# **Neurology**

🧠 **What Is Neurology?**

Neurology is the branch of medicine devoted to the study, diagnosis, and treatment of disorders affecting the nervous system. The nervous system is a highly complex network responsible for regulating and coordinating all bodily functions, thoughts, emotions, and movements.

**The nervous system** includes:

* **Central nervous system (CNS)** – the brain and spinal cord. It processes information, controls movement, and regulates essential bodily functions.
* **Peripheral nervous system (PNS)** – nerves connecting the CNS to the rest of the body. Consists of all nerves outside the brain and spinal cord, including those serving the eyes, ears, skin, and other sensory organs. The PNS transmits signals between the CNS and the rest of the body.
* **Autonomic nervous system (ANS)** – controls involuntary functions like heart rate, digestion, and breathing
* **Muscles** – as affected by neurological conditions (e.g., in neuromuscular disorders)

## Functions of the Nervous System

The nervous system is the body’s command center, responsible for:

* Cognition and memory (thinking, perception, reasoning, decision-making)
* Movement and coordination (muscle control, reflexes, voluntary actions)
* Sensation and perception (vision, hearing, touch, pain, balance)
* Autonomic functions (heartbeat, breathing, digestion, temperature regulation)

# **Neurologist**

A neurologist is a medical doctor who specializes in diagnosing and treating diseases of the brain, spinal cord and nerves. Neurological diseases and conditions can affect nearly every part of your body and affect both adults and children.

## **Overview**

### **What is a neurologist?**

A neurologist is a medical doctor who diagnoses, treats and manages disorders of the brain and nervous system (brain, spinal cord and nerves). A neurologist knows the anatomy, function and conditions that affect your nerves and nervous system. Your nervous system is your body’s command center. It controls everything you think, feel and do — from moving your arm to the beating of your heart.

### **What is a pediatric neurologist?**

A pediatric neurologist is a medical doctor who diagnoses, treats and manages disorders of the brain and nervous system in children — from newborn to adolescent. Many of the conditions they treat are the same as those seen in adults, in addition to inherited and developmental conditions.

### **What is a neurosurgeon?**

A neurosurgeon is a medical doctor who performs surgery on the brain, spinal cord and nerves.

## **What Does a Neurologist Do?**

A **neurologist** is a physician who specializes in treating diseases of the nervous system. Neurologists are trained to investigate, diagnose, and treat a wide range of neurological disorders. They do **not perform surgery** ( surgical interventions are handled by **neurosurgeons**) but often work closely with them.

Neurologists:

* Take patient histories
* Perform physical and neurological exams
* Order and interpret diagnostic tests
* Diagnose neurological disorders
* Prescribe medication and therapies
* Coordinate care with physical therapists, psychiatrists, and surgeons if needed

### **What diseases and conditions does a neurologist treat?**

Some of the most common neurologic disorders a neurologist may treat include:

* [Alzheimer’s disease](https://my.clevelandclinic.org/health/diseases/9164-alzheimers-disease) and other [dementias](https://my.clevelandclinic.org/health/diseases/9170-dementia).
* [Amyotrophic lateral sclerosis](https://my.clevelandclinic.org/health/diseases/16729-amyotrophic-lateral-sclerosis-als) (also called ALS or Lou Gehrig’s disease).
* [Brain injury](https://my.clevelandclinic.org/health/diseases/8874-traumatic-brain-injury), [spinal cord injury](https://my.clevelandclinic.org/health/diseases/12098-spinal-cord-injury) or vascular malformations.
* [Cerebral aneurysms](https://my.clevelandclinic.org/health/diseases/16800-brain-aneurysm) and [arteriovenous malformations](https://my.clevelandclinic.org/health/diseases/16755-arteriovenous-malformation-avm).
* [Cerebral palsy and spasticity.](https://my.clevelandclinic.org/health/diseases/8717-cerebral-palsy)
* [Concussion.](https://my.clevelandclinic.org/health/diseases/15038-concussion)
* [Encephalitis.](https://my.clevelandclinic.org/health/diseases/6058-encephalitis)
* [Epilepsy](https://my.clevelandclinic.org/health/diseases/17636-epilepsy)[.](https://my.clevelandclinic.org/health/diseases/9917-epilepsy-types-and-their-symptoms)
* Facial pain syndromes.
* [Headache](https://my.clevelandclinic.org/health/diseases/9639-headaches)/[migraine](https://my.clevelandclinic.org/health/diseases/5005-migraine-headaches).
* [Hydrocephalus](https://my.clevelandclinic.org/health/diseases/15849-normal-pressure-hydrocephalus-nph).
* [Meningitis.](https://my.clevelandclinic.org/health/articles/14600-meningitis)
* Mental and behavioral health disorders.
* [Multiple sclerosis.](https://my.clevelandclinic.org/health/diseases/17248-multiple-sclerosis)
* [Myasthenia gravis](https://my.clevelandclinic.org/health/diseases/17252-myasthenia-gravis-mg) and myopathies.
* Pain in your neck, back and spine.
* [Parkinson’s disease.](https://my.clevelandclinic.org/health/diseases/8525-parkinsons-disease-an-overview)
* [Peripheral neuropathy.](https://my.clevelandclinic.org/health/diseases/14737-neuropathy)
* [Sleep disorders.](https://my.clevelandclinic.org/health/articles/11429-common-sleep-disorders)
* [Stroke.](https://my.clevelandclinic.org/health/diseases/5601-stroke-understanding-stroke)
* [Tremor](https://my.clevelandclinic.org/health/diseases/11886-essential-tremor), [dystonia](https://my.clevelandclinic.org/health/articles/6006-dystonias).
* Tumors of the [brain](https://my.clevelandclinic.org/health/diseases/17839-brain-lesions), spine and nerves.

### **How do neurologists diagnose conditions?**

Your neurologist will ask about your medical history, family history, medication history and any current symptoms. They’ll also conduct a neurologic examination, including tests of your:

* Coordination, balance, reflexes and gait.
* Muscle strength.
* Mental health.
* Vision, hearing and speech.
* Sensation.

Your neurologist may also order blood, urine or other fluid tests in order to help understand condition severity or check on medication levels. Genetic testing may be ordered to identify inherited disorders. Imaging studies of your nervous system might also be ordered to aid in diagnosis.

Neurologists treat people with medications, physical therapy or other approaches.

### **What types of tests does a neurologist order?**

Common neurologic tests include:

* [Angiography.](https://my.clevelandclinic.org/health/treatments/4977-angiography) Angiography can show if blood vessels in your brain, head or neck are blocked, damaged or abnormal. It can detect such things as aneurysms and blood clots.
* [Biopsy](https://my.clevelandclinic.org/health/diagnostics/17872-fine-needle-aspiration-fna). A biopsy is the removal of a piece of tissue from your body. Biopsies may be taken of muscle, nerve or brain tissue.
* [Cerebrospinal fluid analysis.](https://my.clevelandclinic.org/health/diagnostics/12544-lumbar-puncture-spinal-tap) This test involves the removal of a sample of the fluid that surrounds your brain and spinal cord. The test can detect evidence of a brain bleed, infection, multiple sclerosis and metabolic diseases.
* [Computed tomography (CT)](https://my.clevelandclinic.org/health/diagnostics/4808-ct-computed-tomography-scan), [magnetic resonance imaging (MRI)](https://my.clevelandclinic.org/health/diagnostics/4876-magnetic-resonance-imaging-mri), [X-rays](https://my.clevelandclinic.org/health/diagnostics/10229-spine-x-ray)and[ultrasound](https://my.clevelandclinic.org/health/diagnostics/4995-ultrasound).
* [Electroencephalography (EEG).](https://my.clevelandclinic.org/health/diagnostics/9656-electroencephalogram-eeg) This test measures your brain’s electrical activity and is used to help diagnose seizures and infections (such as encephalitis) brain injury and tumors.
* [Electromyography (EMG).](https://my.clevelandclinic.org/health/articles/4825-electromyograms) This test records the electrical activity in muscles and is used to diagnose nerve and muscle disorders, spinal nerve root compression and [motor neuron disorders](https://my.clevelandclinic.org/health/diseases/motor-neuron-disease-mnd) such as amyotrophic lateral sclerosis.
* Electronystagmography (ENG). This group of tests is used to diagnose involuntary eye movement, dizziness and balance disorders.
* [Evoked potentials.](https://my.clevelandclinic.org/health/diagnostics/12393-evoked-potentials) This test measures how quickly and completely electrical signals reach your brain from your eyes, ears or touch to your skin. The test can help diagnose multiple sclerosis, [acoustic neuroma](https://my.clevelandclinic.org/health/diseases/16400-acoustic-neuroma) and spinal cord injury.
* [Myelography.](https://my.clevelandclinic.org/health/diagnostics/4892-myelogram) This test helps diagnose spinal and spinal cord tumors and herniated disks and fractures.
* Polysomnogram. This test measures brain and body activity during sleep and helps diagnose sleep disorders.
* [Positron emission tomography (PET).](https://my.clevelandclinic.org/health/diagnostics/10123-pet-scan) This imaging test can show tumors or be used to evaluate epilepsy, brain tumors, dementia and Alzheimer’s disease.
* Single-photon emission computed tomography (SPECT). This imaging test can diagnose tumors, infections and assess the location of seizures, degenerative spine disease and stress fractures.
* Thermography. This test measures temperature changes within your body or specific organs and is used to evaluate pain syndromes, peripheral nerve disorders and nerve root compression.

### **When should I make an appointment with a neurologist?**

Some of the more common symptoms for which you may want to see a neurologist (or be referred to one) include:

* Memory disturbances, forgetfulness.
* Loss of consciousness.
* Seizures.
* Taste or smell disturbances.
* Vision problems.
* Numbness and tingling sensations.
* Facial asymmetries (one side of your face doesn’t match the other [eyelid droops, can’t fully smile]).
* Vertigo, ringing in the ears (tinnitus) and deafness.
* Difficulty swallowing, hoarseness in voice, difficulty in shrugging your shoulders or turning your neck, difficulty with tongue movements.
* Muscle weakness, cramps, spasms and twitching.
* Burning or electrical shock-like pain in any body part.
* Neck or back pain, headache.
* Imbalance in gait.
* Tremors.
* Slowness in movement.

### **How should I prepare for my first neurologist appointment?**

To get the most out of your neurologist visit, it’s helpful to be prepared. Ways to prepare include:

* Bring a list of the most important issues you want to discuss with your neurologist.
* Discuss any changes in your overall health.
* Discuss your new symptoms or changes in existing or prior symptoms. Keep a symptom diary (and bring it with you) and record events, including day and time they occurred, how long the event lasted, severity, triggers, symptoms and any action you took to end the event. This is especially useful if you have a condition in which symptoms aren’t constant, such as epilepsy, sleep apnea, headaches or Parkinson’s disease.
* Bring copies of test results, including a CD of images and lab work ordered by other healthcare providers outside of your neurologist’s health care network.
* Bring a list of all current products you take. Include prescription medications, over-the-counter medications and any vitamins, supplements and herbal products. Also, let your neurologist know about any previous medications that didn’t work or that caused side effects.
* Bring a list of your known allergies.
* Bring a friend or relative with you to the appointment to take notes and be another set of ears and eyes. This person can help review your neurologist’s discussion, ask questions and remind you about scheduling tests and follow-up appointments.
* Ask if you should schedule another appointment to discuss any additional concerns.

## **Additional Common Questions**

### **How much schooling does it take to become a neurologist?**

To become a neurologist, doctors must complete:

* Four years of college.
* Four years of medical school.
* One year of an internship (training in neurology and other fields).
* Three years of residency (continued training concentrating on the field of neurology).
* Up to three years of a fellowship. This isn’t mandatory, but a fellowship offers additional training in a neurology subspecialty. This training time may be longer if the neurologist chooses to pursue multiple fellowships.

### **What are some neurology subspecialty fields?**

Some neurology subspecialty fields include:

* Brain injury medicine.
* Child neurology.
* Clinical neurophysiology.
* Epilepsy.
* Headache medicine.
* Geriatric neurology.
* Neurodevelopmental disabilities.
* Neuroimaging.
* Neuro-oncology.
* Pain medicine.
* Sleep medicine.
* Vascular neurology.

### **A note**

A neurologist is a medical doctor who specializes in diseases and conditions affecting your brain, spinal cord and nerves. Your neurologist will examine you, order tests, make a diagnosis, treat your condition with medication or physical therapy or refer you to and work together with other specialists, such as a neurosurgeon or neuro-oncologist, if appropriate. Come prepared with your notes, share your health information and never hesitate to ask questions. Your neurologist is here to help diagnose your condition, treat or manage it as best as possible and support you along the way.

## **Common Neurological Disorders**

| **Category** | **Examples** |
| --- | --- |
| **Neurodegenerative** | Alzheimer's disease, Parkinson's disease, ALS (Lou Gehrig’s disease) |
| **Seizure Disorders** | Epilepsy |
| **Cerebrovascular** | Stroke, Transient Ischemic Attack (TIA) |
| **Demyelinating** | Multiple sclerosis (MS), Guillain-Barré syndrome |
| **Neuromuscular** | Myasthenia gravis, muscular dystrophy |
| **Headaches** | Migraine, cluster headaches, tension headaches |
| **Infections** | Meningitis, encephalitis, brain abscess |
| **Developmental** | Autism spectrum disorder, cerebral palsy |
| **Traumatic** | Traumatic brain injury, spinal cord injury |
| **Tumors** | Brain tumors, spinal tumors |
| **Sleep Disorders** | Narcolepsy, restless leg syndrome, insomnia (neurological causes) |
| **Peripheral Nerve Disorders** | Neuropathies (diabetic, toxic, hereditary) |

## Diagnostic and Therapeutic Tools

Neurology relies on advanced tools and techniques for diagnosis and management, including:

| **Test** | **Purpose** |
| --- | --- |
| **Neuroimaging (MRI, CT scans, PET scans)** | Detailed imaging of brain/spinal cord for tumors, stroke, inflammation |
| **EEG (Electroencephalogram)** | Measures brain electrical activity (used in epilepsy, seizures) |
| **EMG/NCS (Electromyography/Nerve Conduction Study)** | Evaluates nerve and muscle function |
| **Lumbar Puncture (Spinal Tap)** | Tests cerebrospinal fluid (for infections, MS, hemorrhages) |
| **Evoked Potentials** | Measures brain response to stimuli (vision, hearing, touch) |
| **Genetic Testing** | Identifies inherited neurological disorders |
| **Blood Tests:** Laboratory analysis of blood and cerebrospinal fluid | To rule out infections, metabolic or autoimmune causes |

Recent advancements include gene therapy, neuroplasticity research, and brain-computer interfaces, which are transforming the diagnosis and treatment of neurological diseases

## **Treatment in Neurology**

Treatment depends on the specific condition, but may include:

| **Modality** | **Details** |
| --- | --- |
| **Medications** | Antiepileptics, antidepressants, muscle relaxants, corticosteroids, dopamine agonists, etc. |
| **Physical Therapy** | For motor dysfunction and rehabilitation |
| **Occupational Therapy** | Helps patients regain independence in daily life |
| **Speech Therapy** | For patients with swallowing or speech issues |
| **Surgery** | Done by neurosurgeons for tumors, hydrocephalus, severe epilepsy, etc. |
| **Psychological Counseling** | For mood disorders, cognitive issues, and patient/family support |
| **Deep Brain Stimulation** | For Parkinson’s and movement disorders |
| **Lifestyle Changes** | Diet, sleep hygiene, exercise, stress management |

## **Subspecialties in Neurology**

Neurology encompasses several subspecialties, such as:

| **Subfield** | **Focus** |
| --- | --- |
| **Stroke Neurology** | Cerebrovascular diseases |
| **Epileptology** | Seizure disorders |
| **Neuroimmunology** | Multiple sclerosis, autoimmune diseases |
| **Neuro-oncology** | Brain and spinal cord tumors |
| **Child (Pediatric) Neurology** | Neurological/nervous system disorders in children |
| **Neuromuscular Medicine** | Nerve and muscle disorders |
| **Headache Medicine** | Chronic and severe headaches |
| **Sleep Medicine** | Neurologically-linked sleep disorders |
| **Behavioral Neurology** | Cognitive and behavioral changes (dementia, Alzheimer’s) |
| **Neurocritical Care** | Acute brain injuries and life-threatening neuroemergencies |

Others are:

* Neuroimaging
* Neurorehabilitation
* Pain management
* Interventional neurology

## **📊 Global Relevance**

* Neurological disorders are **major causes of disability and death worldwide**
* **Stroke** is a leading cause of death globally
* **Dementia and Parkinson’s disease** are rising due to aging populations
* Increasing focus on **brain health**, **neurorehabilitation**, and **neurotechnology**

**Neurology is a pivotal field because it focuses on the “command center” of the body, influencing every aspect of health and function. Advances in neurology have led to improved diagnosis, treatment, and quality of life for people with previously untreatable or debilitating neurological conditions**

## **Clinical Terminologies & Medical Codes Explained**

**Medical professionals use standardized codes to describe diseases, conditions, and procedures. These codes ensure clear communication, accurate billing, and efficient data management in healthcare.**

**These are standardized systems used in healthcare to:**

* **Document diagnoses and procedures**
* **Communicate medical information clearly**
* **Bill and code for services provided**
* **Support research and statistics**

**There are two major code types listed here:**

### **ICD-10 Codes**

**ICD-10 stands for International Classification of Diseases, 10th Revision.**

* Used to code medical conditions or diagnoses.
* Maintained by the World Health Organization (WHO).
* Helps hospitals and doctors record and report diseases.

### **CPT Codes**

**CPT stands for Current Procedural Terminology.**

* Used in the U.S. healthcare system to code medical, surgical, and diagnostic procedures.
* Maintained by the American Medical Association (AMA).
* Mostly used for billing and reimbursement.

## **ICD-10 Codes: Diagnosing Diseases and Conditions**

**ICD-10 stands for the *International Classification of Diseases, 10th Revision*. It is a globally recognized system for coding diagnoses and health conditions. Each code corresponds to a specific disease or symptom.**

| **ICD-10 Code** | **Condition** | **Description** |
| --- | --- | --- |
| **G40.909** | **Epilepsy, unspecified** | **Used when epilepsy is diagnosed but not further specified by type or cause.** |
| **I63.9** | **Acute ischemic stroke** | **Indicates a stroke caused by blocked blood flow to the brain, without further detail.** |
| **G20** | **Parkinson’s disease** | **Refers to the chronic, progressive neurological disorder affecting movement.** |
| **G35** | **Multiple sclerosis** | **Denotes the autoimmune disease affecting the central nervous system.** |
| **R51.9** | **Headache, unspecified** | **Used for headaches where the specific type is not identified.** |

## CPT Codes: Coding Medical Procedures

**CPT stands for *Current Procedural Terminology*. These codes are used in the United States to document and bill for medical, surgical, and diagnostic services.**

| **CPT Code** | **Procedure** | **Description** |
| --- | --- | --- |
| **95957** | **EEG with video monitoring** | **Records brain electrical activity with simultaneous video, often used for epilepsy evaluation.** |
| **62270** | **Lumbar puncture** | **A procedure to collect cerebrospinal fluid from the lower back for diagnostic testing.** |
| **95816** | **EMG, limb muscles** | **Electromyography to assess electrical activity in limb muscles, used for neuromuscular disorders.** |
| **70551** | **Brain MRI without contrast** | **Magnetic resonance imaging of the brain performed without contrast dye, used for detailed brain imaging.** |

**ICD-10 Codes for Common Conditions:**

* **G40.909** (Epilepsy, unspecified)
* **I63.9** (Acute ischemic stroke)
* **G20** (Parkinson’s disease)
* **G35** (Multiple sclerosis)
* **R51.9** (Headache, unspecified)

**CPT Codes for Procedures:**

* **95957** (EEG with video monitoring)
* **62270** (Lumbar puncture)
* **95816** (EMG, limb muscles)
* **70551** (Brain MRI without contrast)

**List of diseases and conditions managed under Neurology, categorized for clarity:**

1. **Central Nervous System (CNS) Disorders**

* Stroke (Ischemic, Hemorrhagic, TIA)
* Epilepsy & Seizure Disorders
* Multiple Sclerosis (MS)
* Parkinson’s Disease
* Alzheimer’s Disease & Other Dementias
* Huntington’s Disease
* Amyotrophic Lateral Sclerosis (ALS/Lou Gehrig’s Disease)
* Brain Tumors (Benign & Malignant)
* Traumatic Brain Injury (TBI) & Concussion
* Hydrocephalus
* Normal Pressure Hydrocephalus (NPH)
* Cerebral Palsy
* Spinal Cord Injury & Disorders

**2. Peripheral Nervous System (PNS) Disorders**

* Peripheral Neuropathy (Diabetic, Chemotherapy-induced, CIDP, etc.)
* Guillain-Barré Syndrome (GBS)
* Charcot-Marie-Tooth Disease (CMT)
* Bell’s Palsy (Facial Nerve Palsy)
* Trigeminal Neuralgia
* Brachial Plexus Injury

**3. Headache & Pain Disorders**

* Migraine (with/without aura)
* Cluster Headaches
* Tension-Type Headaches
* Trigeminal Autonomic Cephalalgias (TACs)
* Chronic Pain Syndromes (e.g., Fibromyalgia, CRPS)

**4. Movement Disorders**

* Essential Tremor
* Dystonia
* Tourette Syndrome & Tic Disorders
* Restless Legs Syndrome (RLS)
* Ataxia (Spinocerebellar Ataxia, Friedreich’s Ataxia)
* Myoclonus

**5. Neuromuscular Disorders**

* Myasthenia Gravis
* Muscular Dystrophies (Duchenne, Becker, etc.)
* Myopathies (Inflammatory, Metabolic, Congenital)
* Lambert-Eaton Myasthenic Syndrome (LEMS)

**6. Infections & Inflammatory Disorders\***

* Meningitis (Bacterial, Viral, Fungal)
* Encephalitis
* Brain Abscess
* Neurocysticercosis
* Neurosyphilis
* Autoimmune Encephalitis (e.g., Anti-NMDA Receptor Encephalitis)

**7. Sleep Disorders**

* Narcolepsy & Cataplexy
* Sleep Apnea (Neurological Aspects)
* REM Sleep Behavior Disorder (RBD)
* Insomnia (Neurological Causes)

**8. Pediatric & Developmental Neurological Disorders**

* Autism Spectrum Disorder (Neurological Aspects)
* ADHD (Neurological Evaluation)
* Spina Bifida
* Rett Syndrome
* Neurogenetic Disorders (e.g., Down Syndrome with Neurological Complications)

**9. Autonomic Nervous System Disorders**

* Dysautonomia
* Postural Orthostatic Tachycardia Syndrome (POTS)
* Pure Autonomic Failure

**10. Miscellaneous & Rare Neurological Conditions**

* Creutzfeldt-Jakob Disease (Prion Disease)
* Paraneoplastic Syndromes
* Neurological Complications of Cancer (Chemo Brain, Leptomeningeal Disease)
* Mitochondrial Disorders (e.g., MELAS, Leigh Syndrome)

# Overview of Nervous System Disorders

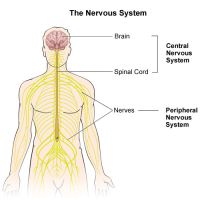
## What is the nervous system?

The nervous system is a complex system that controls and coordinates body activities. It's made up of 2 main divisions:

* **Central nervous system.** This consists of the brain and spinal cord.
* **Peripheral nervous system.** This consists of the peripheral nerves and the autonomic nerves.

The main organs of the nervous system include:

* Brain
* Spinal cord
* Eyes
* Ears
* Sensory organs of taste
* Sensory organs of smell
* Sensory receptors located in the skin, joints, muscles, and other parts of the body



## What are some disorders of the nervous system?

The nervous system can be affected by various disorders. It can be damaged by:

* Injury
* Infections
* Degeneration
* Structural defects
* Tumors
* Blood flow disruption
* Autoimmune disorders

## Disorders of the nervous system

Disorders of the nervous system may include:

* **Vascular disorders**, such as stroke, transient ischemic attack (TIA), subarachnoid hemorrhage, subdural hemorrhage and hematoma, and extradural hemorrhage
* **Infections**, such as meningitis, encephalitis, myelitis, and epidural abscess
* **Structural disorders**, such as brain or spinal cord injury, cervical spondylosis, carpal tunnel syndrome, brain or spinal cord tumors
* **Seizure disorders**, such as epilepsy.
* **Degeneration**, such as Parkinson disease, amyotrophic lateral sclerosis (ALS), Huntington chorea, and Alzheimer disease
* **Autoimmune or inflammatory disorders** , such as Bell palsy, multiple sclerosis, peripheral neuropathy, and Guillain-Barré syndrome
* Mental health disorders, such as mood disorders, depression, and schizophrenia.

## Symptoms of nervous system disorders

These are the most common symptoms of a nervous system disorder. But each person may have slightly different symptoms. Symptoms may include:

* Persistent or sudden onset of a headache
* A headache that changes or is different
* Loss of feeling or tingling
* Weakness or loss of muscle strength
* Loss of sight or double vision
* Memory loss
* Impaired mental ability
* Lack of coordination
* Muscle rigidity
* Tremors and seizures
* Back pain that spreads to the feet, toes, or other parts of the body
* Muscle wasting and slurred speech
* New language impairment (expression or comprehension)

The symptoms of a nervous system disorder may look like other medical conditions or problems. Always see your healthcare provider for a diagnosis.

## Healthcare providers who treat nervous system disorders

The best way to manage nervous system disorders is with the help of a team of healthcare providers. You may not need all members of the team at any given time. But it's good to know who they are and how they can help. Here is a list of some of the healthcare providers that may be involved in treating nervous system disorders:

* **Neurologist.** The doctors who diagnose and treat nervous system disorders are called neurologists. Some neurologists treat acute strokes and cerebral aneurysms.
* **Neurosurgeon.** Surgeons who use surgery to treat nervous system disorders. They are called neurological surgeons or neurosurgeons.
* **Neuroradiologist and interventional radiologist.** This is a radiologist who specializes in diagnosing nervous system conditions using imaging and in treating nervous system conditions, such as cerebral aneurysms, acute strokes, and vertebral fractures. This provider also does biopsies of certain tumors.
* **Psychologist.** Problems, such as anxiety, depression, mood swings, and irritability, are common in nervous system disorders. Your psychologist can help. Psychologists may do testing to find out how much your disorder is affecting the way you think and feel. Psychologists also do counseling to help you deal with the emotional effects caused by nervous system disorders.
* **Psychiatrist.** Like your psychologist, this team member deals with emotional and behavior symptoms caused by nervous system disorders. In most cases, counseling works best for these problems. But if you need medicines to treat symptoms, such as depression or anxiety, this healthcare provider can help.
* **Physiatrist.** Healthcare providers who work with people in the rehab (rehabilitation) process are called physiatrists.
* **Physical therapist.** This is a movement specialist who can help you move and walk well. In physical therapy, you can also work on painful or stiff muscles and joints.
* **Occupational therapist.** This provider helps you learn to handle your day-to-day activities. For example, you might have trouble doing tasks you need to do at work or at home. Your occupational therapist will help you find ways to adjust to any changes in your physical abilities.
* **Speech/language pathologist.** This healthcare provider specializes in communication, including cognitive communication. They also diagnose and treat swallowing problems.

REFERENCES

[Overview of Nervous System Disorders | Johns Hopkins Medicine](https://www.hopkinsmedicine.org/health/conditions-and-diseases/overview-of-nervous-system-disorders) <https://www.hopkinsmedicine.org/health/conditions-and-diseases/overview-of-nervous-system-disordershttps://www.hopkinsmedicine.org/health/conditions-and-diseases/overview-of-nervous-system-disorders>

[**What Is a Neurologist? What They Do & When to See One**](https://my.clevelandclinic.org/health/articles/22277-neurologist)

[**Neurology - Wikipedia**](https://en.wikipedia.org/wiki/Neurology)

**Neurodegenerative Diseases**

**Alzheimer's Disease**

### **Alzheimer’s disease**

While some changes in memory and thinking are a normal part of aging, Alzheimer's is*not*.

Alzheimer's disease is the most common type of dementia.

* Dementia is a general term for the loss of memory, problem-solving and thinking abilities thatinterferes with daily life.

#### ***Alzheimer's disease is...***

* A brain disorder caused by damage to nerve cells in the brain.
* Progressive, meaning that it develops gradually over time.
  + It begins with mild memory loss and can lead to the inability to carry on a conversation, carry out daily activities, or respond to the environment.
* Irreversible, meaning the damage it does to the brain cannot be undone.

### **Who gets Alzheimer's disease**

* The risk of getting this disease increases with age.
* Alzheimer's typically affects people aged 60 or older.
* Younger people can get Alzheimer's disease, but it is less common.
  + In some cases, early signs can appear as early as the mid-40s. This is known as *early-onset Alzheimer's disease*.

### **The number of people with Alzheimer’s disease**

### Did you know?

The number of people living with Alzheimer's is projected to double from 6.9 million in 2020 to nearly 14 million people by 2060.[9]

### **The burden of Alzheimer’s disease in the United States**

Alzheimer's disease is a top 10 leading cause of death in the United States.[8] In 2022, it was the:

* 7th leading cause of death among U.S. adults.[8]
* 6th leading cause of death among adults 65 years or older.[8]

The actual number of older people who die from Alzheimer's may be much higher than what is officially recorded. Alzheimer's and other types of dementia are not always reported on death certificates.[7]

### **Causes**

We do not yet fully understand what causes Alzheimer's disease. There likely is not one single factor, but rather a combination of factors that cause the disease. These factors, which may affect each person differently, include:

* Genes.
* Family history.
* Environmental factors.
* Lifestyle behaviors.

## Signs and symptoms

### **Symptoms of Alzheimer’s disease**

In addition to memory problems, someone with Alzheimer's disease may experience one or more of these problems:

* Memory loss that disrupts daily life.
* Trouble handling money or paying bills.
* Difficulty completing familiar tasks at home, at work, or at leisure.
* Decreased or poor judgment.
* Misplacing things and being unable to retrace steps to find them.
* Changes in mood, personality, or behavior.

Even if you or someone you know has several of these signs, it does NOT mean it's Alzheimer's disease.

### **What to do if you think you might have Alzheimer’s**

Talk to your health care provider to see if your symptoms are related to Alzheimer’s disease or a more treatable condition.

Early and accurate diagnosis may help slow the disease and help some symptoms. Early diagnosis also allows you and your family to consider:

* Treatment options.
* Financial planning.
* Advance directives.
* Clinical trials.
* Future care needs.

Early diagnosis is important for many reasons.

## Risk factors

### **Risk reduction**

Research suggests that people who adopt healthy lifestyle habits can lower the risk of memory loss or slow it down. These habits include staying physically active and keeping your heart healthy.

## Treatment for Alzheimer’s disease

There is no known cure for Alzheimer's disease at this time. But getting proper medical care and treatment can improve the quality of life for people living with Alzheimer's.

Treatment can:

* Help people maintain brain health.
* Manage behavioral symptoms.
* Slow or delay symptoms of the disease.

Treatment of Alzheimer’s depends on the underlying cause and the progression of the disease.

Prescription drugs have been approved by the U.S. Food and Drug Administration (FDA). These drugs:

* Temporarily ease some symptoms.
* Can slow the disease from getting worse.
* Typically work best for people in the early or middle stages of Alzheimer’s.

Medications don’t work for everyone, and they may lose effectiveness over time.

# Signs and Symptoms of Dementia

## WHAT TO KNOW

* It is common to experience changes in functioning as we get older, including some changes in memory.
* But dementia—which blocks a person's ability to remember, think clearly, or make daily decisions—is NOT a normal part of aging.
* Learn the common signs and symptoms of dementia, and how they differ from normal aging.

## Dementia vs. normal aging

A recent survey revealed that nearly half of adults aged 40 and older think they will likely develop dementia.[1]

An estimated 6.9 million Americans aged 65 and older are living with dementia. That is about 1 in 9 people (10.9%) of the U.S. population.[1](https://www.cdc.gov/alzheimers-dementia/signs-symptoms/index.html#cdcreference_1)

The truth is, dementia is not a normal part of normal aging. Many older adults live their entire lives without developing dementia.

Normal aging may include weakening muscles and bones, stiffening arteries and vessels, and some age-related memory changes.

### **Normal age-related memory changes**

As we get older, normal memory changes may include:

* Forgetting where you put your car keys sometimes.
* Struggling to find a word but remembering it later.
* Forgetting the name of an acquaintance.
* Forgetting the most recent events.

These subtle changes can be frustrating. But they should not affect your daily life.

With normal aging, your overall memory, thought, and brain functions stay intact. This includes:

* The knowledge and experiences you gained over years.
* Old memories.
* Language.

## What to look out for

There are many types of dementia that cause problems remembering, thinking, or making daily decisions. Dementia symptoms can vary widely from person to person.

### **Symptoms**

People with dementia have problems with one or more of these things:

* Memory.
* Attention.
* Communication.
* Reasoning, judgment, and problem solving.
* Vision problems such as depth perception, processing visual cues, or recognizing objects.

### **Telltale signs**

Signs that may point to dementia include:

* Getting lost in a familiar neighborhood.
* Using unusual words to refer to familiar objects.
* Forgetting the name of a close family member or friend.
* Forgetting old memories.
* Not being able to complete common tasks on your own.

See your health care provider if you notice any of these signs or symptoms. The sooner you can figure out what’s causing these changes the sooner you can work with your provider to get a diagnosis and figure out next steps.

## When to talk to your doctor

What to do if you think you might have Dementia

Talk to your health care provider to see if your symptoms are related to dementia or a more treatable condition. Early and accurate diagnosis may help slow the progression and alleviate some symptoms. Early diagnosis also allows you and your family to consider:

* Treatment options.
* Financial planning.
* Developing advance directives.
* Enrolling in clinical trials.
* Anticipating any care needs.

### **10 Warning Signs of Alzheimer’s**

People with one or more of these 10 warning signs should see a doctor to find the cause.

1. Memory loss that disrupts daily life.
2. Challenges in planning or solving problems.
3. Difficulty completing familiar tasks at home, at work, or at leisure.
4. Confusion with time or place.
5. Trouble understanding visual images and spatial relations.
6. New problems with words in speaking or writing.
7. Misplacing things and not being able to retrace steps.
8. Decreased or poor judgment.
9. Withdrawal from work or social activities.
10. Changes in mood or personality

# Reducing Risk for Dementia

## PURPOSE

* There are common conditions and lifestyle behaviors that can increase your risk for dementia.
* Learn what they are and the healthy lifestyle habits that can lower your risk of developing dementia, including Alzheimer's disease.

## Risk factors

There are known factors that can increase your risk of dementia. These include:

* Lack of physical activity.
* Uncontrolled diabetes.
* High blood pressure.
* Hearing loss.
* Tobacco and alcohol use.

### **Racial/ethnic differences**

A recent study found that certain racial/ethnic groups, including African American, Hispanic, and American Indian and Alaska Native adults, were more likely to have these risk factors.

* This is important, because those same racial/ethnic groups are also more likely to develop dementia than other groups.

Certain lifestyle factors that can increase risk for dementia.

## Ways to lower your risk of dementia

Healthy lifestyle habits

Healthy habits can benefit brain health by:

* Reducing the chances of worsening memory loss.
* Slowing the progression of dementia, including Alzheimer's.

Here are five lifestyle habits to keep your brain healthy:

1. Stay physically active.

Physical activity is important to keeping your heart, body and brain healthy. What is good for your body is good for your mind.

* Regular physical activity can help you prevent, delay, or manage chronic diseases, like dementia.
* Experts recommend that adults get 150 minutes of physical activity each week (at least 20 minutes/day).

2. Prevent or manage diabetes.

When diabetes is not managed, important organs—like the brain—can be damaged by too much sugar in the bloodstream. The good news is type 2 diabetes can be prevented or delayed.

3. Manage your blood pressure.

High blood pressure can damage blood vessels and limit blood flow to the brain, which does damage to the brain. It also increases the risk of having a stroke, which can also damage the brain.

* Maintaining a healthy weight and taking your prescribed blood pressure medications can help.
* Talk with your health care provider if you’re concerned about high blood pressure.

4. Prevent or correct hearing loss.

Hearing loss is a very important risk factor for dementia. Researchers believe having hearing loss may make the brain work harder at the expense of thinking and memory. Hearing loss also leads people to be less socially engaged, which is important to remaining intellectually stimulated.

* Treating hearing loss (using hearing aids) may reduce the risk of dementia.
* If you have or are concerned about hearing loss, talk to a hearing care professional to prevent, treat, or manage hearing loss.

#### ***5. Try to limit or avoid drinking alcohol and smoking***

Over time, excessive drinking can lead to high blood pressure or brain injuries, both of which increase the risk of dementia. Current smoking also increases the risk of developing dementia, including Alzheimer's disease.

* If you drink alcohol, do so in moderation.
* Quit smoking to reduce your risk dementia. Quitting smoking also reduces other risks for dementia, like stroke, type 2 diabetes, and high blood pressure.

Source:

* Centers for Disease Control and Prevention. (2024) *About Alzheimer's Disease*. Available at: https://www.cdc.gov/alzheimers-dementia/about/alzheimers.html (Accessed: 23 May 2025).

**Alzheimer’s disease**

While some changes in memory and thinking are a normal part of aging, Alzheimer's is not.

Alzheimer's disease is the most common type of dementia.

Dementia is a general term for the loss of memory, problem-solving and thinking abilities that interferes with daily life.

Alzheimer's disease is...

A brain disorder caused by damage to nerve cells in the brain.

Progressive, meaning that it develops gradually over time.

It begins with mild memory loss and can lead to the inability to carry on a conversation, carry out daily activities, or respond to the environment.

Irreversible, meaning the damage it does to the brain cannot be undone.

Who gets Alzheimer's disease

The risk of getting this disease increases with age.

Alzheimer's typically affects people aged 60 or older.

Younger people can get Alzheimer's disease, but it is less common.

In some cases, early signs can appear as early as the mid-40s. This is known as early-onset Alzheimer's disease.

The number of people with Alzheimer’s disease

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Causes

We do not yet fully understand what causes Alzheimer's disease. There likely is not one single factor, but rather a combination of factors that cause the disease. These factors, which may affect each person differently, include:

Genes.

Family history.

Environmental factors.

Lifestyle behaviors.

Signs and symptoms

Symptoms of Alzheimer’s disease

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Trouble handling money or paying bills.

Difficulty completing familiar tasks at home, at work, or at leisure.

Decreased or poor judgment.

Misplacing things and being unable to retrace steps to find them.

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SOURCES

Stokes AC, Weiss J, Lundberg DJ, et al. Estimates of the association of dementia with US mortality levels using linked survey and mortality records. JAMA Neurol. 2020;77(12):1543-1550. https://www.doi.org/10.1001/jamaneurol.2020.2831

CDC WONDER. 2022 15 Leading Causes of Death. Underlying Cause of Death, 2018-2022. https://wonder.cdc.gov/Deaths-by-Underlying-Cause.html

2024 Alzheimer's disease facts and figures. Alzheimers Dement. 2024;20(5):3708-3821. https://www.doi.org/10.1002/alz.13809

**Dementia**

**Key facts**

* **In 2021, 57 million people had dementia worldwide, over 60% of whom live in low-and middle-income countries. Every year, there are nearly 10 million new cases.**
* **Dementia results from a variety of diseases and injuries that affect the brain. Alzheimer disease is the most common form of dementia and may contribute to 60–70% of cases.**
* **Dementia is currently the seventh leading cause of death and one of the major causes of disability and dependency among older people globally.**
* **In 2019, dementia cost economies globally US$ 1.3 trillion, approximately 50% of these costs are attributable to care provided by informal carers (e.g. family members and close friends), who provide on average 5 hours of care and supervision per day.**
* **Women are disproportionately affected by dementia, both directly and indirectly. Women experience higher disability-adjusted life years and mortality due to dementia, but also provide 70% of care hours for people living with dementia.**

**Overview**

Dementia is a term for several diseases that affect memory, thinking, and the ability to perform daily activities.

The illness gets worse over time. It mainly affects older people but not all people will get it as they age.

Things that increase the risk of developing dementia include:

* age (more common in those 65 or older)
* high blood pressure (hypertension)
* high blood sugar (diabetes)
* being overweight or obese
* smoking
* drinking too much alcohol
* being physically inactive
* being socially isolated
* depression.

Dementia is a syndrome that can be caused by a number of diseases which over time destroy nerve cells and damage the brain, typically leading to deterioration in cognitive function (i.e. the ability to process thought) beyond what might be expected from the usual consequences of biological ageing. While consciousness is not affected, the impairment in cognitive function is commonly accompanied, and occasionally preceded, by changes in mood, emotional control, behaviour, or motivation.

Dementia has physical, psychological, social and economic impacts, not only for people living with dementia, but also for their carers, families and society at large. There is often a lack of awareness and understanding of dementia, resulting in stigmatization and barriers to diagnosis and care.

**Signs and symptoms**

Changes in mood and behaviour sometimes happen even before memory problems occur. Symptoms get worse over time. Eventually, most people with dementia will need others to help with daily activities.

Early signs and symptoms are:

* forgetting things or recent events
* losing or misplacing things
* getting lost when walking or driving
* being confused, even in familiar places
* losing track of time
* difficulties solving problems or making decisions
* problems following conversations or trouble finding words
* difficulties performing familiar tasks
* misjudging distances to objects visually.

Common changes in mood and behaviour include:

* feeling anxious, sad, or angry about memory loss
* personality changes
* inappropriate behaviour
* withdrawal from work or social activities
* being less interested in other people’s emotions.

Dementia affects each person in a different way, depending upon the underlying causes, other health conditions and the person’s cognitive functioning before becoming ill.

Most symptoms become worse over time, while others might disappear or only occur in the later stages of dementia. As the disease progresses, the need for help with personal care increases. People with dementia may not be able to recognize family members or friends, develop difficulties moving around, lose control over their bladder and bowls, have trouble eating and drinking and experience behaviour changes such as aggression that are distressing to the person with dementia as well as those around them.

**Common forms of dementia**

Dementia is caused by many different diseases or injuries that directly and indirectly damage the brain. Alzheimer disease is the most common form and may contribute to 60–70% of cases. Other forms include vascular dementia, dementia with Lewy bodies (abnormal deposits of protein inside nerve cells), and a group of diseases that contribute to frontotemporal dementia (degeneration of the frontal lobe of the brain). Dementia may also develop after a stroke or in the context of certain infections such as HIV, as a result of harmful use of alcohol, repetitive physical injuries to the brain (known as chronic traumatic encephalopathy) or nutritional deficiencies. The boundaries between different forms of dementia are indistinct and mixed forms often co-exist.

**Treatment and care**

There is no cure for dementia, but a lot can be done to support both people living with the illness and those who care for them.

People with dementia can take steps to maintain their quality of life and promote their well-being by:

* being physically active
* taking part in activities and social interactions that stimulate the brain and maintain daily function.

In addition, some medications can help manage dementia symptoms:

* Cholinesterase inhibitors like donepezil are used to treat Alzheimer disease.
* NMDA receptor antagonists like memantine are used for severe Alzheimer disease and vascular dementia.
* Medicines to control blood pressure and cholesterol can prevent additional damage to the brain due to vascular dementia.
* Selective serotonin reuptake inhibitors (SSRIs) can help with severe symptoms of depression in people living with dementia if lifestyle and social changes don’t work, but  these should not be the first option.

If people living with dementia are at risk of hurting themselves or others, medicines like haloperidol and risperidone can help, but these should never be used as the first treatment

**Self-care**

For those diagnosed with dementia, there are things that can help manage symptoms:

* Stay physically active.
* Eat healthily.
* Stop smoking and drinking alcohol.
* Get regular check-ups with your doctor.
* Write down everyday tasks and appointments to help you remember important things.
* Keep up your hobbies and do things that you enjoy.
* Try new ways to keep your mind active.
* Spend time with friends and family and engage in community life.

Plan ahead of time. Over time, it may be harder to make important decisions for yourself or your finances:

* Identify people you trust to support you in making decisions and help you communicate your choices.
* Create an advance plan to tell people what your choices and preferences are for care and support.
* Bring your ID with your address and emergency contacts when leaving the house.
* Reach out to family and friends for help.
* Talk to people you know about how they can help you.
* Join a local support group.

It is important to recognize that providing care and support for a person living with dementia can be challenging, impacting the carer’s own health and well-being. As someone supporting a person living with dementia, reach out to family members, friends, and professionals for help. Take regular breaks and look after yourself. Try stress management techniques such as mindfulness-based exercises and seek professional help and guidance if needed.

**Risk factors and prevention**

Although age is the strongest known risk factor for dementia, it is not an inevitable consequence of biological ageing. Further, dementia does not exclusively affect older people – young onset dementia (defined as the onset of symptoms before the age of 65 years) accounts for up to 9% of cases. Studies show that people can reduce their risk of cognitive decline and dementia by , being physically active not smoking, , avoiding harmful use of alcohol controlling their weight, eating a healthy diet, and maintaining healthy blood pressure, cholesterol and blood sugar levels. Additional risk factors include depression, social isolation, low educational attainment, cognitive inactivity and air pollution.

**Human rights**

Unfortunately, people living with dementia are frequently denied the basic rights and freedoms available to others. In many countries, physical and chemical restraints are used extensively in care homes for older people and in acute-care settings, even when regulations are in place to uphold the rights of people to freedom and choice.

An appropriate and supportive legislative environment based on internationally-accepted human rights standards is required to ensure the highest quality of care for people with dementia and their carers.

**WHO response**

WHO recognizes dementia as a public health priority. In May 2017, the World Health Assembly endorsed the  Global action plan on the public health response to dementia 2017-2025. The Plan provides a comprehensive blueprint for action – for policy-makers, international, regional and national partners, and WHO in the following areas: addressing dementia as a public health priority; increasing awareness of dementia and creating a dementia-inclusive society; reducing the risk of dementia; diagnosis, treatment and care; information systems for dementia; support for dementia carers; and, research and innovation

To facilitate the monitoring of the global dementia action plan, WHO developed the  Global Dementia Observatory (GDO), a data portal that collates country data on 35 key dementia indicators across the global action plan’s seven strategic areas. As a complement to the GDO, WHO launched the  GDO Knowledge Exchange Platform,which is a repository of good practices examples in the area of dementia with the goal of fostering mutual learning and multi-directional exchange between regions, countries and individuals to facilitate action globally.

SOURCE:

World Health Organization. (2023) *Dementia*. Available at: https://www.who.int/news-room/fact-sheets/detail/dementia(Accessed: 23 May 2025).

**What Is Parkinson's Disease?**

Parkinson's disease is an illness that affects the part of your  brain that controls how you move your body. It can come on so slowly that you don't even notice it at first. But over time, what starts as a little shakiness in your  hand can have an impact on how you walk, talk, sleep and think.

You're more likely to get it when you're 60 and older. It's also possible for it to start when you're younger, but that doesn't happen nearly as often.

There's no cure for Parkinson's disease, but you can get treatment and support to help manage the symptoms.

**What Does Parkinson's Do to the Brain?**

Deep down in your  brain, there's an area called the substantia nigra, which is in the basal ganglia. Some of its cells make  dopamine, a chemical that carries messages around your brain. When you need to scratch an itch or kick a ball, dopamine quickly carries a message to the nerve cell that controls that movement.

When that system is working well, your body moves smoothly and evenly. But when you have Parkinson's, the cells of your substantia nigra start to die. There's no replacing them, so your dopamine levels drop and you can't fire off as many messages to control smooth body movements.

Early on, you won't notice anything different. But as more and more cells die, you reach a tipping point where you start to have symptoms.

That may not be until 80% of the cells are gone, which is why you can have Parkinson's for quite a while before you realize it.

**How Does Parkinson's Affect the Body?**

The telltale symptoms all have to do with the way you move. You usually notice problems like:

**Rigid muscles**. It can happen on just about any part of your body. Doctors sometimes mistake early Parkinson's for arthritis.

**Slow movements**. You may find that even simple acts, like buttoning a shirt, take much longer than usual.

**Tremors**. Your hands, arms, legs, lips, jaw, or  tongue are shaky when you're not using them.

**Walking and balance problems**. You may notice your arms aren't swinging as freely when you walk. Or you can't take long steps, so you have to shuffle instead.

Parkinson's can also cause a range of other issues, from  depression to bladder problems to acting out dreams. It may be a while before abnormal movements start.

**What Causes Parkinson's?**

Doctors aren't sure why all those  brain cells start dying. They think it's a mix of your genes and something in the environment, but the reason is not straightforward.

Someone could have a change in a gene tied to Parkinson's, but never get the disease. That happens a lot. And a bunch of people could work side by side in a place with chemicals linked to Parkinson's, but only a few of them end up with it.

It's a complex puzzle, and scientists are still trying to put all the pieces together.

**How Will My Doctor Test for It?**

There's no one test for Parkinson's. A lot of it's based on your symptoms and health history, but it could take some time to figure it out. Part of the process is ruling out other conditions that look like Parkinson's. The doctor may do a DaT scan, which looks for dopamine in the brain. This can aid in a diagnosis.

Because there is no single test, it's very important to go to a doctor who knows a lot about it, early on. It's easy to miss.

If you do have it, your doctor might use what's called the Hoehn and Yahr scale to tell you what stage of the disease you're in. It ranks how severe your symptoms are from 1 to 5, where 5 is the most serious.

The stage can help you get a better feel for where your symptoms fall and what to expect as the disease gets worse. But keep in mind, some people could take up to 20 years to move from mild to more serious symptoms. For others, the change is much faster.

**How Is Parkinson's Treated?**

It's all about managing symptoms. Drugs for Parkinson's can often help with tremors, stiff muscles, and slow movements. Your doctor may also suggest physical therapy, occupational therapy, and speech therapy, based on how it affects you. And in some cases, you may need surgery.

**How Will the Disease Affect My Life?**

Most people who have Parkinson’s live a normal to a nearly normal lifespan, but the disease can be life changing.

For some people, treatment keeps the symptoms at bay, and they're mostly mild. For others, the disease is much more serious and really limits what you're able to do.

As it gets worse, it makes it harder and harder to do daily activities like getting out of bed, driving, or going to work. Even writing can seem like a tough task. And in later stages, it can cause dementia.

Even though Parkinson's can have a big impact on your life, with the right treatment and help from your  health care team, you can still enjoy the things you love. It's important to reach out to family and friends for support. Learning to live with Parkinson's means making sure you get the backing you need.

Parkinson's disease is a chronic progressive neurological disease that affects a small area of nerve cells (neurons) in an area of the brain known as the substantia nigra. These cells normally produce dopamine, a chemical (neurotransmitter) that transmits signals between areas in the brain that, when working normally, coordinate smooth and balanced muscle movement. Parkinson's disease causes these nerve cells to die, and as a result, body movements are affected.

"Parkinsonism" is a term that is often used interchangeably with Parkinson's disease. Medically, parkinsonism refers to any condition that causes symptoms similar to Parkinson's disease tremors at rest, muscle rigidity, slow movement, and changes in walking. Parkinson's disease is probably the most common form of parkinsonism. Other conditions that cause it include:

* Medications such as reserpine, Thorazine
* Toxic exposures to carbon monoxide, cyanide
* Hypothyroidism
* Hypoparathyroidism
* A variety of other neurologic conditions affecting the nerves in the substantia nigra such as Wilson's disease (a condition causing abnormal deposition of copper in the brain) and progressive supranuclear palsy

Learn more about other causes of Parkinson's.

## **What Are the Symptoms of Parkinson's Disease?**

Common symptoms of Parkinson's disease include:

* Muscle rigidity
* Tremors
* Bradykinesia (the slowing down of movement and the gradual loss of spontaneous activity)
* Changes in walking pattern and posture
* Changes in speech and handwriting
* Loss of balance and increased falls
* Orthostatic hypotension (a drop in blood pressure when standing, resulting in lightheadedness or fainting)

## **Who Gets Parkinson's Disease?**

Approximately one million Americans have Parkinson's disease, including three out of every 100 people over the age of 60. Over 50,000 Americans are diagnosed with Parkinson's disease each year. There is increasing evidence that Parkinson's disease may be inherited (genetically passed on between family members). Men are slightly more likely to develop the disease than women.

The average age at which it is diagnosed is 60. However, about 4% of those with Parkinson's disease are diagnosed before age 50, and about half of those are diagnosed before age 40. When the diagnosis is made early, it is referred to as "young-onset" Parkinson's disease.

## **Young-Onset Parkinson's Disease**

While the disease presents in much the same way among people in the older age groups, people with young-onset Parkinson's disease will have special concerns because they will be dealing with the disease at a younger age and for a potentially longer period. Potential changes needed may involve making career adjustments and family concerns.

However, there is good news for people with young-onset Parkinson's disease. Young-onset Parkinson's disease is different from older onset Parkinson's disease. In general, younger people have a smoother, longer-term course of the illness. While this may, in part, be a reflection that the younger people have fewer other health problems than older people with the disease; the rate of progression is still significantly slower. Associated problems, such as memory loss, confusion, and balance difficulties, are also less frequent in young people with the disease.

On the other hand, people with young-onset Parkinson's disease often have more movement problems due to the most commonly prescribed medication, levodopa, than older people with the disease. For this reason, young-onset patients are often treated with alternatives to levodopa.

Young-onset patients are also better candidates for many of the new surgical procedures and medical innovations that are used to treat and reduce the symptoms of Parkinson's disease.

## **Is There a Cure for Parkinson's Disease?**

Although research is ongoing, to date there is no known cure or way to prevent Parkinson's disease. But, research has made remarkable progress. There is very real hope that the causes, whether genetic or environmental, will be identified and the precise effects of these causes on brain function will be understood. These remarkable achievements give real hope for the future.

Still, even though there is no cure for Parkinson's disease, by identifying individual symptoms and determining a proper course of treatment, most people with the disease can live enjoyable, fulfilling lives.

Source:

WebMD Editorial Team. (2022) *Parkinson's Disease Overview*. Reviewed by [Name of Reviewer, e.g., Aimee Gallo, MD if available]. WebMD. Available at: https://www.webmd.com/parkinsons-disease/parkinsons-disease-overview (Accessed: 23 May 2025).

About Amyotrophic Lateral Sclerosis (ALS)

HIGHLIGHTS

* ALS also known as Lou Gehrig's disease, is a motor neuron disease.
* ALS is rare, though slightly more common in men than women.
* The disease affects the nerve cells in both the upper and lower parts of the body. It causes the muscles to become weak and leads to paralysis.
* No one knows what causes most cases of ALS.

Overview

ALS is a disease that affects the nerve cells in both the upper and lower parts of the body. This disease causes the nerve cells to stop working and die. The nerves lose the ability to trigger specific muscles, which causes the muscles to become weak and leads to paralysis.

No one knows what causes most cases of ALS. Scientists have been studying many factors that could be linked with ALS, such as heredity and environmental exposures. Other scientists have looked at diet or injury. No cause has been found for most cases of ALS. In the future, scientists may find that many factors together cause ALS.

Health studies have not found definite environmental factors that are linked with either ALS or other MNDs. Some studies suggested a possible link with exposure to heavy metals (e.g., lead and mercury). Other studies suggested a link with exposure to trace elements, solvents, radiation, and agricultural chemicals. No confirmed link was found with infections, diet, physical activity, and injury.

Although no one knows for sure,  reports suggest less than 30,000 people in the United States have ALS; every year about 5,000 people are told by their doctor that they have the disease. Because no records on ALS have been kept throughout the country, it is hard to estimate the number of ALS cases in the United States. CDC does not require doctors to report ALS cases.

How it impacts lives

* ALS is slightly more common in men than women, but recent studies suggest that this difference is decreasing over time. Familial ALS is equally common in men and women.
* ALS is age related; most people with ALS find out they have it when they are between 55 and 75 years of age.
* Most people live from 2 to 5 years after symptoms develop. How long a person lives with ALS seems to be related to age; people who are younger when the illness starts live slightly longer.
* About 5–10% of ALS cases occur within families. This is called familial ALS and it means that two or more people in a family have ALS. These cases are caused by several inherited factors. The most common is in a gene called SOD1.
* Familial ALS is found equally among men and women. People with familial ALS usually do not fare as well as a person with ALS who are not related, and typically live only one to two years after symptoms appear.

# [**Amyotrophic lateral sclerosis (ALS)**](https://www.mayoclinic.org/diseases-conditions/amyotrophic-lateral-sclerosis/symptoms-causes/syc-20354022)

[Request an Appointment](https://www.mayoclinic.org/appointments)

## **Overview of ALS**

Amyotrophic lateral sclerosis (a-my-o-TROE-fik LAT-ur-ul skluh-ROE-sis), known as ALS, is a nervous system disease that affects nerve cells in the brain and spinal cord. ALS causes loss of muscle control. The disease gets worse over time.

ALS is often called Lou Gehrig's disease after the baseball player who was diagnosed with it. The exact cause of the disease is still not known. A small number of cases are inherited.

ALS often begins with muscle twitching and weakness in an arm or leg, trouble swallowing or slurred speech. Eventually ALS affects control of the muscles needed to move, speak, eat and breathe. There is no cure for this fatal disease.

## **Symptoms**

Symptoms of ALS vary from person to person. Symptoms depend on which nerve cells are affected. ALS generally begins with muscle weakness that spreads and gets worse over time. Symptoms might include:

* + Trouble walking or doing usual daily activities.
  + Tripping and falling.
  + Weakness in the legs, feet or ankles.
  + Hand weakness or clumsiness.
  + Slurred speech or trouble swallowing.
  + Weakness associated with muscle cramps and twitching in the arms, shoulders and tongue.
  + Untimely crying, laughing or yawning.
  + Thinking or behavioral changes.

ALS often starts in the hands, feet, arms or legs. Then it spreads to other parts of the body. Muscles get weaker as more nerve cells die. This eventually affects chewing, swallowing, speaking and breathing.

There's generally no pain in the early stages of ALS. Pain also is not common in the later stages. ALS doesn't usually affect bladder control. It also usually doesn't affect the senses, including the ability to taste, smell, touch and hear.

## **Causes**

ALS affects the nerve cells that control voluntary muscle movements such as walking and talking. These nerve cells are called motor neurons. There are two groups of motor neurons. The first group extends from the brain to the spinal cord to muscles throughout the body. They're referred to as upper motor neurons. The second group extends from the spinal cord to muscles throughout the body. They're referred to as lower motor neurons.

ALS causes both groups of motor neurons to gradually deteriorate and then die. When motor neurons are damaged, they stop sending messages to the muscles. As a result, the muscles can't function.

For about 10% of people with ALS, a genetic cause can be identified. For the rest, the cause is not known.

Researchers continue to study possible causes of ALS. Most theories center on a complex interaction between genes and factors in the environment.

## **Risk factors**

Established risk factors for ALS include:

* + **Genetics.** For about 10% of people with ALS, a risk gene was passed down from a family member. This is called hereditary ALS. In most people with hereditary ALS, their children have a 50% chance of inheriting the gene.
  + **Age.** Risk increases with age up to age 75. ALS is most common between the ages of 60 and the mid-80s.
  + **Sex.** Before the age of 65, slightly more men than women develop ALS. This sex difference disappears after age 70.

Environmental factors, such as the following, have been associated with an increased risk of ALS.

* + **Smoking.** Evidence supports that smoking is an environmental risk factor for ALS. Women who smoke seem to be at even higher risk, particularly after menopause.
  + **Environmental toxin exposure.** Some evidence suggests that exposure to lead or other substances in the workplace or at home might be linked to ALS. Much study has been done, but no one agent or chemical has been consistently associated with ALS.
  + **Military service.** Studies indicate that people who have served in the military are at higher risk of ALS. It's not clear what about military service might trigger ALS. It might include exposure to certain metals or chemicals, traumatic injuries, viral infections, or intense exertion.

## **Complications**

As the disease progresses, ALS causes complications, such as:

### Breathing problems

Over time, ALS leads to weakness of the muscles used to breathe. People with ALS might need a device such as a mask ventilator to help them breathe at night. The device is similar to what someone with sleep apnea might wear. This type of device supports the person's breathing through a mask worn over the nose, the mouth or both.

Some people with advanced ALS choose to have a tracheostomy. This is a surgically created hole at the front of the neck leading to the windpipe. A ventilator may work better on a tracheostomy than on a mask.

The most common cause of death for people with ALS is breathing failure. Half of people with ALS die within 14 to 18 months of diagnosis. However, some people with ALS live 10 years or longer.

### Speaking problems

Most people with ALS develop weakness of the muscles used to form speech. This usually starts with slower speech and occasional slurring of words. It then becomes harder to speak clearly. This can progress to the point that others can't understand the person's speech. Other forms of communication and technology are used to communicate.

### Eating problems

People with ALS can develop weakness of the muscles involved with swallowing. This can lead to malnutrition and dehydration. They are also at higher risk of getting food, liquids or saliva into the lungs, which can cause pneumonia. A feeding tube can reduce these risks and ensure proper hydration and nutrition.

### Dementia

Some people with ALS have problems with language and decision-making. Some are eventually diagnosed with a form of dementia called frontotemporal dementia.

## **Diagnosis**

Amyotrophic lateral sclerosis, known as ALS, can be hard to diagnose early because it can have symptoms similar to other diseases. Tests to rule out other conditions or help diagnose ALS might include:

* **Electromyogram (EMG).** A needle is inserted through the skin into various muscles. The test records the electrical activity of the muscles when they contract and when they're at rest. This can determine if there is a problem with the muscles or nerves.
* **Nerve conduction study.** This study measures your nerves' ability to send impulses to muscles in different areas of the body. This test can determine if you have nerve damage. EMG and nerve conduction studies are almost always done together.
* **MRI.** Using radio waves and a powerful magnetic field, an MRI produces detailed images of the brain and spinal cord. An MRI can reveal spinal cord tumors, herniated disks in the neck or other conditions that might be causing your symptoms. The highest resolution cameras may sometimes see ALS changes themselves.
* **Blood and urine tests.** Analyzing samples of your blood and urine in the laboratory might help eliminate other possible causes of your symptoms. Serum neurofilament light levels, which are measured from blood samples, are generally high in people with ALS. The test can help make a diagnosis early in the disease.
* **Spinal tap, known as a lumbar puncture.** This involves removing a sample of spinal fluid for laboratory testing. Spinal fluid is removed using a small needle inserted between two bones in the lower back. The spinal fluid appears typical in people with ALS but may uncover another cause of symptoms.
* **Muscle biopsy.** If your health care provider believes you may have a muscle disease rather than ALS, you might undergo a muscle biopsy. While you're under local anesthesia, a small piece of muscle is removed and sent to a lab for analysis.
* **Nerve biopsy.** If your health care provider believes you may have a nerve disease rather than ALS, you might undergo a nerve biopsy. While you're under local anesthesia, a small piece of nerve is removed and Treatment

Treatments can't reverse the damage of ALS, but they can slow the progression of symptoms. They also can help prevent complications and make you more comfortable and independent.

You might need a team of health care providers and doctors trained in many areas to provide your care. The team works together to prolong your survival and improve your quality of life.

Your team works to select the right treatments for you. You have the right to choose or refuse any of the treatments suggested.

### Medications

The Food and Drug Administration has approved two medicines for treating ALS:

* + **Riluzole (Rilutek, Exservan, Tiglutik).** Taken by mouth, this medicine can increase life expectancy by about 25%. It can cause side effects such as dizziness, gastrointestinal conditions and liver problems. Your health care provider typically monitors your liver function with periodic blood draws while you're taking the medicine.
  + **Edaravone (Radicava).** This medicine may reduce the speed of decline in daily functioning. It's given through a vein in your arm or by mouth as a liquid. The effect on life span isn't yet known. Side effects can include bruising, headache and trouble walking. This medicine is given daily for two weeks each month.

Your health care provider also might prescribe treatments for relief of other symptoms, including:

* + Muscle cramps and spasms.
  + Constipation.
  + Fatigue.
  + Excessive saliva and phlegm.
  + Pain.
  + Depression.
  + Sleep problems.
  + Uncontrolled outbursts of laughing or crying.
  + An urgent need to urinate.
  + Leg swelling.

### Therapies

When ALS affects your ability to breathe, speak and move, therapies and other forms of support can help.

* + **Breathing care.** Most people with ALS eventually have more trouble breathing as muscles weaken. Your health care provider might test your breathing regularly and provide devices known as mechanical ventilation to assist your breathing at night.

You might choose to use a ventilator with a mask that can easily be applied and removed. This is known as noninvasive ventilation. Some people eventually have surgery that creates a hole at the front of the neck leading to their windpipe. This is called a tracheostomy. A tube inserted into the hole connects to a respirator to help them breathe. Sometimes people with ALS who have a tracheostomy also have a type of surgery called a laryngectomy. This surgery prevents food from entering the lungs.

* + **Physical therapy.** A physical therapist can address pain, walking, mobility, bracing and equipment needs that help you stay independent. Practicing low-impact exercises can help maintain your cardiovascular fitness, muscle strength and range of motion for as long as possible.

Regular exercise also can help improve your sense of well-being. Appropriate stretching can help prevent pain and help your muscles function at their best.

A physical therapist also can help you overcome weakness by using a brace, walker or wheelchair. The therapist might suggest devices such as ramps that make it easier for you to get around.

* + **Occupational therapy.** An occupational therapist can help you find ways to remain independent despite hand and arm weakness. Adaptive equipment can help you perform activities such as dressing, grooming, eating and bathing.

An occupational therapist also can help you modify your home to allow accessibility if you have trouble walking safely.

* + **Speech therapy.** A speech therapist can teach you adaptive techniques to make your speech more understandable. Speech therapists also can help you find other ways to communicate. These may include using a smart phone app, alphabet board, or pen and paper.

Ask your therapist about the possibility of recording your own voice to be used by a text-to-speech application.

* + **Nutritional support.** Your team typically works with you and your family members to ensure you are eating foods that are easier to swallow and meet your nutritional needs. You might choose to have a feeding tube placed when it becomes too hard to swallow.
  + **Psychological and social support.** Your team might include a social worker to help with financial issues, insurance, and getting equipment and paying for devices you need. Psychologists, social workers and others may provide emotional support for you and your family.

### Potential future treatments

Based on the current understanding of ALS, researchers are conducting clinical studies on promising medicines and treatments.

## **Coping and support**

Learning you have ALS can be devastating. The following tips may help you and your family cope:

* + **Take time to grieve.** The news that you have a fatal condition that reduces your mobility and independence is hard to hear. You and your family may go through a period of mourning and grief after diagnosis.
  + **Be hopeful.** Your team can help you focus on your abilities and healthy living. Some people with ALS live much longer than the 3 to 5 years usually associated with this condition. Some live 10 years or more. Maintaining an optimistic outlook can help improve quality of life for people with ALS.
  + **Think beyond the physical changes.** Many people with ALS lead rewarding lives despite physical limitations. Try to think of ALS as only one part of your life, not your entire identity.
  + **Join a support group.** You might find comfort in a support group with others who have ALS. Loved ones helping with your care might benefit from a support group of other ALS caregivers. Find support groups in your area by talking to your doctor or by contacting the ALSAssociation.
  + **Make decisions now about your future medical care.** Planning for the future allows you to be in control of decisions about your life and your care. It also lessens the burden for your loved ones. With the help of your health care provider, hospice nurse or social worker, you can decide whether you want certain life-extending procedures.

You also can decide where you want to spend your final days. You might consider hospice care options. Planning for the future can help you and your loved ones calm anxieties.

* + **Considering getting involved in ALS research.** ALS research is working toward finding a cure for ALS. Consider joining a clinical trial, providing samples for research and joining the National ALS Registry. The registry is open to all people with ALS. Many institutions collect samples for research to better understand the disease.

## **Preparing for your appointment**

Your primary care provider may be the first to recognize the symptoms of ALS. Your provider will likely refer you to a doctor trained in nervous system conditions, known as a neurologist, to establish a diagnosis.

### What you can do

You might need many tests to diagnose your condition. The diagnosis process can be stressful and frustrating. These strategies might give you a greater sense of control.

* + **Keep a symptom diary.** Before you see a neurologist, start using a calendar or notebook to jot down when and how you notice symptoms. Record information about your problems with walking, hand coordination, speech, swallowing or involuntary muscle movements. Your notes might show a pattern that's helpful for your diagnosis.
  + **Find a neurologist and care team.** An integrated care team led by your neurologist usually is most appropriate for ALS care. Your team typically communicates with each other and is familiar with your needs.

### What to expect from your doctor

Your primary care provider will likely review your family's medical history and your symptoms. Your neurologist and your primary care provider might conduct a physical and neurological exam. This might include testing your:

* + Reflexes.
  + Muscle strength.
  + Muscle tone.
  + Senses of touch and sight.
  + Coordination.
  + Balance.

Source:

* Centers for Disease Control and Prevention. (2024) *About Amyotrophic Lateral Sclerosis (ALS)*. Available at: https://www.cdc.gov/als/abouttheregistrymain/about-amyotrophic-lateral-sclerosis-als.html (Accessed: 23 May 2025).
* Mayo Clinic Staff. (2023) *Amyotrophic lateral sclerosis (ALS): Symptoms and causes*. Mayo Clinic. Available at: https://www.mayoclinic.org/diseases-conditions/amyotrophic-lateral-sclerosis/symptoms-causes/syc-20354022(Accessed: 23 May 2025).

# **Huntington's Disease**

# **What is Huntington's disease?**

Top of Form

Huntington's disease (HD) is an inherited disorder that causes nerve cells (neurons) in parts of the brain to gradually break down and die. The disease attacks areas of the brain that help to control voluntary (intentional) movement, as well as other areas. People living with HD develop uncontrollable dance-like movements (chorea) and abnormal body postures, as well as problems with behavior, emotion, thinking, and personality.

For example, uncontrolled movements in the person's fingers, feet, face, or torso. These movements are signs of chorea. They can get more intense when the person is nervous or distracted; as HD progresses, the person's movements can become more extreme and obvious.

Symptoms of HD typically appear in middle-aged people (adult HD). They can also appear in children (juvenile HD), but this is rare. The disease gets worse over time.

Early signs of HD can vary, but often include mild clumsiness or problems with balance or movement, cognitive or psychiatric symptoms (problems with thinking or emotion), and changes in behavior.  
  
For some people, chorea can make it harder to walk, which increases the chances of falling. Some people with HD do not develop chorea; instead, they may become rigid (stiff) and move very little or not at all. This condition is called akinesia. Other people may start out with chorea but become rigid as the disease progresses.  
  
In addition to chorea, some individuals have unusual fixed (unchanging) postures, which is known as dystonia. The two movement disorders (akinesia and dystonia) can blend or alternate.  
  
Other symptoms may include tremor (unintentional back-and-forth movement in the person's muscles) and unusual eye movements. The eye movements can happen early in the disease.

Physical changes may include slurred speech and problems with swallowing, eating, speaking, and especially walking. People with HD may lose weight because of problems with feeding, swallowing, choking, and chest infections. Other symptoms may include insomnia (having trouble sleeping), loss of energy, fatigue, and seizures. Eventually the person will need to stay in bed or in a wheelchair.

Changes in thinking (cognitive changes)may include problems with attention or judgment and having difficulty solving problems or making decisions.   
  
Other changes may include trouble with driving, prioritizing (deciding which things are more important to do and which are less important), and organizing, learning new things, remembering a fact, putting thoughts into words, or answering a question.  
  
These cognitive changes get worse as the disease progresses, until people with HD are not able to work, drive, or care for themselves.   
  
When the cognitive problems are severe enough that the person cannot function in daily life, the condition is described as dementia. But many people with HD stay aware of their environment and can express their emotions.

Changes in behavior may include mood swings; feeling irritable (cranky); not being active; or feeling apathetic (uninterested), depressed, or angry. These symptoms may decrease as the disease progresses. But in some people, the symptoms can continue and may include angry outbursts, thoughts of suicide, deep depression, and psychosis (losing touch with reality). People with HD may withdrawal from social activities.

Who is more likely to get Huntington's disease?

HD is an inherited disorder. It is passed from parent to child through a mutation (a change) in a particular gene. When a parent has HD, each child has a 50% chance of inheriting the copy of chromosome 4 that carries the HD mutation. If a child does not inherit the HD mutation, he or she will not develop the disease and cannot pass it on to future generations. When HD occurs without a family history, it is called sporadic HD.

HD is caused by a mutation in the gene for a protein called Huntingtin. The defect causes the building blocks of DNA called cytosine, adenine, and guanine (CAG) to repeat many more times than they normally do.

Most people have fewer than 27 CAG repeats in their HD gene, so they are not at risk for the disease. People who have CAG repeats in the middle range (27 to 35) are not likely to develop the disease, but they could still pass it on to future generations. People with HD may have 36 or more CAG repeats.

Each child of a parent with HD has a 50% chance of inheriting the HD gene. A child who does not inherit the HD gene will not develop the disease, and generally, they cannot pass it on to their children or other future generations.

How is Huntington's disease diagnosed and treated?

### Diagnosing HD

In general, doctors use a combination of tests and other information to see if a person has HD. These include medical history, neurological and lab tests, brain imaging, and genetic testing.

* Neurological exam and medical history—A neurologist will conduct an in-depth interview to obtain a medical and family history for the individual and to rule out other conditions. Neurological and physical exams may review reflexes, balance, movement, muscle tone, hearing, walking, and mental status. Laboratory tests may also be ordered, and individuals with HD may be referred to specialists such as psychiatrists, genetic counselors, clinical neuropsychologists, or speech pathologists for specialized management and/or to support diagnosis.
* Diagnostic imaging—In some cases, especially if a person's family history and genetic testing are inconclusive, the physician may recommend brain imaging, such as computed tomography (CT) or, more likely, magnetic resonance imaging (MRI). As the disease progresses, these scans typically reveal shrinkage in parts of the brain and enlargement of fluid-filled cavities within the brain called ventricles. These changes do not necessarily indicate HD, because they can occur in other disorders. A person can have early symptoms of HD and still have normal findings on a CT or MRI scan.
* Genetic tests—Genetic testing can confirm or rule out a suspected genetic condition or help determine a person's chance of developing or passing on a genetic disorder. Genetic testing makes it possible to predict with a higher degree of certainty if someone will develop HD. The most effective and accurate method of testing for HD—called the direct genetic test—counts the number of CAG repeats in the HD gene, using DNA taken from a blood sample. The presence of 36 or more repeats supports a diagnosis of HD. A test result of 26 or fewer repeats rules out HD. Prenatal testing is an option for people who have a family history of HD and are concerned about passing the disease to a child.

### Treating HD

There is no treatment that can stop or reverse HD, but some of the symptoms can be treated:

* The drugs tetrabenazine and deuterabenazine can treat chorea associated with HD
* Antipsychotic drugs may ease chorea and help to control hallucinations, delusions, and violent outbursts. Some antipsychotic medications can have side effects that make muscle contraction symptoms of HD worse. Individuals using antipsychotic drugs for Huntington's disease symptoms should be closely monitored for side effects.
* Drugs may be prescribed to treat depression and anxiety

Side effects of drugs used to treat the symptoms of HD may include fatigue, sedation, decreased concentration, restlessness, or hyperexcitability. These drugs should be only used when HD symptoms create problems for the person living with HD.

## **What are the latest updates on Huntington's disease?**

Researchers are learning more about Huntington's disease over time. Below are some important updates that may improve how doctors care for this disorder in the future.

### Understanding Huntington's disease mechanisms

NINDS-funded researchers are trying to better understand the cellular and molecular mechanisms involved in HD by investigating, for instance, how the Huntingtin protein affects cell signaling and how its altered structure can contribute to disease. The following provides an overview of this research:

* A new avenue of NINDS-supported research is asking whether additional changes to the Huntington gene during development and in adulthood impact disease onset and severity, and whether the Huntington gene affects the brain's overall ability to maintain healthy, undamaged DNA. This work is a promising area for identifying new modifiers of HD onset and progression that may be attractive drug targets.
* Excessive chemical signaling between cells in the brain may lead to chronic overexcitation (overactivation of neurons to turn on), which is toxic to neurons. Several labs are investigating whether drugs that counteract excitotoxicity might help against HD.
* Cutting-edge methods such as optogenetics (where neurons are activated or silenced in the brains of living animals using light beams) are being used to probe the cause and progression of cell circuit defects in HD.

#### *Biomarkers*

The NINDS-funded PREDICT-HD study and several international studies are working to identify and validate biomarkers for HD. Biomarkers are biological indicators that can be used to predict, diagnose, or monitor a disease. One goal of PREDICT-HD is to determine if the progression of the disease correlates with changes in brain scan images, or with chemical changes in blood, urine, or cerebrospinal fluid. Another goal is to find measurable changes in personality, mood, and cognition that typically precede the appearance of motor symptoms of HD. A third phase of PredictHD is ongoing.

A related NINDS-supported study aims to identify additional human genetic factors that influence the course of the disease. Finding genetic variants that slow or accelerate the pace of disease progression promises to provide important new targets for disease intervention and therapy.

#### *Stem cells*

Through a NINDS-funded consortium, researchers are using cultures of cell lines (created from people with HD who have donated skin and blood samples for research) to understand why neurons malfunction and die in HD, and to rapidly test potential new drugs. Another approach may be to mobilize stem cells that are already there and can move into damaged tissue.

#### *Turning research into treatment*

Testing investigational drugs may lead to new treatments and at the same time improve our understanding of the disease process in HD. Classes of drugs being tested include those designed to control symptoms, slow the rate of progression of HD, block the effects of excitotoxins, provide support factors that improve neuronal health, or suppress metabolic defects that contribute to the development and progression of HD.

Several groups of scientists are using gene-editing or specific molecules that can interfere with the production of the Huntingtin protein in cells or animals to stop production of Htt in inappropriate locations or amounts.

#### *Imaging*

Scientists are using imaging technology to learn how HD affects the chemical systems of the brain, characterize neurons that have died, view changes in the volume and structures of the brain in people with HD, and to understand how HD affects the functioning of different brain regions.

#### *Brain development*

Altered brain development may play an important role in HD. Huntingtin is expressed during embryonic development and throughout life. Studies in animals have shown that the normal HD gene is vital for brain development. Adults who carry the mutant HD gene but have not yet displayed symptoms show measurable changes in the structure of their brain, even up to 20 years before clinical diagnosis.

A NINDS-funded study is evaluating brain structure and function in children, adolescents, and young adults up to age 30 who are at risk for developing the disease because they have a parent or grandparent with HD. This study is trying to capture potential HD effects during the late stages of brain development. Participants who carry the expanded gene will be compared to individuals who carry the gene but have fewer than 9 CAG repeats, as well as to individuals who do not have a history of HD in their family. Changes in brain structure and/or function in the gene-expanded group may point to a developmental component in HD.

**How can I or my loved one help improve care for people with Huntington's disease?**

Consider participating in a clinical trial so clinicians and scientists can learn more about HD. Clinical research uses human volunteers to help researchers learn more about a disorder and perhaps find better ways to safely detect, treat, or prevent disease.

All types of volunteers are needed—those who are healthy or may have an illness or disease—of all different ages, sexes, races, and ethnicities to ensure that study results apply to as many people as possible, and that treatments will be safe and effective for everyone who will use them.

Source:

* National Institute of Neurological Disorders and Stroke. (2024) *Huntington's Disease*. Available at: https://www.ninds.nih.gov/health-information/disorders/huntingtons-disease (Accessed: 23 May 2025).

**Epilepsy**

**Key facts**

* **Epilepsy is a chronic noncommunicable disease of the brain that affects people of all ages.**
* **Around 50 million people worldwide have epilepsy, making it one of the most common neurological diseases globally.**
* **Nearly 80% of people with epilepsy live in low- and middle-income countries.**
* **It is estimated that up to 70% of people living with epilepsy could live seizure-free if properly diagnosed and treated.**
* **The risk of premature death in people with epilepsy is up to three times higher than for the general population.**
* **Three quarters of people with epilepsy living in low-income countries do not get the treatment they need.**
* **In many parts of the world, people with epilepsy and their families suffer from stigma and discrimination.**

**Overview**

Epilepsy is a chronic noncommunicable disease of the brain that affects around 50 million people worldwide. It is characterized by recurrent seizures, which are brief episodes of involuntary movement that may involve a part of the body (partial) or the entire body (generalized) and are sometimes accompanied by loss of consciousness and control of bowel or bladder function.

Seizure episodes are a result of excessive electrical discharges in a group of brain cells. Different parts of the brain can be the site of such discharges. Seizures can vary from the briefest lapses of attention or muscle jerks to severe and prolonged convulsions. Seizures can also vary in frequency, from less than one per year to several per day.

One seizure does not signify epilepsy (up to 10% of people worldwide have one seizure during their lifetime). Epilepsy is defined as having two or more unprovoked seizures. Epilepsy is one of the world’s oldest recognized conditions, with written records dating back to 4000 BCE. Fear, misunderstanding, discrimination and social stigma have surrounded epilepsy for centuries. This stigma continues in many countries today and can impact on the quality of life for people with the disease and their families.

**Signs and symptoms**

Characteristics of seizures vary and depend on where in the brain the disturbance first starts, and how far it spreads. Temporary symptoms occur, such as loss of awareness or consciousness, and disturbances of movement, sensation (including vision, hearing and taste), mood, or other cognitive functions.

People with epilepsy tend to have more physical problems (such as fractures and bruising from injuries related to seizures), as well as higher rates of psychological conditions, including anxiety and depression. Similarly, the risk of premature death in people with epilepsy is up to three times higher than in the general population, with the highest rates of premature mortality found in low- and middle-income countries and in rural areas.

A great proportion of the causes of death related to epilepsy, especially in low- and middle-income countries, are potentially preventable, such as falls, drowning, burns and prolonged seizures.

**Rates of disease**

Epilepsy accounts for a significant proportion of the world’s disease burden, affecting around 50 million people worldwide. The estimated proportion of the general population with active epilepsy (i.e. continuing seizures or with the need for treatment) at a given time is between 4 and 10 per 1000 people.

Globally, an estimated 5 million people are diagnosed with epilepsy each year. In high-income countries, there are estimated to be 49 per 100 000 people diagnosed with epilepsy each year. In low- and middle-income countries, this figure can be as high as 139 per 100 000. This is likely due to the increased risk of endemic conditions such as malaria or neurocysticercosis; the higher incidence of road traffic injuries; birth-related injuries; and variations in medical infrastructure, the availability of preventive health programmes and accessible care. Close to 80% of people with epilepsy live in low- and middle-income countries.

**Causes**

Epilepsy is not contagious. Although many underlying disease mechanisms can lead to epilepsy, the cause of the disease is still unknown in about 50% of cases globally. The causes of epilepsy are divided into the following categories: structural, genetic, infectious, metabolic, immune and unknown. Examples include:

* brain damage from prenatal or perinatal causes (e.g. a loss of oxygen or trauma during birth, low birth weight);
* congenital abnormalities or genetic conditions with associated brain malformations;
* a severe head injury;
* a stroke that restricts the amount of oxygen to the brain;
* an infection of the brain such as meningitis, encephalitis or neurocysticercosis,
* certain genetic syndromes; and
* a brain tumour.

**Treatment**

Seizures can be controlled. Up to 70% of people living with epilepsy could become seizure free with appropriate use of antiseizure medicines. Discontinuing antiseizure medicine can be considered after 2 years without seizures and should take into account relevant clinical, social and personal factors. A documented etiology of the seizure and an abnormal electroencephalography (EEG) pattern are the two most consistent predictors of seizure recurrence.

* In low-income countries, about three quarters of people with epilepsy may not receive the treatment they need. This is called the “treatment gap”.
* In many low- and middle-income countries, there is low availability of antiseizure medicines. A recent study found the average availability of generic antiseizure medicines in the public sector of low- and middle-income countries to be less than 50%. This may act as a barrier to accessing treatment.
* It is possible to diagnose and treat most people with epilepsy at the primary health-care level without the use of sophisticated equipment.
* WHO pilot projects have indicated that training primary health-care providers to diagnose and treat epilepsy can effectively reduce the epilepsy treatment gap.
* Surgery might be beneficial to patients who respond poorly to drug treatments.

**Prevention**

An estimated 25% of epilepsy cases are potentially preventable.

* Preventing head injury, for example by reducing falls, traffic accidents and sports injuries, is the most effective way to prevent post-traumatic epilepsy.
* Adequate perinatal care can reduce new cases of epilepsy caused by birth injury.
* The use of drugs and other methods to lower the body temperature of a feverish child can reduce the chance of febrile seizures.
* The prevention of epilepsy associated with stroke is focused on cardiovascular risk factor reduction, e.g. measures to prevent or control high blood pressure, diabetes and obesity, and the avoidance of tobacco and excessive alcohol use.
* Central nervous system infections are common causes of epilepsy in tropical areas, where many low- and middle-income countries are concentrated. Elimination of parasites in these environments and education on how to avoid infections can be effective ways to reduce epilepsy worldwide, for example those cases due to neurocysticercosis.

**Social and economic impacts**

Epilepsy accounts for more than 0.5% of the global burden of disease, a time-based measure that combines years of life lost due to premature mortality and time lived in less than full health. Epilepsy has significant economic implications in terms of health-care needs, premature death and lost work productivity.

Out-of-pocket costs and productivity losses can create substantial burdens on households. An economic study from India estimated that public financing for both first- and second-line therapy and other medical costs alleviates the financial burden from epilepsy and is cost-effective.

The stigma and discrimination that surround epilepsy worldwide are often more difficult to overcome than the seizures themselves. People living with epilepsy and their families can be targets of prejudice. Pervasive myths that epilepsy is incurable, or contagious, or a result of morally bad behaviour can keep people isolated and discourage them from seeking treatment.

**Human rights**

People with epilepsy can experience reduced access to educational opportunities, a withholding of the opportunity to obtain a driving license, barriers to enter particular occupations, and reduced access to health and life insurance. In many countries legislation reflects centuries of misunderstanding about epilepsy, for example, laws which permit the annulment of a marriage on the grounds of epilepsy and laws that deny people with seizures access to restaurants, theatres, recreational centres and other public buildings.

Legislation based on internationally accepted human rights standards can prevent discrimination and rights violations, improve access to health-care services, and raise the quality of life for people with epilepsy.

**WHO response**

The ﬁrst global report on epilepsy produced in 2019 by WHO and key partners, Epilepsy: A public health imperative, highlighted the available evidence on the burden of epilepsy and the public health response required at global, regional and national levels.

The 75th WHA adopted the Intersectoral global action plan on epilepsy and other neurological disorders 2022–2031, which recognizes the shared preventive, pharmacological and psychosocial approaches between epilepsy and other neurological disorders that can serve as valuable entry points for accelerating and strengthening services and support for these conditions.

Recently, WHO published an epilepsy technical brief, which outlines actions for policy makers and healthcare planners to reduce the burden of epilepsy in countries through finding and prioritizing the most effective solutions in a wide range of societal sectors.

WHO, the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE) led the Global Campaign Against Epilepsy to bring the disease out of the shadows to provide better information and raise awareness about epilepsy and to strengthen public and private efforts to improve care and reduce the disease’s impact.

These efforts have contributed to the prioritization of epilepsy in many countries and projects have been carried out to reduce the treatment gap and morbidity of people with epilepsy, to train and educate health professionals, to dispel stigma, to identify potential prevention strategies, and to develop models integrating epilepsy care into local health systems. Combining several innovative strategies, these projects have shown that there are simple, cost-effective ways to treat epilepsy in low-resource settings. The WHO Programme on reducing the epilepsy treatment gap and the mental health Gap Action Programme (mhGAP) achieved these goals in Ghana, Mozambique, Myanmar and Viet Nam, where 6.5 million more people have access to treatment for epilepsy should they need it.

SOURCE:

* World Health Organization. (2024) *Epilepsy*. Available at: https://www.who.int/news-room/fact-sheets/detail/epilepsy(Accessed: 23 May 2025)

# Stroke

# KEY POINTS

* Stroke causes parts of the brain to become damaged or die.
* Quick treatment is critical for stroke.
* There are two types of stroke: ischemic and hemorrhagic.
* A transient ischemic attack is sometimes called a “mini-stroke."

## What it is

A stroke, sometimes called a brain attack, occurs when something blocks blood supply to part of the brain or when a blood vessel in the brain bursts.

In either case, parts of the brain become damaged or die. A stroke can cause lasting brain damage, long-term disability, or even death.

### **What happens in the brain during a stroke?**

The brain controls our movements, stores our memories, and is the source of our thoughts, emotions, and language. The brain also controls many functions of the body, like breathing and digestion.

To work properly, your brain needs oxygen. Your arteries deliver oxygen-rich blood to all parts of your brain. If something happens to block the flow of blood, brain cells start to die **within minutes,** because they can't get oxygen. This causes a stroke.

A stroke, sometimes call a brain attack, happens in one of two ways: a blocked artery or a ruptured artery.

## Types

There are two types of stroke:

* Ischemic stroke.
* Hemorrhagic stroke.

A transient ischemic attack (TIA) is sometimes called a "mini-stroke." It is different from the major types of stroke. Blood flow to the brain is blocked for only a short time—usually no more than 5 minutes.[1](https://www.cdc.gov/stroke/about/index.html#cdcreference_1)

### **Ischemic stroke**

Most strokes are ischemic strokes. An ischemic stroke occurs when blood clots or other particles block the blood vessels to the brain.

Fatty deposits called plaque can also cause blockages by building up in the blood vessels.

### **Hemorrhagic stroke**

A hemorrhagic stroke happens when an artery in the brain leaks blood or ruptures (breaks open). The leaked blood puts too much pressure on brain cells, which damages them.

High blood pressure and aneurysms—balloon-like bulges in an artery that can stretch and burst—are examples of conditions that can cause a hemorrhagic stroke.

### **Transient ischemic attack (TIA or “mini-stroke”)**

TIAs are sometimes known as "warning strokes." It's important to know that:

* A TIA is a warning sign of a future stroke.
* A TIA is a medical emergency, just like a major stroke.
* Strokes and TIAs require emergency care. **Call 9-1-1** right away if you feel symptoms of a stroke or see signs in another person.
* There is no way to know in the beginning whether symptoms are from a TIA or from a major type of stroke.
* Like ischemic strokes, blood clots often cause TIAs.
* More than a third of people who have a TIA and don't get treatment have a major stroke within 1 year. As many as 10% to 15% of people will have a major stroke within 3 months of a TIA.1

Recognizing and treating TIAs can lower the risk of a major stroke. If you have a TIA, your health care team can find the cause and take steps to prevent a major stroke.

# Signs and Symptoms of Stroke

## KEY POINTS

* During a stroke, every minute counts.
* Fast treatment can lessen the brain damage that stroke can cause.

## Signs and symptoms

By knowing the signs and symptoms of stroke, you can take quick action and perhaps save a life—maybe even your own.

### **What are the signs of stroke in men and women?**

* Sudden numbness or weakness in the face, arm, or leg, especially on one side of the body.
* Sudden confusion, trouble speaking, or difficulty understanding speech.
* Sudden trouble seeing in one or both eyes.
* Sudden trouble walking, dizziness, loss of balance, or lack of coordination.
* Sudden severe headache with no known cause.

Signs of stroke in men and women.

## When to seek emergency help

### **Act F.A.S.T. to identify stroke**

Act F.A.S.T. to help stroke patients get the treatments they need.

The stroke treatments that work best are available only if the stroke is recognized and diagnosed within 3 hours of the first symptoms. Stroke patients may not be eligible for these treatments if they don't arrive at the hospital in time.

If you think someone may be having a stroke, act F.A.S.T. and do the following test:

* **F—Face:** Ask the person to smile. Does one side of the face droop?
* **A—Arms:** Ask the person to raise both arms. Does one arm drift downward?
* **S—Speech:** Ask the person to repeat a simple phrase. Is the speech slurred or strange?
* **T—Time:** If you see any of these signs, call 9-1-1 right away.

Note the time when any symptoms first appear. This information helps health care providers determine the best treatment.

Do not drive to the hospital or let someone else drive you. Call 9-1-1 for an ambulance so that medical personnel can begin life-saving treatment on the way to the emergency room.

### **What should I do to treat a transient ischemic attack ("mini-stroke")?**

If your stroke symptoms go away after a few minutes, you may have had a transient ischemic attack (TIA), also sometimes called a "mini-stroke." Although brief, a TIA is a sign of a serious condition that will not go away without medical help.

Unfortunately, because TIAs clear up, many people ignore them. But paying attention to a TIA can save your life. If you think you or someone you know has had a TIA, tell a health care team about the symptoms right away.

# Treatment and Intervention for Stroke

## KEY POINTS

* If someone you know shows signs of stroke, call 9-1-1 right away.
* If you have had a stroke, you are at high risk for another stroke.

## Overview

If someone you know shows signs of stroke, call 9-1-1 right away.

Your stroke treatment begins the moment emergency medical services (EMS) arrive to take you to the hospital.

Once at the hospital, you may receive emergency care, treatment to prevent another stroke, rehabilitation to treat the side effects of stroke, and/or all three.

### Stroke‎

A stroke, sometimes called a brain attack, occurs when something blocks blood supply to part of the brain or when a blood vessel in the brain bursts.

In either case, parts of the brain become damaged or die. A stroke can cause lasting brain damage, long-term disability, or even death.

## How is stroke treated?

### **On the way to the hospital**

Calling 9-1-1 for an ambulance means that medical staff can begin life-saving treatment on the way to the emergency room.

Do not drive to the hospital or let someone else drive you. The key to stroke treatment and recovery is getting to the hospital quickly.

Stroke patients who are taken to the hospital in an ambulance may get diagnosed and treated more quickly than people who do not arrive in an ambulance. This is because emergency treatment starts on the way to the hospital. The emergency workers may take you to a specialized stroke center to ensure that you receive the quickest possible diagnosis and treatment.

The emergency workers will also collect valuable information that guides treatment and alert hospital medical staff before you arrive at the emergency room, giving them time to prepare.

### **Treating ischemic stroke**

If you get to the hospital within 3 hours of the first symptoms of an ischemic stroke, you may get a type of medicine called a thrombolytic (a "clot-busting" drug) to break up blood clots. Tissue plasminogen activator (tPA) is a thrombolytic.

tPA improves the chances of recovering from a stroke. Studies show that patients with ischemic strokes who receive tPA are more likely to recover fully or have less disability than patients who do not receive the drug. Patients treated with tPA are also less likely to need long-term care in a nursing home.

Recognizing the signs and symptoms and seeking immediate medical attention (by calling 9-1-1) is essential to prevent stroke related disability or death.

Doctors may also treat ischemic stroke with other medicines, such as blood thinners, as well as surgery to remove the clot.

### Ischemic Stroke‎

Most strokes are ischemic strokes. An ischemic stroke occurs when blood clots or other particles block the blood vessels to the brain.

Fatty deposits called plaque can also build up in the blood vessels causing blockages.

### **Treating hemorrhagic stroke**

Other medicines, surgery, or procedures may be needed to stop the bleeding from hemorrhagic stroke and save brain tissue. For example:

* **Endovascular procedures.**Endovascular procedures, which can help repair a weak spot or break in a blood vessel, may be used to treat certain hemorrhagic strokes.
* **Surgical treatment.** Hemorrhagic strokes may be treated with surgery. If the bleeding is caused by a ruptured aneurysm, a metal clip may be put in place to stop the blood loss.

### Hemorrhagic Stroke‎

A hemorrhagic stroke happens when an artery in the brain leaks blood or ruptures (breaks open). The leaked blood puts too much pressure on brain cells, which damages them.

High blood pressure and aneurysms—balloon-like bulges in an artery that can stretch and burst—are examples of conditions that can cause a hemorrhagic stroke.

### **What happens after stroke treatment?**

If you have had a stroke, you are at high risk for another stroke.

* 1 in 4 stroke survivors has another stroke within 5 years.[5](https://www.cdc.gov/stroke/treatment/index.html#cdcreference_5)
* The risk of stroke within 90 days of a transient ischemic attack (TIA) may be as high as 17%, with the greatest risk during the first week.[6](https://www.cdc.gov/stroke/treatment/index.html#cdcreference_6)

Your doctor may give you medications or tell you to change your diet, exercise, or adopt other healthy lifestyle habits. Surgery may also be helpful in some cases. That's why it's important to treat the underlying causes of stroke.

## Prevention

If you have had a stroke, you are at high risk for another stroke. That's why it's important to treat the causes of stroke, including

* Heart disease.
* High blood pressure.
* Atrial fibrillation (fast, irregular heartbeat).
* High cholesterol.
* Diabetes.

You and your health care team can work together to prevent or treat the medical conditions that lead to stroke. Discuss your treatment plan regularly and bring a list of questions to your appointments. Your treatment plan will include medicine or surgery and lifestyle changes to lower your risk for another stroke. Be sure to take your medicine as directed and follow your doctor's instructions.

## Recovery

### **Recovering from stroke: stroke rehabilitation**

Rehabilitation after a stroke begins in the hospital, often within a day or 2 after the stroke. Rehab helps ease the transition from hospital to home and can help prevent another stroke.

Recovery time after a stroke is different for everyone—it can take weeks, months, or even years. Some people recover fully, but others have long-term or lifelong disabilities.

### **What to expect after a stroke**

If you have had a stroke, you can make great progress in regaining your independence. However, some problems may continue:

* Paralysis (inability to move some parts of the body), weakness, or both on one side of the body.
* Trouble with thinking, awareness, attention, learning, judgment, and memory.
* Problems understanding or forming speech.
* Trouble controlling or expressing emotions.
* Numbness or strange sensations.
* Pain in the hands and feet that worsens with movement and temperature changes.
* Trouble with chewing and swallowing.
* Problems with bladder and bowel control.
* Depression.

You and your health care team can discuss what to expect after a stroke. Your health care team will work with you to prevent further strokes.

### **What is stroke rehabilitation?**

Rehab can include working with speech, physical, and occupational therapists.

* Speech therapy helps people who have problems producing or understanding speech.
* Physical therapy uses exercises to help you relearn movement and coordination skills you may have lost because of the stroke.
* Occupational therapy focuses on improving daily activities, such as eating, drinking, dressing, bathing, reading, and writing.

Therapy and medicine may help with depression or other mental health conditions following a stroke. Joining a patient support group may help you adjust to life after a stroke. Talk with your health care team about local support groups, or check with an area medical center.

Support from family and friends can also help relieve fear and anxiety following a stroke. Let your loved ones know how you feel and what they can do to help you.

Source:

Centers for Disease Control and Prevention. (2024) *Stroke Treatment*. Available at: https://www.cdc.gov/stroke/treatment/index.html (Accessed: 23 May 2025).

MOVEMENT DISORDERS

MYOCLONUS

## **What Is Myoclonus?**

Myoclonus (pronounced "my-OCK-lo-nus") is a sudden muscle spasm that you can’t control. It can be a natural reflex – like jumping when something scares you or getting the hiccups from laughing too hard. But sometimes, it can be a sign of a nervous system condition such as multiple sclerosis, dementia, or Parkinson's disease.

Myoclonus can include sudden jerking, quivering, or twitching. You can have one episode or many in a row. And it can be over in seconds or last up to a few minutes.

## **Types of Myoclonus**

The different kinds of myoclonus include:

**Physiological myoclonus**

This type happens in people with no other health problems. Hiccups are one example. Another are twitches when you’re startled.

**Sleep myoclonus**

As you fall asleep, your muscles, especially in your legs, can twitch. You might also feel like you're falling and trying to catch yourself. Also known as hypnic jerks, these are considered a normal type of myoclonus. They're usually not a cause for concern as long as they don't happen often or interfere with your sleep.

You might notice that hypnic jerks happen more often when you're feeling stressed.

**Essential myoclonus**

If you have this kind, twitches or jerks are the only sign. They usually don't become more severe over time. Sometimes, essential myoclonus runs in families.

**Symptomatic (secondary) myoclonus**

Sometimes, myoclonus is caused by another health condition, such as an infection, a stroke, or a brain tumor. It can also be caused because of a prescription drug or other substance, like alcohol or cocaine, that's in your system.

**Stimulus-sensitive myoclonus**

Sometimes, sudden muscle spasms can be triggered by things in the world around you like lights, noise, or movement. Feeling surprised might make this type of myoclonus more likely.

**Cortical reflex myoclonus**

Doctors think this is a kind of epilepsy. If you have it, you're prone to sudden jerk-like movements in your upper limbs and face.

**Palatal myoclonus**

This is a tremor in the roof or soft palate of your mouth. It may involve your face, tongue, diaphragm, and throat. These muscle twitches come fast. You could have as many as 150 in a minute. Bursts of movement can happen while you sleep. You might hear a clicking sound in your ear when they do.

**Reticular reflex myoclonus**

Experts know that this type of myoclonus starts in your brainstem, the part of your brain that controls functions like breathing and your heart rate. Twitching or jerking throughout your whole body is common, but only part of your body could also be affected. Reticular reflex myoclonus is very rare but can interfere with your quality of life.

**Brainstem myoclonus**

This is a broad term that includes both reticular myoclonus and the natural startle response, which puts your body in a defense position when you're surprised. When you're startled, you might not even realize that you're making a face, flexing your knees, or pulling back your arms, but this is a common human reaction. A main feature of brainstem myoclonus is that you're very sensitive to sound.

**Epileptic myoclonus**

If you live with a seizure disorder, muscle spasms can be one symptom or the only symptom you have during a seizure. There are different types of myoclonic seizures. For instance, juvenile myoclonic epilepsy (JME) usually affects your neck, shoulders, or upper arms.

**Progressive myoclonus epilepsy (PME)**

A kind of epileptic myoclonus, this is a group of rare disorders that usually start in kids and teens. The symptoms tend to get more intense over time.

**Action myoclonus**

One of the most severe types of myoclonus, it can affect your arms, legs, and the muscles in your face. Action myoclonus is triggered by movement and could become more severe at times, especially when you're trying to move very precisely and carefully.

## **Myoclonus Symptoms**

Myoclonus spasms aren't easy to define because they vary so much from one person to another. Generally speaking, they:

* Happen without warning
* Don't last long
* Aren't movements that you're able to control
* May feel like little electric shocks
* Can be mild or intense
* Can happen very often or every once in a while
* Can affect one small part of your body or all over
* Are sometimes severe enough to get in the way of daily functions like eating, speaking, or walking

Your muscles can flex or tighten, which is called **positive myoclonus.**

Or they can relax and go limp, which is known as **negative myoclonus.**

Many people have both positive and negative myoclonus.

## **Myoclonus Causes**

Myoclonus often happens because your nervous system isn't working the way it should. Various things, such as neurological disorders, genetic conditions, brain injuries, and exposure to toxins, can cause your nerve cells to misfire and send wrong signals to some of your muscles.

Doctors are aware that several parts of your brain are involved. But more research needs to be done to pinpoint what happens, or doesn't happen, to cause myoclonus. An imbalance of brain chemicals may make the regions of your brain that control movement more active than they need to be. But other times, there's no clear cause.

If you have multiple sclerosis (MS), myoclonus could be due to lesions on your brain or spinal cord.

Other nervous system conditions that can cause myoclonus include:

* Stroke
* Brain tumor
* Alzheimer’s disease
* Parkinson’s disease
* Lewy body dementia
* Creutzfeldt-Jakob disease (CJD)

Sometimes, the cause is a medical condition, such as:

* Autoimmune conditions
* Vitamin or mineral deficiency
* High or low blood sugar
* Genetic disorder you inherited from your parents
* Head or spinal cord injury
* Viral or bacterial infection, like Lyme disease
* Kidney or liver issues
* Stroke or heart attack that keeps your brain from getting oxygen

Both prescribed and recreational drugs can also cause myoclonus. Among the kinds known to do this are:

* Blood pressure medications
* Antibiotics
* Antidepressants
* Anti-seizure drugs
* Surgical anesthetics
* Opioids
* Alcohol
* Cocaine
* Ecstasy
* Heroin
* Amphetamines

## **Myoclonus Diagnosis**

A muscle spasm or twitch every now and then usually isn't a cause for concern. But if your symptoms are frequent or making it a challenge to do things you need or like to do, it's important to see your doctor.

To try to figure out the cause, they'll ask you questions about your health history and which parts of your body have spasms. You might write down some information ahead of time and bring it to your appointment. For instance, it can be helpful for your doctor to know:

* When you first started having spasms
* How often you have them
* How severe your symptoms are
* If you've noticed anything that makes the spasms better or worse

To get more information, your doctor may suggest tests like:

* **Urine and blood tests.**Lab work will provide a general view of your health and can check for conditions like diabetes, kidney disease, or autoimmune disorders.
* **Electroencephalogram (EEG).** This painlessly tracks and records the patterns of electrical activity in your brain to figure out where the myoclonus starts. The doctor will put small discs (called electrodes) on your scalp. They’ll connect them to wires that send signals to a computer.
* **Electromyography (EMG).** This test checks the health of your muscles and the nerve cells that control them. It uses electrodes to sense and record the signals your nerves send to your muscles.
* **Magnetic resonance imaging (MRI).** Your doctor can use this test to get detailed pictures of your brain, spinal cord, and other body parts that might be involved..

## **Myoclonus Treatment**

If another health condition is causing your spasms, your doctor will try to treat it. If it can't be cured, then your doctor will work on lessening your symptoms.

Because so many conditions can cause myoclonus, the treatments vary. Depending on your case, you may need to take several medicines at the same time. They may act on different parts of your brain.

There are no specific myoclonus drugs. But many types of medicines have been found to reduce how often you have spasms and how severe they are. They include:

* **Benzodiazepines.** Clonazepam (Klonopin) is often the first drug doctors use. It relaxes your muscles to keep them from twitching. Common side effects include feeling sleepy and being a bit clumsy. Because of that, your doctor will probably start with a very small dose. They can increase the amount as needed until your symptoms go away.
* **Anti-seizure drugs.** Medicines like levetiracetam (Keppra), primidone (Mysoline), and valproic acid (Valproic) help prevent seizures in people with epilepsy. But they can also help with myoclonus. Side effects include nausea, fatigue, and feeling dizzy.
* **5-hydroxytryptophan (5-HTP).** This is a building block of serotonin, an important neurotransmitter. Some studies have found that 5-HTP helps people with certain forms of myoclonus.
* **Botox shots.** Botulinum toxin "freezes" your muscles and keeps them from twitching. These shots can be helpful if you have frequent spasms on one side of your face.
* **Surgery.** If a brain or spinal cord lesion is causing your symptoms, your doctor may suggest a procedure to remove it.
* **Deep brain stimulation (DBS).** In this surgery, your doctor puts electrodes into your brain and uses wire to connect them with a device implanted in your chest. The device sends out signals that block the ones causing your myoclonus. DBS can lower the number of muscle twitches, but as with all surgeries, there are risks. Doctors are researching its use for multiple sclerosis. Right now, it’s mostly used as a treatment for Parkinson’s disease.

Experts continue to look for new ways to treat myoclonus. Clinical trials are large research studies that rely on volunteers to understand if new treatments work well enough to be available to the general public. If you're interested in being part of one, talk to your doctor about how to apply.

## **Myoclonus Outlook**

Ideally, your doctor will be able to treat the condition that's causing your symptoms. But if not, they can work with you to ease your spasms. Because myoclonus is so complex, it's not uncommon to try more than one treatment or need to see different types of doctors.

## **Myoclonus Injury Prevention**

There’s no way to prevent myoclonus. But you can try to reduce your chances of getting hurt when a severe spasm happens. To do that:

**Get specialized support**. For instance, a neuropsychiatrist can help you spot triggers and learn to manage movement issues. Working with a physical therapist can improve your balance, strength, and coordination.

**Protect yourself.**Wear protective gear so you don't risk further damage to your nervous system or brain. For instance, always wear a seat belt when you're in a car. And wear a helmet to protect your head when you're riding a bike or playing contact sports.

**Follow your doctor's advice**. If you live with another health issue, do your best to manage it. Take any medication as prescribed and see your doctor regularly.

Source

Booth, S. (2024) *Myoclonus: Types, Causes, Symptoms, and Treatment*. Available at: https://www.webmd.com/multiple-sclerosis/myoclonus-muscle-twitching (Accessed: 5 June 2025).

RESTLESS LEG SYNDROME

## **Overview**

Restless legs syndrome (RLS) is a condition that causes a very strong urge to move the legs. The urge to move usually is caused by an uncomfortable feeling in the legs. It typically happens in the evening or at night when sitting or lying down. Moving eases the discomfort for a short time.

Restless legs syndrome can begin at any age and tends to get worse with age. It can disrupt sleep, which interferes with daily activities. RLS also is known as Willis-Ekbom disease.

Simple self-care steps and lifestyle changes may help relieve symptoms. Medicines also help many people with RLS.

## **Symptoms**

The chief symptom of restless legs syndrome is an urge to move the legs. It's common to experience:

* **Uncomfortable sensations that begin while resting.** A feeling in the legs typically begins after you've been lying down or sitting for an extended time. It might happen while sitting in a car, airplane or movie theater.
* **Relief with movement.** The sensation of RLS lessens with movement. Stretching, jiggling the legs, pacing or walking may improve symptoms.
* **Worsening of symptoms in the evening.** Symptoms occur mainly at night.
* **Nighttime leg twitching.** RLS may be associated with another, more common condition called periodic limb movement of sleep. This condition causes the legs to twitch and kick during sleep, possibly throughout the night.

People typically describe RLS symptoms as compelling, unpleasant feelings in the legs or feet. They usually happen on both sides of the body. Less commonly, the sensations affect the arms.

The sensations are felt within the leg rather than on the skin. They're described as:

* Crawling.
* Creeping.
* Pulling.
* Throbbing.
* Aching.
* Itching.
* Electric.

Sometimes the feelings of RLS are hard to explain. People with RLS usually don't describe the condition as a muscle cramp or numbness. They do, however, consistently describe the desire to move the legs.

It's common for symptoms to get better and worse. Sometimes symptoms disappear for periods of time, then come back.

### When to see a doctor

Talk with your healthcare professional if you have symptoms of restless legs syndrome. RLS can interfere with your sleep, cause daytime drowsiness and affect your quality of life.

## **Causes**

Often, there's no known cause for restless legs syndrome. Researchers suspect the condition may be caused by an imbalance of the brain chemical dopamine. Dopamine sends messages to control muscle movement.

### Heredity

Sometimes RLS runs in families, especially if the condition starts before age 40. Researchers have identified sites on the chromosomes where genes for RLS may be present.

### Pregnancy

Pregnancy or hormonal changes may worsen RLS symptoms. Some people get RLS for the first time during pregnancy, especially during the last trimester. However, symptoms usually disappear after delivery.

## **Risk factors**

Restless legs syndrome can develop at any age, even during childhood. The condition is more common with increasing age. It's also more common in women than in men.

RLS usually isn't related to a serious underlying medical condition. However, it sometimes occurs with other conditions, such as:

* **Peripheral neuropathy.** This damage to the nerves in the hands and feet is sometimes due to chronic diseases such as diabetes and alcohol use disorder.
* **Iron deficiency.** Too little iron in the body, known as iron deficiency, can cause or worsen RLS. People who have a history of bleeding from the stomach or bowels may have iron deficiency. Deficiency also may affect people who have heavy menstrual periods or who often donate blood.
* **Kidney failure.** If you have kidney failure, you also may have iron deficiency, often with anemia. When kidneys don't function properly, iron stores in the blood can decrease. This and other changes in body chemistry may cause or worsen RLS.
* **Spinal cord conditions.** Damage to or injury of the spinal cord has been linked to RLS.
* **Parkinson's disease.** People who have Parkinson's disease may have an increased risk of developing RLS.

## **Complications**

Restless legs syndrome symptoms can range from being mild to having a serious impact on people's lives. Many people with RLS find it hard to fall or stay asleep.

Serious symptoms of RLS can affect quality of life and result in depression. Not being able to sleep may lead to excessive daytime drowsiness, but RLS may interfere with napping.

## **Diagnosis**

To diagnose restless legs syndrome, your healthcare professional takes your medical history and asks about your symptoms. A diagnosis of RLS is based on the following criteria, established by the International Restless Legs Syndrome Study Group:

* You have a strong, often irresistible urge to move the legs. This usually occurs with uncomfortable feelings in the legs.
* Your symptoms start or get worse when you're resting, such as sitting or lying down.
* Your symptoms are partially or temporarily relieved by activity, such as walking or stretching.
* Your symptoms are worse at night.
* Symptoms can't be explained solely by another medical or behavioral condition.

Your healthcare professional may conduct a physical and a neurological exam. Blood tests, particularly for iron deficiency, may be ordered to rule out other possible causes of your symptoms.

You may be referred to a sleep specialist. This may involve an overnight stay and a study at a sleep clinic if another sleep condition such as sleep apnea is suspected. However, a diagnosis of RLS usually doesn't require a sleep study.

### Care at Mayo Clinic

[Our caring team of Mayo Clinic experts can help you with your restless legs syndrome-related health concernsStart Here](https://www.mayoclinic.org/diseases-conditions/restless-legs-syndrome/care-at-mayo-clinic/mac-20377180)

## **Treatment**

Symptoms of restless legs syndrome sometimes go away after treating an underlying condition, such as iron deficiency. Correcting an iron deficiency may involve taking an iron supplement by mouth. Or you may be given an iron supplement through a vein in your arm. Take iron supplements only with medical supervision and after having your blood-iron level checked.

Electrical stimulation of a nerve on the side of your knee may help RLS symptoms. Devices for electrical stimulation require a prescription from a healthcare professional.

If you have RLS without an associated condition, treatment focuses on lifestyle changes. If those aren't effective, your healthcare professional may prescribe medicines.

### Medications

Several prescription medicines are available to reduce the restlessness in the legs. Many of the medicines were developed to treat other diseases, but they may help with RLS. They include:

* **Medicines affecting calcium channels.** Medicines such as gabapentin, gabapentin enacarbil and pregabalin are the first line of treatment for most people with RLS. These medicines can cause side effects such as dizziness, unsteadiness, mental fog and weight gain.
* **Medicines that increase dopamine in the brain.** These medicines affect levels of the chemical messenger dopamine in the brain. Rotigotine, pramipexole and ropinirole work at first. But in many people taking these medicines, RLS gets worse over time. The medicines may cause symptoms to return earlier in the day. Some people taking these medicines find that symptoms spread to the arms. This is called augmentation. The medicines also can make it hard to manage impulses, such as compulsive gambling. Because of these risks, dopamine drugs are only used if medicines affecting calcium channels don't work or cause side effects.

People who have occasional RLS symptoms may be prescribed carbidopa-levodopa (Duopa, Rytary, others) to take as needed. But healthcare professionals don't recommend taking this medicine daily or near daily. Daily use of this medicine can cause augmentation.

* **Opioids.** These medicines are used in low doses to treat RLS when other medicines haven't worked or have caused side effects. Most people taking opioids don't have major side effects, and these medicines are effective in managing RLS symptoms. In low doses, addiction is very rare. Some examples of opioids include oxycodone, hydrocodone and buprenorphine.

It may take several trials to find the right medicine or combination of medicines that work best for you.

And some medicines for other conditions may worsen symptoms of RLS. These include some antidepressants, some antipsychotic medicines, some antinausea medicines, and some cold and allergy medicines. Your healthcare professional may recommend that you don't take these medicines, if possible. However, if you need to take them, talk about treatments to help manage RLS.

Most medicines prescribed to treat RLS aren't recommended during pregnancy. Instead, self-care techniques and iron supplements may be recommended to relieve symptoms. But if symptoms are bothersome during your last trimester, your healthcare professional may recommend the use of certain medicines.

## **Lifestyle and home remedies**

Making simple lifestyle changes can help alleviate symptoms of restless legs syndrome:

* **Try baths and massages.** Soaking in a warm bath and massaging the legs can relax the muscles.
* **Apply warm or cool packs.** Use of heat or cold, or alternating use of the two, may lessen the leg sensations.
* **Establish good sleep hygiene.** Fatigue tends to worsen symptoms of RLS, so it's important that you practice good sleep hygiene. Create a cool, quiet, comfortable sleeping environment. Go to bed and rise at the same time daily. Get at least seven hours of sleep nightly.
* **Exercise.** Moderate, regular exercise may relieve symptoms of RLS. But overdoing it or working out too late in the day may make symptoms worse.
* **Avoid caffeine.** Sometimes cutting back on caffeine may help restless legs. Try to avoid caffeine-containing products for a few weeks to see if this helps. This includes cutting out chocolate, coffee, tea and soda.
* **Consider using a foot wrap or a vibrating pad.** A foot wrap specially designed for people with RLS puts pressure under the foot and may help relieve your symptoms. You also may find relief using a pad that vibrates on the back of the legs.

## **Coping and support**

Restless legs syndrome is most often a lifelong condition. It may help you to develop coping strategies that work for you, such as:

* **Tell others about your condition.** Sharing information about RLS helps your family, friends and coworkers better understand what you're going through. It can help explain why you might pace the halls or stand at the back of the theater. It may help coworkers better understand if they see you walk to the water cooler many times during the day.
* **Don't resist your need for movement.** If you attempt to suppress the urge to move, you may find that your symptoms worsen.
* **Keep a sleep diary.** Keep track of the medicines and strategies that help symptoms. Also note what makes symptoms worse. Share this information with your healthcare professional.
* **Stretch and massage.** Begin and end your day with stretching exercises or gentle massage.
* **Seek help.** Support groups bring together family members and people with RLS. By participating in a group, your insights not only can help you but also may help someone else.

## **Preparing for your appointment**

If you have symptoms of restless legs syndrome, make an appointment with your healthcare professional. You may be referred to a doctor who specializes in conditions affecting the nervous system, known as a neurologist, or a sleep specialist.

Here's some information to help you get ready for your appointment.

### What you can do

* **Write down your symptoms,** including when they started and when they tend to occur.
* **Write down key medical information,** including other conditions you have. Also include medicines you take, including prescription, those you get without a prescription, vitamins and supplements. And note whether there's a history of RLS in your family.
* **Take a family member or friend along.** Someone who accompanies you may remember information you missed or forgot.
* **Write down questions to ask.**

Some basic questions to ask about RLS include:

* What is the most likely cause of my symptoms?
* Are there other possible causes?
* What tests do I need?
* What treatment options are available for this condition?
* I have other health conditions. How can I best manage them together?
* What self-care steps might improve my symptoms?
* Do you have educational materials I can have? What websites do you recommend?
* Where can I find a support group for people with RLS?

### What to expect from your doctor

Your healthcare professional is likely to ask you a number of questions, including:

* Do you get an irresistible urge to move your legs?
* What words describe your symptoms?
* Do your symptoms start while you're sitting or lying down?
* Are your symptoms worse at night?
* Does movement make you feel better?
* Have you been told that you kick, shake or otherwise move your legs while sleeping?
* Do you often have trouble falling or staying asleep?
* Are you tired during the day?
* Does anyone else in your family have restless legs?
* How much caffeine do you have daily?
* What is your typical exercise program?
* Are you at risk of low iron due to limiting meat in your diet, donating blood frequently or blood loss from a recent surgery?
* What medicines have you used for RLS? Did they work?

### What you can do in the meantime

To ease your symptoms, try:

* Cutting back on or eliminating caffeine, alcohol and tobacco.
* Massaging your legs while soaking in a warm bath.

Source

Mayo Clinic Staff (2025) *Restless legs syndrome - Diagnosis and treatment*. Available at: https://www.mayoclinic.org/diseases-conditions/restless-legs-syndrome/diagnosis-treatment/drc-20377174 (Accessed: 5 June 2025).

TREMOR

## **Overview**

Essential tremor is a nervous system condition, also known as a neurological condition. It causes rhythmic shaking that you can't control. Essential tremor can affect almost any part of the body, but the trembling happens most often in the hands. The trembling occurs especially when doing simple tasks, such as drinking from a glass or tying shoelaces.

Essential tremor usually is not a dangerous condition. However, it typically worsens over time and can be severe for some people. Other conditions don't cause essential tremor, but essential tremor sometimes is confused with Parkinson's disease.

Essential tremor can happen at any age but is most common in people age 40 and older.

## **Symptoms**

Essential tremor symptoms:

* Begin gradually. They usually are more noticeable on one side of the body.
* Worsen with movement.
* Usually happen in the hands first, affecting one hand or both hands.
* Can include a "yes-yes" or "no-no" double nodding or shaking motion of the head.
* May worsen with emotional stress, fatigue, caffeine or extreme temperatures.

### Essential tremor vs. Parkinson's disease

Many people link tremors with Parkinson's disease. But the two conditions differ in important ways, including:

* **Timing of tremors.** Essential tremor of the hands usually happens when using the hands. Tremors from Parkinson's disease are most noticeable when the hands are resting at the sides of the body or in the lap.
* **Related conditions.** Essential tremor doesn't cause other health problems. However, people with essential tremor sometimes develop other neurological symptoms, such as an unsteady walk. Parkinson's disease is linked to stooped posture, slow movement and dragging the feet when walking.
* **Parts of the body affected.** Essential tremor mainly involves the hands, head and voice. Parkinson's disease tremors usually start in the hands and can affect the legs, chin and other parts of the body.

**Causes**

About half the people with essential tremor appear to have an altered gene. This form of the condition is referred to as familial tremor. It isn't clear what causes essential tremor in people who don't have familial tremor.

**Risk factors**

Known risk factors for essential tremor include:

* **Altered gene.** The inherited variety of essential tremor, known as familial tremor, is an autosomal dominant disorder. That means an altered gene from just one parent is needed to pass on the condition.

Anyone who has a parent with an altered gene for essential tremor has a 50% chance of developing the condition.

* **Age.** Essential tremor is more common in people age 40 and older.

**Complications**

Essential tremor isn't life-threatening, but symptoms often worsen over time. If the tremors become severe, it might be difficult to:

* Hold a cup or glass without spilling.
* Eat without shaking.
* Put on makeup or shave.
* Talk, if the voice box or tongue is affected.
* Write legibly.

**Prevention**

There is no known way to prevent essential tremor.

## **Diagnosis**

Diagnosing essential tremor involves a review of your medical history, family history and symptoms, and a physical examination.

There are no medical tests to diagnose essential tremor. Diagnosing it is often a matter of ruling out other conditions that could be causing symptoms. To do this, your healthcare professional may suggest the following tests.

### Neurological exam

In a neurological exam, your healthcare professional tests how well your nervous system is working. This may include checking your:

* Tendon reflexes.
* Muscle strength and tone.
* Ability to feel certain sensations.
* Posture and coordination.
* Walk and balance.

### Lab tests

Blood and urine may be tested for several factors, including:

* Thyroid disease.
* Metabolic problems.
* Medicine side effects.
* Levels of chemicals that may cause tremor.

### Performance tests

### To evaluate the tremor itself, your healthcare professional may ask you to:

* Drink from a glass.
* Hold your arms outstretched.
* Write.
* Draw a spiral.

A healthcare professional who still is not sure if a tremor is essential tremor or Parkinson's disease might order a dopamine transporter scan. This is a special imaging test that uses an injected medicine to show where the chemical dopamine is found in the brain. It can help the healthcare professional tell the difference between the two types of tremors.

## **Treatment**

Some people with essential tremor don't require treatment if their symptoms are mild. But if your essential tremor is making it difficult to work or perform daily activities, discuss treatment options with your healthcare professional.

Treatment options may include:

### Medicines

* **Beta blockers.** Typically used to treat high blood pressure, beta blockers such as propranolol (Inderal LA, InnoPran XL, Hemangeol) help relieve tremors in some people. Beta blockers may not be an option for people with asthma or certain heart problems. Side effects may include fatigue, lightheadedness or heart problems.
* **Anti-seizure medicines.** Primidone (Mysoline) may be effective in people who don't respond to beta blockers. Other medicines that might be prescribed include gabapentin (Gralise, Neurontin, Horizant) and topiramate (Topamax, Qudexy XR, others). Side effects include drowsiness and nausea, which usually disappear within a short time.
* **Tranquilizers.** Healthcare professionals may use benzodiazepines such as clonazepam (Klonopin) to treat people whose tremors worsen with tension or anxiety. Side effects can include fatigue or mild sedation. These medicines should be used with caution because they can be habit-forming.
* **Nerve-blocking injections.** Injections with onabotulinumtoxinA, also known as Botox, might be useful in treating some types of tremors, especially head and voice tremors. Botox injections can improve tremors for up to three months at a time.

However, if Botox is used to treat hand tremors, it can cause weakness in the fingers. If Botox is used to treat voice tremors, it can cause a hoarse voice and difficulty swallowing.

### Therapy

Healthcare professionals might suggest physical or occupational therapy. Physical therapists can teach you exercises to improve your muscle strength, control and coordination.

Occupational therapists can help you adapt to living with essential tremor. Therapists might suggest adaptive devices to reduce the effect of tremors on your daily activities. These devices may include:

* Heavier glasses and utensils.
* Wrist weights.
* Wider, heavier writing tools, such as wide-grip pens.

### Nerve stimulation devices

A wearable electronic peripheral nerve stimulation device (Cala Trio, Cala kIQ) is a newer treatment option for people with essential tremor. The device is worn as a wristband for 40 minutes twice a day. It works by stimulating nerves and muscles to create a muscle response that reduces tremors. Studies have found that the device can bring some improvement for tremors.

### Surgery

**Deep brain stimulation**

Surgery might be an option if your tremors are severely disabling and you don't respond to medicines.

* **Deep brain stimulation.** This is the most common type of surgery for essential tremor. It involves putting a long, thin electrical probe into the part of the brain that causes the tremors, known as the thalamus. A wire from the probe runs under the skin to a device called a neurostimulator that's placed under the skin in the chest. This device sends painless electrical pulses to interrupt signals from the thalamus that may be causing the tremors.

Side effects of deep brain stimulation can include equipment malfunction and problems with motor control, speech or balance. Headaches and weakness also may be side effects. After some time or adjustment of the device, side effects often go away.

* **Focused ultrasound thalamotomy.** This noninvasive surgery involves using focused sound waves that travel through the skin and skull. The waves generate heat to destroy brain tissue in a specific area of the thalamus to stop a tremor. A surgeon uses MRI to target the correct area of the brain and to be sure the sound waves are generating the exact amount of heat needed for the procedure.

Focused ultrasound thalamotomy is done on one side of the brain. The surgery affects the other side of the body from the one where it's done.

Focused ultrasound thalamotomy creates a lesion that can result in permanent changes to brain function. Some people have experienced altered sensation, trouble with walking or difficulty with movement. However, most complications go away on their own or are mild enough that they don't interfere with quality of life.

## **Lifestyle and home remedies**

To reduce or relieve tremors:

* **Avoid caffeine.** Caffeine and other stimulants can increase tremors.
* **Use alcohol sparingly, if at all.** Some people notice that their tremors improve slightly after they drink alcohol, but drinking isn't a good solution. Tremors tend to worsen once the effects of alcohol wear off. Also, more alcohol eventually is needed to relieve tremors, which can lead to alcohol use disorder.
* **Learn to relax.** Stress and anxiety tend to make tremors worse. Being relaxed may improve tremors. You can't rid your life of all stress. But you can change how you react to stressful situations using a range of relaxation techniques, such as massage or meditation.
* **Make lifestyle changes.** Use the hand that is less affected by tremor more often. Find ways to avoid writing, such as using online banking and debit cards instead of writing checks. Try voice-activated commands on your smartphone and speech-recognition software on your computer.

## **Coping and support**

For many people, essential tremor can have serious social and psychological consequences. If the effects of essential tremor make it difficult to live your life as fully as you once did, consider joining a support group.

Support groups aren't for everyone, but you might find it helpful to have the encouragement of people who understand what you're going through. Or see a counselor or social worker who can help you meet the challenges of living with essential tremor.

## **Preparing for your appointment**

You'll likely start by seeing your primary healthcare professional. Or you might be referred to a doctor trained in brain and nervous system conditions, called a neurologist.

Here's some information to help you get ready for your appointment.

### What you can do

* **Be aware of anything you need to do ahead of time.** At the time you make the appointment, ask if there's anything you need to do in advance, such as restrict your diet.
* **Write down symptoms you have,** including any that may not seem related to the reason you scheduled the appointment.
* **Write down important personal information,** including major stresses or recent life changes.
* **Make a list of all medicines, vitamins and supplements** you're taking and the doses.
* **Take a family member or friend along.** Sometimes it can be hard to remember all the information provided during an appointment. Someone who goes with you may remember something that you missed or forgot.
* **Write down questions to ask** your healthcare team.

Your time with your healthcare team is limited, so preparing a list of questions can help you make the most of your time together. List your questions from most important to least important in case time runs out. For essential tremor, some basic questions to ask include:

* What's the most likely cause of my symptoms?
* Are there other possible causes?
* What tests do I need?
* How does essential tremor usually progress?
* What treatments are available, and which do you recommend?
* I have other health conditions. How can I best manage these conditions together?
* Are there restrictions I need to follow?
* Should I see a specialist? If so, whom do you recommend?
* Are there brochures or other printed materials I can have? What websites do you recommend?

Don't hesitate to ask other questions.

### What to expect from your doctor

Be prepared to answer questions, such as:

* When did your symptoms begin?
* Do you have a family history of tremor?
* Have you ever had a head injury?
* What parts of your body are affected?
* Does anything make your tremors better or worse?

Source:

Mayo Clinic Staff. (2023) *Essential tremor: Diagnosis and treatment*. Mayo Clinic. Available at: https://www.mayoclinic.org/diseases-conditions/essential-tremor/diagnosis-treatment/drc-20350539 (Accessed: 23 May 2025).

**Dystonia**

Dystonia is defined by involuntary maintained contraction of agonist and antagonist muscles yielding abnormal posturing, twisting and repetitive movements, or tremulous and can be initiated or worsened by attempted movement. Dystonia is a dynamic disorder that changes in severity based on the activity and posture. This activity describes the causes, pathophysiology, presentation, and possible treatments of dystonia and highlights the role of the interprofessional team in its management.

**Objectives:**

* Identify the potential causes of dystonia.
* Describe the presentation of dystonia, as well as the findings expected on examination and evaluation.
* Summarize the treatment options available for dystonia.
* Review the importance of improving care coordination among interprofessional team members to improve outcomes for patients affected by dystonia

[.](https://www.statpearls.com/account/trialuserreg/?articleid=20812&utm_source=pubmed&utm_campaign=reviews&utm_content=20812)

**Introduction**

Dystonia is defined by involuntary maintained contraction of agonist and antagonist muscles yielding abnormal posturing, twisting and repetitive movements, or tremulous and can be initiated or worsened by attempted movement.

Dystonia is a dynamic disorder that changes in severity based on the activity and posture. Dystonia may assume a pattern of overextension or over-flexion of the hand, inversion of the foot, lateral flexion or retroflection of the head, torsion of the spine with arching and twisting of the back, forceful closure of the eyes, or a fixed grimace. It may come to an end when the body is in action and during sleep.

Dystonia may vary greatly in severity and may show obvious fluctuations in individual patients. Severe cases result in grotesque and distorted movements. The degree of severity is variable.

It is frequently unrecognized or misdiagnosed because of its variable course and abundant expression.

Usually, people with dystonia can live a relatively normal lifestyle, while others need assistance with all activities of daily living.

Etiology

Dystonia is a heterogeneous entity with diverse etiology and clinical presentation. One of the most useful classifications of dystonia is by etiology: primary and secondary dystonia.

In primary dystonia (familial or sporadic, also called idiopathic torsion dystonia), dystonia is the sole neurologic sign (with exception of the tremor) and other causes of dystonia such as acquired or neurodegenerative processes have been ruled out.

Primary dystonia is further classified into early-onset and adult-onset forms.

Primary dystonia is thought to have a greater genetic contribution, even in the absence of a family history of dystonia. The precise cause of primary dystonia is unknown. There is some genetic susceptibility in conjunction with environmental factors.

Early-onset primary dystonia typically initially affects an extremity and then spreads, in many occurrences becoming generalized. DYT 1 and DYT 6 are the two genes that are responsible for early onset of primary dystonia.

As far as adult-onset dystonia usually involves either cervical, cranial, or brachial muscles, or remains focal or segmental. Worth mentioning that cervical dystonia is the most common form and at the same time is more common than early-onset primary dystonia.

Secondary dystonias are caused by the environmental insult and are brought in by some identified causes, such as head injury, drug side effects (e.g., tardive dyskinesia) or neurological disease (e.g., Wilson disease).

An intermediary category is termed ‘dystonia plus syndromes,’ and consists of disorders in which there is no acquired etiology or neurodegeneration, but in which there are neurologic symptoms other than dystonia. This category includes dopa-responsive dystonia (DRD/DYT5), myoclonus dystonia (MD/DYT11) and rapid-onset dystonia-parkinsonism (RDP/DYT12).

Medications associated with dystonia:

* Antipsychotics
* Metoclopramide
* Antiepileptics
* Dopamine agonists
* MAO inhibitors
* Amphetamines, cocaine
* Caffeine
* Antihistamines
* Beta-adrenergic agents
* Lithium
* Oral contraceptives
* Cimetidine

Epidemiology

Dystonia is the third most prevalent movement disorder, affecting approximately 500,000 adults and children in North America.

After Parkinson, dystonia is the most common movement disorder encountered in movement disorder clinics.

Pathophysiology

The principal cause of dystonia has been thought to be dysfunction of the basal ganglia, which emerged from the concept of the basal ganglia as the brain region responsible for integrating motor control. Also, secondary dystonia is often due to lesions of the basal ganglia, specifically the putamen or globus pallidus.

However, the absence of neurodegeneration in primary dystonia, as well as observations that lesions of brain regions other than the basal ganglia can cause secondary dystonia, has guided to the idea that dystonia is a neuro-functional disorder, i.e. a disorder characterized by abnormal connectivity that may occur in a structurally normal-appearing brain.

Dystonia is considered to be a motor system disorder rather than a disease of a particular motor structure. Studies have provided evidence of dysfunction in almost every region of the central nervous system involved in motor control and sensorimotor integration, including cortex, brainstem, cerebellum, and spinal cord.

Although standard MRIs have not revealed structural pathology, diffusion tensor imaging (DTI) has shown subtle abnormalities in the sensorimotor circuitry of dystonia patients. In DYT 1 mutation carriers there is reduced functional anisotropy (FA) in a sub-gyral white matter of the primary sensorimotor cortex, pons and left superior cerebellar peduncle. Abnormal functional anisotropy has also been observed in the lentiform nucleus and the white matter adjacent to the nucleus in patients with focal dystonia.

Neurophysiological studies demonstrate a variety of changes consistent with abnormalities in inhibitory control, sensorimotor integration, and brain plasticity. The EMG in the dystonia show co-contraction of agonist and antagonist muscles with prolonged bursts and overflow to the muscles.

Dystonia is worsened by stress, fatigue, anxiety, or lack of sleep.

History and Physical

It is important to distinguish between idiopathic and symptomatic dystonia (due to another disease process).

Idiopathic dystonia may be inherited, often has an insidious onset, and may come into sight initially during the execution of a specific, repetitive, well-learned action. In contrast, symptomatic (secondary) dystonia occurs after a stroke, tumor, infection, hypoxia-ischemia, encephalitis, neurodegenerative disease (e.g., hepato-lenticular degeneration or Wilson's disease), and toxins.

The clinical examination in dystonia may exhibit involuntary writhing/twisting movements precipitated by specific voluntary movements, such as walking or writing. Focal task-specific limb dystonia can begin as painful hand cramping or involuntary wrist/finger spasms when writing, while torticollis presents as an uncontrollable head-turning when driving or watching television.

* Oro-mandibular dystonia can manifest as night-time bruxism (jaw spasms producing forceful jaw closure) and may follow dental procedures, oro-mandibular-facial trauma, or temporomandibular joint dysfunction.
* Spasmodic dysphonia can commence as a strained voice. Despite the name dystonia, the tone of affected extremities at rest is often normal at the onset. Deep tendon reflexes may also be normal.
* A tremor in a patient with dystonia (dystonic tremor) is sometimes distinguished from other tremor types by the presence of a null point (e.g., a neutral position at which tremor attenuates).
* In cervical dystonia, head tremor sometimes decreases with the head held in a specific position, and displacement from that position, such as turning the head to one side, may worsen it.
* Dystonic tremor may be nonuniform in amplitude and frequency, can be linked with myoclonus (jerk-like movements), and disappears in sleep. Dystonia may cause hypertrophy and pain in affected muscles such as the sternocleidomastoid in spasmodic torticollis.

In its early stages, it may be viewed as an annoying mannerism or hysteria, and only later due to unremitted postural abnormality, lack of the typical psychological characteristics of hysteria, and becoming an apparent feature of the illness, the correct diagnosis is made.

Dystonic movements tend to be exacerbated by fatigue, stress, and emotional states; they tend to be suppressed with relaxation, hypnosis, and sleep.

A characteristic and almost unique feature of dystonic movements is that they can abate by tactile or proprioceptive sensory tricks (geste antagoniste). For example, patients with cervical dystonia (torticollis) often place a hand on the chin or side of the face to diminish nuchal contractions, and oro-lingual dystonia is often relieved by touching the lips or placing an object in the mouth. Lying down may reduce truncal dystonia; walking backward or running may reduce leg dystonia.

Some dystonic movements last several seconds/minutes but others can last for weeks/months. This can lead to permanent bone deformity, contractures and impairment in function.

Evaluation

Evaluation and work up are based on the type of dystonia where clinical presentation remains the cornerstone of evaluation.

In primary dystonia, clinical evaluation and genetic testing (DYT1 and DYT6) can guide to the correct diagnosis. The gene at the DYT1 locus has been determined to serve as a cause of the dystonia described by Oppenheim. In a vast majority of patients with DYT1 dystonia, symptoms begin in childhood or adolescence, and the mean age of onset is 13 years. Oppenheim dystonia affects most ethnic groups but is considerably wide spread in the Ashkenazi Jewish population.

Dystonia plus syndrome encompasses nondegenerative disorders in which parkinsonism dopa-responsive dystonia (DRD) and rapid-onset dystonia-parkinsonism (RDP) or Myoclonus-Dystonia (M-D) co-occur with dystonia. Dopa responsive dystonia predominantly starts between ages six and 16 but can arise at any age. When it begins in infants has the appearance of cerebral palsy. When it occurs in adults, it often manifests as pure parkinsonism, responding to levodopa with a benign course. Dopa responsive dystonia affects girls more often than boys, has a worldwide distribution and is not known to have a higher specific prevalence in any particular ethnic group. Mutations in the gene for GTP cyclohydrolase 1(GCH1) located at 14q22.1 are accountable for the greater number of dopa-responsive dystonia. Dopa responsive dystonia can be suspected if a young patient with dystonia responds greatly to a low dose of anticholinergics. On the other hand, the most effective agent is levodopa.

Clues suggestive of secondary dystonia emerge from the definition of the disorder that develops as a result of environmental factors that affect the brain, especially the basal ganglia. Spinal cord injury and peripheral injury can serve as a cause of dystonia as well. So the history of possible head trauma, encephalitis, toxin and drug exposure, perinatal anoxia, also the presence of neurologic abnormality independently from dystonia, for example, Parkinsonism, dementia, seizures, ocular symptoms, ataxia, neuropathy, spasticity with abnormal brain imaging will guide to the diagnosis of secondary dystonia.

Because many of the neurodegenerations are a result of genetic abnormalities, the term Heredodegenerative dystonia is applied to this category. Dystonia in Neurodegeneration is a prominent feature. MRI of the brain, ceruloplasmin level, slit-lamp exam, lysosomal screen, peripheral blood smear, nerve conduction studies, creatine kinase (CK) level, vitamin E are a few worth mentioning investigations.

Imaging studies may identify central lesions, hemorrhage or hypoxic damage.

Treatment / Management

The medications that are most potent in the treatment of dystonia include anticholinergics (trihexyphenidyl), GABA agonists (baclofen and benzodiazepines), and dopaminergic agents. The mechanism of action of these drugs is due to modifications in dopaminergic and cholinergic neurotransmission and reduced GABA-mediated inhibition in the dystonic central nervous system (CNS).

Trihexyphenidyl is the first-line medication for management of childhood-onset primary generalized or segmental dystonia.

Focal dystonia can be effectively treated with botulinum toxin injections. The toxin blocks the vesicular release of acetylcholine into the neuromuscular junction, generating temporary local chemo-denervation and muscle weakness, lessening the excessive activity of the affected dystonic muscles.

Botulinum toxin is the first-line treatment for cervical dystonia and blepharospasm and is also habitually used to treat laryngeal dystonia (spasmodic dysphonia), and focal limb dystonia. Apart from its direct peripheral effect of weakening affected muscles, botulinum toxin injections may also reduce afferent feedback from affected muscles, possibly normalizing the abnormal plastic changes in the CNS.

The drug-induced tardive dyskinesia requires specialized treatment.

Historically, dystonia patients were treated surgically with pallidotomy or thalamotomy. These lesional surgeries provided significant benefit to dystonia symptoms in some cases, but also frequently caused permanent, debilitating side effects, particularly dysarthria. Lesional surgeries have now been succeeded by deep brain stimulation (DBS), which resembles a lesional effect but is reversible and adjustable. In the past two decades, DBS has come to the leading edge as an important treatment option for patients with severe medically refractory primary dystonia. The currently established target in DBS for dystonia is the globus pallidus (GPI). DBS is thought to produce its clinical effect by inducing functional changes within the abnormal motor networks in dystonia and ultimately normalizing pathologically overactive motor activation responses. In opposition to the rapid effect of DBS that occurs in Parkinson disease or essential tremor, the effect of DBS is typically delayed in dystonia, often taking weeks to months, confirming  with the concept of dystonia as a disorder of sensorimotor connectivity that compels time to restyle and adapt to changes along the entire motor circuit after DBS.

There is a distinct variability in response to DBS among dystonia patients, with some patients showing dramatic improvement whereas others benefit only modestly or not at all, and no single factor, including DYT1 gene status, has been found to be undeniably predictive of response. The question which patient with primary dystonia will have the best response to DBS remains open and requires further investigation.

Whether DBS should be considered as a treatment option for secondary dystonia is not entirely understood.

Physical therapy may help individuals with focal or segmental dystonic movements. Speech therapists can offer communication aids and provide techniques to relax the jaw.

Differential Diagnosis

* Cerebral palsy
* Lysosomal storage disease
* Neuronal ceroid lipofuscinoses
* Neuro acanthocytosis
* Parkinson-plus syndrome
* Parkinson disease in young adults
* Post-stroke spasticity
* Psychogenic dystonia
* Spinocerebellar ataxia
* Systemic lupus erythematosus (SLE)

Staging

Classification based on anatomy

* Focal dystonia involves a single body part
* Segmental dystonia affects 2 or more contiguous body parts. The classic example is head and neck dystonia
* Multifocal dystonia involves noncontiguous body parts
* Generalized dystonia may involve the trunk and the limbs
* Hemidystonia is typically associated with deficits in the contralateral basal ganglia and also called unilateral dystonia.

Enhancing Healthcare Team Outcomes

Dystonia is a neuro-functional disorder distinguished by modifications at different levels and numerous elements alongside the sensorimotor circuit. Numerous causes can lead to these disruptions and lesions along different points in interconnected pathways can yield similar motor dysfunction. Although the basal ganglia is a crucial brain region, abnormalities exist in many other regions throughout the motor circuit. Ultimately, a full comprehension of the pathophysiology of dystonia would most probably guide to a more effective, logical and directed therapy.

Because of the numerous causes of dystonia, the condition is best managed by an interprofessional team that includes a neurologist, neurosurgeon, internist, pharmacist, primary care provider, therapists, and nurse practitioner. The primary treatment of dystonia is with medications and botulinum toxin. The pharmacist should educate the patient on the importance of medication compliance to control the symptoms. In addition, many patients may benefit from physical and occupational therapy. Speech therapy can retain methods to communicate and offer aids to help with speech. Some patients may require ambulatory devices.

However, treatment is often long term and the drugs also have numerous side effects. Surgery is no longer used to treat dystonia but DBS may be an option. Because dystonia is often life long, many patients develop anxiety and depression, hence a mental health nurse should be involved in the counseling of these patients. Finally, the social workers should be involved to ensure that the patient has adequate support and finances; so care is not neglected. Only through close collaboration between the team can the morbidity of dystonia be minimized.

**Outcomes**

The outlook for most patients with dystonia depends on the cause. In general, while lifespan is not reduced, the quality of life is poor.

Source:

* Singh, V.N., Koneru, V.M. and Chapman, B.C. (2024) *Dystonia*. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing. Available at: https://www.ncbi.nlm.nih.gov/books/NBK448144/ (Accessed: 23 May 2025).

# Ataxia

**Ataxia is a term for a group of disorders that affect co-ordination, balance and speech.**

Any part of the body can be affected, but people with ataxia often have difficulties with:

* balance and walking
* speaking
* swallowing
* tasks that require a high degree of control, such as writing and eating
* vision

The exact symptoms and their severity vary depending on the type of ataxia a person has.

## **Types of ataxia**

There are many different types of ataxia, which can be divided into three broad categories:

* **acquired ataxia** – where symptoms develop as the result of trauma, a stroke, multiple sclerosis (MS), a brain tumour, nutritional deficiencies, or other problems that damage the brain or nervous system
* **hereditary ataxia** – where symptoms develop slowly over many years and are caused by faulty genes that a person inherits from their parents; the most common type is Friedreich's ataxia
* **idiopathic late-onset cerebellar ataxia (ILOCA)** – where the brain is progressively damaged over time for reasons that are unclear

Read more about the main types of ataxia.

## **What causes ataxia?**

Ataxia usually results from damage to a part of the brain called the cerebellum, but it can also be caused by damage to other parts of the nervous system.

This damage can be part of an underlying condition such as MS, or can be caused by a head injury, lack of oxygen to the brain, or long-term, excessive alcohol consumption.

Hereditary ataxia is caused by a faulty gene passed on by family members, who may or may not be affected.

## **How ataxia is treated**

In most cases, there's no cure for ataxia and supportive treatment to control the symptoms is necessary.

This may include:

* speech and language therapy to help with speech and swallowing problems
* physiotherapy to help with movement problems
* occupational therapy to help you cope with the day-to-day problems
* medication to control muscle, bladder, heart and eye problems

In a few cases, it's possible to improve ataxia or stop it getting worse by treating the underlying cause.

## **Outlook**

The outlook for ataxia can vary considerably and largely depends on the type of ataxia you have. Some types may remain relatively stable or even improve with time, but most will get progressively worse over many years.

Life expectancy is generally shorter than normal for people with hereditary ataxia, although some people can live well into their 50s, 60s or beyond. In more severe cases, the condition can be fatal in childhood or early adulthood.

For acquired ataxia, the outlook depends on the underlying cause. Some cases may improve or stay the same, while other cases may get gradually worse over time and reduce life expectancy.

# **Types**-Ataxia

**Some types of ataxia affect children from an early age, while other types may not develop until much later in adulthood.**

Depending on the type of ataxia, the symptoms may stay the same, get progressively worse, or slowly improve.

Some of the main types of ataxia are described below. Read about the causes of ataxia for information about why these different types of ataxia develop.

## **Friedreich's ataxia**

Friedreich's ataxia is the most common type of hereditary ataxia (caused by genes you've inherited). It's thought to affect at least 1 in every 50,000 people.

Symptoms usually first develop before the age of 25, although it can develop in people much older than this.

Signs and symptoms of Friedreich's ataxia can include:

* problems with balance and co-ordination, often causing wobbliness, clumsiness and frequent falls
* increasingly slurred, slow and unclear speech (dysarthria)
* increasing weakness in the legs – many people find walking difficult and need to use a wheelchair after around 10 to 20 years
* difficulty swallowing (dysphagia)
* abnormal curvature of the spine (scoliosis)
* total or partial vision loss and hearing loss
* diabetes
* thickening of the heart muscles (hypertrophic cardiomyopathy), which can cause chest pain, breathlessness and an irregular heartbeat
* loss of sensation in the hands and feet (peripheral neuropathy)

The symptoms of Friedreich's ataxia usually get gradually worse over many years. People with the condition tend to have a shorter life expectancy than normal. Many people live until at least their 30s, and some can live into their 60s or beyond.

## **Ataxia-telangiectasia**

Ataxia-telangiectasia (AT) is a rarer type of hereditary ataxia. Symptoms usually begin in early childhood, although they can sometimes develop later.

Signs and symptoms of AT can include:

* difficulty walking – most children need to use a wheelchair by 10 years of age
* increasingly slurred, slow and unclear speech (dysarthria)
* difficulty swallowing (dysphagia)
* small spider-like clusters of red blood vessels in the corner of their eyes and on their cheeks (telangiectasias)
* very slow eye movements, which may mean the person has to move their head a lot to compensate for this
* a weakened immune system – children with AT are more vulnerable to infections, particularly infections of the sinuses, lungs and airways, such as pneumonia
* an increased risk of cancer, particularly acute lymphoblastic leukaemia or lymphoma

The symptoms of AT tend to get worse quite quickly. People with the condition usually live until the age of 19 to 25, although some may live into their 50s.

## **Spinocerebellar ataxias**

Spinocerebellar ataxias (SCAs) are a group of hereditary ataxias that often don't begin until adulthood, affecting people from the age of 25 up to 80, depending on the type of SCA. Occasionally, some types of SCA begin in childhood.

The symptoms vary depending on the type of SCA. They can include:

* problems with balance and co-ordination – many people find walking difficult and need to use a wheelchair after a few years
* increasingly slurred, slow and unclear speech (dysarthria)
* difficulty swallowing (dysphagia)
* muscle stiffness and cramps
* loss of sensation in the hands and feet (peripheral neuropathy)
* memory loss and difficulties with spoken language
* slow eye movement, which means people have to move their head to compensate
* reduced bladder control (urinary urgency or incontinence)

## **Episodic ataxia**

Episodic ataxia is a rare and unusual type of hereditary ataxia where someone experiences episodes of ataxia, but the rest of the time they have no or only mild symptoms.

During an episode, someone with episodic ataxia may experience:

* problems with balance and co-ordination
* slurred, slow and unclear speech (dysarthria)
* muscle spasms
* involuntary eye movements (nystagmus)
* vertigo, migraines and tinnitus

Episodic ataxia usually first develops during the teenage years. The episodes can last from several minutes to hours and are usually the result of certain triggers, such as sudden movement, stress, exercise, caffeine or alcohol.

The symptoms of episodic ataxia may disappear as a person gets older, although sometimes the condition gets gradually worse over time. Medication can often help control attacks, and life expectancy is usually normal.

## **Other types of ataxia**

There are also a number of other types of ataxia that tend to have similar symptoms to those mentioned above. These include:

* **acquired ataxia** – this can affect people of any age and usually develops very quickly over the course of a few days, or sometimes hours; it may improve over time, stay the same or get slowly worse
* **idiopathic late-onset cerebellar ataxia (ILOCA)** – this usually begins at around 50 years of age and gets slowly worse over time
* **ataxia with vitamin E deficiency** – a similar condition to Friedreich's ataxia caused by problems with the body's ability to use vitamin E in the diet; it's often possible to control the symptoms with vitamin E supplements.

# **Causes**-Ataxia

**Ataxia is usually caused by damage to a part of the brain known as the cerebellum, but it can also be caused by damage to the spinal cord or other nerves.**

The spinal cord is a long bundle of nerves that runs down the spine and connects the brain to all other parts of the body.

The cerebellum is located at the base of the brain and is responsible for controlling:

* walking and sitting balance
* limb co-ordination
* eye movements
* speech

Damage can occur as a result of injury or illness (acquired ataxia) or because the cerebellum or spinal cord degenerates because of an inherited faulty gene (hereditary ataxia).

Sometimes there's no clear reason why the cerebellum and spinal cord become damaged. This is the case for people with idiopathic late-onset cerebellar ataxia (ILOCA).

## **Acquired ataxia**

Acquired ataxia can have a wide range of potential causes, including:

* severe head injury – after a car crash or fall, for example
* bacterial brain infection, such as meningitis or encephalitis (an infection of the brain itself)
* viral infection – some viral infections, such as chickenpox or measles, can spread to the brain, although this is very rare
* conditions that disrupt the supply of blood to the brain, such as a stroke, haemorrhage or a transient ischaemic attack (TIA)
* cerebral palsy – a condition that can occur if the brain develops abnormally or is damaged before, during or shortly after birth
* multiple sclerosis – a long-term condition that damages the nerve fibres of the central nervous system
* sustained long-term alcohol misuse
* an underactive thyroid gland
* vitamin B12 deficiency
* brain tumours and other types of cancer
* certain toxic chemicals, such as mercury and some solvents – these can trigger ataxia if a person is exposed to enough of them
* medications such as benzodiazepines can occasionally trigger ataxia as a side effect

## **Hereditary ataxia**

Hereditary ataxia is caused by a faulty gene. Genes are units of DNA that determine a particular characteristic, such as sex or eye colour. A baby receives two copies of every gene – one from their mother and one from their father.

There are two ways that ataxia can be inherited:

* **autosomal recessive** – Friedreich's ataxia and ataxia-telangiectasia are inherited in this way
* **autosomal dominant** – episodic ataxia and some cases of spinocerebellar ataxia are inherited in this way

These are described in more detail in the following sections.

### Autosomal recessive

When ataxia is autosomal recessive, it means the affected person has inherited the mutated gene from both their mother and their father.

If they only received one mutated gene from either parent, the other normal gene will cancel out the effects of the faulty gene and they will be a carrier of the condition. This means they don't have the condition themselves, but could pass it on to their children if their partner is also a carrier of the faulty gene.

It's estimated around 1 in every 85 people are carriers of the mutated gene that causes Friedreich's ataxia. Fewer people than this are carriers of the mutated gene that causes ataxia-telangiectasia.

If 2 carriers of the mutated gene were to have a baby, there would be a:

* 1 in 4 chance the baby would receive a pair of normal genes
* 1 in 2 chance the baby would receive one normal gene and one mutated gene (be a carrier)
* 1 in 4 chance the baby would receive a pair of mutated genes and develop ataxia

If you have autosomal recessive ataxia and your partner is a carrier, there is a 1 in 2 chance your baby will receive one normal gene and one mutated gene and will be a carrier, and a 1 in 2 chance your baby will receive a pair of mutated genes and develop ataxia.

If you have autosomal recessive ataxia and your partner doesn't and they aren't a carrier, there's no risk of any of your children developing ataxia. This is because your mutated gene will be cancelled out by your partner's normal gene. Your children will be carriers, however.

### Autosomal dominant

When ataxia is autosomal dominant, you can develop the condition if you receive a single faulty gene, either from your mother or father. This is because the mutation is strong enough to override the other normal gene.

If you have autosomal dominant ataxia, any children you have will have a 1 in 2 chance of developing ataxia.

# **Types**-Ataxia

**Some types of ataxia affect children from an early age, while other types may not develop until much later in adulthood.**

Depending on the type of ataxia, the symptoms may stay the same, get progressively worse, or slowly improve.

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Signs and symptoms of Friedreich's ataxia can include:

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* increasingly slurred, slow and unclear speech (dysarthria)
* increasing weakness in the legs – many people find walking difficult and need to use a wheelchair after around 10 to 20 years
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* diabetes
* thickening of the heart muscles (hypertrophic cardiomyopathy), which can cause chest pain, breathlessness and an irregular heartbeat
* loss of sensation in the hands and feet (peripheral neuropathy)

The symptoms of Friedreich's ataxia usually get gradually worse over many years. People with the condition tend to have a shorter life expectancy than normal. Many people live until at least their 30s, and some can live into their 60s or beyond.

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When ataxia is autosomal dominant, you can develop the condition if you receive a single faulty gene, either from your mother or father. This is because the mutation is strong enough to override the other normal gene.

If you have autosomal dominant ataxia, any children you have will have a 1 in 2 chance of developing ataxia.

# **Diagnosis**-Ataxia

**Visit your GP if you or your child have unexplained symptoms such as balance and co-ordination problems or difficulty walking, talking or swallowing.**

## **Family and medical history**

Your GP may ask whether you have any family history of ataxia. They will also want to know about the progression of your symptoms. They might carry out a simple assessment of your balance, walking and co-ordination.

Your GP may also ask how much alcohol you drink and whether you're taking any form of medication. This is because excessive drinking and certain medications can cause ataxia-like symptoms in some people.

You may be referred for a series of tests to rule out other possible causes of your symptoms, such as an infection. The tests will probably include blood and urine tests.

## **Further testing**

If your symptoms suggest you may have acquired ataxia because of a serious underlying condition, it's likely you'll be admitted immediately to your nearest hospital.

Otherwise, you'll be referred to a neurologist (a specialist in brain and nervous system conditions) for further testing or, in the case of children, a paediatrician. Some of the tests you may have are described in the following sections.

### Genetic testing

Genetic testing involves taking a sample of blood and testing the DNA in it for any genetic mutation known to cause ataxia.

Currently, tests can detect the mutations responsible for Friedreich's ataxia, ataxia-telangiectasia and most of the spinocerebellar ataxias.

### Brain scans

Brain scans can be used to check for physical abnormalities in the brain that could be caused by certain types of hereditary ataxia. They can also be used to check for other problems that may affect your brain, such as a brain tumour.

The two most widely used brain imaging scans are:

* magnetic resonance imaging (MRI) scan – this uses a strong magnetic field and radio waves to produce detailed scans of the soft tissue of the brain
* computerised tomography (CT) scan – where a series of X-rays are taken and assembled by a computer into a detailed 3-dimensional image of your brain

### Other tests

Some of the other tests you may have to help diagnose ataxia and determine how severe it is can include:

* a lumbar puncture – where a sample of cerebrospinal fluid is taken from the base of the spine to check it for infection and any other abnormalities
* nerve conduction studies and electromyography (EMG) – tests used to assess the electrical activity in nerves and muscles
* videofluoroscopy – a continuous moving X-ray taken while you swallow different types of food and drink
* an electrocardiogram (ECG) – an assessment of the electrical activity of the heart
* an echocardiogram – an ultrasound scan of the heart

# **Treatment**-Ataxia

**The treatment for ataxia can vary depending on exactly what type of ataxia you have.**

It's sometimes possible to treat the underlying cause of the condition so it improves or stops getting worse, but in most cases this isn't possible and you'll have treatment to relieve your symptoms.

## **Your treatment plan**

You'll usually be cared for by a group of healthcare professionals called a multidisciplinary team (MDT), who will work with you to come up with a care plan. Your MDT will probably include a neurologist, physiotherapist and specialist nurse, among others.

Your care plan will play an important part in the management of your condition. Your physical, social and psychological needs will be assessed, and the plan will outline how these needs can best be met. The plan will also address any future needs you may have.

You'll normally have regular appointments with your MDT or GP to review your progress. In some cases, you may be seen in a specialist ataxia centre.

## **Treating the symptoms**

Treatments for the various symptoms of ataxia are discussed in the following sections, although you may not experience all of the problems described.

### Speech and language therapy

A speech and language therapist will be able to help with two of the most common symptoms of ataxia – slurred speech (dysarthria) and swallowing problems (dysphagia).

The therapist will be able to advise you about how to make your voice sound clearer. For example, they may suggest:

* changing your posture to improve the quality of your voice
* carrying out exercises to strengthen the muscles used when speaking
* speaking more slowly to emphasise each word
* using breathing techniques to improve your speech

If your speech gets worse, you may want to consider using speaking aids such as a laptop computer connected to a voice synthesiser. Your therapist will be able to advise you about the equipment available.

To treat dysphagia, your therapist will be able to teach you exercises to stimulate the nerves used to trigger your swallowing reflex and strengthen the muscles used when swallowing.

You may also be referred to a dietitian for dietary advice. For example, your diet may need to include food that's easier to swallow. Read more about treating dysphagia.

### Occupational therapy

The aim of occupational therapy is to teach you how to adapt to your gradual loss of mobility and develop new skills you can use to carry out daily activities.

An occupational therapist may be able to teach you how to use a wheelchair and other mobility devices. They can also advise you about modifications you can make to your house, such as installing guide rails or a stair lift, to help make your life easier.

### Physiotherapy

If you have ataxia, physiotherapy can help you maintain the use of your arms and legs, and prevent your muscles weakening or getting stuck in one position (contractures).

A physiotherapist will be able to teach you a number of physical exercises you can do every day to help strengthen and stretch your muscles. They may also be able to recommend walking aids to help you get around.

### Muscle problems

If you're experiencing muscle spasms, cramps and stiffness, muscle relaxant medication such as baclofen or tizanidine may be used to control these symptoms.

If these aren't effective, an injection of botulinum toxin (Botox) may be given. This works by blocking the signals from your brain to the affected muscles. The effects of the injection will usually last for up to 3 months.

### Bladder problems

Bladder problems, such as urinary urgency or, more rarely, urinary incontinence, sometimes affect people with ataxia.

In some cases, bladder problems can be controlled using a number of self care techniques, such as limiting fluid intake during the day, planning regular trips to the toilet, and avoiding drinks known to stimulate urine production, such as caffeine and alcohol.

Some people may also require a type of medication known as antimuscarinic. This will help relax the bladder, reducing the frequent urge to urinate. Occasional injections of botulinum toxin into the bladder may also help.

Others may find it difficult to empty their bladder completely when they go to the toilet. This can lead to small amounts of urine leaking out later on. In such cases, it may be necessary to insert a small tube known as a urinary catheter into the bladder to help drain the urine.

### Eye problems

Eye problems are common in some cases of ataxia. Oscillopsia is an eye problem caused by involuntary movement of the eyes from side to side or up and down. It can cause visual disruption, making tasks such as reading difficult. This can sometimes be treated using medication such as gabapentin to control the muscles that move the eyes.

Some people with ataxia experience double vision, where you see 2 images of a single object. It may be possible to treat this by attaching a wedge-shaped piece of glass or plastic called a prism to your glasses.

### Erectile dysfunction

As a result of underlying nerve damage, some men with ataxia will experience difficulty getting or maintaining an erection (erectile dysfunction).

This can often be treated using a group of medications known as phosphodiesterase-5 (PDE-5) inhibitors, such as sildenafil (sold as Viagra). These help increase blood flow to the penis.

### Fatigue

Many people with neurological conditions such as ataxia report feeling extremely tired and lethargic (lacking in energy). It's thought this is partly caused by disturbed sleep and the physical efforts of having to cope with the loss of co-ordination.

A physiotherapist may be able to help you increase your stamina levels, and an occupational therapist can advise you about how to adapt your daily activities to help you cope with fatigue better.

### Nerve pain

Damage to the nerve endings can result in nerve pain. The medical term for nerve pain is neuropathic pain, which is often experienced as a burning, aching or shooting pain, or sometimes tingling, in certain parts of the body.

Traditional painkillers such as paracetamol or ibuprofen aren't usually effective in treating neuropathic pain, so you may be prescribed a number of medications, such as amitriptyline, gabapentin or pregabalin.

### Cardiomyopathy

Cardiomyopathy (damage to the heart muscle) is a common problem in some types of ataxia. This can be serious as it can place strain on the heart, affect the normal blood flow through the heart, and cause heartbeat irregularities (arrhythmias).

If you develop cardiomyopathy, you'll receive regular check-ups from a cardiologist (a heart specialist). You may need to take medication to treat any problems as they develop.

### Depression

Living with a long-term condition such as ataxia can be stressful and can often cause intense feelings of anxiety. In some cases, this can trigger the onset of depression.

Signs that you may be depressed include feeling down or hopeless during the past month and no longer taking pleasure in the things you enjoy.

You should contact your GP or MDT for advice if you think you may be depressed. There are several treatments for depression, such as antidepressants and talking therapies such as cognitive behavioural therapy (CBT).

You may also find it useful to contact Ataxia UK, a leading charity for people affected by ataxia. Their helpline number is 0800 995 6037, open Monday to Thursday, 10.30am to 2.30pm.

## **Treating the underlying cause**

In a few cases of ataxia, it may be possible to improve the condition or stop it getting worse by treating the underlying cause.

For example:

* **ataxia with vitamin E deficiency** can often be controlled or improved with vitamin E supplements
* **episodic ataxia** can often be controlled with a medication called acetazolamide and by avoiding triggers such as stress, alcohol and caffeine
* **acquired ataxia** can sometimes be treated depending on the specific cause – for example, antibiotic or antiviral medication may help if it's caused by an infection

If acquired ataxia is caused by serious underlying brain damage, such as damage from a stroke or a severe head injury, it may not be possible to improve the condition. If this is the case, the treatments mentioned above can be used to control your symptoms.

Source

NHS (2021) *Ataxia - Treatment*. Available at: https://www.nhs.uk/conditions/ataxia/treatment/ (Accessed: 5 June 2025).

TOURRETTE SYNDROME/TIC

# Diagnosis for Tic Disorders

## KEY POINTS

* There are three main types of tic disorders.
* Health professionals consider the type of tic present and how long the symptoms have lasted to diagnosis a specific tic disorder.
* Talk to your child's healthcare provider if your child makes sudden and repeated twitches, movements, or sounds.

## Why diagnosis is important

Although there is no cure for tic disorders, there are treatments available to help manage the tics. Medication and behavioral treatments are available if tics cause pain or injury; interfere with school, work, or social life; or cause stress.

## Types of tic disorders

The American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (*DSM-5-TR)* is used by health professionals to help diagnose tic disorders.

Three tic disorders are included in the *DSM-5-TR*:

* Tourette syndrome (TS, sometimes called Tourette disorder)
* Persistent (sometimes called chronic) motor or vocal tic disorder
* Provisional tic disorder

The tic disorders differ from each other in terms of the type of tic present (motor or vocal, or a combination of both), and how long the symptoms have lasted. People with Tourette syndrome have both motor *and* vocal tics and have had tic symptoms for at least 1 year. People with persistent motor or vocal tic disorders have either motor *or* vocal tics and have had tic symptoms for at least 1 year. People with provisional tic disorders can have motor or vocal tics, or both, but have had their symptoms less than 1 year.

### **Tourette syndrome**

To be diagnosed with TS, a person must

* Have two or more motor tics (for example, blinking or shrugging the shoulders) *and* at least one vocal tic (for example, humming, clearing the throat, or yelling out a word or phrase), although they might not always happen at the same time.
* Have had tics for at least a year. The tics can occur many times a day (usually in bouts) nearly every day, or off and on.
* Have tics that begin before age 18 years.
* Have symptoms that are not due to taking medicine or other drugs or due to having another medical condition (for example, seizures, Huntington disease, or postviral encephalitis).

### **Persistent (chronic) motor or vocal tic disorder**

To be diagnosed with a persistent tic disorder, a person must

* Have one or more motor tics (for example, blinking or shrugging the shoulders) or vocal tics (for example, humming, clearing the throat, or yelling out a word or phrase), but *not*both.
* Have tics that occur many times a day nearly every day or on and off throughout a period of more than a year.
* Have tics that start before age 18 years.
* Have symptoms that are not due to taking medicine or other drugs, or due to having a medical condition that can cause tics (for example, seizures, Huntington disease, or postviral encephalitis).
* Not have been diagnosed with TS.

### **Provisional tic disorder**

To be diagnosed with a provisional tic disorder, a person must

* Have one or more motor tics (for example, blinking or shrugging the shoulders) or vocal tics (for example, humming, clearing the throat, or yelling out a word or phrase).
* Have been present for no longer than 12 months in a row.
* Have tics that start before age 18 years.
* Have symptoms that are not due to taking medicine or other drugs, or due to having a medical condition that can cause tics (for example, Huntington disease or postviral encephalitis).
* Not have been diagnosed with TS or persistent motor or vocal tic disorder.

### Tics after a strep infection

In some children, tics may suddenly appear, or suddenly become worse, following a streptococcal (strep) infection, such as strep throat or scarlet fever.

### **Sudden onset of tic-like behaviors**

Sometimes people have tic-like behaviors that look like tics, but that are distinctly different from those typically seen in Tourette syndrome and other tic disorders. The people who develop these tic-like behaviors are often experiencing movement symptoms for the first time, with no reported history of tics. These types of tic-like behaviors are more common among teenagers and more often seen in girls than boys. Sometimes these tics can happen in groups of children. Many experts believe these sudden onset tic-like behaviors can happen for different reasons, and tic-like behaviors may need different treatment compared to tic disorders including Tourette syndrome. The best first step is usually to talk to a healthcare provider who is familiar with tics and get a thorough assessment.

## What to do when your child is diagnosed with Tourette syndrome

Taking an active role, learning about TS, and understanding treatment and ways to manage symptoms can help you make the best possible choices for your child and for your family.

* Talk to a healthcare provider about any questions or concerns.
* Learn as much as you can about TS. You can start by reading our pages on the following topics: Facts, Treatments, and Other Concerns & Conditions.
* Ask your provider about concerns and symptoms beyond tics. Most children with TS also have been diagnosed with at least one additional mental, behavioral, or developmental condition and these conditions often add to stress and difficulty in managing health care. Many children with TS also experience learning difficulties. Getting proper treatment and coordinated care is very important.
* Visit the website of the Tourette Association of America to find information, resources, newsletters, videos, and more. In addition, the Tourette Association can be helpful with finding local healthcare providers.

## Finding support

Parenting is often challenging and parenting a child with a chronic condition like TS can add additional stress to the day-to-day challenges. If you are the parent of a child with TS, it might be helpful to talk with other parents who have a child with the same condition, to share concerns and information. Similarly, if you are an adult with TS, talking to other adults with TS might be helpful.

Remember that the choices for another family might not be best for your family, so it's important to understand all options and discuss them with your healthcare providers.

* Your local Tourette Association chapter can help you connect with other families through conferences, support groups and other events.
* Parent-to-Parent Programs provide information and emotional support to families of children who have special needs.

Risk Factors for Tourette Syndrome

KEY POINTS

* The risk factors for and causes of Tourette syndrome are not well understood.
* Current research shows that genes play an important role.
* Scientists are studying other possible causes and environmental factors that may increase risk for Tourette syndrome.

What increases risk

Scientists are studying the causes of and risk factors for Tourette syndrome (TS) in an effort to understand it better, and to find better ways to manage TS and to reduce the chances of a person having TS. The causes of TS and other tic disorders are not well understood.

Genes play an important role in a person's risk of Tourette syndrome.

Although the risk factors for and causes of TS are unknown, current research shows that genes play an important role. Some research has shown that TS is a genetically complex disorder that likely occurs as a result of the effects of multiple genes interacting with other factors in the environment. Scientists are studying other possible causes and environmental risk factors that might contribute to TS. Some studies have shown that the following factors might be associated with TS, but additional research is needed to better understand these associations:

* Smoking during pregnancy.
* Pregnancy complications.
* Low birthweight.
* Infection. Researchers have found mixed results about whether certain children are more likely to develop tics following infections.

# Treatment of Tourette Syndrome

## KEY POINTS

* Although there is no cure for Tourette syndrome (TS), medication and behavioral treatments can help manage tics if they get in the way of daily life.
* Training and other educational resources can help parents and schools support children with TS in achieving their full potential.

## Treatment overview

Although there is no cure for Tourette syndrome (TS), there are treatments to help manage the tics caused by TS. Many people with TS have tics that do not get in the way of their living their daily life and do not need any treatment. However, medication and behavioral treatments are available if tics cause pain or injury; interfere with school, work, or social life; or cause stress.

It is common for people with TS to have other conditions, particularly attention-deficit/hyperactivity disorder (ADHD), anxiety, and obsessive-compulsive disorder (OCD). People with additional conditions will require different treatments based on the symptoms. Sometimes treating these other conditions can help reduce tics. To develop the right treatment plan, people with tics, parents, and healthcare providers can work together and include teachers, child care providers, coaches, therapists, and other family members. Taking advantage of all the resources available will help guide success.

## Treatments and interventions

### **Medications**

Medications can be used to reduce severe or disruptive tics that might have led to problems in the past with family and friends, other students, or coworkers. Medications also can be used to reduce symptoms of related conditions, such as ADHD or OCD.

Medications do not eliminate tics completely. However, they can help some people with TS in their everyday life. There is no one medication that is best for all people. Most medications prescribed for TS have not been approved by the US Food and Drug Administration (FDA) for treating tics.

Medications affect each person differently. One person might do well with one medication, but not another. When deciding the best treatment, a doctor might try different medications and doses, and it may take time to find the treatment plan that works best. The doctor will want to find the medication and dose that have the best results and the fewest side effects. Doctors often start with small doses and slowly increase as needed.

As with all medications, those used to treat tics can have side effects. Side effects can include weight gain, stiff muscles, tiredness, restlessness, and social withdrawal. The side effects need to be considered carefully when deciding whether or not to use any medication to treat tics. In some cases, the side effects can be worse than the tics.

Even though medications often are used to treat the symptoms of TS, they might not be helpful for everyone. Two common reasons for not using medications to treat TS are unpleasant side effects and failure of the medications to work as well as expected.

### **Behavioral therapy**

Behavioral therapy is a treatment that teaches people with TS ways to manage their tics. Behavioral therapy is not a cure for tics. However, it can help reduce the number of tics, the severity of tics, the impact of tics, or a combination of all of these. It is important to understand that even though behavioral therapies might help reduce the severity of tics, this does not mean that tics are just psychological or that anyone with tics should be able to control them.

#### ***Habit reversal***

Habit reversal is one of the most studied behavioral interventions for people with tics. It has two main parts: awareness training and competing response training. In the awareness training part, people identify each tic out loud. In the competing response part, people learn to do a new behavior that cannot happen at the same time as the tic. For example, if the person with TS has a tic that involves head rubbing, a new behavior might be for that person to place their hands on their knees, or to cross their arms so that the head rubbing cannot take place.

#### ***Comprehensive behavioral intervention for tics***

Comprehensive behavioral intervention for tics (CBIT) is an evidence-based type of behavioral therapy for TS and chronic tic disorders. CBIT includes habit reversal in addition to other strategies, including education about tics and relaxation techniques. CBIT has been shown to be effective at reducing tic symptoms and tic-related impairment among children and adults.

In CBIT, a therapist will work with a child (and their parents) or an adult with TS to better understand the types of tics the person is having and to understand the situations in which the tics are at their worst. Changes to the surroundings may be made, if possible, and the person with TS will also learn to do a new behavior instead of the tic (habit reversal). This helps to decrease how often the tic occurs by doing a new behavior. CBIT skills can be learned with practice, with the help of an experienced therapist, and with the support and encouragement of those close to the person with TS.

A therapist trained in CBIT can best support a child with Tourette syndrome to manage their tics.

In recent years, more health professionals have recognized that behavioral therapy can be very effective in managing the symptoms of TS. So far, few clinicians have been trained in these types of treatments specifically for TS and tic disorders. The CDC and The Tourette Association of America have been working to educate more health professionals in this approach to managing TS symptoms.

Source:

* Singh, V.N., Koneru, V.M. and Chapman, B.C. (2024) *Dystonia*. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing. Available at: https://www.ncbi.nlm.nih.gov/books/NBK448144/ (Accessed: 23 May 2025).

NEUROMUSCULAR DISORDERS

Multiple sclerosis

## **Key facts**

* **Multiple sclerosis (MS) affects function in cognitive, emotional, motor, sensory, or visual areas and occurs as a result of a person’s immune system attacking their brain and spinal cord.**
* **It is estimated that over 1.8 million people have MS worldwide.**
* **People of all ages can be affected, but it is more common in young adults and in females.**
* **MS can improve or stabilize by being treated with medicines early in the course of the disease and treatments will be different for each person depending on the severity of the disease and symptoms.**

## **Overview**

Multiple sclerosis (MS) is a condition that happens when the immune system attacks the brain and spinal cord.

Symptoms of MS vary from person to person and depend on the location and severity of nerve fibre damage. These often include vision problems, tiredness, trouble walking and keeping balance, and numbness or weakness in the arms and legs. Symptoms can come and go or last for a long time.

The causes of MS are not known but a family history of the disease may increase the risk.

While there is no cure for MS, treatment can reduce symptoms, prevent further relapses and improve quality of life.

MS can present in a variety of ways including:

* clinically isolated syndrome (CIS): describes an episode of neurologic symptoms that are the first clinical sign of possible MS;
* relapsing remitting (RRMS): the most common form of MS characterized by intermittent attacks of symptoms (relapses), followed by a short or long period of no clinical attacks (remissions);
* secondary progressive (SPMS): after living with RRMS for a long period of time, relapses decrease and symptoms continue progressively without relapses or remissions; and
* primary progressive (PPMS): starting from the initial symptoms, the disease gradually progresses and gets worse without any clear relapses or remissions.

MS is not always easy to diagnose in its early stages. Typically, people who have been diagnosed with MS will have been through several diagnostic stages, which can be an unsettling and frightening experience.

## **Symptoms**

Symptoms of multiple sclerosis can be different from person to person. They can come and go or get worse over time. MS can affect any part of the central nervous system.

MS symptoms can worsen with heat or during other infections such as urinary tract or respiratory infections.

Symptoms can include:

* vision problems
* difficulty walking or keeping balance
* difficulty thinking clearly
* numbness or weakness especially in the arms and legs
* muscle stiffness
* depression
* problems with sexual function or urination
* feeling very tired.

## **Causes**

MS is an inflammatory demyelinating condition that results from an autoimmune attack on myelin, the fatty insulation that surrounds the nerves in the brain and spinal cord. This disrupts the electrical impulses that are sent through the nerves to the rest of the body and results in scars (plaques or sclerosis).

It is not known what triggers the immune system to attack myelin, but genetic and environmental factors are thought to play a role. MS happens most commonly in young to middle-aged adults, more in females than males, and is more common in higher latitudes, possibly due to sun exposure and vitamin D.

## **Diagnosis**

MS is a diagnosis of exclusion and there are no definitive diagnostic tests. Magnetic resonance imaging (MRI) can help with diagnosis by showing plaques or sclerosis on the brain and spinal cord. Other tests such as lumbar puncture, optical coherence tomography (OCT) and visual evoked potentials can also help support the diagnosis.

## **Treatment and care**

Treatments for MS will be different for each person. They depend on the stage of the disease and symptoms.

The goals of MS treatment are to reduce the frequency and severity of relapses, slow disease progression, manage symptoms, and improve quality of life.

Specific MS disease modifying therapies (DMTs) are started as early as possible to slow disease progression and prevent relapses.

Steroids are sometimes used in the short term to treat relapses. Other medicines can be used to reduce the symptoms of MS such as fatigue, muscle tightening, depression and urinary or sexual problems. These medicines do not change the course of the disease but help manage the symptoms.

Rehabilitation specialists can help improve functioning, quality of life and reduce muscle stiffness and spasms.

Many people feel fatigue with multiple sclerosis. Ways to manage fatigue include:

* regular exercise
* healthy sleep patterns
* avoiding medicines that make fatigue worse.

In the past twenty years treatment options for MS have improved dramatically. In high income countries many oral, intravenous and injectable options exist to treat MS. However, most of these medications are not available in low- and middle-income countries and there is still a lack of treatment options for progressive types of MS.

People with MS and their families should be encouraged to seek services and guidance from local and national Organizations of Disabled People (ODPs) and other disability focused organizations, which can provide vital advice about legal rights, economic opportunities and social engagement to ensure that people disabled by MS or other neurological disorders are able to live full and rewarding lives.

SOURCE

* World Health Organization. (2023) *Multiple sclerosis*. Available at: https://www.who.int/news-room/fact-sheets/detail/multiple-sclerosis (Accessed: 23 May 2025).

What is multiple sclerosis?

Multiple sclerosis (MS) is a chronic neurological disorder. It is an autoimmune disorder, meaning that in MS the immune system—which normally protects us from viruses, bacteria, and other threats—mistakenly attacks healthy cells. MS symptoms usually begin in young adults, between the ages of 20 and 40.

MS affects people differently. A small number of people with MS will have mild symptoms with little disability, whereas others will experience worsening symptoms that will lead to increased disability over time. Most people with MS have short periods of symptoms that resolve fully or partially after they appear. These periods are followed by long stretches without noticeable symptoms. Most people with MS have a normal life expectancy.

### Myelin and the immune system

In MS, the immune system attacks myelin in the central nervous system. Myelin is a mixture of protein and fatty acids that makes up the protective cover (known as the myelin sheath) that coats nerve fibers (axons). Myelin is what gives the brain’s white matter its whitish appearance and helps with communication between neurons. The central nervous system is made up of the brain, the spinal cord, and the optic nerves, which connect the eyes to the brain

In addition to causing damage to the myelin sheath, MS also damages the nerve cell bodies, which are found in the brain's gray matter, as well as the axons themselves. As the disease progresses, the outermost layer of the brain, called the cerebral cortex, shrinks. This process is known as cortical atrophy. The way that cortical atrophy happens in MS may connect it with some neurodegenerative disorders.

Sclerosis is a medical term for the distinctive areas of scar-like tissue (also called plaques or lesions) that result from the attack on myelin by the immune system. These areas are visible on an MRI (magnetic resonance imaging). The patches of scar-like tissue can be as small as the head of a pin or as large as a golf ball.

The symptoms of MS depend on the severity of the attacks as well as the location and size of the plaques.

### Types of multiple sclerosis

The course of MS is different for each person, which makes it difficult to predict how an individual will do with the disease. While many different courses or progressions of MS have been used over the years, these are changing as the scientific and medical community better understands different ways the disease can progress.

Currently, the five courses used to describe MS are:

1. **Clinically isolated syndrome**—Symptoms come from a single attack (also called "exacerbation" or "relapse") followed by complete or near-complete recovery. MRI and other tests, such as a spinal tap or electrical vision tests, may show “silent” damage in other places in the central nervous system. If this damage is identified, it could allow a full diagnosis of MS even after a single attack.
2. **Relapsing-remitting MS**—Symptoms come in the form of recurrent attacks with total or partial recovery. The periods of disease inactivity between MS attacks are referred to as remission. Weeks, months, or even years may pass before another attack occurs, followed again by a period of inactivity. Treatment with disease-modifying therapies can reduce the frequency of attacks or eliminate them entirely. Most people with MS are initially diagnosed with this form.
3. **Secondary-progressive MS**—Relapsing-remitting MS can gradually evolve into secondary-progressive MS. Attacks become less and less common but may still occur, and people gradually develop steady symptoms with deterioration in their functioning over time. Secondary-progressive MS with attacks is called “active,” whereas secondary-progressive MS without attacks is called “non-relapsing.” Disease-modifying therapy for relapsing-remitting MS can delay and sometimes prevent secondary progressive MS, but the transition can occur even with treatment.
4. **Primary-progressive MS**—This course of MS is less common and is characterized by progressively worsening symptoms from the beginning, with no noticeable acute attacks, although there may be temporary or minor worsening of, or relief from, symptoms.
5. **Radiologically isolated syndrome**—This is the rarest course of MS in which a person has abnormal MRI results that look like MS, but doesn’t have MS symptoms. However, symptoms (attacks or progression) may occur in the future.

### Symptoms of MS

Early MS symptoms often include:

* Vision problems, such double vision or optic neuritis (inflammation of the optic nerve), which causes pain with eye movement and vision loss
* Muscle weakness, often in the arms and legs, and muscle stiffness with painful muscle spasms
* Tingling, numbness, or pain in the arms, legs, trunk, or face
* Clumsiness, especially difficulty staying balanced when walking
* Bladder control problems
* Intermittent or constant dizziness

MS may also cause other symptoms, such as:

* Mental or physical fatigue
* Mood changes such as depression or difficulty with emotional expression or control
* Cognitive changes, including problems concentrating, multitasking, thinking, or learning, or difficulties with memory or judgment

Muscle weakness, stiffness, and spasms may be severe enough to affect walking or standing. In some cases, MS leads to partial or complete paralysis. The use of a wheelchair is not uncommon, particularly in individuals who are untreated or have advanced disease. Many people with MS find that their symptoms are worse when they have a fever or are exposed to heat or following common infections.

Pain is rarely the first sign of MS, but pain often occurs with optic neuritis and trigeminal neuralgia. Painful limb spasms and sharp pain shooting down the legs or around the abdomen can also be symptoms of MS.

**Who is more likely to get multiple sclerosis?**

Women are more likely to get MS than men. People of all races and ethnicities can get MS, but it is most common in White people.

Having a parent or sibling with MS increases the likelihood of a person getting MS, although MS itself is not an inherited disorder. Research suggests that hundreds of genes and gene variants combine to create vulnerability to MS. Some of these genes have been identified, and most are associated with functions of the immune system. Some of the known genes are similar to those that have been identified in people with other autoimmune diseases, such as inflammatory bowel disease, celiac disease, type 1 diabetes, rheumatoid arthritis, or lupus.

Several viruses have been found in people with MS, but the virus most consistently linked to the development of MS is the Epstein-Barr virus (EBV) which causes infectious mononucleosis. Almost everyone has been infected by EBV at some point in their lives. Only about 5% of the population has not been infected, and these individuals are at a lower risk for developing MS than those who have been infected. People who got EBV during childhood are at a lower risk of getting MS than people who infected with EBV in adolescence or adulthood. However, the vast majority of people who get infected with EBV are not going to develop MS.

Research indicates that people who spend more time in the sun, and those with relatively higher levels of vitamin D, are less likely to develop MS than those who do not. Additionally, people with MS who spend significant time in the sun and/or have higher vitamin D levels have a less severe course of disease and fewer relapses. Bright sunlight helps human skin produce vitamin D. Researchers believe that vitamin D may help regulate the immune system in ways that reduce the risk of MS and autoimmune disorders in general. People from regions near the equator, where there is a great deal of bright sunlight, generally have a much lower risk of MS than people from temperate areas such as the U.S. and Canada, where sunshine is highly variable throughout the year.

Studies have found that people who smoke are more likely to develop MS and have a more aggressive disease course. They also tend to have more brain lesions and brain shrinkage than non-smokers.

### How is multiple sclerosis diagnosed and treated?Diagnosing MS

There is no single test used to diagnose MS. Doctors use different tests to rule out or confirm the diagnosis. In addition to a complete medical history, physical examination, and a detailed neurological examination, a doctor may recommend MRI scans of the brain and spinal cord to look for the characteristic lesions of MS. A special dye or contrast agent may be injected into a vein to enhance the brain images.

In addition, a doctor may recommend:

* Lumbar puncture (sometimes called a spinal tap) to obtain a sample of cerebrospinal fluid and examine it for proteins and inflammatory cells associated with the disease. This can also test for diseases that may look like MS.
* Evoked potential tests, which use electrodes placed on the skin and painless electric signals to measure how quickly and accurately the nervous system responds to stimulation
* MRI of the optic nerves, optic coherence tomography (OCT), or visual evoked potentials to detect optic nerve lesions

In most cases, doctors can diagnose MS by assessing symptoms and identifying characteristic MS signs on an MRI.

### Treating MS

There is no cure for MS, but there are treatments that can reduce the number and severity of relapses and delay the long-term progression of the disease.

Corticosteroids, such as methylprednisolone, are prescribed over for three to five days and are usually injected into a vein. Corticosteroids quickly and potently suppress the immune system and reduce inflammation. They may be followed by a tapered dose of oral corticosteroids. Clinical trials have shown that these drugs hasten recovery from MS attacks but do not alter the long-term outcome of the disease.

#### *Disease-modifying treatments*

Current therapies approved by the U.S. Food and Drug Administration (FDA) for MS are designed to modulate or suppress the inflammatory reactions of the disease. They are most effective for relapsing-remitting MS or secondary-progressive MS with residual attacks. They are also effective in some cases of radiologically isolated syndrome to prevent development of clinical MS. Radiologically isolated syndrome is a condition in which a person has abnormal MRI results that look like MS, but doesn’t have MS symptoms.

Infusion treatments include:

* Natalizumab (brand name: Tysabri®) works by preventing cells of the immune system from entering the central nervous system. It is very effective but is associated with an increased risk of a serious and potentially fatal viral infection of the brain called progressive multifocal leukoencephalopathy (PML). Regular blood tests for antibodies to the virus that causes PML can help address this risk.
* Ocrelizumab (brand name: Ocrevus®) treats adults with relapsing-remitting, active secondary-progressive, or primary-progressive MS. It is currently the only FDA-approved disease-modifying therapy for primary-progressive MS. The drug targets circulating immune cells (“B cells”) that have many functions, including giving rise to the cells that produce antibodies. Side effects include infusion-related reactions and increased risk of infections. Ocrelizumab may slightly increase the risk of cancer and reduce the effectiveness of some vaccines.
* Alemtuzumab targets proteins on the surface of immune cells. Because this drug increases the risk of autoimmune disorders, it is usually used in those who have not responded sufficiently to two or more MS therapies.

Oral treatments include:

* Fingolimod (brand name: Gilenya®) reduces the MS relapse rate in adults and children. It is the first FDA-approved drug to treat MS in adolescents and children age 10 and older. The drug prevents white blood cells called lymphocytes from leaving the lymph nodes and entering the blood, brain, and spinal cord. Fingolimod may result in a slow heart rate and eye problems when first taken. Fingolimod can also increase the risk of infections, such as herpes virus infections, or in rare cases be associated with PML. Siponimod has a similar mechanism of action to fingolimod. Siponimod has been approved by the FDA to treat secondary-progressive MS.
* Dimethyl fumarate (brand name: Tecfidera®) is used to treat relapsing forms of MS. Its exact mechanism of action is not currently known. Side effects of dimethyl fumarate are flushing (temporary reddening of the skin), diarrhea, nausea, and lowered white blood cell count. Diroximel fumarate (brand name: Vumerity®) is a drug similar to dimethyl fumarate, but with fewer gastrointestinal side effects.
* Teriflunomide (brand name: Aubagio®) reduces the rate of growth in the number of activated immune cells. Teriflunomide side effects can include nausea, diarrhea, liver damage, and hair loss.
* Cladribine (brand names: Mavenclad® and Leustatin® DSC) targets certain types of white blood cells that drive immune attacks in MS. The drug may increase the person’s risk of developing cancer.

Injectable medications include:

* Beta interferon drugs, which were once the most commonly used treatments for MS but are rarely used now. Potential side effects of these drugs include flu-like symptoms (which usually fade with continued therapy), depression, or elevation of liver enzymes.
* Glatiramer acetate, which can reduce the frequency of attacks in relapsing-remitting MS.

Clinical trials have shown that cladribine, diroximel fumarate, and dimethyl fumarate decrease the number of relapses, delay the progression of physical disability, and slow the development of brain lesions.

### Managing MS symptoms

MS causes a variety of symptoms that can interfere with daily activities. Fortunately, many of the symptoms of MS can usually be treated or managed. Neurologists with advanced training in the treatment of MS can prescribe specific medications to treat these problems.

#### *Eye and vision problems*

Eye and vision problems are common in people with MS but rarely result in permanent blindness. Symptoms may include blurred or grayed vision, temporary blindness in one eye, loss of normal color vision, issues with depth perception, or loss of vision in parts of the visual field. Uncontrolled horizontal or vertical eye movements (nystagmus), “jumping vision" (opsoclonus), and double vision (diplopia) are common in people with MS. Vision therapy exercises, special eyeglasses, and resting the eyes may be helpful.

#### *Muscle and mobility problems*

Muscle weakness and spasticity are common in MS. It is very important that people with MS stay physically active because physical inactivity can contribute to worsening stiffness, weakness, pain, fatigue, and other symptoms. Stretching and exercising muscles through water therapy, yoga, or physical therapy (PT) can help manage mild spasticity. Medications can also help reduce spasticity.

Tremor, or uncontrollable shaking, develops in some people with MS. Assistive devices are sometimes helpful for people with tremor. Deep brain stimulation and medications may also help.

Many people with MS have difficulty with balance and walking. The most common walking problem is ataxia—unsteady, uncoordinated movements—due to damage to the areas of the brain that coordinate muscle balance. People with severe ataxia generally benefit from the use of a cane, walker, or other assistive device. Physical therapy can also reduce walking problems. Occupational therapy (OT) can help people learn how to walk using an assistive device or in a way that saves physical energy. The FDA has approved the drug dalfampridine to improve walking speed in people with MS.

#### *Fatigue*

Fatigue is a common symptom of MS and may be both physical (tiredness in the arms or legs) and cognitive (slowed processing speed or mental exhaustion). Daily physical activity programs of mild to moderate intensity can significantly reduce fatigue, although people should avoid excessive physical activity and minimize exposure to high temperatures. PT and OT can sometimes help manage fatigue. PT provides personalized treatments, while OT teaches ways to use energy wisely. They also help find the right changes in the person’s environment. Stress management programs or relaxation training may help some people.

#### *Bladder control and constipation issues*

Problems with bladder control and constipation may include problems with frequency of urination, urgency, or the loss of bladder control. A small number of individuals retain large amounts of urine. Medical treatments are available for bladder-related problems. Constipation is also common and can be treated with a high-fiber diet, laxatives, and stool softeners.

#### *Sexual dysfunction*

Sexual dysfunction can result from damage to nerves running through the spinal cord. Sexual problems may also stem from MS symptoms, including fatigue, muscle symptoms, and psychological factors. Some of these problems can be corrected with medications. Counseling (therapy) may be helpful.

#### *Mental and emotional problems*

Clinical depression is frequent among people with MS. MS may cause depression as part of the disease process and chemical imbalance in the brain. Depression can intensify symptoms of fatigue, pain, and sexual dysfunction. It is most often treated with cognitive behavioral therapy and selective serotonin reuptake inhibitor (SSRI) antidepressant medications, which are less likely than other antidepressant medications to cause fatigue.

Inappropriate and involuntary expressions of laughter, crying, or anger—called pseudobulbar symptoms—are sometimes associated with MS, although this is not as common as in some other neurological disorders. These expressions are often incongruent with mood; for example, people with MS may cry when they are actually happy or laugh when they are not especially happy. The combination treatment of the drugs dextromethorphan and quinidine can treat pseudobulbar affect, as can other drugs such as amitriptyline or citalopram.

#### *Cognitive problems*

Cognitive impairment—a decline in the ability to think, learn, and remember—affects up to 75% of people with MS. These cognitive changes may appear at the same time as the physical symptoms, or they may develop gradually over time. Sometimes, cognitive impairment in people with MS is caused by depression. It is important to rule out depression, first. If cognitive impairment is caused by depression, it can be treated. Drugs such as donepezil may be helpful in some cases.

#### *Complementary approaches*

Some people with MS report improvement in their symptoms from complementary or alternative approaches. These include acupuncture, aromatherapy, ayurvedic medicine, touch and energy therapies, physical movement disciplines such as yoga and tai chi, herbal supplements, and biofeedback

Because of the risk of interactions between alternative and conventional therapies, people with MS should discuss all the therapies they are using with their doctor, especially herbal supplements. Herbal supplements have biologically active ingredients that could have harmful effects on their own or interact harmfully with other medications.

What are the latest updates on multiple sclerosis?

NINDS, a component of the National Institutes of Health (NIH), is the leading federal funder of research on the brain and nervous system, including research on MS. Other components of NIH are funding research on topics relevant to MS, including cognitive impairment, rehabilitation strategies, and telehealth.

Although researchers have not been able to identify the exact cause(s) of MS, there has been excellent progress in other areas of MS research—especially in the development of new treatments to prevent exacerbations of the disease. New discoveries are improving and expanding MS treatment options and helping to reduce MS-related disability.

NINDS-supported research projects cover a wide range of topics. These include co-occurring conditions, mechanisms of cognitive impairment, blood-brain barrier breakdown in MS, the role of sleep and circadian rhythms, rehabilitation strategies, and telehealth. Other topics include:

* Biomarkers to accurately diagnose MS and monitor disease progression and treatment response, including blood and imaging tests
* Genetic and environmental risk factors for MS
* The role of the gut microbiome and diet in MS
* Mechanisms that underlie sex differences in the incidence and presentation of MS
* MS risk factors and disease course in African American and Hispanic populations
* Social determinants of health that influence disease outcome and disparities in care
* The role of the immune system in MS, including its function in the central nervous system
* The role and crosstalk of various cell types in the central nervous system with relation to MS
* Basic functions of myelination, demyelination, and axonal degeneration, and strategies to overcome axonal and myelin loss

Genetic research funded by NINDS is exploring the roles of "susceptibility genes"—genes that are associated with an increased risk for MS. Several candidate genes have been identified and researchers are studying their function in the nervous system to discover how they may lead to the development of MS.

Other studies aim to develop better neuroimaging tools, such as more powerful MRI methods, to diagnose MS, track disease progression, and assess treatments. Investigators are also using MRI to study the natural history of MS and to help define the mechanism of action and cause of side effects of disease modifying therapies.

### Intramural research programs on MS

NINDS and other NIH Institutes have a very active MS intramural research program among scientists working at NIH (known as “intramural” research). Together, they have:

* Established and continue to develop MRI as a critical tool for examining the natural course of MS in humans, monitoring disease progression, assessing effects of treatments in clinical trials, and understanding MS biology.
* Played an important role in understanding why some people develop a rare and potentially fatal brain infection (called progressive multifocal leukoencephalopathy) when taking potent MS drugs. Research teams are now developing new treatments for this infection.
* Unraveled mechanisms by which viruses contribute to the development of MS.
* Conducted next-generation treatment trials targeting specific mechanisms of disease progression, using advanced MRI and fluid biomarkers as outcome measures.
* Developed the first MRI method to visualize the lymph vessels surrounding the brain, which play a critical role in neuro-immune communication.

### Translational research

NIH supports translational studies to develop therapies that will stop or reverse the course of the disease, focusing on pathways that modify immune system function in the peripheral and central nervous system, repair damaged myelin, or protect neurons from damage. Researchers are also developing improved disease models of MS in animals to more accurately predict drug response in human disease.

### Progressive MS therapies

While scientists continue to study relapsing-remitting MS, research is also investigating treatments that slow or prevent the steady decline in function in progressive MS. In the MS-SPRINT trial, the NINDS NeuroNEXT clinical trials network tested the drug ibudilast as a potential neuroprotective drug for progressive MS and showed that the drug slowed the rate of brain shrinkage as compared to a placebo. NINDS intramural scientists are conducting proof-of-concept clinical trials on a key driver of clinical progression called the “chronic active lesion.”

### Biomarkers for MS

As part of a larger effort to develop and validate effective biomarkers (signs that may indicate risk of a disease or be used to monitor its progression) for neurological disease, NINDS is supporting two definitive multicenter MS studies:

1. The Central Vein Sign in MS (CAVS-MS) study, which is testing whether a rapid MRI approach designed by NINDS scientists can use the detection of a central vein passing through brain plaques to differentiate MS from other common neurological disorders that can mimic MS. The goal is to develop a reliable imaging test for MS in order to achieve rapid yet accurate diagnosis and reduce misdiagnosis, which may affect up to 20% of people currently diagnosed with MS.
2. A study to test whether a simple new blood test that measures small amounts of neuron-derived proteins (neurofilaments) can be used to predict the severity of disease and help determine whether MS drugs are working to protect brain tissues.

In addition to NINDS, other NIH Institutes fund research on multiple sclerosis. Find more information on NIH research efforts through NIH RePORTER, a searchable database of current and past research projects supported by NIH and other federal agencies. RePORTER also includes links to publications and patents citing support from these projects.

SOURCE:

* National Institute of Neurological Disorders and Stroke. (2024) *Multiple Sclerosis*. Available at: https://www.ninds.nih.gov/health-information/disorders/multiple-sclerosis (Accessed: 23 May 2025).

MYASTHENIA GRAVIS

## **Overview**

Myasthenia gravis (my-us-THEE-nee-uh GRAY-vis) causes muscles under your voluntary control to feel weak and get tired quickly. This happens when the communication between nerves and muscles breaks down.

There's no cure for myasthenia gravis. Treatment can help with symptoms. These symptoms can include weakness of arm or leg muscles, double vision, drooping eyelids, and problems with speaking, chewing, swallowing and breathing.

This disease can affect people of any age, but it's more common in women younger than 40 and in men older than 60.

## **Symptoms**

Muscle weakness caused by myasthenia gravis gets worse when the affected muscle is used. Because symptoms usually get better with rest, muscle weakness can come and go. However, the symptoms tend to progress over time. They usually reach their worst within a few years after the disease begins.

Myasthenia gravis may affect any of the muscles that you can control. Certain muscle groups are more commonly affected than others.

### Eye muscles

In more than half the people who develop myasthenia gravis, their first symptoms affect the eyes. Symptoms include:

* + Drooping of one or both eyelids, called ptosis.
  + Double vision, called diplopia, which may be horizontal or vertical, and improves or resolves when one eye is closed.

### Face and throat muscles

In about 15% of people with myasthenia gravis, the first symptoms involve face and throat muscles. These symptoms can:

* + **Make speaking difficult.** Your speech might sound soft or nasal, depending on which muscles are affected.
  + **Cause problems with swallowing.** You might choke easily, making it difficult to eat, drink or take pills. Sometimes, liquids you're trying to swallow come out your nose.
  + **Affect chewing.** The muscles used for chewing might tire halfway through a meal. This is especially true if you've been eating something hard to chew, such as steak.
  + **Change facial expressions.** For example, your smile might look like a snarl.

### Neck and limb muscles

Myasthenia gravis also can cause weakness in the neck, arms and legs. Weakness in the legs can affect how you walk. Weak neck muscles make it hard to hold up the head.

### When to see a doctor

Talk to your health care provider if you have problems:

* + Breathing.
  + Seeing.
  + Swallowing.
  + Chewing.
  + Walking.
  + Using your arms or hands.
  + Holding up your head.

## **Causes**

### Antibodies

**Receptors**

Your nerves communicate with your muscles by releasing chemicals, called neurotransmitters, that fit into places on the muscle cells, called receptor sites, at the nerve-muscle junction.

In myasthenia gravis, the immune system makes antibodies that block or destroy many of your muscles' receptor sites for a neurotransmitter called acetylcholine (as-uh-teel-KOH-leen). With fewer receptor sites available, your muscles receive fewer nerve signals. This causes weakness.

Antibodies also can block a protein called muscle-specific receptor tyrosine kinase (TIE-roh-seen KIE-nays), sometimes referred to as MuSK. This protein helps form the nerve-muscle junction. Antibodies against this protein can lead to myasthenia gravis.

Antibodies against another protein, called lipoprotein-related protein 4 (LRP4), can play a part in this condition. Research studies have found other antibodies and the number of antibodies involved will likely grow over time.

Some people have myasthenia gravis that isn't caused by antibodies blocking acetylcholine, MuSK or LRP4. This type of myasthenia gravis is called seronegative myasthenia gravis, also known as antibody-negative myasthenia gravis. In general, researchers believe that this type of myasthenia gravis still comes from a problem with autoimmunity, but the antibodies involved just can't be found yet.

### Thymus gland

**Thymus gland**

The thymus gland is a part of your immune system. This gland is located in the upper chest beneath the breastbone. Researchers believe that the thymus gland makes or helps produce the antibodies that block acetylcholine.

The thymus gland is large in babies and small in healthy adults. In some adults with myasthenia gravis, however, the thymus gland is larger than usual. Some people with myasthenia gravis also have tumors of the thymus gland, called thymomas. Usually, thymomas aren't cancerous, also known as malignant. But thymomas can become cancerous.

### Other causes

Rarely, mothers with myasthenia gravis have children who are born with myasthenia gravis. This is called neonatal myasthenia gravis. If treated immediately, children usually recover within two months after birth.

Some children are born with a rare, hereditary form of myasthenia gravis, called congenital myasthenic syndrome.

Factors that can make myasthenia gravis worse include:

* Fatigue.
* Illness or infection.
* Surgery.
* Stress.
* Some medicines — such as beta blockers, quinidine gluconate, quinidine sulfate, quinine (Qualaquin), phenytoin (Dilantin), certain anesthetics and some antibiotics.
* Pregnancy.
* Menstrual periods.

## **Complications**

Complications of myasthenia gravis are treatable, but some can be life-threatening.

### Myasthenic crisis

Myasthenic crisis is a life-threatening condition. It happens when the muscles that control breathing become too weak to work. Emergency treatment and mechanical assistance with breathing are needed. Medicines and therapies that filter the blood help people to breathe on their own.

### Thymus gland tumors

Some people with myasthenia gravis have a tumor in the thymus gland. The thymus is a gland under the breastbone that is part of the immune system. Most of these tumors, called thymomas, aren't cancerous.

### Other disorders

People with myasthenia gravis are more likely to have the following conditions:

* **Underactive or overactive thyroid.** The thyroid gland in the neck secretes hormones that regulate the metabolism. If the thyroid is underactive, you might have problems dealing with cold, weight gain and other issues. An overactive thyroid can cause problems dealing with heat, weight loss and other issues.
* **Autoimmune conditions.** People with myasthenia gravis might be more likely to have autoimmune conditions, such as rheumatoid arthritis or lupus.

## **Diagnosis**

Your health care provider will look at your symptoms and medical history and conduct a physical examination. Your provider might use several tests, including:

### Neurological examination

Your provider may check your neurological health by testing:

* Reflexes.
* Muscle strength.
* Muscle tone.
* Senses of touch and sight.
* Coordination.
* Balance.

Tests to help confirm a diagnosis of myasthenia gravis might include:

### Ice pack test

If you have a droopy eyelid, your provider might put a bag filled with ice on your eyelid. After two minutes, your provider removes the bag and analyzes your droopy eyelid for improvement.

### Blood analysis

A blood test might show nontypical antibodies that interrupt the receptor sites where nerves signal your muscles to move.

### Repetitive nerve stimulation

In this nerve conduction study, providers attach electrodes to your skin over the muscles to be tested. Small pulses of electricity run through the electrodes. These pulses measure whether the nerve can send a signal to the muscle.

During this test, the nerve is tested several times to see if its ability to send signals gets worse with fatigue. Results from this test help inform a diagnosis of myasthenia gravis.

### Single-fiber electromyography (EMG)

This test measures the electrical activity traveling between your brain and your muscle. It involves inserting a fine wire electrode through your skin and into a muscle to test a single muscle fiber.

### Imaging

Your provider might order a CT scan or an MRI to check if there's a tumor or other problem with your thymus.

### Pulmonary function tests

These tests measure whether your condition is affecting your breathing.

## **Treatment**

Various treatments, alone or together, can help with symptoms of myasthenia gravis. Your treatment will depend on your age, how severe your disease is and how fast it's progressing.

### Medications

* **Cholinesterase inhibitors.** Medicines such as pyridostigmine (Mestinon, Regonal) improve communication between nerves and muscles. These medicines aren't a cure, but they can improve muscle contraction and muscle strength in some people.

Possible side effects include gastrointestinal upset, diarrhea, nausea, and too much salivation and sweating.

* **Corticosteroids.** Corticosteroids such as prednisone (Rayos) block the immune system, making it less able to produce antibodies. Use of corticosteroids over a long period of time, however, can lead to serious side effects. These include bone thinning, weight gain, diabetes and higher risk of some infections.
* **Immunosuppressants.** Your provider also might prescribe other medicines that change your immune system. These medicines could include azathioprine (Azasan, Imuran), mycophenolate mofetil (Cellcept), cyclosporine (Sandimmune, Gengraf, others), methotrexate (Trexall) or tacrolimus (Astagraf XL, Prograf, others). These medicines, which can take months to work, might be used with corticosteroids.

Side effects of immunosuppressants, such as higher risk of infection and liver or kidney damage, can be serious.

### Intravenous therapy

The following therapies are usually used for a short time to treat symptoms that suddenly get worse or before surgery or other therapies.

* **Plasmapheresis (plaz-muh-fuh-REE-sis).** This procedure uses a filtering process that's like dialysis. Your blood is put through a machine that removes the antibodies that block transmission of signals from your nerve endings to your muscles. However, the good effects from this procedure usually last only a few weeks. Having several procedures can lead to problems finding veins for the treatment.

Risks of plasmapheresis include a drop in blood pressure, bleeding, heart rhythm problems or muscle cramps. Some people have an allergic reaction to the solutions used to replace the plasma.

* **Intravenous immunoglobulin (IVIg).** This therapy provides your body with typical antibodies, which alters your immune system response. Benefits are usually seen in less than a week and can last 3 to 6 weeks.

Side effects, which usually are mild, can include chills, dizziness, headaches and fluid retention.

* **Monoclonal antibody.** Rituximab (Rituxan) and eculizumab (Soliris) are medicines given by vein for myasthenia gravis. These medicines are usually used when other treatments don't work. They can have serious side effects.

### Surgery

Some people with myasthenia gravis have a tumor in the thymus gland. If you have a tumor, called a thymoma, you'll need surgery to remove the thymus gland, called thymectomy.

Even if you don't have a tumor in the thymus gland, removing the gland might improve your symptoms. However, the benefits of this surgery can take years to develop.

The thymectomy can be performed as an open surgery or as a minimally invasive surgery. In open surgery, the surgeon splits the central breastbone, called the sternum,) to open the chest and remove the thymus gland.

Minimally invasive surgery to remove the thymus gland uses smaller cuts, called incisions. It might also involve:

* **Video-assisted thymectomy.** In one form of this surgery, surgeons make a small opening in the neck or a few small openings in the side of the chest. They then use a long, thin camera, called a video endoscope, and small instruments to see and remove the thymus gland.
* **Robot-assisted thymectomy.** In this form of thymectomy, surgeons make several small openings in the side of the chest. They use a robotic system to remove the thymus gland. This system includes a camera arm and mechanical arms.

These procedures might cause less blood loss, less pain, lower mortality rates and shorter hospital stays compared with open surgery.

## **Clinical trials**

Explore Mayo Clinic studies testing new treatments, interventions and tests as a means to prevent, detect, treat or manage this condition.

## **Lifestyle and home remedies**

To help you make the most of your energy and cope with the symptoms of myasthenia gravis:

* **Adjust your eating routine.** Try to eat when you have good muscle strength. Take your time chewing your food, and take a break between bites of food. You might find it easier to eat small meals several times a day. Also, try eating mainly soft foods and avoid foods that require more chewing, such as raw fruits or vegetables.
* **Use safety precautions at home.** Install grab bars or railings in places where you need support, such as next to the bathtub or next to steps. Keep your floors clean, and move area rugs. Outside your home, keep paths, sidewalks and driveways cleared of leaves, snow and other debris that could cause you to trip.
* **Use electric appliances and power tools.** To save your energy, try using an electric toothbrush, electric can openers and other electrical tools to perform tasks.
* **Wear an eye patch.** If you have double vision, an eye patch can help. Try wearing one to write, read or watch television. Switch the eye patch to the other eye regularly to help reduce eyestrain.
* **Plan.** If you have chores, shopping or errands to do, plan the activity for when you have the most energy.

## **Coping and support**

Coping with myasthenia gravis can be difficult for you and your loved ones. Stress can make your condition worse, so find ways to relax. Ask for help when you need it.

Learn all you can about your condition, and have your loved ones learn about it as well. You all might benefit from a support group, where you can meet people who understand what you and your family members are going through.

## **Preparing for your appointment**

You're likely to first see your primary care provider, who will then refer you to a doctor trained in nervous system conditions, called a neurologist, for further evaluation.

Here's information to help you get ready for your appointment.

### What you can do

Take a friend or family member along to help you understand the information you're given. Make a list of:

* **Your symptoms** and when they began.
* **All medicines, vitamins or supplements** you take, including doses.
* **Questions to ask** your provider.

For myasthenia gravis, questions to ask your provider include:

* What is likely causing my symptoms?
* What tests do I need?
* What course of action do you recommend?
* What are the alternatives to the approach you're suggesting?
* I have other health conditions. How can I best manage them together?
* Are there restrictions I need to follow?
* Are there brochures or other printed materials I can have? What websites do you recommend?

Don't hesitate to ask other questions.

### What to expect from your doctor

Be prepared to answer questions your provider is likely to ask, such as:

* Have your symptoms been continuous or occasional?
* How severe are your symptoms?
* What, if anything, seems to improve your symptoms?
* What, if anything, appears to worsen your symptoms?

Source:

* Mayo Clinic Staff. (2024) *Myasthenia gravis: Diagnosis and treatment*. Mayo Clinic. Available at: https://www.mayoclinic.org/diseases-conditions/myasthenia-gravis/diagnosis-treatment/drc-20352040 (Accessed: 23 May 2025).

PERIPHERAL NEUROPATHY

Continuing Education Activity

About 2.4% of the population is affected by peripheral neuropathy. The prevalence increases to 8% in older populations. Peripheral neuropathy can be a manifestation of a wide range of pathologies that require further evaluation or treatment. Furthermore, peripheral neuropathies must be addressed before they result in complications, such as falls with subsequent hip fractures or pedal infections necessitating amputation. Interprofessional team members must recognize and evaluate peripheral neuropathy so that any underlying cause can be addressed and complications can be prevented, improving patient outcomes. This activity highlights considerations when evaluating and treating patients with peripheral neuropathies and demonstrates the critical role that interprofessional care teams play in caring for patients suffering from peripheral neuropathies.

**Objectives:**

* Identify the etiology of peripheral neuropathy.
* Determine the appropriate evaluation of a patient with peripheral neuropathy.
* Assess the treatment and management options available for peripheral neuropathy.
* Communicate the importance of improving care coordination amongst the interprofessional team to enhance care delivery for patients with peripheral neuropathy.

Introduction

Peripheral neuropathies encompass disorders of peripheral nerve cells and fibers, manifesting secondary to a wide range of pathologies. These include cranial nerves, spinal nerve roots and ganglia, nerve trunks and division, and autonomic nervous system nerves. Several methods classify peripheral neuropathies, including mononeuropathies, multifocal neuropathies, and polyneuropathies. Further subclassifications can be made by separating peripheral neuropathies as axonal, demyelinating, or mixed, essential for treatment and management. The most frequently encountered symptoms of peripheral neuropathy include numbness and paresthesias; pain, weakness, and loss of deep tendon reflexes may accompany these symptoms. Peripheral neuropathies usually develop over months to years, while some may develop more rapidly and be progressive. Peripheral neuropathies have a broad range of severity and clinical manifestations, as they can affect motor, sensory, and autonomic fibers.

Etiology

Peripheral neuropathies stem from a variety of origins, including metabolic, systemic, and toxic causes. Underlying etiologies to consider include:

* Diabetes mellitus
* Chronic alcoholism
* Nutritional deficiencies (eg, B1, B6, B12, and vitamin E)
* Inflammatory conditions (eg, vasculitis)
* Hypothyroidism
* Autoimmune disease (eg, Sjögren syndrome, lupus, rheumatoid arthritis)
* Infections (eg, Lyme disease, Epstein-Barr virus, hepatitis C, shingles, leprosy, HIV)
* Guillain-Barre syndrome
* Toxins (heavy metals, chemicals)
* Chemotherapy agents
* Medications (antibiotics, cardiovascular medications)
* Tumors (secondary to compression or associated paraneoplastic syndromes)
* Inherited conditions (eg, Charcot-Marie-Tooth disease, familial amyloidosis)
* Trauma or injury
* Multiple myeloma and its treatments
* Monoclonal gammopathy of undetermined significance (MGUS)

In some cases, a direct cause may not be apparent.

Epidemiology

About 2.4% of the world population is affected by peripheral nerve disorders; the prevalence increases to 8% in older populations. Diabetic neuropathy occurs in approximately half of individuals with chronic type 1 and type 2 diabetes. Globally, leprosy remains a common cause of peripheral neuropathy, with the highest prevalence in Southeast Asia.

The most common genetic sensorimotor polyneuropathy is Charcot-Marie-Tooth disease, specifically, type 1a. The most common mononeuropathy is carpal tunnel syndrome.

Pathophysiology

The exact pathophysiology of peripheral neuropathy depends on the underlying disease. Although a wide assortment of distinct diseases can ultimately lead to peripheral neuropathies, the mechanisms by which peripheral nerves suffer injury exhibit similar patterns.

**Segmental Demyelination**

Segmental demyelination refers to the degeneration of the myelin sheath, with sparing of the nerve axon. This type of reaction can present in mononeuropathies, sensorimotor, or, principally, motor neuropathies. These are often inflammatory and sometimes immune-mediated. About 20% of symmetrical peripheral neuropathies result from damage to the myelin. Examples include Charcot-Marie-Tooth and neuropathy associated with monoclonal gammopathy of undetermined significance.

**Wallerian Degeneration**

Wallerian degeneration occurs after a nerve axon degenerates due to a lesion or physical compression; the portion distal to the axon passively wastes away, likely due to a lack of nutrients from the cell body. This reaction results in focal mononeuropathy that is secondary to trauma or infarction of the nerve. Wallerian degeneration is immunohistochemically distinct by the localization of neuropeptide Y-Y1 receptor markers.

**Axonal Degeneration**

Axonal degeneration, also known as the dying-back phenomenon: This type of degeneration usually manifests as symmetrical polyneuropathy (around 80%) and tends to cause weakness, most notably weakness in dorsiflexion of the ankles and foot, with accompanied trophic changes to muscle. The axon degenerates in a pattern that starts distal and progresses proximally; this is thought to be because the most distal portion of the axon is particularly vulnerable due to its distance from the cell body, which provides metabolic support. A proposed mechanism is that insult to the nerve causes impaired delivery of local axonal survival factors, resulting in an increased level of calcium intra-axonal, leading to a calcium-dependent cytoskeletal breakdown. Examples of diseases causing axonal degeneration include diabetes, HIV, hepatitis C virus, and Guillain-Barre syndrome.

History and Physical

The clinical presentation of peripheral neuropathy widely varies depending on the underlying disease process. Patients may complain of symptoms initially starting in their digits and progressing to their proximal limbs. Symptoms range and include changes in sensation, weakness, atrophy, pain, numbness, and even autonomic disturbances. Clinically, these symptoms may resemble those of myelopathies, radiculopathies, autoimmune diseases, and diseases of muscles. Advanced disease may progress to reduced or absent deep tendon reflexes, stocking-glove pattern sensory loss, muscle wasting, and weakness. Obtaining a thorough history is vital in helping to uncover the primary cause of neuropathy. Aside from a meticulous review of past medical history, providers should inquire about toxic exposures, present and past medications, trauma, dietary and nutritional deficiencies, and alcohol use.

Evaluation

Evaluating patients with neuropathy involves a detailed history and physical, including a review of current and past medications. Although there are no standard laboratory or imaging studies to test for peripheral neuropathies, the following studies may aid in the diagnosis and help narrow down the underlying cause of the neuropathy (eg, inflammatory, infectious, metabolic):

* Complete blood count (macrocytic anemia may clue the clinician to vitamin B12 or folate deficiency, or even alcohol abuse)
* Metabolic panels such as basic metabolic panel or complete metabolic panel (look for electrolyte imbalances contributing to neuropathy and renal failure as uremia can also lead to neuropathy).
* Hemoglobin A1c Testing (Diabetes is a common cause of neuropathy)
* Testing for vitamin and mineral deficiencies such as copper, thiamine, pyridoxine, folate, B12, and vitamin E play fundamental roles in nervous system development and maintenance.
* Heavy metal toxicities such as mercury, lead, and arsenic are known to cause peripheral nerve toxicities along with CNS disturbances
* Infectious workup for Lyme disease, Epstein-Barr virus, hepatitis C, HIV, and syphilis as a long-standing disease may manifest with peripheral neuropathies and paresthesias
* Thyroid function testing
* Antibody testing for specific autoimmune diseases known to cause peripheral neuropathies, such as Sjögren syndrome, lupus, and rheumatoid arthritis
* Nerve conduction study and electromyography
* MRI or CT scans in cases where compression of the nerve is of concern
* Nerve biopsy
* Genetic testing (for inherited neuropathies)
* Urine Test (looking for Bence-Jones proteins as multiple myeloma and its treatments can cause peripheral neuropathy)

Treatment / Management

Treatment of peripheral neuropathies should focus on the treatment of the underlying disease process. For example, glucose control in diabetic neuropathy and alcohol cessation in alcoholic neuropathy. Nutritional deficiencies can be treated with the supplementation of depleted vitamins or minerals. Unfortunately, not all peripheral neuropathies are reversible. Physical and occupational therapy can be initiated to aid in improving a patient's overall strength and function. Chronic inflammatory demyelinating neuropathy is initially treated using corticosteroids but can also be treated using intravenous immunoglobulin, plasma exchange, and some immunosuppressant drugs.

A referral to a pain specialist can be beneficial for those patients who are suffering from neuropathic pain. Neuropathic pain, particularly in those suffering from small-fiber neuropathies, does not typically respond to simple analgesics. Instead, effective treatment for pain associated with peripheral neuropathies can be with membrane stabilizers, certain anti-epileptics, and tricyclic antidepressants. Transcutaneous electrical nerve stimulation (TENS) is also an option as a noninvasive intervention for pain relief.

Differential Diagnosis

Differentials to consider greatly vary depending on clinical presentation. Symptoms of peripheral neuropathies may resemble those of myelopathies, radiculopathies, autoimmune diseases, and diseases of muscles.

Prognosis

In those diseases where peripheral nerves suffer damage through Wallerian or axonal degeneration, the prognosis is poorer, as the recovery of the nerve is more challenging. The axon must regenerate itself and reinnervate the affected muscle or organ for clinical improvement. The prognosis of diseases that occur secondary to segmental demyelination is more favorable because remyelination is achieved more quickly, allowing the return of function of the axon.

Complications

Complications of peripheral neuropathies include pain, altered sensation, muscle atrophy, and weakness. Diabetic peripheral neuropathy is infamous for complications, including foot ulcers, which can lead to gangrenous digits and limbs, sometimes progressing to amputation.

Consultations

Consultations and referrals to consider for patients suffering from peripheral neuropathy include:

* Neurologist
* Chronic pain physician
* Physical therapy
* Occupational therapy
* Endocrinologist
* Rheumatologist
* Psychiatry and addiction medicine (for those with alcohol-induced peripheral neuropathy)
* Infectious disease specialist
* Surgeon (for neuropathy secondary to compression)
* Hematology or oncology (for those with neuropathy related to cancer)

Deterrence and Patient Education

Patients require education on the signs and symptoms of peripheral neuropathy. Patients should be made aware that they have an increased risk of injury due to loss of sensation; they should be conscious of any new cuts or damage to their skin as wound healing can be delayed, and the risk for infection increases. Recommend always wearing socks with closed-toed shoes to decrease the risk of infection. Patients should take caution when exposing themselves to hot or cold environments to avoid burns and frostbite. Patients with diabetes should receive counseling on managing their diabetes appropriately. Patients with alcohol-induced neuropathy should get information on cessation.

Pearls and Other Issues

* Charcot-Marie-Tooth is the most commonly inherited cause of peripheral neuropathy
* Demyelinating neuropathies are commonly inflammatory and often treatable
* Neurophysiological tests can differentiate axonal from demyelinating neuropathies
* Overall, the most common polyneuropathy is diabetic sensorimotor polyneuropathy
* Peripheral neuropathy can be divided into mono-neuropathies, multifocal neuropathies, and polyneuropathies, with further subclassifications into axonal, demyelinating, or mixed types.
* Neuropathic pain can be effectively treated with membrane stabilizers, certain antiepileptics, and tricyclic antidepressants

Enhancing Healthcare Team Outcomes

A wide range of disease processes can lead to peripheral neuropathies, which routinely require an interprofessional team approach to diagnosis and treatment. This team should include physicians, specialists, specialty-trained nurses, and, when necessary, pharmacists, all working collaboratively to achieve optimal patient care and outcomes. Neuropathies can be both painful and debilitating for patients. Thus, it is vital to acquire a prompt diagnosis of the underlying condition followed by the initiation of appropriate treatment(s) to reverse, slow, or stop the progression of the disease. Identifying patients most at risk for neuropathies and implementing a preventative approach to their care can undoubtedly improve outcomes for patients, as seen in the case of diabetic neuropathy. As primary care providers and nurse practitioners are often the first to work with these patients, they must be familiar with the full range of etiologies that play a role in developing peripheral neuropathies, including testing and referrals to the appropriate specialists.

Source:

* Singh, V.N. and Waseem, M. (2024) *Peripheral Neuropathy*. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing. Available at: https://www.ncbi.nlm.nih.gov/books/NBK542220/ (Accessed: 23 May 2025).

PERIPHERAL NEUROPATHY

## **Overview**

Peripheral neuropathy happens when the nerves that are located outside of the brain and spinal cord (peripheral nerves) are damaged. This condition often causes weakness, numbness and pain, usually in the hands and feet. It also can affect other areas and body functions including digestion and urination.

The peripheral nervous system sends information from the brain and spinal cord, also called the central nervous system, to the rest of the body through motor nerves. The peripheral nerves also send sensory information to the central nervous system through sensory nerves.

Peripheral neuropathy can result from traumatic injuries, infections, metabolic problems, inherited causes and exposure to toxins. One of the most common causes of neuropathy is diabetes.

People with peripheral neuropathy usually describe the pain as stabbing, burning or tingling. Sometimes symptoms get better, especially if caused by a condition that can be treated. Medicines can reduce the pain of peripheral neuropathy.

## **Symptoms**

Every nerve in the peripheral system has a specific job. Symptoms depend on the type of nerves affected. Nerves are divided into:

* Sensory nerves that receive sensation, such as temperature, pain, vibration or touch, from the skin.
* Motor nerves that control muscle movement.
* Autonomic nerves that control functions such as blood pressure, sweating, heart rate, digestion and bladder function.

Symptoms of peripheral neuropathy might include:

* Gradual onset of numbness, prickling, or tingling in your feet or hands. These sensations can spread upward into your legs and arms.
* Sharp, jabbing, throbbing or burning pain.
* Extreme sensitivity to touch.
* Pain during activities that shouldn't cause pain, such as pain in your feet when putting weight on them or when they're under a blanket.
* Lack of coordination and falling.
* Muscle weakness.
* Feeling as if you're wearing gloves or socks when you're not.
* Inability to move if motor nerves are affected.

If autonomic nerves are affected, symptoms might include:

* Heat intolerance.
* Excessive sweating or not being able to sweat.
* Bowel, bladder or digestive problems.
* Drops in blood pressure, causing dizziness or lightheadedness.

Peripheral neuropathy can affect one nerve, called mononeuropathy. If it affects two or more nerves in different areas, it's called multiple mononeuropathy, and if it affects many nerves, it's called polyneuropathy. Carpal tunnel syndrome is an example of mononeuropathy. Most people with peripheral neuropathy have polyneuropathy.

### When to see a doctor

Seek medical care right away if you notice unusual tingling, weakness, or pain in your hands or feet. Early diagnosis and treatment give you the best chance for controlling your symptoms and preventing further damage to your peripheral nerves.

## **Causes**

Peripheral neuropathy is nerve damage caused by several different conditions. Health conditions that can cause peripheral neuropathy include:

* **Autoimmune diseases.** These include Sjogren's syndrome, lupus, rheumatoid arthritis, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy and vasculitis. Also, some cancers related to the body's immune system can cause polyneuropathy. These are a form of autoimmune disorder called paraneoplastic syndrome.
* **Diabetes and metabolic syndrome.** This is the most common cause. Among people with diabetes, more than half will develop some type of neuropathy.
* **Infections.** These include certain viral or bacterial infections, including Lyme disease, shingles, hepatitis B and C, leprosy, diphtheria, and HIV.
* **Inherited disorders.** Disorders such as Charcot-Marie-Tooth disease are hereditary types of neuropathy that run in families.
* **Tumors.** Cancerous growths, also called malignant, and noncancerous growths, also called benign, can grow on or press on nerves.
* **Bone marrow disorders.** These include a protein in the blood that isn't usually there, called monoclonal gammopathies, a rare form of myeloma that affects the bones, lymphoma and the rare disease amyloidosis.
* **Other diseases.** These include metabolic conditions such as kidney disease or liver disease, and an underactive thyroid, also known as hypothyroidism.

Other causes of neuropathies include:

* **Alcohol use disorder.** Unhealthy dietary choices made by people with alcohol use disorder, also known as alcoholism, and poor absorption of vitamins can lead to low amounts of essential vitamins in the body.
* **Exposure to poisons.** Toxic substances include industrial chemicals and heavy metals such as lead and mercury.
* **Medicines.** Certain medicines, especially chemotherapy used to treat cancer, can cause peripheral neuropathy.
* **Injury or pressure on the nerve.** Injuries, such as from motor vehicle accidents, falls or sports injuries, can sever or damage peripheral nerves. Nerve pressure can result from having a cast or using crutches or repeating a motion such as typing many times.
* **Low vitamin levels.** B vitamins, including B-1, B-6 and B-12, as well as copper and vitamin E are crucial to nerve health.

In some cases, no cause can be identified. This is called idiopathic peripheral

## **Risk factors**

Peripheral neuropathy risk factors include:

* Diabetes, especially if your sugar levels are not controlled well.
* Alcohol misuse.
* Low levels of vitamins in the body, especially vitamin B-12.
* Infections, such as Lyme disease, shingles, hepatitis B and C, and HIV.
* Autoimmune diseases, such as rheumatoid arthritis and lupus, in which the immune system attacks your own tissues.
* Kidney, liver or thyroid disorders.
* Exposure to toxins.
* Repetitive motion, such as those performed for certain jobs.
* Family history of neuropathy.

## **Complications**

Complications of peripheral neuropathy can include:

* **Burns, skin injuries and wounds on the feet.** You might not feel temperature changes or pain on parts of your body that are numb.
* **Infection.** Your feet and other areas that lack sensation can become injured without your knowing. Check these areas regularly, wear close-toed, well-fitting shoes and treat minor injuries before they become infected, especially if you have diabetes.
* **Falls.** Weakness and loss of sensation may be associated with lack of balance and falling. Installing handrails in the bathroom, using canes or walkers when needed, and ensuring that you are walking only in well-lit rooms can decrease fall risk.

## **Prevention**

### Manage underlying conditions

The best way to prevent peripheral neuropathy is to manage medical conditions that put you at risk.

### Make healthy lifestyle choices

These habits support your nerve health:

* **Eat a diet rich in fruits, vegetables, whole grains and lean protein to keep nerves healthy.** Protect against low levels of vitamin B-12 by eating meats, fish, eggs, low-fat dairy foods and fortified cereals. If you're vegetarian or vegan, fortified cereals are a good source of vitamin B-12, but talk to your health care professional about B-12 supplements.
* **Exercise regularly.** With a health care professional's OK, try to get at least 30 minutes to one hour of exercise at least three times a week.
* **Avoid factors that may cause nerve damage.** These factors can include repetitive motions, exposure to toxic chemicals, smoking and drinking too much alcohol.

## **Diagnosis**

Peripheral neuropathy has many possible causes. Besides a physical exam, which may include blood tests, diagnosis usually requires:

* **A full medical history.** Your health care professional will look at your medical history. The history will include your symptoms, lifestyle, exposure to toxins, drinking habits and a family history of nervous system, or neurological, diseases.
* **Neurological exam.** Your care professional might check your tendon reflexes, muscle strength and tone, ability to feel certain sensations, and balance and coordination.

### Tests

A health care professional may order tests, including:

* **Blood tests.** These can detect low levels of vitamins, diabetes, signs of inflammation or metabolic issues that can cause peripheral neuropathy.
* **Imaging tests.** CT or MRI scans can look for herniated disks, pinched nerves, also called compressed nerves, growths or other problems affecting the blood vessels and bones.
* **Nerve function tests.** Electromyography (EMG) measures and records electrical activity in your muscles to find nerve damage. A thin needle (electrode) is inserted into the muscle to measure electrical activity as you contract the muscle.

During an EMG, a nerve conduction study is typically also done. Flat electrodes are placed on the skin and a low electric current stimulates the nerves. A health care professional will record how the nerves respond to the electric current.

* **Other nerve function tests.** These might include an autonomic reflex screen. This test records how the autonomic nerve fibers work. Other tests can include a sweat test that measures your body's ability to sweat and sensory tests that record how you feel touch, vibration, cooling and heat.
* **Nerve biopsy.** This involves removing a small portion of a nerve, usually a sensory nerve, to try to find the cause of the neuropathy.
* **Skin biopsy.** A small portion of skin is removed to look at the number of nerve endings.

## **Treatment**

Treatment goals are to manage the condition causing your neuropathy and to improve symptoms. If your lab tests show no condition that's causing the neuropathy, your health care professional might recommend watchful waiting to see if your neuropathy stays the same or gets better.

### Medicines

Medicines can be used to treat conditions associated with peripheral neuropathy. There also are medicines used to improve peripheral neuropathy symptoms. These medicines include:

* **Pain relievers.** Medicines available without a prescription, such as nonsteroidal anti-inflammatory drugs, can improve mild symptoms.
* **Anti-seizure medicines.** Medicines such as gabapentin (Gralise, Neurontin, Horizant) and pregabalin (Lyrica), developed to treat epilepsy, often improve nerve pain. Side effects can include drowsiness and dizziness.
* **Topical treatments.** Lidocaine cream that is available without a prescription can be applied to the skin.

Lidocaine patches are another treatment you apply to the skin to improve pain. Side effects can include drowsiness, dizziness and numbness at the site of the patch.

* **Antidepressants.** Certain tricyclic antidepressants, such as amitriptyline and nortriptyline (Pamelor), can help improve pain. These medicines interfere with chemical processes in the brain and spinal cord that cause you to feel pain.

The serotonin and norepinephrine reuptake inhibitor duloxetine (Cymbalta) and the extended-release antidepressants venlafaxine (Effexor XR) and desvenlafaxine (Pristiq) also might improve peripheral neuropathy pain caused by diabetes.

Side effects of antidepressants may include dry mouth, nausea, drowsiness, dizziness, changes in appetite, weight gain and constipation.

### Therapies

Various therapies and procedures might help with the symptoms of peripheral neuropathy.

* **Scrambler therapy.** This treatment uses electrical impulses to send nonpain messages to the brain. These messages replace the pain messages the nerves send to the brain. The goal is to retrain the brain to think there is no pain.
* **Spinal cord stimulation.** This type of therapy works through devices put into the body. These devices are called neurostimulators. They send low-level electrical impulses that can block pain signals from reaching the brain.
* **Plasma exchange, steroids and intravenous immune globulin.** These treatments are often used if inflammation or autoimmune conditions are causing neuropathy with weakness, numbness or imbalance. These therapies are not used to treat pain alone.
* **Physical therapy.** If you have muscle weakness or issues with balance, physical therapy can help improve your ability to move. You also may need hand or foot braces, a cane, a walker, or a wheelchair.
* **Surgery.** Neuropathies caused by pressure on nerves, such as from tumors, might require surgery.

## **Alternative medicine**

Some people with peripheral neuropathy try complementary treatments for relief. Researchers haven't studied these techniques as thoroughly as they have most medicines. But the following therapies have shown some promise:

* **Acupuncture.** Inserting thin needles into various points on your body might lower peripheral neuropathy symptoms. You might need multiple sessions before you see improvement. Acupuncture is generally considered safe when done by a certified practitioner using sterile needles.
* **Alpha-lipoic acid.** This has been used as a treatment for peripheral neuropathy in Europe for years and there is some evidence that it can be helpful in those with painful diabetic neuropathy. Discuss using alpha-lipoic acid with your health care professional because it can affect blood sugar levels. Other side effects can include stomach upset and skin rash.
* **Amino acids.** Amino acids, such as acetyl-L-carnitine, might benefit people who have undergone chemotherapy and people with diabetes. Side effects might include nausea and vomiting.

## **Lifestyle and home remedies**

To help you manage peripheral neuropathy:

* **Take care of your feet, especially if you have diabetes.** Check daily for blisters, cuts or calluses. Wear soft, loose cotton socks and padded shoes. You can use a semicircular hoop, which is available in medical supply stores, to keep bedcovers off hot or sensitive feet.
* **Exercise.** Regular exercise, such as walking three times a week, can lower neuropathy pain, improve muscle strength and help control blood sugar levels. Gentle routines such as yoga and tai chi also might help. If you have painful neuropathy in your feet, you may want to try pool-based exercise such as swimming.
* **Quit smoking.** Cigarette smoking can cause problems with circulation. This increases the risk of foot problems and other neuropathy complications.
* **Eat healthy meals.** Good nutrition is especially important to make sure that you get important vitamins and minerals. Include fruits, vegetables, whole grains and lean protein in your diet.
* **Avoid excessive alcohol.** Alcohol can make peripheral neuropathy worse.
* **Monitor your blood sugar levels.** If you have diabetes, this will help keep your blood sugar under control and might help improve your neuropathy.

## **Preparing for your appointment**

You're likely to start by seeing your health care professional. You may then be referred to a doctor trained in nervous system disorders, also called a neurologist.

Here's information to help you get ready for your appointment.

### What you can do

When you make the appointment, ask if there's anything you need to do in advance, such as fasting for a specific test. Make a list of:

* **Your symptoms,** including any that may seem like they're not related to your reason for scheduling the appointment.
* **Key personal information,** including recent stresses or major life changes, family medical history and alcohol use.
* **All medicines,** vitamins or other supplements you take, including doses.
* **Questions to ask** your health care professional.

Take a family member or friend along, if possible, to help you remember the information you're given.

For peripheral neuropathy, basic questions to ask include:

* What's the most likely cause of my symptoms?
* Are there other possible causes?
* What tests do I need?
* Is this condition temporary or long lasting?
* What treatments are available, and which do you recommend?
* What side effects can I expect from treatment?
* Are there alternatives to the approach you're suggesting?
* I have other health conditions. How can I best manage them together?
* Do I need to limit activities?
* Are there brochures or other printed material I can take? What websites do you recommend?

Don't hesitate to ask other questions.

### What to expect from your doctor

Your health care professional is likely to ask you questions, such as:

* Do you have health conditions, such as diabetes or kidney disease?
* When did your symptoms begin?
* Have your symptoms been continuous or occasional?
* How severe are your symptoms?
* Does anything seem to improve your symptoms?
* What, if anything, appears to worsen your symptoms?
* Does anyone in your family have symptoms similar to yours?
* Have you fallen in the past year?
* Have you had any injuries to your feet?

Source:

* Mayo Clinic Staff. (2024) *Peripheral neuropathy: Diagnosis and treatment*. Mayo Clinic. Available at: https://www.mayoclinic.org/diseases-conditions/peripheral-neuropathy/diagnosis-treatment/drc-20352067 (Accessed: 23 May 2025).

**Myopathy**

Myopathy is a general term that refers to diseases that affect the muscles that connect to your bones (skeletal muscles). Myopathies may be passed on in families (inherited) or they may develop later in life (acquired). People living with myopathy may have difficulty performing activities of daily living like bathing, combing their hair or standing up from a chair.

**Overview**

**What is myopathy?**

Myopathy refers to diseases that affect skeletal muscles (muscles that connect to your bones). These diseases attack muscle fibers, making your muscles weak.

**Are there different types of myopathies?**

Myopathy can be categorized by its cause. Basically, myopathies are separated into two categories: inherited and acquired.

**Inherited myopathies**

**Inherited myopathies**are those that you’re born with, often from inheriting an abnormal gene mutation from a parent that causes the disease. Conditions that are inherited myopathies include:

**Congenital myopathies**

Symptoms of congenital myopathies usually start at birth or in early childhood, but may not appear until the teen years or even later in adulthood. Congenital myopathies are somewhat unique compared with other inherited myopathies, as weakness typically affects all muscles (not just the ones closest to the center of your body) and is often not progressive.

**Mitochondrial myopathies**

Mitochondrial myopathy is caused by a defect in the mitochondria, which are the energy-producing part of cells. These conditions have muscle weakness, but also a variety of other symptoms, as mitochondrial disorders typically affect other organ systems like your heart, brain and gastrointestinal tract. Diseases in this group can be caused by gene mutations with or without a family history.

**Metabolic myopathies**

Defects in genes that code for enzymes that are needed for normal muscle function and movement cause metabolic myopathies. They often show as exercise intolerance, exertional muscle pains in your shoulders and thighs, or non-traumatic rhabdomyolysis (muscle fiber condition). These can also happen with episodes of weakness that come and go with other times of normal strength.

**Muscular dystrophies**

Muscular dystrophies are characterized by progressive degeneration of muscle tissue due to abnormal or insufficient structural support proteins being present. They all involve your arms and/or legs to varying degrees, and some involve the muscles of your eyes or face.

**Acquired myopathies**

**Acquired myopathies** develop later in life and can be due to other medical disorders, infections, exposure to certain medications or electrolyte imbalances, among other possibilities. Conditions that are acquired myopathies include:

**Autoimmune/inflammatory myopathy**

Autoimmune/inflammatory myopathies are diseases in which your body attacks itself, causing problems with muscle function.

**Toxic myopathy**

Toxic myopathy happens when a toxin or medication interferes with muscle structure or function.

* **Toxins:**Alcohol and toluene (a vapor in spray paint and other substances that can be inhaled by people who abuse substances).
* **Medications:** Checkpoint inhibitor immunotherapy (pembrolizumab, nivolumab), corticosteroids (prednisone), cholesterol-lowering drugs (statins), amiodarone, colchicine, chloroquine, antivirals and protease inhibitors used in the treatment of HIV infection, omeprazole.

**Endocrine myopathies**

Endocrine myopathies happen when hormones interfere with muscle function.

* **Thyroid:** Low thyroid (hypothyroidism) is more common, but increased thyroid (hyperthyroidism) can also be problematic.
* **Parathyroid:** Hyperparathyroidism resulting in increased calcium levels.
* **Adrenal:** Addison’s disease and Cushing syndrome.

**Infectious myopathies**

Infectious myopathies occur as the result of infections that affect muscle function. These include:

* Viral infections like HIV, influenza, Epstein-Barr.
* Bacterial pyomyositis.
* Lyme disease.
* Parasitic infections like trichinosis, toxoplasmosis, cysticercosis.
* Fungal infections like Candida, Coccidiomycosis.

**Electrolyte imbalance**

High or low levels of the following electrolytes can interfere with muscle function:

* **Potassium:** Hypokalemia (low), hyperkalemia (high).
* **Magnesium:** Hypermagnesemia (high).

**Critical illness myopathy**

Critical illness myopathy is a disease of your limbs and the muscles that help you breathe (respiratory muscles). It develops while you’re being cared for in an intensive care unit, and may be caused in part by being in bed for a long period of time (prolonged immobility), or by the medications used during your care, such as muscle relaxants, corticosteroids or sedatives.

**Symptoms and Causes**

**Who gets myopathy and how common is it?**

Anyone can get a myopathy.

Factors that might increase your risk include:

* **Having a family history of myopathy.** This increases the likelihood you might inherit an abnormal gene that causes muscle disease.
* **Being male.** Some myopathies are carried on the X chromosome, and actually affect more men than women. Other inherited forms of myopathy carried on other chromosomes affect everyone equally.
* **Having an autoimmune, metabolic or endocrine disorder.**
* **Being exposed to certain medications or toxins** (see toxic myopathy below for a list of some of these medications).

How common myopathies are depends on their type. In acquired myopathies, for example:

* Inflammatory and endocrine myopathies are more common than other types and are more common in females than males.
* The number of people diagnosed with inflammatory myopathy is between 9 and 32 per 100,000.
* Anywhere from 25% to 79% of adults with hypothyroidism will develop muscle symptoms; though, overt myopathy might be as low as 10%.

The most common inherited myopathies are muscular dystrophies and these are typically more common in males.

* Duchenne’s and Becker’s muscular dystrophies are the most common, with 7 per 100,000 people worldwide.
* Mitochondrial disorders affect 1 in 5,000 people, and most affect skeletal muscle. Other forms of inherited myopathies are rare.

**What are the symptoms of myopathy?**

Many myopathies share common symptoms. These common symptoms include:

* Muscle weakness, most commonly of your upper arms and shoulders and thighs (more common and more severe).
* Muscle cramps, stiffness and spasms.
* Fatigue with exertion.
* Lack of energy.

**What does myopathy feel like?**

Most myopathies share the common symptom of symmetric muscle weakness (similar on both sides of your body), especially in proximal muscles. Proximal muscles are those closest to the center of your body, such as the muscles in your shoulders, upper arms, hips and thighs. This can lead to the following:

* Difficulty performing activities of daily living such as bathing, dressing or combing your hair.
* Trouble getting out of a chair, climbing stairs or performing tasks that require reaching over your head, like changing a ceiling light bulb.
* Muscle cramps or spasms.
* Muscle fatigue with activity.
* Shortness of breath with exertion.

The muscles in your hands or feet aren’t usually affected.

Other symptoms vary depending on the type of myopathy.

* Muscle weakness can be either non-progressive, or very slowly progressive.
* In some disorders, muscle weakness is intermittent with other normal periods of strength.
* Slow development of skills requiring the use of muscles in children (such as walking, hopping, climbing stairs or grasping a spoon or pencil).
* Children who can’t keep up with their peers during sports or games like tag.
* Trouble with the muscles that control your swallowing and speech, which can lead to choking and slurring of words.

**Diagnosis and Tests**

**What do I do if I think I have myopathy?**

You should first contact your primary care doctor to alert them to the symptoms you’re concerned about. Depending on the nature of your symptoms, you might be referred to a specialist such as a neurologist or a rheumatologist.

**How is myopathy diagnosed?**

Your healthcare provider will ask about your medical and family history, prescription drug history and your symptoms. Your healthcare provider will conduct a physical exam, which will include an exam of your skin, reflexes, muscle strength, balance, and sensation.

Tests your healthcare provider may order include:

* Blood tests:
  + Muscle enzymes such as creatine kinase (CK) or aldolase may be elevated in certain myopathies as a result of the breakdown of muscle fibers.
  + Electrolyte levels such as sodium, magnesium, potassium, calcium and phosphorus.
  + Autoimmune disease testing such as antinuclear antibodies (ANA), rheumatoid factor, sedimentation rate and c-reactive protein.
  + Endocrine testing such as thyroid hormone.
* Electromyography (EMG and nerve conduction studies), including testing the electrical conduction of your nerves and needle examination of your muscles to assess the type and degree of muscle damage.
* Magnetic resonance imaging (MRI) of your muscles.
* Genetic tests.
* Muscle biopsy, in which your healthcare provider surgically removes a small piece of muscle tissue for testing.

**Management and Treatment**

**How is myopathy treated?**

After determining your specific type of myopathy, your healthcare provider will develop a treatment plan specific to your symptoms.

Most treatments include physical therapy, occupational therapy and some form of exercise. Other treatments are more specific and based on the type of myopathy. In general, most acquired myopathies can be well controlled and treated to minimize weakness and symptoms. Some inherited myopathies have specific treatments that can stop the progression of the disease. At the present time, most inherited myopathies don’t have specific treatments, but people can benefit from physical therapy and certain types of exercise.

**Inflammatory and autoimmune-related myopathies**

The goal of treatment is to decrease inflammation and your body’s autoimmune response. These myopathies are often treated with:

* Immunomodulatory/immunosuppressant drugs such as methotrexate, cyclosporine, tacrolimus, azathioprine, mycophenolate, rituximab and intravenous (IVIg) or subcutaneous (SubQIg) immunoglobulin.
* Corticosteroids such as prednisone or methylprednisolone.

**Inherited and genetic myopathies**

Most inherited and genetic myopathies don’t have a specific treatment or cure. Management is largely based on symptom control and different forms of therapy. There are multiple ongoing clinical trials in various areas of research looking at treatments and gene therapy.

Duchenne muscular dystrophy and Pompe disease are disorders that can be treated with specific medication.

**Other acquired myopathies**

Healthcare providers manage acquired myopathies including endocrine, toxic and infectious myopathies by treating the underlying disease causing the myopathy. Toxin-related myopathies are treated by stopping the offending agent (alcohol or toluene, for example) or medication (statins, for example). Muscle symptoms that result from infections caused by bacteria, viruses or other infectious organisms are improved by treating the infection directly with antibiotics.

**Living With**

**How do I take care of myself?**

Although myopathy is a long-term (chronic) disease whether inherited or acquired, you can take steps to improve your health to help control your illness. These might include:

* Eat a healthy, well-balanced diet full of a variety of fruits and vegetables.
* Stay active with mild cardiovascular exercise. It may be recommended to avoid certain types of weight lifting depending on your myopathy type, and you should discuss this with your doctor prior to starting any exercise routine.
* Maintain a healthy weight.
* If you have a dermatomyositis rash, protect your skin from sunlight, which can worsen the rash. Wear full-cover clothing and a hat when able. Be sure to apply sunscreen with a sun-protective factor (SPF) of at least 30 before going outdoors.
* If you have trouble swallowing, eat soft or semisolid foods. Consider pureeing your food. If you’re bedbound, eat sitting up in bed.
* Take all medications as prescribed.
* Participate in your therapies if recommended — physical, occupational or speech.

Source

Cleveland Clinic (2022) *Myopathy: Causes, Symptoms, Diagnosis & Treatment*. Available at: https://my.clevelandclinic.org/health/diseases/17256-myopathy (Accessed: 5 June 2025).

# **Lambert-Eaton myasthenic syndrome**

**Lambert-Eaton myasthenic syndrome (LEMS) is a rare condition that affects the signals sent from the nerves to the muscles.**

It means the muscles are unable to tighten (contract) properly, resulting in muscle weakness and a range of other symptoms.

More than half of LEMS cases occur in middle-aged or older people with lung cancer. The remaining cases are not associated with cancer and can start at any age.

LEMS is also known as myasthenic syndrome or Eaton-Lambert syndrome.

## **Symptoms of LEMS**

The symptoms of LEMS develop gradually over weeks or months.

The main symptoms are weakness in the legs, arms, neck and face, as well as problems with automatic body functions, such as controlling blood pressure.

Common symptoms include:

* aching muscles
* feeling very tired all the time (fatigue)
* difficulty walking and climbing stairs
* difficulty lifting objects or raising the arms
* drooping eyelids, dry eyes and blurred vision
* swallowing problems
* dizziness upon standing
* a dry mouth
* constipation
* erectile dysfunction
* muscle weakness that gets worse with time

See a GP if you have a combination of these symptoms.

## **Causes of LEMS**

LEMS is caused by the body's natural defences (the immune system) mistakenly attacking and damaging the nerves.

Normally, nerve signals travel down the nerves and stimulate the nerve endings to release a chemical called acetylcholine. This chemical then helps activate the muscles.

If the nerve endings are damaged, the amount of acetylcholine they produce decreases, which means nerve signals do not reach the muscles properly.

It's not known what triggers the immune system to attack the nerves. It's often associated with lung cancer, but can occur in people without cancer.

## **Tests for LEMS**

The GP will first check your medical history, ask about your symptoms, carry out a physical examination, and test your reflexes.

If they think you have a problem with your nerves, they may refer you to a specialist called a neurologist for further tests to determine the cause.

Tests you may have include:

* **blood tests** – a blood test can detect substances in the blood (antibodies) resulting from the immune system attacking the nerves
* **nerve studies** – a needle may be inserted into your skin to check how well signals are reaching the muscles from the nerves
* **scans** – you may have a CT scan or PET scan to check for lung cancer

If initial scans do not find cancer, you may be advised to have regular scans every few months for a few years to check that it does not develop later on.

## **Treatments for LEMS**

There's currently no cure for LEMS, but a number of treatments can help reduce the symptoms.

These include:

* **treatment for lung cancer** – if you have lung cancer, treating it can significantly improve the symptoms of LEMS
* **medicine to help nerve signals reach the muscles** – commonly used medicines include 3,4-diaminopyridine and pyridostigmine
* **medicine to reduce the activity of the immune system (immunosuppressants)** – commonly used medicines include steroid tablets (such as prednisolone), azathioprine and methotrexate
* **plasmapheresis** – a procedure to redirect your blood through a machine that filters out the antibodies attacking your nerves
* **immunoglobulin therapy** – injections of antibodies from donated blood that temporarily stop your immune system attacking your nerves

Medicine is the main treatment, although plasmapheresis and immunoglobulin therapy may be recommended in the short term, or if muscle weakness is severe and other treatments have not helped.

## **Outlook for LEMS**

Some people respond well to treatment and find that treatment helps keep their symptoms under control.

Others respond less well and find the condition affects their everyday activities and quality of life.

LEMS does not affect life expectancy if it's not associated with cancer. But people with lung cancer and LEMS tend to have a shorter life expectancy because by this point it's very difficult to treat.

Source

NHS (2023) *Lambert-Eaton myasthenic syndrome*. Available at: https://www.nhs.uk/conditions/lambert-eaton-myasthenic-syndrome/ (Accessed: 5 June 2025).

SPINAL CORD DISORDERS

Spinal cord injury

Key facts

* **Globally, over 15 million people are living with spinal cord injury (SCI).**
* **Most SCI cases are due to trauma, including falls, road traffic injuries or violence, and are thus preventable.**
* **People with SCI are at risk of developing debilitating and even life-threatening secondary conditions, which can cause premature mortality.**
* **SCI is associated with lower school enrolment and economic participation rates, carrying substantial individual and societal costs.**
* **Effective prevention, treatment, rehabilitation, and ongoing health care are essential to alleviate the global burden of SCI.**

## **Overview**

The term spinal cord injury (SCI) refers to damage to the spinal cord resulting from trauma (e.g. from falls and road traffic injuries) or non-traumatic causes like tumors, degenerative and vascular conditions, infections, toxins or birth defects.

The extent of SCI related impairment depends on injury severity and location in the spinal cord. SCI results in complete or incomplete loss of sensory and/or motor functions below injury level. In paraplegia arm functions are preserved; in tetraplegia they are affected. Autonomic nervous system dysfunction affecting diverse functions can occur at any level of injury.

Inappropriate management of SCI related impairments and secondary conditions often causes premature mortality.

SCI can diminish the capacity to perform daily activities, including walking, using one’s hands, physiological emptying of bowel/bladder or washing and dressing oneself. Limitations are compounded by misconceptions, negative attitudes and physical barriers to basic mobility, restricting independence and full societal participation. SCI is a major cause of long-term disability, accounting for over 4.5 million years of life lived with disability (YLDs) in 2021.

Importantly, many restrictions in performing activities and participating in meaningful life areas do not result from the condition itself, but from insufficient or inadequate medical care, rehabilitation and assistive technologies access, a high economic burden, and from barriers in the physical, social and policy environments. For example, globally, only 5–35% have wheelchair access.

## **Scope of the problem**

Global estimates suggest that in 2021, approximately 15.4 million people were living with SCI.

Males are more commonly affected by SCI than females, with consistently higher prevalence and YLDs attributed to this demographic.

Life expectancy in people with SCI strongly correlates with neurological impairment and preventable secondary conditions. People with SCI often die earlier because of health system factors such as insufficient access to or poor quality health services. For people with SCI, the in-hospital mortality rate is nearly three times higher in low- and middle-income countries than in high-income countries.

Misconceptions, negative attitudes and mobility barriers prevent many individuals from full societal participation. Children with SCI are less likely than their peers to start school, and once enrolled, less likely to advance. Adults with SCI face similar barriers to economic participation, with unemployment rates exceeding 60%.

Many people with SCI, their carers and families face substantial social and economic consequences. While existing data limit global cost estimates of SCI, its economic burden is significant. Indirect costs (for example, lost earnings) often exceed direct costs, which are highest in the first year after SCI onset, with much of the cost borne by people with SCI.

## **Signs and symptoms**

Depending on injury severity and location, people with SCI can experience

* partial or complete loss of sensory and/or motor functions (including respiratory muscle functions)
* bowel, bladder and sexual dysfunction
* dysregulation of blood pressure, heart rate, and/or body temperature.

SCI is often associated with a risk of developing complications, including debilitating and potentially life-threatening secondary conditions, such as

* spasticity
* (chronic) pain
* urinary tract infections
* pressure ulcers
* respiratory complications
* autonomic dysreflexia
* deep vein thrombosis
* osteoporosis.

Furthermore, people with SCI may develop clinical signs of depression, negatively impacting functional improvements and overall health.

Mortality risk is highest in the first year after injury, remaining high compared to the general population.  Injury level and severity, availability of timely, quality medical care, transfer method to hospital after injury and time to hospital admission are important factors.

## **Cause, risk factors and prevention**

Traumatic SCIs from falls and road traffic accidents are the leading cause of SCI, followed by violence (including self-harm and attempted suicide) and work or sports-related injuries. Emergencies can also result in surges in SCI. Earthquakes, for example, can cause increases in SCI due to blunt trauma; conflicts may cause surges in penetrating injuries. Non-traumatic SCIs are also increasing, specifically in ageing populations, given increases in non-communicable diseases such as tumors, degenerative and vascular conditions that can cause spinal cord damage.

Effective interventions are available to prevent many causes of traumatic SCI. These include improvements in road infrastructure, vehicles and people’s road behaviors to avoid road traffic accidents, window guards to prevent falls, policies to thwart the harmful use of alcohol and access to firearms to reduce violence, and domestic violence and suicide prevention strategies (including equitable mental health services). Prevention of non-traumatic SCI includes early diagnosis and treatment of the underlying health condition.

The prevention, early diagnosis and treatment of SCI related secondary conditions are essential to increase life expectancy.

## **Treatment, rehabilitation and management**

Timely access to prehospital management, emergency and acute care and rehabilitation is essential to ensure survival and restore optimal levels of functioning, aimed at minimizing long-term disability. Long-term management is indispensable to maintain functioning and to prevent secondary conditions and premature mortality. Essential measures include the following:

* timely, appropriate pre-hospital management: quick recognition of suspected SCI, rapid evaluation and initiation of injury management, including spine immobilization, as needed;
* acute care (including surgical intervention) appropriate to injury type and severity, degree of instability, presence of neural compression, and in accordance with the person’s and their family’s wishes;
* access to acute, post-acute and ongoing multidisciplinary rehabilitation including mental health services to address the existing impairments and optimize functioning, independence, community integration including vocational reintegration, and overall well-being;
* access to assistive products that enable people to perform everyday activities they otherwise couldn’t are essential to increase functioning and independency;
* access to ongoing health care to detect and manage complications and reduce risks of secondary conditions; and
* specialized knowledge on SCI and skills among medical care and rehabilitation providers.

Persons with disabilities such as SCI continue to experience substantial health inequities. According to the Convention on the Rights of Persons with Disabilities, Member States must ensure that persons with SCI can access the same range, quality and standard of free or affordable health care and social support as others. Addressing inequities is essential to realize this mandate.

## **Self-care**

Appropriate self-management is indispensable to manage SCI related impairments, restore optimal levels of functioning and prevent secondary conditions. Self-management requires competencies to apply effective self-care strategies as independently as possible and implement a healthy lifestyle.

However, people with more severe SCI often require ongoing care and support provided largely by informal carers. Challenges for carers include stress, role strain, financial burden, social isolation, lack of community services and bereavement in the event of loss of loved ones. Caring for a person with SCI may affect the carer’s own health, well-being and social relationships. Effective carer support and self-care interventions for health can significantly alleviate carer strain and enhance quality of care and participation of people with SCI.

Self-care interventions provided by health workers aim to empower people with SCI and their families to care for their health, prevent secondary conditions, maintain optimal levels of functioning, and foster coping strategies.

## **WHO response**

WHO works across the spectrum from primary prevention of SCI, improving trauma care, strengthening health and rehabilitation services, and supporting inclusion of people with SCI. Major initiatives include the following.

* The Intersectoral global action plan on epilepsy and other neurological disorders 2022–2031 addresses the challenges and gaps in providing care and services for people with neurological disorders like SCI that exist worldwide, ensuring a comprehensive, coordinated response across sectors.
* WHO serves as the secretariat for the United Nations Decade of Action for Road Safety 2021–2030, aimed at reducing road traffic deaths and injuries by at least 50% by 2030. This includes convening a global network of heads of national road safety agencies, producing global status reports, and providing technical assistance.
* WHO supports efforts to address injuries and violence in many ways. Activities include technical country support and monitoring progress towards the Sustainable Development Goal targets linked to injury, violence prevention, mental health and substance use through global status reports on road safety, violence prevention, and alcohol and health, and world reports on preventing suicide – amongst other actions.
* In 2017, WHO launched Rehabilitation 2030, emphasizing health system strengthening and calling for stakeholders worldwide to: improve leadership and governance; develop a strong multidisciplinary rehabilitation workforce; expand financing for rehabilitation; and improve data collection and research on rehabilitation. The WHO Package of interventions for rehabilitation, Module 3 Neurological conditions provides specific guidance on evidence-based and essential interventions for rehabilitation for SCI. Furthermore, WHO launched the World Rehabilitation Alliance (WRA) to support the Rehabilitation 2030 Initiative through advocacy.
* WHO has included specific guidance on SCI care in its Emergency Medical Teams publications, and in emergencies often works with Member States and partners to improve the care available for people with new SCI.

Source:

* World Health Organization. (2023) *Spinal cord injury*. Available at: https://www.who.int/news-room/fact-sheets/detail/spinal-cord-injury (Accessed: 23 May 2025).

**Spinal Stenosis**

**What is spinal stenosis?**

Spinal stenosis is the narrowing of one or more spaces within your spinal canal. Your spinal canal is the tunnel that runs through each of the vertebrae in your spine. It contains your spinal cord. Less space within your spinal canal cramps your spinal cord and the nervesthat branch off it (nerve roots).

A tightened space can cause your spinal cord or nerves to become irritated, compressed or pinched. This can lead to back pain and other nerve issues, like sciatica. Several conditions and injuries can lead to a narrowed spinal canal.

Spinal stenosis can affect anyone, but it’s most common in people over the age of 50.

The condition most commonly affects two areas of your spine:

* **Lower back (lumbar spinal stenosis)**: Your lumbar spine consists of five bones (vertebrae) in your lower back. Your lumbar vertebrae, known as L1 to L5, are the largest of your entire spine.
* **Neck (cervical spinal stenosis)**: Your cervical spine consists of seven vertebrae in your neck. These vertebrae are labeled C1 to C7.

Your middle back (thoracic spine) can also have spinal stenosis, but this is rare.

**How common is spinal stenosis?**

Spinal stenosis is fairly common. Degenerative spinal changes affect up to 95% of people by the age of 50. Spinal stenosis is one of those changes. For people over 65 undergoing spine surgery, lumbar spinal stenosis is the most common diagnosis.

**Symptoms and Causes**

**What are the symptoms of spinal stenosis?**

Depending on where and how severe your spinal stenosis is, you might feel the following in your neck, back, arms, legs, hands or feet:

* Pain
* Numbness.
* Tingling.
* Weakness.

Spinal stenosis usually develops slowly over time. For this reason, you may not have any symptoms for a while, even if it shows up on X-rays or other imaging tests. Symptoms may come and go and affect each person differently.

**Symptoms of lumbar spinal stenosis**

Symptoms of lumbar (low back) spinal stenosis include:

* Pain in your low back.
* Pain that begins in your buttocks and extends down your leg. It may continue into your foot.
* A heavy feeling in your legs, which may lead to cramping in one or both legs.
* Numbness or tingling (“pins and needles”) in your buttocks, leg or foot.
* Pain that worsens when you stand for long periods of time, walk or walk downhill.
* Pain that lessens when you lean forward, walk uphill or sit.

**Symptoms of cervical spinal stenosis**

You can feel symptoms of cervical spinal stenosis anywhere below the point of the nerve compression in your neck. Symptoms include:

* Neck pain.
* Numbness or tingling in your arm, hand, leg or foot.
* Weakness or clumsiness in your arm, hand, leg or foot.
* Balance problems.
* Decreased function in your hands, like having issues writing or buttoning shirts.

**What does spinal stenosis pain feel like?**

Pain from spinal stenosis can feel different from person to person. Some describe it as a dull ache or tenderness. Others describe it as an electric-like or burning sensation. The pain can come and go.

**What causes spinal stenosis?**

Spinal stenosis has several causes. Many different changes or injuries in your spine can cause a narrowing of your spinal canal. The causes are split into two main groups:

* Acquired (developing after birth).
* Congenital (from birth).

Acquired spinal stenosis is more common. It usually happens from “wear and tear” changes that naturally occur in your spine as you age. Only 9% of cases result from congenital causes.

**Acquired causes of spinal stenosis**

Acquired spinal stenosis means you develop it later in life (after birth) — most commonly after the age of 50. These cases usually happen from an injury or changes in your spine that occur as you age (degenerative changes).

Causes of acquired spinal stenosis include:

* **Bone overgrowth**: Osteoarthritis is the “wear and tear” condition that breaks down the cartilage in your joints, including your spine. Cartilage is the protective covering of joints. As your cartilage wears away, your bones begin to rub against each other. Your body responds by growing new bone. Bone spurs, or an overgrowth of bone, commonly form. Bone spurs on your vertebrae extend into your spinal canal, narrowing the space and pinching nerves in your spine. Paget’s disease of the bone can also cause an overgrowth of bone in your spine.
* **Bulging or herniated disks**: Between each vertebra is a flat, round cushioning pad (vertebral disk) that acts as a shock absorber. As you age, the disks can dry out and flatten. Cracking in the outer edge of the disks can cause the gel-like center to break through. The bulging disk then presses on the nerves near the disk.
* **Thickened** **ligaments**: Ligaments are the fiber bands that hold your spine together. Arthritis can cause ligaments to thicken over time and bulge into your spinal canal.
* **Spinal** **fractures** **and injuries**: Broken or dislocated bones in your vertebrae or near your spine can narrow your canal space. Inflammation from injuries near your spine can also cause issues.
* **Spinal cysts or** **tumors**: Growths within your spinal cord or between your spinal cord and vertebrae can narrow your spinal canal.

**Congenital causes of spinal stenosis**

Congenital spinal stenosis affects babies and children. It can happen due to:

* Issues with spine formation during fetal development.
* Genetic (inherited) conditions that affect bone growth. These are due to genetic mutations(changes).

Some congenital causes of spinal stenosis include:

* **Achondroplasia**: A bone growth disorder that results in dwarfism due to a genetic mutation.
* **Spinal dysraphism**: When the spine, spinal cord or nerve roots don’t form properly during fetal development. Spina bifida and other neural tube defects are examples.
* **Congenital** **kyphosis**: When your child’s spine curves outward more than it should. As a result, their upper back looks overly rounded. This happens due to an issue with fetal spine development.
* **Congenital short pedicles**: When your baby is born with vertebrae pedicles (the bony “sides” of the spinal canal) that are shorter in length. This decreases their spinal canal size.
* **Osteopetrosis**: A rare genetic condition that causes your child’s bones to grow abnormally and become overly dense.
* **Morquio syndrome:** A rare genetic condition that affects your child’s bones, spine and other body systems.
* **Hereditary multiple exostoses (diaphyseal aclasis)**: A rare genetic condition that causes several small bone growths (protrusions). They can grow on your child’s vertebrae and affect their spinal canal.

**Diagnosis and Tests**

**How is spinal stenosis diagnosed?**

Your healthcare provider will review your medical history, ask about your symptoms and do a physical exam. Your provider may feel your spine, pressing on different areas to see if it causes pain. They’ll likely ask you to bend in different directions to see if certain spine positions bring on symptoms.

You’ll also have imaging tests so your provider can “see” your spine and determine the exact location, type and extent of the problem. These tests may include:

* **Spine X-ray**: X-rays use a small amount of radiation and can show changes in bone structure. For example, they can show a loss of disk height or bone spurs.
* **MRI**: Magnetic resonance imaging (MRI) uses radio waves and a powerful magnet to create cross-sectional images of your spine. MRI provides detailed images of your nerves, disks and spinal cord. It can reveal any tumors as well.
* **CT scan** **or CT** **myelogram**: A computed tomography (CT) scan is a combination of X-rays that creates cross-sectional images of your spine. A CT myelogram uses a contrast dye so your provider can more clearly see your spinal cord and nerves.

**Management and Treatment**

**What is the treatment for spinal stenosis?**

There are many treatment options for spinal stenosis. What’s best for you depends on:

* The cause.
* The location of the issue.
* The severity of your symptoms.

If your symptoms are mild, your healthcare provider may recommend at-home care first. If these methods don’t work and as symptoms worsen, your provider may recommend physical therapy, medications, injections and, finally, surgery.

**At-home care for spinal stenosis**

At-home care may include:

* **Applying heat**: Heat usually is the better choice for osteoarthritis pain. Heat increases blood flow, which relaxes your muscles and relieves aching joints. Be careful when using heat — a high heat setting can burn you.
* **Applying cold**: If heat isn’t easing your symptoms, try ice, like an ice pack, frozen gel pack or a frozen bag of peas. Apply the ice for 20 minutes on and 20 minutes off. Ice reduces swelling, tenderness and inflammation.
* **Exercising**: Check with your healthcare provider first, but exercise can help relieve pain. It also strengthens your muscles to support your spine and improves your flexibility and balance.

**Nonsurgical treatment for spinal stenosis**

Nonsurgical treatments mainly help manage symptoms of spinal stenosis. They include:

* **Oral medications**: Over-the-counter nonsteroidal anti-inflammatory medications (NSAIDs) can help relieve inflammation and provide pain relief from spinal stenosis. Be sure to talk with your provider to learn about the possible long-term problems of taking these medicines. Your provider may also recommend prescription medications with pain-relieving properties. These may include the antiseizure medication called gabapentin or tricyclic antidepressants, like amitriptyline. If you have muscle cramps or spasms, muscle relaxants may help.
* **Physical therapy**: Physical therapists will work with you to develop a back-healthy exercise program to help you gain strength and improve your balance, flexibility and spine stability. Strengthening your back and abdominal muscles (your core) will make your spine more resilient. Physical therapists can teach you how to walk in a way that opens up your spinal canal, which can help ease pressure on your nerves.
* **Steroid injections**: Getting corticosteroid injections in the space around pinched spinal nerves may help reduce inflammation, pain and irritation.

**Surgery for spinal stenosis**

Spinal stenosis is complex, and your spine is a delicate area. Because of this, providers consider surgery only if all other treatment options haven’t worked. Fortunately, most people who have spinal stenosis don’t need surgery.

Types of spine surgery include:

* **Laminectomy** **(decompression surgery)**: This is the most common type of surgery for spinal stenosis. It involves removing the lamina, which is a portion of your vertebra. The surgeon may also remove some ligaments and bone spurs. The procedure makes more room for your spinal cord and nerves.
* **Laminotomy**: This is a partial laminectomy. The surgeon only removes a small part of the lamina — the area causing the most pressure on the nerve.
* **Laminoplasty**: This surgery is just for your neck (cervical spinal stenosis). The surgeon removes part of the lamina to provide more canal space. They use metal plates and screws to create a hinged bridge across the area where they removed bone.
* **Foraminotomy**: The foramen is the area in your vertebrae where the nerve roots exit. This procedure involves removing bone or tissue in this area to provide more space for the nerve roots.
* **Interspinous process spacers**: This is a minimally invasive surgery for some people with lumbar spinal stenosis. The surgeon inserts spacers between the bones that extend off the back of each vertebrae called the spinous processes. The spacers help keep your vertebrae apart, creating more space for nerves.
* **Spinal fusion**[:](https://health.clevelandclinic.org/is-spinal-fusion-right-for-you/) Healthcare providers use spinal fusion as a last option. They only consider it if you have radiating nerve pain from spinal stenosis, your spine is not stable and other treatments haven’t helped. Spinal fusion surgery permanently joins (fuses) two vertebrae together.

**Prevention**

**Can I prevent spinal stenosis?**

As most causes of spinal stenosis are normal age-related “wear and tear” conditions, you can’t totally prevent spinal stenosis. But you can take certain steps to keep your spine healthy. They may help lower your risk or slow the progression of spinal stenosis. These steps include:

* Eating healthy foods. Be sure you’re getting enough calcium in your diet to keep your bones strong.
* Maintaining a weight that’s healthy for you.
* Avoiding smoking or quitting smoking. Smoking damages your arteries, which can contribute to back pain and make it difficult for any injuries to heal.
* Practicing good posture.
* Exercising regularly. Keeping your muscles strong, especially your back and core muscles, helps to keep your spine healthy.

**Outlook / Prognosis**

**What is the prognosis for spinal stenosis?**

The prognosis (outlook) for spinal stenosis varies based on several factors, like:

* Its location.
* Its severity.
* Your overall health.

In most cases, the prognosis for spinal stenosis is good. Many people with spinal stenosis can live full and active lives with nonsurgical treatment. But it’s important to remember that spinal stenosis affects each person differently, so not every treatment works for everyone.

**What are the complications of spinal stenosis?**

In severe cases, spinal stenosis can cause a loss of bladder or bowel control (incontinence). It can also cause sexual dysfunction due to nerve issues, like erectile dysfunction or anorgasmia.

It’s very rare, but extreme cases of spinal stenosis can cause partial or complete leg paralysis.

**Living With**

**When should I see my healthcare provider about spinal stenosis?**

If you notice new back pain or other symptoms, like tingling or weakness in your extremities, talk to a healthcare provider.

If you’re receiving treatment for spinal stenosis and it’s not working to help your symptoms, talk to your provider about other options.

**Source:**

* Cleveland Clinic. (2024) *Spinal Stenosis*. Available at: https://my.clevelandclinic.org/health/diseases/17499-spinal-stenosis (Accessed: 23 May 2025).

HERNIATED DISK

Could I Have a Herniated Disk?

Back pain can sneak up on you when you least expect it. One minute you're sitting comfortably in front of the TV, and the next you try to stand up, and a sharp pain radiates through your lower back.

Could you have a slipped or herniated disk? You might.

A herniated disk happens when there's a tear or puncture in a disk in your spine. Your doctor can help diagnose your herniated disk and recommend appropriate treatment. (Photo Credit: Science Photo Library/Getty Images)

The adult spine is made of 24 bones called vertebrae. Between the vertebrae are disks, which allow the spine to move and bend. Inside each disk is a soft, jelly-like center called the nucleus pulposus. The outer band is called the annulus fibrosus. In the case of a herniated disk, the outer band of your disk becomes torn or punctured, causing the inner nucleus to leak into the spinal canal.

Herniated disk vs. bulging disk

A herniated disk can often be confused with a bulging disk. While these conditions have some similar symptoms, they do differ. A herniated disk happens when the outer layer of the disk becomes ruptured, often during an acute, sudden injury. For bulging disks, it's possible to happen due to injury, but often it's because the soft center of each disk begins to wear down and deflate gradually as you age. Multiple disks can be affected at the same time and cause other spine-related issues.

Herniated and bulging disks share the following symptoms, depending on the location of the disk:

Pain in lower back, buttocks, leg (lumbar spine)

Pain in the neck, shoulder, arm (cervical spine)

Numbness, tingling, weakness

Some differences between the conditions include:

Herniated disk Bulging disk

Acute, sudden injury

Disk covering has a hole or tear

May affect one spinal disk at a time

Usually happens to people ages 30 to 50, and it's more common in men

Progressive, degenerative condition

Disk decompresses and presses outward

Can happen to multiple disks at the same time

Generally happens around age 40 and older

Herniated Disk Symptoms

If you have a herniated disk, you may not have any symptoms. Symptoms vary depending on the injury's severity and the disk's location. Symptoms include:

Numbness or tingling

Sharp, burning, or shooting pain in the lower back, buttocks, leg, calf, or foot (lower back herniated disk)

Sharp, burning, or shooting pain in the arm or shoulder (neck herniated disk)

Muscle weakness surrounding the area of pain

Symptoms located on one side of the body

If you don't have symptoms, your herniated disk may appear on a spinal image.

What does a herniated disk feel like?

Herniated disks can occur in any area of the spine, but they are most common in the lower back (the lumbar spine), just above the hips. The pain may spread from the back to the buttocks, thighs, and even your calves.

Herniated disks in the neck (the cervical spine) may extend to the shoulder and arm. Pain in the lumbar or cervical spine can feel sharp or burning. It's common to have numbness and tingling that affects the area of pain and then radiates through a nearby limb. You'll likely feel weakened muscles near the source of pain, too.

Discomfort from a herniated disk usually worsens when you're active and lessens when you're resting. Even coughing, sneezing, and sitting can worsen your symptoms because they put pressure on pinched nerves.

Herniated disk emergency symptoms

While a herniated disk can often be treated at home, there are occasions when you need to seek emergency medical care. If your pain becomes so severe you're unable to do daily activities, it’s time to see the doctor. Seek emergency care immediately if you experience any of the following after an injury:

Leg or arm weakness

Infection or fever

Loss of feeling in the rectum or genital area

Bladder or bowel dysfunction

If you have a history of metastatic cancer, it's also important to have your condition checked by a doctor.

Herniated Disk Diagnosis

The best way to tell if you have a herniated disk is to see your doctor. They’ll likely do a physical exam to find the source of your pain, which is usually the only test you’ll need to confirm a diagnosis. Your doctor will check your back or neck for sore or painful spots. They may ask you to lie on your back and lift or move your legs or neck in various directions.

They may also check:

Your reflexes at the knee and ankle(for lower back pain) or your arms and shoulders (for neck pain)

Your leg or arm strength, depending on the area of pain

How you walk on your heels and toes

Whether you can feel light touches or vibrations

RELATED:

Tips for Traveling When You Have Back Pain

If your doctor wants to rule out other sources of your pain or pinpoint specific nerves that are aggravated, they may do further testing, including:

X-rays. While a standard X-ray can't show if you have a herniated disk, it can show your doctor the outline of your spine and rule out whether your pain is caused by something else, such as a fracture or tumor.

Myelogram. This test uses dye injected into your spinal fluid and an X-ray to locate the pressure on the spinal cord.

CT scan. A computerized tomography (CT) scan takes several X-rays from different angles and combines them to create images of your spinal cord and the structures surrounding it.

MRI. Magnetic resonance imaging (MRI) uses radio waves, a magnetic field, and a computer to create detailed 3D images of the spinal cord and surrounding areas. MRI images can locate the position of the herniated disk, look inside it, and determine which nerves are affected.

Electromyogram (EMG). Your doctor might use these tests to see if any nerves are damaged or compressed. The EMG test uses a device to detect the tiny amount of electricity muscle cells make when stimulated by nerves connected to them. A needle electrode put into a muscle records its electrical activity and looks for anything that isn’t as it should be.

Nerve conduction studies (NCS). NCS are often done simultaneously with the EMG. In this test, an electrode stimulates the nerves with tiny electrical impulses at one point on the body while other electrodes detect the impulses at a different point. The time it takes for the electrical impulses to travel between electrodes tells your doctor whether there is nerve damage.

Takeaways

A sudden injury can cause a herniated disk. Symptoms include sharp or burning pain at the point of injury, numbness, tingling, and weakness. A herniated disk in the lower back can trigger traveling pain into the buttocks, hip, and leg. A herniated disk in the neck can trigger pain in the shoulder and arm. Your doctor can help diagnose your herniated disk and may recommend treatment including rest, anti-inflammatory drugs, and physical therapy. Most cases of a herniated disk resolve within a few weeks or months. If your pain continues, talk to your doctor about further treatment.

Do herniated disks heal on their own?

Typically, a herniated disk will heal with rest, time, and an occasional over-the-counter anti-inflammatory medicine. It's important to avoid triggering exercises and activities during your healing process. If the pain isn’t resolved within 6 months, your doctor may prescribe physical therapy. Surgery is typically not recommended unless your doctor detects spinal compression or your daily movement is severely restricted.

What is the fastest way to heal a herniated disk?

The fastest way to heal a herniated disk is to avoid triggering activities, to rest, and to take an over-the-counter anti-inflammatory medicine. During the initial onset, apply ice to help ease pain. In the days and weeks following, heat can help relax and soothe sore muscles. Try incorporating short walks, gentle stretches, and stabilizing exercises, but only if they help reduce pain, not worsen it. If your symptoms don’t get better within a few weeks, speak with your doctor.

**How do I know if I have herniated my disk?**

The only way to know if you have a herniated disk is to see your doctor for an examination and diagnosis. During your exam, your doctor will guide you through various movements to assess your range of motion and strength.

Your doctor may also run diagnostic tests. An electromyogram (EMG) will help find the exact nerve root that is triggered. A myelogram can show the size and location of the herniated disk. An MRI or CT scan can show where the herniated disk is putting pressure on the spine. A nerve conduction test can reveal any possible nerve damage. A spinal X-ray may be used to see if other physical issues are connected to the herniated disk, although it won’t show a herniated disk alone.

**Do you have a herniated disk for life?**

Most people recover from a herniated disk within a few weeks or months. If the pain lingers, your doctor may prescribe pain relief medications and muscle relaxants or give you a steroid shot. Physical therapy can help reduce pain, build supportive muscles around the area of injury, and teach correct posture and alignment to reduce the chances

SOURCES:

* WebMD Editorial Team. (2024) *Do I Have a Herniated Disk?*. Reviewed by [Name of Reviewer, e.g., Aimee Gallo, MD if available]. WebMD. Available at: https://www.webmd.com/pain-management/do-i-have-a-herniated-disk (Accessed: 23 May 2025).

**INFECTIONS OF THE NERVOUS SYSTEM**

# **Meningitis**

## **Key facts**

* Meningitis is a devastating disease that can be deadly and often results in serious long-term health issues.
* Meningitis remains a major global public health challenge.
* Many organisms can cause meningitis, including bacteria, viruses, fungi and parasites.
* Bacterial meningitis is of particular concern. Around 1 in 6 people who get this type of meningitis die and 1 in 5 have severe complications.
* Epidemics of meningitis are seen across the world, particularly in sub-Saharan Africa.
* Vaccines are the most effective way to deliver long-lasting protection.

## **Overview**

Meningitis is the inflammation of the tissues surrounding the brain and spinal cord. It can be infectious or non-infectious in origin, can be associated with high risk of death and long-term complications, and requires urgent medical care.

Meningitis remains a significant global health threat. It can be caused by several species of bacteria, viruses, fungi and parasites. Injuries, cancers and drugs cause a small number of cases.

Bacterial meningitis is the most serious type of meningitis. It is a severe, life-threatening condition that can often lead to long-term adverse health consequences. There are four main causes of acute bacterial meningitis:

* *Neisseria meningitidis* (meningococcus)
* *Streptococcus pneumoniae* (pneumococcus)
* *Haemophilus influenzae*
* *Streptococcus agalactiae* (group B streptococcus).

These bacteria are responsible for more than half of the deaths from meningitis globally and can cause other severe diseases like sepsis and pneumonia.

Additional important causes of meningitis worldwide include other bacteria species (e.g. *Mycobacterium tuberculosis*, non-typhoidal *Salmonella spp*, Listeria monocytogenes), viruses (e.g. enteroviruses, herpesviruses an arboviruses), fungi (e.g. *Cyptococcus spp.),*and parasites (e.g. some species of amoebae).

## **Who is at risk?**

Meningitis can affect anyone anywhere, and at any age. The pathogens that cause it can vary, based on a person’s age and immune system, and level of exposure to risk, which can be influenced by their living conditions and geographical location.

Newborn babies are most at risk from Group B streptococcus, whereas children and adolescents are at most risk of meningococcus, pneumococcus and *Haemophilus influenzae*. Pneumococcus and meningococcus also account for most cases of bacterial meningitis among adults.

Immunocompromised and/or people living with HIV are at increased risk of different types of meningitis.

Globally, the highest burden of disease is seen in a region of sub-Saharan Africa, known as the African meningitis belt, which stretches from Senegal to Ethiopia, and is at high risk of recurrent epidemics of meningococcal meningitis.

Meningococcal meningitis outbreaks occur more frequently under special risk conditions, such as crowded settings where people are in close proximity, mining areas, mass gatherings, such as religious or sporting events, settings with refugees or displaced persons, closed institutions, military camps and areas with high migration, such as high-traffic markets and border areas.

## **Transmission**

The route of transmission varies by organism. Most bacteria that cause meningitis, including meningococcus, pneumococcus and *Haemophilus influenzae*, are carried in the human nose and throat. They are spread from person to person by respiratory droplets or throat secretions. Group B streptococcus is often carried in the human gut or vagina and can spread from mother to child around the time of birth.

Carriage of these organisms is usually harmless and contributes to building up immunity against infection, but the bacteria occasionally invade the body, causing meningitis, sepsis and other forms of invasive disease.

## **Signs and symptoms**

The symptoms of meningitis can differ based on the cause, how quickly the disease progresses, how long it lasts, brain involvement, and other serious complications like sepsis.

Common symptoms of meningitis are fever, neck stiffness, confusion or altered mental status, headache, sensitivity to light, nausea and vomiting. Less frequent symptoms include seizures, coma and neurological deficits, such as weakness of the limbs.

Infants often have different symptoms compared to adults:

* unusual behaviour, such as the child being less active and difficult to wake
* irritability
* weak, continuous cry
* poor feeding
* bulging of the soft spot in their head.

Some bacterial pathogens may also account for other symptoms as a result of bloodstream infection, which can quickly lead to sepsis, including cold hands and feet, fast breathing and low blood pressure. A characteristic, non-blanching skin rash may appear with meningococcal sepsis.

## **Complications and sequelae**

One in 5 people surviving an episode of bacterial meningitis may have long lasting after-effects. These after-effects include hearing loss, seizures, limb weakness, difficulties with vision, speech, language, memory and communication, as well as scarring and limb amputations after sepsis.

## **Prevention**

Vaccines offer the best protection against common types of bacterial meningitis.

Vaccines can prevent meningitis caused by:

* meningococcus
* pneumococcus
* *Haemophilus influenzae* type b (Hib).

Maternal Group B streptococcus vaccines to prevent invasive GBS disease in infants are in the final stages of clinical development.

Bacterial and viral meningitis can spread from person to person. If you live with someone who has either type of meningitis, you should:

* talk to your doctor or nurse about taking antibiotics (in case of bacterial meningitis)
* wash hands frequently, especially before eating
* avoid close contact and sharing cups, utensils or toothbrushes.

### 1. Vaccination

Licensed vaccines against meningococcal, pneumococcal and *Haemophilus influenzae* disease have been available for many years. These bacteria have several different strains (known as serotypes or serogroups) and vaccines are designed to protect against the most harmful strains. No universal vaccine exists.

Hib vaccine is used in most national childhood immunization programmes globally. WHO also recommends universal use pneumococcal conjugate vaccines (PCV). Meningococcal vaccinesinclude multivalent polysaccharide conjugate vaccines (MMCV), which include 4 to 5 meningococcal serogroups (A,C,W,Y,X); protein-based vaccines, which include meningococcal serogroup B, and combination vaccines combining the latter with 4-valent MMCV. Polysaccharide vaccines are still marketed internationally but are gradually being replaced by MMCV.

In the African meningitis belt, meningococcus serogroup A accounted for 80–85% of meningitis epidemics before the large-scale deployment of a meningococcal A conjugate vaccine starting in 2010. In 2023, the first pentavalent MMCV protecting against serogroups A, C, W, Y and X (Men5CV) was prequalified by WHO and recommended for use in countries of the African meningitis belt. Roll-out of Men5CV has the potential to eliminate meningitis epidemics and make the meningitis belt history.

### 2. Antibiotics for prevention (chemoprophylaxis)

Post-exposure prophylaxis with antibiotics is given to close contacts of individuals with meningococcal disease to eradicate asymptomatic meningococcal carriage in the nose and decrease the risk of transmission.

Identifying mothers whose babies are at risk of getting Group B streptococcal (GBS) disease is recommended in many countries. Mothers at risk of transmitted GBS to their babies are offered intravenous penicillin during labour to prevent their babies developing GBS infection.

## **Diagnosis**

To diagnose meningitis, a lumbar puncture is needed to examine the cerebrospinal fluid (CSF). This should be done before starting antibiotics; however, if bacterial meningitis is suspected based on the signs and symptoms, a lumbar puncture should never delay antibiotic treatment.

Laboratories will then perform specific tests with CSF or blood to identify the pathogen causing the infection. The tests will also help identify the treatments needed, and specifically for bacterial infections the susceptibility to types of antibiotics, as well as identify the strain(s) of the pathogen responsible and inform public health responses.

## **Treatment**

Meningitis is a medical emergency and requires urgent medical attention in an appropriate health-care facility.

Antibiotic treatment should be started as soon as possible when bacterial meningitis is suspected. The first dose of antibiotic treatment should not be delayed until the results of the lumbar puncture are available. The choice of antibiotic treatment should consider the age of the patient, presence of immunosuppression, and local prevalence of antimicrobial resistance patterns. In non-epidemic settings, intravenous corticosteroids (e.g., dexamethasone) are initiated with the first dose of antibiotics to reduce the inflammatory response and the risk of neurological sequelae and death,

Those who have lived through meningitiscan have complications such as deafness, learning impairment or behavioural problem and require long-term treatment and care. The ongoing psychosocial impacts of disability from meningitis can have medical, educational, social and human rights-based implications. Access to both services and support for these conditions is often insufficient, especially in low- and middle-income countries.

Individuals and families with members disabled by meningitis should be encouraged to seek services and guidance from local and national organizations of disabled people and other disability focused organizations, which can provide vital advice about legal rights, economic opportunities and social engagement to ensure people disabled by meningitis are able to live full and rewarding lives.

WHO has also developed an Intersectoral global action plan on epilepsy and other neurological disorders to address the many challenges and gaps in providing care and services for people with epilepsy and other neurological disorders that exist worldwide, including those suffering from meningitis sequelae.

## **Surveillance**

Surveillance, from case detection to investigation and laboratory confirmation, is essential to the control of meningitis. Main objectives include:

* detect and confirm outbreaks;
* monitor the incidence trends, including the distribution and evolution of serogroups and serotypes;
* estimate the disease burden;
* monitor the antibiotic resistance profile;
* monitor the circulation, distribution, and evolution of specific strains (clones); and
* estimate the impact of meningitis control strategies, particularly preventive vaccination programmes.

## **WHO response**

In 2020, the 73rd World Health Assembly approved resolution (WHA73.9), in which all Member States committed to implementing the Defeating meningitis by 2030 global road map.

The roadmap sets a comprehensive vision “Towards a world free of meningitis” and has 3 visionary goals:

* elimination of bacterial meningitis epidemics;
* reduction of cases of vaccine-preventable bacterial meningitis by 50% and deaths by 70%; and
* reduction of disability and improvement of quality of life after meningitis due to any cause.

Source:

* World Health Organization. (2023) *Meningitis*. Available at: https://www.who.int/news-room/fact-sheets/detail/meningitis(Accessed: 23 May 2025).

**ENCEPHALITIES**

## **Overview**

Encephalitis (en-sef-uh-LIE-tis) is inflammation of the brain. It can be caused by viral or bacterial infections, or by immune cells mistakenly attacking the brain. Viruses that can lead to encephalitis can be spread by insects such as mosquitos and ticks.

When inflammation is caused by an infection in the brain, it's known as infectious encephalitis. And when it's caused by the immune system attacking the brain, it's known as autoimmune encephalitis. Sometimes there is no known cause.

Encephalitis can sometimes lead to death. Getting diagnosed and treated right away is important because it's hard to predict how encephalitis may affect each person.

## **Symptoms**

Encephalitis may cause many different symptoms including confusion, personality changes, seizures or trouble with movement. Encephalitis also may cause changes in sight or hearing.

Most people with infectious encephalitis have flu-like symptoms, such as:

* + Headache.
  + Fever.
  + Aches in muscles or joints.
  + Fatigue or weakness.

Typically, these are followed by more-serious symptoms over a period of hours to days, such as:

* + Stiff neck.
  + Confusion, agitation or hallucinations.
  + Seizures.
  + Loss of feeling or being unable to move certain areas of the face or body.
  + Irregular movements.
  + Muscle weakness.
  + Trouble with speech or hearing.
  + Loss of consciousness, including coma.

In infants and young children, symptoms also might include:

* + Bulging of the soft spots of an infant's skull.
  + Nausea and vomiting.
  + Stiffness affecting the whole body.
  + Poor feeding or not waking for a feeding.
  + Irritability.

In autoimmune encephalitis, symptoms may develop more slowly over several weeks. Flu-like symptoms are less common but can sometimes happen weeks before more-serious symptoms start. Symptoms are different for everyone, but it's common for people to have a combination of symptoms, including:

* + Changes in personality.
  + Memory loss.
  + Trouble understanding what is real and what is not, known as psychosis.
  + Seeing or hearing things that aren't there, known as hallucinations.
  + Seizures.
  + Changes in vision.
  + Sleep problems.
  + Muscle weakness.
  + Loss of sensation.
  + Trouble walking.
  + Irregular movements.
  + Bladder and bowel symptoms.

### When to see a doctor

Get medical care right away if you experience any of the more-serious symptoms associated with encephalitis. A bad headache, fever and change in consciousness require urgent care.

Infants and young children with any symptoms of encephalitis also need urgent care.

## **Causes**

In about half of patients, the exact cause of encephalitis is not known.

In those for whom a cause is found, there are two main types of encephalitis:

* **Infectious encephalitis.** This condition usually occurs when a virus infects the brain. The infection may affect one area or be widespread. Viruses are the most common causes of infectious encephalitis, including some that can be passed by mosquitoes or ticks. Very rarely, encephalitis may be caused by bacteria, fungus or parasites.
* **Autoimmune encephalitis.** This condition occurs when your own immune cells mistakenly attack the brain or make antibodies targeting proteins and receptors in the brain. The exact reason why this happens is not completely understood. Sometimes autoimmune encephalitis can be triggered by cancerous or noncancerous tumors, known as paraneoplastic syndromes of the nervous system. Other types of autoimmune encephalitis such as acute disseminated encephalomyelitis (ADEM) can be triggered by an infection in the body. This is known as post-infectious autoimmune encephalitis. In many instances, no trigger for the immune response is found.

### Common viral causes

The viruses that can cause encephalitis include:

* **Herpes simplex virus (HSV).** Both HSV type 1 and HSV type 2 can cause encephalitis. HSV type 1 causes cold sores and fever blisters around the mouth, and HSV type 2 causes genital herpes. Encephalitis caused by HSV type 1 is rare but can result in significant brain damage or death.
* **Other herpes viruses.** These include the Epstein-Barr virus, which commonly causes infectious mononucleosis, and the varicella-zoster virus, which commonly causes chickenpox and shingles.
* **Enteroviruses.** These viruses include the poliovirus and the coxsackievirus, which usually cause an illness with flu-like symptoms, eye inflammation and abdominal pain.
* **Mosquito-borne viruses.** These viruses can cause infections such as West Nile, La Crosse, St. Louis, western equine and eastern equine encephalitis. Symptoms of an infection might appear within a few days to a couple of weeks after exposure to a mosquito-borne virus.
* **Tick-borne viruses.** The Powassan virus is carried by ticks and causes encephalitis in the Midwestern United States. Symptoms usually appear about a week after a bite from an infected tick.
* **Rabies virus.** Infection with the rabies virus, which is usually transmitted by a bite from an infected animal, causes a rapid progression to encephalitis once symptoms begin. Rabies is a rare cause of encephalitis in the United States.

## **Risk factors**

Anyone can develop encephalitis. Factors that may increase the risk include:

* **Age.** Some types of encephalitis are more common or more serious in certain age groups. In general, young children and older adults are at greater risk of most types of viral encephalitis. Similarly, some forms of autoimmune encephalitis are more common in children and young adults, whereas others are more common in older adults.
* **Weakened immune system.** People who have HIV/AIDS, take immune-suppressing medicines or have another condition causing a weakened immune system are at increased risk of encephalitis.
* **Geographical regions.** Mosquito- or tick-borne viruses are common in particular geographical regions.
* **Season of the year.** Mosquito- and tick-borne diseases tend to be more common in summer in many areas of the United States.
* **Autoimmune disease.** People who already have an autoimmune condition may be more prone to develop autoimmune encephalitis.
* **Smoking.** Smoking increases the chances of developing lung cancer, which in turn increases the risk of developing paraneoplastic syndromes including encephalitis.

## **Complications**

The complications of encephalitis vary, depending on factors such as:

* Your age.
* The cause of your infection.
* The severity of your initial illness.
* The time from disease onset to treatment.

People with relatively mild illness usually recover within a few weeks with no long-term complications.

### Complications of serious illness

Inflammation can injure the brain, possibly resulting in a coma or death.

Other complications may last for months or may be permanent. Complications can vary widely and can include:

* Fatigue that doesn't go away.
* Weakness or lack of muscle coordination.
* Personality changes.
* Memory problems.
* Hearing or vision changes.
* Trouble with speech.

## **Prevention**

The best way to prevent viral encephalitis is to take precautions to avoid exposure to viruses that can cause the disease. Try to:

* **Practice good hygiene.** Wash hands often and thoroughly with soap and water, especially after using the toilet and before and after meals.
* **Don't share utensils.** Don't share tableware and drinks.
* **Teach your children good habits.** Make sure they practice good hygiene and avoid sharing utensils at home and school.
* **Get vaccinations.** Keep your own and your children's vaccinations current. Before traveling, talk to your healthcare professional about recommended vaccinations for different destinations.

### Protection against mosquitoes and ticks

To minimize your exposure to mosquitoes and ticks:

* **Dress to protect yourself.** Wear long-sleeved shirts and long pants outside. This is especially important if you're outside between dusk and dawn when mosquitoes are most active. It's also important when you're in a wooded area with tall grasses and shrubs where ticks are more common.
* **Apply mosquito repellent.** Chemicals such as DEET can be applied to both the skin and clothes. To apply repellent to your face, spray it on your hands and then wipe it on your face. If you're using both sunscreen and a repellent, apply sunscreen first.
* **Use insecticide.** The Environmental Protection Agency recommends the use of products containing permethrin, which repels and kills ticks and mosquitoes. These products can be sprayed on clothing, tents and other outdoor gear. Permethrin shouldn't be applied to the skin.
* **Avoid mosquitoes.** Stay away from places where mosquitoes are most common. If possible, don't do outdoor activities from dusk till dawn when mosquitoes are most active. Repair broken windows and screens.
* **Get rid of water sources outside your home.** Eliminate standing water in your yard, where mosquitoes can lay their eggs. Common places include flowerpots or other gardening containers, flat roofs, old tires, and clogged gutters.
* **Look for outdoor signs of viral disease.** If you notice sick or dying birds or animals, report your observations to your local health department.

### Protection for young children

Insect repellents aren't recommended for use on infants younger than 2 months of age. Instead, cover an infant carrier or stroller with mosquito netting.

For older infants and children, repellents with 10% to 30% DEET are considered safe. Products containing both DEET and sunscreen aren't recommended for children. This is because reapplying for sunscreen protection can expose the child to too much DEET.

Tips for using mosquito repellent with children include:

* Always assist children with the use of mosquito repellent.
* Spray on clothing and exposed skin.
* Apply the repellent when outdoors to lessen the risk of inhaling the repellent.
* Spray repellent on your hands and then apply it to your child's face. Take care around the eyes and ears.
* Don't use repellent on the hands of young children who may put their hands in their mouths.
* Wash treated skin with soap and water when you come indoors.

## **Diagnosis**

To diagnose encephalitis, a member of your healthcare team does a physical exam and takes your medical history.

Your healthcare professional might then recommend:

* **Brain imaging.** MRI or CT images can reveal any swelling of the brain or another condition that might be causing your symptoms, such as a tumor.
* **Spinal tap, known as a lumbar puncture.** A needle inserted into your lower back removes a small amount of cerebrospinal fluid (CSF), the protective fluid that surrounds the brain and spinal column. Changes in this fluid can point to infection and inflammation in the brain. Sometimes samples of CSF can be tested to identify the cause. This may include testing for infection or the presence of antibodies associated with autoimmune encephalitis.
* **Other lab tests.** Samples of blood, urine or excretions from the back of the throat can be tested for viruses or other infectious agents.
* **Electroencephalogram (EEG).** Electrodes attached to your scalp record the brain's electrical activity. Certain patterns may point to encephalitis.
* **Body imaging.** Sometimes, autoimmune encephalitis may be triggered by an immune response to a tumor in the body. The tumor may be noncancerous or cancerous. Your healthcare professional may order imaging studies, such as ultrasound, MRI, CT or PET-CT scans. These scans may look at your chest, stomach area or pelvis to check for these tumors. If a mass is found, a small piece of it may be removed to study it in a lab. This is known as a biopsy.
* **Brain biopsy.** Rarely, a small sample of brain tissue might be removed for testing. A brain biopsy is usually done only if symptoms are worsening and treatments are having no effect.

## **Treatment**

Treatment for mild encephalitis usally consists of:

* + Bed rest.
  + Plenty of fluids.
  + Anti-inflammatory medicines — such as acetaminophen (Tylenol, others), ibuprofen (Advil, Motrin IB, others) and naproxen sodium (Aleve) — to relieve headaches and fevers.

### Antiviral medicines

Encephalitis caused by certain viruses usually requires antiviral treatment.

Antiviral medicines commonly used to treat encephalitis include:

* + Acyclovir (Zovirax, Sitavig).
  + Ganciclovir.
  + Foscarnet (Foscavir).

Some viruses, such as insect-borne viruses, don't respond to these treatments. But because the specific virus may not be identified right away or at all, you may be treated with acyclovir. Acyclovir can be effective against HSV, which can result in serious complications when not treated quickly.

Antiviral medicines are generally well tolerated. Rarely, side effects can include kidney damage.

### Autoimmune encephalitis

If the tests show an autoimmune cause of encephalitis, then medicines that target your immune system, known as immunomodulatory medicines, or other treatments may be started. These may include:

* + Intravenous or oral corticosteroids.
  + Intravenous immunoglobulin.
  + Plasma exchange.

Some people with autoimmune encephalitis need long-term treatment with immunosuppressive medicines. These may include azathioprine (Imuran, Azasan), mycophenolate mofetil (CellCept), rituximab (Rituxan) or tocilizumab (Actemra).

Autoimmune encephalitis caused by tumors may require treatment of those tumors. This may include surgery, radiation, chemotherapy or a combination of treatments.

### Supportive care

People who are hospitalized with serious encephalitis might need:

* + Breathing assistance, as well as careful monitoring of breathing and heart function.
  + Intravenous fluids to ensure proper hydration and levels of essential minerals.
  + Anti-inflammatory medicines, such as corticosteroids, to reduce swelling and pressure within the skull.
  + Anti-seizure medicines to stop or prevent seizures.

### Follow-up therapy

If you experience complications of encephalitis, you might need additional therapy, such as:

* + **Brain rehabilitation** to improve cognition and memory.
  + **Physical therapy** to improve strength, flexibility, balance, motor coordination and mobility.
  + **Occupational therapy** to develop everyday skills and to use adaptive products that help with everyday activities.
  + **Speech therapy** to relearn muscle control and coordination to produce speech.
  + **Psychotherapy** to learn coping strategies and new behavioral skills to improve mood disorders or address personality changes.

## **Preparing for your appointment**

Serious illness associated with encephalitis is usually severe and relatively sudden, so seek emergency medical care. Your healthcare team will likely include specialists in infectious diseases and in the brain and nervous system, known as neurologists.

### Questions from your doctor

You may need to answer these questions, or answer them on behalf of your child or another person with a serious illness:

* + When did the symptoms begin?
  + Have you recently started taking any new medicines? If so, what is the medicine?
  + Have you been bitten by a mosquito or tick during the past few weeks?
  + Have you traveled recently? Where?
  + Have you recently had a cold, flu or other illness?
  + Are you up to date on your immunizations? When was your last one?
  + Have you had any exposure to wild animals or known toxins recently?
  + Have you had unprotected sex with a new or long-term sexual partner?
  + Do you have a condition or take any medicines that result in a weakened immune system?
  + Do you have an autoimmune condition or do autoimmune conditions run in the family?

Source:

Mayo Clinic Staff. (2023) *Encephalitis: Symptoms and causes*. Mayo Clinic. Available at: https://www.mayoclinic.org/diseases-conditions/encephalitis/symptoms-causes/syc-20356136 (Accessed: 23 May 2025).

# **Sleep Disorder**

Continuing Education Activity

Sleep disorders encompass several clinical problems encountered in outpatient settings. Sleep disorders have a broad differential diagnosis; therefore, standardized definitions and classifications are essential. There are many different types of sleep disorders. Using the International Classification of Sleep Disorders (ICSD) helps in providing a standardized classification and definitions for sleep disorders. Sleep disorders are common in both adults and children. However, children with sleep disorders may present with different symptoms than adults. This activity reviews the evaluation and management of sleep disorders and highlights the role of the interprofessional team in evaluating and treating patients with this condition.

**Objectives:**

* Identify the etiology of sleep disorders.
* Describe the evaluation of sleep disorders.
* Explain the management options available for sleep disorders.
* Summarize an interprofessional approach to coordinating care in treating patients with sleep disorders to achieve the best patient outcomes.

**INTRODUCTION**

Sleep disorders are a group of conditions that disturb normal sleep patterns. Sleep disorders are one of the most common clinical problems encountered. Inadequate or non-restorative sleep can interfere with normal physical, mental, social, and emotional functioning. Sleep disorders can affect overall health, safety, and quality of life. A study showed significant impairment in the quality of life in patients with insomnia.

There are many different types of sleep disorders. The International Classification of Sleep Disorders (ICSD) helps provide a standardized classification and definitions for sleep disorders. Specifically, the third edition of the ICSD (ICSD-3) includes the following categories of sleep disorders:

* Insomnia
* Sleep-disordered breathing
* Central disorders of hypersomnolence
* Circadian rhythm sleep-wake disorders
* Parasomnias
* Sleep-related movement disorders

Sleep disorders are common in both adults and children. However, children with sleep disorders may present with different symptoms than adults. Children with sleep problems may exhibit motor overactivity, inattentiveness, irritability, or oppositional behavior rather than overt sleepiness. Here we will review sleep disorders in adults, and sleep disorders in pediatrics will be discussed in a different section.

ETIOLOGY

There are different causes for different sleep disorders. For each sleep disorder listed below, more details are discussed in the pertinent section referenced below.

**Insomnia**

The exact causes of insomnia are unknown. Some contributing factors include environmental, genetic, psychological, and behavioral, leading to hyperarousal.

**Sleep-Disordered Breathing (SDB)**

The causes of SDB range from breathing control to upper airway and chest wall mechanics, causing compromised ventilatory and resistive loading. SDB is a spectrum of disorders ranging from  syndrome to OSA and central sleep apnea (CSA). In the obstructive type of SDB, obesity plays a key role, and more information is discussed in the sections on OSA, CSA, and obesity hypoventilation syndrome.

**Central Disorders of Hypersomnolence**

The central causes of hypersomnolence are commonly due to intrinsic abnormalities in the central nervous system's control of sleep-wake. Central hypersomnia is usually divided into three main subtypes: narcolepsy type 1, narcolepsy type 2, and idiopathic hypersomnia (IH), which are reviewed in more detail in separate sections. In addition, other causes of central hypersomnolence include Kleine-Levin syndrome, hypersomnia due to a medical disorder, medication or substance, psychiatric disorder, and sleep insufficiency syndrome.

**Circadian Rhythm Sleep-Wake Disorders (CRSD)**

The responsible causes of CRSD can be divided into two major groups (1): the environment is not well aligned with the internal circadian timing (e.g., shift work, jetlag); and (2) those occurring when the circadian timing system becomes altered relative to the external environment (e.g., delayed sleep phase syndrome, non-24, advanced sleep phase syndrome, irregular sleep-wake rhythm). More details are outlined in separate review articles.

**Parasomnias**

The causes of parasomnia vary from environmental, genetic, and gene-environment interactions, all of which may play a significant role in the origin of parasomnias. Parasomnia is divided into the following major categories: Non-rapid eye movement (NREM)-related parasomnias, rapid eye movement (REM)-related parasomnias, and other parasomnias. NREM-related parasomnia includes confusional arousal, sleepwalking, sleep terrors, and a sleep-related eating disorder. REM-related parasomnias include REM sleep behavior disorder (RBD) and nightmare disorder. The etiology of various types of parasomnia is discussed in a separate article.

**Sleep-Related Movement Disorders**

Abnormal movements during sleep are disorders of motor control excitation or disinhibition often associated with sleep disturbances. The etiology of various movements condition during sleep depends on the type of that disorder. For example, in restless legs syndrome (RLS), the etiology could be primarily due to familial and genetic predisposition or secondary to iron deficiency. More details on the etiology of RLS are discussed in a separate article. Other sleep-related movement disorders include categories based on the type of movements: simple, periodic, rhythmic, or complex conditions (some of which are associated with parasomnias). This will be discussed in detail in a dedicated section.

Epidemiology

The prevalence of sleep disorders differs based on the specific condition. A link between SDB, short sleep duration, and non-restorative sleep has recently been reported. A recent study has linked poor sleep to other sleep disorders; for example, among a sample of patients with diabetes, 61% reported poor sleep, 47% of the participants screened positive for RLS, and 51% had an increased risk for OSA. We will briefly list the prevalence of each major sleep disorder as classified by the ICSD-3.

**Insomnia**

Difficulty sleeping or insomnia symptoms are among the most common medical complaints affecting nearly a third of the adult population. When the symptoms are severe enough to cause daytime consequences, the prevalence is estimated to be approximately 10% and is higher among women than among men (17.6% vs. 10.1%%, respectively). In addition, insomnia is found to be a persistent disorder (lasting over five years) and affects over 40% of patients if they have severe insomnia symptoms at presentation.

**Sleep-Disordered Breathing (SDB)**

The prevalence of SDB is dependent on the type of disease. As people age, the incidence of sleep problems also rises. Approximately 50% of older adults have sleep problems. Details on the prevalence of specific SDB (obstructive, central, upper airway resistance syndrome, sleep-related hypoventilation syndrome, or obesity hypoventilation) as outlined in their respective articles.

**Central Disorders of Hypersomnia**

The prevalence of narcolepsy in the general population is approximately 142,600 individuals (44.3 per 100,000 persons), but there is a reported trend of increase over the last decade (by 14% from 38.9 in 2013 to 44.3 in 2016).

Likewise, The prevalence of idiopathic hypersomnia also increased by 32% (from 7.8 to 10.3 per 100,000 persons), with similar rates between both sexes.

**Circadian Rhythm Sleep-Wake Disorders (CRSD)**

The prevalence of CRSD among the general population depends on the type and is reported to be between 0.13 to 0.17%. However, the prevalence is higher among individuals with comorbid psychiatric illnesses. Delayed sleep phase syndrome (DSPD) is common in adolescents and young adults, with an estimated prevalence of 7 to 16%.

**Parasomnia**

Parasomnia, such as sleepwalking, confusional arousals, sleep terrors, sleep talking, and nightmares, are prevalent, including during childhood. The overall parasomnia prevalence in the no OSA group is approximately 3% in the NREM group (such as in sleepwalking, sexual acts during sleep, and sleep-related eating), 43.8% in nightmares, and the prevalence of RBD is estimated to be 8.7 per 100,000 people (with men to women ratio is 3:1).

**Sleep-Related Movement Disorders**

Restless leg syndrome and periodic limb movement disorder are also more prevalent in the elderly. Primary insomnia is more common in women over 50 than their male counterparts. The prevalence of periodic leg movements disorder (PLMD) is approximately 40 per 100,000 persons and has increased in the last decade about 30%.

There are gender differences in many of these sleep disorders. The prevalence of insomnia is higher in women than men throughout most of life (with a ratio of 1.4:1.0). The prevalence of RLS is twice as high for women as for men (9.0% vs. 5.4%) across all ages. In contrast, the prevalence of SDB is higher in men than in premenopausal women (with a ratio of 2:1). In the Wisconsin Sleep Cohort Study (WSCS), the prevalence of SDB increased over time n both sexes (26.4 to 33.9 % in men and 13.2 to 17.4 % in women). Several possibilities for this increase in prevalence were contemplated, including increased obesity and aging of the general population, in addition to improved diagnostic techniques.

There are also racial and ethnic differences in the prevalence of sleep disorders. In the Multi-Ethnic Study of Atherosclerosis (MESA), Hispanics and Chinese individuals had higher odds of SDB and short sleep than Whites. Likewise, Black have higher odds (1.8) for sleep apnea syndrome (AHI > five events per hour associated with excessive daytime sleepiness) compared to white after adjusting for age, gender and BMI.

History and Physical

The clinical presentations of sleep disorders depend on the specific disease. In general, sleep disturbances can present with a wide range of clinical pictures and commonly include insomnia, hypersomnia, or unusual sleep-related behaviors. Early identification of the underlying sleep disorder is essential to prevent complications and health consequences. A detailed history, sleep habits, and work schedule are critical to the assessment. Obtaining a complete list of medications (both prescribed and over-the-counter) is essential in assessing patients with sleep disturbances. In addition, evaluating detailed family and social history is very important, including any substances used by patients that can affect sleep and/or breathing.

**Insomnia**

Insomnia may present as difficulty falling asleep and/or staying asleep. Patients report taking thirty minutes or more to fall asleep (for those with sleep initiation difficulties) or spending thirty minutes or more awake during the night (for those with sleep maintenance difficulties). The diagnosis of insomnia also requires the presence of compromised daytime function, which includes one or more symptoms like fatigue, daytime sleepiness, poor attention, increased accidents, aggression, reduced motivation, or energy. Insomnia can often be a persistent or recurrent condition with exacerbations connected to medical, psychiatric, and psychosocial stressors. Recently insomnia was classified as a short-term and chronic type.

The ICSD-3 criteria of the diagnosis of chronic insomnia disorder include the following three conditions: (1) difficulty in sleep initiation or maintenance, (2) adequate opportunity to sleep, and (3) presence of daytime consequences due to difficulty sleeping. These conditions should last for at least three months and thrice weekly. Early identification of insomnia is crucial and requires a low threshold for suspicion. Clinical features that predispose, precipitate, and perpetuate insomnia symptoms should be identified from history.

**Hypersomnia**

Patients with hypersomnia complain of disabling excessive daytime sleepiness. They find it difficult to maintain alertness during significant waking hours, with sleep occurring unintentionally or at inappropriate times that interfere with the daily routine. Many patients describe a considerable impact on their cognitive function, calling it brain fog. In addition, in idiopathic hypersomnia, there has been an association between excessive sleepiness and depressive symptom, and low quality of life. Fatigue can present in a broad range of sleep disorders and can be confused with sleepiness.

The severity of hypersomnia and fatigue are commonly measured by questionnaires such as the Epworth sleepiness scale and fatigue severity scale. Other sleepiness features are related to sleep duration, such as idiopathic hypersomnia (IH) or specific neurobiological disorder such as narcolepsy. IH has distinctive clinical features in addition to the severity of hypersomnia, such as prolonged nighttime sleep (more than 10 hours) and sleeps inertia. Narcolepsy, however, is a chronic neurological disorder due to the brain's inability to control sleep and wakefulness. It is associated with a low cerebrospinal fluid level of orexin-A/hypocretin-1.

Patients with narcolepsy complain of excessive chronic daytime sleepiness with cataplexy (type I) or without cataplexy (type II) (transient loss of muscle tone in response to intense emotion such as laughter), hallucinations while falling asleep (hypnagogic hallucinations), or hallucinations while waking (hypnopompic hallucinations), and sleep paralysis (inability to move immediately after awakening). Cataplexy can be manifested commonly (more than 50% of the time) as nontypical presentations (including spontaneous cataplectic attacks or cataplexy induced by non-humorous triggers such as anger) and 30% as partial cataplexy (involves the jaw and the face).

Excessive daytime sleepiness is one of the most common clinical presentations of sleep-disordered breathing (SDB) (reported usually in up to 50% of patients), in addition to loud snoring and observed apnea or gasping by a bed partner. However, many patients with SDB are asymptomatic, particularly in special populations with heart failure, stroke, and other neurological disorders. More details on SDB are described in separate articles.

**Unusual Sleep-Related Behaviors**

Features of specific behavior before, during, or after sleep can provide essential clues to certain sleep disorders such as movement disorders, eating disorders, or parasomnia. For example, reporting sleep-related movement disorders such as the urge to move legs during a specific time of the evening could suggest restless leg movements or periodic leg movements, and further questions are needed to confirm the diagnosis. Confusional arousal or sleep drunkenness during arousal or awakening from sleep is a common manifestation of hypersomnolence disorder, such as idiopathic hypersomnia or, less commonly, sleep-related sex (sexsomnia). Sexsomnia is abnormal sexual behaviors without recollection, including sexual intercourse with a bed partner, masturbation, or sexual vocalizations.

Patients who report movements during sleep, such as kicking, punching, arm-flailing, or jumping from bed in response to violent dreams, could suffer from REM sleep behavior disorder (RBD). The patient can recall the dream if he awakens during the episode. This disorder may be associated with other medical conditions such as Parkinson disease, Lewy body dementia, or multiple system atrophy. Other sleep-related symptoms that require detailed history to reach a clinical diagnosis include sleepwalking, sleep talking, and night terrors (common in children aged 2 to 12) and usually resolve spontaneously as the child ages). They mainly occur in non-REM sleep, without memory of the event. On the other hand, nightmares occur during REM sleep, usually in the middle of the night and early morning. During a nightmare, the person may scream and yell out things.

The difference between nightmares and night terrors is that the person can become fully alert when awakened during a nightmare. Also, there is a memory of the event in a nightmare, i.e., a person can recall a nightmare. Sleep-eating disorders are other unusual sleep-related behaviors that require detailed histories to differentiate from each other.Sleep-related eating disorders (SRED) manifest as recurrent episodes of involuntary eating during the first one-third of sleep with reduced consciousness. However, night eating syndrome (NES) manifests by excessive eating between dinner and bedtime or after a complete awakening from sleep. Complex sleep behaviors are nonrapid eye movement (NREM)-related behaviors such as sleepwalking resulting in serious injuries or death, particularly among middle-aged and older patients with chronic insomnia.

The symptoms associated with sleep disorders are commonly exacerbated by sleep deprivation, physical or emotional stress, traumatic events, and the use and abuse of substances or medications. Some of the medicines that are commonly linked to unusual sleep-related behaviors are antipsychotics and psychotropic medications (e.g., anticholinergics), sedatives, and hypnotic agents, particularly the class of Z drugs or nonbenzodiazepine benzodiazepine receptor agonists (e.g., zolpidem and eszopiclone) which now have a black box warning from US Food and Drug Administration (FDA) due to increased risk of complex sleep behaviors.

Evaluation

A variety of information is required to evaluate sleep problems. After a detailed medical history, medication history, and physical examination, some clinical and investigative tools could help narrow the differential diagnosis and help identify the type of sleep disorders. Here is a list of some of these questionnaires and tests

**Epworth sleepiness scale (ESS):**ESS is an eight-item self-administered questionnaire that measures the presence and severity of sleepiness.

**Fatigue severity scale (FSS):** FSS is a nine-item instrument that can help distinguish sleepiness from fatigue and estimate fatigue severity.

**Insomnia Severity Index (ISI):** ISI is the most widely accepted clinical assessment tool that helps identify and monitor insomnia severity  in addition to a sleep diary.

**Sleep diary:** The sleep diary, or sleep log, is a personal paper record of sleep and wakefulness over weeks to months. Patients should record a detailed description of sleep, such as bedtime, duration until sleep onset, the number of awakenings, duration of awakenings, and nap times.

**Sleep studies:** Objective measures of sleep may be obtained by sleep studies such as home sleep apnea testing (HSAT) or polysomnography (PSG). PSG is the gold standard for diagnosing OSA and other sleep disorders. During PSG, numerous monitoring devices are connected to the patient, allowing the patient to sleep. Various physiologic parameters such as respiratory effort, sleep stages, electrocardiography, airflow, body position, and limb movements are assessed. The information obtained from these parameters helps to diagnose various REM & NREM sleep disorders and determine the causes of sleep disturbance. In cases with a diagnosis of OSA and residual hypersomnia despite PAP therapy with adequate adherence, follow-up PSG can be used to reassess patients and ensure adequate PAP. However, a follow-up sleep study (PSG or HSAT) is *not* recommended in asymptomatic patients as a routine test.

**Laboratory studies:** Some of the lab studies appropriate for those with sleep disorders include:

* Arterial blood gases (ABG)
* Thyroid function tests
* Drug and alcohol toxicity screening
* Iron studies and ferritin level
* Cerebrospinal fluid (CSF) hypocretin-1 deficiency (<110 pg/ml).

**Actigraphy:** In this test, an actigraph device is worn on the wrist like a watch. The signals are detected when there is movement, and very few to no signs are recorded during sleep/inactivity. This device can assess sleep-wake cycles or circadian rhythm over an extended period and thus diagnose advanced or delayed sleep phase syndrome.

**Multiple sleep latency testing (MSLT):** This objective test determines the degree of sleepiness. This test is often called a nap study. On the day following an overnight PSG study, the patient is asked to take four or five naps for 8 to 10 hours. Each nap lasts about 20 minutes. These tests help identify the causes of excessive daytime sleepiness, which can be present in various disorders such as sleep apnea, hypersomnia, and narcolepsy.

Treatment / Management

Treatments for sleep disorders depend on the type of sleep disorder.

Treatment of insomnia can be broadly categorized into non-pharmacological and pharmacological treatments.

**Non-pharmacological**

* Cognitive-behavioral therapy for insomnia (CBT-I) includes a set of psychological and behavioral techniques specific to treating insomnia. Studies report that CBT-I is the psychological treatment of choice, using individual or group therapy techniques and, recently, digital CBT-I formats.
* A meta-analysis of 61 randomized controlled trials, which included 11,571 participants and assessed different CBT-I delivery formats (individual, group, guided self-help, digital assisted, and unguided self-help ) with control conditions found that CBT-I not only significantly increases sleep parameters such as sleep efficiency and total sleep time but reduces sleep onset latency, wake after sleep onset, and insomnia severity. CBT-I therapy is particularly important in groups of patients that may not tolerate pharmacological treatment, such as older patients, due to increased risk of side effects and addiction and tolerance to using Z drugs. Other interventions are not proven to have a clinical effect if used alone. These interventions include:
  + Sleep restriction therapy (SRT): SRT limits the total time allowed in bed to increase the drive to sleep.
  + Stimulus control therapy helps change sleep habits so that the patients don't have difficulty falling asleep. Patients should not go to bed until they are sleepy. Also, the bed should be used only for sleeping and not for watching television or reading books.
  + Relaxation therapy: Relaxation techniques may be implemented before sleep. Meditation and breathing exercises are some of the relaxation techniques.
  + Sleep hygiene: A set of education about lifestyle and environmental factors (e.g., light, noise, temperature) that may interfere with sleep. Sleep hygiene may include education about normal sleep, avoidance of substance use, regular exercise, bedroom environment, sleep and wake times, and avoidance of daytime naps. However, sleep hygiene education alone is less effective than CBT-I in individuals with poor sleep or insomnia.

**Pharmacologic**

* Histamine type 1 receptor blockers (e.g., chlorpheniramine and diphenhydramine) are commonly used for difficulty sleeping due to their sedative effects. However, due to their anticholinergic effect, these drugs should be avoided.
* Benzodiazepines (BZD): these drugs are commonly used to treat insomnia. The drugs bind to a particular benzodiazepine site on the gamma-aminobutyric acid (GABA) receptor complex, enhancing the activity of neurotransmitters. These drugs suppress REM sleep and reduce stage 3 sleep while increasing stage 2 sleep. Examples include flurazepam and temazepam.
* Non-benzodiazepine hypnotics or z-drugs: these agents are used to treat acute and short-term insomnia. These drugs have non-BZD-like chemical structures but interact with the GABA-BZD receptor, causing sedation. Examples include zolpidem and zaleplon.
* Melatonin receptor agonists: the melatonin receptors MT1 and MT2 are implicated in regulating sleepiness and the sleep-wake cycle. Melatonin receptor agonists act on these receptors and improve sleep through the endogenous regulating system. These drugs are used in circadian rhythm sleep disorders, jet lag, and delayed sleep-wake phase disorder (insomnia with difficulty in sleep onset). An example includes ramelteon.
* Orexin receptor antagonists: orexin promotes wakefulness. Thus, the antagonism of this receptor helps in sleep. An example includes suvorexant, which improved ISI through improvement in sleep onset and maintenance.

Treatment of OSA includes primarily mechanical positive airway therapy (PAP), lifestyle changes, and options of oral appliances or surgical procedures in certain patients.. The use of drug treatment such as solriamfetol, stimulants (such as amphetamines or modafinil), and norepinephrine reuptake inhibitors to increase wakefulness in patients with OSA and persistent hypersomnia despite adequate PAP adherence and elimination of respiratory events can be considered in selected patients to treat their day time symptoms. A long-term study of the safety and efficacy of solriamfetol under open-label and double-blind, placebo-controlled conditions demonstrated long-term efficacy of solriamfetol and reported side effects in less than 5% of patients with OSA or narcolepsy such as headache, nausea, nasopharyngitis, insomnia, dry mouth, anxiety, decreased appetite, and upper respiratory tract infection.

A number of medications can be used for the treatment of narcolepsy. Modafinil, a non-amphetamine stimulant that promotes wakefulness, is considered first-line therapy for narcolepsy as it reduces daytime sleepiness, is well tolerated, and has less abuse potential compared to traditional stimulants (amphetamines, methylphenidate). These traditional drugs are second-line drugs. Patients with significant cataplexy may benefit from REM-suppressing medications such as anti-depressants and sodium oxybate.

Light-phase shift therapy is useful for sleep disturbances associated with circadian rhythm abnormalities. Patients may be exposed to bright light to help normalize their sleep schedule.

Gabapentin enacarbil, a prodrug formulation of gabapentin, significantly improves restless leg syndrome and hence can alleviate sleep disturbance.

Differential Diagnosis

The differential diagnosis of sleep disorders are as follows:

* Post-traumatic stress disorder (PTSD)
* Depression
* Anxiety disorder
* Bipolar disorder
* Opioid abuse
* Alcoholism
* Stimulants abuse (amphetamine)
* Chronic obstructive pulmonary disease (COPD)
* Hyperthyroidism

Prognosis

Insufficient sleep can result in industrial or motor vehicle accidents, decreased work performance, and cognitive dysfunction. The prognosis of sleep disorders depends widely on the cause of the sleep disorder. Insomnia due to OSA generally resolves with treatment, whereas patients with chronic insomnia have an increased risk of depression, anxiety, and reduced quality of life.

Complications

Untreated sleep disorders may lead to an increased risk of accidents and the development of various serious complications. Mood and anxiety disorders may develop. Sleep deprivation can lead to false memory and a decline in cognitive functioning.

Patients with periodic limb movement sleep disorder may have a higher risk of cerebrovascular accidents.

Untreated OSA (especially if severe and associated with hypersomnia) can lead to various cardiovascular disorders.

Deterrence and Patient Education

All patients should be educated well and encouraged to practice good sleep hygiene. "Sleep hygiene" is a term used to describe good sleep habits.

The following advice should be given to the patients to practice good sleep hygiene:

* Maintain a regular schedule, i.e., go to bed and wake up at the same time every day
* Use the bed for sleep and sex only. Avoid watching television, looking at phones, or reading in the bed
* Exercise almost every day, but not right before bedtime
* Avoid caffeine or smoking, mainly during the evening
* Maintain a dark, calm, and quiet environment in the bedroom
* Avoid struggling to fall asleep in bed. If you can't sleep, get up and try again later or change the bed.

Also, if the patient takes sedative-hypnotic medications, this should be documented in the medical record. Patients should be counseled to avoid driving and operating machines when under these medications.

Enhancing Healthcare Team Outcomes

The proper management of sleep disorders requires the efforts of an interprofessional healthcare team that includes clinicians (MDs, DOs, NPs, and PAs), specialists, pharmacists, nursing staff, psychological professionals (social workers, counselors, etc.), and in some cases a sleep clinic, and a dietician. Surgical consultations are required for some of the underlying causes of insomnia, such as in cases of OSA, which may require palate surgery. Interprofessional collaboration is essential for good patient outcomes in sleep disorders.

Nurses can coordinate activities between the managing clinicians and other health professionals on the case, as well as counsel the patient and answer any questions. The pharmacist will verify the medication dosing, check for interactions, and counsel patients on proper administration. Sleep clinics will look deeper into the case, including potential sleep studies, when indicated. Psychological professionals will work with any issues that may contribute to sleep problems and report to the rest of the interprofessional team. Clinicians will do well to consider input from all team members in deciding their course of therapy; the patient and possibly family (e.g., spouses, parents) are also members of the care team.

All interprofessional team members are responsible for maintaining accurate and updated records regarding the patient's case with every interaction or intervention taken. They must also be free to openly communicate with all other team members when there are any concerns about the patient's condition or progress. This interprofessional model will help drive optimal outcomes for those patients who experience issues with sleep disorders of any type.

Source

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**Brain Cancer (Brain Tumor)**

Brain tumors can be malignant (cancerous) or benign (noncancerous) and can affect children and adults. But whether they’re cancerous or not, brain tumors can impact your brain function if they grow large enough to press on surrounding tissues. There are several treatment options for brain tumors.

**What is a brain tumor?**

A brain tumor is an abnormal growth or mass of cells in or around your brain. Together, spinal tumors and brain tumors are called central nervous system (CNS) tumors.

Brain tumors can be malignant (cancerous) or benign (noncancerous). Some tumors grow quickly, while others are slow growing.

Only about one-third of brain tumors are cancerous. But whether they’re cancerous or not, brain tumors can impact brain function and your health if they grow large enough to press on surrounding nerves, blood vessels and tissue.

Tumors that develop in your brain are called primary tumors. Tumors that spread to your brain after forming in a different part of your body are called secondary tumors, or metastatic brain tumors. This article focuses on primary brain tumors.

**What are the types of brain tumors?**

Researchers have identified more than 150 different brain tumors.

Healthcare providers categorize primary tumors as glial (composed of glial cells in your brain) or non-glial (developed on or in the structures of your brain, including nerves, blood vessels and glands) and benign (noncancerous) or malignant (cancerous).

Many types of brain tumors can also form in your spinal cord or column.

Usually benign brain tumors

Types of brain tumors that are usually benign include:

**Chordomas**: These slow-growing tumors typically begin at the base of your skull and the bottom part of your spine. They’re mostly benign.

**Craniopharyngiomas**: These tumors usually arise from a portion of your pituitary gland. They’re difficult tumors to remove because of their location near critical structures deep in your brain.

Gangliocytomas, gangliomas and anaplastic gangliogliomas: These are rare tumors that form in neurons (nerve cells).

**Glomus jugulare:** These tumors are typically located just under the base of your skull at the top of your jugular vein (neck vein). They’re the most common form of glomus tumor.

**Meningiomas:** These are the most common type of primary brain tumors. Meningiomas typically develop slowly. They form in the meninges, the layers of tissue that protect your brain and spinal cord. In rare cases, a meningioma can be malignant.

**Pineocytomas:** These slow-growing tumors form in your pineal gland, which is located deep in your brain and secretes the hormone melatonin.

**Pituitary adenomas:** These tumors form in your pituitary gland, which is located at the base of your brain. Your pituitary gland makes and controls hormones in your body. Pituitary adenomas are usually slow growing and they may release excess pituitary hormones.

**Schwannomas:** These are common benign brain tumors in adults. They develop from the Schwann cells in your peripheral nervous system or cranial nerves. Schwann cells assist the conduction of nerve impulses. Acoustic neuromas are the most common schwannoma. These tumors occur on your vestibular nerve (the nerve that leads from your inner ear to your brain).

Cancerous (malignant) brain tumors

Approximately 78% of cancerous primary brain tumors are gliomas. These tumors develop in glial cells, which surround and assist nerve cells. Types of gliomas include:

Astrocytoma: These tumors are the most common type of glioma. They form in the star-shaped glial cells called astrocytes. They can form in many parts of your brain, but most commonly occur in your cerebrum.

Ependymomas: These tumors often occur near the ventricles in your brain. Ependymomas develop from ependymal cells (called radial glial cells).

Glioblastoma (GBM): These tumors form in glial cells called astrocytes. GBMs are the fastest-growing astrocytoma.

Oligodendroglioma: These uncommon tumors begin in cells that create myelin (a layer of insulation around nerves in your brain).

Medulloblastoma is another type of cancerous brain tumor. These tumors are fast growing and form at the base of your skull. They’re the most common cancerous brain tumor in children.

**Who do brain tumors affect?**

Brain tumors can affect anyone. They're slightly more common in males.

Meningioma, which is usually benign, is the only type of brain tumor that’s more common in females.

The most serious type of brain tumor, glioblastoma, is becoming more common among people who are as the general population ages.

**How common are primary brain tumors?**

Primary brain tumors (tumors that originate in your brain) are uncommon. Only about 5 per 100,000 people are diagnosed with a primary brain tumor each year in the United States.

About 4,100 children under the age of 15 are diagnosed with a brain or central nervous system tumor each year in the United States.

**How serious are brain tumors?**

Brain tumors — whether cancerous or not — can cause serious problems. This is because your skull is rigid and doesn’t provide room for the tumor to expand. Also, if a tumor develops near parts of your brain that control vital functions, it may cause symptoms, such as:

* Weakness.
* Difficulty walking.
* Problems with balance.
* Partial or complete loss of vision.
* Difficulty understanding or using language.
* Memory issues.

**Brain tumors can cause problems by:**

* Directly invading and destroying healthy brain tissue.
* Putting pressure on nearby tissue.
* Increasing pressure within your skull (intracranial pressure).
* Causing fluid to build up in your brain.
* Blocking the normal flow of cerebrospinal fluid (CSF) through the spaces within your brain, causing those spaces to enlarge.
* Causing bleeding in your brain.

However, some people have brain tumors that never cause symptoms or grow large enough to compress surrounding tissues.

**Symptoms and Causes**

Medical illustration of a pink brain with a yellow mass inside it, indicating a tumor.

Brain tumors can be benign (not cancerous) or malignant (cancerous). There are over 150 different types of brain tumors.

**What are the signs and symptoms of brain tumors?**

Some people who have a brain tumor experience no symptoms, especially if it’s very small.

Signs and symptoms of a brain tumor vary depending on the tumor’s location, size and type. They can include:

* Headaches that may be more severe in the morning or wake you up at night.
* Seizures.
* Difficulty thinking, speaking or understanding language.
* Personality changes.
* Weakness or paralysis in one part or one side of your body.
* Balance problems or dizziness.
* Vision issues.
* Hearing issues.
* Facial numbness or tingling.
* Nausea or vomiting.
* Confusion and disorientation.

It’s important to see your healthcare provider if you’re experiencing these symptoms.

**What causes brain tumors?**

Researchers know brain tumors develop when certain genes on the chromosomes of a cell are damaged and no longer function properly, but they aren’t sure why this happens. Your DNA in your chromosomes tells cells throughout your body what to do — it tells them when to grow, when to divide or multiply and/or when to die.

When brain cell DNA changes, it gives your brain cells new instructions. Your body develops abnormal brain cells that grow and multiply faster than normal and sometimes live longer than normal. When that happens, the ever-growing crowd of abnormal cells takes over space in your brain.

In some cases, a person may be born with changes in one or more of these genes. Environmental factors, such as exposure to large amounts of radiation from X-rays or previous cancer treatment, may then lead to further damage.

In other cases, the environmental injury to the genes may be the only cause.

There are a few rare, inherited (passed down from parent to child) genetic syndromes that are associated with brain tumors, including:

* Neurofibromatosis type 1 (NF1 gene).
* Neurofibromatosis type 2 (NF2 gene).
* Turcot syndrome (APC gene).
* Gorlin syndrome (PTCH gene).
* Tuberous sclerosis complex (TSC1 and TSC2 genes).
* Li-Fraumeni syndrome (TP53 gene).
* Only about 5% to 10% of people with brain tumors have a family history of a brain tumor.

**Diagnosis and Tests**

**How are brain tumors diagnosed?**

Diagnosing a brain tumor can be a complicated process and may involve several specialists. In some cases, though, healthcare providers may discover a brain tumor when performing imaging tests for another medical issue.

If you’re experiencing symptoms of a brain tumor, your healthcare provider will perform a physical exam. They’ll also ask questions about your:

**Symptoms.**

* Past and current health conditions.
* Current medications.
* Surgeries and medical treatments.
* Family medical history.

They may also perform a neurological exam, which involves looking for changes in your:

* Balance and coordination.
* Mental status.
* Hearing.
* Vision.
* Reflexes.

These changes can point to the part of your brain that may be affected by a tumor.

If your healthcare provider suspects you may have a brain tumor, a brain scan, most often an MRI, is usually the next step.

**What tests will be done to diagnose a brain tumor?**

Healthcare providers use several tests to diagnose a brain tumor, including:

Brain MRI or CT scan: Magnetic resonance imaging (MRI) is the best imaging test for identifying brain tumors. Computed tomography (CT) is a good alternative if you’re unable to undergo an MRI. Before these tests, a substance that makes the tumor easier to see called a contrast agent is injected into one of your veins. These tests can show the tumor’s size and exact position in specific detail. Your healthcare provider may also look at other parts of your body, such as your lungs, colon or breasts, to see if the tumor has spread.

Biopsy: Healthcare providers usually need to do a biopsy of the tumor (removal of a sample of the tumor for examination under a microscope) to identify the type of tumor and if it’s cancerous. A neurosurgeon may perform a biopsy during surgery in which they remove all or part of the tumor. If the tumor is difficult to reach, they may perform a stereotactic biopsy, which involves creating a small hole in your skull and using a needle to take a sample of tissue from the tumor.

Spinal tap (lumbar puncture): For this procedure, your healthcare provider uses a small needle to remove cerebrospinal fluid (CSF) from around your spine. A laboratory examines this fluid to look for cancer cells. Healthcare providers use this procedure when they suspect that the tumor has invaded the layers of tissues that cover your brain (meninges).

Specialized tests: Certain tests can sometimes help with the diagnosis. For example, your healthcare provider may order tests that check your blood and cerebrospinal fluid for substances that certain tumors release called tumor markers. They can also test for gene abnormalities that are characteristic of certain tumors.

Management and Treatment

**How are brain tumors treated?**

Brain tumor treatment depends on several factors, including:

* The tumor’s location, size and type.
* The number of tumors.
* Your age.
* Your overall health.

Benign (noncancerous) brain tumors can usually be successfully removed with surgery and don’t usually grow back. It often depends on if your neurosurgeon can safely remove all of the tumor.

Treatments that are fairly well tolerated by the brains of adults, such as radiation therapy, may prevent the normal development of a child’s brain, especially in children younger than age five.

Healthcare providers often use a combination of therapies to treat a tumor. Your treatment options might include:

Brain surgery (craniotomy): When possible, neurosurgeons remove the tumor. They work very carefully, sometimes performing surgery when you’re awake (you won’t feel pain), to minimize damage to functional areas of your brain.

Radiation therapy: High doses of X-rays destroy brain tumor cells or shrink the tumor in this type of treatment.

Radiosurgery: This is a type of radiation therapy that uses very focused beams of radiation (gamma rays or proton beams) to destroy a tumor. It’s not actually surgery because it doesn’t require an incision (cut).

Brachytherapy: This is a form of radiation therapy. It involves surgically placing radioactive seeds, capsules or other implants directly in or near the cancerous tumor.

Chemotherapy: This therapy consists of anticancer drugs that kill cancer cells in your brain and throughout your body. You might receive chemotherapy through an injection into a vein or take it as a pill. Your healthcare provider may recommend chemotherapy after surgery to kill any cancer cells left behind or to prevent remaining tumor cells from growing.

Immunotherapy: Immunotherapy, also called biological therapy, is a type of treatment that uses your body’s immune system to fight cancer. The therapy mainly consists of stimulating your immune system to help it do its job more effectively.

Targeted therapy: With this treatment, drugs target specific features in cancer cells without harming healthy cells. Your healthcare provider may recommend targeted therapy if you have trouble tolerating the side effects of chemotherapy, such as fatigue and nausea.

Watchful waiting/active surveillance: If you have a brain tumor that’s very small and isn’t causing symptoms, your healthcare provider may recommend closely monitoring the tumor for signs of growth with regular testing.

Other treatments that help with symptoms caused by brain tumors include:

Shunts: If the tumor causes pressure within your skull to increase, you may need to have a shunt (a thin piece of tubing) surgically placed in your brain to drain excess cerebrospinal fluid.

Drugs such as mannitol and corticosteroids: These medications can help reduce pressure within your skull. They reduce swelling around the tumor.

Palliative care: This is a specialized form of care that provides symptom relief, comfort and support to people living with serious illnesses. It also provides support to caregivers and those impacted by a loved one’s condition.

Prevention

Can brain tumors be prevented?

Unfortunately, you can’t prevent a brain tumor. You can reduce your risk of developing a brain tumor by avoiding environmental hazards such as smoking and excessive radiation exposure.

If you have a first-degree biological relative (sibling or parent) who has been diagnosed with a brain tumor, it’s important to tell your healthcare provider. They may recommend genetic counseling to see if you have an inherited genetic syndrome that’s associated with brain tumors.

Outlook / Prognosis

What is the prognosis (outlook) for brain tumors?

The prognosis (outlook) for people with brain tumors varies greatly. Factors that affect the prognosis include:

The tumor’s type, grade and location.

If the whole tumor has been surgically removed.

Your age and overall health.

In many cases, healthcare providers can successfully treat a brain tumor. Some people live active and fulfilling lives with brain tumors that don’t cause symptoms. For some people, brain tumors can recur (return) after treatment. If this happens to you, you may need to continue treatments, including chemotherapy or radiation, to keep the tumor from growing or spreading.

What is the survival rate for brain tumors?

Survival rates are different for each type of brain tumor and vary based on your age, race and overall health. Survival rates are estimates based on averages. The five-year survival rate tells you what percent of people live at least five years after they’re diagnosed with a brain tumor. The five-year survival rates for meningioma, the most common type of benign (noncancerous) primary brain tumor, are:

Over 96% for children ages 14 and under.

97% in people ages 15 to 39.

Over 87% in adults 40 and older.

Survival rates vary widely and depend on several factors. Talk with your healthcare provider about what to expect with your diagnosis.

Living With

When should I see my healthcare provider about my brain tumor?

If you’ve been diagnosed with a brain tumor, you’ll need to see your healthcare team regularly to receive treatment and monitor your symptoms.

You should see your healthcare provider if your brain tumor symptoms get worse or you have new symptoms.

Even after brain tumor treatment, you should follow up with your healthcare provider regularly.

What questions should I ask my doctor about a brain tumor diagnosis?

If you’ve been diagnosed with a brain tumor, it may be helpful to ask your healthcare provider the following questions:

Is the tumor malignant or benign?

What kind of tumor do I have?

What type of treatment is best for me?

Will my treatment cause side effects?

What type of specialists will be part of my care?

What’s my prognosis?

Are my family members at risk of developing a brain tumor?

Do you know of any online or in-person support groups for people with brain tumors?

**Source**

Cleveland Clinic. (2024) *Brain Cancer (Brain Tumor)*. Available at: https://my.clevelandclinic.org/health/diseases/6149-brain-cancer-brain-tumor (Accessed: 23 May 2025).

**TRAUMATIC BRAIN INJURY(TBI)**

## **Overview**

Traumatic brain injury usually results from a violent blow or jolt to the head or body. An object that goes through brain tissue, such as a bullet or shattered piece of skull, also can cause traumatic brain injury.

Mild traumatic brain injury may affect your brain cells temporarily. More-serious traumatic brain injury can result in bruising, torn tissues, bleeding and other physical damage to the brain. These injuries can result in long-term complications or death.

Symptoms

Traumatic brain injury can have wide-ranging physical and psychological effects. Some signs or symptoms may appear immediately after the traumatic event, while others may appear days or weeks later.

Mild traumatic brain injury

The signs and symptoms of mild traumatic brain injury may include:

Physical symptoms

o Headache

o Nausea or vomiting

o Fatigue or drowsiness

o Problems with speech

o Dizziness or loss of balance

Sensory symptoms

o Sensory problems, such as blurred vision, ringing in the ears, a bad taste in the mouth or changes in the ability to smell

o Sensitivity to light or sound

Cognitive, behavioral or mental symptoms

o Loss of consciousness for a few seconds to a few minutes

o No loss of consciousness, but a state of being dazed, confused or disoriented

o Memory or concentration problems

o Mood changes or mood swings

o Feeling depressed or anxious

o Difficulty sleeping

o Sleeping more than usual

Moderate to severe traumatic brain injuries

Moderate to severe traumatic brain injuries can include any of the signs and symptoms of mild injury, as well as these symptoms that may appear within the first hours to days after a head injury:

Physical symptoms

o Loss of consciousness from several minutes to hours

o Persistent headache or headache that worsens

o Repeated vomiting or nausea

o Convulsions or seizures

o Dilation of one or both pupils of the eyes

o Clear fluids draining from the nose or ears

o Inability to awaken from sleep

o Weakness or numbness in fingers and toes

o Loss of coordination

Cognitive or mental symptoms

o Profound confusion

o Agitation, combativeness or other unusual behavior

o Slurred speech

o Coma and other disorders of consciousness

Children's symptoms

Infants and young children with brain injuries might not be able to communicate headaches, sensory problems, confusion and similar symptoms. In a child with traumatic brain injury, you may observe:

o Change in eating or nursing habits

o Unusual or easy irritability

o Persistent crying and inability to be consoled

o Change in ability to pay attention

o Change in sleep habits

o Seizures

o Sad or depressed mood

o Drowsiness

o Loss of interest in favorite toys or activities

When to see a doctor

Always see your doctor if you or your child has received a blow to the head or body that concerns you or causes behavioral changes. Seek emergency medical care if there are any signs or symptoms of traumatic brain injury following a recent blow or other traumatic injury to the head.

The terms "mild," "moderate" and "severe" are used to describe the effect of the injury on brain function. A mild injury to the brain is still a serious injury that requires prompt attention and an accurate diagnosis.

## **Causes**

Traumatic brain injury is usually caused by a blow or other traumatic injury to the head or body. The degree of damage can depend on several factors, including the nature of the injury and the force of impact.

Common events causing traumatic brain injury include the following:

* + **Falls.** Falls from bed or a ladder, down stairs, in the bath, and other falls are the most common cause of traumatic brain injury overall, particularly in older adults and young children.
  + **Vehicle-related collisions.** Collisions involving cars, motorcycles or bicycles — and pedestrians involved in such accidents — are a common cause of traumatic brain injury.
  + **Violence.** Gunshot wounds, domestic violence, child abuse and other assaults are common causes. Shaken baby syndrome is a traumatic brain injury in infants caused by violent shaking.
  + **Sports injuries.** Traumatic brain injuries may be caused by injuries from a number of sports, including soccer, boxing, football, baseball, lacrosse, skateboarding, hockey, and other high-impact or extreme sports. These are particularly common in youth.
  + **Explosive blasts and other combat injuries.** Explosive blasts are a common cause of traumatic brain injury in active-duty military personnel. Although how the damage occurs isn't yet well understood, many researchers believe that the pressure wave passing through the brain significantly disrupts brain function.

Traumatic brain injury also results from penetrating wounds, severe blows to the head with shrapnel or debris, and falls or bodily collisions with objects following a blast.

## **Risk factors**

The people most at risk of traumatic brain injury include:

* + Children, especially newborns to 4-year-olds
  + Young adults, especially those between ages 15 and 24
  + Adults age 60 and older
  + Males in any age group

## **Complications**

Several complications can occur immediately or soon after a traumatic brain injury. Severe injuries increase the risk of a greater number of and more-severe complications.

### Altered consciousness

Moderate to severe traumatic brain injury can result in prolonged or permanent changes in a person's state of consciousness, awareness or responsiveness. Different states of consciousness include:

* + **Coma.** A person in a coma is unconscious, unaware of anything and unable to respond to any stimulus. This results from widespread damage to all parts of the brain. After a few days to a few weeks, a person may emerge from a coma or enter a vegetative state.
  + **Vegetative state.** Widespread damage to the brain can result in a vegetative state. Although the person is unaware of surroundings, he or she may open his or her eyes, make sounds, respond to reflexes, or move.

It's possible that a vegetative state can become permanent, but often individuals progress to a minimally conscious state.

* + **Minimally conscious state.** A minimally conscious state is a condition of severely altered consciousness but with some signs of self-awareness or awareness of one's environment. It is sometimes a transitional state from a coma or vegetative condition to greater recovery.
  + **Brain death.** When there is no measurable activity in the brain and the brainstem, this is called brain death. In a person who has been declared brain dead, removal of breathing devices will result in cessation of breathing and eventual heart failure. Brain death is considered irreversible.

### Physical complications

* + **Seizures.** Some people with traumatic brain injury will develop seizures. The seizures may occur only in the early stages, or years after the injury. Recurrent seizures are called post-traumatic epilepsy.
  + **Fluid buildup in the brain (hydrocephalus).** Cerebrospinal fluid may build up in the spaces in the brain (cerebral ventricles) of some people who have had traumatic brain injuries, causing increased pressure and swelling in the brain.
  + **Infections.** Skull fractures or penetrating wounds can tear the layers of protective tissues (meninges) that surround the brain. This can enable bacteria to enter the brain and cause infections. An infection of the meninges (meningitis) could spread to the rest of the nervous system if not treated.
  + **Blood vessel damage.** Several small or large blood vessels in the brain may be damaged in a traumatic brain injury. This damage could lead to a stroke, blood clots or other problems.
  + **Headaches.** Frequent headaches are very common after a traumatic brain injury. They may begin within a week after the injury and could persist for as long as several months.
  + **Vertigo.** Many people experience vertigo, a condition characterized by dizziness, after a traumatic brain injury.

Sometimes, any or several of these symptoms might linger for a few weeks to a few months after a traumatic brain injury. When a combination of these symptoms lasts for an extended period of time, this is generally referred to as persistent post-concussive symptoms.

Traumatic brain injuries at the base of the skull can cause nerve damage to the nerves that emerge directly from the brain (cranial nerves). Cranial nerve damage may result in:

* + Paralysis of facial muscles or losing sensation in the face
  + Loss of or altered sense of smell or taste
  + Loss of vision or double vision
  + Swallowing problems
  + Dizziness
  + Ringing in the ear
  + Hearing loss

### Intellectual problems

Many people who have had a significant brain injury will experience changes in their thinking (cognitive) skills. It may be more difficult to focus and take longer to process your thoughts. Traumatic brain injury can result in problems with many skills, including:

Cognitive problems

* + Memory
  + Learning
  + Reasoning
  + Judgment
  + Attention or concentration

Executive functioning problems

* + Problem-solving
  + Multitasking
  + Organization
  + Planning
  + Decision-making
  + Beginning or completing tasks

### Communication problems

Language and communications problems are common following traumatic brain injuries. These problems can cause frustration, conflict and misunderstanding for people with a traumatic brain injury, as well as family members, friends and care providers.

Communication problems may include:

* + Difficulty understanding speech or writing
  + Difficulty speaking or writing
  + Inability to organize thoughts and ideas
  + Trouble following and participating in conversations

Communication problems that affect social skills may include:

* + Trouble with turn taking or topic selection in conversations
  + Problems with changes in tone, pitch or emphasis to express emotions, attitudes or subtle differences in meaning
  + Difficulty understanding nonverbal signals
  + Trouble reading cues from listeners
  + Trouble starting or stopping conversations
  + Inability to use the muscles needed to form words (dysarthria)

### Behavioral changes

People who've experienced brain injury may experience changes in behaviors. These may include:

* + Difficulty with self-control
  + Lack of awareness of abilities
  + Risky behavior
  + Difficulty in social situations
  + Verbal or physical outbursts

### Emotional changes

Emotional changes may include:

* + Depression
  + Anxiety
  + Mood swings
  + Irritability
  + Lack of empathy for others
  + Anger
  + Insomnia

### Sensory problems

Problems involving senses may include:

* + Persistent ringing in the ears
  + Difficulty recognizing objects
  + Impaired hand-eye coordination
  + Blind spots or double vision
  + A bitter taste, a bad smell or difficulty smelling
  + Skin tingling, pain or itching
  + Trouble with balance or dizziness

### Degenerative brain diseases

The relationship between degenerative brain diseases and brain injuries is still unclear. But some research suggests that repeated or severe traumatic brain injuries might increase the risk of degenerative brain diseases. But this risk can't be predicted for an individual — and researchers are still investigating if, why and how traumatic brain injuries might be related to degenerative brain diseases.

A degenerative brain disorder can cause gradual loss of brain functions, including:

* + Alzheimer's disease, which primarily causes the progressive loss of memory and other thinking skills
  + Parkinson's disease, a progressive condition that causes movement problems, such as tremors, rigidity and slow movements
  + Dementia pugilistica — most often associated with repetitive blows to the head in career boxing — which causes symptoms of dementia and movement problems

## **Prevention**

Follow these tips to reduce the risk of brain injury:

* + **Seat belts and airbags.** Always wear a seat belt in a motor vehicle. A small child should always sit in the back seat of a car secured in a child safety seat or booster seat that is appropriate for his or her size and weight.
  + **Alcohol and drug use.** Don't drive under the influence of alcohol or drugs, including prescription medications that can impair the ability to drive.
  + **Helmets.** Wear a helmet while riding a bicycle, skateboard, motorcycle, snowmobile or all-terrain vehicle. Also wear appropriate head protection when playing baseball or contact sports, skiing, skating, snowboarding or riding a horse.
  + **Pay attention to your surroundings.** Don't drive, walk or cross the street while using your phone, tablet or any smart device. These distractions can lead to accidents or falls.

### Preventing falls

The following tips can help older adults avoid falls around the house:

* + Install handrails in bathrooms
  + Put a nonslip mat in the bathtub or shower
  + Remove area rugs
  + Install handrails on both sides of staircases
  + Improve lighting in the home, especially around stairs
  + Keep stairs and floors clear of clutter
  + Get regular vision checkups
  + Get regular exercise

### Preventing head injuries in children

The following tips can help children avoid head injuries:

* + Install safety gates at the top of a stairway
  + Keep stairs clear of clutter
  + Install window guards to prevent falls
  + Put a nonslip mat in the bathtub or shower
  + Use playgrounds that have shock-absorbing materials on the ground
  + Make sure area rugs are secure
  + Don't let children play on fire escapes or balconies

Diagnosis

Traumatic brain injuries may be emergencies. In the case of more-severe TBIs, consequences can worsen rapidly without treatment. Doctors or first responders need to assess the situation quickly.

Glasgow Coma Scale

This 15-point test helps a doctor or other emergency medical personnel assess the initial severity of a brain injury by checking a person's ability to follow directions and move their eyes and limbs. The coherence of speech also provides important clues.

Abilities are scored from three to 15 in the Glasgow Coma Scale. Higher scores mean less severe injuries.

Information about the injury and symptoms

If you saw someone sustain an injury or arrived immediately after an injury, you may be able to provide medical personnel with information that's useful in assessing the injured person's condition.

Answers to the following questions may be beneficial in judging the severity of injury:

How did the injury occur?

Did the person lose consciousness?

How long was the person unconscious?

Did you observe any other changes in alertness, speaking, coordination or other signs of injury?

Where was the head or other parts of the body struck?

Can you provide any information about the force of the injury? For example, what hit the person's head, how far did he or she fall, or was the person thrown from a vehicle?

Was the person's body whipped around or severely jarred?

Imaging tests

Computerized tomography (CT) scan. This test is usually the first performed in an emergency room for a suspected traumatic brain injury. A CT scan uses a series of X-rays to create a detailed view of the brain. A CT scan can quickly visualize fractures and uncover evidence of bleeding in the brain (hemorrhage), blood clots (hematomas), bruised brain tissue (contusions), and brain tissue swelling.

Magnetic resonance imaging (MRI). An MRI uses powerful radio waves and magnets to create a detailed view of the brain. This test may be used after the person's condition stabilizes, or if symptoms don't improve soon after the injury.

Intracranial pressure monitor

Tissue swelling from a traumatic brain injury can increase pressure inside the skull and cause additional damage to the brain. Doctors may insert a probe through the skull to monitor this pressure.

More Information

Brain magnetic resonance imaging

CT scan

MRI

Treatment

Treatment is based on the severity of the injury.

Mild injury

Mild traumatic brain injuries usually require no treatment other than rest and over-the-counter pain relievers to treat a headache. However, a person with a mild traumatic brain injury usually needs to be monitored closely at home for any persistent, worsening or new symptoms. He or she may also have follow-up doctor appointments.

The doctor will indicate when a return to work, school or recreational activities is appropriate. Relative rest — which means limiting physical or thinking (cognitive) activities that make things worse — is usually recommended for the first few days or until your doctor advises that it's OK to resume regular activities. It isn't recommended that you rest completely from mental and physical activity. Most people return to normal routines gradually.

Immediate emergency care

Emergency care for moderate to severe traumatic brain injuries focuses on making sure the person has enough oxygen and an adequate blood supply, maintaining blood pressure, and preventing any further injury to the head or neck.

People with severe injuries may also have other injuries that need to be addressed. Additional treatments in the emergency room or intensive care unit of a hospital will focus on minimizing secondary damage due to inflammation, bleeding or reduced oxygen supply to the brain.

Medications

Medications to limit secondary damage to the brain immediately after an injury may include:

Anti-seizure drugs. People who've had a moderate to severe traumatic brain injury are at risk of having seizures during the first week after their injury.

An anti-seizure drug may be given during the first week to avoid any additional brain damage that might be caused by a seizure. Continued anti-seizure treatments are used only if seizures occur.

Coma-inducing drugs. Doctors sometimes use drugs to put people into temporary comas because a comatose brain needs less oxygen to function. This is especially helpful if blood vessels, compressed by increased pressure in the brain, are unable to supply brain cells with normal amounts of nutrients and oxygen.

Diuretics. These drugs reduce the amount of fluid in tissues and increase urine output. Diuretics, given intravenously to people with traumatic brain injury, help reduce pressure inside the brain.

Surgery

Emergency surgery may be needed to minimize additional damage to brain tissues. Surgery may be used to address the following problems:

Removing clotted blood (hematomas). Bleeding outside or within the brain can result in a collection of clotted blood (hematoma) that puts pressure on the brain and damages brain tissue.

Repairing skull fractures. Surgery may be needed to repair severe skull fractures or to remove pieces of skull in the brain.

Bleeding in the brain. Head injuries that cause bleeding in the brain may need surgery to stop the bleeding.

Opening a window in the skull. Surgery may be used to relieve pressure inside the skull by draining accumulated cerebrospinal fluid or creating a window in the skull that provides more room for swollen tissues.

Rehabilitation

Most people who have had a significant brain injury will require rehabilitation. They may need to relearn basic skills, such as walking or talking. The goal is to improve their abilities to perform daily activities.

Therapy usually begins in the hospital and continues at an inpatient rehabilitation unit, a residential treatment facility or through outpatient services. The type and duration of rehabilitation is different for everyone, depending on the severity of the brain injury and what part of the brain was injured.

Rehabilitation specialists may include:

Physiatrist, a doctor trained in physical medicine and rehabilitation, who oversees the entire rehabilitation process, manages medical rehabilitation problems and prescribes medication as needed

Occupational therapist, who helps the person learn, relearn or improve skills to perform everyday activities

Physical therapist, who helps with mobility and relearning movement patterns, balance and walking

Speech and language therapist, who helps the person improve communication skills and use assistive communication devices if necessary

Neuropsychologist, who assesses cognitive impairment and performance, helps the person manage behaviors or learn coping strategies, and provides psychotherapy as needed for emotional and psychological well-being

Social worker or case manager, who facilitates access to service agencies, assists with care decisions and planning, and facilitates communication among various professionals, care providers and family members

Rehabilitation nurse, who provides ongoing rehabilitation care and services and who helps with discharge planning from the hospital or rehabilitation facility

Traumatic brain injury nurse specialist, who helps coordinate care and educates the family about the injury and recovery process

Recreational therapist, who assists with time management and leisure activities

Vocational counselor, who assesses the ability to return to work and appropriate vocational opportunities and who provides resources for addressing common challenges in the workplace.

A number of strategies can help a person with traumatic brain injury cope with complications that affect everyday activities, communication and interpersonal relationships. Depending on the severity of injury, a family caregiver or friend may need to help implement the following approaches:

* **Join a support group.** Talk to your doctor or rehabilitation therapist about a support group that can help you talk about issues related to your injury, learn new coping strategies and get emotional support.
* **Write things down.** Keep a record of important events, people's names, tasks or other things that are difficult to remember.
* **Follow a routine.** Keep a consistent schedule, keep things in designated places to avoid confusion and take the same routes when going to frequently visited destinations.
* **Take breaks.** Make arrangements at work or school to take breaks as needed.
* **Alter work expectations or tasks.** Appropriate changes at work or school may include having instructions read to you, allowing more time to complete tasks or breaking down tasks into smaller steps.
* **Avoid distractions.** Minimize distractions such as loud background noise from a television or radio.
* **Stay focused.** Work on one task at a time.

Source

Mayo Clinic Staff. (2023) *Traumatic brain injury: Diagnosis and treatment*. Mayo Clinic. Available at: https://www.mayoclinic.org/diseases-conditions/traumatic-brain-injury/diagnosis-treatment/drc-20378561 (Accessed: 23 May 2025).

# **Cerebral Palsy**

## KEY POINTS

* Cerebral palsy (CP) affects a person’s ability to move and maintain balance and posture.
* The symptoms vary from person to person.
* CP does not worsen over time, though the exact symptoms can change over a person’s lifetime.
* There is no cure for CP, but treatment can improve the lives of those who have the condition.

**What it is**

Cerebral palsy (CP) is a group of disorders that affect a person's ability to move and maintain balance and posture.

* "Cerebral" means having to do with the brain
* "Palsy" means weakness in or problems with using the muscles

CP is caused by abnormal brain development or damage to the developing brain that affects a person's ability to control their muscles. CP is the most common motor disability in childhood.

The symptoms of CP vary from person to person. A person with severe CP might need to use special equipment to be able to walk or might not be able to walk at all and might need lifelong care. A person with mild CP, on the other hand, might walk a little awkwardly, but might not need any special help. CP does not get worse over time, though the exact symptoms can change over a person's lifetime.

All people with CP have problems with movement and posture. Many also have related conditions such as the following:

* Intellectual disability
* Seizures
* Problems with vision, hearing, or speech
* Changes in the spine (such as scoliosis)
* Joint problems (such as contracturesB)

## Types

Doctors classify CP according to the main type of movement disorder involved. Depending on which areas of the brain are affected, one or more of the following movement disorders can occur:

* Stiff muscles (spasticity)
* Uncontrollable movements (dyskinesia)
* Poor balance and coordination (ataxia)

### **There are four main types of CP:**

#### ***Spastic cerebral palsy***

The most common type of CP is spastic CP. Spastic CP affects about 80% of people with CP.

People with spastic CP have increased muscle tone. This means their muscles are stiff and, as a result, their movements can be awkward. Spastic CP usually is described by which parts of the body are affected:

* Spastic diplegia/diparesis: Muscle stiffness is mainly in the legs, with the arms less affected or not affected at all. Tight hip and leg muscles cause legs to pull together, turn inward, and cross at the knees (also known as scissoring), making walking difficult.
* Spastic hemiplegia/hemiparesis: Affects only one side of a person's body; usually the arm is more affected than the leg.
* Spastic quadriplegia/quadriparesis: Most severe form of spastic CP and affects all four limbs, the trunk, and the face. People with spastic quadriparesis usually cannot walk and often have other developmental disabilities such as intellectual disability; seizures; or problems with vision, hearing, or speech.

#### ***Dyskinetic cerebral palsy***

People with dyskinetic CP have problems controlling the movement of their hands, arms, feet, and legs, making it difficult to sit and walk.

Dyskinetic CP includes athetoid, choreoathetoid, and dystonic cerebral palsies. The movements are uncontrollable and can be slow and writhing or rapid and jerky. Sometimes the face and tongue are affected, and the person has a hard time sucking, swallowing, and talking. A person with dyskinetic CP has muscle tone that can change (varying from too tight to too loose) not only from day to day, but even during a single day.

#### ***Ataxic cerebral palsy***

People with ataxic CP have problems with balance and coordination. They might be unsteady when they walk. They might have a hard time with quick movements or movements that need a lot of control, like writing. They might have a hard time controlling their hands or arms when they reach for something.

#### ***Mixed cerebral palsy***

Some people have symptoms of more than one type of CP. The most common type of mixed CP is spastic-dyskinetic CP.

## Signs and symptoms

There is no cure for CP, but treatment can improve the lives of those who have the condition.

The signs of CP vary greatly because there are many different types and levels of disability. The main sign that a child might have CP is a delay reaching motor or movement milestones (such as rolling over, sitting, standing, or walking). Following are some other signs of possible CP. It is important to note that some children without CP also might have some of these signs.

### **In a baby younger than 6 months of age**

* Their head lags when you pick him up while he's lying on his back.
* They feel stiff.
* They feel floppy.
* When held cradled in your arms, they seem to overextend his back and neck, constantly acting as if they are pushing away from you.
* When you pick them up, their legs get stiff, and they cross or scissor.

### **In a baby older than 6 months of age**

* They don't roll over in either direction.
* They cannot bring her hands together.
* They have difficulty bringing their hands to their mouth.
* They reach out with only one hand while keeping the other fisted.

### **In a baby older than 10 months of age**

* They crawl in a lopsided manner, pushing off with one hand and leg while dragging the opposite hand and leg.
* They scoot around on their buttocks or hops on their knees but do not crawl on all fours.

Tell your child's doctor or nurse if you notice any of these signs.

## Causes

CP is caused by abnormal development of the brain or damage to the developing brain that affects a child's ability to control their muscles. There are several possible causes of the abnormal development or damage. People used to think that CP was mainly caused by lack of oxygen during the birth process. Now, scientists think that this causes only a small number of CP cases.

The abnormal development of the brain or damage that leads to CP can happen before birth, during birth, within a month after birth, or during the first years of a child's life, while the brain is still developing. CP related to abnormal development of the brain or damage that occurred before or during birth is called congenital CP. The majority of CP (85% to 90%) is congenital. In many cases, the specific cause is not known.

A small percentage of CP is caused by abnormal development of the brain or damage that occurs more than 28 days after birth. This is called acquired CP and usually is associated with an infection (such as meningitis) or head injury.

## Screening and diagnosis

Diagnosing CP at an early age is important to the well-being of children and their families. Diagnosing CP can take several steps:

### **Developmental monitoring**

Developmental monitoring (also called surveillance) means tracking a child's growth and development over time. If any concerns about the child's development are raised during monitoring, then a developmental screening test should be given as soon as possible.

### **Developmental screening**

During developmental screening, a short test is given to see if the child has specific developmental delays, such as motor or movement delays. If the results of the screening test are cause for concern, then the doctor will make referrals for developmental and medical evaluations.

### **Developmental and medical evaluations**

The goal of a developmental evaluation is to diagnose the specific type of disorder that affects a child.

## Treatment and intervention services

There is no cure for CP, but early identification and treatment can help improve the lives of those who have the condition. It is important to begin a treatment program as early as possible.

After a CP diagnosis is made, a team of health professionals works with the child and family to develop a plan to help the child reach his or her full potential. Common treatments include medicines; surgery; braces; and physical, occupational, and speech therapy. No single treatment is the best one for all children with CP. Before deciding on a treatment plan, it is important to talk with the child's doctor to understand all the risks and benefits.

# Screening for Cerebral Palsy

## KEY POINTS

* Diagnosing cerebral palsy (CP) at an early age is important to the well-being of children and their families. It can take several steps.
* Developmental monitoring tracks a child's growth and development over time.
* Developmental screening checks for developmental delays.
* Developmental and medical evaluation diagnoses the specific disorder.

## Developmental monitoring

Developmental monitoring (also called surveillance) means tracking a child's growth and development over time. At each well-child office visit, to monitor the child's development, the doctor may do the following:

* Ask parents if they have any concerns about their child's development
* Take or update the child's developmental history
* Watch the child during the exam to see how they move

If any concerns about the child's development are raised during monitoring, then a developmental screening test should be given as soon as possible.

### Fact‎

It is important for doctors to monitor the development of all children, but especially those who are at a higher risk for developmental problems due to preterm birth or low birthweight.

## Developmental screening

A short developmental screening test is routinely given to see if the child has specific developmental delays, such as motor or movement delays. Some tests are in the form of interviews or questionnaires completed by parents, others are given to the child by the doctor. The American Academy of Pediatrics recommends that all children be screened for developmental delays during regular well-child office visits at

* **9 months**: Many issues involving movement are seen easily at this age.
* **18 months**: Mild movement delays might be easier to see at this point.
* **24 or 30 months**: Most movement delays can be found at this age.

A developmental screening test also can be given whenever the child's parents, doctor, or other caregivers have concerns about the child's development. Concerns from the test results can prompt the doctor to make referrals for both of the following:

* Developmental and medical evaluations AND
* Early intervention or early childhood services

## Developmental and medical evaluations

The goal of a developmental evaluation is to diagnose the specific type of disorder that affects a child. To evaluate movement or motor delays, the doctor will look closely at the child's motor skills, muscle tone, reflexes, and posture and take a careful medical history from the parents. The doctor will try to rule out other disorders that could cause similar problems.

Because many children with CP also have related developmental conditions such as intellectual disability; seizures; or vision, hearing, or speech problems, it is important to evaluate the child to find these disorders as well.

The developmental evaluation can be performed by the primary care doctor or by a specialist. Specialists who can do this type of developmental evaluation include

* Developmental pediatricians or neurodevelopment pediatricians (doctors with special training in child development and in evaluating children's developmental problems)
* Child neurologists (doctors with special training in childhood diseases of the brain, spine, and nerves)
* Pediatric physiatrists or pediatric rehabilitation doctors (doctors with special training in physical medicine and rehabilitation for children)

In addition to the developmental evaluation, additional tests can be done to look for a cause of CP. Specialists might suggest brain imaging tests, such as x-ray, computed tomography (CT scan), or magnetic resonance imaging (MRI). An electroencephalogram (EEG), genetic testing, or metabolic testing, or a combination of these, also might be done.

## Diagnosis

CP generally is diagnosed during the first or second year after birth. But if a child's symptoms are mild, it is sometimes difficult to make a diagnosis until the child is a few years older.

## What to do if you are concerned

If you think your child is not meeting movement milestones or might have CP, you can take the following steps to find help:

* Contact your doctor or nurse and share your concerns.
* Ask for a referral to a specialist who can do a more in-depth evaluation of your child.
* Call your state or territory's early intervention program to request a free or reduced cost evaluation.

# Risk Factors for Cerebral Palsy

## KEY POINTS

* Cerebral palsy (CP) is caused by abnormal development of the brain or damage to the developing brain that affects a child’s ability to control their muscles.
* CP related to events before or during birth is called congenital CP and describes the majority of cases (85%–90%).
* CP can also occur during the first years of a child’s life (known as acquired CP).

**What increases risk**

Some things increase the chance that a child will have CP. These are called risk factors. It is important to remember that having a risk factor does not mean that a child will have CP.

Some of the risk factors for congenital CP are:

* **Low birthweight**: Children who weigh less than 5 pounds, 8 ounces (2,500 grams) at birth, and especially those who weigh less than 3 pounds, 5 ounces (1,500 grams) have a greater chance of having CP.
* **Premature birth**: Children who were born before the 37th week of pregnancy, especially if they were born before the 32nd week of pregnancy, have a greater chance of having CP. Intensive care for premature infants has improved a lot over the past several decades. Babies born very early are more likely to live now, but many have medical problems that can put them at risk for CP.
* **Multiple births**: Twins, triplets, and other multiple births have a higher risk for CP, especially if a baby's twin or triplet dies before birth or shortly after birth. Some, but not all, of this increased risk is due to the fact that children born from multiple pregnancies often are born early or with low birthweight, or both.
* **Assisted reproductive technology (ART)** **infertility treatments:** Children born from pregnancies resulting from the use of some infertility treatments have a greater chance of having CP. Most of the increased risk is explained by preterm delivery or multiple births, or both; both preterm delivery and multiple births are increased among children conceived with ART infertility treatments.
* Infections during pregnancy: Infections can lead to increases in certain proteins called cytokines that circulate in the brain and blood of the baby during pregnancy. Some types of infection that have been linked with CP include viruses such as chickenpox, rubella (German measles), and cytomegalovirus (CMV), and bacterial infections such as infections of the placenta or fetal membranes, or maternal pelvic infections.
* **Jaundice and kernicterus:**Jaundice is the yellow color seen in the skin of many newborns. When severe jaundice goes untreated for too long, it can cause a condition called kernicterus. This can cause CP and other conditions. Sometimes, kernicterus results from ABO or Rh blood type difference between the mother and baby.
* **Medical conditions of the mother:**Mothers with thyroid problems, intellectual disability, or seizures have a slightly higher risk of having a child with CP.
* **Birth complications**: Detachment of the placenta, uterine rupture, or problems with the umbilical cord during birth can disrupt oxygen supply to the baby and result in CP.

## Prevention of cerebral palsy before, during, and after birth

### **What we know**

In many cases, the cause or causes of CP are not fully known, which means that currently little can be done to prevent it.

CP related to genetics is not preventable. However, there are actions people can take before and during pregnancy, as well as after birth that might help reduce the risk of developmental problems, including CP.

Taking steps to help ensure a healthy pregnancy can help prevent developmental problems, including CP. Acquired CP, which is CP that occurs after birth, often is related to an infection or injury, and some of these cases can be prevented.

### Did you know?

Developmental disabilities are a group of conditions due to an impairment in physical, learning, language, or behavior areas. These conditions begin during the developmental period, may impact day-to-day functioning, and usually last throughout a person's lifetime.

### **Before pregnancy**

#### ***Being as healthy as possible before pregnancy***

* Make sure any infections in the mother are treated and health conditions are in control, ideally before pregnancy occurs.
* Get vaccinated for certain diseases (such as chickenpox and rubella) that could harm a developing baby. It is important to have many of these vaccinations *before* becoming pregnant.
* If assistive reproductive technology (ART) infertility treatments are used to get pregnant, consider ways to reduce the chance of a multiple pregnancy (twins, triplets, or more), such as transferring only one embryo at a time.

### **During pregnancy**

Talk to your doctor about important steps to take during pregnancy to keep you and your developing baby healthy.

#### ***Important steps to a healthy pregnancy***

* Get early and regular prenatal care, both for your health and for that of your developing baby.
* Contact your health care provider if you get sick, have a fever, or have other signs of infection during pregnancy.
* Wash your hands often with soap and water to help reduce the risk of infections that might harm your developing baby.
* A flu shot is your best protection against serious illness from the flu. A flu shot can protect pregnant women and their unborn babies, both before and after birth.
* Find out your blood type and talk to your doctor about ways to prevent potential problems. If there is a difference in the blood type or Rh incompatibility between mother and baby, it can cause jaundice and kernicterus. Doctors can treat the mother with Rh immune globulins (RhoGAM) at the 28th week of pregnancy and again shortly after giving birth to prevent kernicterus from occurring.
* Talk to your doctor about ways to prevent problems if you are at risk for preterm delivery. Research has shown that taking magnesium sulfate before anticipated early preterm birth reduces the risk of CP among surviving infants.

#### ***Keeping your baby healthy and safe after birth***

* Ask your doctor or nurse about a jaundice bilirubin test. Any baby can get jaundice. Severe jaundice that is not treated can cause brain damage, called kernicterus. Kernicterus is a cause of CP that potentially can be prevented. Your baby should be checked for jaundice in the hospital and again within 48 hours after leaving the hospital.
* Make sure your child is vaccinated against infections that can cause meningitis and encephalitis, including *Haemophilus* *influenzae* type B (HiB vaccine) and *Streptococcuspneumoniae*(pneumococcal vaccine).

# Treatment and Intervention for Cerebral Palsy

## KEY POINTS

* There is no cure for cerebral palsy (CP), but early identification and treatment can improve the lives of those who have the condition.
* There are steps you can take if you are concerned about your child's development.
* The Individuals with Disabilities Education Act (IDEA) can help children and families access early intervention services and services for school-aged children.

## What to do if you are concerned

### **Talk to your child's healthcare provider**

If you think your child is not meeting movement milestones or might have CP, **contact your doctor or nurse and share your concerns**.

If you or your doctor is still concerned, **ask for a referral to a specialist** who can do a more in-depth evaluation of your child and assist in making a diagnosis.

### **Contact your state or territory's early intervention program**

In addition to talking to your child's healthcare provider, call your state or territory's early intervention program to request a free or reduced cost evaluation to find out if your child qualifies for intervention services. This is sometimes called a Child Find evaluation.

### Early intervention services can start even before a CP diagnosis is made.‎

*You do not need to wait for a doctor's referral or a medical diagnosis to call your state or territory's early intervention program.*

Where to call for a free or reduced cost evaluation from the state or territory depends on your child's age:

* **If your child is not yet 3 years old,** contact your local early intervention system. You can find the right contact information for your state by calling the Early Childhood Technical Assistance Center (ECTA) at 919-962-2001 or visit the Early Childhood Technical Assistance Center.
* **If your child is 3 years of age or older,** contact your local public school system. Even if your child is not yet old enough for kindergarten or enrolled in a public school, call your local elementary school or board of education and ask to speak with someone who can help you have your child evaluated. If you're not sure who to contact, you can call the Early Childhood Technical Assistance Center (ECTA) at 919-962-2001 or visit the Early Childhood Technical Assistance Center.

## Individuals with Disabilities Education Act (IDEA) Services

Both early intervention and school-aged services are available through our nation’s special education law—the Individuals with Disabilities Education Act (IDEA).

* Part C applies to early intervention services (ages birth to 36 months).
* Part B applies to services for school-aged children (ages 3 to 22 years).

Even if your child has not been diagnosed with CP, he or she may be eligible for IDEA services.

### **Part C of IDEA: Early Intervention for Babies and Toddlers**

Early intervention services can help children from birth through 36 months of age learn new skills, whether they have been identified recently with motor and movement delays or already have a CP diagnosis. Early intervention services can start even before a CP diagnosis is made.

Depending on the child's needs, early intervention services might include

* family training, counseling, and home visits;
* occupational, physical, or speech therapy;
* hearing loss services;
* health, nutrition, social work, and assistance with service coordination;
* assistive technology devices and services; and
* transportation.

Before Part C services start, an **Individual Family Service Plan (IFSP)** is developed by a team, which includes the parents and all providers who work with the child and the family. The IFSP describes the child's present level of development, the family's strengths and needs, the specific services to be provided to the child and the family, and a plan to transition to public school.

### **Part B of IDEA: Services for School-Aged Children**

Services for school-aged children with developmental disabilities (3 to 22 years of age) are provided free of charge through the public school system.

Among the services covered under IDEA are

* special education;
* related services such as physical, occupational, and speech therapy; and
* supplementary aids and services, such as adaptive equipment or special communication systems.

Before Part B services start, an **Individualized Education Plan (IEP)** is developed for children 3 to 22 years of age who qualify for special education services from school districts. An IEP is similar to an IFSP, but more focused on the child's goals rather than on the family's goals.

Source

Centers for Disease Control and Prevention (2024) *Treatment and Intervention for Cerebral Palsy*. Available at: https://www.cdc.gov/cerebral-palsy/treatment/index.html (Accessed: 5 June 2025).

**PERIPHERAL NERVOUS SYSTEM(PNS) DISORDERS**

* Peripheral Neuropathy

Peripheral neuropathy refers to any condition that affects the nerves outside your brain or spinal cord. This can happen for several reasons, from trauma to infections to inherited conditions. There are also many possible symptoms. Many causes, forms or symptoms of this condition are treatable, but this can vary widely from person to person.

Overview

Peripheral neuropathy conditions affect the peripheral nerves, which are nerves outside your brain and spinal cord.

Peripheral neuropathy can affect nerves anywhere in your body. It can disrupt your body’s control of automatic processes, as well as your sense of touch and muscle control.

**What is peripheral neuropathy?**

Peripheral neuropathy is an umbrella term for nerve diseases that affect a specific subdivision of your nervous system. Many different conditions can cause peripheral neuropathy, which means a wide range of symptoms is also possible. Peripheral neuropathy can also affect different body parts, depending on how and why it happens.

**What this name means**

The term “peripheral” is from the Greek word that means “around.” “Peripheral” in this context means outside of or away from the “central” nervous system. The term neuropathy combines two words that trace their origins back to ancient Greek:

Neuro-: From the Greek word “neuron,” meaning “nerve.”

-pathy: From the Greek word “pathos,” meaning “affliction” or “condition.”

Your nervous system has two parts, the central nervous system and the peripheral nervous system. Your brain and spinal cord are the two components that make up your central nervous system. Your peripheral nervous system consists of all the other nerves in your body. It also includes nerves that travel from your spinal cord and brain to supply your face and the rest of your body.

Peripheral neuropathy can refer to any condition affecting your peripheral nerves. Healthcare providers often use the terms “neuropathy” and “polyneuropathy” (meaning “disease of many nerves”) interchangeably with “peripheral neuropathy.” Peripheral nerves are farthest from the central nervous system, and they often show the earliest and most severe effects of these conditions

**Who does peripheral neuropathy affect?**

Peripheral neuropathy can affect anyone, regardless of age, sex, race or ethnicity, personal circumstances, medical history, etc. However, some people are at greater risk for specific types of peripheral neuropathy (see below under Causes and Symptoms for more about this).

Peripheral neuropathy is also very common with some age-related diseases. That means the risk of developing peripheral neuropathy increases as you get older.

**How common is this condition?**

Peripheral neuropathy is common, partly because this term refers to so many conditions. About 2.4% of people globally have a form of peripheral neuropathy. Among people 45 and older, that percentage rises to between 5% and 7%.

How does this condition affect my body?

To understand how peripheral neuropathy affects your body, it helps to know a little about the structure of neurons, a key type of cell that makes up your nerves. Neurons send and relay signals through your nervous system using electrical and chemical signals. Each neuron consists of the following:

Cell body: This is the main part of the cell.

Axon: This is a long, arm-like part that extends outward from the cell body. At the end of the axon are several finger-like extensions where the electrical signal in the neuron becomes a chemical signal. These extensions, known as synapses, lead to nearby nerve cells.

Dendrites: These are small branch-like extensions (their name comes from a Latin word that means “tree-like”) on the cell body. Dendrites are the receiving point for chemical signals from the synapses of other nearby neurons.

Myelin: This is a thin layer composed of fatty chemical compounds. Myelin surrounds the axon of many neurons and acts as a protective covering.

Disease types

Peripheral neuropathy happens in two main ways:

Demyelinating neuropathy: This happens when the myelin coating on the axon deteriorates or can’t form correctly. That affects the way signals travel through the neuron.

Axonal degeneration: This causes the axon to deteriorate and die off. The longer a neuron is, the worse the effect. That’s why axonal degeneration conditions tend to involve your legs and feet, which are farthest from your spinal cord and rely on connections using longer axons. Axonal degeneration is the most common pattern seen with peripheral neuropathy.

How quickly does peripheral neuropathy develop?

How peripheral neuropathy develops, particularly the timeline of its progress, depends very much on what causes it. Injuries can cause it to develop instantaneously or within minutes or hours. Some toxic and inflammation-based forms of peripheral neuropathy may develop rapidly over days or weeks, while most other conditions take months, years or even decades to develop.

Symptoms and Causes

Learn more about peripheral neuropathy.

What are the symptoms of peripheral neuropathy?

There are many different symptoms of peripheral neuropathy. This condition can affect a single nerve, a connected group of related nerves, or many nerves in multiple places throughout your body. The symptoms also depend on the type of nerve signals affected, and multiple signal types may be involved.

The symptom types (with more about them below) are:

* Motor.
* Sensory and pain.
* Autonomic.

Motor symptoms

Your peripheral nervous system carries motor signals, which are commands sent from your brain to your muscles. These signals are what make it possible for you to move around. Your muscles need nerve connections to the brain to stay healthy and work properly.

Motor symptoms include:

Muscle weakness and paralysis. Nerve deterioration from peripheral neuropathy weakens the connected muscles. That can cause paralysis, which may cause difficulty moving the toes, foot drop and hand weakness. Weakness can also affect muscles in the thighs, arms and elsewhere.

Muscle atrophy. Loss of nerve connection can cause muscles to shrink in size, as well as weaken. This especially happens in the feet, lower legs and hands with peripheral neuropathy. Sometimes there are deformities of the feet and hands because of muscle loss.

Uncontrolled muscle movements. Sometimes, nerves that lose their connection to the brain because of peripheral neuropathy become hyperactive on their own, causing cramps.

Sensory symptoms

Your peripheral nerves convert information about the outside world into nerve signals. Those signals then travel to your brain, which processes those signals into what you can sense of the world around you. Peripheral neuropathy can disrupt what your senses pick up from the outside world or the ability of those senses to communicate with your brain.

The sensory symptoms of peripheral neuropathy include:

Tingling. This happens when there’s a problem with nerves that carry signals to your brain. This is like radio static you hear when you’re too far from the broadcasting station.

Numbness. This happens when nerves can’t send or relay sensory signals, causing the loss of specific types of sensations. An example of this would be picking up a cold pop can, but not feeling the smoothness or coldness of the can, or not being able to feel the texture of carpet or the temperature of the floor through your feet.

Imbalance and clumsiness. Nerves also carry sensations that your brain uses to keep track of the location of your hands and feet. You’re not consciously aware of these sensations, but they’re critical for balance and coordination. Without these sensations, you can experience a loss of balance, especially in the dark, and clumsiness with your hands.

Pain. Nerve damage from peripheral neuropathy can cause malfunctions in how and when nerves send pain signals, making pain signals more intense (hyperalgesia) or happen too easily (allodynia). It can even cause nerves to generate pain signals spontaneously. This is known as “neuropathic” pain, and it’s the most noticeable and disruptive symptom of peripheral neuropathy.

Autonomic symptoms

Your body has several autonomic processes. These are the automatic functions of your body that happen without your thinking or even being aware of them. They include things like sweating, digestion, blood pressure control, etc. Autonomic nerve fibers carry autonomic signals. Disruptions in autonomic signals mean your body’s automatic processes can’t work correctly. Some may work off and on, while others may not work at all.

**Autonomic symptoms of peripheral neuropathy can include:**

Blood pressure changes. Your body automatically manages blood pressure, but damage to your peripheral nerves can disrupt this. That can cause sudden drops in blood pressure or increases in heart rate, especially when you stand up.

Sweating too much or not enough. Your body automatically manages its internal temperature, using sweating to shed heat. Peripheral nerve damage can cause you to sweat too much or not enough. That can lead to dryness and scaling on your feet, or excessive sweating after eating.

Bowel and bladder problems. Autonomic signals control your bowel and bladder without you having to think about them. Nerve fiber disruption can affect bowel movements (constipation or diarrhea), and can occasionally affect bladder control, too.

Sexual dysfunction. Your autonomic nervous system controls sexual arousal. That’s why autonomic problems can cause sexual dysfunction.

Other symptoms. Autonomic changes from peripheral neuropathy can also cause skin color changes, swelling, changes in the pupils of the eyes and blurry vision.

What causes peripheral neuropathy?

Peripheral neuropathy can happen for many reasons. These include:

Type 2 diabetes. The most common cause of peripheral neuropathy is unmanaged type 2 diabetes. When your blood sugar is too high for too long, it damages your peripheral nerves. That’s why people with type 2 diabetes can lose feeling in their feet and lower legs.

Alcohol use disorder. Excessive intake of alcohol, especially over long periods of time, can damage nerves. Alcohol use disorder is a common cause of peripheral neuropathy, and it can also contribute to vitamin deficiencies that lead to peripheral neuropathy.

Vitamin and nutrient deficiencies. People can develop nerve damage because they have deficiencies in certain vitamins. The deficiencies that are most likely to cause this are copper and vitamins B1, B6, B9, B12, folic acid (B9) and E. Too much vitamin B6 can also cause this.

Autoimmune and inflammatory conditions. Guillain-Barré syndrome and chronic inflammatory demyelinating polyneuropathy (CIDP) can cause severe weakness. They’re also very treatable. Neuropathy can happen due to lupus, rheumatoid arthritis, Sjögren syndrome, vasculitis and more.

Medications and toxins. Chemotherapy and certain other medications (antibiotics, and medications that treat arrhythmia and gout) can cause peripheral neuropathy. Exposure to some heavy metals and industrial chemicals can also cause it.

Tumors. Malignant tumors (cancer) and benign (noncancerous) tumors can both disrupt your peripheral nervous system.

Genetic conditions. Genetic conditions are ones you inherit from one or both parents. Examples of these causing peripheral neuropathy include amyloidosis, Fabry disease and Charcot-Marie-Tooth disease. There are treatments for familial amyloidosis and Fabry disease.

Infections. Nerve damage from infections can happen because of viruses, such as HIV, or bacteria — such as Borrelia burgdorferi, which causes Lyme disease. Another common example is having shingles, which can lead to lingering nerve pain.

Hansen disease (better known as leprosy). While the effects of this disease — which is rare in developed countries — are most visible on the skin, it also damages your peripheral nerves. It’s a very common cause of peripheral neuropathy in developing nations. worldwide

Trauma and surgery. Injuries and damage directly to nerves can happen from trauma or from medical procedures. Swelling or stretching can also damage nerves. This kind of damage is usually only in one location. It can be long-term or even permanent.

Vascular disorders (circulation-related problems). Lack of blood flow can cause peripheral neuropathy. A harmless, temporary form of this happens when you sit or lay a certain way and an arm or leg falls asleep. This goes away quickly if you shift position enough for circulation to return. More severe circulation problems can cause serious and permanent nerve damage.

Idiopathic neuropathy. It’s common for peripheral neuropathy to happen for unknown reasons. This type of neuropathy is known as “idiopathic” or “cryptogenic” (hidden or obscure cause).

Is peripheral neuropathy contagious?

Peripheral neuropathy isn’t contagious. While it can happen because of infectious diseases, this condition doesn’t spread from person to person on its own. The only exception is Hansen disease, which can spread from person to person but doesn’t spread easily.

Diagnosis and Tests

How is peripheral neuropathy diagnosed?

Diagnosing peripheral neuropathy usually involves a combination of methods. These include:

Symptoms and medical history. Your healthcare provider will likely ask questions about your medical history and any recent symptoms or changes you’ve noticed. They may also ask about other medical conditions and factors, such as type 2 diabetes, and your nutrition, habits and lifestyle.

Physical and neurological exams. These involve a healthcare provider looking for physical signs of peripheral neuropathy, including changes in your ability to feel sensations, muscle weakness, changes in your reflexes or trouble with walking and balance.

Lab, diagnostic and imaging tests. A wide range of tests can help with diagnosing peripheral neuropathy.

What tests will be done to diagnose peripheral neuropathy?

The most common types of tests for peripheral neuropathy (either to confirm the diagnosis or rule out other conditions) include:

Blood tests (these can detect many problems, ranging from immune system problems to toxins and poisons, especially metals like mercury or lead).

* Electromyogram.
* Nerve ultrasound.
* Nerve biopsy.
* Genetic testing.
* Magnetic resonance imaging (MRI).

Management and Treatment

How is peripheral neuropathy treated, and is there a cure?

The treatment for peripheral neuropathy can vary widely depending on its cause. Other factors can also affect treatment, including your medical history, personal preferences and more. Your healthcare provider is the best person to tell you more about the treatment(s) they recommend and the likely recovery timeline. In general, the following treatment methods are more common for peripheral neuropathy:

Medications. Many medications can treat peripheral nervous system problems. These can come in many forms, including injections, pills you take by mouth, patches that stick to your skin, slow-release medication and more.

Surgery. Surgery can help reconnect cut nerves and relieve pain due to trapped nerves. It can also sever or remove damaged or malfunctioning nerves to keep their signals from reaching the brain and vice versa.

Physical therapy. This can help you recover from injuries or medical procedures, or improve pain symptoms. It can also help you adapt to nervous system changes, including improving balance and preventing falls.

Devices and wearable equipment. These include medical devices like braces, canes and walkers, prescribed footwear and more. These may not directly treat peripheral neuropathy, but they can help prevent complications from it. An example is special footwear for people who have peripheral neuropathy because of type 2 diabetes.

Podiatry and foot care. Peripheral neuropathy commonly affects your feet. That can cause soft tissue and bone changes, including sores and infections, especially in people with type 2 diabetes. Many people with peripheral neuropathy need to see a podiatrist (foot specialist).

Other pain treatments. If your pain from peripheral neuropathy or nerve injury doesn’t improve with standard medications, pain specialists may occasionally offer other treatments such as acupuncture, transcutaneous electrical nerve stimulation, injections or surgery to implant a spinal cord stimulator.

What are the possible complications or side effects of peripheral neuropathy treatments?

The possible side effects and complications of treatments for peripheral neuropathy depend on many factors. These include the specific cause of the neuropathy, other conditions you have, the specific treatments you receive and more. Your healthcare provider is the best person to tell you more about the possible side effects and complications you might experience.

**How do I take care of myself or manage symptoms of peripheral neuropathy?**

Peripheral neuropathy is a sign of a problem with the nerve signals traveling between parts of your body and your brain. While this can happen for minor reasons that aren’t serious, it can also happen because of severe or dangerous conditions. It’s also sometimes possible to stop or reverse certain types of neuropathies if treatment begins quickly enough. Because of these factors, you shouldn’t try to self-diagnose and self-treat it. A healthcare provider is the best person to guide you in managing this condition.

**Outlook / Prognosis**

**What can I expect if I have this condition?**

The effects of peripheral neuropathy depend on the cause, the nerves it affects, your medical history, treatments you receive and more. Your healthcare provider is the best person to tell you more about what you can expect in your case.

**How long does peripheral neuropathy last?**

Peripheral neuropathy can be a temporary concern, or it can be permanent. How long it lasts depends on what caused it, the extent of the damage — if any — that it caused, the treatments and more.

Peripheral neuropathy is most likely to be permanent with chronic conditions like type 2 diabetes, autoimmune diseases and genetic conditions. However, this can still vary, so it’s best to ask your healthcare provider about what’s most likely in your case.

**What’s the outlook for this condition?**

Peripheral neuropathy is usually not dangerous, but it can have very disruptive effects on your life. These effects are usually not as severe when it only affects one nerve or a limited group of nerves. The more nerves it affects, the greater the potential impact.

The outlook also depends partly on your symptoms. Pain from peripheral neuropathy is usually the most disruptive symptom, but medications or other treatments may help. Autonomic symptoms are among the most serious because they involve your body’s vital functions. When those don’t work correctly, it can have very severe — and sometimes dangerous — effects.

Motor and sensory symptoms can also greatly disrupt your ability to work and go about your daily activities. They can cause problems — sometimes severe — with mobility, balance and coordination. Sensory symptoms are also disruptive, especially when they involve pain or affect your ability to control what you do with the affected body part(s).

Lastly, treatments can make a big difference in outlook. Some treatments can greatly reduce or even stop symptoms, but this varies. Your healthcare provider is the best source of information on the outlook for your case and what you can do to help.

**Prevention**

How can I reduce my risk of developing peripheral neuropathy or prevent it entirely?

Some of the possible causes of peripheral neuropathy are preventable. You can also lower your chances of developing it by preventing or delaying certain conditions. In general, the best preventive or precautionary steps you can take include:

Eating a balanced diet. Certain vitamin deficiencies, especially vitamin B12 deficiency, can affect your nervous system and cause major problems. Other vitamins, especially B6, are toxic and cause peripheral neuropathy at high levels.

Staying physically active and maintaining a healthy weight. This, along with managing your diet, can help prevent or delay the onset of type 2 diabetes, which damages your peripheral nerves over time.

Wearing safety equipment as needed. Injuries are a major source of nerve damage. Using safety equipment during work and play activities can protect you from these injuries or limit how severe the injuries are.

Managing chronic conditions as recommended. If you have a chronic condition that can affect your peripheral nerves, especially type 2 diabetes, it’s important to manage it as your healthcare provider recommends. That can limit the effects of the condition or delay how long it takes to get worse.

Avoiding alcohol in excess. Excessive consumption of alcohol is a proven cause of peripheral neuropathy. You can reduce your risk of neuropathy (and some other medical complications) by avoiding alcohol, or consuming it in moderation only.

Avoiding exposures to toxins, poisons and heavy metals. Heavy metals like lead and mercury can cause severe damage to your nervous system. Mercury exposure is rare thanks to environmental regulations, but older thermometers or thermostats may still contain it. Older homes may also contain lead-based paint. Local, state and national agencies may have resources and services to help you avoid exposure to toxic metals and chemicals. If you work around such metals and chemicals, follow all safety regulations and use recommended or required protective gear.

**Living With**

**How do I take care of myself?**

If you have peripheral neuropathy, it’s important to follow your healthcare provider’s guidance. That includes seeing them as recommended, taking medications or treatments as prescribed and modifying your life to protect yourself and manage your symptoms. The actions you can take also vary widely depending on many factors, and what helps one person may not be as effective for another.

**When should I see my healthcare provider, or when should I seek care?**

If you have symptoms of peripheral neuropathy, you should see a healthcare provider as soon as possible. In some cases, peripheral neuropathy symptoms start before the condition causes permanent changes or damage, so it may be possible to limit the effects or even reverse them.

If you receive a diagnosis of peripheral neuropathy, you should see your healthcare provider as recommended or if you notice changes in your symptoms. You should also talk to them if you experience side effects from any treatments. Talking to your healthcare provider can be especially helpful when you have symptom changes or side effects that affect your usual routine and activities. Your provider may be able to modify your treatment or find ways to adapt to these changes and limit their effects.

**When should I go to the ER?**

In general, peripheral neuropathy isn’t likely to cause life-threatening complications or symptoms. However, there are a few conditions that fall under peripheral neuropathy that are severe and need immediate medical attention.

There are also conditions that share symptoms with peripheral neuropathy. You should go to the ER if you have symptoms of certain conditions that can be especially dangerous, such as:

Stroke: Look for weakness, paralysis or numbness, often on one side. An easily recognizable example of this is a droop on one side of the face or weakness in one arm or leg. A stroke can also cause a person to have trouble walking.

Guillain-Barré syndrome. This condition is when your immune system attacks your nerves. This condition can quickly cause life-threatening complications. Symptoms of this condition include numbness or tingling in the hands and feet, muscle weakness that starts in the feet and moves up the body, trouble breathing or swallowing and unusual heart rate and blood pressure shifts.

You should also go to the ER if you have autonomic symptoms of peripheral neuropathy, such as:

Irregular heart rate or a heart rate that’s unusually fast (more than 100 beats per minute) or slow (under 60 beats per minute).

Dizziness or passing out when standing or sitting up (especially if you fall and have a possible injury to your head, neck or back).

Changes in bathroom habits, especially severe pain or trouble peeing (urinating).

**Additional Common Questions**

**Can peripheral neuropathy be reversed?**

Peripheral neuropathy may be reversible in some cases, but many factors influence whether or not this is possible. Because there are so many factors involved, your healthcare provider should be the one to answer this question for you. The information they provide will be the most accurate and relevant for your specific case and circumstances.

**Is fatigue a symptom of peripheral neuropathy?**

Fatigue is a symptom that can happen with conditions that can cause peripheral neuropathy. It can also happen due to living with severe or long-term pain due to peripheral neuropathy, or because of autonomic problems from peripheral neuropathy. However, it isn’t a direct symptom of peripheral neuropathy itself.

**Is peripheral neuropathy serious?**

Peripheral neuropathy can be serious, but there are many reasons why it might not be. Whether or not it’s serious depends on many factors, including the symptoms it causes, how severely it affects nerves and more. Your healthcare provider is the best person to tell you about the seriousness of your case and what that means for you.

How do I know if I have peripheral neuropathy?

Peripheral neuropathy isn’t something you can self-diagnose. A qualified and trained healthcare provider can diagnose it, but the diagnosis process almost always involves some form of diagnostic, imaging or laboratory testing. You may suspect you have peripheral neuropathy based on the symptoms you experience, but you should see a healthcare provider to be sure.

What is the most common treatment for peripheral neuropathy?

There’s no one common treatment for peripheral neuropathy. The treatments depend on what’s causing it and the symptoms you experience. Some causes of peripheral neuropathy are directly treatable. For others, treating and minimizing the symptoms and their effects is the best approach.

Can peripheral neuropathy ever go away?

Yes, peripheral neuropathy can sometimes go away, but this isn’t universal. Many factors can influence how long peripheral neuropathy lasts. The condition that causes peripheral neuropathy is a major factor in whether or not it will go away, as are the treatments you receive. It’s also important to remember that what works for one person may not work for another, because peripheral neuropathy can happen very differently from person to person.

Peripheral neuropathy is an umbrella term for any condition, disease or disorder that affects your peripheral nerves, which are all the nerves outside of your spinal cord and brain. There are many different ways that peripheral neuropathy can happen, so this condition is common.

For some people, peripheral neuropathy is temporary, treatable or both. For others, it’s permanent and incurable. Thanks to advances in medical science and technology, many symptoms or forms of peripheral neuropathy are now treatable. That offers many people a chance to manage this condition, meaning they can live longer and with fewer restrictions or impacts from the related conditions and symptoms.

**Peripheral Neuropathy**

Peripheral neuropathy refers to any condition that affects the nerves outside your brain or spinal cord. This can happen for several reasons, from trauma to infections to inherited conditions. There are also many possible symptoms. Many causes, forms or symptoms of this condition are treatable, but this can vary widely from person to person.

**Overview**

Peripheral neuropathy can affect nerves anywhere in your body. It can disrupt your body’s control of automatic processes, as well as your sense of touch and muscle control.

**What is peripheral neuropathy?**

Peripheral neuropathy is an umbrella term for nerve diseases that affect a specific subdivision of your nervous system. Many different conditions can cause peripheral neuropathy, which means a wide range of symptoms is also possible. Peripheral neuropathy can also affect different body parts, depending on how and why it happens.

**What this name means**

The term “peripheral” is from the Greek word that means “around.” “Peripheral” in this context means outside of or away from the “central” nervous system. The term neuropathy combines two words that trace their origins back to ancient Greek:

* Neuro-: From the Greek word “neuron,” meaning “nerve.”
* -pathy: From the Greek word “pathos,” meaning “affliction” or “condition.”

Your nervous system has two parts, the central nervous system and the peripheral nervous system. Your brain and spinal cord are the two components that make up your central nervous system. Your peripheral nervous system consists of all the other nerves in your body. It also includes nerves that travel from your spinal cord and brain to supply your face and the rest of your body.

Peripheral neuropathy can refer to any condition affecting your peripheral nerves. Healthcare providers often use the terms “neuropathy” and “polyneuropathy” (meaning “disease of many nerves”) interchangeably with “peripheral neuropathy.” Peripheral nerves are farthest from the central nervous system, and they often show the earliest and most severe effects of these conditions

**Who does peripheral neuropathy affect?**

Peripheral neuropathy can affect anyone, regardless of age, sex, race or ethnicity, personal circumstances, medical history, etc. However, some people are at greater risk for specific types of peripheral neuropathy (see below under Causes and Symptoms for more about this).

Peripheral neuropathy is also very common with some age-related diseases. That means the risk of developing peripheral neuropathy increases as you get older.

**How common is this condition?**

Peripheral neuropathy is common, partly because this term refers to so many conditions. About 2.4% of people globally have a form of peripheral neuropathy. Among people 45 and older, that percentage rises to between 5% and 7%.

**How does this condition affect my body?**

To understand how peripheral neuropathy affects your body, it helps to know a little about the structure of neurons, a key type of cell that makes up your nerves. Neurons send and relay signals through your nervous system using electrical and chemical signals. Each neuron consists of the following:

* **Cell body**: This is the main part of the cell.
* **Axon**: This is a long, arm-like part that extends outward from the cell body. At the end of the axon are several finger-like extensions where the electrical signal in the neuron becomes a chemical signal. These extensions, known as synapses, lead to nearby nerve cells.
* **Dendrites**: These are small branch-like extensions (their name comes from a Latin word that means “tree-like”) on the cell body. Dendrites are the receiving point for chemical signals from the synapses of other nearby neurons.
* **Myelin**: This is a thin layer composed of fatty chemical compounds. Myelin surrounds the axon of many neurons and acts as a protective covering.

**Disease types**

Peripheral neuropathy happens in two main ways:

* **Demyelinating neuropathy**: This happens when the myelin coating on the axon deteriorates or can’t form correctly. That affects the way signals travel through the neuron.
* **Axonal degeneration**: This causes the axon to deteriorate and die off. The longer a neuron is, the worse the effect. That’s why axonal degeneration conditions tend to involve your legs and feet, which are farthest from your spinal cord and rely on connections using longer axons. Axonal degeneration is the most common pattern seen with peripheral neuropathy.

**How quickly does peripheral neuropathy develop?**

How peripheral neuropathy develops, particularly the timeline of its progress, depends very much on what causes it. Injuries can cause it to develop instantaneously or within minutes or hours. Some toxic and inflammation-based forms of peripheral neuropathy may develop rapidly over days or weeks, while most other conditions take months, years or even decades to develop.

**Symptoms and Causes**

Learn more about peripheral neuropathy.

**What are the symptoms of peripheral neuropathy?**

There are many different symptoms of peripheral neuropathy. This condition can affect a single nerve, a connected group of related nerves, or many nerves in multiple places throughout your body. The symptoms also depend on the type of nerve signals affected, and multiple signal types may be involved.

The symptom types (with more about them below) are:

* Motor.
* Sensory and pain.
* Autonomic.

**Motor symptoms**

Your peripheral nervous system carries motor signals, which are commands sent from your brain to your muscles. These signals are what make it possible for you to move around. Your muscles need nerve connections to the brain to stay healthy and work properly.

Motor symptoms include:

* **Muscle weakness** **and paralysis.** Nerve deterioration from peripheral neuropathy weakens the connected muscles. That can cause paralysis, which may cause difficulty moving the toes, foot drop and hand weakness. Weakness can also affect muscles in the thighs, arms and elsewhere.
* **Muscle atrophy**. Loss of nerve connection can cause muscles to shrink in size, as well as weaken. This especially happens in the feet, lower legs and hands with peripheral neuropathy. Sometimes there are deformities of the feet and hands because of muscle loss.
* **Uncontrolled muscle movements**. Sometimes, nerves that lose their connection to the brain because of peripheral neuropathy become hyperactive on their own, causing cramps.

**Sensory symptoms**

Your peripheral nerves convert information about the outside world into nerve signals. Those signals then travel to your brain, which processes those signals into what you can sense of the world around you. Peripheral neuropathy can disrupt what your senses pick up from the outside world or the ability of those senses to communicate with your brain.

The sensory symptoms of peripheral neuropathy include:

* **Tingling**. This happens when there’s a problem with nerves that carry signals to your brain. This is like radio static you hear when you’re too far from the broadcasting station.
* **Numbness**. This happens when nerves can’t send or relay sensory signals, causing the loss of specific types of sensations. An example of this would be picking up a cold pop can, but not feeling the smoothness or coldness of the can, or not being able to feel the texture of carpet or the temperature of the floor through your feet.
* **Imbalance and clumsiness**. Nerves also carry sensations that your brain uses to keep track of the location of your hands and feet. You’re not consciously aware of these sensations, but they’re critical for balance and coordination. Without these sensations, you can experience a loss of balance, especially in the dark, and clumsiness with your hands.
* **Pain**. Nerve damage from peripheral neuropathy can cause malfunctions in how and when nerves send pain signals, making pain signals more intense (hyperalgesia) or happen too easily (allodynia). It can even cause nerves to generate pain signals spontaneously. This is known as “neuropathic” pain, and it’s the most noticeable and disruptive symptom of peripheral neuropathy.

**Autonomic symptoms**

Your body has several autonomic processes. These are the automatic functions of your body that happen without your thinking or even being aware of them. They include things like sweating, digestion, blood pressure control, etc. Autonomic nerve fibers carry autonomic signals. Disruptions in autonomic signals mean your body’s automatic processes can’t work correctly. Some may work off and on, while others may not work at all.

Autonomic symptoms of peripheral neuropathy can include:

* **Blood pressure changes**. Your body automatically manages blood pressure, but damage to your peripheral nerves can disrupt this. That can cause sudden drops in blood pressure or increases in heart rate, especially when you stand up.
* **Sweating too much or not enough**. Your body automatically manages its internal temperature, using sweating to shed heat. Peripheral nerve damage can cause you to sweat too much or not enough. That can lead to dryness and scaling on your feet, or excessive sweating after eating.
* **Bowel and bladder problems**. Autonomic signals control your bowel and bladder without you having to think about them. Nerve fiber disruption can affect bowel movements (constipation or diarrhea), and can occasionally affect bladder control, too.
* **Sexual dysfunction**. Your autonomic nervous system controls sexual arousal. That’s why autonomic problems can cause sexual dysfunction.
* **Other symptoms**. Autonomic changes from peripheral neuropathy can also cause skin color changes, swelling, changes in the pupils of the eyes and blurry vision.

**What causes peripheral neuropathy?**

Peripheral neuropathy can happen for many reasons. These include:

* **Type 2 diabetes**. The most common cause of peripheral neuropathy is unmanaged type 2 diabetes. When your blood sugar is too high for too long, it damages your peripheral nerves. That’s why people with type 2 diabetes can lose feeling in their feet and lower legs.
* **Alcohol use disorder**. Excessive intake of alcohol, especially over long periods of time, can damage nerves. Alcohol use disorder is a common cause of peripheral neuropathy, and it can also contribute to vitamin deficiencies that lead to peripheral neuropathy.
* **Vitamin and nutrient deficiencies**. People can develop nerve damage because they have deficiencies in certain vitamins. The deficiencies that are most likely to cause this are copper and vitamins B1, B6, B9, B12, folic acid (B9) and E. Too much vitamin B6 can also cause this.
* **Autoimmune and inflammatory conditions**. Guillain-Barré syndrome and chronic inflammatory demyelinating polyneuropathy (CIDP) can cause severe weakness. They’re also very treatable. Neuropathy can happen due to lupus, rheumatoid arthritis, Sjögren syndrome, vasculitis and more.
* **Medications and toxins.**Chemotherapy and certain other medications (antibiotics, and medications that treat arrhythmia and gout) can cause peripheral neuropathy. Exposure to some heavy metals and industrial chemicals can also cause it.
* **Tumors**. Malignant tumors (cancer) and benign (noncancerous) tumors can both disrupt your peripheral nervous system.
* **Genetic conditions**. Genetic conditions are ones you inherit from one or both parents. Examples of these causing peripheral neuropathy include amyloidosis, Fabry disease and Charcot-Marie-Tooth disease. There are treatments for familial amyloidosis and Fabry disease.
* **Infections**. Nerve damage from infections can happen because of viruses, such as HIV, or bacteria — such as *Borrelia burgdorferi*, which causes Lyme disease. Another common example is having shingles, which can lead to lingering nerve pain.
* **Hansen disease (better known as leprosy)**. While the effects of this disease — which is rare in developed countries — are most visible on the skin, it also damages your peripheral nerves. It’s a very common cause of peripheral neuropathy in developing nations. worldwide
* **Trauma and surgery**. Injuries and damage directly to nerves can happen from trauma or from medical procedures. Swelling or stretching can also damage nerves. This kind of damage is usually only in one location. It can be long-term or even permanent.
* **Vascular disorders (circulation-related problems).**Lack of blood flow can cause peripheral neuropathy. A harmless, temporary form of this happens when you sit or lay a certain way and an arm or leg falls asleep. This goes away quickly if you shift position enough for circulation to return. More severe circulation problems can cause serious and permanent nerve damage.
* **Idiopathic neuropathy**. It’s common for peripheral neuropathy to happen for unknown reasons. This type of neuropathy is known as “idiopathic” or “cryptogenic” (hidden or obscure cause).

**Is peripheral neuropathy contagious?**

Peripheral neuropathy isn’t contagious. While it can happen because of infectious diseases, this condition doesn’t spread from person to person on its own. The only exception is Hansen disease, which can spread from person to person but doesn’t spread easily.

**Diagnosis and Tests**

**How is peripheral neuropathy diagnosed?**

Diagnosing peripheral neuropathy usually involves a combination of methods. These include:

* **Symptoms and medical history**. Your healthcare provider will likely ask questions about your medical history and any recent symptoms or changes you’ve noticed. They may also ask about other medical conditions and factors, such as type 2 diabetes, and your nutrition, habits and lifestyle.
* **Physical and neurological exams**. These involve a healthcare provider looking for physical signs of peripheral neuropathy, including changes in your ability to feel sensations, muscle weakness, changes in your reflexes or trouble with walking and balance.
* **Lab, diagnostic and imaging tests**. A wide range of tests can help with diagnosing peripheral neuropathy.

**What tests will be done to diagnose peripheral neuropathy?**

The most common types of tests for peripheral neuropathy (either to confirm the diagnosis or rule out other conditions) include:

* Blood tests (these can detect many problems, ranging from immune system problems to toxins and poisons, especially metals like mercury or lead).
* Electromyogram.
* Nerve ultrasound.
* Nerve biopsy.
* Genetic testing.
* Magnetic resonance imaging (MRI).

**Management and Treatment**

**How is peripheral neuropathy treated, and is there a cure?**

The treatment for peripheral neuropathy can vary widely depending on its cause. Other factors can also affect treatment, including your medical history, personal preferences and more. Your healthcare provider is the best person to tell you more about the treatment(s) they recommend and the likely recovery timeline. In general, the following treatment methods are more common for peripheral neuropathy:

* **Medications**. Many medications can treat peripheral nervous system problems. These can come in many forms, including injections, pills you take by mouth, patches that stick to your skin, slow-release medication and more.
* **Surgery**. Surgery can help reconnect cut nerves and relieve pain due to trapped nerves. It can also sever or remove damaged or malfunctioning nerves to keep their signals from reaching the brain and vice versa.
* **Physical therapy**. This can help you recover from injuries or medical procedures, or improve pain symptoms. It can also help you adapt to nervous system changes, including improving balance and preventing falls.
* **Devices and wearable equipment**. These include medical devices like braces, canes and walkers, prescribed footwear and more. These may not directly treat peripheral neuropathy, but they can help prevent complications from it. An example is special footwear for people who have peripheral neuropathy because of type 2 diabetes.
* **Podiatry and foot care.**Peripheral neuropathy commonly affects your feet. That can cause soft tissue and bone changes, including sores and infections, especially in people with type 2 diabetes. Many people with peripheral neuropathy need to see a podiatrist (foot specialist).
* **Other pain treatments**. If your pain from peripheral neuropathy or nerve injury doesn’t improve with standard medications, pain specialists may occasionally offer other treatments such as acupuncture, transcutaneous electrical nerve stimulation, injections or surgery to implant a spinal cord stimulator.

**What are the possible complications or side effects of peripheral neuropathy treatments?**

The possible side effects and complications of treatments for peripheral neuropathy depend on many factors. These include the specific cause of the neuropathy, other conditions you have, the specific treatments you receive and more. Your healthcare provider is the best person to tell you more about the possible side effects and complications you might experience.

**How do I take care of myself or manage symptoms of peripheral neuropathy?**

Peripheral neuropathy is a sign of a problem with the nerve signals traveling between parts of your body and your brain. While this can happen for minor reasons that aren’t serious, it can also happen because of severe or dangerous conditions. It’s also sometimes possible to stop or reverse certain types of neuropathies if treatment begins quickly enough. Because of these factors, you shouldn’t try to self-diagnose and self-treat it. A healthcare provider is the best person to guide you in managing this condition.

**Outlook / Prognosis**

**What can I expect if I have this condition?**

The effects of peripheral neuropathy depend on the cause, the nerves it affects, your medical history, treatments you receive and more. Your healthcare provider is the best person to tell you more about what you can expect in your case.

**How long does peripheral neuropathy last?**

Peripheral neuropathy can be a temporary concern, or it can be permanent. How long it lasts depends on what caused it, the extent of the damage — if any — that it caused, the treatments and more.

Peripheral neuropathy is most likely to be permanent with chronic conditions like type 2 diabetes, autoimmune diseases and genetic conditions. However, this can still vary, so it’s best to ask your healthcare provider about what’s most likely in your case.

**What’s the outlook for this condition?**

Peripheral neuropathy is usually not dangerous, but it can have very disruptive effects on your life. These effects are usually not as severe when it only affects one nerve or a limited group of nerves. The more nerves it affects, the greater the potential impact.

The outlook also depends partly on your symptoms. Pain from peripheral neuropathy is usually the most disruptive symptom, but medications or other treatments may help. Autonomic symptoms are among the most serious because they involve your body’s vital functions. When those don’t work correctly, it can have very severe — and sometimes dangerous — effects.

Motor and sensory symptoms can also greatly disrupt your ability to work and go about your daily activities. They can cause problems — sometimes severe — with mobility, balance and coordination. Sensory symptoms are also disruptive, especially when they involve pain or affect your ability to control what you do with the affected body part(s).

Lastly, treatments can make a big difference in outlook. Some treatments can greatly reduce or even stop symptoms, but this varies. Your healthcare provider is the best source of information on the outlook for your case and what you can do to help.

**Prevention**

**How can I reduce my risk of developing peripheral neuropathy or prevent it entirely?**

Some of the possible causes of peripheral neuropathy are preventable. You can also lower your chances of developing it by preventing or delaying certain conditions. In general, the best preventive or precautionary steps you can take include:

* **Eating a balanced diet**. Certain vitamin deficiencies, especially vitamin B12 deficiency, can affect your nervous system and cause major problems. Other vitamins, especially B6, are toxic and cause peripheral neuropathy at high levels.
* **Staying physically active and maintaining a healthy weight**. This, along with managing your diet, can help prevent or delay the onset of type 2 diabetes, which damages your peripheral nerves over time.
* **Wearing safety equipment as needed.**Injuries are a major source of nerve damage. Using safety equipment during work and play activities can protect you from these injuries or limit how severe the injuries are.
* **Managing chronic conditions as recommended**. If you have a chronic condition that can affect your peripheral nerves, especially type 2 diabetes, it’s important to manage it as your healthcare provider recommends. That can limit the effects of the condition or delay how long it takes to get worse.
* **Avoiding alcohol in excess**. Excessive consumption of alcohol is a proven cause of peripheral neuropathy. You can reduce your risk of neuropathy (and some other medical complications) by avoiding alcohol, or consuming it in moderation only.
* **Avoiding exposures to toxins, poisons and heavy metals.**Heavy metals like lead and mercury can cause severe damage to your nervous system. Mercury exposure is rare thanks to environmental regulations, but older thermometers or thermostats may still contain it. Older homes may also contain lead-based paint. Local, state and national agencies may have resources and services to help you avoid exposure to toxic metals and chemicals. If you work around such metals and chemicals, follow all safety regulations and use recommended or required protective gear.

**Living With**

**How do I take care of myself?**

If you have peripheral neuropathy, it’s important to follow your healthcare provider’s guidance. That includes seeing them as recommended, taking medications or treatments as prescribed and modifying your life to protect yourself and manage your symptoms. The actions you can take also vary widely depending on many factors, and what helps one person may not be as effective for another.

**When should I see my healthcare provider, or when should I seek care?**

If you have symptoms of peripheral neuropathy, you should see a healthcare provider as soon as possible. In some cases, peripheral neuropathy symptoms start before the condition causes permanent changes or damage, so it may be possible to limit the effects or even reverse them.

If you receive a diagnosis of peripheral neuropathy, you should see your healthcare provider as recommended or if you notice changes in your symptoms. You should also talk to them if you experience side effects from any treatments. Talking to your healthcare provider can be especially helpful when you have symptom changes or side effects that affect your usual routine and activities. Your provider may be able to modify your treatment or find ways to adapt to these changes and limit their effects.

**When should I go to the ER?**

In general, peripheral neuropathy isn’t likely to cause life-threatening complications or symptoms. However, there are a few conditions that fall under peripheral neuropathy that are severe and need immediate medical attention.

There are also conditions that share symptoms with peripheral neuropathy. You should go to the ER if you have symptoms of certain conditions that can be especially dangerous, such as:

* **Stroke**: Look for weakness, paralysis or numbness, often on one side. An easily recognizable example of this is a droop on one side of the face or weakness in one arm or leg. A stroke can also cause a person to have trouble walking.
* **Guillain-Barré syndrome**. This condition is when your immune system attacks your nerves. This condition can quickly cause life-threatening complications. Symptoms of this condition include numbness or tingling in the hands and feet, muscle weakness that starts in the feet and moves up the body, trouble breathing or swallowing and unusual heart rate and blood pressure shifts.

You should also go to the ER if you have autonomic symptoms of peripheral neuropathy, such as:

* Irregular heart rate or a heart rate that’s unusually fast (more than 100 beats per minute) or slow (under 60 beats per minute).
* Dizziness or passing out when standing or sitting up (especially if you fall and have a possible injury to your head, neck or back).
* Changes in bathroom habits, especially severe pain or trouble peeing (urinating).

**Additional Common Questions**

**Can peripheral neuropathy be reversed?**

Peripheral neuropathy may be reversible in some cases, but many factors influence whether or not this is possible. Because there are so many factors involved, your healthcare provider should be the one to answer this question for you. The information they provide will be the most accurate and relevant for your specific case and circumstances.

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There’s no one common treatment for peripheral neuropathy. The treatments depend on what’s causing it and the symptoms you experience. Some causes of peripheral neuropathy are directly treatable. For others, treating and minimizing the symptoms and their effects is the best approach.

**Can peripheral neuropathy ever go away?**

Yes, peripheral neuropathy can sometimes go away, but this isn’t universal. Many factors can influence how long peripheral neuropathy lasts. The condition that causes peripheral neuropathy is a major factor in whether or not it will go away, as are the treatments you receive. It’s also important to remember that what works for one person may not work for another, because peripheral neuropathy can happen very differently from person to person.

**A note from Cleveland Clinic**

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Source

Cleveland Clinic (2022) *Peripheral Neuropathy: What It Is, Symptoms & Treatment*. Available at: https://my.clevelandclinic.org/health/diseases/14737-peripheral-neuropathy (Accessed: 5 June 2025).

**HYDROCEPHALUS**

## **Overview**

Hydrocephalus is the buildup of fluid in cavities called ventricles deep within the brain. The excess fluid increases the size of the ventricles and puts pressure on the brain.

Cerebrospinal fluid usually flows through the ventricles and bathes the brain and spinal column. But the pressure of too much cerebrospinal fluid can damage brain tissues and cause a range of symptoms related to brain function.

Hydrocephalus can happen at any age, but it occurs more often among infants and among adults 60 and older. Surgery can restore and maintain healthy cerebrospinal fluid levels in the brain. Therapies can manage symptoms resulting from hydrocephalus.

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## **Symptoms**

The symptoms of hydrocephalus can vary by age.

### Infants

Common symptoms of hydrocephalus in infants include:

#### *Changes in the head*

* A head that is larger than usual.
* A rapid increase in the size of an infant's head.
* A bulge or tense soft spot on the top of the head.

#### *Physical symptoms*

* Nausea and vomiting.
* Sleepiness or sluggishness, known as lethargy.
* Irritability.
* Poor eating.
* Seizures.
* Eyes fixed downward, known as sunsetting of the eyes.
* Problems with muscle tone and strength.

### Toddlers and older children

Among toddlers and older children, symptoms might include:

#### *Physical symptoms*

* Headache.
* Blurred or double vision.
* Eye movements that are not usual.
* Enlargement of a toddler's head.
* Sleepiness or sluggishness.
* Nausea or vomiting.
* Trouble with balance.
* Poor coordination.
* Poor appetite.
* Loss of bladder control or urinating often.

#### *Behavioral and cognitive changes*

* Irritability.
* Change in personality.
* Decline in school performance.
* Delays or problems with earlier gained skills, such as walking or talking.

### Young and middle-aged adults

Common symptoms in this age group include:

* Headache.
* Sluggishness.
* Loss of coordination or balance.
* Loss of bladder control or needing to urinate often.
* Vision problems.
* Decline in memory, concentration and other thinking skills that may affect job performance.

### Older adults

Among adults 60 and older, the more common symptoms of hydrocephalus are:

* Loss of bladder control or needing to urinate often.
* Memory loss.
* Progressive loss of other thinking or reasoning skills.
* Trouble walking, often described as shuffling or the feeling of the feet being stuck.
* Poor coordination or balance.

### When to see a doctor

**Seek emergency medical care for infants and toddlers** with these symptoms:

* A high-pitched cry.
* Problems with sucking or feeding.
* Recurrent vomiting with no clear cause.
* Seizures.

**Seek prompt medical attention** for other hydrocephalus symptoms in any age group.

More than one condition can cause the problems associated with hydrocephalus. It's important to get a timely diagnosis and appropriate care.

## **Causes**

Hydrocephalus is caused by an imbalance between how much cerebrospinal fluid is produced and how much is absorbed into the bloodstream.

Tissues lining the ventricles of the brain produce cerebrospinal fluid. It flows through the ventricles by way of channels. The fluid eventually flows into spaces around the brain and spinal column. It's absorbed primarily by blood vessels in tissues on the surface of the brain.

Cerebrospinal fluid plays an important role in brain function by:

* Allowing the relatively heavy brain to float within the skull.
* Cushioning the brain to prevent injury.
* Removing waste products of the brain's metabolism.
* Flowing back and forth between the brain cavity and spinal column. This flow maintains a constant pressure within the brain and allows for changes in blood pressure in the brain.

Too much cerebrospinal fluid in the ventricles can occur for one of the following reasons:

* **Obstruction.** Partial blockage of the flow of cerebrospinal fluid is the most common cause of too much cerebrospinal fluid in the ventricles. A blockage may happen from one ventricle to another or from the ventricles to other spaces around the brain.
* **Poor absorption.** Less common is a problem with absorbing cerebrospinal fluid. This is often related to inflammation of brain tissues from disease or injury.
* **Overproduction.** Rarely, cerebrospinal fluid is created more quickly than it can be absorbed.

## **Risk factors**

Much of the time, the cause of hydrocephalus is not known. However, developmental or medical problems can contribute to or trigger hydrocephalus.

### Newborns

Hydrocephalus may be present at or before birth, known as congenital hydrocephalus. Or it can occur shortly after birth. Any of the following incidents may cause hydrocephalus in newborns:

* The central nervous system developed in a way that blocks the flow of cerebrospinal fluid.
* Bleeding occurred within the ventricles. This is a possible complication of premature birth.
* There was an infection in the uterus during pregnancy, such as rubella or syphilis. An infection can cause swelling in the brain tissues of an unborn baby.

### Other contributing factors

Other factors that can contribute to hydrocephalus among any age group include:

* Tumors of the brain or spinal cord.
* Central nervous system infections, such as bacterial meningitis or mumps.
* Bleeding in the brain from a stroke or head injury.
* Other traumatic injury to the brain.

## **Complications**

In most cases, hydrocephalus worsens. Without treatment, hydrocephalus leads to complications. Complications may include learning disabilities or developmental and physical disabilities. Complications of this condition also can result in death. When hydrocephalus is mild and it's treated, there may be few, if any, serious complications.

## **Diagnosis**

A diagnosis of hydrocephalus is usually based on:

* Your symptoms.
* A general physical exam.
* A neurological exam.
* Brain-imaging tests.

### Neurological exam

The type of neurological exam depends on a person's age. A health care professional might ask questions and conduct simple tests to judge muscle condition, movement, well-being and function of sensory abilities.

### Brain imaging

Imaging tests can help diagnose hydrocephalus. They also can pinpoint underlying causes of symptoms. Imaging tests include:

* **Ultrasound.** This test is often the first test for infants because it's a simple, low-risk procedure. The ultrasound device is placed over the soft spot on the top of the baby's head. Ultrasound also might find hydrocephalus before birth during routine prenatal exams.
* **MRI.** This test uses radio waves and a magnetic field to produce detailed images of the brain. This test is painless, but it is noisy and requires lying still.

MRI scans can show enlarged ventricles caused by excess cerebrospinal fluid. MRI also can be used to find causes of hydrocephalus or other conditions contributing to symptoms.

Children might need medicine to help them feel calm, known as mild sedation, for some MRI scans. However, some hospitals use a fast version of MRI that usually doesn't require sedation.

* **CT scan.** This specialized X-ray technology produces cross-sectional views of the brain. Scanning is painless and quick. But this test also requires lying still, so a child usually receives a mild sedative.

CT scans show less detail than do MRI scans. And CT technology causes exposure to a small amount of radiation. CT scans for hydrocephalus usually are used only for emergency exams.

## **Treatment**

One of two surgical treatments can be used to treat hydrocephalus.

### Shunt

The most common treatment for hydrocephalus is the surgical insertion of a drainage system, called a shunt. It consists of a long, flexible tube with a valve that keeps fluid from the brain flowing in the right direction and at the proper rate.

One end of the tubing is usually placed in one of the brain's ventricles. The tubing is then tunneled under the skin to another part of the body such as the stomach or a heart chamber. This allows excess fluid to be more easily absorbed.

People who have hydrocephalus usually need a shunt system for the rest of their lives. They require regular monitoring.

### Endoscopic third ventriculostomy

Some people may have a surgery called endoscopic third ventriculostomy. The surgeon uses a small video camera to see inside the brain. Then the surgeon makes a hole in the bottom of a ventricle. This allows cerebrospinal fluid to flow out of the brain.

### Complications of surgery

Both surgical procedures can result in complications. Shunt systems can stop draining cerebrospinal fluid. Or shunt systems may poorly regulate drainage because of mechanical problems, a blockage or infections. Complications of ventriculostomy include bleeding and infections.

Complications of surgery require prompt attention. Another surgery or other interventions may be needed. Fever or symptoms of hydrocephalus should prompt an appointment with your health care professional.

### Other treatments

Some people with hydrocephalus, particularly children, might need supportive therapies. Need for these therapies depends on the long-term complications of hydrocephalus.

Children's care teams might include:

* **Pediatrician or physiatrist,** who oversees the treatment plan and medical care.
* **Pediatric neurologist,** who specializes in diagnosing and treating neurological conditions in children.
* **Occupational therapist,** who specializes in therapy to develop everyday skills.
* **Developmental therapist,** who specializes in therapy to help your child develop age-appropriate behaviors, social skills and interpersonal skills.
* **Mental health professional,** such as a psychologist or psychiatrist.
* **Social worker,** who helps the family get needed services and plan for transitions in care.

Children who are in school may need special education. Special education teachers address learning disabilities, determine educational needs and help find needed resources.

Adults with more serious complications might need the services of occupational therapists or social workers. Or they may need to see specialists in dementia care or other medical specialists.

## **Coping and support**

With the help of therapies and educational services, many people with hydrocephalus live with few limitations.

If you have a child with hydrocephalus, there are many resources available to provide emotional and medical support. Children with developmental disabilities might be eligible for government-sponsored health care and other support services. Check with your state or county social services agency.

Hospitals and organizations serving people with disabilities are good resources for emotional and practical support. Members of your health care team also can help. Ask for help connecting with other families who are coping with hydrocephalus.

Adults living with hydrocephalus might find valuable information from organizations dedicated to hydrocephalus education and support, such as the Hydrocephalus Association.

### Should you be vaccinated against meningitis?

Ask your child's or your health care team if you or your child should receive a vaccine against meningitis, once a common cause of hydrocephalus. The Centers for Disease Control and Prevention recommends meningitis vaccination for preteen children and boosters for teenagers. Vaccination also is recommended for younger children and adults who might be at increased risk of meningitis for any of the following reasons:

* Traveling to countries where meningitis is common.
* Having an immune system disease called terminal complement deficiency.
* Having a damaged spleen or having had the spleen removed.
* Living in a college dormitory.
* Joining the military.

## **Preparing for your appointment**

The timing of diagnosing a child with hydrocephalus can depend on how bad the symptoms are and when problems appeared. It also may depend on whether there were risk factors for hydrocephalus during the pregnancy or delivery. Sometimes hydrocephalus can be diagnosed at birth or before birth.

### Well-baby visits

It's important to take your child to all regularly scheduled well-baby visits. Health care professionals monitor your child's development in key areas, including:

* Head size, rate of head growth and overall body growth.
* Muscle strength and tone.
* Coordination.
* Posture.
* Age-appropriate motor skills.
* Sensory abilities such as vision, hearing and touch.

Questions you should be prepared to answer during regular checkups might include:

* What concerns do you have about your child's growth or development?
* How well does your child eat?
* How does your child respond to touch?
* Is your child reaching certain milestones in development, such as rolling over, pushing up, sitting up, crawling, walking or speaking?

### Preparing for other health care visits

You'll likely start by seeing your child's or your health care professional. You may then be referred to a doctor who specializes in brain and nervous system conditions, known as a neurologist.

Be prepared to answer the following questions about your symptoms or on your child's behalf:

* What symptoms have you noticed? When did they begin?
* Have these symptoms changed over time?
* Do these symptoms include nausea or vomiting?
* Have you or your child had any vision problems?
* Have you or your child had a headache or fever?
* Have you noticed personality changes, including increased irritability?
* Has your child's school performance changed?
* Have you noticed new problems with movement or coordination?
* Is your child having trouble sleeping or lacking in energy?
* Has your infant had seizures?
* Has your infant had problems with eating or breathing?
* In older children and adults, have symptoms included loss of bladder control and urinating often?
* Have you or your child had a recent head injury?
* Have you or your child recently begun a new medicine?

Source

Mayo Clinic Staff (2023) *Hydrocephalus - Symptoms and causes*. Available at: https://www.mayoclinic.org/diseases-conditions/hydrocephalus/symptoms-causes/syc-20373604 (Accessed: 5 June 2025).

**BRAIN TUMORS**

## What is a brain tumor?

A brain tumor is a growth of abnormal cells in the brain. The anatomy of the brain is very complex, with different parts responsible for different nervous system functions. Brain tumors can develop in any part of the brain or skull, including its protective lining, the underside of the brain (skull base), the brainstem, the sinuses and the nasal cavity, and many other areas. There are more than 120 different types of tumors that can develop in the brain, depending on what tissue they arise from.

### How common are brain tumors, and are they dangerous?

In the United States, brain and nervous system tumors affect about 30 adults out of 100,000. Brain tumors are dangerous because they can put pressure on healthy parts of the brain or spread into those areas. Some brain tumors can also be cancerous or become cancerous. They can cause problems if they block the flow of fluid around the brain, which can lead to an increase in pressure inside the skull. Some types of tumors can spread through the spinal fluid to distant areas of the brain or the spine.

### How is a tumor different from a brain lesion?

A brain tumor is a specific type of brain lesion. A lesion describes any area of damaged tissue. All tumors are lesions, but not all lesions are tumors. Other brain lesions can be caused by stroke, injury, encephalitis and arteriovenous malformation.

## Brain Tumor vs. Brain Cancer

All brain cancers are tumors, but not all brain tumors are cancerous. Noncancerous brain tumors are called benign brain tumors.

Benign brain tumors typically grow slowly, have distinct borders and rarely spread. Benign tumors can still be dangerous. They can damage and compress parts of the brain, causing severe dysfunction. Benign brain tumors located in a vital area of the brain can be life-threatening. Very rarely, a benign tumor can become malignant. Examples of typically benign tumors include meningioma, vestibular schwannoma and pituitary adenoma.

Malignant brain tumors are cancerous. They typically grow rapidly and invade surrounding healthy brain structures. Brain cancer can be life-threatening due to the changes it causes to the vital structures of the brain. Some examples of malignant tumors that originate in or near the brain include olfactory neuroblastoma, chondrosarcoma and medulloblastoma.

Primary vs. Metastatic Brain Tumors

Primary brain tumors are tumors that start in the brain. Examples of tumors that most often originate in the brain include meningioma and glioma. Very rarely, these tumors can break away and spread to other parts of the brain and spinal cord. More commonly, tumors spread to the brain from other parts of the body.

Metastatic brain tumors, also called secondary brain tumors, are malignant tumors that originate as cancer elsewhere in the body and then metastasize (spread) to the brain. Metastatic brain tumors are about four times more common than primary brain tumors. They can grow rapidly, crowding or invading nearby brain tissue.

Common cancers that can spread to the brain are:

* Breast cancer
* Colon cancer
* Kidney cancer
* Lung cancer
* Skin cancer (melanoma)

## Brain Tumor Locations

Brain tumors can form in any part of the brain, but there are certain regions where specific tumors form:

* Meningiomas form in the meninges, the protective lining of the brain.
* Pituitary tumors develop in the pituitary gland.
* Medulloblastoma tumors arise from the cerebellum or brainstem.
* Skull base tumors grow on the underside of the brain, called the skull base.

Other brain tumors are described by the kinds of cells they are made of. For instance, gliomas are composed of glial cells.

## Brain Tumors in Children

Brain tumors are the most common solid tumor in children and adolescents, affecting about 5,000 children in the U.S. each year. Several different types of brain tumors can occur in children, including astrocytomas (e.g., glioblastoma multiforme), gliomas, ependymomas and medulloblastomas.

## Brain Tumor Symptoms

Different parts of the brain control different functions, so brain tumor symptoms will vary depending on the tumor’s location. For example, a brain tumor located in the cerebellum at the back of the head may cause trouble with movement, walking, balance and coordination. If the tumor affects the optic pathway, which is responsible for sight, vision changes may occur.

The tumor’s size and how fast it’s growing also affect which symptoms a person will experience.

In general, the most common symptoms of a brain tumor may include:

* Headaches
* Seizures or convulsions
* Difficulty thinking, speaking or finding words
* Personality or behavior changes
* Weakness, numbness or paralysis in one part or one side of the body
* Loss of balance, dizziness or unsteadiness
* Loss of hearing
* Vision changes
* Confusion and disorientation
* Memory loss

Can you have a brain tumor with no symptoms?

Brain tumors don’t always cause symptoms. In fact, the most common brain tumor in adults, meningioma, often grows so slowly that it goes unnoticed. Tumors may not start causing symptoms until they become large enough to interfere with healthy tissues inside the brain.

## Brain Tumor Causes and Risk Factors

Doctors don’t know why some cells begin to form into tumor cells. It may have something to do with a person’s genes or his or her environment, or both. Some potential brain tumor causes and risk factors may include:

* Cancers that spread from other parts of the body
* Certain genetic conditions that predispose a person to overproduction of certain cells
* Exposure to some forms of radiation

Are brain tumors hereditary?

Genetics are to blame for a small number (fewer than 5%) of brain tumors. Some inherited conditions put individuals at greater risk of developing tumors, including:

* Neurofibromatosis
* Von Hippel-Lindau disease
* Li-Fraumeni syndrome
* Familial adenomatous polyposis
* Lynch syndrome
* Basal cell nevus syndrome (Gorlin syndrome)
* Tuberous sclerosis
* Cowden syndrome



## Brain Tumor Diagnosis

Diagnosing a brain tumor usually involves a neurological exam, brain scans and a biopsy, if it can be done safely.

* A neurological exam may include a variety of tests to evaluate neurological functions such as balance, hearing, vision and reflexes.
* A variety of imaging techniques, including CT (or CAT) scan, MRI, occasionally an angiogram or X-rays can be used to identify the tumor, pinpoint its location and/or assess the function of your brain.
* If doctors cannot safely perform a biopsy (tissue sample collection and analysis), they will diagnose the brain tumor and plan the treatment based on other test results. If a biopsy was possible, doctors can use it to determine the tumor grade (how aggressive it is), as well as study the tumor tissue for any biomarkers that can help personalize the treatment approach.

Depending on your symptoms, doctors may also perform these tests to help confirm the diagnosis and rule out other conditions:

* Lumbar puncture to collect a sample of cerebrospinal fluid and see if it contains traces of the tumor cells.
* Evoked potentials studies to measure electrical activity in the nerves and/or electroencephalography (EEG) to measure electrical activity in the brain.
* Neurocognitive assessment to evaluate any changes in cognition and well-being.
* Neuro-ophthalmological examination to assess for signs of tumor affecting the eyes.
* Endocrinological evaluation to assess hormone function.

Proper diagnosis is essential in determining the best course of treatment.

### Brain Tumor Grading

The grade of a brain tumor defines how serious it is. Using the biopsy sample, a pathologist will examine the tumor under a microscope to determine its grade. Brain tumor grading is a category system that describes the brain tumor cells and indicates how likely the tumor is to grow and spread.

Brain tumor grading uses a scale from 1 (least aggressive) to 4 (most aggressive).

(World Health Organization tumor grading system)

#### *Grade I brain tumor*

* Benign (noncancerous)
* Slow-growing
* Cells look almost normal under a microscope
* Usually associated with long-term survival
* Rare in adults

#### *Grade II brain tumor*

* Relatively slow-growing
* Sometimes spreads to nearby normal tissue and comes back (recurs)
* Cells look slightly abnormal under a microscope
* Sometimes comes back as a higher grade tumor

#### *Grade III brain tumor*

* Malignant (cancerous)
* Actively reproduces abnormal cells
* Tumor spreads into nearby normal parts of the brain
* Cells look abnormal under a microscope
* Tends to come back, often as a higher grade tumor

#### *Grade IV brain tumor*

* Malignant
* Most aggressive
* Grows fast
* Easily spreads into nearby normal parts of the brain
* Actively reproduces abnormal cells
* Cells look very abnormal under a microscope
* Tumor forms new blood vessels to maintain rapid growth
* Tumors have areas of dead cells in their center (called necrosis)

#### *A changing diagnosis*

The grade of a brain tumor might change, usually to a higher grade, often without a cause. It’s also possible that the biopsy sample might not represent the entire tumor, giving an inaccurate initial data for the grade.

A change from a low-grade tumor to a high-grade tumor happens more often in adults than in children.

Brain Tumor Staging

Staging refers to how far a tumor has spread. If a tumor has migrated to other parts of the body, it has metastasized. Staging is often done for other types of tumors but *not*primary brain tumors. This is because brain tumors are unlikely to spread beyond the nervous system.

Conversely, other types of tumors (e.g., lung cancer) can spread to the brain. Tumors that have spread to the brain are advanced stage.

What does the size of a brain tumor mean?

Because larger tumors are more likely to interfere with normal brain function, they more often cause symptoms and complications.

## Brain Tumor Treatment

The most common treatment for brain tumors is surgery. For some tumors, surgical removal and continued monitoring may be the only treatment needed. Common surgical approaches to brain tumor removal include craniotomy, neuroendoscopy, laser ablation and laser interstitial thermal therapy.

Chemotherapy and radiation therapy can be used to treat brain cancer by helping shrink the tumor, slowing down its growth and/or preventing it from coming back. External beam radiation therapy, stereotactic radiosurgery and proton therapy are some of the radiation treatments for brain tumor.

## Brain Tumor Prognosis

Brain tumor can be a frightening diagnosis. It’s important to partner with a medical team you trust to determine the best next steps, whether it’s observation, surgery, radiation therapy or another treatment. How successful your personal outcome will be depends on many factors, including:

* The type of brain tumor, its size, grade and location
* Whether the tumor has spread within the brain or to other parts of the body
* Your age and overall health
* How long you had symptoms before you were diagnosed with a brain tumor
* How much the brain tumor affects your ability to function
* Your treatment preferences
* The expertise of your treatment team

There is no projected survival rate for those diagnosed with a brain tumor, as individual circumstances play a big role. For example, some malignant tumors can be successfully controlled by radiation therapy. Others, because of their location, may be life-threatening even if they are benign. Doctors have to look at thousands of patients with similar characteristics to see a trend in how certain tumors progress and how different treatments affect them.

Your overall outlook and prognosis are likely to change as you undergo various treatments. If you have surgery, how much of the tumor the neurosurgeon can remove will impact what will happen next. Other brain tumor treatments will determine future steps as well.

Source

Johns Hopkins Medicine (2025) *Brain Tumors and Brain Cancer*. Available at: https://www.hopkinsmedicine.org/health/conditions-and-diseases/brain-tumor (Accessed: 5 June 2025).

# Guillain-Barré Syndrome

* Guillain-Barré syndrome (GBS) is a rare condition that causes nerve damage.
* Symptoms include muscle weakness, tingling, and sometimes paralysis.
* *Campylobacter*infection is one of the most common causes of GBS in the United States.

## Overview

Guillain-Barré (Ghee-YAN Bah-RAY) syndrome happens when a person’s immune system harms their nerves. This harm causes muscle weakness and sometimes paralysis.

### **Symptoms**

Early symptoms of GBS include weakness and tingling.

People with GBS usually first feel these symptoms in both legs. Then, they might feel these symptoms in their arms and upper body.

Symptoms can progress over hours, days, or weeks.

The weakness can increase until people cannot use some muscles. In severe cases, people can become paralyzed.

### **Outlook**

People with GBS need to be hospitalized.

Most people start to recover 2–3 weeks after symptoms start. Recovery may take as little as a few weeks or as long as a few years.

Most people recover fully, but some have permanent nerve damage. Some people have died from GBS.

## Causes of GBS

### ***Campylobacter*infection**

*Campylobacter*infection is one of the most common causes of GBS in the United States.

* About 1 in every 1,000 people with *Campylobacter*infection gets GBS.
* At least 1 in every 20 people with GBS had a recent *Campylobacter*infection.
  + Some studies found as many as 8 in every 20 people with GBS had a recent *Campylobacter* infection.

### **Other causes**

Several other things can lead to GBS. These include:

* **Diarrhea or a respiratory illness**: About 2 in every 3 people had diarrhea or a respiratory illness before developing GBS.
* **Viral infection**: Some people with GBS had the flu or infection with cytomegalovirus, Epstein Barr virus, Zika virus, or other viruses.
* **Vaccination**: Very rarely, people have developed GBS after getting certain vaccines.

### Keep in mind‎

Benefits of vaccination far outweigh the risks. For example, studies have shown that people are more likely to get GBS after having the flu than after getting a flu vaccine.

## Other information about GBS

### **Number of people affected**

GBS is rare. CDC estimates that only about 3,000–6,000 people develop GBS each year in the United States.

### **Risk factors**

Anyone can develop GBS. However, in the United States, GBS is more common in men and people older than 50.

### **Outbreaks**

GBS is not contagious and outbreaks of GBS are very rare.

Most often, an outbreak of GBS is linked to another outbreak. For example, a GBS outbreak can happen if more than one person involved in an outbreak of *Campylobacter*infections develops GBS.

What is Guillain-Barré syndrome?

Guillain-Barré syndrome (GBS) (pronounced Ghee-yan Bah-ray) is a rare neurological disorder in which a person’s immune system mistakenly attacks part of their peripheral nervous system—the network of nerves that carries signals from the brain and spinal cord to the rest of the body.

GBS begins suddenly and can increase in intensity over a period of hours, days, or weeks until certain muscles cannot be used at all. Some cases of GBS are very mild and only marked by brief weakness. Others cause nearly devastating paralysis, leaving the person unable to breathe on their own. In these cases, the disorder is life-threatening—potentially interfering with breathing, blood pressure, or heart rate. Fortunately, most people eventually recover from even the most severe cases of GBS. After recovery, people may continue to have some weakness.

### Symptoms of Guillain-Barré syndrome

* **Weakness**: The weakness seen in GBS usually comes on quickly and worsens over hours or days. Often, feet are affected first, and weakness may move up the body to eventually impact the legs, arms, face, and breathing muscles. The person may first notice unexpected difficulty climbing stairs or walking. Less commonly, symptoms start in the face and move down to the legs and feet. Most people reach the greatest stage of weakness within the first two weeks after symptoms appear; by the third week 90% of affected people are at their weakest.
* **Sensation changes**: In GBS, the brain may receive abnormal sensory signals from the rest of the body due to the nerve damage associated with the condition. This results in unexplained, spontaneous sensations, called paresthesias, that the person may feel as tingling, a sense of insects crawling under the skin (called formications), and pain. Some people with GBS feel a deep muscular pain in the back and/or legs. Unexplained sensations often happen first, such as tingling in the feet or hands, or even pain (especially in children), often starting in the legs or back. Children will also begin to have difficulty walking and may refuse to walk. These sensations tend to disappear before the major, longer-term symptoms appear.

Other symptoms of Guillain-Barré syndrome may include:

* Difficulty with eye muscles and vision
* Difficulty swallowing, speaking, or chewing
* Pricking or pins and needles in the hands and feet
* Pain that can be severe, particularly at night
* Coordination problems and unsteadiness
* Abnormal heart rate or blood pressure
* Problems with digestion and/or bladder control

The body’s nerves have a central conducting core called the axon that carries an electric signal. The axon is surrounded by an insulating layer (or sheath) called myelin. The myelin sheath surrounding the axon speeds up the transmission of nerve signals and allows the transmission of signals over long distances. In the most common type of GBS, called acute inflammatory demyelinating polyradiculoneuropathy (AIDP), the immune system damages the myelin sheath. In two other types of GBS, called acute motor axonal neuropathy (AMAN) and acute motor-sensory axonal neuropathy (AMSAN), the immune system may damage the axons themselves. As a result, the nerves cannot transmit signals efficiently and the muscles begin to lose their ability to respond to the brain's commands, which causes weakness and abnormal or no reflexes.

Miller Fisher syndrome is another type of GBS involving the cranial nerves, which extend from the brain to areas of the head and neck. The main symptoms are weakness or paralysis of the muscles that move the eyes, problems with balance and coordination, and abnormal or no reflexes. People with this disorder may have other common GBS symptoms like muscle weakness.

Who is more likely to get Guillain-Barré syndrome?

GBS can affect anyone of any sex or age, but most often affects adults and people older than 50. GBS is not contagious or inherited and the exact cause is unknown.

Since the body's own immune system does the damage, GBS is called an autoimmune disease (“auto” meaning “self”). Normally the immune system uses antibodies (molecules produced in an immune response) and special white blood cells to protect us by attacking infecting bacteria and viruses. In GBS, however, the immune system mistakenly attacks the healthy nerves. This attack may start as a fight against an infection. One possible reason for this is that some chemicals seen on bacteria and viruses resemble those on nerve cells. The immune system may not be able to distinguish bacteria and viruses from healthy nerve cells which also become targets of attack.

GBS usually starts a few days or weeks following a respiratory or gastrointestinal bacterial or viral infection. One of the most common risk factors for GBS is infection with the bacteria *Campylobacter jejuni*, which causes gastroenteritis (including nausea, vomiting, and diarrhea). Sometimes, surgery will trigger the syndrome. In very rare cases certain vaccinations may increase the risk of GBS. Some countries worldwide reported an increased incidence of GBS following infection with the COVID-19, Zika, cytomegalovirus, or Epstein-Barr viruses.

### How is Guillain-Barré syndrome diagnosed and treated?

### Diagnosing GBS

Cases of GBS begin differently for different people, and there are several disorders with similar symptoms. Therefore, it may be difficult to diagnose GBS in its earliest stages. Doctors may perform the following:

* **History and physical exam**: A doctor will perform a physical exam and review the person’s medical history. They will assess how the person’s muscles and nerves are working. The doctor will note whether symptoms appear on both sides of the body (which is typical in GBS) and how fast the symptoms appeared. This is helpful because in other disorders, muscle weakness may progress over months rather than days or weeks. They will also check the reflexes, as some reflexes are lost in people with GBS.
* **Nerve conduction velocity test (NCV)**: This test measures the nerve's ability to send a signal. In GBS, the signals traveling along the damaged nerves are slowed because of damage to the myelin sheath.
* **Cerebrospinal fluid analysis**: A doctor may also conduct an analysis of the cerebrospinal fluid that bathes the spinal cord. This fluid contains more protein and fewer immune cells in people with GBS.
* **Imaging**: In some cases, an MRI (magnetic resonance imaging) of the spinal cord or even brain may help find any other potential causes of muscle weakness.

### Treating GBS

Currently, there is no cure for GBS. However, some therapies can reduce its severity and shorten recovery time. There are also several ways to treat the complications of the disease.

People with GBS are usually admitted to the hospital and treated in the intensive care unit due to possible complications of muscle weakness. At the hospital, people with GBS are closely monitored to track the progression of their muscle weakness, breathing, and heart rate. If an intervention is needed, it can be quickly provided by the hospital staff.

#### *Acute care for Guillain-Barré syndrome*

Two treatments are commonly used to interrupt immune-related nerve damage. Both are equally effective if started within two weeks of GBS symptoms.

* **Plasma exchange (PE)**, also called plasmapheresis, involves removing some blood through a catheter. Plasma (the liquid part of the blood) is separated from the blood cells. These cells, along with replacement fluid, are returned to the body. PE may work by removing the bad antibodies in the plasma that have been damaging the nerves.
* **Intravenous immunoglobulin therapy (IVIg)** involves injections of immunoglobulins—proteins that your immune system naturally makes to attack infecting organisms. The immunoglobulins are developed from a pool of thousands of healthy donors. IVIg can lessen the immune attack on the nervous system and shorten recovery time. Researchers believe this treatment also reduces the effectiveness of antibodies that attack the nerves by both “diluting” them with non-specific antibodies and reducing the number of harmful antibodies.

Anti-inflammatory steroid hormones called corticosteroids have also been tried to reduce the severity of GBS, but clinical trials have shown this treatment is not effective.

Supportive care is very important to address the many complications of paralysis as the body recovers and damaged nerves begin to heal. Since respiratory failure can occur in GBS, a person’s breathing should be closely monitored. Sometimes a mechanical ventilator is used to help support or control breathing. The autonomic nervous system (that regulates the functions of internal organs and some of the muscles in your body) can also be disturbed, causing changes in heart rate, blood pressure, digestion, or sweating, so the person should be put on a heart monitor or other equipment that measures and tracks body function. If the person has problems swallowing, they may also need special care to prevent choking, which can cause pneumonia.

#### *Rehabilitative care*

As people with GBS begin to improve, they may be transferred from the acute care unit at a hospital to a rehabilitation setting. They can receive physical rehabilitation and other therapy to regain strength and resume activities of daily living.

Because GBS can affect several parts of the body, different methods and approaches may be needed to prevent or treat complications. For example, a physical therapist can manually move and position the person’s limbs to help keep the muscles flexible and prevent muscle shortening. Muscle strength may not return in the same way. Muscles that get stronger faster may take over a function that weaker muscles normally perform (this process is called substitution). A physical therapist can select specific exercises to improve the strength of weaker muscles so their original function can be regained.

Occupational and vocational therapy can help people learn new ways to handle everyday functions that may be affected. They can also help the person manage work demands and identify the need for assistive devices and other adaptive equipment and technology.

#### *Long-term outlook for people with GBS*

GBS can be a devastating disorder because of its sudden and rapid, unexpected onset of weakness—and often paralysis. Fortunately, most people with GBS have a full recovery. With careful intensive care and successful treatment of infection, autonomic dysfunction, and other medical complications, even people who have respiratory failure usually survive.

Recovery can be slow–anywhere from a few weeks to a few years. Some people do not recover completely and experience long-term weakness, numbness, fatigue, or pain. People recovering from GBS may face physical challenges and emotionally painful periods. It can be extremely difficult to adjust to sudden paralysis and dependence on others for help with routine daily activities. Some people with GBS need mental health counseling to help them adapt. Support groups can often ease emotional strain and provide valuable information.

What are the latest updates on Guillain-Barré syndrome?

The National Institute of Neurological Disorders and Stroke (NINDS), a part of the National Institutes of Health (NIH), is the nation's leading federal funder of research on neurological disorders. NINDS, the National Institute of Allergy and Infectious Diseases (NIAID), and several other components of NIH conduct research on disorders including GBS and fund research at major institutions and universities. Neuroscientists, immunologists, virologists, and pharmacologists are working collaboratively to learn how to prevent GBS and to make new and better therapies.

Scientists are looking at how the immune system works to find which cells are responsible for beginning and carrying out the attack on the nervous system seen in GBS. The fact that GBS often begins after a viral or bacterial infection suggests that certain features of some viruses and bacteria may activate the immune system inappropriately. Investigators are searching for what those triggers may be. Certain proteins or peptides in viruses and bacteria may appear similar to the immune system as those found in myelin, and the production of antibodies to neutralize the invading viruses or bacteria could trigger the attack on the myelin sheath. Researchers are studying a treatment to stop the disruption of myelin junctions (gaps) to prevent myelin from being removed (demyelination) when the immune system damages the myelin sheath.

Some studies show that normal variations in certain genes could increase risk of developing GBS; however, more research is needed to identify and confirm associated genes. Since many of the genes that may increase the risk of GBS are involved in the immune system, their roles in fighting infection might contribute to the development of the condition.

NIH-funded researchers make use of a mouse model with an altered autoimmune regulator gene that generates autoimmunity against the peripheral nervous system (PNS). Using this model, scientists hope to identify which PNS proteins are at greatest risk of autoimmune attack and which parts of the immune system contribute to the autoimmune response against the PNS. A greater understanding of how the immune system damages the PNS could lead to better treatments for autoimmune disorders such as GBS.

Other NINDS-funded researchers are investigating the mechanisms by which IVIg treatment lessens the symptoms of GBS. By understanding these mechanisms, it may be possible to develop more effective treatments. For example, even with IVIg treatment, some people with GBS are left permanently disabled. Antibodies from the immune system directed against axonal or myelin antigens (substances that trigger an immune system reaction) play an important role in inflammatory responses and the eventual damage to the nerve fibers. Researchers are testing a new treatment that can reduce macrophage inflammation in the nerves of animal models.

Source

* Centers for Disease Control and Prevention (2024) *Guillain-Barré Syndrome*. Available at: https://www.cdc.gov/campylobacter/signs-symptoms/guillain-barre-syndrome.html (Accessed: 5 June 2025).
* National Institute of Neurological Disorders and Stroke (2025) *Guillain-Barré Syndrome*. Available at: https://www.ninds.nih.gov/health-information/disorders/guillain-barre-syndrome (Accessed: 5 June 2025).

**Charcot-Marie-Tooth disease**

**Charcot-Marie-Tooth disease (CMT) is a group of inherited conditions that damage the peripheral nerves.**

It's also known as hereditary motor and sensory neuropathy (HMSN) or peroneal muscular atrophy (PMA).

The peripheral nerves are found outside the main central nervous system (brain and spinal cord).

They control the muscles and relay sensory information, such as the sense of touch, from the limbs to the brain.

People with CMT may have:

* muscle weakness in their feet, ankles, legs and hands
* an awkward way of walking (gait)
* highly arched or very flat feet
* numbness in the feet, arms and hands

The symptoms of CMT usually start to appear between the ages of 5 and 15, although they sometimes do not develop until well into middle age or later.

CMT is a progressive condition. This means the symptoms slowly get worse, making everyday tasks increasingly difficult.

## **What causes CMT?**

CMT is caused by an inherited fault in one of the many genes responsible for the development of the peripheral nerves. This fault means the nerves become damaged over time.

A child with CMT may have inherited the genetic fault responsible for the condition from 1 or both of their parents.

There's no single faulty gene that causes CMT. There are many types of CMT that are caused by different genetic faults and these can be inherited in several different ways.

The chances of passing CMT to your child depend on the specific genetic faults you and your partner carry.

## **Testing for CMT**

See your GP if you think you may have symptoms of CMT.

If they suspect CMT, they'll refer you to a doctor who specialises in treating conditions of the nervous system (a neurologist) for further tests to confirm the diagnosis.

You should also see your GP if you or your partner have a family history of CMT and are considering having a baby.

Your GP can refer you for genetic counselling, where you can discuss your concerns and the options available with a genetics specialist.

## **How CMT is treated**

There's currently no cure for CMT. But treatments can help relieve symptoms, aid mobility, and increase independence and quality of life for people with the condition.

These treatments may include:

* physiotherapy and certain types of exercise
* occupational therapy
* walking aids

In some cases, surgery may be needed to correct problems such as flat feet and muscle contractures, where muscles shorten and lose their normal range of movement.

## **Living with CMT**

CMT is not life threatening and most people with the condition have the same life expectancy as a person without the condition.

But it can make everyday activities very difficult. Living with a long-term progressive condition can also have a significant emotional impact.

Some people find it helpful to speak to others with the condition through support groups.

You may also benefit from a talking therapy, such as cognitive behavioural therapy (CBT).

**The symptoms of Charcot-Marie-Tooth disease (CMT) can differ from person to person, even among relatives with the condition.**

Symptoms can vary depending on the type of CMT, and even people with the same type can experience it differently.

SYMPTOMS

For example, it's not possible to predict the age at which symptoms will first appear, how quickly the condition will progress, or its severity.

## **Early symptoms of CMT**

CMT is a progressive condition, which means the symptoms gradually get worse over time.

This means it may be difficult to spot symptoms in young children who have CMT.

Signs that a young child may have CMT include:

* appearing unusually clumsy and accident-prone for their age
* difficulty walking because they may have problems lifting their feet from the ground
* their toes dropping forward as they lift their feet (foot drop)

## **Main symptoms of CMT**

The main symptoms of CMT usually appear between the ages of 5 and 15, although they sometimes do not develop until well into middle age or later.

Some of the main symptoms of CMT include:

* muscle weakness in the feet, ankles and legs at first
* feet that are very highly arched, which can make the ankle unstable, or having very flat feet
* curled toes (hammer toes)
* an awkward or high step and difficulty using the ankle muscles to lift the foot, which makes walking more difficult
* a lack of sensation in the arms and feet
* cold hands and feet caused by poor circulation
* wasting of the muscles in the lower legs, causing legs to have a distinctive "upside-down champagne bottle" shape
* feeling tired a lot of the time as a result of the extra effort it takes to move around

Some people also develop additional problems, such as:

* uncontrollable tremor or shaking hands
* abnormal curvature of the spine (scoliosis)
* problems speaking, breathing or swallowing (dysphagia) – these symptoms are rare in CMT

## **Later symptoms of CMT**

As CMT progresses, the muscle weakness and lack of sensation gets worse and starts to affect your hands and arms more.

This can lead to problems with both manual dexterity and hand strength, making tasks like doing up the buttons of a shirt very difficult.

Persistent problems with walking and posture can put excessive strain on your body, which often leads to muscle and joint pain.

Less commonly, damaged nerves may also cause pain, known as neuropathic pain.

Problems with mobility and walking tend to get worse with age. It's uncommon to lose the ability to walk completely, but older people with CMT often need a walking aid to get around.

CAUSES

**Charcot-Marie-Tooth disease (CMT) is caused by mutations (faults) in genes that cause the peripheral nerves to become damaged.**

The peripheral nerves are a network of nerves that run from the brain and spinal cord (the central nervous system).

They carry impulses to and from the rest of the body, such as the limbs and organs, and are responsible for the body's senses and movements.

A peripheral nerve is similar to an electrical cable, and is made up of 2 parts:

* the axon – which transmits electrical information between your brain and limbs, similar to the wiring in an electrical cable
* the myelin sheath – which is wrapped around the axon to protect it and ensure the electrical signal is not broken, similar to the insulation around electrical cable

In some types of CMT, faulty genes cause the myelin sheath to break down.

Without protection, the axons become damaged, which affects the transmission of messages between the brain and the muscles and senses. This leads to muscle weakness and numbness.

In other types of CMT, the axons are directly affected and do not transmit electrical signals at the normal strength.

This means the muscles and senses do not get used enough, leading to symptoms of muscle weakness and numbness.

**How CMT is inherited**

A child with CMT may have inherited the genetic fault responsible for the condition from 1 or both parents.

No single faulty gene causes CMT. The many types of CMT are caused by different genetic mutations and the faulty genes can be inherited in several different ways.

**Autosomal dominant**

Autosomal dominant inheritance of CMT occurs when 1 copy of a mutated gene is enough to cause the condition.

If either parent carries a faulty gene, there's a 1 in 2 chance the condition will be passed on to each child they have.

**Autosomal recessive**

Autosomal recessive inheritance of CMT occurs when 2 copies of the defective gene are needed to cause the condition.

You inherit 1 copy from each parent. As your parents only have 1 copy of the gene, they don't develop CMT themselves.

If both you and your partner are carriers of the autosomal recessive CMT gene, there's a:

* 1 in 4 chance each child you have will develop CMT
* 1 in 2 chance each child you have will inherit 1 of the defective genes and be able to pass the condition to any children they have (known as being a carrier) – although they will not have any of the symptoms of CMT themselves
* 1 in 4 chance each child you have will receive a pair of healthy genes and will not develop CMT

If only 1 parent has the autosomal recessive gene, your children will not develop CMT. But there's a 1 in 2 chance each child will be a carrier.

**X-linked inheritance**

In X-linked inheritance, the mutated gene is located on the X chromosome and passed from mother to son. Chromosomes are the parts of cells that carry your genes.

Men have XY sex chromosomes. They receive the X chromosome from their mother and the Y chromosome from their father.

Women have XX chromosomes. They receive 1 X chromosome from their mother and the other X chromosome from their father.

A woman with the defective X chromosome will usually have no or very mild symptoms because the other healthy X chromosome counters the effect of the defective one.

But there's a 1 in 2 chance she'll pass on the defective gene to her son and he'll develop CMT.

If a woman with the defective X chromosome only has daughters, CMT can skip a generation until one of her grandsons inherits it.

**Types of CMT**

There are many different types of CMT that are all caused by different mutations (changes) in your genes.

The main types of CMT are:

* CMT 1 – the most common type, caused by defective genes that cause the myelin sheath to slowly break down
* CMT 2 – a less common and usually less severe type than CMT 1, caused by defects in the axon
* CMT 3 (Dejerine-Sottas syndrome) – a rare and severe type of CMT that affects the myelin sheath, causing severe muscle weakness and sensory problems to begin developing in early childhood
* CMT 4 – another rare and severe type of CMT that affects the myelin sheath, which begins developing in early childhood and causes many people to eventually lose the ability to walk
* CMT X – caused by a mutation in the X chromosome, and more common in men than women

DIAGNOSIS

**If you have early symptoms of Charcot-Marie-Tooth disease (CMT), your GP will ask about your symptoms and may carry out a physical examination.**

They may want to know:

* when your symptoms started
* how severe your symptoms are
* if anyone in your family has CMT

During a physical examination, your GP will look for evidence of the condition, such as muscle weakness, poor or absent reflexes, and foot deformities, such as high arches or flat feet.

## **Further tests**

If CMT is suspected, you may be referred to a doctor who specialises in treating conditions of the nervous system (a neurologist) for further testing.

Here are some tests you may have.

### Nerve conduction test

A nerve conduction test measures the strength and speed of signals transmitted through your peripheral nerves, the network of nerves that run from the brain and spinal cord to and from the rest of the body, such as the limbs and organs.

Small metal discs called electrodes are placed on your skin, which release a small electric shock that stimulates the nerves.

The speed and strength of the nerve signal is measured. An unusually slow or weak signal could indicate CMT.

### Electromyography (EMG)

Electromyography (EMG) uses a small needle-shaped electrode placed in your skin to measure the electrical activity of your muscles.

Some types of CMT cause a distinctive change in the pattern of electrical activity that can be detected by an EMG.

### Genetic testing

Genetic testing involves taking a blood sample and testing it for defective genes known to cause CMT.

So far, many of these genes have been found, but there may be more not yet identified.

Most people with CMT should be able to have their diagnosis confirmed by genetic testing and find out exactly which type of CMT they have.

For others, genetic testing may prove inconclusive because an unidentified gene may be involved.

### Nerve biopsy

In a small number of cases where other tests have been inconclusive, a test called a nerve biopsy may be carried out.

This is a minor surgical procedure where a sample of a peripheral nerve is removed from your leg for testing.

CMT can cause physical changes to the shape of the nerve, which can be seen under a microscope.

The biopsy is carried out under a local anaesthetic, so you'll be awake but will not feel any pain.

## **Being diagnosed with CMT**

Everyone reacts differently when told they have CMT.

You may experience feelings of shock, denial, confusion or fear. Some people are relieved that there's finally an explanation for their symptoms.

If you have recently been diagnosed with CMT, you may find it useful to:

* take all the time you need – do not rush into making important decisions about your health
* find the support you need – talk to your family and friends when you feel ready; you may also find it helpful to contact other people with CMT through the charity Charcot-Marie-Tooth UK
* find out what you can about CMT – both from your healthcare team and reliable online resources, such as Charcot-Marie-Tooth UK
* get involved in your care – work closely with your healthcare team to come up with a treatment plan that best suits you

## **Tests before and during pregnancy**

Couples with a family history of CMT who are thinking of having a baby can be referred to a genetics specialist for advice.

A genetic counsellor can help you work through the decision-making process and explain possible tests that can be carried out and any alternatives you may want to consider, such as adoption.

The main tests that can be carried out during pregnancy to check if a baby will develop certain types of CMT are:

* chorionic villus sampling (CVS) – where a small sample of placenta is removed from the womb and tested for known CMT genes, usually during weeks 11 to 14 of pregnancy
* amniocentesis – where a sample of amniotic fluid is taken for testing, usually during weeks 15 to 20 of pregnancy

If these tests show that your child is likely to have CMT, you can discuss with your genetic counsellor whether you want to continue the pregnancy or have a termination (abortion).

It's important to be aware that the results of these tests will not indicate how serious your child's CMT will be.

This is because the symptoms and progression of the condition can vary widely, even among family members with the same type of CMT.

It's also important to bear in mind that both tests can slightly increase your chances of having a miscarriage.

### Pre-implantation genetic diagnosis

For some couples at risk of having a child with CMT, pre-implantation genetic diagnosis (PGD) may be an option.

PGD involves using in vitro fertilisation (IVF), where eggs are removed from a woman's ovaries before being fertilised with sperm in a laboratory.

After a few days, the resulting embryos can be tested for certain types of CMT and a maximum of 2 unaffected embryos transferred into the womb.

TREATMENT

**There's no cure for Charcot-Marie-Tooth disease (CMT), but therapies are available to help reduce your symptoms and enable you to live as independently as possible.**

As CMT gets worse over time, you'll need to be assessed regularly to check for any changes in your condition.

How often you're assessed depends on the type of CMT you have and the severity of your symptoms.

Your treatment programme may involve a number of healthcare professionals working together in a multidisciplinary team (MDT).

A doctor will usually co-ordinate your treatment programme, and makes sure every aspect of your condition is closely monitored and treated if necessary.

## **Physiotherapy**

Physiotherapy is one of the most important therapies for improving the symptoms of CMT and reducing the risk of muscle contractures, where muscles shorten and lose their normal range of movement.

Physiotherapy uses physical methods, such as massage and manipulation, to promote healing and wellbeing.

It usually involves low-impact exercises such as stretching, swimming and moderate weight training.

There's a lack of good-quality medical research into the benefits of exercise for people with CMT, but it's possible that some types of exercise are beneficial.

For example:

* strengthening exercises that focus on improving muscle strength, such as lifting weights, may help improve overall strength and reduce foot drop
* aerobic exercise, such as walking or swimming, which raises your heart rate and makes you breathe harder, may improve your fitness and your ability to function on a day-to-day basis
* posture and balance exercises, such as yoga, may also be beneficial

Any exercise needs to be carefully planned as part of a personalised exercise programme.

A certain level of exercise may be safe, but you risk making your symptoms worse if you do not follow proper instructions or overexert yourself.

Speak to your GP or physiotherapist about arranging a suitable exercise programme that will allow you to pace yourself.

## **Occupational therapy**

Occupational therapy involves identifying problem areas in your everyday life, such as dressing yourself, then working out practical solutions.

Occupational therapy will be useful if muscle weakness in your arms and hands makes it difficult for you to do day-to-day tasks, such as dressing or writing.

An occupational therapist will teach you how to use adaptive aids to compensate for your difficulties, such as clothing with clasps instead of buttons and magnetic tubes that allow you to pick up objects.

## **Orthoses and walking aids**

Orthoses are devices worn inside your shoes or on your legs to improve the strength and functionality of your limbs, or to correct your gait (the way you walk).

There are several different types of orthoses, including:

* insoles in your shoes
* custom-made shoes that support your ankles
* ankle or leg braces
* thumb splints that can improve your hand strength

It's unusual for a person with CMT to completely lose the ability to walk.

But moving around can be difficult, so using a wheelchair every now and again can help by giving you a chance to rest.

## **Taking care of yourself**

In addition to the treatment you receive, there are some general precautions you can take to avoid further problems.

These may include:

* trying to maintain a healthy weight – being overweight can make moving around more difficult and put more strain on your body
* taking good care of your feet – make sure you check and clean your feet regularly, as there's a risk of injury and infection if you have reduced sensation in your feet
* avoiding drinking too much alcohol – this has many health risks, which may be worse if you have CMT
* avoiding caffeine (found in tea, coffee, cola and energy drinks) and nicotine (found in tobacco) if you have tremors (shaking) – they can make this worse
* avoid medicines that can cause nerve damage – Charcot-Marie-Tooth UK has a list of medications to avoid or use with caution if you have CMT

Ask your MDT if they have specific lifestyle advice for you, as risks may vary from person to person.

## **Controlling pain**

There are 2 types of pain associated with CMT:

* joint and muscle pain – caused by the stresses that CMT places on your body
* neuropathic pain – caused by damage to your nerves (this is less common)

Joint and muscle pain can usually be controlled by taking non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen.

Neuropathic pain may be treated with tricyclic antidepressants (TCAs) or an anticonvulsant medication (a medicine often used to prevent seizures).

These medications were not originally designed to be painkillers, but there's evidence to suggest they're effective in treating long-term nerve pain in some people.

## **Surgery**

If CMT causes significant deformities, surgery may be needed to correct them.

### Osteotomy

An osteotomy is a surgical procedure used to correct severe flatness of the feet.

A cut (incision) is made in your foot and the surgeon removes or repositions the bones in your foot to correct its shape.

After surgery, your foot (or feet) will need to be kept in plaster for several weeks until the bones have healed.

### Arthrodesis

Arthrodesis involves fusing the 3 main joints in the back of your feet to strengthen your feet, correct their shape and relieve pain.

It can be used to correct flat feet and heel deformities, and relieve joint pain.

After surgery, your foot (or feet) will be put in plaster, and you will not be able to place any weight on them for 6 weeks.

During this time, you'll need to use crutches or a wheelchair.

Once you can put weight on your feet, you'll need to wear the cast for another 6 weeks (12 weeks in total).

But it may take up to 10 months for you to fully recover from the operation.

### Plantar fascia release

Plantar fascia release is a surgical procedure used to relieve persistent heel pain caused by inflamed tendons. Tendons are the fibrous cords that join bones to muscle.

During the procedure, part of the tendon is removed and the remaining tendon repositioned and allowed to heal.

Afterwards, you'll need to wear a cast for 3 weeks and will not be able to put any weight on your feet during this time.

### Spinal surgery

Although abnormal curvature of the spine (scoliosis) can often be treated using a back brace, corrective surgery may be needed.

## **Research into treatments**

There's some promising research that may provide new ways of treating people with CMT.

This research includes:

* using stem cells (cells at an early stage of development) to repair nerve damage
* using hormones (powerful chemicals) and gene therapy to slow the progression of the condition

## **Living with CMT**

Living with CMT can be challenging. The condition can have an impact on many aspects of your life.

These include:

* driving and getting around
* employment and finances
* holidays and leisure activities
* your emotional health

Source

NHS (2022) *Charcot-Marie-Tooth disease - Treatment*. Available at: https://www.nhs.uk/conditions/charcot-marie-tooth-disease/treatment/ (Accessed: 5 June 2025).

BELLS PALSY (FACIAL NERVE PALSY)

Continuing Education Activity

Bell palsy is the most common paralysis of the seventh cranial nerve, with an onset that is typically rapid and hemifacial. The condition affects 15 to 40 of every 100,000 people annually and recurs in approximately 10% of cases. In addition to unilateral facial paralysis, Bell palsy often also involves a prodrome of otalgia, and many patients additionally report ipsilateral xerophthalmia, epiphora, hyperacusis, nasal obstruction, and dysgeusia. The facial asymmetry accompanying Bell palsy may cause dysarthria, oral incompetence, and difficulty expressing emotions nonverbally, resulting in social isolation and emotional distress.

Fortunately, 70% to 80% of patients will recover completely even without treatment, and over 95% recover with prompt pharmacological therapy. In rare cases, surgical intervention may be indicated to protect the eye or improve recovery of facial nerve function. Imaging and laboratory evaluation are unnecessary in most cases, but patients with severe paralysis may undergo electrodiagnostic testing for its prognostic value and to establish candidacy for facial nerve decompression surgery. For patients who do not fully recover from Bell palsy, spastic and dyscoordinated facial contractions (synkinesis) usually develop, necessitating long-term treatment with physiotherapy, botulinum toxin injections, and potential surgical interventions.

This activity for healthcare professionals reviews key aspects of Bell palsy, including its etiology, clinical presentation, differential diagnosis, and current approaches to treatment and rehabilitation, from initial presentation to long-term management. The activity also highlights the role of an interprofessional team in improving outcomes for affected patients.

**Objectives:**

* Identify the most common symptoms and clinical findings of Bell palsy to facilitate early diagnosis.
* Assess the severity of Bell palsy using the House-Brackmann Facial Nerve Grading System or an alternative classification scale.
* Apply current evidence-based guidelines for diagnosing and managing acute and recurrent cases of Bell palsy.
* Collaborate with all members of an interprofessional team to optimize outcomes and minimize complications for patients with Bell palsy.

Introduction

Named for Sir Charles Bell, the Scottish neurologist and anatomist who first described the condition, Bell palsy is the most common paralysis of the seventh cranial nerve, accounting for 38% to 83% of cases of facial weakness (see **Image**. Sir Charles Bell). In 1821, Bell presented his paper titled *On the Nerves: Giving an Account of Some Experiments on Their Structure and Functions, Which Lead to a New Arrangement of the System* to the Royal Society, in which he described, among other things, the course and function of the facial nerves.Prior to Bell's anatomical studies, it was not known that the seventh cranial nerve controlled the muscles of facial expression, and this nerve was occasionally sacrificed during treatments for facial pain, thereby resulting in hemifacial paralysis. Bell was a prolific researcher and artist, and his name remains associated with several anatomical structures and physical findings, including the Bell phenomenon, or palpebral oculogyric reflex, which elevates the globes in order to protect the cornea when the eyelids close. This reflex is particularly critical for patients with facial paralysis, whose corneas are at greater risk for exposure and ulceration in the absence of effective eye closure.

When Bell palsy occurs, patients typically present complaining of weakness and often "numbness" of one side of the face, usually preceded 1 to 2 days prior by a dull ache behind or within the ipsilateral ear. Patients may report a dry eye over the course of the day prior to presentation, noting drooling while brushing their teeth before going to bed, and potentially numbness of the tongue or a metallic taste in the mouth. Some patients will also describe ipsilateral ear pain with loud noises. Upon awakening, the patient or partner will frequently notice facial asymmetry and may be concerned about the possibility of a stroke, which often leads to an emergency department visit. Generally, however, distinguishing between a stroke and Bell palsy is very straightforward, and patients can be reassured and discharged with steroids, antivirals, and eye lubricant as long as there is no suspicion for Ramsay Hunt syndrome, Lyme disease, or any other conditions that may cause a facial nerve palsy.

Fortunately, over 80% of patients with Bell palsy will recover on their own, with 90% to 97% improving if provided with appropriate medical management in a timely fashion. For this reason, the most important early intervention for most patients is corneal protection in the event that eye closure is impaired; this consists of artificial tears, eyelid taping, and potentially upper eyelid weight placement. For the patients unfortunate enough to recover incompletely, spastic and dyscoordinated facial contractions (synkinesis) will develop, for which a broad range of treatments is available, from physiotherapy to botulinum toxin injections and surgery.

Etiology

Historically, Bell palsy has been considered a diagnosis of exclusion, to be applied when no other causes of acute-onset facial paralysis are readily apparent. If a patient with hemifacial palsy were to present in the absence of an auriculofacial rash, history of a tick bite, other neurological deficits, and imaging or laboratory abnormalities, Bell palsy would be diagnosed. Ironically, however, the term "Bell palsy" is often misused in an overly nonspecific manner to refer to any hemifacial paralysis, regardless of etiology, for example, describing the manifestations of a coronavirus infection as "upper and lower respiratory symptoms with polyneuropathy and Bell palsy."

While it remains difficult to pin down the exact cause of Bell palsy for any individual patient, there is evidence to suggest that *Human herpesvirus 1* is responsible for most of the cases. This virus has been identified in the epineurial fluid of 79% of the patients with Bell palsy but in none of the patients with Ramsay Hunt or other facial palsy conditions in a 1996 study performed by Murakami et al. Testing epineurial fluid for herpes simplex deoxyribonucleic acid by polymerase chain reaction is clinically impractical in most patients, but because of the ubiquity of this virus and its close relatives (other herpes simplex viruses, cytomegalovirus, Epstein-Barr virus), the diagnosis of Bell palsy is now typically made clinically if the history and physical examination are consistent.

Another unsolved mystery regarding Bell palsy is its association with coronavirus disease (COVID) 2019  and the immunizations to prevent this infection. Facial paralysis, as well as other cranial neuropathies, are known to accompany SARS-CoV-2 infection, particularly affecting the olfactory, oculomotor, and abducens nerves, but also the trigeminal, auditory, vagus, glossopharyngeal, and hypoglossal nerves. More controversial, however, is the potential relationship between Bell palsy and the various available COVID vaccinations. A large metanalysis published by Rafati et al in 2023 provided results determining that the risk of developing Bell palsy after messenger ribonucleic acid (mRNA) vaccination was 3.6 times higher than in the unvaccinated population, but that there was no significant increase in the risk of Bell palsy with viral vector vaccines. However, results from a 2021 study that compared the incidence of Bell palsy after immunization with the Pfizer/BioNTech mRNA vaccine to that after the CoronaVac/Sinovac inactivated virus vaccine found the incidence to be over twice as high with the CoronaVac/Sinovac injection. Regardless, the chance of developing facial palsy is significantly higher (relative risk of 3.23) with COVID infection than it is after COVID vaccination.

Epidemiology

The annual incidence of Bell palsy is 15 to 40 per 100,000 individuals, and the lifetime risk is 1 in 60, with a recurrence rate of 8% to 12%. There is no sex, ethnic, or laterality predilection, and Bell palsy can occur at any age; there is a bimodal distribution with incidence peaks between 20 and 30 years and between 60 and 70. There are multiple known risk factors for developing Bell palsy, including diabetes, pregnancy, preeclampsia, obesity, dental procedures, and, debatably, hypertension. Pregnant patients and those with diabetes are specifically at higher risk for worse outcomes and are potentially more likely to present with worse paralysis than patients without diabetes and who aren't pregnant with Bell palsy.

According to a 2022 paper published by Escalante et al, the most common severity of Bell palsy is House-Brackmann grade III (mild-moderate), accounting for 41.9% of patients. Grade VI palsy (total hemifacial paralysis) occurs in 20.1% of patients. House-Brackmann grades II (mild) and V (severe) each comprise 16.3% of patients, and grade IV accounts for only 5.4%. The same study also assessed the chance of recovery as a function of palsy severity and found that patients with House-Brackmann grade VI palsy had a 60% chance of recovery to grade I or II, and grade V patients had an 83% chance if provided steroids and antivirals. Patients with grade II to IV paralysis all recovered to grade I or II in this series.

**Pathophysiology**

Bell palsy, which is a unilateral hemifacial palsy of rapid onset, results from inflammation of the facial nerve, typically originating in the labyrinthine segment (see **Image**. Bell Palsy). The labyrinthine segment is the second intratemporal segment of the facial nerve and the narrowest, with an average diameter of 0.7 mm and a length of 3 to 5 mm. The narrowness of this portion of the facial nerve's canal through the temporal bone of the skull (the Fallopian canal) predisposes it to dysfunction, potentially due to edema and subsequent impairment of perfusion when inflammation occurs, with Bell palsy more likely to occur in patients who have narrow labyrinthine segments of the facial canal.

Proximal to the labyrinthine segment is the canalicular segment, which runs in the internal auditory canal superior to the cochlear nerve and anterior to the superior vestibular nerve. The labyrinthine segment ends distally at the geniculate ganglion, where the greater superficial petrosal nerve branches off to supply parasympathetic innervation to the lacrimal gland and the mucous glands of the nasal cavity and palate. At the distal end of the geniculate ganglion, also known as the first genu of the facial nerve, the tympanic segment enters the middle ear and courses superior to the oval window before turning inferiorly at the second genu and entering the mastoid cavity. The mastoid segment courses downwards to the stylomastoid foramen, where the nerve exits the temporal bone on its path to the parotid gland, within which it divides into the five main branches that innervate the muscles of facial expression. These branches are the frontal, zygomatic, buccal, marginal mandibular, and cervical (see **Image**. The Facial Nerve).

Bell palsy is thought to result from compression of the seventh cranial nerve within the labyrinthine segment of the Fallopian canal. Not only is this segment the narrowest along the nerve's course within the temporal bone, but it also appears to have the most tenuous blood supply, with very fine arterioles connecting the angiosomes supplied by the internal auditory branch of the anterior inferior cerebellar artery proximally and the petrosal branch of the middle meningeal artery distally. The final segment of the intratemporal facial nerve is perfused by the stylomastoid artery, a branch of the posterior auricular artery. Further implicating the labyrinthine segment as the primary site of Bell palsy inflammation is the appearance of the nerve on magnetic resonance imaging (MRI): 59% of patients with acute Bell palsy have asymmetric enhancement of the labyrinthine segment, and a further 33% have enhancement of both the labyrinthine segment and the geniculate ganglion (see **Image**. Left-Sided Bell Palsy, Magnetic Resonance Image).

The severity of this inflammation may depend upon several factors, including the patient's immune status, blood glucose level, blood pressure, and age. There is a hypothesis that edema of the nerve within the Fallopian canal compromises perfusion, leading to nerve dysfunction. The extent of the dysfunction and the prognosis for recovery depend on the degree of disruption of the internal architecture of the facial nerve, in which each axon has a myelin sheath and an endoneurial membrane surrounding it, with the axons grouped together into fascicles surrounded by perineurial membranes, and the fascicles together constituting the nerve itself, which is invested in epineurium (see **Image**. Neurology, Nerve Fascicle, Fasciculus, Epineurium).

A mild injury may only cause a temporary conduction block with or without focal demyelination, known as neuropraxia in the Seddon grading system, or a Sunderland class I injury. Actual axonal damage occurs in a Sunderland class II injury, but all of the internal architecture of the nerve is otherwise preserved, virtually ensuring that the axons regrow correctly along their original paths. In the case of a Sunderland class III injury, the axons undergo Wallerian degeneration as they do in a class II injury. However, the endoneurial membranes that surround the damaged axons are violated, which permits mild misdirection of the regenerating axons that may result in discoordinated movements and spasms (synkinesis). A Sunderland class IV injury adds perineurial damage to the class III injury, which results in disruption of the fascicular organization of the nerve and greater potential for synkinesis. Sunderland class II to IV injuries are collectively known as axonotmesis in the Seddon grading system, and a Sunderland class V injury is known as neuronotmesis. Neuronotmesis is a complete transection of the nerve, including the epineurium, guaranteeing severe synkinesis even if the nerve is repaired microsurgically (see **Image**. Seddon and Sunderland Classifications of Nerve Injury).

History and Physical

Patients with Bell palsy present with progressive hemifacial paralysis that typically reaches a peak in severity within 24 to 72 hours of onset. Most patients will also report prodromal dull pain within or behind the ipsilateral ear. Other common associated symptoms include hyperacusis due to stapedius muscle weakness, a metallic taste on the ipsilateral side of the tongue or ipsilateral tongue numbness due to chorda tympani involvement, paradoxical eye dryness with tearing due to impairment of both eye closure and the lacrimal pump function of the orbicularis oculi muscle, ipsilateral nasal obstruction due to nasalis muscle weakness, oral incompetence and dysarthria due to orbicularis oris dysfunction, aesthetic self-consciousness because of facial asymmetry, and ipsilateral facial numbness. The latter may be a mischaracterization of facial weakness by some patients but may also represent a manifestation of the poorly understood connections between branches of the facial and trigeminal nerves that have been observed in laboratory studies.

If the patient notes skin or mucosal rashes, an alternative diagnosis, such as Ramsay Hunt syndrome or Lyme disease, should be considered. Similarly, if the patient mentions significant, burning pain rather than a dull otalgia, a herpes zoster diagnosis may be appropriate even in the absence of a vesicular outbreak. Most importantly, there should not be an element of the history that implicates a specific etiology for facial paralysis, such as head trauma, otologic infection, or neoplasm.

Upon physical examination, all branches of the facial nerve are roughly equally impaired on the affected side of the face in patients with Bell palsy. In contrast, a cortical stroke will typically leave forehead movement intact on the affected side due to bilateral upper motor neuron contributions to the facial nucleus. A stroke will typically also present with other neurological signs or cranial neuropathies, while Bell palsy will not. Like Bell palsy though, a brainstem stroke will cause hemifacial weakness that does not preserve forehead movement; this too will most often present with other neurological symptoms as expected with a cortical stroke.

The unilaterality of Bell palsy is an important feature that helps to differentiate it from other facial paralyses, such as Lyme disease and Guillain-Barré syndrome, which often present with bilateral, albeit asymmetric, facial paralysis. Similarly, the presence of a cutaneous or mucosal rash of the head or face along with hemifacial palsy should shift focus to a diagnosis of Ramsay Hunt syndrome; a targetoid rash anywhere on the body may indicate Lyme disease. Patients presenting with chronic facial movement dysfunction from Bell palsy rather than acute, flaccid paralysis may report facial tension, fatigue, and pain instead of frank weakness, although they may mistake this synkinetic dyscoordination and asymmetry of facial expression for persistent paralysis. Another phenomenon that may accompany facial synkinesis is Bogorad syndrome, or "crocodile tears," in which aberrant reinnervation of the lacrimal gland leads to tearing that accompanies salivation.

An assessment of facial nerve function should be performed in a systematic fashion to ensure no findings are overlooked (see **Video**. Acute Bell Palsy with a Severe Presentation). Evaluating each extratemporal branch of the facial nerve individually is critical, both at rest and with movement. Resting forehead rhytid and brow symmetry, as well as symmetry with elevation, should be assessed; the examiner's thumb may be used to hold the glabella still to prevent transmission of movement from the normal side to the paralyzed brow if there is any doubt about the presence of movement on the affected side. The resting appearance of the palpebral fissures should be compared, and any increased opening on the affected side should be noted, as well as whether the increased opening is due to upper eyelid retraction or lower eyelid laxity. There may be asymmetry of the lateral periocular rhytids (crow's feet) as well, with the affected side having fewer or shallower wrinkles. Gentle eye closure (with a normal blink) and eye closure with full effort should be assessed, although it is not necessary to attempt to pry open the patient's eyes manually, as this maneuver has no prognostic or diagnostic value.

If eye closure is incomplete, the Bell phenomenon should be assessed to help determine the risk of corneal exposure. The Bell phenomenon is the reflex by which the globe rolls superolaterally to protect the cornea when the eye closes; this reflex may serve to protect the cornea even if eye closure is incomplete (see **Image**. Bell Phenomenon). The reflex is present in 70% to 80% of the population and tends to diminish with age. If, on the other hand, eye closure is complete, the finding should be considered in the context of the rest of the history and physical examination. If several days have passed since the onset of paralysis and the rest of the hemiface also demonstrates some movement, the paralysis is likely only of mild to moderate severity. If there is slow but complete eye closure and no discernable movement in the rest of the hemiface with paralysis of recent onset, the eye closure is likely due to gravity rather than volitional movement and does not indicate any retained facial nerve function. Paralytic lagophthalmos in this situation will likely develop over the ensuing 24 to 48 hours.

Evaluation of midfacial motor function begins with a comparison of the nasolabial folds at rest. The affected side's fold may be shallower and/or more vertically oriented than the unaffected side. There may also be unilaterally diminished contraction of the nasalis muscle, although, like the eyebrows, this may be difficult to discern without placing a thumb in the center of the nose to prevent transmitted movement. A Cottle maneuver, in which the examiner's thumb is used to suspend the nasal base by retracting the cheek laterally, will identify any nasal valve collapse.

In the lower face, the oral commissure may be inferiorly malpositioned, and the philtrum may be pulled towards the unaffected side due to a lack of resting muscle tone on the affected side. The smile may be asymmetric, with decreased oral commissure excursion, upper lip elevation, and lower lip depression on the affected side. Lastly, there may be asymmetric platysmal contraction or even loss of resting platysmal banding on the affected side in an older patient.

The overall function can then be categorized using the House-Brackmann scale, which was published in 1985 as a means of describing acute otologic facial paralysis, although it also works well for documenting the severity of acute Bell palsy (see **Table**. House-Brackmann Facial Nerve Grading System). For patients with chronic facial movement disorders due to incompletely recovered Bell palsy, the use of a more detailed scale, such as the House-Brackmann 2.0, Sunnybrook, Yanagihara, or eFace, is appropriate and conveys additional useful information (see **Staging** section). These patients require a more detailed physical examination; after assessing resting symmetry and voluntary movement as described above, the location and degree of synkinesis should be evaluated. Doing so requires the same facial movements previously detailed, but the examiner directs attention to the regions of the face that are not requested to move. For example, with eye closure, the clinician will look for zygomaticus muscle and platysmal contraction, or with lip pucker, there may be involuntary winking (see **Video**. Post-Bell Palsy Synkinesis). Other common areas in which synkinesis is seen are the mentalis, depressor anguli oris, and frontalis muscles.

Table. House-Brackmann Facial Nerve Grading System .

\*In the first 1 to 2 days after paralysis onset, eye closure on the affected side may remain complete due to gravity even if there is a severe facial nerve dysfunction. Lagophthalmos may present in a delayed fashion even if the rest of the face is paralyzed, and this preserved eye closure should not be considered in the overall House-Brackmann assessment.

Additional physical examination techniques may be employed to assess ocular health, such as slit-lamp evaluation with fluorescein to identify corneal defects and Schirmer testing to evaluate tear production. The Schirmer test involves placing a strip of filter paper in the fornix of the lower eyelid for 5 minutes and measuring how far the moisture has diffused at the end of that period; 10 mm or more is considered normal. Photographs, videos, and patient-reported quality-of-life instruments should also be completed in order to facilitate objective tracking of recovery.

The Sir Charles Bell Society of International Facial Paralysis Experts recommends obtaining the following photographs of every facial paralysis patient at every visit: in repose, elevation of eyebrows, gentle eye closure, tight eye closure, wrinkling the nose, small closed-mouth smile, large smile showing teeth, lip puckering, depressing the lower lip to show the bottom teeth, and a nasal base "worm's eye" view. The same movements should be recorded on video as well. Lastly, an outcomes survey, such as the Facial Clinimetric Evaluation scale (FaCE), should be documented at each visit to track the effect of any interventions performed and monitor the patient's progress over time.

Patients who present with incomplete paralysis less than 72 hours after palsy onset should have a follow-up visit within 1 week to determine whether the paralysis progresses to House-Brackmann grade VI and requires evaluation with electrodiagnostic testing (see **Evaluation** section). Patients should also be advised to follow up immediately if eye pain, photophobia, or a foreign body sensation develops, which can indicate a corneal abrasion and necessitate ophthalmological evaluation. Vesicles ipsilateral to the paralysis appearing on the ear, scalp, face, or in the mouth within a few days after initial presentation should trigger the diagnosis of Ramsay Hunt syndrome, which necessitates a higher dose of antivirals than Bell palsy and a prolonged steroid course.

Evaluation

The history and physical examination determine the need for additional evaluation, which is not required in typical cases of Bell palsy. There is some evidence to suggest that a neutrophil-to-lymphocyte ratio higher than 3.53:1 is a reliable predictor of poor recovery, but this has not achieved widespread acceptance as a standard part of the evaluation of patients with Bell palsy, given the high spontaneous recovery rate and the cost of drawing blood.

When a patient presents with House-Brackmann grade VI paralysis, some surgeons will offer facial nerve decompression under specific circumstances. While the outcomes of the operation are somewhat variable and the practice controversial, the most widely adopted candidacy criteria require electroneuronography (ENoG) and electromyography (EMG). ENoG is a form of evoked EMG in which a transcutaneous stimulator is placed over the stylomastoid foramen, and cutaneous electrodes on the face record the compound muscle action potentials that result from facial nerve stimulation. The muscles typically monitored are the orbicularis oculi and the zygomaticus major. The ENoG requires an unaffected side to act as a control for comparison with the affected side, and the test, therefore, works best when only 1 side of the face is weak, as is generally the case for Bell palsy. If the compound muscle action potential amplitude is reduced by 90% or more on the paralyzed side relative to the unaffected side, the ENoG is considered positive, and the EMG is then performed.

The EMG following a positive ENoG is performed by placing percutaneous needle electrodes into the same muscles monitored with the ENoG and looking for motor units that contract when the patient attempts voluntary facial movement. If motor units are identified, the nerve injury is considered incomplete, but if no motor units are present, the patient meets the criteria for operative facial nerve decompression. The procedure, depending on how it is performed, requires a craniotomy or, at the very least, a mastoidectomy, and many patients are either reluctant to proceed or are not good candidates due to medical comorbidities. For these patients, performing an ENoG can still be useful because of its prognostic value. When treated medically, patients with House-Brackmann grade VI paralysis who meet decompression criteria are essentially guaranteed to develop synkinesis without surgery, whereas patients with House-Brackmann grade VI paralysis who do not meet decompression criteria have a roughly 60% chance of developing synkinesis.

Laboratory investigations and imaging are more commonly performed in patients whose diagnosis of Bell palsy is questionable due to the presence of skin or mucosal lesions, other neurological symptoms, insidious paralysis onset, or repeated episodes of paralysis. Magnetic resonance imaging (MRI) can rule out space-occupying lesions, such as meningiomas or schwannomas, and contrast-enhanced computed tomography effectively assesses for geniculate ganglion vascular malformations, otologic pathology, and extratemporal masses. Enhancement in the labyrinthine segment of the facial nerve, the cerebellopontine angle, the internal auditory canal, or the parotid gland is abnormal, while enhancement when limited to the geniculate ganglion and the tympanic and mastoid segments of the nerve is mostly likely normal "physiological" enhancement. More recently, there has been increasing interest in using ultrasound to identify the location and severity of edema within the facial nerve, thereby providing prognostic information. For patients with a history of travel to an endemic area, Lyme titers may be drawn, and numerous other conditions can cause facial paralysis as well, including human immunodeficiency virus infection, syphilis, West Nile virus, tuberculosis, leprosy, COVID, polio, and myriad autoimmune diseases.

Historically, the maximal stimulation test (MST) and the nerve excitability test (NET) have been used to assess facial nerve function, but both have been largely supplanted by ENoG, which, despite the variability of its results, remains more objective and consistent than either the MST or NET. The NET involves stimulation of the face with an increasing electrical current and determining the difference between the lowest current amplitudes that produce visible contraction on each side. The MST is similar in that it requires a cooperative patient and the examiner's subjective evaluation of movement, but it involves stimulating the unaffected side with increasing electrical current until no additional contraction is achieved and then recording how much contraction is produced on the affected side with the same stimulation. Various other studies may also be employed to evaluate the autonomic and sensory functions of the facial nerve, including saliva flow, taste testing, and stapedial reflex testing.

**Treatment / ManagementAcute Bell Palsy**

Once Bell palsy is diagnosed, management is very straightforward and follows a predictable algorithm (see **Image**. Management of Acute Bell Palsy). Steroids and antiviral medications are prescribed, with antihyperglycemic medications added or adjusted as necessary for patients with diabetes. Corneal protection is provided, and electrodiagnostic studies are performed if a House-Brackmann grade VI paralysis is present, with surgery offered if candidacy criteria are met. Patients at high risk for exposure keratopathy are given a scleral contact lens or undergo minor surgery, such as upper eyelid loading, tarsorrhaphy, or lateral tarsal strip canthopexy. Electrical stimulation has also been shown to improve outcomes when combined with medical management, expediting recovery and enhancing facial function. Acupuncture, on the other hand, provides questionable benefits to patients with Bell palsy according to the poor quality studies conducted thus far; it does appear to be safe for those who wish to receive the treatment.

**Medical management**

Ideally, patients with acute Bell palsy should be seen as soon as possible and given corticosteroids within 72 hours of paralysis onset. A common regimen is 1 mg/kg daily up to 60 mg of prednisone or an equivalent dose of prednisolone for 5 to 7 days with or without a taper. There is strong evidence that steroids alone improve Bell palsy outcomes, but there is some controversy regarding the addition of antivirals. A 2007 paper published by Sullivan et al reported that patients receiving prednisolone alone had a 94.4% chance of recovery to House-Brackmann grade I or II function by 9 months post-paralysis, but that the addition of acyclovir actually decreased the chance of a similar recovery to 92.7%. On the other hand, results from a study published that same year by Hato et al found that adding valacyclovir to a course of prednisolone improved the recovery rate to 96.5%.

In addition to steroids and antivirals, corneal protection during recovery is a critical intervention for patients without complete eye closure. Depending upon the severity, this may be an ocular lubricant at night only or periocular surgery. Most patients are well served with artificial tear drops to use throughout the day and lubricant ointment to use at night, with or without eyelid taping (see **Video**. Taping the Eyelid). Upper eyelid stretching 2 to 3 times per day is also very helpful for alleviating the unopposed contraction of the levator palpebrae superioris muscle that further hinders eye closure in the absence of a strong orbicularis oculi muscle (see **Video**. Stretching the Upper Eyelid). For patients who continue to have ocular discomfort despite these conservative measures or who are at high risk for exposure keratopathy (corneal anesthesia, absent Bell phenomenon, slow or prolonged recovery, only seeing eye), placement of a scleral contact lens or minor surgical procedures may be required to protect the cornea until a spontaneous eye blink is restored.

**Periocular procedures**

Due to the expense and time required to manufacture a custom scleral contact lens, periocular procedures are more often employed for patients with long-term flaccid facial paralysis due to nerve trauma or resection; scleral contact lenses can be very useful in cases of acute Bell palsy to prevent or treat exposure keratopathy. Surgical options for improving eye closure include placement of a weight or a spring into the upper eyelid, tightening of the lower eyelid with medial or lateral canthopexy and tarsal strip, and tarsorrhaphy or tarsoconjunctival flap transfer (see **Image**. Interventions for Corneal Protection).

Of these options, the most common is upper eyelid loading, often performed with a gold or platinum weight. The weight can be placed onto the tarsal plate (pretarsal placement) via a supratarsal crease incision, as for blepharoplasty, or the weight can be located on the levator aponeurosis (postseptal placement), again via a supratarsal crease incision. The latter approach keeps the weight hidden behind the preaponeurotic fat so that its contour is not visible externally, but because the weight sits higher than the equator of the globe, it may paradoxically cause the eyelid to open when the patient is supine. A pretarsal placement, approximately 2 mm superior to the lash line, provides a greater mechanical advantage and, therefore, employs a smaller weight, but the thin skin in this location usually renders the outline of the weight visible. In either case, the implant is typically centered over the medial limbus, which is the point of maximum lagophthalmos in most cases of facial paralysis (see **Image**. Pretarsal Upper Eyelid Weight Placement).

The appropriate mass for the implant can be determined by trying a set of different adhesive weights on the patient's upper eyelid and identifying the one that provides the best eye closure while causing minimal blepharoptosis. For patients who are surgery-averse, the use of a skin color-matched adhesive weight is an alternative to surgical implantation, but the adhesive may be irritating to the thin skin of the upper eyelid, and weights often fall off and are lost due to their small size. For pretarsal placement, 1.2 g is a common size, while postseptal weights usually need to be slightly heavier. Heavier weights, particularly in a pretarsal location, can cause blepharoptosis even if complete eye closure is not achieved; patients should be informed of this lack of "Goldilocks" size preoperatively, ie, there is rarely an implant of just the right weight to produce complete eye closure without adverse effects.

Another common adverse event is astigmatism, which results from the mass pressing downward on the globe and distorting it. Fortunately, most astigmatism tends to correct itself spontaneously once the weight is removed. One way to minimize the astigmatism is to place an articulated chain rather than a solid weight, although doing so increases the risk of implant extrusion over time, and the thickness of a chain relative to that of a solid weight makes its contour more visible. Material is also an important consideration, as, despite its inert characteristics, gold can still cause tissue reactions in 3.2% to 9.5% of the population; platinum is less reactive (<1%) and slightly denser, therefore possessing a thinner profile and potentially being less apparent under the skin.

When lower eyelid laxity produces paralytic ectropion, loading the upper eyelid will not be sufficient to provide complete eye closure, and repositioning the lower eyelid will be required. This can be accomplished by tightening the eyelid at the medial canthus, the lateral canthus, or both, with the lateral tarsal strip procedure most commonly performed (see **Image**. Tarsal Strip-Lateral Canthopexy). Some degree of overcorrection is required with this technique, as the lower eyelid begins to loosen fairly quickly, and the overcorrected appearance will not last long. As a caveat, if the cornea protrudes substantially beyond the infraorbital rim, tightening the lower lid may cause a paradoxical retraction; therefore, this "negative vector" configuration must be identified preoperatively. When addressing paralytic lagophthalmos, some surgeons prefer to address the upper and lower eyelids simultaneously, and this can be accomplished by means of a tarsorrhaphy, either with a temporary suture or with a reversible surgical procedure that adheres the upper and lower eyelids together along the grey line (see **Image**. Interventions for Corneal Protection). In either case, the aesthetic implications of a tarsorrhaphy are significant, and many patients decline this option for that reason. A more cosmetically acceptable means of linking the upper and lower eyelids together, thereby decreasing the height of the palpebral fissure, is the tarsoconjunctival flap, which preserves the separation of the upper and lower lash lines and does not obstruct vision (see **Image**. Interventions for Corneal Protection).

**Facial nerve decompression**

Surgery on the facial nerve itself, such as grafting or transfer, is not commonly performed in cases of acute Bell palsy; decompression of the facial nerve may be offered to patients who meet the electrodiagnostic criteria enumerated above and who are both willing and able to undergo the operation. Decompression of the tympanic through the mastoid segments of the facial nerve may be accomplished via a postauricular mastoidectomy approach (see **Image**. Transmastoid Facial Nerve Decompression), although some surgeons do not consider this to be a thorough decompression because the neuritis in Bell palsy usually involves the labyrinthine segment, which may be best accessed via a middle fossa craniotomy. Accessing the labyrinthine segment of the facial nerve via a transmastoid approach may require removal of the incus and subsequent ossicular chain reconstruction in some cases, which can adversely impact postoperative hearing. Nevertheless, some authors do stand by the transmastoid technique because it spares the patient a craniotomy and intensive care unit admission; outcomes of this procedure are not consistently better than those after non-operative management, however.

More recently, some surgeons have begun to employ a transcanal endoscopic approach to facial nerve decompression; this minimally invasive procedure provides somewhat limited access to the facial nerve, although the geniculate ganglion can be exposed effectively. Large studies with consistent resulting data are lacking with this technique, however. To access the more proximal facial nerve, ie, the meatal foramen and canalicular portions, a middle fossa decompression approach is often employed or added to the transmastoid operation (see **Image**. Middle Fossa Craniotomy Approach to Facial Nerve Decompression). Regardless of the approach selected, the earlier intervention appears to result in better outcomes. Patients who meet criteria for facial nerve decompression but are not willing or able to undergo surgery may be offered alternative medical management, including ultra-high-dose oral corticosteroids (up to 200 mg of prednisone per day), intratympanic dexamethasone injections, and operative electrical stimulation to improve chances of satisfactory recovery.

**Chronic facial nerve dysfunction**

While every patient with true Bell palsy recovers facial motor function to some extent, many will develop synkinesis, particularly if presenting with severe or total hemifacial paralysis. The clinician is responsible for identifying these aberrant facial movements, as patients may not recognize the difference between the initial flaccid weakness and the hypertonicity that follows it, characterizing the chronic movement disorder as a continuation of the acute palsy rather than as a different, but related, clinical entity. Nevertheless, persistent facial asymmetry and mimetic dysfunction can have major adverse impacts on quality of life, causing patients to seek care. Physiotherapy and chemodenervation are sufficient for most individuals, although operative options do exist for patients who are dissatisfied with the results of conservative measures or who would prefer to avoid a prolonged course of regular botulinum toxin injections.

**Physiotherapy**

Facial rehabilitation therapy comprises a wide range of techniques, including neuromuscular reeducation, surface EMG biofeedback, mime therapy, video self-modeling, massage, stretching, and relaxation. Neuromuscular reeducation (NMR) consists of exercises to produce small but controlled movements on the affected side of the face while concentrating on symmetry and avoiding synkinetic muscle contraction. This can be performed with a mirror or EMG biofeedback that provides an audible tone when contraction is detected in the desired muscle, such as the zygomaticus major. Patients with more severe synkinesis may need to begin the course of therapy with relaxation, stretching, massage, and meditation before progressing to a point at which beginning NMR is even feasible. Exercises, such as NMR, require dozens of repetitions a few times a day to help build the neural pathways that will improve mimetic muscle coordination and symmetry of movement. These same techniques are also applied to patients who undergo nerve or muscle transfer for facial reanimation, as they need to learn to use the transferred nerve or muscle to produce the desired movement, typically biting down to smile.

**Chemodenervation**

The use of botulinum toxin injection to alleviate spasms and dyscoordinated or asymmetric movement due to facial palsy has been well-documented and found to be effective in both pediatric and adult populations. There are currently several commercially available botulinum toxin preparations, but the most commonly used one is onabotulinumtoxinA, which is also the best studied, although any can be used effectively. Several muscles typically become problematic with the development of synkinesis, and these are, therefore, most often the primary targets for chemodenervation. The orbicularis oculi is often injected to alleviate involuntary eye closure, particularly with mouth movement. Injections into this muscle are usually performed laterally, just deep to the skin, close to—but not medial to—the lateral orbital rim to prevent inadvertent weakening of the lateral rectus muscle and ensuing diplopia. A good starting dose is 2 aliquots of 5 units of onabotulinumtoxinA, or its equivalent in a different botulinum toxin preparation. When lower eyelid spasms persist despite lateral orbicularis oculi injections, small aliquots of 1 to 2 units may also be placed in the pretarsal portion of the inferior orbicularis oculi muscle (see **Image**. Injection of Botulinum Toxin for Facial Synkinesis). Care should be taken to avoid causing lower lid laxity that may result in lagophthalmos or blepharoptosis from medial injection of the upper eyelid that weakens the levator palpebrae superioris muscle. When injecting the orbicularis oculi muscle in addition to other facial muscles, it may be helpful to inject the orbicularis oculi first, while the needle is sharpest, because the thin skin in this region of the face is sensitive and prone to bruising. A fine, short needle on a small syringe is best for ensuring precise doses of toxin are administered to the desired targets; a 30- or 33-gauge needle is recommended on a 1 cc syringe. For onabotulinumtoxinA, diluting a 100-unit vial with 2 ccs of sterile, normal saline with preservatives provides 50 units in each 1 cc syringe, or 5 units per 0.1 cc, which makes keeping track of doses during injections comparatively straightforward. The preservatives in the saline improve comfort during injection, as they have a mild local anesthetic effect.

Other targets frequently injected include the platysma muscle, which, along with the depressor anguli oris muscle, can pull the oral commissure downwards when a patient is trying to smile, thus turning the expression into an unpleasant sneer. Twenty units, 4 injections of 5 units each, make a good starting point for treating the platysma. The mentalis, treated with 5 units, is also a common injection site because it tends to wrinkle with eye closure or brow elevation in patients with synkinesis (see **Image**. Botulinum Toxin Injection for Facial Synkinesis). Injecting the midface can be challenging, with some clinicians treating the zygomaticus major or upper lip elevators if they contract involuntarily or are hyperactive at rest and others electing to forego these injections because of the risk of causing an upper lip or oral commissure droop. Some clinicians prefer instead to treat the buccinator muscle to alleviate some midfacial tension as well as accidental cheek biting during mastication; this injection is typically performed via an intraoral approach. While not strictly for synkinesis, injection of the depressor labii inferioris muscle on the unaffected side, also with 5 units, may improve smiling symmetry by correcting the crooked appearance of the lower lip caused by unilateral depression. Other less common targets include the posterior belly of the digastric muscle, which can cause pain when hypertonic, and the lacrimal gland, which helps to alleviate Bogorad syndrome.

Before injection of onabotulinumtoxinA, patients should be counseled that effects will not be appreciable immediately as it may take 3 to 5 days for any improvement to occur and 1 to 2 weeks to reach maximum effect. The duration of the improvement is 3 to 4 months, and patients, therefore, typically schedule injection appointments at that interval to avoid significant recurrence of synkinesis between treatments. These intervals are, however, somewhat variable among individual patients and may be shorter or longer if a different botulinum toxin preparation is used. Over time, typically several years, repeat injections of large doses of botulinum toxin may lead to neutralizing antibody development that generally manifests as a shorter duration of effect after an injection. This can be addressed by increasing the doses up to a point or by switching to a different preparation of the toxin. Many patients are satisfied with the symptom improvement they achieve with chemodenervation with or without physiotherapy and do not proceed to surgical intervention. To maximize the effect of these nonsurgical interventions, however, it is imperative to start physiotherapy prior to botulinum toxin treatments so that patients have the opportunity to practice their facial exercises before the injections additionally impair muscle movement.

**Myomectomy**

Patients who have undergone botulinum toxin injections with good results but who desire a longer-term solution or who are losing the effectiveness of the injections due to antibody development may be candidates for myomectomy procedures, in which a segment of muscle is removed to reduce synkinetic contraction. Common targets include the platysma and the depressor anguli oris, in which diminished function will improve smile excursion, and the orbicularis oculi, whose myomectomy will reduce involuntary eye closure and squinting. A full-thickness horizontal strip of platysma muscle may be excised under local anesthesia through a 2 cm lateral transverse cervical incision, interrupting visible platysmal bands and the abnormal contraction that pulls down on the corner of the mouth. The platysma is a large muscle, however, and over the course of several months, it will often restore its continuity, leading to the return of some of its synkinetic activity. Resection of a portion of the depressor anguli oris muscle, also to permit greater movement of the oral commissure during smiling, is performed via an intraoral approach. This procedure involves a 3 cm vertical incision made along the lateral margin of the orbicularis oris muscle, with dissection proceeding through the buccinator, a portion of which is also excised, before reaching the depressor anguli oris, the majority of which is then resected as a strip perpendicular to the vector of contraction. Less commonly performed is resection of a strip of orbicularis oculi muscle from the lower eyelid, with or without its innervating branches of the facial nerve, via a skin-muscle flap lower blepharoplasty approach.

**Selective neurectomy**

Like removing portions of abnormally-contracting muscles, resection of segments of nerve branches that innervate these muscles can supplement or replace long-term botulinum toxin injections, or be performed as an adjunct to myomectomy. As with myomectomy, selective neurectomy is often performed to limit involuntary eye closure or improve the symmetry of the smile, but unlike myomectomy, an extraparotid facial nerve dissection is required, and thus general anesthesia is necessary (see **Image**. Selective Neurectomy for Facial Synkinesis). A 2-step highly selective neurectomy is a technique that identifies zygomatic branches of the facial nerve that innervate the orbicularis oculi muscle, employing a facial nerve exploration under general anesthesia. Loops of the identified branches are then externalized via percutaneous stab incisions for resection after the patient has emerged from anesthesia, thus permitting precise titration of the number of neurectomies required to balance reduction of involuntary eyelid contraction against creating lagophthalmos.

Patients report early symptomatic improvement with this technique, but nerve branches to the orbicularis oculi muscle tend to regenerate after a few months, thereby negating the effects of the surgery. In the lower face, however, longer-term results appear more achievable with modified selective neurectomy of the branches that control the lower facial depressor muscles, as described by Azzizadeh et al. When performing selective neurectomy, it is important to maintain excellent communication between the surgeon and the anesthesia provider, as identification of nerve branches requires not only that the patient remain still, but also that the patient remain still in the absence of paralytic drugs, the use of which would prevent electronic nerve stimulators from facilitating nerve branch identification via muscle contraction. Additionally, it may be prudent to inject the surgical field preoperatively with epinephrine only, rather than lidocaine and epinephrine, as local anesthetic medications occasionally diffuse deeply enough to block action potential conduction of the motor nerves in question and, therefore, prevent their identification with an electronic stimulator. Selective neurectomy may be combined with myomectomy to maximize relief of synkinesis and may also be combined with nerve or muscle transfer.

**Nerve transfer**

While historically employed for restoring function in cases of flaccid facial paralysis, typically either traumatic or iatrogenic, nerve transfer may also be used to improve coordination of a particular muscle or muscle group by "disconnecting" it from the synkinetic control of the facial nerve and reinnervating it with a different motor nerve, such as the hypoglossal or masseteric nerve (the latter being a branch of the mandibular division of the trigeminal nerve). For reanimation of the flaccid face, nerve transfer is ideally performed within the first 6 to 12 months after the onset of paralysis to ensure that viable muscle remains to reinnervate, as irreversible muscle atrophy and fibrosis occur with prolonged denervation. In the case of synkinesis, however, the muscles are not denervated but rather aberrantly reinnervated, and therefore, there is no time constraint for surgical intervention.

Nerve transfer for smile rehabilitation most often involves rerouting the nerve to the masseter into the facial nerve's buccal branch that controls the zygomaticus major muscle. This procedure may be performed independently or in combination with selective neurectomy or myomectomy. The procedure is performed via a modified Blair incision, as one might use for a parotidectomy or facelift, and as with selective neurectomy, long-acting paralytics and preoperative injection of lidocaine should be avoided (see **Image**. Masseteric Nerve Transfer). The masseteric nerve is reliably located at a point 3 cm anterior to the tragus, 1 cm inferior to the zygomatic arch, and 1.5 cm deep to the parotidomasseteric fascia. Once exposed, it is transected as distally (inferiorly) as possible, just proximal to its branch point, to provide as much length as possible to reflect the cut end of the proximal segment out of the masseter muscle to facilitate the neurorrhaphy; proximal circumferential dissection of the nerve up to the zygomatic arch will further improve its mobility.

The buccal branch that innervates the zygomaticus major muscle is consistently found at Zuker point, located halfway along a line between the root of the helix and the oral commissure. This buccal branch courses deep to the parotid fascia but is superficial and just superior to the masseteric nerve, in the same plane as the parotid duct and the transverse facial vessels, which are located inferior to it. The buccal branch is transected as proximally as possible without including branches to other muscles. The use of a nerve stimulator will verify the correct receiving buccal branch for the nerve transfer. Provided the masseteric nerve is mobilized adequately, it should reach the distal segment of the buccal branch without tension. Both nerves are roughly 2 mm in diameter. The neurorrhaphy is generally performed under an operating microscope, using 9-0 or 10-0 interrupted nylon sutures on a cutting or spatula-tip needle. Several weeks to months may pass before seeing any improvement in the patient's smile, and the patient may not notice anything until the surgeon points out the movement. Initially, contraction of the zygomaticus major muscle will require intentional biting to trigger an action potential in the masseteric nerve, but over time, most patients can smile without the need to clench the jaw if they comply with the postoperative physiotherapy regimen. Significant improvements in smile symmetry and oral commissure excursion (approximately 5 mm) are expected with a successful nerve transfer.

**Muscle transfer**

For patients in whom nerve transfer has failed or who desire greater smile excursion than is anticipated with nerve transfer, muscle transfer techniques, such as those used for smile reanimation in a flaccidly paralyzed face, may be employed. Of these, the best studied is the gracilis free muscle transfer, which takes a portion of the gracilis muscle from the medial thigh and transfers it into the face between the modiolus of the oral commissure and the temporalis fascia. This location and vector allow the gracilis to assume the function of the zygomaticus major muscle, thus permitting the patient to produce a close-lipped smile (see **Image**. Gracilis Free Flap for Facial Reanimation).

The adductor artery and vena comitans in the gracilis' vascular pedicle are typically anastomosed to the facial artery and vein, while the obturator nerve to the gracilis is usually coapted to the masseteric nerve, although a cross-face nerve graft may be used instead of the masseteric nerve or added via an end-to-side neurorrhaphy. The monitoring of flap perfusion may be achieved with an implantable Doppler sensor, duplex ultrasound the day after surgery, or a handheld Doppler probe. As with a masseteric nerve transfer, postoperative physiotherapy is critical, and the patient will initially have to bite down to smile, although this movement may not be required in the long term.

More recently, the use of dual-vector cervical strap muscle-free flaps has been described for smile restoration and, like the gracilis, has been applied to the reanimation of the flaccid face and smile rehabilitation in the context of synkinesis. The advantage of the sterno-omohyoid flap over the gracilis is that it introduces less bulk into the face, thereby minimizing postoperative volume asymmetry, and it also provides 2 contractile muscle bellies that can be used to produce a smile with the dental show, replacing both the zygomaticus major and the levator labii superioris muscles' functions (see **Image**. Sterno-Omohyoid Flap for Facial Reanimation). This flap also relies upon the facial vessels for blood supply, although the flap's vessels, the superior thyroid artery and vein, are less reliable than the gracilis' adductor vessels, making the strap muscle flap potentially more challenging. The ansa cervicalis provides the innervation for the strap flap, and because there are 2 ends to this loop of nerve, both the masseteric nerve and a cross-face nerve graft may be coapted simultaneously in an end-to-end fashion. As with nerve transfers, muscle transfer may be combined with myomectomy and selective neurectomy.

Differential Diagnosis

The differential diagnosis for acute hemifacial palsy is broad and includes infectious, neoplastic, vascular, traumatic, toxic, and metabolic etiologies. In most cases, however, a patient presenting with rapid-onset, hemifacial weakness without other neurological or dermatological signs or symptoms and without a history of trauma, chemical exposure, or severe metabolic derangement will be experiencing Bell palsy.

The most common condition that may be mistaken for Bell palsy is Ramsay Hunt syndrome, particularly when it presents as zoster sine herpete, ie, hemifacial palsy without a rash but still with significant pain. Lyme disease is another fairly common cause of acute facial paralysis, although it can usually be identified by the pathognomonic targetoid rash, a history of tick bite or travel to an endemic area, and potentially bilateral facial weakness. Other viral infections, such as Epstein-Barr virus, cytomegalovirus, and human immunodeficiency virus, may also present with unilateral facial paralysis but often also cause vague systemic symptoms, such as fevers, fatigue, and malaise. Tuberculosis and COVID may also cause facial paralysis, but typically with accompanying respiratory symptoms. Neoplasms, such as facial nerve schwannoma and parotid gland mucoepidermoid carcinoma, as well as autoimmune disorders, such as Sjögren syndrome, are more likely to cause an insidious onset of facial paralysis but may nevertheless present acutely.

Cerebrovascular accident is often considered high on the differential diagnosis when a patient presents with Bell palsy, leading to unnecessary imaging. A patient with acute onset hemifacial weakness in the absence of other neurological symptoms or vital sign instability is unlikely to be experiencing cerebral ischemia, particularly if the forehead is paralyzed. A brainstem stroke, unlike a cortical stroke, will cause hemifacial weakness that includes the forehead but will typically also cause other cranial neuropathies as well as vertigo, nausea, and vomiting. Recurrent episodes of hemifacial paralysis may represent Bell palsy, which recurs in 8% to 12% of affected patients. Still, patients with more than 2 episodes without other risk factors should be evaluated further with imaging and laboratory studies, as facial nerve schwannomas and autoimmune diseases, such as Melkersson-Rosenthal syndrome, may present this way.

Sometimes, risk factors may not be apparent, even with a detailed history and physical examination. For example, a patient may deny a history of head trauma but fail to mention self-contained underwater breathing apparatus (scuba) diving or air travel, either of which can result in otic barotrauma and subsequent facial paralysis. Similarly, a patient with a distant cancer may suffer facial paralysis as a result of brain metastasis or chemotherapy. Misadventures with botulinum toxin injections can cause facial paralysis as well, which some patients may be reluctant to disclose. Last, otologic disease should not be overlooked, whether in the context of acute otitis media or a chronic cholesteatoma.

Staging

The original House-Brackmann scale is simple and easy to use for surgeons, emergency medicine providers, and primary care clinicians, but it provides very little detail, particularly concerning the function of individual zones of the face or synkinetic movement. While it is a sound staging system for acute Bell palsy, there are a number of more detailed classification systems that are better suited to describing the chronic facial movement dysfunction that may follow Bell palsy or other forms of facial paralysis that may affect different zones of the face differently, such as facial nerve trauma, iatrogenic injury, congenital anomalies, poliomyelitis, and multiple sclerosis.

The first facial paralysis grading scheme published was that of Naoaki Yanagihara in 1976, requiring patients to perform 9 facial movements and a resting evaluation. The strength of each is graded as 4 points (normal or nearly normal), 2 points (weak), or 0 points (no movement). Thus, a score of 40 is normal, and a score of 0 corresponds to a House-Brackmann grade of VI. The 9 movements are eyebrow elevation, gentle eye closure, forceful eye closure, closure of the affected eye only, wrinkling the nose, puffing out the cheek, whistling, smiling, and depressing the lower lip. Scoring Bell palsy with this system requires a thorough facial nerve examination. This scale is still commonly used in Asia.

In 1996, Ross and her colleagues published the Sunnybrook Facial Grading System, named for the Sunnybrook Health Science Center in Toronto, Canada. This scale goes 1 step beyond that of Yanagihara, evaluating resting asymmetry, voluntary movement, and synkinetic movement separately for each facial zone, thus providing a very detailed assessment of a patient's facial function, but at the expense of the rapidity and convenience of the House-Brackmann scale. For resting asymmetry, the Sunnybrook system individually scores the palpebral fissure height, nasolabial fold depth, and oral commissure position, with a maximum of 15 points for asymmetry across all 3 zones. For voluntary movement, eyebrow elevation, gentle eye closure, open mouth smile, snarl, and lip pucker are evaluated, with 100 points indicating normal function. Synkinetic movement is evaluated with the same facial expressions, with 15 points for severe synkinesis in all zones. The resting asymmetry and synkinesis scores are subtracted from the voluntary movement score to determine the composite Sunnybrook score.

An update to the House-Brackmann Facial Nerve Grading System with the "Facial Nerve Grading System 2.0" was devised by Vrabec et al in 2009. This scale, like the Sunnybrook system, assesses the eyebrow, the eye, the nasolabial fold, and the oral commissure separately, assigning a score between 1 (normal symmetry) and 6 (no movement) for each region's function that takes into account both movement and resting symmetry. Up to 3 more points can be added to the total for disfiguring synkinesis, with 2 points indicating obvious synkinesis and 1 point signifying slight synkinesis. Because no synkinesis points can be scored when there is no movement, the maximum score is 24 points, which equates to a House-Brackmann grade VI on the original scale.

More recently, technology has been leveraged to improve the granularity and the convenience of grading facial functions. Massachusetts Eye & Ear Infirmary's eFACE application was released in 2015 and validated by a group of international facial nerve experts in 2017. This app-based approach to evaluating facial paralysis uses multiple Likert scales to assess resting symmetry, voluntary movement, and synkinetic movement. Then, it provides a set of scores that reproducibly quantify function in terms of static symmetry, dynamic symmetry, and synkinesis, as well as regional function for the periocular area, lower face and neck, midface and smile, and smile alone (see **Image**. The eFACE Software Application). Further development of the software grading concept resulted in the auto-eFACE, which analyzes a set of standardized photographs to evaluate the severity of facial dysfunction using the eFACE scale.

Numerous other facial nerve grading scales, such as the FAME, MoReSS, Sydney, and Toronto systems, have been developed and compared with the original House-Brackmann Facial Nerve Grading System, with many of them providing good interrater reliability and correlation with the House-Brackmann scale. However, the Sir Charles Bell Society recommends using the Sunnybrook scale because of its high reliability and ability to evaluate resting asymmetry, flaccid palsy, and synkinesis.

Prognosis

Bell palsy resolves completely without treatment in approximately 80% of cases, with the remaining patients developing synkinesis to some degree. Oral corticosteroids with or without antivirals increase the chance of recovery from 90% to 97%. Recurrence does occur in 8% to 12% of affected individuals, with a mean latency of 10 years between episodes. Cases of multiple recurrent Bell palsy may be due to narrow Fallopian canals that exacerbate vascular insufficiency caused by nerve inflammation and edema within the enclosed space of the canal.

Risk factors associated with the development of synkinesis include complete paralysis, age 60 years or older, and decreased salivation or taste on the ipsilateral side. While some patients are typically young and healthy with incomplete palsy and may exhibit complete recovery in as few as 2 weeks, most patients will take several months to a year to recover. The longer it takes for clinical recovery to begin and the slower the recovery once it does, the more likely synkinesis will occur. Similarly, patients who present with more severe paralysis are more likely to have worse outcomes. Escalante et al reported that House-Brackmann grade V paralysis evolves into synkinesis in 17% of patients and House-Brackmann grade VI paralysis does so in 40% of patients; conversely, no patients with a severity of House-Brackmann grade II developed synkinesis in their series. Other factors that adversely affect outcomes include diabetes, pregnancy, history of a recent dental procedure, progression to complete paralysis within 24 hours of onset, and loss of more than 90% of the compound muscle action potential amplitude on electroneuronography, ENoG. Debate remains regarding the impact of hypertension on recovery from Bell palsy, with some studies reporting worse outcomes and others no difference between hypertensive and non-hypertensive patients. Regardless of risk factors, the mean time to development of synkinesis is roughly 5 months for patients who fail to recover completely.

Complications

Despite its high spontaneous recovery rate, Bell palsy may cause synkinesis in approximately 15% of patients and corneal exposure keratopathy in about 40% of patients. Beyond physical sequelae, psychological distress and quality-of-life decrements are known to occur with facial paralysis, particularly for women, older patients, and in cases of long-standing paralysis. Fortunately, keratopathy and decreased quality of life tend to resolve as facial function recovers.

Postoperative and Rehabilitation Care

Physiotherapy remains a critical element of the treatment of severe Bell palsy, whether as an aspect of nonoperative management in conjunction with botulinum toxin injection or as part of the postoperative recovery regimen. Facial rehabilitation therapy, provided by physical therapists, occupational therapists, or speech-language pathologists, may involve stretching, massages, and exercises performed in the mirror to improve facial muscle coordination. In some cases, transcutaneous electrical stimulation is also employed. Postoperatively, therapy most often centers on helping the patient use a transferred nerve, with or without a transferred muscle, to produce a smile on the paralyzed side and to integrate it with the smile on the unaffected side to create a symmetric expression.

Consultations

Most cases of acute Bell palsy are managed successfully by emergency medicine or primary care professionals, who can prescribe the appropriate medications and educate patients regarding corneal protection. Patients who have House-Brackmann grade VI paralysis should be seen as soon as possible by a neurologist for electrodiagnostic testing and then referred to an otologist for consideration for facial nerve decompression, if appropriate. If an intratympanic steroid injection is planned, an otologist or otolaryngologist will be required. If conservative corneal protection interventions are inadequate, an ophthalmologist, plastic surgeon, or facial plastic surgeon may be needed to place an eyelid weight or perform another periocular procedure. In some cases, an adjustment disorder may develop, particularly in young women or patients with a history of depression; mental health evaluation may be appropriate for these patients.

For patients with chronic facial dysfunction after Bell palsy, facial rehabilitation can be performed by a physical therapist, occupational therapist, or speech-language pathologist. A plastic surgeon, neurologist, or facial plastic surgeon may offer botulinum toxin injections for synkinesis, or the injections may be performed by a trained injection nurse, nurse practitioner, or physician assistant in 1 of those specialties. Plastic or facial plastic surgeons typically perform surgical interventions, including myomectomy, neurectomy, nerve transfer, and muscle transfer

Deterrence and Patient Education

The most critical intervention for optimizing facial functional outcomes in Bell palsy is the prescription of oral corticosteroids, although patients should be strongly encouraged to take antiviral medications as well. That said, most patients will recover completely or nearly completely from Bell palsy with or without medical management, so the argument can be made that the most important intervention in cases of acute Bell palsy is the protection of the cornea with eyedrops, ointment, taping, and eyelid stretching exercises. Patients should be counseled strongly that inadequate eye care can result in long-term ocular sequelae despite the temporary nature of the Bell palsy itself. Beyond that, while there are no known effective strategies for preventing the occurrence or recurrence of Bell palsy, maintaining tight glucose control for diabetic patients may improve outcomes or even decrease the risk of developing the condition.

Enhancing Healthcare Team Outcomes

Due to its effects on emotional expression, oral competence, articulation, ocular health, and quality of life, Bell palsy can have myriad consequences for severely affected patients. Clinicians must be skilled in accurately diagnosing and managing Bell palsy, including recognizing early signs, applying corticosteroid and antiviral treatments, and managing chronic complications like synkinesis. Physicians, advanced practitioners, and nurses should be adept at monitoring patient progress and coordinating care with other specialties. Pharmacists play a crucial role in ensuring safe medication management and patient education. While an otolaryngologist or neurologist is typically tasked with managing the patient overall if the paralysis is severe or complicated, an interprofessional team of healthcare providers should be engaged to optimize outcomes for patients with Bell palsy.

Patients with House-Brackmann grade VI paralysis have the greatest need for an effective interprofessional team because they require prompt referral for electrodiagnostic testing and may require major surgery shortly after diagnosis. These patients are also at greatest risk for developing synkinesis and are, therefore, most likely to require facial rehabilitation therapy. Likewise, patients with House-Brackmann grade VI paralysis typically take the longest to recover and are most likely to require intervention to prevent corneal injury. Having a team assembled whose members effectively communicate and collaborate will expedite and streamline care for patients with Bell palsy, ensuring timely and appropriate intervention while minimizing complications.

Source

Hohman, M.H., Warner, M.J. and Varacallo, M.A. (2025) ‘Bell Palsy’, in *StatPearls*. StatPearls Publishing. Available at: https://www.ncbi.nlm.nih.gov/books/NBK482290/#article-18195.s1 (Accessed: 5 June 2025).

# [**Trigeminal neuralgia**](https://www.mayoclinic.org/diseases-conditions/trigeminal-neuralgia/symptoms-causes/syc-20353344)

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## **TRIGEMINAL NEURALGIA**

## **Overview**

Trigeminal neuralgia (try-JEM-ih-nul nu-RAL-juh) is a condition that causes intense pain similar to an electric shock on one side of the face. It affects the trigeminal nerve, which carries signals from the face to the brain. Even light touch from brushing your teeth or putting on makeup may trigger a jolt of pain. Trigeminal neuralgia can be long-lasting. It's known as a chronic pain condition.

People with trigeminal neuralgia may at first experience short, mild episodes of pain. But the condition can get worse, causing longer periods of pain that happen more often. It's more common in women and people older than 50.

But trigeminal neuralgia, also known as tic douloureux, doesn't mean living a life of pain. It usually can be managed with treatment.

## **Symptoms**

Trigeminal neuralgia symptoms may include one or more of these patterns:

* Episodes of intense shooting or jabbing pain that may feel like an electric shock.
* Sudden episodes of pain or pain triggered by touching the face, chewing, speaking or brushing your teeth.
* Episodes of pain lasting from a few seconds to several minutes.
* Pain that occurs with facial spasms.
* Episodes of pain lasting days, weeks, months or longer. Some people have periods when they experience no pain.
* Pain in areas supplied by the trigeminal nerve. These areas include the cheek, jaw, teeth, gums or lips. Less often, the eye and forehead may be affected.
* Pain on one side of the face at a time.
* Pain focused in one spot. Or the pain may be spread in a wider pattern.
* Pain that rarely occurs while sleeping.
* Episodes of pain that become more frequent and intense over time.

### When to see a doctor

See your healthcare professional if you experience pain in your face, particularly if it's long-lasting or comes back after going away. Also get medical attention if you have chronic pain that doesn't go away with pain medicine that you buy off the shelf.

## **Causes**

In trigeminal neuralgia, the trigeminal nerve's function is disrupted. Contact between a blood vessel and the trigeminal nerve at the base of the brain often causes the pain. The blood vessel may be an artery or a vein. This contact puts pressure on the nerve and doesn't allow it to function as usual.

But while compression by a blood vessel is a common cause, there are many other potential causes. Multiple sclerosis or a similar condition that damages the myelin sheath protecting certain nerves can cause trigeminal neuralgia. A tumor pressing against the trigeminal nerve also can cause the condition.

Some people may experience trigeminal neuralgia as a result of a stroke or facial trauma. An injury of the nerve due to surgery also can cause trigeminal neuralgia.

### Triggers

Several triggers may set off the pain of trigeminal neuralgia, including:

* Shaving.
* Touching your face.
* Eating.
* Drinking.
* Brushing your teeth.
* Talking.
* Putting on makeup.
* A light breeze blowing over your face.
* Smiling.
* Washing your face.

## **Risk factors**

Research has found that some factors put people at higher risk of trigeminal neuralgia, including:

* **Sex.** Women are more likely than men to experience trigeminal neuralgia.
* **Age.** Trigeminal neuralgia is more common among people 50 and older.
* **Certain conditions.** For example, hypertension is a risk factor for trigeminal neuralgia. In addition, people with multiple sclerosis are at higher risk of trigeminal neuralgia.

## **Diagnosis**

Your healthcare professional diagnoses trigeminal neuralgia mainly based on your description of the pain, including:

* **Type.** Pain related to trigeminal neuralgia is sudden, feels like an electric shock and is brief.
* **Location.** The parts of your face affected by pain can tell your healthcare professional if the trigeminal nerve is involved.
* **Triggers.** Eating, talking, light touch of your face or even a cool breeze can bring on pain.

Your healthcare professional may conduct tests to diagnose trigeminal neuralgia. Tests also can help find the causes of the condition. They may include:

* **A neurological exam.** Touching and examining parts of your face can help determine exactly where the pain is occurring. If you appear to have trigeminal neuralgia, the exam can help uncover which branches of the trigeminal nerve may be affected. Reflex tests can help determine if your symptoms are caused by a compressed nerve or another condition.
* **Magnetic resonance imaging (MRI).** You may need an MRI to look for possible causes of trigeminal neuralgia. An MRI may reveal signs of multiple sclerosis or a tumor. Sometimes a dye is injected into a blood vessel to view the arteries and veins to show blood flow.

Your facial pain may be caused by many different conditions, so an accurate diagnosis is important. Your healthcare professional also may order other tests to rule out other conditions.

## **Treatment**

Trigeminal neuralgia treatment usually starts with medications, and some people don't need any additional treatment. However, over time, some people with the condition may stop responding to medications, or they may experience unpleasant side effects. For those people, injections or surgery provide other trigeminal neuralgia treatment options.

If your condition is due to another cause, such as multiple sclerosis, you need treatment for the underlying condition.

### Medications

To treat trigeminal neuralgia, healthcare professionals prescribe medicines to lessen or block the pain signals sent to your brain.

* **Anti-seizure medicines.** Healthcare professionals often prescribe carbamazepine (Tegretol, Carbatrol, others) for trigeminal neuralgia. It has been shown to be effective in treating the condition.

Other anti-seizure medicines that may be used include oxcarbazepine (Trileptal, Oxtellar XR), lamotrigine (Lamictal), and phenytoin (Dilantin, Phenytek, Cerebyx). Other medicines that may be used include topiramate (Qudexy XR, Topamax, others), pregabalin (Lyrica) and gabapentin (Neurontin, Gralise, Horizant).

If the anti-seizure medicine you're using becomes less effective, your healthcare professional may increase the dose or switch to another type. Side effects of anti-seizure medicines may include dizziness, confusion, drowsiness and nausea. Also, carbamazepine can trigger a serious reaction in some people, mainly in those of Asian descent. Genetic testing may be recommended before you start carbamazepine.

* **Muscle relaxants.** Muscle-relaxing medicines such as baclofen (Gablofen, Fleqsuvy, others) may be used alone or in combination with carbamazepine. Side effects may include confusion, nausea and drowsiness.
* **Botox injections.** Small studies have shown that onabotulinumtoxinA (Botox) injections may reduce pain from trigeminal neuralgia in people who are no longer helped by medicines. However, more research needs to be done before this treatment is widely used for this condition.

### Surgery

Surgical options for trigeminal neuralgia include:

* **Microvascular decompression.** This procedure involves moving or removing blood vessels that touch the trigeminal nerve to stop the nerve from malfunctioning. A cut, known as an incision, is made behind the ear on the side where you feel the pain. Then, through a small hole in your skull, your surgeon moves any arteries that are in contact with the trigeminal nerve. The surgeon also places a soft cushion between the nerve and the arteries.

If a vein is compressing the nerve, your surgeon may remove it. Part of the trigeminal nerve may be cut if arteries aren't pressing on the nerve. This is known as a neurectomy.

Microvascular decompression can stop or reduce pain for many years. Long-term pain relief depends on the location of pain, type of pain and age of the person. People with a blood vessel that is seen to be compressing the nerve can remain pain free for years after the procedure. Only a small number of people may have pain come back in 3 to 5 years after surgery. Microvascular decompression has some risks, including decreased hearing, facial weakness, facial numbness, stroke or other complications. Most people who have this procedure have no facial numbness afterward.

* **Brain stereotactic radiosurgery, also known as Gamma Knife.** In this procedure, a surgeon aims a focused dose of radiation to the root of the trigeminal nerve. The radiation damages the trigeminal nerve to reduce or stop pain. Pain relief occurs gradually and may take up to a month.

Brain stereotactic radiosurgery is successful in stopping pain for most people. But like all procedures, there is a risk that pain may come back, often within 3 to 5 years. If pain returns, the procedure can be repeated or you may have another procedure. Facial numbness is a common side effect, and may occur months or years after the procedure.

Other procedures may be used to treat trigeminal neuralgia, such as a rhizotomy. In a rhizotomy, your surgeon destroys nerve fibers to reduce pain. This causes some facial numbness. Types of rhizotomy include:

* **Glycerol injection.** A needle that goes through the face and into an opening in the base of the skull delivers medicine to reduce pain. The needle is guided to a small sac of spinal fluid that surrounds the area where the trigeminal nerve divides into three branches. Then a small amount of sterile glycerol is injected. The glycerol damages the trigeminal nerve and blocks pain signals.

This procedure often relieves pain. However, pain returns in some people. Many people experience facial numbness or tingling after a glycerol injection.

* **Balloon compression.** This procedure involves inserting a hollow needle through the face. It's guided it to a part of the trigeminal nerve that goes through the base of the skull. Then a thin, flexible tube called a catheter with a balloon on the end is threaded through the needle. The balloon inflates with enough pressure to damage the trigeminal nerve and block pain signals.

Balloon compression successfully controls pain in most people, at least for a period of time. Most people undergoing this procedure experience at least some temporary facial numbness.

* **Radiofrequency thermal lesioning.** This procedure selectively destroys nerve fibers associated with pain. While you're sedated, your surgeon inserts a hollow needle through your face. The surgeon guides the needle to a part of the trigeminal nerve that goes through an opening at the base of your skull.

Once the needle is positioned, your surgeon briefly wakes you from sedation. Your surgeon inserts an electrode through the needle and sends a mild electrical current through the tip of the electrode. You're asked to say when and where you feel tingling.

When your surgeon locates the part of the nerve involved in your pain, you're returned to sedation. Then the electrode is heated until it damages the nerve fibers, creating an area of injury known as a lesion. If the lesion doesn't get rid of your pain, your doctor may create additional lesions.

Radiofrequency thermal lesioning usually results in some temporary facial numbness after the procedure. Pain may return after 3 to 4 years.

## **Alternative medicine**

Alternative treatments for trigeminal neuralgia haven't been as well studied as medicines or surgical procedures. There's often little evidence to support their use.

However, some people have found improvement with treatments such as acupuncture, biofeedback, chiropractic, and vitamin or nutritional therapy. Be sure to check with your doctor before trying an alternative treatment because it may interact with your other treatments.

## **Coping and support**

Living with trigeminal neuralgia can be difficult. The disorder may affect your interaction with friends and family, your productivity at work, and the overall quality of your life.

You may find encouragement and understanding in a support group. Group members often know about the latest treatments and tend to share their own experiences. If you're interested, your doctor may be able to recommend a group in your area.

## **Preparing for your appointment**

Make an appointment with your healthcare professional if you have symptoms of trigeminal neuralgia. After your initial visit, you may see a doctor trained in brain and nervous system conditions, known as a neurologist.

### What you can do to prepare

* **Write down any symptoms you've been having,** and for how long.
* **Note any triggers** that bring on facial pain.
* **Make a list of your key medical information,** including any other conditions for which you're being treated. Also include the names of any medicines, vitamins or supplements you're taking.
* **Take a family member or friend along,** if possible. Someone who comes with you may remember something that you missed or forgot.
* **Write down your questions in advance.** It can help you make the most of your time with your healthcare professional.

For possible trigeminal neuralgia, some basic questions to ask include:

* What's the most likely cause of my pain?
* Do I need any diagnostic tests?
* What treatment approach do you recommend?
* If you're recommending medicines, what are the possible side effects?
* Will I need treatment for the rest of my life?
* How much do you expect my symptoms will improve with treatment?
* Is surgery an option?

In addition to the questions that you've prepared, don't hesitate to ask any others that come up during your visit. Also ask questions if you don't understand something.

### What to expect from your doctor

You're likely to be asked a number of questions. Being ready to answer them may give you more time to go over points you want to discuss further. Your healthcare professional may ask:

* What are your symptoms and where are they located?
* When did you first develop these symptoms?
* Have your symptoms gotten worse over time?
* How often do you experience periods of facial pain? Have you noticed if anything seems to trigger your facial pain?
* How long does facial pain typically last?
* How much are these symptoms affecting your quality of life?
* Have you ever had dental surgery or surgery on or near your face, such as sinus surgery?
* Have you had any facial trauma, such as an injury or accident that affected your face?
* Have you tried any treatments for your facial pain so far? Has anything helped?
* What side effects have you experienced from treatment?

Sources

Mayo Clinic Staff (2023) *Trigeminal neuralgia - Diagnosis and treatment*. Available at: https://www.mayoclinic.org/diseases-conditions/trigeminal-neuralgia/diagnosis-treatment/drc-20353347 (Accessed: 5 June 2025).

# **Brachial Plexus Injury**

## **What is a brachial plexus injury?**

The brachial plexus is a network of nerves that carries signals from the upper parts of the spinal cord to your shoulder, arm, and hand. These nerves involve movement and sensation and allow you to raise your arm and move your hand and wrists. Brachial plexus injuries (also known as Erb's palsy and Dejerine-Klumpke palsy) are caused by damage to those nerves, typically from trauma, tumors, inflammation, pressure, athletic injuries, or being stretched too far. Some brachial plexus injuries can happen to babies during birth.

Erb's palsy refers to numbness and paralysis of the upper brachial plexus. Dejerine-Klumpe palsy (also known as Klumpke's palsy) refers to loss of sensation in the wrist and hand and paralysis of the lower brachial plexus. A rare syndrome called Parsonage-Turner Syndrome, or brachial plexitis, causes inflammation of the brachial plexus without any obvious shoulder injury.

Symptoms of a brachial plexus injury may include:

* A limp or paralyzed arm
* Lack of muscle control in the arm, hand, or wrist
* A lack of feeling or sensation in the arm or hand
* Sudden pain in the shoulder or arm that may be stinging or burning

Although injuries can occur at any time, many brachial plexus injuries happen when a baby's shoulders become impacted during delivery and the brachial plexus nerves stretch or tear.

Types of brachial plexus injuries are:

* Neuropraxia or stretch, the mildest form in which the nerve has been damaged but not torn and causes some problems with nerve signaling
* Neuroma, in which the nerve has torn and healed but scar tissue puts pressure on the injured nerve and prevents it from conducting signals to the muscles
* Rupture, in which the nerve is torn but not at the spinal attachment
* Avulsion, the most severe type, in which the nerve is cut or torn from the spinal cord. There is also an incomplete form of avulsion in which part of the nerve is damaged and which leaves some opportunity for the nerve to slowly recover function

The severity of a brachial plexus injury depends on the nerves affected and the extent of the injury. Some injuries may be temporary, while others are chronic. Some brachial plexus injuries may heal without treatment. Some children who are injured during birth improve or recover on their own by 3 to 4 months of age. Most children recover some function through physical and occupational therapy.

In some cases (such as avulsion and rupture injuries), surgery is needed. Medications can help with pain management and assistive devices, such as splints or braces, may be needed by some individuals.

How can I or my loved one help improve care for people with a brachial plexus injury?

Consider participating in a clinical trial so clinicians and scientists can learn more about brachial plexus injury. Clinical research uses human volunteers to help researchers learn more about a disorder and perhaps find better ways to safely detect, treat, or prevent disease.

All types of volunteers are needed—those who are healthy or may have an illness or disease—of all different ages, sexes, races, and ethnicities to ensure that study results apply to as many people as possible, and that treatments will be safe and effective for everyone who will use them.

## **Summary**

The brachial plexus is a network of nerves that sends signals from the spine to the shoulder, arm, and hand. Damage to the brachial plexus can cause symptoms such as:

* A limp or paralyzed arm
* Lack of muscle control in the arm, hand, or wrist
* Lack of feeling or sensation in the arm or hand

Brachial plexus injuries can happen because of shoulder trauma, tumors, or inflammation. Sometimes they happen during childbirth when a baby's shoulders become stuck during delivery and the nerves stretch or tear.

Some brachial plexus injuries may heal without treatment. Many children who are injured during birth improve or recover by 3 to 4 months of age. Treatment includes physical therapy and, in some cases, surgery.

# **Brachial plexopathy**

Brachial plexopathy is a form of peripheral neuropathy. It occurs when there is damage to the brachial plexus. This is a group of nerves that run from the lower neck through the upper shoulder area. These nerves provide the shoulder, arm, and hand with movement and sensation through the radial, median, and ulnar nerves.

Damage to the nerves of the brachial plexus results in pain, decreased movement, or decreased feeling in the arm and shoulder.

## **Causes**

Damage to the brachial plexus may occur due to:

* Direct injury to the nerve
* Stretching injuries (including birth trauma)
* Pressure from tumors in the area (especially from lung tumors)
* Damage from radiation therapy

Brachial plexus dysfunction may also be associated with:

* Birth defects that put pressure on the neck area
* Exposure to toxins, chemicals, or medicines and illegal drugs
* General anesthesia, used during surgery
* Inflammatory conditions, such as those due to a virus or immune system problem
* Hereditary causes, such as hereditary neuralgic amyotrophy

In some cases, no cause can be identified.

## **Symptoms**

Symptoms may include:

* Numbness of the shoulder, arm, or hand
* Shoulder pain
* Tingling, burning, pain, or abnormal sensations (location depends on the area injured)
* Weakness of the shoulder, arm, hand, or wrist

## **Exams and Tests**

An exam of the arm, hand and wrist can reveal a problem with the nerves of the brachial plexus. Signs may include:

* Deformity of the arm or hand
* Difficulty moving the shoulder, arm, hand, or fingers
* Diminished arm reflexes
* Wasting of the muscles
* Weakness of hand flexing

A detailed history may help determine the cause of the brachial plexopathy. Age and sex are important, because some brachial plexus problems are more common in certain groups. For example, young men more often have inflammatory or post-viral brachial plexus disease called Parsonage-Turner syndrome.

Tests that may be done to diagnose this condition include:

* Blood tests
* Chest x-ray
* Electromyography (EMG) to check the muscles and nerves that control the muscles
* MRI of the head, neck, and shoulder
* Nerve conduction to check how fast electrical signals move through a nerve
* Nerve biopsy to examine a piece of nerve under the microscope (rarely needed)
* Ultrasound
* Genetic tests to look for hereditary causes of neuropathy

## **Treatment**

Treatment is aimed at correcting the underlying cause and allowing you to use your hand and arm as much as possible. In some cases, no treatment is needed and the problem gets better on its own.

Treatment options include any of the following:

* Medicines to control pain
* Physical therapy to help maintain muscle strength
* Braces, splints, or other devices to help you use your arm
* Nerve block, in which medicine is injected into the area near the nerves to reduce pain
* Surgery to repair the nerves or remove something pressing on the nerves

You may need occupational therapy or counseling to suggest changes in the workplace.

Medical conditions such as diabetes and kidney disease can damage nerves. In these cases, treatment is also directed at the underlying medical condition.

## **Outlook (Prognosis)**

A good recovery is possible if the cause is found and properly treated. In some cases, there is partial or complete loss of movement or sensation. Nerve pain may be severe and may last for a long time.

## **Possible Complications**

Complications may include:

* Deformity of the hand or arm, mild to severe, which can lead to contractures
* Partial or complete arm paralysis
* Partial or complete loss of sensation in the arm, hand, or fingers
* Recurrent or unnoticed injury to the hand or arm due to diminished sensation

## **When to Contact a Medical Professional**

Contact your health care provider if you experience pain, numbness, tingling, or weakness in the shoulder, arm, or hand.

## **Alternative Names**

Neuropathy - brachial plexus; Brachial plexus dysfunction; Parsonage-Turner syndrome; Pancoast syndrome

Source

* National Institutes of Health (2024) *Brachial Plexus Injuries*. Available at: https://medlineplus.gov/brachialplexusinjuries.html (Accessed: 5 June 2025).
* A.D.A.M., Inc. (2025) *Brachial plexopathy*. Available at: https://medlineplus.gov/ency/article/001418.htm (Accessed: 5 June 2025).
* National Institute of Neurological Disorders and Stroke (2024) *Brachial Plexus Injury*. Available at: https://www.ninds.nih.gov/health-information/disorders/brachial-plexus-injury (Accessed: 5 June 2025).

## **Headache & Pain Disorders: Comprehensive Definition and Description**

Headache and pain disorders encompass a wide range of conditions characterized by pain in the head or face, often with distinct patterns, triggers, and associated symptoms. These disorders can be primary—occurring independently, such as migraines, cluster headaches, tension-type headaches, and trigeminal autonomic cephalalgias (TACs)—or secondary, resulting from another medical condition.

## **General Definition of Headache**

A headache is pain occurring in any region of the head, which may be unilateral or bilateral, localized or diffuse, and can vary in intensity and duration. The pain can be sharp, throbbing, or dull and may appear suddenly or develop gradually. Headaches are among the most common nervous system disorders, affecting about 49% of adults globally each year.

## **What can cause headaches?**

According to the International Headache Society, there are primary and secondary headaches. Both types of pain have different reasons for appearing.

**1. Primary Headaches**

Primary headaches are an illness that stands alone from other diseases and are caused by overactivity or problems with pain-sensitive structures in the head, such as the blood vessels, muscles, and nerves of the head and neck. It also can be a result of the changes in brain chemical activity.

The list of most typical primary headaches includes tension headaches, cluster headaches, and migraines. Some types of headaches can combine qualities of the primary and secondary. It can happen because they may be an isolated ailment or be a result of another illness. They can involve:

1. A headache that appears because of the direct physical stimuli (temperature or external pressure);
2. Pain that spread over the scalp (epicranial);
3. Physical strain
4. Also, there can be other miscellaneous headaches.

**2. Secondary Headaches**

It is headaches, which are symptoms of another condition that influences the pain-sensitive nerves of the head. There are a great number of reasons that can cause secondary headaches, beginning with the severity of an alcohol-induced hangover and ending with a brain tumor.

Besides the two examples listed above, secondary headaches can be caused by

* Blood clots
* Brain freeze (ice cream headaches)
* Carbon monoxide poisoning
* Concussion
* Dehydration
* Glaucoma
* Influenza
* Overuse of pain medication
* Panic attacks
* Stroke.

## **Types of Headache & Pain Disorders**

## **Migraine (With and Without Aura)**

**Definition & Description:** Migraine is a neurological disorder marked by recurrent, often severe headaches, typically accompanied by nausea, vomiting, and sensitivity to light and sound.

Migraines are divided into:

* **Migraine with aura:** Involves sensory disturbances (visual, auditory, or speech changes) that precede or accompany the headache. Auras can include flashing lights, zigzag lines, or tingling sensations and affect about 25% of migraine sufferers.

**Migraine aura with a headache:** With this type, you have aura symptoms shortly before or at the same time as a migraine headache. You might hear it called "classic migraine," although most people with migraine don't get auras.

**Migraine with a brainstem aura:** This is when the aura starts in the base of your brain (brainstem) or on both sides of your brain. This type includes neurological symptoms like slurred speech, dizziness, ringing in the ears, and double vision.

**Hemiplegic migraine:** With this rare type, the aura causes weakness on one side of your body (hemiplegia).

**Retinal migraine:** You have vision changes in one eye before the headache begins.

* **Migraine without aura:** The most common type, characterized by a throbbing headache usually on one side of the head, without preceding sensory warnings. Attacks last from 4 hours to 3 days and are often aggravated by physical activity.

‘Aura’ is a warning sign of a migraine. It is most commonly a symptom that affects your sight, such as blind spots or seeing flashing lights. If you have migraine without aura, you won’t get a warning sign that a migraine attack is about to start.

Attacks of migraine without aura usually last between four hours and three days if they are not treated or if the treatment is not effective. The frequency of these attacks varies. They could happen every few years or several times a week.

Migraine without aura used to be called ‘common migraine’ or ‘hemicrania simplex.’

# **Causes & Risk Factors:**

* **Genetics (30–60% heritability)**

**Genes linked to migraine**

Researchers have identified several genes related to migraine susceptibility. For example, variations in the TRPM8 gene, which is involved in cold sensation, to migraine risk.

A 2023 study showed that the CACNA1A gene, affecting calcium channels in the brain, is linked to familial hemiplegic migraine, a [rare and severe form](https://www.ncbi.nlm.nih.gov/books/NBK513302/) of migraine.

Other genes linked to this type of migraine and other familial types of migraine [include](https://www.ncbi.nlm.nih.gov/books/NBK560787/):

* ATP1A2
* SCN1A
* PRRT2
* SLC4A4
* **Hormonal changes (especially in women)**  
  A [2020 study](https://onlinelibrary.wiley.com/doi/10.1111/ene.15778), which grouped participants into female and male categories, found that female participants are more than twice as likely to experience migraine as males and prone to having more severe migraine symptoms. Some research suggests the risk may be [three to four times greater](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9176156/) in females.

Hormonal fluctuations, particularly related to [estrogen](https://www.healthline.com/health/womens-health/estrogen-vs-progesterone), are a major contributing factor. These changes [can occur](https://www.ninds.nih.gov/health-information/disorders/migraine) during menstruation, pregnancy, or menopause or as a side effect of oral contraceptive use. [Hormonal changes](https://www.healthline.com/health/hormonal-headaches) can trigger or worsen migraine by altering certain neurotransmitters and brain chemicals, affecting your body’s response to pain.

* **AGE:**

While a migraine can start at any age, it’s [most common](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8904749/) in late teens and early adulthood and typically becomes less frequent as people get older. However, for some people, migraine may persist into [older age](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10676778/) due to changes in hormone levels and brain chemistry, which can cause the symptoms to develop or worsen. [Research](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10676778/) indicates that some aging processes, specifically social aging and [related stress](https://www.healthline.com/health/migraine-from-stress), may influence migraine experiences in older adults. Social aging is based on society’s expectations, such as managing older parents’ emotional challenges or supporting younger colleagues as they adapt to the work environment. Aging is also associated with an increased likelihood of having other health conditions that may worsen migraine attacks.

* **Environmental triggers (stress, certain foods, sleep changes, etc.)**

### **Depression**

Changes in brain chemicals and neurotransmitter levels due to depression can increase sensitivity to pain and trigger migraine attacks. A [2020 study review](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7357317/) found a strong link between migraine and [major depressive disorder](https://www.healthline.com/health/migraine/link-between-chronic-migraine-and-depression) due to shared genetic factors and chemical pathways.

### **Sleep disorders**

[Sleep disorders](https://www.healthline.com/health/sleep/disorders) like insomnia [may increase the risk](https://thejournalofheadacheandpain.biomedcentral.com/articles/10.1186/s10194-020-01192-5) of migraine by causing sleep cycle disruptions, triggering abnormal brain activity, and altering the regulation of neurotransmitters and chemicals linked to migraine onset.

### **Hypertension**

[Research](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10840219/) suggests a strong link between hypertension (high blood pressure) and migraine. The two conditions share similar pathways of development and may actually influence each other. [Hypertension](https://www.healthline.com/health/high-blood-pressure-hypertension) may also increase the frequency of migraine headaches, causing people with episodic migraine to develop [chronic migraine](https://www.healthline.com/health/migraine-vs-chronic-migraine).

### **Head trauma**

While headaches are common after a [head injury](https://www.healthline.com/health/head-injury), people with traumatic brain injuries (TBIs) may also be more likely to develop migraines. A [2023 study](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9959615/) found that people with a TBI were 48.4% more likely to develop migraine. The risk of migraine was 67% higher after major head trauma.

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### **Epilepsy**

People with [epilepsy](https://www.healthline.com/health/epilepsy) may experience migraine due to the neurological disturbances caused by abnormal electrical activity in the brain. A 2023 study found an [80% increased lifetime risk](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10796653/) of migraine in people with epilepsy compared to people without, consistent with results from earlier studies.

**Smoking**

[Nicotine](https://www.healthline.com/health/nicotine-and-related-disorders) can constrict blood vessels, leading to decreased blood flow to the brain and triggering migraine episodes.

A [2023 review](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10006570/) found that people who currently smoke have a higher chance of experiencing severe headaches or migraine than those who do not smoke. The chances of headaches increase with the quantity of cigarettes smoked and a longer smoking history.

* **Family history increases risk.**

# **Triggers that make migraine worse**

Several factors [can worsen](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10632231/) migraine for people who are prone to migraine, making episodes more frequent or severe. These include:

* [emotional stress](https://www.healthline.com/health/emotional-symptoms-of-stress)
* lack of sleep or irregular sleep patterns
* hormonal changes, especially in people assigned female at birth
* [certain foods](https://www.healthline.com/nutrition/migraine-diet)
* environmental factors, including bright lights, loud noises, and strong smells
* changes in weather or [barometric pressure](https://www.healthline.com/health/headache/barometric-pressure-headache)
* [intense physical activity](https://www.healthline.com/health/migraine/exercise-induced-migraines)
* [overuse of acute pain medications](https://www.healthline.com/health/migraine/rebound-migraine)

# **Signs & Symptoms:**

* Severe, pulsating headache
* A headache that is usually on one side of your head. This is often a throbbing pain. It will worsen when you move, such as if you walk or climb the stairs. It is so severe that it means you can’t do your normal daily activities.
* Feeling sick (nausea) or being sick (vomiting).
* Being sensitive to light (photophobia), sound (phonophobia), and/or smells.
* Nausea/vomiting
* Sensitivity to light, sound, and smells
* Visual or sensory aura (in some cases)
* Prodrome and postdrome phases with mood, appetite, or cognitive changes.

# **Diagnosis:**

* Clinical history and symptom assessment
* Neurological examination
* Imaging (MRI/CT) to rule out secondary causes if atypical features are present.

# **Treatment:**

* Acute: NSAIDs, triptans, antiemetics
* Preventive: Beta-blockers, anticonvulsants, CGRP inhibitors
* Lifestyle modifications, trigger avoidance, behavioral therapy

# **Prevention:**

While one may not be able to change certain migraine risk factors, such as genetics, there are steps one can take to [prevent](https://www.ncbi.nlm.nih.gov/books/NBK328460/) migraines, and they include:

* Regular sleep, stress management, avoiding known triggers
* Manage stress through [relaxation techniques](https://www.healthline.com/health/10-ways-to-relieve-stress) like yoga and meditation.
* Track migraine triggers by keeping a [headache diary](https://www.healthline.com/health/headache/headache-diary) to identify and avoid specific triggers.
* Maintain a regular sleep schedule with consistent patterns and adequate rest.
* Monitor your diet by avoiding known food triggers.
* Exercise regularly with moderate physical activity to reduce stress.
* Consider taking dietary supplements such as [magnesium](https://www.healthline.com/health/magnesium-for-migraines).
* Avoid exposure to bright lights, loud noises, and strong smells.
* Consider [preventive medications](https://www.healthline.com/health/migraine-prevention-medications) by talking with a healthcare professional about options that may help.

# **Prognosis:**

* Chronic in some, but often manageable with treatment

**Complications:**

* Medication overuse headache, chronic migraine, depression[1](https://www.nyneurologists.com/blog/headaches-definition-and-causes)

**When to See a Doctor/Red Flags:**

* Sudden, severe headache
* Neurological deficits
* Headache with fever, neck stiffness, or altered consciousness.

**Differential Diagnosis:**

* Tension-type headache, cluster headache, sinus headache, secondary causes.

**Epidemiology:**

* Affects 12–15% of the population, more common in women.

## **Cluster Headaches**

**Definition & Description:**Cluster headaches are extremely painful, unilateral headaches, typically centered around one eye. They occur in cyclical patterns (clusters) lasting weeks to months, followed by remission periods.

## **Causes & Risk Factors:**

* Unknown, but hypothalamic involvement suspected
* Male predominance
* **Sex.** Men are more likely to have cluster headaches than women are.
* **Age.** Most people who develop cluster headaches are between the ages of 20 and 50. But the condition can start at any age.
* **Smoking.** Many people who get cluster headaches are smokers. But quitting smoking usually doesn't stop the headaches.
* **Alcohol use.** If you have cluster headaches, drinking alcohol during a cluster period may increase the risk of an attack.
* **Family history.** Having a parent, brother, or sister who has cluster headaches might increase the risk.

## 

## **Signs & Symptoms:**

* Excruciating, stabbing pain around one eye
* Red,
* watery eye
* nasal congestion
* Sweating
* eyelid droop on affected side
* Restlessness/agitation during attacks

### **Cluster periods**

A cluster period usually lasts for several weeks to months. Each cluster period may start at about the same time of year and last about the same length of time. For example, cluster periods can come during certain seasons, such as every spring or every fall.

For most people with cluster headaches, the cluster period lasts from one week to a year. Then there's a pain-free period, known as remission, for three months or longer before the next cluster headache comes. This is known as episodic cluster headache.

Cluster periods might go on for more than a year. Pain-free periods might last less than one month. If a cluster period lasts a year without letup, it's called chronic cluster headache.

**During a cluster period:**

* Headaches usually come every day, often several times a day.
* A single attack can last from 15 minutes to three hours, but more often lasts 30 to 45 minutes.
* The attacks often occur at the same time each day.
* Most attacks occur at night, usually 1 to 2 hours after bedtime.

The pain usually ends as suddenly as it begins. After attacks, most people are pain-free but exhausted.

## **Diagnosis:**

* Clinical criteria based on attack pattern and associated symptoms
* Imaging to exclude secondary causes

## **Treatment:**

* Acute: High-flow oxygen, triptans
* Preventive: Verapamil, corticosteroids, lithium

## 

## **Prevention:**

* Avoiding alcohol during cluster periods

## **Prognosis:**

* Chronic or episodic; can be disabling but not life-threatening

## **Complications:**

## Suicide risk due to severity of pain

## **When to See a Doctor/Red Flags:**

* Sudden, severe headache, new neurological symptoms

See a health care provider if you've just started to have cluster headaches. Your provider can rule out other illnesses and suggest treatment.

Even bad headache pain isn't usually the result of another disease. But headaches can sometimes mean a serious medical condition. This can include a brain tumor or tear of a weakened blood vessel, known as a dissection. Also, if you have a history of headaches, see your health care provider if there's a change in how they feel or how often they occur.

## **Differential Diagnosis:**

* Migraine
* trigeminal neuralgia
* sinusitis.

## **Epidemiology:**

* Rare (<1% of population), more common in men.

### 

### **Seek emergency care**

If you have any of these symptoms:

* A severe headache that comes on all of a sudden, often like a clap of thunder.
* A headache with a fever, nausea or vomiting, a stiff neck, confusion, seizures, numbness, or trouble speaking. These might point to a stroke, meningitis, encephalitis, a brain tumor, or other problems.
* A headache after a head injury, especially if it gets worse — even if the injury was a minor fall or bump.
* A sudden, severe headache unlike any other.
* A headache that worsens over days and changes in pattern.

## **Tension-Type Headaches**

**Definition & Description:**The most common primary headache, characterized by mild to moderate, diffuse pain described as a tight band around the head.

## **Causes & Risk Factors:**

* Stress, anxiety, poor posture, muscle tension
* Fatigue, dehydration

## **Signs & Symptoms:**

* Dull, aching pain
* Tightness or pressure across forehead or back of head
* Tenderness in scalp, neck, shoulders

## **Diagnosis:**

* Clinical history and exclusion of other causes

## **Treatment:**

* NSAIDs, acetaminophen

## Stress management, physical therapy

## **Prevention:**

* Regular exercise, stress reduction, ergonomic adjustments

## **Prognosis:**

* Generally good, but chronic forms can impact quality of life

## **Complications:**

* Chronic daily headache, medication overuse

## **When to See a Doctor/Red Flags:**

* New or worsening headaches, neurological symptoms

## **Differential Diagnosis:**

* Migraine, secondary headaches.

## **Epidemiology:**

* Most common headache type, affects up to 80% of adults at some point.

## **Trigeminal Autonomic Cephalalgias (TACs)**

**Definition & Description:** A group of primary headaches characterized by unilateral pain and prominent cranial autonomic symptoms (tearing, nasal congestion, etc.). Includes cluster headache, paroxysmal hemicrania, SUNCT/SUNA, and hemicrania continua.

## **Causes & Risk Factors:**

* Unknown, but involve trigeminal and autonomic nervous systems

## **Signs & Symptoms:**

* Severe, lateralized headache
* Ipsilateral autonomic features: conjunctival injection, lacrimation, rhinorrhea

## **Diagnosis:**

* Clinical criteria (ICHD-IIIb), attack duration and frequency help distinguish subtypes
* Imaging to rule out secondary causes

## **Treatment:**

* Varies by subtype: indomethacin (paroxysmal hemicrania, hemicrania continua), oxygen/triptans (cluster headache)

## **Prevention:**

* Subtype-specific preventive medications

## **Prognosis:**

* Varies; some forms highly responsive to specific treatments

## **Complications:**

* Chronic pain, impact on daily life

## **When to See a Doctor/Red Flags:**

* Sudden severe headache, new neurological findings

## **Differential Diagnosis:**

* Migraine, trigeminal neuralgia, sinusitis.

## **Epidemiology:**

* Rare compared to other headache types

## **Chronic Pain Syndromes**

**Definition & Description:**Chronic pain syndromes refer to persistent pain conditions, including chronic daily headache, chronic migraine, and others, often lasting more than three months.

## **Causes & Risk Factors:**

* Repeated headache attacks, medication overuse, psychological factors, underlying medical conditions

## **Signs & Symptoms:**

* Persistent or frequently recurring pain
* Associated symptoms depend on underlying headache type

## **Diagnosis:**

* Clinical history, exclusion of secondary causes, sometimes imaging or lab work

## **Treatment:**

* Multimodal: medications, behavioral therapy, physical therapy, sometimes procedures

## **Prevention:**

* Avoid medication overuse, manage triggers, address comorbidities

## **Prognosis:**

* Variable; can be disabling if not managed

## **Complications:**

* Depression, anxiety, reduced quality of life

## **When to See a Doctor/Red Flags:**

* Persistent or worsening pain, new symptoms

## **Differential Diagnosis:**

* Fibromyalgia, neuropathic pain, secondary headaches

## **Epidemiology:**

* Chronic headache affects about 3–5% of the population

## **Recent Guidelines and Updates**

* The International Classification of Headache Disorders (ICHD-III) provides updated diagnostic criteria for all primary and secondary headaches.
* Major health organizations (WHO, CDC, Mayo Clinic) emphasize early diagnosis, appropriate use of medications, and the importance of preventive strategies.

## **Summary Table: Key Features of Major Headache Types**

| **Disorder** | **Pain Location & Quality** | **Key Features** | **Prevalence** | **Treatment Highlights** |
| --- | --- | --- | --- | --- |
| Migraine (with/without aura) | Unilateral, throbbing | Nausea, photophobia, aura | 12–15% | Triptans, NSAIDs, preventives |
| Cluster Headache | Unilateral, orbital | Severe, autonomic symptoms | <1% | Oxygen, triptans, verapamil |
| Tension-Type Headache | Bilateral, band-like | Mild-moderate, muscle tenderness | Up to 80% | NSAIDs, stress management |
| TACs (incl. CH, PH, SUNCT) | Unilateral, severe | Cranial autonomic symptoms | Rare | Indomethacin, oxygen, triptans |

## **When to Seek Medical Attention (Red Flags)**

* Sudden, severe ("thunderclap") headache
* New headache in individuals >50 years old
* Neurological deficits (weakness, vision loss)
* Headache with fever, neck stiffness, or altered mental status
* Headache after trauma

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# **Sleep Disorders**

Sleep disorders are a broad category of medical conditions that affect the quality, timing, and amount of sleep, leading to significant distress and impairment in daytime functioning. These disorders can have neurological, psychological, and physiological origins, often co-occurring with other medical or mental health conditions such as depression, anxiety, or cognitive disorders. They impact physical health, emotional well-being, cognitive performance, and social functioning. Other sleep-wake disorders include obstructive sleep apnea, parasomnias, narcolepsy, and restless leg syndrome.

Sleep difficulties are linked to both physical and emotional problems. Sleep problems can both contribute to or exacerbate mental health conditions and can be a symptom of other mental health conditions.

About one-third of adults report insomnia symptoms, and 4-22 meet the criteria for insomnia disorder.

## **1. Narcolepsy & Cataplexy**

## **Definition and Neurological Basis:**

Narcolepsy is a chronic neurological disorder characterized by the brain's impaired ability to regulate sleep-wake cycles, resulting in excessive daytime sleepiness and sudden sleep attacks. It is often associated with cataplexy, a sudden loss of muscle tone triggered by strong emotions, resembling the muscle paralysis normally occurring during REM sleep.

## **Types:**

* **Type 1 Narcolepsy (with cataplexy):** Diagnosed by low levels of hypocretin (orexin), a neurotransmitter that regulates wakefulness, or by the presence of cataplexy and excessive daytime sleepiness confirmed by sleep tests.
* **Type 2 Narcolepsy (without cataplexy):** Characterized by excessive daytime sleepiness without cataplexy and normal hypocretin levels.

A condition known as secondary narcolepsy can result from a brain injury to the hypothalamus, a region deep in the brain that helps regulate sleep. In addition to experiencing the typical symptoms of narcolepsy, individuals with secondary narcolepsy may also have other severe neurological problems and sleep for long periods (more than 10 hours) each night.

## **Causes and Risk Factors:**

* Loss of hypocretin-producing neurons in the hypothalamus (autoimmune or genetic factors).
* Secondary narcolepsy can result from brain injury affecting sleep regulation centers.

## **Signs and Symptoms:**

* Excessive daytime sleepiness with irresistible sleep attacks.

All individuals with narcolepsy have periods of EDS. It is often the most obvious symptom. Everyone with narcolepsy has some daytime sleepiness, but the severity of sleepiness varies among individuals. EDS causes severe daytime sleepiness that doesn't improve, even after getting enough sleep at night. Sleepiness in narcolepsy is often like a “sleep attack,” where an overwhelming feeling of sleepiness comes on quickly. In between sleep attacks, individuals can have normal levels of alertness, particularly if doing activities that keep their attention.

* Cataplexy: sudden muscle weakness triggered by emotions.

This symptom leads to sudden episodes of muscle weakness, often triggered by strong emotions such as laughter, fear, anger, stress, or excitement. Cataplexy may appear weeks or even years after the onset of EDS. Some people may only have one or two attacks in a lifetime, while others may experience many attacks a day. In about 10% of cases of narcolepsy, cataplexy is the first symptom to appear. Sometimes, it can be misdiagnosed as a seizure disorder. Attacks may be mild and involve only brief, minor weakness in a few muscles, such as a slight drooping of the eyelids. The most severe attacks result in a total body collapse during which individuals are unable to move, speak, or keep their eyes open. Even during the most severe episodes, people remain fully conscious, a characteristic that makes cataplexy different from fainting or seizure disorders. The person remains fully conscious, even if unable to speak, during the episode, which usually lasts a few seconds to several minutes and resolves on its own. While scary, the episodes are not dangerous as long as the individual is in a safe place.

* Sleep paralysis and hypnagogic/hypnopompic hallucinations.

This temporary inability to move or speak while falling asleep or waking up usually lasts only a few seconds or minutes and is similar to the reductions of voluntary muscle activity brought on by REM sleep. Sleep paralysis resembles cataplexy, except that it occurs at the edges of sleep. Very vivid, dreamlike, and sometimes frightening visual, auditory, or tactile hallucinations can accompany sleep paralysis and usually occur when people are falling asleep or waking up.

* Fragmented nighttime sleep and REM sleep behavior disorder (RBD), where muscle paralysis during REM sleep is absent, causing dream enactment.

While individuals with narcolepsy are very sleepy during the day, they usually also experience difficulties staying asleep at night. They may wake up several times each night for 10–20 minutes, which can worsen daytime sleepiness. Sleep may be disrupted by insomnia, vivid dreaming, [sleep apnea](https://www.ninds.nih.gov/archived/health-information/disorders/sleep-apnea), acting out dreams, and periodic leg movements.

* REM sleep behavior disorder (RBD)— Usually, when people dream, the body's muscles become temporarily paralyzed. This keeps people from physically acting out their dreams. However, people with RBD don't experience this paralysis. As a result, they might punch, kick, shout, or grab while asleep, disturbing their sleep and the sleep of people around them. RBD can be a problem on its own, or it could be a sign of another neurological disorder like narcolepsy.

## **Who is more likely to get narcolepsy?**

Narcolepsy affects men and women equally. Symptoms usually begin between ages 7 and 25 but can start at any age. People with narcolepsy are often misdiagnosed with other conditions like psychiatric disorders, so it can take years to get the correct diagnosis. Nearly all people with narcolepsy type 1 have extremely low levels of hypocretin. Although the causes of narcolepsy are not completely understood, current research suggests that narcolepsy may be the result of a combination of factors working together to cause a lack of hypocretin.

**These factors include**

* Autoimmune disorders—Autoimmune disorders occur when the body's immune system turns against itself and mistakenly attacks healthy cells or tissue. When cataplexy is present, the cause is most often the loss of brain cells that produce hypocretin. Although the reason for this cell loss is unknown, it appears to be linked to abnormalities in the immune system. Researchers believe that in individuals with narcolepsy, the body's immune system selectively attacks the hypocretin-containing brain cells because of a combination of genetic and environmental factors.
* Family history—Most cases of narcolepsy are sporadic, meaning the disorder occurs in individuals with no known family history. However, clusters in families sometimes occur—up to 10% of individuals diagnosed with Type 1 narcolepsy report having a close relative with similar symptoms.
* Brain injuries—Rarely, narcolepsy results from traumatic injury to parts of the brain that regulate wakefulness and REM sleep or from tumors and other diseases in the same regions.

Groups of neurons in several parts of the brain interact to control sleep, and many genes control the activity of these neurons. In the past few decades, scientists have made considerable progress in understanding narcolepsy and identifying genes strongly associated with the disorder. The loss of hypocretin neurons in the hypothalamus is the main cause of type 1 narcolepsy. These neurons help stabilize sleep and wake states.

The human leukocyte antigen (HLA) system of genes plays an important role in regulating the immune system. This gene family provides instructions for making a group of related proteins called the HLA complex, which helps the immune system distinguish between good proteins from an individual's own body and bad proteins made by foreign invaders like viruses and bacteria.

One of the genes in this family is HLA-DQB1. A variation in this gene, called HLA-DQB1\*06:02, increases the chance of developing narcolepsy, particularly Type 1 narcolepsy. HLA-DQB1\*06:02 and other HLA gene variations may increase susceptibility to an immune attack on hypocretin neurons, causing these cells to die. Most people with narcolepsy have this gene variation and may also have specific versions of closely related HLA genes.

Narcolepsy follows a seasonal pattern and is more likely to develop in the spring and early summer after the winter season, a time when people are more likely to get sick. By studying people soon after they develop the disorder, scientists have discovered that individuals with narcolepsy have high levels of certain antibodies, indicating an immune response to a recent bacterial infection (such as strep throat). Also, the H1N1 influenza epidemic in 2009 resulted in a large increase in the number of new cases of narcolepsy. Together, this suggests that individuals with the HLA-DQB1\*06:02 gene variation are at risk for developing narcolepsy after they are exposed to a specific trigger, like certain infections that trick the immune system into attacking the body.

## **Diagnosis:**

* Clinical history emphasizing daytime sleepiness and cataplexy.
* Polysomnography (overnight sleep study) and Multiple Sleep Latency Test (MSLT) to measure sleep onset and REM sleep tendency.

**Polysomnogram (PSG or sleep study):** This overnight test records brain activity, muscle movements, breathing, and eye movements during sleep. It helps determine if REM sleep happens too early in the sleep cycle and checks for other conditions like sleep apnea.  
**Multiple sleep latency test (MSLT):** This test measures how quickly a person falls asleep and whether they enter REM sleep.

* Cerebrospinal fluid hypocretin-1 levels and HLA typing may be used in some cases.

## **Treatment:**

Although there is no cure for narcolepsy, some of the symptoms can be managed with a combination of medications and lifestyle changes. Treatments target a person’s symptoms, rather than the underlying disease. Treatment varies widely by person, and it often takes a long time to find the right combination of treatments.

Research has shown that people with narcolepsy are at a higher risk for heart disease and other serious heart problems. Their heart health should be monitored regularly by a doctor and taken into consideration when considering medications or other therapies.

#### **Medications**

Medications are important for managing symptoms, and many people with narcolepsy take multiple medications to help. Treatments affect each person differently. Therefore, finding effective treatment with medications that produce the greatest benefits with the fewest problems can take time.

* Stimulants (e.g., modafinil) to reduce daytime sleepiness. In cases where modafinil is not effective, doctors may prescribe amphetamine-like stimulants (such as methylphenidate) to alleviate EDS. However, these medications must be carefully monitored for serious side effects.
* Sodium oxybate for cataplexy and sleep consolidation. This drug (also known as gamma hydroxybutyrate or GHB) has been approved by the U.S. Food and Drug Administration (FDA) to treat cataplexy and excessive daytime sleepiness in individuals with narcolepsy. Due to safety concerns associated with its use, the distribution of sodium oxybate is tightly restricted. A similar drug, called mixed salt oxybate (or low sodium oxybate) contains a combination of salts, including calcium, magnesium, and potassium, in addition to sodium. This formulation has significantly less sodium compared to sodium oxybate.
* Antidepressants to manage cataplexy and REM-related symptoms. Two classes of antidepressant drugs have proven effective in controlling cataplexy in many individuals: tricyclics (including imipramine, desipramine, clomipramine, and protriptyline) and selective serotonin and noradrenergic reuptake inhibitors (including venlafaxine, fluoxetine, and atomoxetine).
* Histamine 3 receptor antagonist/inverse agonist—Pitolisant is the only non-scheduled product for treating excessive daytime sleepiness and cataplexy in adults with narcolepsy. It has also been approved to treat excessive daytime sleepiness in children 6 years of age and older. Pitolisant, which has been commercially available in the U.S. since 2019, is thought to increase histamine levels in the brain.
* Behavioral strategies include scheduled naps and good sleep hygiene.

People with narcolepsy should consider lifestyle changes in addition to medications to best manage symptoms. Consider the following tips:

1. Take short naps. Many individuals take short, regularly scheduled naps at times when they tend to feel sleepiest.
2. Maintain a regular sleep schedule. Going to bed and waking up at the same time every day, even on the weekends, can help people sleep better.
3. Avoid caffeine or alcohol before bed. Individuals should avoid alcohol and caffeine for several hours before bedtime.
4. Avoid smoking, especially at night.
5. Cognitive behavioral therapy (CBT). CBT, a form of talk therapy, can help people with narcolepsy sleep better, feel less sleepy during the day, and improve their overall health.
6. Exercise. Exercising for at least 20 minutes most days at least four or five hours before bedtime improves sleep quality. Regular exercise has been shown to reduce excessive daytime sleepiness in people with narcolepsy.
7. Eat healthy and avoid large, heavy meals late in the day. Because of increased risk for heart problems, people with narcolepsy should follow a heart-healthy diet. There is no specific diet for narcolepsy, but emerging research suggests that following a ketogenic diet (high in healthy fats and low in carbohydrates) may help reduce EDS in people with narcolepsy type 1. Eating very close to bedtime can make it harder to sleep.
8. Relax before bed. Relaxing activities such as a warm bath before bedtime can help promote sleepiness. Try to keep the sleep space cool and comfortable.
9. Take safety precautions. Taking steps to stay safe, especially when driving, is important for people with narcolepsy. Avoiding driving when sleepy is one way to stay safe. Additionally, the Americans with Disabilities Act (ADA) requires employers to allow adults with narcolepsy to ask for work adjustments, like flexible schedules for naps or doing challenging tasks when they are most awake. Kids and teens with narcolepsy can also work with their schools to adjust schedules, take medicine during the day, and use other strategies to manage their condition.

Support groups can help people with narcolepsy and their families develop connections and share stories and strategies with others living with the same condition.

## **Prognosis and Complications:**

* Chronic condition requiring lifelong management.
* Increased risk of accidents due to sudden sleep episodes.
* Social and psychological impacts, including isolation and anxiety.

## **Epidemiology:**

* Narcolepsy affects approximately 0.02-0.05% of the population, often presenting in adolescence or early adulthood.

## **2. Sleep Apnea (Neurological Aspects)**

## **Definition:**

Sleep apnea is a disorder characterized by repeated interruptions in breathing during sleep, leading to fragmented sleep and reduced oxygen saturation. Neurologically, it involves dysfunction in the brainstem centers that regulate breathing and upper airway muscle tone.

## **Types:**

* Obstructive Sleep Apnea (OSA): airway obstruction during sleep.
* Central Sleep Apnea (CSA): failure of the brain to send proper signals to breathing muscles.

## **Causes and Risk Factors:**

* Anatomical abnormalities, obesity, and aging for OSA.
* Neurological diseases affecting respiratory control (e.g., stroke, Parkinson’s disease) for CSA.

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## **Signs and Symptoms:**

* Loud snoring, gasping, or choking during sleep.
* Excessive daytime sleepiness, morning headaches, and cognitive impairment.
* Mood disturbances and cardiovascular complications.

## **Diagnosis:**

* Polysomnography with monitoring of airflow, respiratory effort, oxygen levels, and brain activity.
* Home sleep apnea testing in some cases.

## **Treatment:**

* Continuous Positive Airway Pressure (CPAP) therapy is first-line for OSA.
* Oral appliances, weight loss, and positional therapy.
* For CSA, addressing underlying neurological causes and adaptive servo-ventilation devices.

**Complications:**

* Increased risk of hypertension, stroke, heart disease, and neurocognitive decline.

## **Prevention:**

* Weight management,
* avoiding alcohol
* sedatives,
* and treating nasal congestion.

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## **3. REM Sleep Behavior Disorder (RBD)**

## **Definition:**

RBD is a parasomnia characterized by the absence of normal muscle paralysis during REM sleep, leading to physical enactment of dreams, which can cause injury to the patient or bed partner. Individuals who suffer from RBD have high levels of physical activity during REM sleep, especially during disturbing dreams. These behaviors vary widely, but they can include kicking, punching, scratching, yelling, and behaving like an animal that has been frightened or attacked. People who suffer from this disorder can injure themselves or their sleeping partners when engaging in these behaviors. Furthermore, these types of behaviors ultimately disrupt sleep, although affected individuals have no memories that these behaviors have occurred (Arnulf, 2012).

This disorder is associated with a number of neurodegenerative diseases, such as Parkinson’s disease. In fact, this relationship is so robust that some view the presence of RBD as a potential aid in the diagnosis and treatment of a number of neurodegenerative diseases (Ferini-Strambi, 2011). Clonazepam, an anti-anxiety medication with sedative properties, is most often used to treat RBD. It is administered alone or in conjunction with doses of melatonin (the hormone secreted by the pineal gland). As part of treatment, the sleeping environment is often modified to make it a safer place for those suffering from RBD (Zangini, Calandra-Buonaura, Grimaldi, & Cortelli, 2011).

## **Neurological Basis:**

* Dysfunction in brainstem regions responsible for REM sleep muscle atonia.
* Often associated with neurodegenerative diseases such as Parkinson’s disease and narcolepsy.

## **Signs and Symptoms:**

* Violent movements during sleep, such as punching, kicking, and shouting.
* Dream enactment behaviors are often vivid and frightening.

## **Diagnosis:**

* Polysomnography showing REM sleep without atonia.
* Clinical history of dream enactment and injury.

## **Treatment:**

* Clonazepam and melatonin are commonly used.
* Safety measures to prevent injury (e.g., padding the bed area).

## **Prognosis:**

* RBD can precede neurodegenerative disorders by years.
* Monitoring for the development of Parkinsonism or dementia is advised.

## **4. Insomnia (Neurological Causes)**

## **Definition:**

Insomnia is the difficulty in initiating or maintaining sleep, or non-restorative sleep, despite adequate opportunity, leading to daytime impairment. Neurological causes include hyperarousal of the central nervous system, neurochemical imbalances, and circadian rhythm disruptions.

## **Causes and Risk Factors:**

* Stress, anxiety, depression.
* Neurological disorders like Parkinson’s, Alzheimer’s disease, and chronic pain conditions.
* Medications and substance use.

## **Signs and Symptoms:**

* Difficulty falling asleep, frequent awakenings, and early morning awakenings.
* Daytime fatigue, irritability, impaired concentration.

## **Diagnosis:**

* Clinical evaluation including sleep history and questionnaires.
* Polysomnography or actigraphy if other sleep disorders are suspected.

## **Treatment:**

* Cognitive Behavioral Therapy for Insomnia (CBT-I) is first-line.
* Short-term use of hypnotics or sedative medications.
* Addressing underlying neurological or psychiatric conditions.

## **Complications:**

* Increased risk of depression, anxiety, cardiovascular disease, and impaired quality of life.

## **Prevention:**

* Good sleep hygiene, stress management, and a regular sleep schedule.

## **General Notes on Sleep Disorders**

* Sleep disorders affect a significant portion of the population; for example, insomnia symptoms affect about one-third of adults, with 4-22% meeting criteria for insomnia disorder.
* Sleep disorders can exacerbate or be symptoms of other medical or psychiatric conditions, requiring comprehensive evaluation.
* Diagnosis often involves polysomnography, actigraphy, clinical history, and sometimes specialized lab tests (e.g., hypocretin levels for narcolepsy).
* Treatment is multidisciplinary, combining pharmacological, behavioral, and sometimes surgical interventions depending on the disorder.
* Early diagnosis and management improve prognosis and reduce complications such as accidents, cardiovascular disease, and neurodegeneration.

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# **Infections & Inflammatory Disorders**

Infections and inflammatory disorders of the central nervous system (CNS) encompass a range of conditions with varying etiologies, clinical presentations, and management strategies. Below is a detailed analysis of the specified disorders, organized by key clinical categories.

# **Meningitis**

Meningitis is an infection that causes inflammation of the membranes (meninges) that protect the brain and spinal cord. Depending on the type of infection, meningitis could go away without treatment in a matter of weeks or become dangerous and even life-threatening.

## **Causes and Risk Factors**

* **Bacterial**: Commonly caused by *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Listeria monocytogenes*. Risk factors include crowded living conditions (e.g., college dormitories), age extremes (infants, elderly), and immunocompromise.

Bacterial meningitis is caused by bacteria. Usually, the bacteria enter the bloodstream and then travel to the meninges. It’s also possible to introduce bacteria directly into the meninges through sinus infections or ear infections.

Bacterial meningitis is a medical emergency and must be treated quickly. It can be life-threatening if it’s not treated rapidly.

You should be kept in the hospital while being treated with antibiotic medication. With prompt and proper antibiotic treatment, the risk of death as a result of meningitis isn’t likely.

**Several bacteria can cause meningitis:**

* Pneumococcus disease results from the bacteria *Streptococcus pneumoniae*. It causes pneumonia, ear, and sinus infections. It’s the most common culprit in bacterial meningitis.
* *Neisseria meningitidis* and, less often, *Staphylococcus aureus* can also cause meningitis.
* *Haemophilus influenzae* type b (Hib) was once the most common cause of bacterial meningitis until the Hib vaccine became standard in children.
* Meningococcus refers to infections caused by *N. meningitidis*. It’s the most contagious bacteria behind meningitis and is known for causing outbreaks in college dorms.
* Listeria is found in some meats and cheeses and can be dangerous to pregnant women and the elderly.
* **Viral:** Enteroviruses (most common), herpesviruses. Higher risk in children under 5 and immunocompromised individuals.

A viral infection is the most common cause of meningitis in the United States. Several viruses can lead to meningitis. Most of these causal viruses are in the enterovirus family.

Less commonly, other viruses like HIV, herpes simplex, and the West Nile virus can lead to meningitis. Most often, when a virus is to blame, the infection is usually fairly mild and may even go away without treatment.

In most cases, no treatment is necessary for viral meningitis. Certain treatments can be helpful, depending on the virus that caused the infection. Also, some people may require in-patient care if they fall into a higher-risk category. This includes:

* people with weakened immune systems
* older adults
* newborns and infants
* **Fungal:** *Cryptococcus* species, often seen in HIV/AIDS or prolonged corticosteroid use.

A fungal infection is the least common cause of meningitis in most parts of the world. It’s not usually spread from an infected person to other people. Generally, it affects people with weakened immune systems.

People with HIV or cancer are at higher risk of fungal meningitis. The fungi usually responsible are Cryptococcus, which can be inhaled from bird droppings, and Histoplasma, found in bird or bat droppings.

Fungal meningitis is usually treated with antifungal medications. These medications are injected into a vein. If you have fungal meningitis, you can expect to enter the hospital for treatment. The length of your stay depends on the condition of your immune system. In some cases, you will need to continue maintenance treatment for a long period of time.

## **Signs and Symptoms**

* Classic triad: fever, headache, stiff neck.
* Altered mental status, photophobia, and seizures in severe cases.

**Viral meningitis may cause:**

* [headaches](https://www.healthline.com/health/headache)
* fever
* [stiff neck](https://www.healthline.com/health/neck-pain)
* [seizures](https://www.healthline.com/health/what-does-a-seizure-feel-like)
* sensitivity to bright light
* sleepiness
* [lethargy](https://www.healthline.com/health/lethargy)
* [nausea](https://www.healthline.com/health/nausea) and vomiting
* decreased appetite
* altered mental state

**Bacterial meningitis symptoms develop suddenly. They may include:**

* altered mental status
* nausea
* vomiting
* [sensitivity to light](https://www.healthline.com/health/photophobia)
* irritability
* headache
* fever
* chills
* stiff neck
* purple areas of skin that resemble bruises
* sleepiness
* lethargy

**Symptoms of fungal meningitis resemble the other types of this infection. These may include:**

* nausea
* vomiting
* sensitivity to light
* neck stiffness
* fever
* headache
* a [general sense of being unwell](https://www.healthline.com/health/malaise)
* confusion or disorientation

**Meningitis symptoms in infants**

Babies [who develop meningitis](https://www.healthline.com/health/meningitis-baby) may show different symptoms than adults. These can include:

* fever
* body or neck stiffness
* high-pitched crying
* inconsolable behaviors
* sleepy and difficulty waking
* irritable and grumpy
* doesn’t feel well and has a weak suck during feeding

Viruses that cause colds, cold sores, flu, and diarrhea can also cause viral meningitis.

Bacterial meningitis typically spreads from a severe infection in a nearby area of the body. For example, bacteria from a severe ear infection or sinus infection can enter the bloodstream and travel to the brain or spinal cord.

## **Meningitis symptoms in children**

Meningitis becomes more common in children as they grow older and reach high school and college ages. Symptoms of viral and bacterial meningitis in children are similar to symptoms in adults. These include:

* sudden fever
* body and neck aches
* confusion or disorientation
* nausea
* vomiting
* tiredness or fatigue

## **Diagnosis**

* Lumbar puncture: CSF analysis for cell count, protein, glucose, and culture.
* Imaging: CT/MRI to rule out increased intracranial pressure before lumbar puncture.

**Diagnosing meningitis starts with a health history and physical exam. During the physical exam, your doctor may check you for:**

* fever
* skin issues
* increased heart rate
* neck stiffness
* [reduced consciousness](https://www.healthline.com/health/consciousness-decreased)

**They will also order tests to accurately diagnose meningitis. These can include:**

* A [lumbar puncture](https://www.healthline.com/health/lumbar-puncture), also called a spinal tap, extracts cerebrospinal fluid to look for signs of infection.
* [Blood cultures](https://www.healthline.com/health/blood-culture) identify bacteria in the blood. Bacteria can travel from the blood to the brain. N. meningitidis and S. pneumonia, among others, can cause both [sepsis](https://www.healthline.com/health/sepsis) (a blood infection) and meningitis.
* A [complete blood count (CBC)](https://www.healthline.com/health/cbc) with differential checks your number of red and white blood cells. Meningitis usually causes a raised white blood cell count.
* [Chest X-rays](https://www.healthline.com/health/chest-x-ray) can reveal [pneumonia](https://www.healthline.com/health/pneumonia), [tuberculosis](https://www.healthline.com/health/tuberculosis), or fungal infections. Meningitis can occur after pneumonia.
* A [CT scan](https://www.healthline.com/health/ct-scan) of the head may show problems like a [brain abscess](https://www.healthline.com/health/brain-abscess) or intercranial pressure. Bacteria can spread from the sinuses to the meninges.

Testing can also determine the best antibiotic for treatment.

**Treatment**

* **Bacterial:** Immediate empiric antibiotics (e.g., ceftriaxone + vancomycin). It requires immediate hospitalization. Early diagnosis and treatment with intravenous (IV) antibiotics and steroids may prevent brain damage and death.
* **Viral:** Supportive care; acyclovir for suspected herpes simplex. This may resolve on its own, but doctors treat some causes with IV antiviral medications.
* **Fungal:** Amphotericin B + flucytosine.
* **Parasitic meningitis** may either involve treating just symptoms or the infection directly. If it worsens, a doctor may try to treat the infection itself.
* **Chronic meningitis:** requires treating the underlying cause, such as a fungal infection, or an autoimmune issue, such as rheumatoid arthritis

## **Prevention**

* Vaccines: Hib, pneumococcal, meningococcal.
* Prophylaxis for close contacts of meningococcal meningitis.

While it’s difficult to prevent all types of meningitis, you may be able to prevent bacterial meningitis, the most common and serious type, with vaccines.

If you’re at an elevated risk for meningitis due to your age, job, or overall health, consider talking with a doctor about your options for [vaccination](https://www.healthline.com/health/vaccinations/meningococcal).

**You may be able to reduce your risk of meningitis by:**

* avoiding contact with people who are sick
* contacting a doctor immediately if you were in contact with someone who has a bacterial meningococcal infection, as they may be able to prescribe preventive antibiotics
* taking precautions against viral infections, such as frequent handwashing and wearing a mask in crowded places
* taking precautions against foodborne illness, especially if you are [pregnant](https://www.healthline.com/health/food-safety-pregnancy) or have a weakened immune system
* avoiding sharing personal items, such as drinks, utensils, toothbrushes

**Certain practices may also support your overall immune system health and reduce your risk of illness that could lead to meningitis. This can include:**

* quitting [smoking](https://www.healthline.com/health/smoking/effects-on-body) if you smoke
* getting enough rest
* eating a balanced diet
* getting regular physical activity

**What are the complications of meningitis?**

These complications are typically associated with meningitis:

* seizures
* hearing loss
* vision loss
* memory problems
* migraine headaches
* [brain damage](https://www.healthline.com/health/head-injury)
* [hydrocephalus](https://www.healthline.com/health/hydrocephalus)
* a subdural empyema, or a buildup of fluid between the brain and the skull

A meningitis infection may produce bacteria in the bloodstream. These bacteria multiply, and some release toxins. This can damage blood vessels and leak blood into the skin and organs.

A serious form of this blood infection can be life-threatening. Gangrene may damage skin and tissue. In rare cases, amputation may be necessary. Several other serious complications may occur in people with meningitis who do not receive proper treatment.

## **Prognosis**

* Bacterial meningitis mortality: 10–15%.
* Viral cases often resolve without sequelae.

# **Encephalitis**

Encephalitis (en-sef-uh-LIE-tis) is inflammation of the brain. It can be caused by viral or bacterial infections or by immune cells mistakenly attacking the brain. Viruses that can lead to encephalitis can be spread by insects such as mosquitos and ticks.

When inflammation is caused by an infection in the brain, it's known as infectious encephalitis. And when it's caused by the immune system attacking the brain, it's known as autoimmune encephalitis. Sometimes there is no known cause.

Encephalitis can sometimes lead to death. Getting diagnosed and treated right away is important because it's hard to predict how encephalitis may affect each person.

## **Causes**

* Infectious: HSV-1, arboviruses (e.g., West Nile), rabies.

This condition usually occurs when a virus infects the brain. The infection may affect one area or be widespread. Viruses are the most common causes of infectious encephalitis, including some that can be passed by mosquitoes or ticks. Very rarely, encephalitis may be caused by bacteria, fungus or parasites.

* Autoimmune: Anti-NMDA receptor antibodies, often post-herpesviral or associated with ovarian teratomas.

This condition occurs when your own immune cells mistakenly attack the brain or make antibodies targeting proteins and receptors in the brain. The exact reason why this happens is not completely understood. Sometimes autoimmune encephalitis can be triggered by cancerous or noncancerous tumors, known as paraneoplastic syndromes of the nervous system. Other types of autoimmune encephalitis, such as acute disseminated encephalomyelitis (ADEM), can be triggered by an infection in the body. This is known as post-infectious autoimmune encephalitis. In many instances, no trigger for the immune response is found.

**The viruses that can cause encephalitis include:**

* **Herpes simplex virus (HSV).** Both HSV type 1 and HSV type 2 can cause encephalitis. HSV type 1 causes cold sores and fever blisters around the mouth, and HSV type 2 causes genital herpes. Encephalitis caused by HSV type 1 is rare but can result in significant brain damage or death.
* **Other herpes viruses.** These include the Epstein-Barr virus, which commonly causes infectious mononucleosis, and the varicella-zoster virus, which commonly causes chickenpox and shingles.
* **Enteroviruses.** These viruses include the poliovirus and the coxsackievirus, which usually cause an illness with flu-like symptoms, eye inflammation, and abdominal pain.
* **Mosquito-borne viruses.** These viruses can cause infections such as West Nile, La Crosse, St. Louis, western equine, and eastern equine encephalitis. Symptoms of an infection might appear within a few days to a couple of weeks after exposure to a mosquito-borne virus.
* **Tick-borne viruses.** The Powassan virus is carried by ticks and causes encephalitis in the Midwestern United States. Symptoms usually appear about a week after a bite from an infected tick.
* **Rabies virus.** Infection with the rabies virus, which is usually transmitted by a bite from an infected animal, causes a rapid progression to encephalitis once symptoms begin. Rabies is a rare cause of encephalitis in the United States.

## **Symptoms**

* Altered consciousness,
* seizures,
* focal neurologic deficits,
* and psychiatric symptoms (e.g., psychosis in anti-NMDA encephalitis).

**Most people with infectious encephalitis have flu-like symptoms, such as:**

* Headache.
* Fever.
* Aches in muscles or joints.
* Fatigue or weakness.

**Typically, these are followed by more serious symptoms over a period of hours to days, such as**

* Stiff neck.
* Confusion, agitation, or hallucinations.
* Seizures.
* Loss of feeling or being unable to move certain areas of the face or body.
* Irregular movements.
* Muscle weakness.
* Trouble with speech or hearing.
* Loss of consciousness, including coma.

**In infants and young children, symptoms also might include:**

* Bulging of the soft spots of an infant's skull.
* Nausea and vomiting.
* Stiffness affecting the whole body.
* Poor feeding or not waking for a feeding.
* Irritability.

In autoimmune encephalitis, symptoms may develop more slowly over several weeks. Flu-like symptoms are less common but can sometimes happen weeks before more serious symptoms start.

**Symptoms are different for everyone, but it's common for people to have a combination of symptoms, including**

* Changes in personality.
* Memory loss.
* Trouble understanding what is real and what is not, known as psychosis.
* Seeing or hearing things that aren't there is known as hallucinations.
* Seizures.
* Changes in vision.
* Sleep problems.
* Muscle weakness.
* Loss of sensation.
* Trouble walking.
* Irregular movements.
* Bladder and bowel symptoms.

## **Risk factors**

Anyone can develop encephalitis. Factors that may increase the risk include:

* **Age.** Some types of encephalitis are more common or more serious in certain age groups. In general, young children and older adults are at greater risk of most types of viral encephalitis. Similarly, some forms of autoimmune encephalitis are more common in children and young adults, whereas others are more common in older adults.
* **Weakened immune system.** People who have HIV/AIDS, take immune-suppressing medicines or have another condition causing a weakened immune system are at increased risk of encephalitis.
* **Geographical regions.** Mosquito- or tick-borne viruses are common in particular geographical regions.
* **Season of the year.** Mosquito- and tick-borne diseases tend to be more common in summer in many areas of the United States.
* **Autoimmune disease.** People who already have an autoimmune condition may be more prone to develop autoimmune encephalitis.
* **Smoking.** Smoking increases the chances of developing lung cancer, which in turn increases the risk of developing paraneoplastic syndromes, including encephalitis.

## **Complications**

The complications of encephalitis vary, depending on factors such as

* Your age.
* The cause of your infection.
* The severity of your initial illness.
* The time from disease onset to treatment.

People with relatively mild illnesses usually recover within a few weeks with no long-term complications.

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### **Complications of serious illness**

Inflammation can injure the brain, possibly resulting in a coma or death.

Other complications may last for months or may be permanent. Complications can vary widely and can include:

* Fatigue that doesn't go away.
* Weakness or lack of muscle coordination.
* Personality changes.
* Memory problems.
* Hearing or vision changes.
* Trouble with speech.

## **Diagnosis**

* MRI: Hyperintense lesions in temporal lobes (HSV).
* CSF analysis: PCR for viral DNA; antibody testing (e.g., NMDA receptor antibodies).

## **Treatment**

* HSV encephalitis: IV acyclovir.
* Autoimmune: Immunotherapy (steroids, IVIG, rituximab) and tumor resection if present.

## **Prognosis**

* Anti-NMDA encephalitis: 80% recover with early treatment; mortality ~4%.

# **Brain Abscess**

A brain abscess is a collection of pus, immune cells, and other material in the brain, caused by a bacterial or fungal infection.

## **Causes**

* Bacterial (e.g., *Staphylococcus aureus*) or fungal spread from sinus/ear infections, endocarditis, or trauma.

Brain abscesses commonly occur when bacteria or fungi infect part of the brain. As a result, swelling and irritation (inflammation) develop. Infected brain cells, white blood cells, live and dead bacteria or fungi collect in an area of the brain. Tissue forms around this area and creates a mass or abscess.

The germs that cause a brain abscess can reach the brain through the blood. Or, they enter the brain directly, such as during brain surgery. In some cases, a brain abscess develops from an infection in the sinuses.

The source of the infection is often not found. However, the most common identified source is a lung infection. Less often, a heart infection is the cause.

The following raise your chance of developing a brain abscess:

* A weakened immune system (such as in people with HIV/AIDS)
* Chronic diseases, such as [cancer](https://medlineplus.gov/ency/article/001289.htm)
* Medicines that suppress the immune system (corticosteroids or [chemotherapy](https://medlineplus.gov/ency/article/002324.htm))
* [Congenital heart disease](https://medlineplus.gov/ency/article/001114.htm)

## **Symptoms**

* Headache (70–90%), fever, focal deficits (e.g., hemiparesis), and seizures.

## **Diagnosis**

* MRI/CT: Ring-enhancing lesion with edema.
* Biopsy: Culture-guided antimicrobial therapy.

## **Treatment**

* Antibiotics: Ceftriaxone + metronidazole for 6–8 weeks.
* Surgery: Aspiration or excision for large/ruptured abscesses.

## **Complications**

* Herniation, hydrocephalus, and permanent neurologic deficits.

# **Neurocysticercosis**

## **Causes**

* *Taenia solium* larvae ingestion via contaminated food/water; endemic in Latin America, Asia, and Africa.

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## **Symptoms**

* Seizures (70%),
* intracranial hypertension,
* and focal deficits depending on cyst location.
* [Changes in mental status](https://medlineplus.gov/ency/article/003205.htm), such as confusion, slow response or thinking, unable to focus, or sleepiness
* [Decreased ability to feel touch or pain](https://medlineplus.gov/ency/article/003206.htm) (sensory loss)
* Fever and chills
* Headache, or stiff neck
* Language problems
* Loss of muscle function, typically on one side
* Vision changes
* Vomiting
* Weakness in a limb (such as an arm or leg)

## **Diagnosis**

* Imaging: MRI/CT showing cysts with scolex.
* Serology: ELISA for antibodies.
* [Blood cultures](https://medlineplus.gov/ency/article/003744.htm)
* [Chest x-ray](https://medlineplus.gov/ency/article/003804.htm)
* [Complete blood count](https://medlineplus.gov/ency/article/003642.htm) (CBC)
* [Head CT scan](https://medlineplus.gov/ency/article/003786.htm)
* [Electroencephalogram](https://medlineplus.gov/ency/article/003931.htm) (EEG)

A needle [biopsy](https://medlineplus.gov/ency/article/003416.htm) is usually performed to identify the cause of the infection

## **Treatment**

* Antiparasitics: Albendazole + praziquantel (for viable cysts).
* Steroids: To reduce inflammation (e.g., dexamethasone).

A brain abscess is a medical emergency. Pressure inside the skull may become high enough to be life-threatening. You will need to stay in the hospital until the condition is stable. Some people may need life support.

Medicine, such as an antibiotic, rather than surgery, is recommended if you have:

* A small abscess less than 0.79 inches (in) or 2 centimeters (cm)
* An abscess deep in the brain
* An abscess and [meningitis](https://medlineplus.gov/ency/article/000680.htm)
* Several abscesses (rare)
* Shunts in the brain for [hydrocephalus](https://medlineplus.gov/ency/article/001571.htm) (in some cases, the shunt may need to be removed temporarily or replaced)
* An infection called [toxoplasmosis](https://medlineplus.gov/ency/article/000637.htm) in a person with HIV/AIDS

You may be prescribed several different types of antibiotics to make sure treatment works.

Antifungal medicines may also be prescribed if the infection is likely caused by a fungus.

**Surgery is needed if:**

* Increased pressure in the brain continues or gets worse
* The brain abscess does not get smaller after medicine
* The brain abscess contains gas (produced by some types of bacteria)
* The brain abscess might break open (rupture)
* The brain abscess is large (more than 0.79 in or 2 cm)

Surgery consists of opening the skull, exposing the brain, and draining the abscess. Lab tests are often done to examine the fluid. This helps identify the cause of the infection so that the right antibiotics or antifungal medicine can be prescribed.

Needle [aspiration](https://medlineplus.gov/ency/article/002216.htm) guided by CT or MRI scan may be needed for a deep abscess. During this procedure, medicines may be injected directly into the mass.

Certain diuretics (medicines that reduce fluid in the body) and steroids may be used to reduce brain swelling.

## **Prevention**

* Improved sanitation and pork inspection in endemic regions.

## **Prognosis**

If untreated, a brain abscess is almost always deadly. With treatment, the death rate is about 10% to 30%. The earlier treatment is received, the better.

Some people may have long-term brain or nerve damage after a brain abscess or surgery.

## **Possible Complications**

Complications may include:

* Brain damage
* Meningitis that can be severe and life threatening
* Return (recurrence) of the infection
* [Seizures](https://medlineplus.gov/ency/article/003200.htm)

## **When to Contact a Medical Professional**

Go to a hospital emergency room or call 911 or the local emergency number if you have symptoms of a brain abscess.

# **Neurosyphilis**

Neurosyphilis is a bacterial infection of the brain or spinal cord. It usually occurs in people who have had untreated [syphilis](https://medlineplus.gov/ency/article/000861.htm) for many years.

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## **Causes**

* *Treponema pallidum* infection progressing untreated for 10–20 years.

Neurosyphilis is caused by Treponema pallidum bacteria. Neurosyphilis usually occurs about 10 to 20 years after a person is first infected with syphilis. Not everyone who has syphilis develops this complication.

**There are four different forms of neurosyphilis:**

* [Asymptomatic](https://medlineplus.gov/ency/article/002217.htm) (most common form)
* [General paresis](https://medlineplus.gov/ency/article/000748.htm)
* Meningovascular
* [Tabes dorsalis](https://medlineplus.gov/ency/article/000729.htm)

Asymptomatic neurosyphilis occurs before [symptomatic](https://medlineplus.gov/ency/article/002293.htm) syphilis. Asymptomatic means there aren't any symptoms.

## **Symptoms**

* Early: Asymptomatic.
* Late: Dementia, tabes dorsalis (gait instability), Argyll Robertson pupils.

Symptoms usually affect the nervous system. Depending on the form of neurosyphilis, symptoms may include any of the following:

* Abnormal walk (gait) , or unable to walk
* Numbness in the toes, feet, or legs
* Problems with thinking, such as confusion or poor concentration
* Mental problems, such as [depression](https://medlineplus.gov/ency/article/003213.htm) or irritability
* Headache, [seizures](https://medlineplus.gov/ency/article/003200.htm), or stiff neck
* Loss of bladder control ([incontinence](https://medlineplus.gov/ency/article/003142.htm))
* [Tremors](https://medlineplus.gov/ency/article/003192.htm), or weakness
* [Visual problems](https://medlineplus.gov/ency/article/003029.htm), even blindness

## **Exams and Tests**

Your health care provider will do a physical examination and may find the following:

* Abnormal reflexes
* [Muscle atrophy](https://medlineplus.gov/ency/article/003188.htm)
* Muscle contractions
* Mental changes

Blood tests can be done to detect substances produced by the bacteria that cause syphilis. This includes

* Treponema pallidum particle agglutination assay (TPPA)
* Venereal disease research laboratory ([VDRL](https://medlineplus.gov/ency/article/003515.htm)) test
* Fluorescent treponemal antibody absorption ([FTA-ABS](https://medlineplus.gov/ency/article/003512.htm))
* Rapid plasma reagin ([RPR](https://medlineplus.gov/ency/article/003533.htm))

With neurosyphilis, it is important to [test the spinal fluid](https://medlineplus.gov/ency/article/003768.htm) for signs of syphilis.

Tests to look for problems with the nervous system may include:

* [Cerebral angiogram](https://medlineplus.gov/ency/article/003799.htm)
* [Head CT scan](https://medlineplus.gov/ency/article/003786.htm)
* [Lumbar puncture](https://medlineplus.gov/ency/article/003428.htm) (spinal tap) and [cerebrospinal fluid (CSF) analysis](https://medlineplus.gov/ency/article/003369.htm)
* [MRI](https://medlineplus.gov/ency/article/003335.htm) scan of the brain, brainstem, or spinal cord

## **Diagnosis**

* CSF-VDRL: Positive in active disease.
* Imaging: Cerebral atrophy or gummas on MRI.

## **Treatment**

Penicillin (an antibiotic) is used to treat neurosyphilis. It can be given in different ways:

* Injected into a vein several times a day for 10 to 14 days.
* By mouth 4 times a day, combined with daily muscle injections, both taken for 10 to 14 days.

You must have follow-up blood tests at 3, 6, 12, 24, and 36 months to make sure the infection is gone. You will need follow-up lumbar punctures for CSF analysis every 6 months. If you have HIV/AIDS or another medical condition, your follow-up schedule may be different.

## **Prognosis**

Neurosyphilis is a life-threatening complication of syphilis. How well you do depends on how severe the neurosyphilis is before treatment. The goal of treatment is to prevent further deterioration. Many of these changes will be permanent.

* Partial recovery is possible with early treatment;
* Irreversible damage occurs in late stages.

## **When to Contact a Medical Professional**

Contact your provider if you have had syphilis in the past and now have signs of nervous system problems

## **Prevention**

Prompt diagnosis and treatment of the original syphilis infection can prevent neurosyphilis.

# **Autoimmune Encephalitis (Anti-NMDA Receptor)**

## **Causes**

* Paraneoplastic (50% linked to ovarian teratomas) or post-infectious (e.g., herpes encephalitis).

## **Symptoms**

* Psychiatric features (psychosis, agitation),
* dyskinesias,
* autonomic instability.

## **Diagnosis**

* CSF antibodies: NMDA receptor IgG.
* Imaging: Often normal; ovarian ultrasound for teratomas.

## **Treatment**

* First-line: steroids, IVIG, plasmapheresis.
* Second-line: Rituximab or cyclophosphamide.

## **Epidemiology**

* Incidence: 1.5 per million/year; 80% female, median age 21.

## **Differential Diagnosis**

| **Condition** | **Key Distinguishing Features** |
| --- | --- |
| Meningitis vs Encephalitis | Meningitis: Nuchal rigidity, no focal deficits. Encephalitis: Altered mentation, seizures. |
| Brain Abscess vs Tumor | Abscess: Ring-enhancing lesion with fever. Tumor: Gradual progression, no systemic signs. |
| Neurocysticercosis vs Epilepsy | Neurocysticercosis: Cystic lesions on imaging, endemic exposure. |

## **When to Seek Immediate Care**

* Red flags: sudden fever with altered consciousness, seizures, or focal neurologic deficits.

## **Epidemiology Insights**

* Neurocysticercosis: accounts for 30% of epilepsy cases in endemic regions.
* Anti-NMDA encephalitis: 40% of cases occur in children.

This synthesis integrates current guidelines, including 2025 BMJ recommendations for encephalitis management and CDC-endorsed protocols for meningitis prevention. Early diagnosis and tailored therapies are critical to mitigating morbidity and mortality across these conditions.

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# **Paediatric & Developmental Neurological Disorders**

## **1. Autism Spectrum Disorder (Neurological Aspects)**

Autism spectrum disorder is a condition related to brain development that affects how people see others and socialize with them. This causes problems in communication and getting along with others socially. The condition also includes limited and repeated patterns of behavior. The term "spectrum" in autism spectrum disorder refers to the wide range of symptoms and the severity of these symptoms. Autism spectrum disorder includes conditions that were once thought to be separate — autism, Asperger's syndrome, childhood disintegrative disorder and a form of widespread developmental disorder that isn't specified. Autism spectrum disorder begins in early childhood. Over time, it can cause difficulty functioning in society. For example, people with autism spectrum disorder may have problems being social or when in school or at work. Often children show symptoms of autism within the first year of life. A small number of children with the condition appear to develop as expected in the first year. Then between 18 and 24 months of age, they may lose some skills and develop autism symptoms. There is no cure for autism spectrum disorder. But getting treatment early, during the preschool years, can make a big difference in the lives of many children with the condition.

## **Symptoms**

Some children show signs of autism spectrum disorder in early infancy, such as less eye contact, not responding to their names or not being interested in caregivers. Other children may not develop as expected for the first few months or years of life. Then they suddenly become withdrawn or aggressive or lose the language skills they had before. Signs usually are seen by ages 2 to 3 years old. Some people in the mild range on the autism spectrum may have more symptoms that aren't noticed early on. They may not be diagnosed until middle to late childhood, when there is a greater need to communicate and be social. Sometimes a diagnosis is made for the first time in adulthood, though symptoms were likely present during childhood. Each child with autism spectrum disorder is likely to have a unique pattern of behavior that depends on whether symptoms are mild, moderate or severe. Some children with autism spectrum disorder have trouble learning, and some have signs of lower than usual intelligence. Other children with the condition have usual to high intelligence. These children learn quickly but have trouble communicating, applying what they know in everyday life and adjusting to social situations.Because each child can have a unique mix of symptoms, sometimes it can be hard to tell how severe the condition is. It's generally based on how severe the symptoms are and how much those symptoms affect a child being able to function. Below are some common signs shown by people who have autism spectrum disorder.

## **Social communication and interaction**

People with autism spectrum disorder may have problems getting along with others and communicating. They may have a mix of these and other symptoms:

* Don't respond to their name, or they don't seem to hear at times.
* Don't want to be cuddled or held and prefer to play alone, retreating into their own worlds.
* Have poor eye contact and have no expression on their faces.
* Don't speak or have delayed speech or lose the ability to say words or sentences as they could before.
* Can't start a conversation or keep one going, or only start one to make requests or label items.
* Speak with an unusual tone or rhythm and may use a singsong voice or robotlike speech.
* Repeat words or phrases word for word but don't know how to use them.
* Don't seem to understand simple questions or directions.
* Don't show emotions or feelings and don't seem to be aware of how others feel.
* Don't point at or bring objects to share interest.
* Are passive, aggressive or disruptive when interacting with others.
* Have a hard time figuring out what it means when people have different looks on their faces, position their bodies differently or speak in different tones of voice.

## **Patterns of behavior**

People with autism spectrum disorder may have limited, repetitive patterns of behavior, interests or activities, including a mix of these and other signs:

* Make the same movement over and over again, such as rocking, spinning or hand-flapping.
* Do activities where they could hurt themselves, such as biting or head-banging.
* Create specific routines or rituals and become upset at even small changes.
* Aren't coordinated and may be clumsy, or they move in patterns that aren't usual, such as walking on toes.
* Have unusual, stiff or exaggerated body language.
* Are fascinated by details of an object, such as the spinning wheels of a toy car, but they don't know what the object is for or how it works.
* Are sensitive to light, sound or touch but may not be affected by pain or temperature.
* Don't mimic others or take part in make-believe play.
* Fixate on an object or activity with unusual intensity or focus.
* Prefer specific foods, such as eating only a few foods or not wanting to eat foods with certain textures.

As they get older, some children with autism spectrum disorder interact more with others and show fewer disturbances in behavior. Some, usually those with the least severe problems, eventually may lead typical or nearly typical lives. But others continue to have trouble with language or social skills. And the teenage years can bring more behavioral and emotional challenges.

## **Causes**

Autism spectrum disorder has no single known cause. Since the condition is complex and symptoms and severity vary, there could be many causes. Both genetics and the environment may play a role.

* **Genetics.** Several genes seem to be involved in autism spectrum disorder. For some children, autism spectrum disorder can be related to a genetic condition, such as Rett syndrome or fragile X syndrome. For other children, genetic changes, also known as mutations, may raise the risk of autism spectrum disorder. Still other genes may affect the way that the brain develops or brain cells communicate. Or those genes may affect how severe symptoms are. While some genetic changes seem to be inherited, others aren't.
* **Environmental factors.** Researchers are exploring whether factors such as viral infections, medicines, complications during pregnancy or air pollutants play a role in causing autism spectrum disorder.

## **No link between vaccines and autism spectrum disorder**

One of the greatest controversies in autism spectrum disorder centers on whether there is a link between the condition and childhood vaccines. Many well-done research studies show no link between autism spectrum disorder and any vaccines. In fact, the original study that started the debate years ago was retracted due to poor design and questionable research methods.

When your child doesn't get vaccines, your child and other children could catch and spread viruses that cause serious diseases. These diseases include whooping cough, also known as pertussis, as well as measles, mumps and others.

## **Risk factors**

The number of children diagnosed with autism spectrum disorder is rising. It isn't clear whether this is due to better ways to diagnose and report the condition, a real increase in the number of children with the condition, or both. Autism spectrum disorder affects children of all races and nationalities. But certain factors raise a child's risk, including:

* **Your child's sex.** Boys are about four times more likely to be diagnosed with autism spectrum disorder than girls are. While boys may get autism spectrum disorder more often than girls, it's possible that some girls aren't diagnosed.
* **Family history.** Families who have one child with autism spectrum disorder have a higher risk of having another child with the condition. Sometimes parents or relatives of a child with autism spectrum disorder may have minor problems being social or communicating, or they may show certain behaviors typical of the condition.
* **Other conditions.** Children with certain medical conditions have a higher risk of autism spectrum disorder or symptoms similar to autism. Examples include fragile X syndrome, an inherited condition that causes intellectual disability; tuberous sclerosis, a condition in which benign tumors develop in the brain; and Rett syndrome, a genetic condition that almost always occurs in girls and causes slowing of head growth, intellectual disability and loss of purposeful hand use.
* **Early birth.** Babies born before 26 weeks of a parent's pregnancy may have a higher risk of autism spectrum disorder.
* **Parents' ages.** There may be a connection between children born to older parents and autism spectrum disorder. But more research is needed to show this link.

## **Complications**

Because people with autism spectrum disorder often have a hard time interacting socially, communicating or behaving, this can lead to problems with:

* School and learning.
* Getting a job.
* Not being able to live on their own.
* Being isolated socially.
* Stress within the family.
* Being a victim and being bullied.

## **Prevention**

There's no known way to prevent autism spectrum disorder. But many studies have been done to see if taking folic acid and other vitamins before and during pregnancy can lower the risk of having a baby with autism spectrum disorder. A review of studies on what are known as prenatal vitamins shows no clear answer. This is due to the quality of the research. More high-quality studies are needed. Getting diagnosed and treated early is most helpful in improving behavior, skills and language development. But getting treatment is helpful at any age. Though children usually don't outgrow autism spectrum disorder symptoms, they may learn to function well.

## **Diagnosis**

Your child's healthcare professional looks for signs of developmental delays at regular well-child checkups. If your child shows any symptoms of autism, you'll likely be referred to a specialist who treats children with autism spectrum disorder for an evaluation. This specialist could be a child psychiatrist or psychologist, a pediatric neurologist, or a developmental pediatrician. Because autism spectrum disorder symptoms and how severe they are can vary widely, it may be hard to make a diagnosis. There is no specific medical test to diagnose autism spectrum disorder. Instead, a specialist may:

* Observe your child and ask how your child has developed or changed over time in terms of interacting socially, communicating and behaving.
* Give your child tests covering hearing, speech, language, level of development, and social and behavioral issues.
* Present structured social and communication interactions to your child and score the performance.
* Include other specialists in coming up with a diagnosis.
* Recommend genetic testing to figure out whether your child has a genetic condition such as Rett syndrome or fragile X syndrome

## **Treatment**

There is no cure for autism spectrum disorder, and there is no one-size-fits-all treatment. Treatment seeks to support your child's learning, development and behavior. Getting treated early, during the preschool years, can help your child learn critical social, communication, functional and behavioral skills. The range of home-based and school-based treatments for autism spectrum disorder can be overwhelming, and your child's needs may change over time. Your healthcare professional can recommend options and help find resources in your area. If your child is diagnosed with autism spectrum disorder, talk with experts about creating a treatment strategy and build a team of health professionals to meet your child's needs.

Treatment options may include:

* **Behavior and communication therapies.** Many programs address the range of social, language and behavioral difficulties linked with autism spectrum disorder. Some programs focus on reducing challenging behaviors and teaching new skills. Other programs focus on teaching children how to act in social situations or communicate better with others. Applied behavior analysis can help children learn new skills and adapt these skills to many situations by motivating them with rewards.
* **Educational therapies.** Children with autism spectrum disorder often respond well to highly structured educational programs. Successful programs usually include a team of specialists and various activities to improve social skills, communication and behavior. Preschool children who get intensive, individualized behavioral treatments often show good progress.
* **Family therapies.** Parents and other family members can learn how to play and interact with children who have autism in ways that support social interaction skills, manage challenging behaviors, and teach daily living skills and communication.
* **Other therapies.** Depending on your child's needs, speech therapy to make communication skills better, occupational therapy to teach activities of daily living, and physical therapy to make movement and balance better may help. A psychologist can recommend ways to manage problem behavior.
* **Medicines.** Medicine can't make the core signs of autism spectrum disorder better, but specific medicines can help control symptoms. For example, certain medicines may be prescribed if your child is hyperactive. Sometimes healthcare professionals prescribe antipsychotic medicines to treat severe behavioral symptoms. Or they may prescribe antidepressants for anxiety. Keep all healthcare professionals updated on any medicines or supplements your child takes. Some medicines and supplements can affect how one medicine acts with another, causing dangerous side effects.

## **Managing other medical and mental health conditions**

In addition to autism spectrum disorder, children, teenagers and adults also can have:

* **Medical health issues.** Children with autism spectrum disorder also may have medical issues such as epilepsy, sleep disorders, limited food preferences or stomach problems. Ask your child's healthcare professional how to best manage these conditions together.
* **Problems with transition to adulthood.** Teens and young adults with autism spectrum disorder may have a hard time understanding body changes. Also, social situations become more complex during the teen years, and there may be less tolerance for individual differences. Behavior also may be challenging at this time.
* **Other mental health conditions.** Teens and adults with autism spectrum disorder often have other mental health conditions, such as anxiety disorders; depression; attention-deficit-hyperactivity disorder, also known as ADHD; and substance misuse. Your healthcare professional, mental health professional, and community advocacy and service organizations can help.
* **Behavioral health concerns.** In addition to autism spectrum disorder, your child could be irritable or aggressive and may not pay attention. Your child also could be hyperactive, have sudden outbursts or try self-harm. Work with your healthcare professional, mental health professional and other team members to look for a cause, such as pain, distress or frustration, and to manage these challenges if they occur.

## **Treatment**

**Alternative medicine**

Because autism spectrum disorder can't be cured, many parents seek alternative or complementary therapies. But there's little or no research on these therapies to show whether they're helpful. And some alternative treatments could be dangerous. Talk with your child's healthcare professional about whether research supports any therapy that you're thinking about for your child.

Examples of complementary and alternative therapies that may offer some benefit when used along with proven treatments include:

* **Creative therapies.** Some parents choose to include art or music therapy along with educational and medical therapies. Doing so can make a child less sensitive to touch or sound.
* **Sensory-based therapies.** Therapists may use brushes, squeeze toys, trampolines and other materials to stir the senses, such as touch, balance and hearing. But research has not proved that these therapies work. It's possible that they may help when used with other treatments.
* **Melatonin.** Research shows that melatonin could help with sleep issues related to autism spectrum disorder when taken as directed. But it's important to work on developing healthy sleep habits first.
* **Massage.** While massage may be relaxing, there isn't enough evidence to show that it improves symptoms of autism spectrum disorder.
* **Pet or horse therapy.** Pets can give your child a companion and a fun time. But more research is needed to determine whether being with animals improves symptoms of autism spectrum disorder.

Some complementary and alternative therapies may not be harmful, but there's no evidence that they help. Some also may be costly and hard to carry out. Examples of these therapies include:

* **Vitamin supplements and probiotics.** Although not harmful when used in the usual amounts, there is no evidence they help autism spectrum disorder symptoms. Also, supplements can be costly. Talk with your healthcare professional about vitamins and other supplements and the right dose for your child.
* **Acupuncture.** This therapy has been used to improve autism spectrum disorder symptoms, but research doesn't show that it works.

Some complementary and alternative treatments aren't proved to help, and they could be dangerous. Examples of complementary and alternative treatments that aren't recommended for autism spectrum disorder include:

* **Special diets that limit nutrients.** There's no evidence that special diets effectively treat autism spectrum disorder. And for growing children, restrictive diets can mean that children won't get enough nutrients. If you decide to pursue a restrictive diet, work with a registered dietitian to create a proper meal plan for your child that has all the needed nutrients.
* **Chelation therapy.** This treatment is said to remove mercury and other heavy metals from the body, but there's no known link between these metals and autism spectrum disorder. Research doesn't support that chelation therapy works, and it can be very dangerous. In some cases, children treated with chelation therapy have died.
* **Hyperbaric oxygen treatments.** Hyperbaric oxygen involves breathing oxygen inside a pressurized chamber. This treatment has not been shown to be effective in treating autism spectrum disorder symptoms, and the U.S. Food and Drug Administration (FDA) has not approved it for this use.
* **Intravenous immunoglobulin (IVIg) infusions.** There is no evidence that using IVIg infusions improves autism spectrum disorder symptoms. The FDA has not approved immunoglobulin products for this use.
* **Other treatment claims.** Treatments that may not be safe or are not proved to help include CBD oil, secretin, antifungal therapy, and clay baths that supposedly remove toxins.

## **Source**

<https://www.mayoclinic.org/diseases-conditions/autism-spectrum-disorder/symptoms-causes/syc-20352928>

<https://www.mayoclinic.org/diseases-conditions/autism-spectrum-disorder/diagnosis-treatment/drc-20352934>

2. ADHD- Attention-deficit/hyperactivity disorder

Attention-deficit/hyperactivity disorder, also called ADHD, is a long-term condition that affects millions of children. It often continues into adulthood. ADHD includes a mix of ongoing problems. These can include having a hard time paying attention, being hyperactive and being impulsive. Children with ADHD also may have low self-esteem and troubled relationships and do poorly in school. Symptoms sometimes lessen with age. Some people never completely outgrow their ADHD symptoms but they can learn strategies to be successful. While treatment won't cure ADHD, it can help a great deal with symptoms. Besides giving education about ADHD, treatment can involve medicines and behavior therapies. Early diagnosis and treatment can make a big difference in results.

## **Symptoms**

The main features of ADHD include not paying attention and being hyperactive and impulsive. ADHD symptoms usually start before age 12. In some children, they can be seen as early as 3 years of age. ADHD symptoms can be mild, moderate or severe. Symptoms need to be seen in two or more settings, such as at home and at school. The symptoms cause problems with development and daily life and may continue into adulthood. ADHD occurs more often in boys than in girls. Behaviors can be different in boys and girls. For example, boys may be more hyperactive and girls may tend to quietly not pay attention.

There are three types of ADHD:

* **Predominately inattentive.** In this type, most symptoms fall under inattention. This means having trouble focusing and staying on a task. It also includes trouble getting and staying organized.
* **Predominately hyperactive and impulsive.** In this type, most symptoms involve being hyperactive and impulsive. Hyperactive means being too active and having too much energy. It may include disruptive behavior. Being impulsive means acting without thinking ahead about the results or effects of behavior.
* **Combined.** This type is a mix of inattentive symptoms and hyperactive and impulsive symptoms. The person meets the criteria for both predominately inattentive and predominately hyperactive and impulsive types of ADHD.

## **Inattentive symptoms**

A child who shows a pattern of inattention may often:

* Fail to pay close attention to details or make careless mistakes in schoolwork.
* Have trouble staying focused in tasks or play.
* Seem not to listen, even when spoken to directly.
* Have a hard time following through on instructions and not finish schoolwork or chores.
* Have trouble organizing tasks and activities.
* Stay away from or not like tasks that need focused mental effort, such as homework.
* Lose items needed for tasks or activities, for example, toys, school assignments, pencils.
* Be easily distracted by other things, thoughts or activities rather than finishing a task.
* Forget to do some daily activities, such as forgetting to do chores.

## **Hyperactive and impulsive symptoms**

A child who shows a pattern of hyperactive and impulsive symptoms may often:

* Fidget with or tap hands or feet, or squirm in the seat.
* Have a hard time staying seated in the classroom or in other situations.
* Be on the go, in constant motion.
* Run around or climb in situations when it's not proper.
* Have trouble playing or doing an activity quietly.
* Talk too much.
* Blurt out answers, interrupting the questioner.
* Have trouble waiting for a turn.
* Interrupt others' conversations, games or activities.

## **Typical development versus ADHD**

Most healthy children are inattentive, hyperactive or impulsive at one time or another. It's typical for preschoolers to have short attention spans and not be able to stick with one activity for long. Even in older children and teenagers, attention span often depends on the level of interest. The same is true of hyperactivity. Young children are naturally energetic. They often are still full of energy long after they've tired their parents. And some children just naturally have a higher activity level than others do. Children should never be classified as having ADHD just because they're different from their friends or siblings. Children who have problems in school but get along well at home or with friends may likely have a concern other than ADHD. The same is true of children who are hyperactive or inattentive at home but whose schoolwork and friendships aren't affected.

## **Causes**

While the exact cause of ADHD is not clear, research efforts continue. Factors that may be involved in the development of ADHD include genetics, the environment or central nervous system conditions at key moments in development.

## **Risk factors**

Risk factors for ADHD may include:

* Having a blood relative, such as a parent or sibling, with ADHD or another mental health condition.
* Being around environmental toxins such as lead, which is found mainly in paint and pipes in older buildings.
* Being born to a parent who used recreational drugs, alcohol or tobacco during pregnancy.
* Being born too early, also called premature birth.

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## **Complications**

ADHD can make life hard for children. Children with ADHD:

* Often have trouble in the classroom, which can lead to failing grades and being judged by other children and adults.
* Tend to have more accidents and injuries of all kinds than do children who don't have ADHD.
* Tend to have poor self-esteem.
* Are more likely to have trouble interacting with and being accepted by peers and adults.
* Are at higher risk of alcohol and drug misuse and other behavior that can cause problems with the law.
* Have a higher risk of suicidal thoughts and suicide.
* Have sleep disorders.

**Conditions often linked with ADHD**

ADHD does not cause other mental health or developmental problems. But children with ADHD are more likely than others to also have conditions such as:

* **Oppositional defiant disorder.** This condition is generally defined as a pattern of negative, defiant and hostile behavior toward people who are in authority.
* **Conduct disorder.** This involves antisocial behavior such as stealing, fighting, destroying property, and harming people or animals.
* **Disruptive mood dysregulation disorder.** This involves irritability and problems handling frustration.
* **Learning disabilities.** These can include problems with reading, writing, understanding and communicating.
* **Substance use disorders.** This involves misuse of drugs, alcohol, marijuana or nicotine.
* **Anxiety.** This results in constant worry and nervousness that affect daily life.
* **Obsessive-compulsive disorder, also called OCD.** OCD is a pattern of unwanted thoughts and fears that lead to repetitive behaviors. These get in the way of daily activities and cause a lot of distress.
* **Mood disorders.** These include depression and bipolar disorder. Bipolar disorder includes depression and manic behavior.
* **Autism spectrum disorder.** This condition is related to brain development. It impacts how a person thinks of and socializes with others.
* **Tic disorders.** These conditions involve repetitive movements or unwanted sounds, called tics, that can't be easily controlled.

## **Prevention**

To help lower your child's risk of ADHD:

* **During pregnancy,** avoid anything that could harm your baby's development before birth. For example, don't drink alcohol, use drugs or smoke cigarettes.
* **Protect your child from exposure to pollutants and toxins,** including cigarette smoke and lead paint.
* **Limit screen time.** Although still not proved, it may be a good idea for young children to limit TV, video games and other screen time.

## **Diagnosis**

In general, a diagnosis of attention-deficit/hyperactivity disorder is made if the core symptoms of ADHD start early in life — before age 12 — and create major problems at home and at school on an ongoing basis. There's no specific test for ADHD. An evaluation can help find out whether symptoms are related to ADHD or another problem. Making a diagnosis will likely include:

* **A medical exam.** This can help rule out other possible causes of symptoms.
* **Information gathering.** This includes reviewing any current medical conditions, personal and family medical history, and school records.
* **Interviews or surveys.** These may include information from family members, teachers or other people who know your child well, such as caregivers, babysitters and coaches. This information can show how your child behaves in different situations.
* **ADHD rating scales.** These help collect and evaluate information about your child.

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## **Diagnosing ADHD in young children**

Signs of ADHD can sometimes be noticed in preschoolers or even younger children. But diagnosing the condition in very young children is harder. That's because developmental conditions such as language delays can be mistaken for ADHD. Children preschool age or younger suspected of having ADHD are more likely to need evaluation by a specialist, such as a psychologist or psychiatrist, speech pathologist, or developmental pediatrician.

## **Other conditions with symptoms like those of ADHD**

Some medical conditions or their treatments may cause symptoms much like those of ADHD. Examples include:

* Learning or language delays.
* Mood disorders such as depression.
* Anxiety disorders.
* Seizure disorders.
* Vision or hearing conditions.
* Autism spectrum disorder.
* Medical conditions or medicines that affect thinking or behavior.
* Sleep disorders.
* Brain injury.

## **Treatment**

Standard treatments for ADHD in children include medicines, behavior therapy, counseling and education services. These treatments can lessen many of the symptoms of ADHD, but they don't cure it. Treatment also can help prevent some complications caused by ADHD. It may take some time to find what works best for your child.

## **Stimulant medicines**

Stimulant medicines, also called psychostimulants, are currently the most prescribed medicines for ADHD. Stimulants appear to boost and balance levels of brain chemicals called neurotransmitters. The medicines help lessen the symptoms of inattention and hyperactivity. They can sometimes help in a short period of time.

Examples of stimulant medicines include:

* **Amphetamines.** These include dextroamphetamine (Dexedrine Spansule), dextroamphetamine-amphetamine (Adderall XR, Mydayis) and lisdexamfetamine (Vyvanse).
* **Methylphenidates.** These include methylphenidate (Concerta, Ritalin, others), dexmethylphenidate (Focalin) and dexmethylphenidate-serdexmethylphenidate (Azstarys).

Stimulant medicines are available in short-acting and long-acting forms. Long-acting patches of methylphenidate (Daytrana) or dextroamphetamine (Xelstrym) are available. They can be worn on the hip.

The right dose varies from child to child, so it may take time to find what works for your child. And the dose may need to be adjusted if side effects occur or as your child matures. Ask your healthcare professional about possible side effects of stimulant medicines.

## **Stimulant medicines and certain health risks**

Some research suggests that using ADHD stimulant medicines with certain heart problems may be a concern. Weight and growth may be affected. Also, the risk of certain mental health symptoms may be higher when using stimulant medicines.

* **Heart conditions.** Stimulant medicines may cause a rise in blood pressure or heart rate. But the higher risk of serious side effects or sudden death is still not proved. The healthcare professional evaluates your child for any heart condition or family history of heart disease before prescribing a stimulant medicine. The healthcare professional also monitors your child when stimulant medicines are used.
* **Appetite changes, weight loss and slowed growth.** Stimulant medicines can affect appetite and cause weigh loss. These medicines also can slightly affect height growth.
* **Mental health conditions.** Stimulant medicines may rarely raise the risk for agitation or irritability. Uncommonly, manic symptoms or losing touch with reality can happen. Contact your child's healthcare professional right away if your child has sudden new or worsening behavior or sees or hears things that aren't real while taking stimulant medicine.

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## **Source**

<https://www.mayoclinic.org/diseases-conditions/adhd/symptoms-causes/syc-20350889>

<https://www.mayoclinic.org/diseases-conditions/adhd/diagnosis-treatment/drc-20350895>

## **3. Spina bifida**

Spina bifida is a condition that occurs when the spine and spinal cord don't form properly. It's a type of neural tube defect. The neural tube is the structure in a developing embryo that later becomes the baby's brain and spinal cord and the tissues that enclose them. Typically, the neural tube forms early in pregnancy and closes by the 28th day after conception. In babies with spina bifida, a portion of the neural tube doesn't close all the way. This affects the spinal cord and bones of the spine.

## **Types**

**Spina bifida occulta**

Occulta means hidden. Spina bifida occulta is the mildest and most common type. This type of spina bifida results in a small separation or gap in one or more of the bones of the spine, called vertebrae. Many people who have spina bifida occulta don't know they have it. It may be found during an imaging test such as an X-ray that is done for another reason.

**Myelomeningocele**

Myelomeningocele is the most serious type. It also is known as open spina bifida. The spinal canal is open along several vertebrae in the lower or middle back. Part of the spinal cord, including the spinal cord's protective covering and spinal nerves, push through this opening at birth, forming a sac on the baby's back. Tissues and nerves usually are exposed. This makes the baby prone to dangerous infections. This type also may cause loss of movement in the legs, and bladder and bowel dysfunction.

**Meningocele**

This is a rare type of spina bifida. In this type, a sac of spinal fluid bulges through an opening in the spine. No nerves are affected and the spinal cord isn't in the fluid sac. Babies with meningocele may have some minor trouble with functioning, including with the bladder and bowels.

## **Symptoms**

Symptoms of spina bifida vary by type and from one person to another.

* **Spina bifida occulta.** Typically, there aren't any symptoms of spina bifida occulta because the spinal nerves aren't involved. But you can sometimes see symptoms on the newborn's skin above the small gap in the spine. You might see a tuft of hair, a small dimple or a birthmark. Sometimes, these skin marks can be symptoms of a spinal cord issue that can be found with MRI or a spinal ultrasound in a newborn.
* **Meningocele.** This type may affect bladder and bowel function.
* **Myelomeningocele.** In this most serious type of spina bifida, the spinal canal remains open along several vertebrae in the lower or middle back. The membranes and part of the spinal cord or nerves protrude at birth, forming a sac. Tissues and nerves usually are exposed, though sometimes skin covers the sac. Babies with this type of spina bifida may have trouble with bladder and bowel function. They also may experience weakness or lack of movement in the legs. Babies may have a buildup of fluid in the brain called hydrocephalus that can put pressure on brain tissue

## **Causes**

The cause of spina bifida is not known. It's thought that a combination of genetic, nutritional and environmental risk factors causes the condition. This includes having a family history of neural tube defects and getting too little folate, also known as vitamin B-9, during pregnancy.

## **Risk factors**

Spina bifida is more common among Hispanic people and white people. Also, female babies are affected more often than male babies. Although healthcare professionals and researchers don't know why spina bifida occurs, they have identified some risk factors:

* **Too little folate in the pregnant person's body.** Folate, the natural form of vitamin B-9, is important to the development of a healthy baby. Folic acid is the synthetic form that's found in supplements and fortified foods. If folate levels are too low, it's known as a deficiency. Folate deficiency increases the risk of spina bifida and other conditions that affect the neural tube.
* **Family history of neural tube defects.** Having one child with a condition that affects the neural tube slightly increases the chance of having another baby with the same condition. The risk increases even more if two previous children have been affected by the condition.

Also, being born with a neural tube defect increases the chance of giving birth to a child with spina bifida. However, most babies with spina bifida are born to parents with no known family history of the condition.

* **Some medicines.** Taking anti-seizure medicines such as valproic acid during pregnancy increases the risk of having a baby with spina bifida. This might happen because the medicines interfere with the body's ability to use folate and folic acid.
* **Diabetes.** Having diabetes that is not well controlled before becoming pregnant increases the risk of having a baby with spina bifida.
* **Obesity.** Obesity at the time of pregnancy also is associated with an increased risk of spina bifida.
* **Increased body temperature.** Some evidence suggests that increased body temperature in the early weeks of pregnancy may increase the risk of spina bifida. A high core body temperature can be caused by a fever or by using a sauna or hot tub.

## **Prevention**

You can greatly reduce your risk of having a baby with spina bifida or other neural tube defects by taking folic acid supplements. Begin taking the supplements at least one month before becoming pregnant and continue taking them through the first trimester of pregnancy.

**Get folic acid first**

Having enough folic acid in your body by the early weeks of pregnancy is critical to prevent spina bifida. But many people don't discover that they're pregnant until this time. For this reason, experts recommend that all people of childbearing age take a supplement of 400 micrograms (mcg) of folic acid a day.

It's also helpful to eat foods that contain folate or have had folic acid added to them, known as fortification. Foods that are fortified with folic acid include:

* Enriched bread.
* Pasta.
* Rice.
* Some breakfast cereals.

Folic acid may be listed on food packages as folate, which is the natural form of folic acid found in foods.

**Planning pregnancy**

Adults who are planning pregnancy or who could become pregnant need to get 400 to 800 mcg of folic acid a day.

The body doesn't absorb folate as easily as it absorbs folic acid, and most people don't get the recommended amount of folate through diet alone. Vitamin supplements that include folic acid are necessary to prevent spina bifida. It's also possible that folic acid may help lower the risk of other conditions that may be present at birth. These conditions include a cleft lip, a cleft palate and some heart conditions.

It's also a good idea to eat a healthy diet that includes foods rich in folate or fortified with folic acid. This vitamin is present naturally in many foods, including:

* Beans and peas.
* Citrus fruits and juices.
* Egg yolks.
* Cow's milk.
* Avocados.
* Dark green vegetables, such as broccoli and spinach.

**When higher doses are needed**

If you have spina bifida or if you've previously given birth to a child with spina bifida, you need extra folic acid before you become pregnant. If you're taking anti-seizure medicines or you have diabetes, you also may benefit from a higher dose of this B vitamin. Check with your healthcare professional before taking additional folic acid supplements.

## **Diagnosis**

Tests before the birth of a baby, known as prenatal screening, can check for spina bifida and other conditions. The tests aren't perfect. Some people who have positive blood tests have babies without spina bifida. Even if the results are negative, there's still a small chance that spina bifida is present. Talk with your healthcare professional about prenatal testing, its risks and what the results mean.

**Blood tests**

Spina bifida can be screened with blood tests during pregnancy, but typically the diagnosis is made with an ultrasound exam.

* **Maternal serum alpha-fetoprotein (MSAFP) test.** For the MSAFP test, a sample of blood is drawn and tested for alpha-fetoprotein (AFP). This is a protein produced by the baby. It's typical for a small amount of AFP to cross the placenta and enter the pregnant parent's bloodstream. But high levels of AFP suggest that the baby may have a neural tube defect such as spina bifida. However, high levels of AFP don't always occur in spina bifida.
* **Test to confirm high AFP levels.** Varying levels of AFP can be caused by other factors such as a wrong estimate of the unborn baby's age or the presence of multiple babies. You may need a follow-up blood test to confirm the results. If levels of AFP are still high, you need further evaluation, including an ultrasound exam.
* **Other blood tests.** Your healthcare professional may perform the MSAFP test with two or three other blood tests. These tests screen for other conditions, such as trisomy 21 syndrome, also known as Down syndrome. They are commonly done with the MSAFP test.

## **Ultrasound**

An ultrasound is the most accurate way to diagnose spina bifida in your baby before delivery. During pregnancy, an ultrasound may be done in the first 11 to 14 weeks of pregnancy, known as the first trimester. Or it may be done at 18 to 22 weeks, known as the second trimester. Spina bifida can be more accurately diagnosed during the second trimester ultrasound exam. This exam is crucial to identify and rule out conditions that may be present at birth. An advanced ultrasound can detect symptoms of spina bifida, such as an open spine or features in the baby's brain. Sometimes ultrasound also can help your healthcare professional see how serious spina bifida is.

## **Amniocentesis**

If the prenatal ultrasound confirms the diagnosis of spina bifida, your healthcare professional may request a test cal led amniocentesis. During this test, a needle is used to remove a sample of fluid from the amniotic sac that surrounds the baby. This exam may be important to rule out genetic diseases. Talk to your healthcare professional about the potential risks of amniocentesis. There's a slight risk of loss of the pregnancy.

## **Treatment**

Spina bifida treatment depends on how serious the condition is in your baby. Spina bifida occulta often doesn't need any treatment at all, but other types of spina bifida do.

**Surgery before birth**

Nerve function in babies with spina bifida can get worse if it's not treated. Prenatal surgery for spina bifida, also known as fetal surgery, takes place before the 26th week of pregnancy. Surgeons open the pregnant person's stomach and then the womb, also known as the uterus. The unborn baby's spinal cord is repaired. Then the surgeon closes the uterus and stomach. Sometimes this procedure can be done less invasively with a special surgical tool called a fetoscope. Instruments are inserted into the uterus through tiny ports to perform surgery on the unborn baby. Research suggests that children with spina bifida who have fetal surgery may have less disability and be less likely to need crutches or other walking devices. Fetal surgery also may lower the risk of hydrocephalus. Ask your healthcare professional whether this procedure may be right for you. Ask about the potential benefits. Also ask about the risks to you and your baby, such as premature delivery and other complications. It's important to have a comprehensive evaluation to determine whether fetal surgery can be done. This specialized surgery should only be done at a healthcare facility with experienced fetal surgery experts, a multispecialty team and neonatal intensive care. Typically, the team includes a fetal surgeon, a pediatric neurosurgeon, a maternal-fetal medicine specialist, a fetal cardiologist and a neonatologist.

**Cesarean birth**

Many babies with myelomeningocele tend to be in a feet-first position, known as breech. Cesarean birth may be a safer way to deliver if your baby is breech or has a large cyst or sac.

**Surgery after birth**

Myelomeningocele requires surgery to close the opening in the baby's back within 72 hours of birth. Early surgery can help lower the risk of infection associated with the exposed nerves. It also may help protect the spinal cord from more trauma. During the procedure, a neurosurgeon places the spinal cord and exposed tissue inside the baby's body and covers them with muscle and skin. At the same time, the neurosurgeon may place a shunt in the baby's brain to control hydrocephalus.

## **Source**

<https://www.mayoclinic.org/diseases-conditions/spina-bifida/symptoms-causes/syc-20377860>

<https://www.mayoclinic.org/diseases-conditions/spina-bifida/diagnosis-treatment/drc-20377865>

## **4. Rett Syndrome**

Rett syndrome is a rare genetic neurological and developmental disorder that affects the way the brain develops. This disorder causes a progressive loss of motor skills and language. Rett syndrome primarily affects females. Most babies with Rett syndrome seem to develop as expected for the first six months of life. These babies then lose skills they previously had — such as the ability to crawl, walk, communicate or use their hands. Over time, children with Rett syndrome have increasing problems with the use of muscles that control movement, coordination and communication. Rett syndrome can also cause seizures and intellectual disabilities. Unusual hand movements, such as repetitive rubbing or clapping, replace purposeful hand use. Although there's no cure for Rett syndrome, potential treatments are being studied. Current treatment focuses on improving movement and communication, treating seizures, and providing care and support for children and adults with Rett syndrome and their families.

## **Symptoms**

Babies with Rett syndrome usually are born after an uncomplicated pregnancy and delivery. Most infants with Rett syndrome seem to grow and behave as expected for the first six months. After that, signs and symptoms start to appear. The most pronounced changes generally occur at 12 to 18 months of age, over a period of weeks or months. Symptoms and their severity vary greatly from child to child.

The main signs and symptoms include:

* **Slowed growth.** Brain growth slows after birth. Smaller than usual head size (microcephaly) is sometimes the first sign that a child has Rett syndrome. As children get older, there is delayed growth in other parts of the body.
* **Loss of movement and coordination abilities.** The first signs often include reduced hand control and a decreasing ability to crawl or walk. At first, this loss of abilities occurs rapidly, and then it continues more gradually. Eventually muscles become weak or stiff, with unusual movement and positioning.
* **Loss of communication abilities.** Children with Rett syndrome typically begin to lose the ability to speak, to make eye contact and to communicate in other ways. They may become disinterested in other people, toys and their surroundings. Some children have rapid changes, such as a sudden loss of language. Over time, children may gradually regain eye contact and develop nonverbal communication skills.
* **Unusual hand movements.** Children with Rett syndrome usually develop repetitive, purposeless hand movements, which differ from child to child. Hand movements may include hand-wringing, squeezing, clapping, tapping or rubbing.

Other signs and symptoms can include:

* **Unusual eye movements.** Children with Rett syndrome tend to have unusual eye movements, such as intense staring, blinking, crossed eyes or closing one eye at a time.
* **Breathing problems.** These include breath holding, rapid breathing (hyperventilation), forcefully blowing out air or saliva, and swallowing air. These problems tend to occur during waking hours. Other breathing disturbances such as shallow breathing or short periods of stopping breathing (apnea) can occur during sleep.
* **Irritability and crying.**Children with Rett syndrome may become increasingly agitated and irritable as they get older. Periods of crying or screaming may begin suddenly, for no apparent reason, and last for hours. Some children may experience fears and anxiety.
* **Other unusual behaviors.** These may include, for example, sudden, odd facial expressions and long bouts of laughter, hand licking, and grasping of hair or clothing.
* **Intellectual disabilities.** Loss of skills may be connected to losing the ability to think, understand and learn.
* **Seizures.** Most people who have Rett syndrome experience seizures at some time during their lives. Multiple seizure types may occur and are associated with changes on an electroencephalogram (EEG).
* **Sideways curvature of the spine (scoliosis).** Scoliosis is common with Rett syndrome. It typically begins between 8 and 11 years of age and progresses with age. Surgery may be required if the curvature is severe.
* **Irregular heartbeat.** This is a life-threatening problem for many children and adults with Rett syndrome and can result in sudden death.
* **Sleep disturbances.** Problems with sleep patterns can include irregular sleep times, falling asleep during the day and being awake at night, or waking in the night with crying or screaming.
* **Other symptoms.** A variety of other symptoms can occur, such as a decreased response to pain; small hands and feet that are usually cold; problems with chewing and swallowing; problems with bowel function; and teeth grinding.

## **Stages of Rett syndrome**

Rett syndrome is commonly divided into four stages:

* **Stage 1: Early onset.** Signs and symptoms are subtle and easily overlooked during the first stage, which starts between 6 and 18 months of age. Stage 1 can last for a few months or a year. Babies in this stage may show less eye contact and start to lose interest in toys. They may also have delays in sitting or crawling.
* **Stage 2: Rapid deterioration.** Starting between 1 and 4 years of age, children lose the ability to perform skills they previously had. This loss can be rapid or more gradual, occurring over weeks or months. Symptoms of Rett syndrome occur, such as slowed head growth, abnormal hand movements, hyperventilating, screaming or crying for no apparent reason, problems with movement and coordination, and a loss of social interaction and communication.
* **Stage 3: Plateau.** The third stage usually begins between the ages of 2 and 10 years, and it can last for many years. Although problems with movement continue, behavior may slightly improve, with less crying and irritability, and there may be some improvement in hand use and communication. Seizures may begin in this stage and generally don't occur before the age of 2.
* **Stage 4: Late motor deterioration.** This stage usually begins after the age of 10 and can last for years or decades. It's marked by reduced mobility, muscle weakness, joint contractures and scoliosis. Understanding, communication and hand skills generally remain stable or improve slightly, and seizures may occur less often.

## **Causes**

Rett syndrome is a rare genetic disorder. Classic Rett syndrome, as well as several variants (atypical Rett syndrome) with milder or more-severe symptoms, occur based on several specific genetic changes (mutations). The genetic changes that cause Rett syndrome occur randomly, usually in the MECP2 gene. Very few cases of this genetic disorder are inherited. The genetic changes appear to result in problems with the protein production critical for brain development. However, the exact cause is not fully understood and is still being studied.

**Rett syndrome in males**

Because males have a different chromosome combination from females, males who have the genetic changes that cause Rett syndrome are affected in devastating ways. Most of them die before birth or in early infancy. A very small number of males have a different genetic change that results in a less destructive form of Rett syndrome. Similar to females with Rett syndrome, these males are likely to live to adulthood, but they're still at risk of a number of intellectual and developmental problems.

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## **Risk factors**

Rett syndrome is rare. The genetic changes known to cause the disease are random, and no risk factors have been identified. In a very small number of cases, inherited factors — for instance, having close family members with Rett syndrome — may play a role.

## **Complications**

Complications of Rett syndrome include:

* Sleep problems that cause significant sleep disruption to the person with Rett syndrome and family members.
* Difficulty eating, leading to poor nutrition and delayed growth.
* Bowel and bladder problems, such as constipation, gastroesophageal reflux disease (GERD), bowel or urinary incontinence, and gallbladder disease.
* Pain that may accompany problems such as gastrointestinal issues or bone fractures.
* Muscle, bone and joint problems.
* Anxiety and problem behavior that may hinder social functioning.
* Needing lifelong care and assistance with activities of daily living.
* Shortened life span. Although most people with Rett syndrome live into adulthood, they may not live as long as the average person because of heart problems and other health complications.

## **Prevention**

There's no known way to prevent Rett syndrome. In most cases, the genetic changes that cause the disorder occur spontaneously. Even so, if you have a child or other family member with Rett syndrome, you may want to ask your health care provider about genetic testing and genetic counselling.

## **Diagnosis**

Diagnosing Rett syndrome involves careful observation of your child's growth and development and answering questions about medical and family history. The diagnosis is usually considered when slowing of head growth is noticed or loss of skills or developmental milestones occurs. For a diagnosis of Rett syndrome, other conditions with similar symptoms must be ruled out.

## **Evaluating other causes for the symptoms**

Because Rett syndrome is rare, your child may have certain tests to determine whether other conditions are causing some of the same symptoms as Rett syndrome. Some of these conditions include:

* Other genetic disorders
* Autism spectrum disorder
* Cerebral palsy
* Hearing or vision problems
* Metabolic disorders, such as phenylketonuria (PKU)
* Disorders that cause the brain or body to break down (degenerative disorders)
* Brain disorders caused by trauma or infection
* Brain damage before birth (prenatal)

What tests your child needs depends on specific signs and symptoms. Tests may include:

* Blood tests
* Urine tests
* Imaging tests such as magnetic resonance imaging (MRI) or computerized tomography (CT) scans
* Hearing tests
* Eye and vision exams
* Brain activity tests (electroencephalograms, also called EEGs)

## **Core symptoms**

Diagnosis of classic Rett syndrome includes these core symptoms, which may start to show up anytime from 6 to 18 months of age:

* Partial or complete loss of purposeful hand skills
* Partial or complete loss of spoken language
* Walking problems, such as difficulty walking or not being able to walk
* Repetitive purposeless hand movements, such as hand-wringing, squeezing, clapping or tapping, putting hands in the mouth, or washing and rubbing movements

Additional symptoms that typically occur with Rett syndrome can support the diagnosis.

Guidelines for diagnosis of atypical Rett syndrome may vary slightly, but the symptoms are the same, with varying degrees of severity.

## **Genetic testing**

If your child's health care provider suspects Rett syndrome after evaluation, genetic testing (DNA analysis) may be needed to confirm the diagnosis. The test requires drawing a small amount of blood from a vein in your child's arm. The blood is then sent to a lab, where the DNA is examined for clues about the cause and severity of the disorder. Testing for changes in the MEPC2 gene confirms the diagnosis. Genetic counseling can help you understand gene changes and their effects.

## **Treatment**

Although there is no cure for Rett syndrome, treatments address symptoms and provide support. These may improve the potential for movement, communication and social participation. The need for treatment and support doesn't end as children become older — it's usually necessary throughout life. Treating Rett syndrome requires a team approach.

Treatments that can help children and adults with Rett syndrome include:

* **Regular medical care.** Management of symptoms and health problems may require a multispecialty team. Regular monitoring of physical changes such as scoliosis, gastrointestinal (GI) issues and heart problems is needed.
* **Medications.** Though medications can't cure Rett syndrome, they may help control some signs and symptoms that are part of the disorder. Medications may help with seizures, muscle stiffness, or problems with breathing, sleep, the GI tract or the heart.
* **Physical therapy.** Physical therapy and the use of braces or casts can help children who have scoliosis or require hand or joint support. In some cases, physical therapy can also help maintain movement, create a proper sitting position, and improve walking skills, balance and flexibility. Assistive devices such as a walker or wheelchair may be helpful.
* **Occupational therapy.** Occupational therapy may improve purposeful use of the hands for activities such as dressing and feeding. If repetitive arm and hand movements are a problem, splints that restrict elbow or wrist motion may be helpful.
* **Speech-language therapy.** Speech-language therapy can help improve a child's life by teaching nonverbal ways of communicating and helping with social interaction.
* **Nutritional support.** Proper nutrition is extremely important for healthy growth and for improved mental, physical and social abilities. A high-calorie, well-balanced diet may be recommended. Feeding strategies to prevent choking or vomiting are important. Some children and adults may need to be fed through a tube placed directly into the stomach (gastrostomy).
* **Behavioral intervention.** Practicing and developing good sleep habits may be helpful for sleep disturbances. Therapies may help improve problem behaviors.
* **Support services.** Early intervention programs and school, social and job-training services may help with integration into school, work and social activities. Special adaptations may make participation possible.

## **Source**

<https://www.mayoclinic.org/diseases-conditions/rett-syndrome/symptoms-causes/syc-20377227>

<https://www.mayoclinic.org/diseases-conditions/rett-syndrome/diagnosis-treatment/drc-20377233>

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# **5. Neurogenetic Disorders**

## **Down Syndrome**

Down syndrome is a genetic condition caused when an unusual cell division results in an extra full or partial copy of chromosome 21. This extra genetic material causes the developmental changes and physical features of Down syndrome. The term "syndrome" refers to a set of symptoms that tend to happen together. With a syndrome, there is a pattern of differences or problems. The condition is named after an English physician, John Langdon Down, who first described it. Down syndrome varies in severity among individuals. The condition causes lifelong intellectual disability and developmental delays. It's the most common genetic chromosomal cause of intellectual disabilities in children. It also commonly causes other medical conditions, including heart and digestive system problems. Better understanding of Down syndrome and early interventions can greatly improve the quality of life for children and adults with this condition and help them live fulfilling lives.

## **Symptoms**

Each person with Down syndrome is an individual. Problems with intellect and development are usually mild to moderate. Some people are healthy while others have serious health issues such as heart problems that are present at birth. Children and adults with Down syndrome have distinct face and body features. Though not all people with Down syndrome have the same features, some of the more common features include:

* Flattened face and small nose with a flat bridge.
* Small head.
* Short neck.
* Tongue that tends to stick out of the mouth.
* Upward slanting eyelids.
* Skin fold of the upper eyelid that covers the inner corner of the eye.
* Small, rounded ears.
* Wide, small hands with a single crease in the palm and short fingers.
* Small feet with a space between the first and second toes.
* Tiny white spots on the colored part of the eye called the iris. These white spots are called Brushfield's spots.
* Short height.
* Poor muscle tone in infancy.
* Joints that are loose and too flexible.

Infants with Down syndrome may be average size, but typically they grow slowly and remain shorter than other children the same age.

## **Developmental delays**

Children with Down syndrome take longer to reach developmental milestones, such as sitting, talking and walking. Occupational therapy, physical therapy, and speech and language therapy can help improve physical functioning and speech.

## **Intellectual disabilities**

Most children with Down syndrome have mild to moderate cognitive impairment. This means that they have problems with memory, learning new things, focusing and thinking, or making decisions that affect their everyday life. Language and speech are delayed. Early intervention and special education services can help children and teens with Down syndrome reach their full potential. Services for adults with Down syndrome can help support living a full life.

## **Causes**

Human cells usually contain 23 pairs of chromosomes. One chromosome in each pair comes from the sperm, the other from the egg. Down syndrome results from an unusual cell division involving chromosome 21. This unusual cell division results in an extra partial or full chromosome 21. This extra genetic material changes how the body and brain develop. It is responsible for the physical features and developmental problems of Down syndrome.

Any one of three genetic changes can cause Down syndrome:

* **Trisomy 21.** About 95% of the time, Down syndrome is caused by trisomy 21. This means the person has three copies of chromosome 21, instead of the usual two copies. The extra chromosome 21 is in all cells in the body. Trisomy 21 results from an unusual cell division during the development of the sperm cell or the egg cell.
* **Mosaic Down syndrome.** This is a rare form of Down syndrome. People with mosaic Down syndrome have only some cells with an extra copy of chromosome 21. This mosaic of typical and changed cells is caused by an unusual cell division after the egg has been fertilized by the sperm.
* **Translocation Down syndrome.** In a small number of people, Down syndrome can occur when a part of chromosome 21 becomes attached, also called translocated, onto another chromosome. This can happen before or at conception. The person has the usual two copies of chromosome 21, but also has extra genetic material from chromosome 21 attached to another chromosome.

**Is it inherited?**

Most of the time, Down syndrome is not passed down in families. The condition is caused by a random unusual cell division. This can happen during the development of the sperm cell or the egg cell or during early development of the baby in the womb. Translocation Down syndrome can be passed from parent to child. But only a small number of children with Down syndrome have translocation and only some of them inherited it from one of their parents. Either parent may have a balanced translocation. The parent has some rearranged genetic material from chromosome 21 on another chromosome, but no extra genetic material. This means the parent has no signs of Down syndrome, but can pass an unbalanced translocation on to children, causing Down syndrome in the children.

## **Risk factors**

Some parents have a greater risk of having a baby with Down syndrome. Risk factors include:

* **Older age.** Chances of giving birth to a child with Down syndrome goes up with age because older eggs have a greater risk of unusual chromosome division. The risk of having a child with Down syndrome increases after a pregnant person is 35 years of age. But most children with Down syndrome are born to pregnant people under age 35 because they have far more babies.
* **Being carriers of the genetic translocation for Down syndrome.** Either parent can pass the genetic translocation for Down syndrome on to their children.
* **Having had one child with Down syndrome.** Both parents who have one child with Down syndrome and parents who have a translocation themselves are at higher risk of having another child with Down syndrome. A genetic counselor can help parents understand the risk of having a second child with Down syndrome.

## **Complications**

Health concerns that result from having Down syndrome can be mild, moderate or severe. Some children with Down syndrome are healthy, while others may have serious health problems. Some health concerns may become more of a problem as the person gets older.

Health concerns can include:

* **Heart problems.** About half the children with Down syndrome are born with some type of heart condition that is present at birth. These heart problems can be life-threatening and may require surgery in early infancy.
* **Problems with the digestive system and digesting food.** Stomach and intestinal conditions occur in some children with Down syndrome. These may include changes in the structure of the stomach and intestines. There is a higher risk of developing digestive problems, such as intestinal blockage, heartburn called gastroesophageal reflux disease (GERD) or celiac disease.
* **Problems with the immune system.** Because of differences in their immune systems, people with Down syndrome are at higher risk of developing autoimmune disorders, some forms of cancer and infectious diseases such as pneumonia.
* **Sleep apnea.** Soft tissue and spinal changes can lead to blockage of the airways. Children and adults with Down syndrome are at greater risk of obstructive sleep apnea.
* **Being overweight.** People with Down syndrome are more likely to be overweight or obese compared with the general population.
* **Spinal problems.** In some people with Down syndrome, the top two vertebrae in the neck may not line up as they should. This is called atlantoaxial instability. The condition puts people at risk of serious injury to the spinal cord from activities that bend the neck too far. Some examples of these activities include contact sports and horseback riding.
* **Leukemia.** Young children with Down syndrome have a higher risk of leukemia.
* **Alzheimer's disease.** Having Down syndrome greatly raises the risk of developing Alzheimer's disease. Also, dementia often occurs at an earlier age than in the general population. Symptoms may begin around age 50.
* **Other problems.** Down syndrome also may also be linked with other health conditions, such as thyroid problems, dental problems, seizures, ear infections, and hearing and vision problems. Conditions such as depression, anxiety, autism and attention-deficit hyperactivity disorder (ADHD) also may be more common.

## **Life expectancy**

Over the years, there have been advances in healthcare for children and adults with Down syndrome. Because of these advances, children born today with Down syndrome are likely to live a longer life than in the past. People with Down syndrome can expect to live more than 60 years, depending on how severe their health problems are.

## **Prevention**

There's no way to prevent Down syndrome. If you're at higher risk of having a child with Down syndrome or you already have one child with Down syndrome, you may want to talk with a genetic counselor before becoming pregnant.

A genetic counselor can help you understand your chances of having a child with Down syndrome. The counselor also can explain the prenatal tests that are available and help explain the pros and cons of testing.

## **Diagnosis**

The American College of Obstetricians and Gynecologists recommends offering the option of screening tests and diagnostic tests for Down syndrome to all who are pregnant, no matter what age.

* **Screening tests** can suggest the likelihood or chances that you're carrying a baby with Down syndrome. But these tests can't tell for sure whether your baby has Down syndrome.
* **Diagnostic tests** can tell for sure whether your baby has Down syndrome.

## **Screening tests during pregnancy**

Screening for Down syndrome is offered as a routine part of care before the baby's birth, called prenatal care. Although screening tests can only tell your risk of carrying a baby with Down syndrome, they can help you make decisions about the need for diagnostic tests.

Screening tests include the first trimester combined test and the integrated screening test. The first trimester means about the first three months of pregnancy.

## **The first trimester combined test**

The first trimester combined test is done in two steps. These include:

* **Blood test.** This blood test measures the levels of pregnancy-associated plasma protein-A (PAPP-A) and the pregnancy hormone known as human chorionic gonadotropin (HCG). Levels of PAPP-A and HCG outside the standard range may indicate a problem with the baby.
* **Nuchal translucency screening test.** During this test, an ultrasound is used to measure a specific area on the back of your baby's neck. When certain conditions caused by chromosome changes are present, more fluid than usual tends to collect in this neck tissue.

Using your age and the results of the blood test and the ultrasound, your healthcare professional or genetic counselor can estimate the risk that your baby has Down syndrome.

## **Integrated screening test**

The integrated screening test is done in two parts during the first and second trimesters of pregnancy. The results are combined to estimate the risk of your baby having Down syndrome.

* **First trimester.** Part one includes a blood test to measure PAPP-A and an ultrasound to measure nuchal translucency.
* **Second trimester.** The quad screen measures your blood level of four substances present in pregnancy: alpha fetoprotein, estriol, HCG and inhibin A.

## **Cell-free DNA testing**

A small amount of DNA is released from the placenta into a pregnant person's bloodstream. This cell-free DNA in the blood can be examined for the extra chromosome 21 material of Down syndrome. For those at risk of having an infant with Down syndrome, the test can be done starting at 10 weeks of pregnancy. If the test is positive, diagnostic testing is usually needed to confirm that the baby has Down syndrome.

## **Diagnostic tests during pregnancy**

If your screening test results are positive or uncertain, or you're at high risk of having a baby with Down syndrome, you might consider more testing to confirm the diagnosis. Your healthcare professional can help you weigh the pros and cons of these tests.

Diagnostic tests that can identify Down syndrome include:

* **Chorionic villus sampling (CVS).** In CVS, cells are taken from the placenta. The cells are used to look at the baby's chromosomes. This test is usually done in the first trimester, between 10 and 14 weeks of pregnancy. The risk of pregnancy loss, called a miscarriage, from a CVS is very low.
* **Amniocentesis.** A sample of the amniotic fluid surrounding the baby in the womb is withdrawn through a needle inserted into the mother's uterus. This sample is then used to look at the chromosomes of the baby. This test is usually done in the second trimester, after 15 weeks of pregnancy. This test also carries a very low risk of miscarriage.

Couples who are being treated for infertility through in vitro fertilization (IVF) who know that they are at increased risk of passing on certain genetic conditions to their children may choose to have the embryo tested for genetic changes before it's implanted in the womb.

## **Diagnostic tests for newborns**

A physical exam is usually enough to identify Down syndrome in an infant in the first 24 hours after birth. If your healthcare professional thinks that your infant has Down syndrome, your healthcare professional orders a test called a chromosomal karyotype to confirm the diagnosis. Using a sample of blood, this test looks at your child's chromosomes. If there's an extra full or partial chromosome 21 in all or some cells, the diagnosis is Down syndrome.

## **Treatment**

Early intervention for infants and children with Down syndrome can make a major difference in improving their quality of life. Because each child with Down syndrome is unique, treatment will depend on your child's needs. Also, as your child gets older and enters different stages of life, your child may need different care or services. For people with Down syndrome, ongoing services, including healthcare, education and life skills support, are important throughout life. Getting routine medical care and treating issues when needed can help keep a healthy lifestyle.

## **Team care**

If your child has Down syndrome, you'll likely rely on a team of specialists that can provide medical care and help your child develop skills as fully as possible. Depending on your child's needs, your team may include some of these experts:

* Primary care pediatrician to coordinate and give routine childhood care.
* Pediatric heart specialist called a cardiologist.
* Pediatric digestive system specialist called a gastroenterologist.
* Pediatric specialist in treating hormone-related conditions called an endocrinologist.
* Developmental pediatrician.
* Pediatric nervous system specialist called a neurologist.
* Pediatric ear, nose and throat (ENT) specialist.
* Pediatric eye doctor called an ophthalmologist.
* Hearing professional called an audiologist.
* Speech and language therapist called a speech-language pathologist.
* Physical therapist.
* Occupational therapist.

You'll need to make important decisions about your child's treatment, services and education. Build a team of healthcare professionals, teachers and therapists you trust. These professionals can help find resources in your area and explain state and federal programs for children and adults with disabilities. You may find it helpful to look for a developmental pediatrician, a specialist with expertise about Down syndrome. Also, some areas have a child Down syndrome specialty clinic that offers a range of services in one place. These experts give special attention to needs and issues that are more common in people with Down syndrome. They can work together with your primary care professional.

## **Adults with Down syndrome**

As your child with Down syndrome becomes an adult, healthcare needs can change. Besides general health screenings recommended for all adults, ongoing healthcare includes evaluation and treatment for conditions that are more common in adults with Down syndrome. You may choose to visit an adult Down syndrome specialty clinic, if available.

Conditions common in adults with Down syndrome include:

* Vision and hearing problems.
* Dental issues.
* Low thyroid levels called hypothyroidism.
* Diabetes.
* Celiac disease and GERD.
* Heart disease, stroke and high cholesterol.
* Obesity.
* Sleep apnea.
* Mood and behavior changes.
* Alzheimer's disease.
* Bone problems, such as spine problems, arthritis and osteoporosis.

In addition to meeting health needs, caring for your adult loved one with Down syndrome includes planning for current and future life needs, such as:

* Living arrangements.
* Social and recreational opportunities.
* Support programs and jobs.
* Financial support.
* Guardianship.

## **Source**

<https://www.mayoclinic.org/diseases-conditions/down-syndrome/symptoms-causes/syc-20355977>

<https://www.mayoclinic.org/diseases-conditions/down-syndrome/diagnosis-treatment/drc-20355983>

## **B. Autonomic Nervous System Disorders**

## **1. Dysautonomia/ Autonomic Dysfunction**

For children and young adults with autonomic dysfunction (AD) and postural orthostatic tachycardia syndrome (POTS), a holistic treatment approach is important to improving functionality and quality of life. We provide multidisciplinary care in the Autonomic Dysfunction (AD) Clinic at Johns Hopkins All Children’s Hospital in St. Petersburg, Florida. Our clinic is one of the only pediatric AD clinics in the Southeastern United States. The autonomic nervous system (ANS) regulates many of our automatic processes, such as blood pressure, breathing, digestion, and other functions we do not consciously think about. It also helps us feel and process sensations like hunger, happiness, anxiety and temperature. Autonomic dysfunction (sometimes called dysautonomia) describes a general state where the ANS is not functioning and communicating between organ systems as expected. Postural orthostatic tachycardia syndrome (POTS) is one of several disorders that fall into the category of autonomic dysfunction. Patients with AD can experience inappropriate heart rates, stomach problems, brain fog, fatigue, dizziness, lightheadedness, temperature intolerance, and other symptoms. Mood disturbances like anxiety and depression, and attention issues, such as ADHD, are also common in AD. AD and POTS can be difficult to diagnose. We have the expertise to recognize and appropriately diagnose our patients so they can receive the care that best meets their needs.

## **What causes autonomic dysfunction?**

We’ve found through our experience and research that there is rarely a singular cause of autonomic dysfunction. This is part of what can make diagnosis and treatment challenging. Anything that causes dysregulation to the autonomic nervous system, such as an infection, an autoimmune response, and/or a traumatic life event, can lead to AD. Additionally, disruption to other organ systems or bodily processes, including emotional disruption, can put stress on the autonomic nervous system and make it more susceptible to dysregulation.

## **How is postural orthostatic tachycardia syndrome (POTS) diagnosed?**

Postural orthostatic tachycardia syndrome (POTS) is one of the most well-known disorders of the autonomic nervous system. In youth, specific criteria are needed for diagnosis including an increase in heart rate of 30-40 beats per minute during performance of orthostatic vital signs (changing positions from lying to sitting to standing) without a significant decrease in blood pressure. However, diagnosis of POTS requires more than just identification of an increase in heart rate with position change. Individuals with POTS will also have abnormalities in other organ systems the autonomic nervous system is involved in regulating. Notably, patients do not have to have a diagnosis of POTS to experience challenging and impairing symptoms of AD.

## **Treatment**

**Consistent hydration and salt**

Consistent and adequate fluid and salt intake has been shown to help with many of the common AD symptoms, such as dizziness and fainting (syncope). We work with patients to set goals for daily fluid (water and electrolytes) intake, as well as salt (sodium) intake, which can be achieved by adding it to food or using salt supplements, such as tablets or electrolyte additives.

**Physical activity**

An individually appropriate exercise regimen performed consistently has been proven to be an essential part of re-integrating the ANS and cardiovascular system, and increasing cardiovascular conditioning is one of the strongest predictors of long-term symptom improvement. Our exercise physiologist works with our patients to develop exercise plans that are right for them.

**Mental wellness**

Many individuals with AD deal with anxiety or other mood disturbance. For some, the mood disturbance was present before other symptoms of AD and for others, the mood challenges may have developed due to living with the complex symptoms of AD. Unfortunately, some individuals with AD and POTS have been told their symptoms are solely due to anxiety or depression. We know this to not be true; however, untreated or under treated mood disturbance will make it difficult to significantly improve ANS functioning and will often worsen symptoms of AD and POTS. We know that the psychological mind and physical body do not operate independently of each other, so coping activities are critical to adjusting to and managing symptoms.

## **Additional treatments as needed**

Once these strategies have been implemented, we may add supplemental therapies, such as medications, that can be helpful in reducing specific symptoms, depending on the patient’s individual needs. It is also important to identify other sources of abnormal input into the autonomic nervous system from other organ systems. Conditions like anemia, thyroid disease, autoimmune disorders, chronic infections, and sleep disorders can stimulate the ANS in abnormal ways, resulting in development of symptoms similar to those of autonomic dysfunction and POTS. Over time, if some of these conditions are not identified and addressed, they can result in changes to how the ANS functions and processes signals. Our team monitors patients for signs of these conditions and can provide referrals to related specialists at Johns Hopkins All Children’s as needed.

## **Source**

<https://www.hopkinsmedicine.org/all-childrens-hospital/services/heart-institute/heart-institute-programs-and-services/pediatric-cardiology-services/autonomic-dysfunction-clinic>

## **2. Postural Orthostatic Tachycardia Syndrome (POTS)**

Postural orthostatic tachycardia syndrome (POTS) is a blood circulation disorder characterized by two factors:

* A specific group of symptoms that frequently occur when standing upright
* A heart rate increase from horizontal to standing (or as tested on a tilt table) of at least 30 beats per minute in adults, or at least 40 beats per minute in adolescents, measured during the first 10 minutes of standing

POTS is diagnosed only when orthostatic hypotension is ruled out and when there is no acute dehydration or blood loss. Orthostatic hypotension is a form of low blood pressure: 20mm Hg drop in systolic or a 10mm Hg drop in diastolic blood pressure in the first three minutes of standing upright.

## **What does POTS stand for?**

* Postural: related to the position of your body
* Orthostatic: related to standing upright
* Tachycardia: increased heart rate
* Syndrome: a group of symptoms

## **Why does heart rate increase excessively with POTS?**

In most patients with POTS, the structure of the heart itself is normal. POTS symptoms arise from a combination of the following:

* Lower amount of blood in the circulation
* Excessive pooling of blood below the level of the heart when upright
* Elevated levels of certain hormones such as epinephrine (also known as adrenaline since it is released by the adrenal glands) and norepinephrine (mainly released by nerves).

When we stand, gravity pulls more blood into the lower half of the body. In a healthy person, to ensure that a sufficient amount of blood reaches the brain, the body activates several nervous system responses. One such response is releasing hormones that help tighten blood vessels and cause a modest increase in heart rate. This leads to better blood flow to the heart and brain. Once the brain is receiving enough blood and oxygen, these nervous system responses settle back to normal. In people with POTS, for unclear reasons that may differ from person to person, the blood vessels don’t respond efficiently to the signal to tighten. As a result, the longer you are upright, the more blood pools in the lower half of your body. This leads to not enough blood returning to the brain, which can be felt as lightheadedness (faintness), brain fog and fatigue. As the nervous system continues to release epinephrine and norepinephrine to tighten the blood vessels, the heart rate increases further. This may cause shakiness, forceful or skipped heartbeats, and chest pain. Some people with POTS can develop hypotension (a drop in blood pressure) with prolonged standing (more than three minutes upright). Others can develop an increase in blood pressure (hypertension) when they stand.

## **Types and Causes of POTS**

The causes of POTS vary from person to person. Researchers don’t entirely understand the origins of this disorder. The classification of POTS is the subject of discussion, but most authorities recognize different characteristics in POTS, which occur in some patients more than others. Importantly, these characteristics are not mutually exclusive; person with POTS may experience more than of these at the same time:

**Neuropathic POTS** is a term used to describe POTS associated with damage to the small fiber nerves (small-fiber neuropathy). These nerves regulate the constriction of the blood vessels in the limbs and abdomen.

**Hyperadrenergic POTS** is a term used to describe POTS associated with elevated levels of the stress hormone norepinephrine.

**Hypovolemic POTS** is a term used to describe POTS associated with abnormally low levels of blood (hypovolemia).

**Secondary POTS** means that POTS is associated with another condition known to potentially cause autonomic neuropathy, such as diabetes, Lyme disease, or autoimmune disorders such as lupus or Sjögren’s syndrome.

## **What are the symptoms of postural orthostatic tachycardia syndrome?**

POTS symptoms vary from person to person and may include:

* Severe and/or long-lasting fatigue
* Lightheadedness with prolonged sitting or standing that can lead to fainting
* Brain fog: trouble focusing, remembering or paying attention
* Forceful heartbeats or heart palpitations (a feeling of the heart pounding or skipping a beat)
* Nausea and vomiting
* Headaches
* Excessive sweating
* Shakiness
* Intolerance of exercise or a prolonged worsening of general symptoms after increased activity
* A pale face and purple discoloration of the hands and feet if the limbs are lower than the level of the heart

POTS symptoms typically get worse:

* In warm environments, such as a hot bath or shower, a hot room or on a hot day
* In situations involving a lot of standing, such as waiting for a bus or when shopping
* If fluid and salt intake have not been adequate, such as after skipping a meal

POTS symptoms may also get worse when you get a common cold or an infection. In severe cases, POTS symptoms can prevent a person from being upright for more than a couple of minutes. This can greatly affect all aspects of personal, school, work and social life.

## **How is POTS diagnosed?**

POTS diagnosis can be complicated because the symptoms can affect a wide range of organ systems, and the most bothersome symptom for each patient may differ. In most instances, symptoms have been present for months before the diagnosis is made. Your doctor will perform a physical exam, order bloodwork and arrange a standing test or a head-up tilt table test to confirm POTS.

## **Tilt Table Test for POTS**

During the tilt table test, you are secured on a table while lying flat. Then the table is raised to an almost upright position. Your heart rate, blood pressure and often blood oxygen and exhaled carbon dioxide levels are measured during this test.

You might have POTS if you meet all three of these criteria:

* Your body produces an abnormal heart rate response to being upright
* Your symptoms worsen when upright
* You don’t develop orthostatic hypotension in the first three minutes of testing

## **Other POTS Tests**

In some cases, other tests are warranted. They may include:

* Valsalva maneuver to test the response of the autonomic nerves that control the heart.
* Quantitative sudomotor axon reflex test (QSART) to measure response of the autonomic nerves responsible for regulating sweating.
* Although less common, your physician may also schedule an MRI and other imaging tests to rule out tumors or other abnormalities.

## **Similar Conditions**

Many conditions share the same symptoms as POTS. POTS can complicate any other chronic health condition, from asthma to inflammatory bowel disease. The vast majority of adolescents and young adults with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) have POTS or related forms of orthostatic intolerance. The intensity of the fatigue, exercise intolerance and other symptoms are greater in those with ME/CFS and POTS than in those with POTS alone. Another condition similar to POTS is inappropriate sinus tachycardia, in which the resting heart rate is usually above 100 beats per minute. Fibromyalgia patients, those with gastrointestinal motility disorders (such as irritable bowel syndrome), excessive sweating (hyperhidrosis) and many other conditions can also develop POTS.

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## **How is POTS treated?**

Treatment for POTS should be tailored to each individual, because the symptoms and underlying conditions may vary widely. Although there is no known cure for POTS, the condition can be managed in most patients with diet, exercise and medications.

## **Postural Orthostatic Tachycardia Syndrome Diet**

The foundation of treating POTS is to drink fluids frequently throughout the day. For most POTS patients, the goal is at least 64-80 ounces (about 2-2.5 liters) a day. You would also need to increase your intake of salty foods and add more salt to your diet with a saltshaker or salt tablets. These dietary modifications help keep water in the bloodstream, which helps more blood reach the heart and the brain. Certain foods or drinks can have an adverse effect on POTS symptoms in some patients. For example, alcohol almost always aggravates POTS. It diverts blood away from the central circulation to the skin and increases loss of fluids through urine. Caffeine can make some people more nervous and lightheaded, but for some it can help improve constriction of blood vessels. Your regular physician or POTS specialist can help you determine how your diet and certain medications could be helping or hindering your treatment.

## **Exercise for Postural Orthostatic Tachycardia Syndrome**

Physical therapy can make a difference for some people with POTS. Because sometimes POTS symptoms can worsen with exercise, physical therapy has to start slowly and advance based on your tolerance rather than a rigid plan. As your blood circulation improves with medications and diet, the exercise intensity may be gradually increased. The goal is to retrain the autonomic nervous system to allow for more exercise, which then helps increase the blood volume. Those who can’t stand upright may start exercising in a horizontal or reclined position. Aquatic therapy may work for some POTS patients due to the water creating pressure around the body. Many experts find that manual physical therapy that addresses issues with nerve tightness and range of motion works as a bridge to build better tolerance of exercise.

## **POTS Medications**

While no single medication is effective for everyone with POTS, most people with frequent symptoms affecting their quality of life need some form of medication. The search for the right medication or combination of medications requires patience and persistence on the part of both physicians and patients. These medications may focus on:

* Improving blood volume
* Helping the kidneys retain sodium (e.g., fludrocortisone)
* Reducing heart rate or blocking the effect of adrenal hormones on the heart (e.g., beta blockers)
* Improving blood vessel constriction (e.g., midodrine)

## **Source**

<https://www.hopkinsmedicine.org/health/conditions-and-diseases/postural-orthostatic-tachycardia-syndrome-pots>

C. **CLASSIC CREUTZFELDT-JAKOB DISEASE**

• Classic CJD is a quick-moving, always fatal disease that occurs worldwide.

• It affects the brain and causes dementia and other problems.

• CJD mostly occurs in older adults.

• There is no treatment or cure.

• It usually leads to death within a year from when symptoms begin.

## **Overview**

CJD is caused by a prion, a type of infectious protein. Prions trigger normal proteins in the body to misfold, leading to CJD. CJD causes dementia and other neurologic problems. Once symptoms begin, it can lead to death in months to a year. Classic CJD occurs worldwide in older adults, with the average age in the late 60s. Very few cases occur in people who are younger than 30 years old. CJD occurs worldwide with an estimated rate of about one to two illness per one million population members per year. In recent years in the United States, about 500-600 cases have been reported per year.

## **Types**

There are three main types of CJD infection:

**Sporadic**

The vast majority of all CJD cases reported (about 85 percent) are called sporadic. These types of cases occur when prion proteins already in the body misfold for some unknown reason. The result is disease that breaks down the brain's functions. Some cases are fatal within a few months of the first symptoms, and most are fatal within a year.

**Familial**

About 5-15 percent of CJD cases occur because the person has inherited a mutation in the prion protein gene. A person with CJD with a first-degree relative (parent, sibling, or child) who also has the disease would have familial CJD.

**Iatrogenic**

Iatrogenic cases are caused by contact with prions in a healthcare setting or due to biological products. There have been six known CJD cases caused by surgical or medical equipment contaminated with prions is used on another patient.

People who received prion-contaminated human growth hormone prior to 1978 may also develop iatrogenic CJD. Even 50 years later, cases are still being identified.

Finally, cases can occur in people who receive a transplant of specific materials. These include corneal (eye) grafts or dura mater (a membrane in the brain and spinal cord) grafts. If the donor had CJD that was not discovered before the donation, recipients can contract CJD.

## **How it affects your body**

People with CJD suffer from dementia. Other symptoms may include trouble walking, sudden jerky movements, and visual disturbances. CJD patients usually die within one year following the onset of symptoms.

## **Testing and diagnosis**

Healthcare providers can diagnose an illness as a suspect case based on:

• Symptoms and course of illness

• Tests of a person's spinal fluid

• Magnetic Resonance Imaging (MRI), a brain scan

• EEG, a test of electrical activity in the brain.

The only way to confirm CJD is through testing brain tissue from a biopsy or an autopsy.

## **Treatment and Prognosis**

Classic CJD is always fatal, usually within a few months. There is unfortunately no therapy that will slow or stop the progression of disease. So, treatment involves supportive care to make the patient more comfortable.

## **Similar diseases**

Though they have very similar names, CJD and variant CJD (vCJD) are not the same disease. Both are prion diseases. However, variant CJD is tied to eating meat from cows infected with bovine spongiform encephalopathy (sometimes called Mad Cow Disease). CJD, sometimes called "classic CJD" to avoid confusion, mostly occurs sporadically. Unlike variant CJD, classic CJD is not caused by any other prion disease.

In general, classic CJD affects people older than 55 while vCJD cases were younger, with an average age of 28. Classic CJD progresses much more quickly, causing death in an average of 4-5 months, while vCJD averages more than a year.

## **Source**

Centers for Disease Control and Prevention (2024) Classic Creutzfeldt-Jakob Disease. Available at: https://www.cdc.gov/creutzfeldt-jakob/about/index.html (Accessed: 12 June 2025).

# **CREUTZFELDT-JAKOB DISEASE**

## **Prevention**

Creutzfeldt-Jakob disease (CJD) is a rare and fatal condition that affects the brain. It causes brain damage that worsens rapidly over time.

## **Symptoms of CJD**

Symptoms of CJD include:

• loss of intellect and memory

• changes in personality

• loss of balance and co-ordination

• slurred speech

• vision problems and blindness

• abnormal jerking movements

• progressive loss of brain function and mobility

Most people with CJD will die within a year of the symptoms starting, usually from infection.

This is because the immobility caused by CJD can make people with the condition vulnerable to infection.

## **What causes CJD?**

CJD appears to be caused by an abnormal infectious protein called a prion. These prions accumulate at high levels in the brain and cause irreversible damage to nerve cells.

While the abnormal prions are technically infectious, they're very different from viruses and bacteria.

For example, prions aren't destroyed by the extremes of heat and radiation used to kill bacteria and viruses, and antibiotics or antiviral medicines have no effect on them.

## **Types of CJD**

There are 4 main types of CJD.

**Sporadic CJD**

Sporadic CJD is the most common type.

The precise cause of sporadic CJD is unclear, but it's been suggested that a normal brain protein changes abnormally ("misfolds") and turns into a prion. Most cases of sporadic CJD occur in adults aged between 45 and 75. On average, symptoms develop between the ages of 60 and 65. Despite being the most common type of CJD, sporadic CJD is still very rare, affecting only 1 or 2 people in every million each year in the UK. In 2020, there were 131 recorded deaths from sporadic CJD in the UK.

**Variant CJD**

Variant CJD (vCJD) is likely to be caused by consuming meat from a cow that had bovine spongiform encephalopathy (BSE, or "mad cow" disease), a similar prion disease to CJD. Since the link between variant CJD and BSE was discovered in 1996, strict controls have proved very effective in preventing meat from infected cattle entering the food chain. But the average time it takes for the symptoms of variant CJD to occur after initial infection (the incubation period) is still unclear. The incubation period could be very long (more than 10 years) in some people, so those exposed to infected meat before the food controls were introduced can still develop variant CJD. The prion that causes variant CJD can also be transmitted by blood transfusion, although this has only happened 5 times in the UK. In 2020, there were no recorded deaths from variant CJD in the UK.

**Familial or inherited CJD**

Familial CJD is a very rare genetic condition where one of the genes a person inherits from their parent (the prion protein gene) carries a mutation that causes prions to form in their brain during adulthood, triggering the symptoms of CJD. It affects about 1 in every 9 million people in the UK. The symptoms of familial CJD usually first develop in people when they're in their early 50s. In 2020, there were 6 deaths from familial CJD and similar inherited prion diseases in the UK.

**Iatrogenic CJD**

Iatrogenic CJD is where the infection is accidentally spread from someone with CJD through medical or surgical treatment. For example, a common cause of iatrogenic CJD in the past was growth hormone treatment using human pituitary growth hormones extracted from deceased individuals, some of whom were infected with CJD. Synthetic versions of human growth hormone have been used since 1985, so this is no longer a risk. Iatrogenic CJD can also occur if instruments used during brain surgery on a person with CJD aren't properly cleaned between each surgical procedure and are reused on another person. But increased awareness of these risks means iatrogenic CJD is now very rare. In 2020, there was 1 death from iatrogenic CJD in the UK caused by receiving human growth hormone before 1985.

## **How CJD is treated**

There's currently no cure for CJD, so treatment aims to relieve symptoms and make the affected person feel as comfortable as possible. This can include using medicine such as antidepressants to help with anxiety and depression, and painkillers to relieve pain. Some people will need nursing care and assistance with feeding.

## **Symptoms-Creutzfeldt-Jakob disease**

The pattern of symptoms can vary depending on the type of Creutzfeldt-Jakob disease (CJD). In sporadic CJD, the symptoms mainly affect the workings of the nervous system (neurological symptoms) and these symptoms rapidly worsen in the space of a few months. In variant CJD, symptoms that affect a person's behaviour and emotions (psychological symptoms) will usually develop first. These are then followed by neurological symptoms around 4 months later, which get worse over the following few months. Familial CJD has the same sort of pattern as sporadic CJD, but it often takes longer for the symptoms to progress – usually around 2 years, rather than a few months. The pattern of iatrogenic CJD is unpredictable, as it depends on how a person became exposed to the infectious protein (prion) that caused CJD.

## **Initial neurological symptoms**

Initial neurological symptoms of sporadic CJD can include:

• difficulty walking caused by problems with balance and co-ordination

• slurred speech

• numbness or pins and needles in different parts of the body

• dizziness

• vision problems, such as double vision

• hallucinations (seeing or hearing things that aren't really there)

## **Initial psychological symptoms**

Initial psychological symptoms of variant CJD can include:

• severe depression

• withdrawal from family, friends and the world around you

• anxiety

• irritability

• difficulty sleeping (insomnia)

## **Advanced neurological symptoms**

Advanced neurological symptoms of all forms of CJD can include:

• loss of physical co-ordination, which can affect a wide range of functions, such as walking, speaking and balance (ataxia)

• muscle twitches and spasms

• loss of bladder control (urinary incontinence) and bowel control (bowel incontinence)

• blindness

• swallowing difficulties (dysphagia)

• loss of speech

• loss of voluntary movement

## **Advanced psychological symptoms**

Advanced psychological symptoms of all forms of CJD include:

• loss of memory, which is often severe

• problems concentrating

• confusion

• feeling agitated

• aggressive behaviour

• loss of appetite, which can lead to weight loss

• paranoia

• unusual and inappropriate emotional responses

## **Final stages**

As the condition progresses to its final stages, people with all forms of CJD will become totally bedridden. They often become totally unaware of their surroundings and require around-the-clock care. They also often lose the ability to speak and can't communicate with their careers. Death will inevitably follow, usually either as a result of an infection, such as pneumonia, or respiratory failure, where the lungs stop working and the person is unable to breathe. Nothing can be done to prevent death in these circumstances. Advancements in end of life care (the treatment of incurable conditions) mean that people with CJD often have a peaceful death.

## **Causes-Creutzfeldt-Jakob disease**

Creutzfeldt-Jakob disease (CJD) is caused by an abnormal infectious protein in the brain called a prion. Proteins are molecules made up of amino acids that help the cells in our body function. They begin as a string of amino acids that then fold themselves into a 3-dimensional shape. This "protein folding" allows them to perform useful functions within our cells. Normal (harmless) prion proteins are found in almost all body tissues, but are at the highest levels in brain and nerve cells. The exact role of normal prion proteins is unknown, but it's thought they may play a role in transporting messages between certain brain cells. Mistakes sometimes occur during protein folding and the prion protein can't be used by the body. Normally, these misfolded prion proteins are recycled by the body, but they can build up in the brain if they aren't recycled.

## **How prions cause CJD**

Prions are misfolded prion proteins that build up in the brain and cause other prion proteins to misfold as well. This causes the brain cells to die, releasing more prions to infect other brain cells. Eventually, clusters of brain cells are killed and deposits of misfolded prion protein called plaques may appear in the brain. Prion infections also cause small holes to develop in the brain, so it becomes sponge-like. The damage to the brain causes the mental and physical impairment associated with CJD, and eventually leads to death. Prions can survive in nerve tissue, such as the brain or spinal cord, for a very long time, even after death.

## **Types of CJD**

The different types of CJD are all caused by a build-up of prions in the brain. But the reason why this happens is different for each type.

**Sporadic CJD**

Even though sporadic CJD is very rare, it's the most common type of CJD, accounting for around 8 in every 10 cases. It's not known what triggers sporadic CJD, but it may be that a normal prion protein spontaneously changes into a prion, or a normal gene spontaneously changes into a faulty gene that produces prions. Sporadic CJD is more likely to occur in people who have specific versions of the prion protein gene. At present, nothing else has been identified that increases the risk of developing sporadic CJD.

**Variant CJD**

There's clear evidence that variant CJD (vCJD) is caused by the same strain of prions that causes bovine spongiform encephalopathy (BSE, or "mad cow" disease). In 2000, a government inquiry concluded that the prion was spread through cattle that were fed meat-and-bone mix containing traces of infected brains or spinal cords. The prion then ended up in processed meat products, such as beef burgers, and entered the human food chain. Strict controls have been in place since 1996 to prevent BSE entering the human food chain, and the use of meat-and-bone mix has been made illegal. It appears not everyone who's exposed to BSE-infected meat will go on to develop vCJD. Almost all definite cases of vCJD occurred in people with a specific version (MM) of the prion protein gene, which affects how the body makes a number of amino acids. It's estimated up to 4 in 10 of the UK population have this version of the gene. Cases of vCJD peaked in the year 2000, in which there were 28 deaths from this type of CJD. There have been no confirmed deaths from 2017 to 2020. Some experts believe that the food controls have worked and further cases of vCJD will continue to decline, but this doesn't rule out the possibility that other cases may be identified in the future. It's also possible for vCJD to be transmitted by blood transfusion, although this is very rare and measures have been put in place to reduce the risk of it happening. We don't know how many people in the UK population could develop vCJD in the future and how long it'll take for symptoms to appear, if they ever will. A study published in October 2013 that tested random tissue samples suggested around 1 in 2,000 people in the UK population may be infected with vCJD, but show no symptoms to date.

**Familial or inherited CJD**

Familial or inherited CJD is a rare form of CJD caused by an inherited mutation (abnormality) in the gene that produces the prion protein. The altered gene seems to produce misfolded prions that cause CJD. Everyone has 2 copies of the prion protein gene, but the mutated gene is dominant. This means you only need to inherit 1 mutated gene to develop the condition. So if 1 parent has the mutated gene, there's a 50% chance it will be passed on to their children. As the symptoms of familial CJD don't usually begin until a person is in their 50s, many people with the condition are unaware that their children are also at risk of inheriting this condition when they decide to start a family.

**Iatrogenic CJD**

Iatrogenic CJD (iCJD) is where the infection is spread from someone with CJD through medical or surgical treatment. Most cases of iatrogenic CJD have occurred through the use of human growth hormone to treat children with restricted growth. Between 1958 and 1985, thousands of children were treated with the hormone, which at the time was extracted from the pituitary glands (a gland at the base of the skull) of human corpses. A minority of those children developed CJD, as the hormones they received were taken from glands infected with CJD. Since 1985, all human growth hormone in the UK has been artificially manufactured, so there's now no risk. But a small number of people exposed before 1985 are still developing iCJD. A few other cases of iCJD have occurred after people received transplants of infected dura mater (tissue that covers the brain) or came into contact with surgical instruments that were contaminated with CJD. This happened because prions are tougher than viruses or bacteria, so the normal process of sterilising surgical instruments had no effect. Once the risk was recognised, the Department of Health tightened the guidelines on organ donation and the reuse of surgical equipment. As a result, cases of iCJD are now very rare.

## **BSE ('MAD COW' DISEASE)**

Bovine spongiform encephalopathy (BSE), also known as "mad cow" disease, is a relatively new disease that first occurred in the UK during the 1980s. One theory about why BSE developed is that an older prion disease that affects sheep, called scrapie, may have mutated. The mutated disease may have then spread to cows that were fed meat-and-bone mix from sheep containing traces of this new mutated prion.

**Is CJD contagious?**

In theory, CJD can be transmitted from an affected person to others, but only through an injection or consuming infected brain or nervous tissue. There's no evidence that sporadic CJD is spread through ordinary day-to-day contact with those affected or by airborne droplets, blood or sexual contact. But in the UK, variant CJD has been transmitted on 5 occasions by blood transfusion.

## **Diagnosis-Creutzfeldt-Jakob disease**

A diagnosis of Creutzfeldt-Jakob disease (CJD) is usually based on medical history, symptoms and a series of tests. A neurologist (a doctor who specialises in conditions of the nervous system) will carry out the tests to rule out other conditions with similar symptoms, such as Alzheimer's disease, Parkinson's disease, or a brain tumour. The only way to confirm a diagnosis of CJD is to examine the brain tissue by carrying out a brain biopsy or, more commonly, after death in a post-mortem examination of the brain.

## **Tests for CJD**

A clinical neurologist will rule out other conditions with similar symptoms. They'll also check for some common signs of CJD by carrying out the following tests:

• an MRI brain scan – uses strong magnetic fields and radio waves to produce a detailed image of the brain, and can show up abnormalities particular to CJD

• an EEG – records brain activity and may pick up abnormal electrical patterns seen in sporadic CJD

• a lumbar puncture – a procedure where a needle is inserted into the lower part of the spine to draw out a sample of cerebrospinal fluid (which surrounds your brain and spinal cord) so it can be tested for a certain protein that indicates you may have CJD

• a prototype blood test for variant CJD has also been developed by the prion unit at the Medical Research Council (MRC) and is available through the National Prion Clinic

• tonsil biopsy – a small piece of tissue can be taken from the tonsils and checked for the abnormal prions found in variant CJD (they're not present in other types of CJD)

• genetic test – a simple blood test to find out whether you have a mutation (fault) in the gene that produces normal protein; a positive result may indicate familial (inherited) prion disease

Brain biopsy

During a brain biopsy, a surgeon drills a tiny hole into the skull and removes a small piece of brain tissue using a very thin needle.

It's carried out under general anaesthetic, which means the person will be unconscious during the procedure.

As a brain biopsy carries the risk of causing brain damage or seizures (fits), it's only performed in a few cases where there's a concern that someone doesn't have CJD but some other treatable condition.

## **Treatment-Creutzfeldt-Jakob disease**

There's no proven cure for Creutzfeldt-Jakob disease (CJD), but clinical studies are under way at the National Prion Clinic to investigate possible treatments.

At present, treatment involves trying to keep the person as comfortable as possible and reducing symptoms with medicines.

For example, psychological symptoms of CJD, such as anxiety and depression, can be treated with sedatives and antidepressants, and muscle jerks or tremors can be treated with medicines like clonazepam and sodium valproate.

Any pain experienced can be relieved using powerful opiate-based painkillers.

Advance directive

Many people with CJD draw up an advance directive (also known as an advance decision).

An advance directive is where a person makes their treatment preferences known in advance in case they can't communicate their decisions later because they're too ill.

Issues that can be covered by an advance directive include:

• whether a person with CJD wants to be treated at home, in a hospice, or in a hospital once they reach the final stages of the condition

• what type of medicines they'd be willing to take in certain circumstances

• whether they'd be willing to have a feeding tube if they were no longer able to swallow food and liquid

• whether they're willing to donate any of their organs for research after they die (the brains of people with CJD are particularly important for ongoing research)

• if they lose lung function, whether they'd be willing to be resuscitated by artificial means – for example, by having a breathing tube inserted into their neck

Your care team can provide more advice about making an advance directive.

Treating symptoms of CJD

• treating ataxia (loss of physical co-ordination)

• treating urinary incontinence (loss of bladder control)

• bowel incontinence (loss of bowel control)

• treating dysphagia (swallowing difficulties)

• dystonia (muscle spasms and stiffness)

• blindness or vision loss

Care and support in the advanced stages of CJD

As CJD progresses, people with the condition will need significant nursing care and practical support.

As well as help with feeding, washing and mobility, some people may also need help peeing. A tube inserted into the bladder to drain urine (a catheter) is often required.

Many people will also have problems swallowing, so they may have to be given nutrition and fluids through a feeding tube.

It may be possible to treat someone with CJD at home, depending on the severity and progression of their condition.

Caring for someone with CJD can be distressing and difficult to cope with, so many carers prefer to use the specialist services of a hospital or hospice.

## **Prevention-Creutzfeldt-Jakob disease**

Although Creutzfeldt-Jakob disease (CJD) is very rare, the condition can be difficult to prevent.

This is because most cases occur spontaneously for an unknown reason (sporadic CJD) and some are caused by an inherited genetic fault (familial CJD).

Sterilisation methods used to help prevent bacteria and viruses spreading also aren't completely effective against the infectious protein (prion) that causes CJD.

But tightened guidelines on the reuse of surgical equipment mean that cases of CJD spread through medical treatment (iatrogenic CJD) are now very rare.

There are also measures in place to prevent variant CJD spreading through the food chain and the supply of blood used for blood transfusions.

Protecting the food chain

Since the link between bovine spongiform encephalopathy (BSE, or "mad cow" disease) and variant CJD was confirmed, strict controls have been in place to stop BSE entering the human food chain.

These controls include:

• a ban on feeding meat-and-bone mix to farm animals

• the removal and destruction of all parts of an animal's carcass that could be infected with BSE

• a ban on mechanically recovered meat (meat residue left on the carcass that's pressure-blasted off the bones)

• testing on all cattle more than 30 months old (experience has shown that infection in cattle under 30 months of age is rare, and even cattle that are infected haven't yet developed dangerous levels of infection)

Blood transfusions

In the UK, there have been 5 cases where variant CJD has been transmitted by blood transfusion.

In each case, the person received a blood transfusion from a donor who later developed variant CJD.

3 of the 5 recipients went on to develop variant CJD, while the other 2 recipients died before developing variant CJD but were found to be infected following a post-mortem examination.

It's not certain whether the blood transfusion was the cause of the infection, as those involved could have contracted variant CJD through dietary sources.

Nevertheless, steps were taken to minimise the risk of the blood supply becoming contaminated.

These steps include:

• not allowing people potentially at risk from CJD to donate blood, tissue or organs (including eggs and sperm for fertility treatments)

• not accepting donations from people who have received a blood transfusion in the UK since 1980

• removing white blood cells, which may carry the greatest risk of transmitting CJD, from all blood used for transfusions

Source

NHS (2024) Creutzfeldt-Jakob disease (CJD) - Prevention. Available at: https://www.nhs.uk/conditions/creutzfeldt-jakob-disease-cjd/prevention/ (Accessed: 12 June 2025).

# **PARANEOPLASTIC SYNDROMES**

## **Overview**

What is a paraneoplastic syndrome?

A paraneoplastic syndrome is a set of signs and symptoms that can occur when you have cancer. The symptoms develop when a malignant tumor causes changes in your body that aren’t directly caused by the cancer itself. The tumor may secrete a hormone or protein that affects a particular body system. Often with paraneoplastic syndromes, your immune system releases antibodies to destroy the tumor. During this process, the antibodies also damage healthy cells (autoimmune response). Paraneoplastic syndromes can affect multiple body systems and organs, including your nervous system, endocrine system (hormones), kidneys, bones, joints, skin and blood, etc. Often, the symptoms of a paraneoplastic syndrome are the first signs of cancer.

## **Who is affected by paraneoplastic syndromes?**

You’re more likely to have a paraneoplastic syndrome if you’re middle-aged or older and you have lung, lymphatic, ovarian or breast cancer. The same factors that increase your cancer risk can increase your chances of developing a paraneoplastic syndrome.

## **How common are paraneoplastic syndromes?**

About 8% to 20% of people with cancer develop paraneoplastic syndromes.

## **What cancers are associated with paraneoplastic syndromes?**

Anyone with a cancerous tumor can develop a paraneoplastic syndrome. The types of cancer most commonly associated with paraneoplastic syndromes are:

• Breast cancer.

• Stomach cancer.

• Leukemia.

• Lymphoma.

• Lung cancer (especially small-cell lung cancer).

• Ovarian cancer.

• Pancreatic cancer.

• Prostate cancer.

• Kidney cancer.

• Testicular cancer.

## **Symptoms and Causes**

## **What causes paraneoplastic syndromes?**

Some cancerous tumors secrete substances, like hormones or proteins, that cause certain organs in your body to work atypically. As a result, you may experience symptoms that wouldn’t occur without the tumor. These substances can permanently damage an organ or system without treatment. Often, paraneoplastic syndromes occur because your body’s immune system mistakenly harms healthy tissue. Your immune system makes a substance called antibodies. Antibodies protect you from disease by identifying and destroying abnormal cells, like cancer cells. Sometimes, the signals get crossed, and antibodies attack healthy cells and tissue instead, causing symptoms associated with a paraneoplastic syndrome.

## **What are the symptoms of paraneoplastic syndromes?**

Symptoms of paraneoplastic syndromes vary depending on the organ systems affected. In more than half of cases (60%), people experience symptoms before receiving a cancer diagnosis. Identifying a paraneoplastic syndrome early can help your healthcare provider diagnose cancer in its early stages when it’s easiest to treat.

Common symptoms of a paraneoplastic syndrome include:

• Fever.

• Loss of appetite and weight.

• Night sweats.

Paraneoplastic syndromes that affect particular organs or body systems may cause system-specific symptoms. Nervous system Paraneoplastic syndromes affecting your central nervous system (brain, spinal cord) and your peripheral nervous system (nerves outside of your brain and spinal cord) may cause:

• Dizziness.

• Double vision.

• Speech difficulty.

• Memory loss.

• Seizures.

• Muscle weakness.

• Reduced reflexes, sensation or coordination.

• Loss of feeling in your arms and legs.

Endocrine system

Paraneoplastic syndromes affecting your endocrine system may cause:

• Fatigue.

• High blood pressure.

• Muscle weakness.

• Nausea and vomiting.

• Unexplained weight gain.

Joints, bones and muscles (rheumatologic)

Paraneoplastic syndromes affecting your joints, bones, muscles and connective tissue may cause:

• Arthritis.

• Joint pain, swelling or stiffness.

Skin

Paraneoplastic syndromes affecting your skin may cause:

• Itching.

• Flushing (redness).

• Thickened skin.

• Benign (noncancerous) skin growths.

What are the types of paraneoplastic syndromes?

There are several paraneoplastic syndromes, including those that affect your nervous system, endocrine system, joints, blood, skin, kidneys, etc.

Nervous system paraneoplastic syndromes

Examples include:

• Cerebellar degeneration.

• Dysautonomia.

• Encephalitis.

• Encephalomyelitis.

• Lambert-Eaton myasthenic syndrome (LEMS).

• Myasthenia gravis (MG).

• Myelopathy.

• Neuromyotonia.

• Opsoclonus-myoclonus syndrome.

• Neuropathy (peripheral neuropathy).

• Stiff-person syndrome.

Endocrine system paraneoplastic syndromes

Examples include:

• Cushing’s syndrome.

• Hypercalcemia.

• Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH).

Rheumatic paraneoplastic syndromes

Examples include:

• Eosinophilic fasciitis.

• Erythromelalgia.

• Hypertrophic osteoarthropathy.

• Palmar fasciitis.

• Paraneoplastic polyarthritis.

Blood paraneoplastic syndromes

Examples include:

• Paraneoplastic erythrocytosis.

• Paraneoplastic thrombocytosis.

Skin paraneoplastic syndromes

Examples include:

• Acanthosis nigricans.

• Dermatomyositis.

• Leukocytoclastic vasculitis.

• Paraneoplastic pemphigus.

• Sweet syndrome.

• Paraneoplastic glomerulonephritis is a paraneoplastic syndrome that affects your kidneys.

## **Diagnosis and Tests**

## **How are paraneoplastic syndromes diagnosed?**

Your healthcare provider will diagnose paraneoplastic syndromes with a medical history, physical exam and several tests.

• Neurological exam: Paraneoplastic syndromes often affect your nervous system, impacting your brain and muscle function. Your provider may ask you to perform specific tasks to check how your nervous system functions. They’ll want to judge any change in your abilities related to strength, memory and coordination.

• Imaging: Your provider may use imaging tests such as CT scans, MRIs and ultrasounds to look for a tumor that may be causing symptoms.

• Blood tests: Blood tests can reveal suspicious findings that suggest a tumor or that confirm you have antibodies linked to paraneoplastic syndromes. Blood tests can also help your provider rule out other conditions that may be causing your symptoms, like an infection, a hormone disorder or a metabolic disorder.

• Spinal tap: In some instances, your provider may perform a spinal tap (lumbar puncture) to test your cerebrospinal fluid for signs of antibodies attacking healthy cells. During a spinal tap, your provider inserts a needle into your lower back to withdraw a fluid sample. Later, your healthcare provider will test the liquid for antibodies.

## **Management and Treatment**

## **How are paraneoplastic syndromes managed or treated?**

Your healthcare provider will treat the underlying cancer that’s causing your symptoms. They’ll also work to manage your symptoms to decrease any damage to your body’s organs or systems. Therapies used to manage paraneoplastic syndromes include:

• Corticosteroids: Medications, such as cortisone or prednisone, that reduce inflammation (swelling).

• Immunosuppression: Drugs that decrease your body’s immune response. The drug therapies your provider prescribes will be tailored to your paraneoplastic syndrome.

• Intravenous immunoglobulin: Treatment that destroys the harmful antibodies causing the syndrome. During the procedure, your provider gives you a shot of healthy antibodies that destroy the harmful ones.

• Plasmapheresis: A procedure that decreases the number of antibodies by removing plasma (liquid) from your blood. The plasma contains the antibodies that damage healthy tissue.

• Physical and speech therapy: Muscle exercises that can help improve functions like speech and movement. You may need this therapy if you have a neurological paraneoplastic syndrome.

## **Outlook / Prognosis**

## **What can I expect if I have a paraneoplastic syndrome?**

Your prognosis mostly depends on your cancer. In some instances, paraneoplastic syndromes cause mild, temporary symptoms. In others, paraneoplastic syndromes cause severe symptoms that must be managed long-term.

Talk to your healthcare provider about how your stage of cancer and response to treatment will affect your prognosis.

## **What complications are associated with paraneoplastic syndromes?**

You may experience a broad range of complications, some of which are minor and some that may be more serious or even life-threatening without treatment. Your healthcare provider will discuss potential complications and treatment options with you.

## **Source**

Cleveland Clinic (2022) Paraneoplastic Syndromes: Symptoms, Types & Treatment. Available at: <https://my.clevelandclinic.org/health/diseases/17938-paraneoplastic-syndromes> (Accessed: 12 June 2025).

## **Neurologic Complications of Cancer and its Treatment**

The central nervous system (CNS) and peripheral nervous system (PNS) are very susceptible to cancer and its treatment. The most direct involvement of the nervous system manifests in the development of primary brain and spinal cord tumors. Many cancers exhibit a propensity toward spread to the CNS, and brain metastases are common problems seen in malignancies such as lung, breast, and melanoma. Such spread may involve the brain or spine parenchyma or the subarachnoid space. In the PNS, spread is usually through direct infiltration of nerve roots, plexi, or muscle by neighboring malignancies. In some cases, cancer has sudden, devastating effects on the nervous system: epidural spinal cord compression or cord transection from pathologic fractures of vertebra involved by cancer; increased intracranial pressure from intracranial mass lesion growth and edema; and uncontrolled seizure activity as a result of intracranial tumors (status epilepticus), which are neuro-oncologic emergencies. The best known indirect or remote effects of cancer on the nervous system are the neurologic paraneoplastic syndromes. Cancer can also result in a hypercoagulable state causing cerebrovascular complications. Treatment of cancer can have neurologic complications. The commonest of these complications are radiation-induced injury to the brain, spine, and peripheral nerves and chemotherapy-induced peripheral neuropathy. The suppressant effect of cancer and its treatment on the body’s immune system can result in infectious complications within the nervous system.

## **Introduction**

Cancer often affects the nervous system and may result in significant neurologic morbidity and mortality. These effects may be direct—with direct cancer involvement of the brain, spine, or peripheral nervous system (PNS)—or indirect as in paraneoplastic neurologic syndromes. Treatment of cancer can also damage the nervous system. This article discusses the effects of systemic cancers and their treatment on the nervous system, although the complications of primary brain and spine tumors are not discussed.

## **Epidemiology**

Cancer takes a huge toll on the human race. In 2009, it was estimated that almost 1.5 million new cases of cancer would be diagnosed in the United States, resulting in more than half a million deaths . Many of these patients are expected to develop complications in sites distant to the original tumor location. The nervous system is very susceptible to such complications. In a prospective evaluation in a large cancer center, slightly less than half (45.2%) of more than 800 cancer patients seen in neurologic consultation during a 6-month period had metastases to the nervous system .

## **Direct Cancer Complications**

## **Brain Metastases**

Metastases to the brain from systemic malignancies are the most common direct form of nervous system involvement by cancer. It is estimated that in the United States as many as 200,000 cases of brain metastases (BMs) are diagnosed each year . The most common cancers resulting in BMs are lung, breast, and melanoma. BMs are rare in prostate cancer and quite uncommon in cancers of the female reproductive tract . Gastrointestinal cancers and hematologic malignancies are less likely to result in parenchymal brain metastases. Leukemia and lymphoma are more likely to result in leptomeningeal metastases. Most brain metastases develop in the cerebral hemispheres (80%) in accordance with higher blood flow to the supratentorial compartment .

## **Clinical Presentation and Diagnosis**

Seizures, headaches, and focal neurologic deficits, depending on location, usually lead to the diagnosis of brain metastases. Examination may reveal focal neurologic deficits such as focal weakness, numbness, or language problems. Head CT scans will reveal single or multiple discreet areas of contrast enhancement and associated vasogenic edema. Brain MRI may uncover metastases too small for CT resolution and prove more effective in defining size and location of lesions.

## **Treatment**

Treatment of brain metastases includes symptomatic therapy for seizures and vasogenic edema. Although there are several anticonvulsants available, nonenzyme-inducing newer generation anticonvulsants are tolerated better and pose less risk of drug–drug interactions than older enzyme-inducing agents. Examples of nonenzyme-inducing anticonvulsants include levetiracetam, lacosamide, and pregabalin. Although seizure prophylaxis is still used, no evidence supports this practice. However, hemorrhagic metastases are more likely to cause seizures and prophylaxis may be prudent in these situations. Vasogenic edema is treated with corticosteroids, usually dexamethasone. Depending on the degree of vasogenic edema and the presence or absence of mass effect, midline shift, and herniation of brain structures, high doses of corticosteroids (dexamethasone 12–24 mg daily) may be necessary. Short-term complications include hyperglycemia, psychoses, and weight gain. Once patients are controlled on symptomatic therapy, more directed therapy for the metastastic lesions is planned. The most important modalities of treatment are surgery and radiation therapy. Chemotherapy has a modest role in the management of this cancer complication. Radiation therapy includes whole brain radiation therapy (WBRT) and stereotactic radiosurgery (SRS). The best treatment for patients with BMs depends on several factors. Age, performance status, and the presence of systemic metastatic disease emerged as the most important factors in a recursive portioning analysis (RPA) of the Radiation Therapy Oncology Group (RTOG) trials that demonstrated benefit from WBRT . The prognostic classes from this analysis were defined as follows. RPA class I is characterized by younger than 65 years old and Karnofsky Performance Status greater than 70; no extracranial disease and primary tumor not progressive; and median survival of 7.1 months. RPA class II is characterized by patients other than those in RPA class I or III and median survival of 4.2 months. RPA class III is characterized by Karnofsky Performance Status less than 70 and median survival of 2.3 months. Tumor histology and number of brain metastases are also important factors in determining treatment. The following guidelines apply given current available data. WBRT is indicated in RPA class I and II patients with single metastasis after surgical resection and as palliative therapy in patients with a poor performance status (RPA class III). WBRT may also be used in RPA class I and II patients with multiple metastases but emerging data indicate that SRS alone as a first-line intervention may be preferable in these patients given the early development of cognitive dysfunction with WBRT .

## **Leptomeningeal Metastases**

The largest autopsy series to date indicates that 8% of patients with cancer have leptomeningeal seeding at autopsy. This complication is seen mostly in small cell lung cancer , breast cancer , and melanoma. In hematologic and lymphoid malignancies, non-Hodgkin’s lymphoma (NHL) and acute nonlymphocytic leukemia account for most cases.

## **Clinical Presentation, Pathophysiology, and Diagnosis**

Patients present with evidence of spinal cord or nerve root involvement, cranial neuropathies, or symptoms and signs referable to the cerebral hemispheres Patients may present with limb weakness, pain referable to the involved nerve roots or bladder, and bowel disturbances in spine and sacral root involvement. Examination confirms weakness, sensory loss, and changes in deep tendon reflexes. Cranial nerve VI, III, and IV dysfunction result in diplopia and optic nerve involvement causes visual blurring. The fifth cranial nerve is also involved in some cases. Extraocular nerve abnormalities or facial sensory deficits are present. Multiple cranial neuropathies in a patient with cancer are highly indicative of leptomeningeal metastases (LM).

## **Cerebral Symptoms**

Cancer cells gain access to the cerebrospinal fluid (CSF) in three ways. The most common route is hematogenous, but direct extension from cancer sites contiguous to the central nervous system (CNS) and entry via perineural and perivascular spaces is also possible . The diagnosis of LM should be confirmed with CSF examination. This study also helps exclude other causes of cerebral, cranial nerve, and spinal/nerve root dysfunction in patients with cancer such as chronic (opportunistic) infections. The presence of malignant cells in the CSF is diagnostic; additionally high protein, low glucose, elevated opening pressures, and increased white cell count support the diagnosis when cytology is negative. A repeat CSF analysis increases the yield in such cases and should be performed. Flow cytometry and polymerase chain reaction techniques are useful in cases of NHL with suspected lymphomatous meningitis . Before CSF analysis, neuroimaging should be performed. MRI of the brain and entire spine is indicated in such cases to help stage the extent of LM and guide management. LM is often associated with increased intracranial pressure and concomitant parenchymal metastatic disease with mass effect. In such cases, a lumbar puncture (LP) for CSF analysis may be contraindicated. MRI imaging may demonstrate LM enhancement, which may be linear or more nodular. Cranial nerve enhancement, especially in the presence of cranial neuropathies, is highly indicative of LM disease. MRI sensitivity is low (<50%) although it is considered more sensitive than CT. CSF flow analysis in patients with LM is another important diagnostic and prognostic tool. Abnormal CSF flow is common in LM and 111indium-diethylenetriamine pentaacetic acid or 99Tc macroaggregated albumin tracers may be used to define the extent and location of such disturbances.

## **Treatment**

Treatment is palliative, and the patient and family should be made aware of this fact, as well as of prognostic implications. Surgery, radiation, and chemotherapy play a role, as the multidisciplinary care of these patients is very important. Patients with LM may require ventriculoperitoneal shunting for hydrocephalus. Surgery is also required for placement of Ommaya reservoirs for administration of intrathecal chemotherapy. Radiation therapy may have significant palliative value in patients with LM. Radionuclide studies may demonstrate CSF flow abnormalities. Radiation therapy to areas of CSF block has been shown to be of benefit . Patients who have cerebral LM and concomitant brain metastases are treated with WBRT. Finally, focused radiation to bulky tumor involving the spine can help stabilize or improve neurologic function. Chemotherapy has shown activity in LM, especially lymphomatous and leukemic meningitis. The responses and palliation seen with chemotherapy in solid tumors are less robust but some benefit can also be derived in these cases. Most commonly, chemotherapy is administered via an Ommaya reservoir. DepoCyt (Enzon; New Brunswick, NJ) is considered the drug of choice for such administration. DepoCyt is sustained-release cytarabine (a liposomal formulation) and has shown benefit in patients with lymphomatous meningitis and solid tumor LM . In lymphomatous meningitis, Glantz et al. demonstrated high response rates and better quality of life when liposomal cytarabine was compared with standard cytarabine. In solid tumors, the response rates noted to DepoCyt were similar to what had been reported for methotrexate administration . However, the less-frequent administration of DepoCyt compared with methotrexate was felt to benefit the patient. This drug is also less toxic to the CNS than methotrexate. Direct spinal fluid injection of methotrexate, cytarabine, thiotepa, etoposide, topotecan, and rituximab have all been used in patients with LM. Chamberlain provided a very recent and comprehensive review on this subject.

## **Spine Metastases**

Spine metastases are common in cancer patients. The most common form of involvement is metastases to the bone of the spine with or without encroachment on the epidural space. This represents up to 98% of cases of spine metastases. Metastases to the parenchyma of the spinal cord are uncommon. Epidural spinal cord compression (ECSS) is a consequence of metastases to the vertebral bone with encroachment on the epidural space. Cancers most likely to result in ESCC are breast, lung, and prostate cancer, but NHL, melanoma, and adenocarcinoma of unknown primary were also noted in ESCC in a retrospective series of patients . The pathophysiology mainly involves hematogenous dissemination of cancer cells to the vertebral body.

## **Clinical Presentation and Diagnosis**

The presenting features of ESCC depend on the level of involvement but pain is essentially universal in such patients. Pain may be reflective of nerve root involvement and have radicular or axial features. Thoracic spine involvement is most common so that mid-back pain, bilateral lower extremity weakness, and sensory disturbances tend to be the most common presenting symptoms. Patients may also develop bowel and bladder symptoms. Such dysfunction may be very prominent in compression occurring at the level of the conus medullaris or cauda equina. The diagnosis of ESCC is clinical. However, neuroimaging is required to confirm the level of compression, assess for the presence of other levels of bone and epidural involvement, and determine the presence of LM. Chamberlain and Kormanik [27] found involvement at more than one level in 29% of cases within their series. In the occasional patient who cannot undergo MRI, CT or CT myelography can also be diagnostic.

## **Treatment**

Supportive care includes high-dose steroid therapy, usually with dexamethasone to reduce edema. This often helps with pain control and stabilization and improvement of neurologic function. We usually use immediate intravenous administration of 10 mg of dexamethasone followed by 6 mg every 4 hours. Pain control is very important and specific pain therapy besides corticosteroids is almost always necessary. For definitive therapy, early liaison with a radiation oncologist and a neurosurgeon are key to success. The neurosurgeon may use vertebroplasty or kyphoplasty for pain relief in collapsed vertebrae, corpectomy to resect tumor in the vertebral body and decompress the spine (anterior decompression), or a laminectomy (posterior decompression). Radiation therapy is the most common therapeutic modality available to patients with ESCC and may be the only source of palliation for patients who are not surgical candidates. The various radiation therapy modalities include stereotactic radiotherapy, intensity modulated radiotherapy (IMRT), and conventional external beam radiation therapy. Conventional fractionated external beam radiation therapy is most commonly administered. Radiation therapy is administered one level above and below the site of compression to reduce the risk of recurrence from epidural tumor extension. Success with radiation is highly dependent on tumor histology (eg, melanoma and renal cell carcinoma are radioresistant).

## **Peripheral Nervous System Metastases**

The peripheral nervous system may be directly involved by cancer. Metastases to individual nerves is rare; more commonly noted is direct infiltration or compression of nerve roots, plexi (cervical, brachial, or lumbosacral), individual nerves, or muscles.

## **Clinical Presentation and Diagnosis**

Cancer may infiltrate a nerve plexus causing pain and sensorimotor deficits in one limb. Examination in such cases may reveal evidence of partial or complete injury to the plexus. In the case of the lumbosacral plexus, injury to the entire plexus from infiltrating neoplasm is seen in 18% of cases, upper plexus involvement (L1-L4) is seen in 31% and the lower plexus (L4-S1) in 51%. Patients with extensive lumbosacral plexus involvement would have weakness of thigh flexion, eversion and adduction, as well as leg extension. Sensory loss over the genitoinguinal region, thigh, and medical aspect of the lower leg as well as loss of the patellar reflex would also be expected signs in such cases. Similarly, involvement of the cervical or brachial plexus by cancer may cause typical findings on examination; the reader is referred to comprehensive texts on this subject. Weakness or numbness may also result from individual nerve involvement. Metastases to a nerve are rare but involvement of nerves from bone, soft tissue, or CSF metastases is not. The numb chin syndrome (NCS) caused by malignant infiltration of the mental or inferior alveolar nerve is one example. Patients present with orofacial numbness involving the chin or lower lip. The most common cause is bone involvement by cancer and nerve compression, although some cases are associated with leptomeningeal metastases . Appropriate diagnostic studies such as a Panorex radiograph of the jaw and cerebrospinal analysis often determines the etiology.

Neuroimaging with MRI is the diagnostic modality of choice for most cases of tumor-related compression neuropathy or plexopathy. It may show direct infiltration of a nerve plexus or a mass compressing an individual nerve. Neuroimaging of plexus lesions may be difficult to interpret, especially when previous radiation therapy to the area (eg, brachial plexus) raises the possibility of radiation plexopathy. In such cases, electrodiagnostic studies with electromyography and nerve conduction studies may be very helpful. This differential is discussed later under nervous system complications from radiation therapy (see below). Treatment of PNS involvement by cancer includes steroids and analgesics to reduce pain. Pain relief may be accomplished using tricyclic or other antidepressants such as duloxetine as well as anticonvulsants. Pregabalin and gabapentin are often the first choices. More definitive therapy includes both radiation and chemotherapy, depending on the underlying histology and site of involvement.

**Indirect Complications of Cancer**

**Paraneoplastic Syndromes**

Neurologic paraneoplastic syndromes (NPNS) are disorders caused by cancer without direct infiltration, metastases, or compression of the CNS or PNS structure involved as determined by clinical presentation. The mechanism is autoimmune and recognition of these syndromes is very important as it may lead to an early cancer diagnosis. Additionally, these syndromes are treatable by control of the underlying malignancy and immunomodulatory therapies. A classic paraneoplastic syndrome, Lambert-Eaton myasthenic syndrome, is discussed and summarized, along with other well-recognized syndromes,

Pathology and clinical presentation of the paraneoplastic syndromes

| **Paraneoplastic Syndrome** | **Antibody** | **Clinical presentation** | **Usual cancer association** | **Pathology** | **Treatment**[**a**](https://pmc.ncbi.nlm.nih.gov/articles/PMC3637950/#TFN1) |
| --- | --- | --- | --- | --- | --- |
| Paraneoplastic  cerebellar  degeneration | Anti-Hu, anti-  Yo, anti-Tr,  anti-Ri | Gait disturbance,  nausea, dizziness,  diplopia | SCLC, ovarian,  breast,  Hodgkin’s  lymphoma | Purkinje cell loss,  dentate, and olivary  nuclei degeneration | Plasmapheresis and  IVIg |
| Paraneoplastic  limbic encephalitis | Anti-Hu, anti-  Ma-2, anti-  NMDAR | Seizures, memory loss,  insomnia | SCLC | Loss of neurons, limbic  microglial  proliferation,  perivascular and  interstitial  inflammation | Corticosteroids and  IVIg or plasma  exchange |
| Paraneoplastic  encephalomyelitis  and associated  paraneoplastic  phenomena | Anti-Hu, anti-  CV-2/  CRMP5, anti-  Ma proteins,  anti-NMDAR | Brainstem: diplopia,  dysphagia, dysarthria;  autonomic: orthostatic  hypotension,  arrhythmias | SCLC, thymoma,  testicular (germ  cell), non-SCLC,  ovarian terato-  mas |  | Plasma exchange, IVIg  or cyclophosphamide  (for anti-CV2/  CRMP5 and anti-  NMDAR) |
| Paraneoplastic stiffman  syndrome | Anti-  amphiphysin | Generalized rigidity | Breast, SCLC | Motor neurons and  interneurons anterior  horn cell loss | IVIG, benzodiazepines |
| Paraneoplastic  sensorimotor  neuropathy | ? | Motor and sensory loss  in extremities | Multiple, usually  advanced | Axonal degeneration or  demyelination | Corticosteroids, IVIg |
| Paraneoplastic  sensory  neuronopathy | Anti-Hu | Sensory loss (limbs,  trunk, face) | SCLC | Neuronal degeneration | Steroids |
| Paraneoplastic  opsoclonusmyoclonus | ? | Falls, ataxia,  opsoclonus, | Neuroblastoma  (children),  SCLC (adults) |  | Corticosteroids, IVIg,  ACTH; adults: IVIg |
| Lambert-Eaton  myasthenic  syndrome | Anti P/Q-type  VGCC | Weakness, fatigue,  autonomic  dysfunction | SCLC | P/Q type VGCC  antibody | Immunotherapy, 3,4-  DAP, pyridostigmine,  guanidine |
| Polymyositis and  dermatomyositis  [ | ? | Proximal myopathy,  neck flexion  weakness, eyelid rash  in DM | Ovarian, breast,  lung,  gastrointestinal | Immune-mediated  vasculopathy, muscle  necrosis with elevated  creatine kinase | Corticosteroids, IVIg  and chemotherapy  (eg, azathioprine) |
| Myeloma associated  sensorimotor  neuropathy | ? | Neuropathy (sensory,  sensori-motor) | Multiple myeloma |  | None specific |

Refers to specific treatment modalities. In most cases treatment of the underlying tumor is usually the most effective treatment of the paraneoplastic syndrome.

ACTH—adrenocorticotropic hormone; CRMP5—collapsin response mediator protein 5; IVIg—intravenous immunoglobin; NDMR—N-methyl-D-aspartate receptor; SCLC—small cell lung cancer; VGCC—voltage-gated calcium channel.

# **LAMBERT-EATON MYASTHENIC SYNDROME**

Patients with small cell lung cancer (SCLC) sometimes present with a neuromuscular syndrome consisting of fluctuating weakness, fatigue, and autonomic dysfunction caused by a defect in acetylcholine release from the presynaptic terminal at the neuromuscular junction. In turn, this is caused by antibodies to presynaptic voltage-gated calcium channels (VGCC). Examination confirms limb (especially lower extremity) weakness and hyporeflexia. Electromyography (EMG)/NCS show a decremental response to low-frequency repetitive nerve stimulation and an incremental response to higher frequency stimulation. Detection of VGCC antibodies in the presence of such findings should prompt an aggressive search for an underlying malignancy, usually SCLC. Treatment includes 3,4-diaminopyridine to improve acetylcholine release, pyridostigmine, and guanidine. Immunomodulatory therapy with intravenous Ig and plasmapheresis, as well as long-term steroid therapy, may also be necessary .

## **Cerebrovascular Complications of Cancer**

## **Ischemic Stroke**

Cancer patients are at risk for cerebrovascular complications for three reasons: 1) cancer and its treatment result in disorders of coagulation; 2) cancer may directly affect blood vessels; and 3) infections in individuals who are immunocompromised may result in secondary stroke . Cancer induces a hypercoagulable state. Tumors produce procoagulant factors, such as tissue factor and cancer procoagulant, and interaction of these with the host blood vessels result in abnormal clotting. Additionally, there is some downregulation of anticoagulant pathways, activated protein C resistance, or an imbalance between tissue factor expression and tissue factor plasminogen inhibitor . The normal coagulation balance tips in favor of a hypercoagulable state resulting in localized thrombosis or even a chronic disseminated intravascular coagulation (DIC) in cancer patients. As recently reviewed by Rogers, there are two thrombotic syndromes in cancer that may result in cerebrovascular disease: nonbacterial thrombotic endocarditis (NBTE) and cerebral intravascular thrombosis without NBTE. Graus et al. described nonbacterial thrombotic endocarditis as the most common cause of stroke in cancer patients. This complication—often seen in patients with lung or gastrointestinal mucin-producing adenocarcinoma—results from cardiac vegetations that embolize to main cerebral arteries, often the middle cerebral. As a result, patients present with typical stroke symptoms such as aphasia, focal weakness, and numbness. Heparin has been recommended in such cases, as well as consideration for valve replacement if the patient is felt to have a reasonable prognosis. In non-NBTE cerebral thrombosis, the process of thrombosis is more widespread and affects smaller blood vessels than in NBTE cases; heparin is also recommended in such cases. Because the process is multifocal, more generalized presentations (eg, encephalopathy) than in NBTE are common. There are also documented cases of embolic stroke from tumor cell embolization and tumors can cause direct compression of blood vessels, especially venous sinuses. In such cases, direct management of the tumor is the only therapy possible. Venous sinus thrombosis occurring in cancer patients is yet another manifestation of hypercoagulability. Diagnosis is confirmed with magnetic resonance venography and this complication is treated with anticoagulation.

## **Hemorrhagic Stroke**

Intracranial blood may be seen in patients with hemorrhagic metastases. Melanoma, lung cancer, and renal cell cancer are the most likely metastatic histologies to be hemorrhagic. Such cases may present with seizures, headache, and are diagnosed and managed in a similar manner to nonhemorrhagic metastases. The occurrence of a consumptive coagulopathy (DIC) may result in intracranial hemorrhage in hematologic malignancy.

**Neurologic Complications of Cancer Treatment**

**Nervous System Complications from Radiation Therapy**

The central and peripheral nervous system may be affected by radiation therapy. In the brain and spinal cord this is believed to be caused by a combination of vascular damage and damage to glia, mainly oligodendrocytes. The timing of radiation complications has led to a classification of such injury and this is helpful in predicting reversibility. During or immediately after radiation therapy, patients may develop acute injury, usually manifest mainly by headache, nausea, and vomiting. Injury to capillaries and leakage with edema are the likely mechanism and this injury is steroid-responsive. Complications occurring beyond a month and up to 6 months from completion of radiation therapy are termed early-delayed injury. In these cases, patients may develop drowsiness, fatigue, and cognitive problems (somnolence syndrome). In addition, patients may also develop brain MRI changes suggestive of tumor progression. These changes are reversible and improvement may be hastened by steroids. Conversely, late injury is associated with permanent diffuse white matter changes (leukoencephalopathy), focal areas of necrosis, and cognitive impairment. This is irreversible and the most severe forms result in a severe dementia and, ultimately, death. The most important risk factors in the development of leukoencephalopathy and cognitive impairment are older age, radiation dose, brain volume receiving radiation, and combination with chemotherapy . The combination of radiation therapy with methotrexate for treatment of primary CNS lymphoma is the best example of this; very severe forms of leukoencephalopathy may be seen in patients treated with such combinations especially when methotrexate is administered concomitantly with radiation. Radiation-induced cognitive impairment presents a spectrum of severity ranging from mild impairment to frank dementia . Neuroimaging shows white matter abnormalities and in cases associated with dementia, significant atrophy may be noted. There are no effective therapies although psychostimulants have been advocated for the attention and memory problems associated with mild to moderate cognitive dysfunction . Focal areas of necrosis in the brain raise concern about possible tumor progression because the appearance can be very similar with heterogenous enhancement and lesional areas consistent with necrosis. Surgery may be necessary when such areas are symptomatic and to exclude tumor progression requiring further treatment.

**Spinal Cord Injury**

In the spinal cord, radiation-induced damage may be early-delayed, which is almost always reversible and late-delayed, which is more likely to be permanent . Because the former improves spontaneously, specific treatment is not really necessary. Leung et al. noted Lhermitte’s sign in 121 (10.3%) of 1171 nasopharyngeal carcinoma patients treated with radiation. They also noted that median development time for such signs was 3 months and that it was more likely to happen when the dose to the cervical cord exceeded 48.9 Gy. In rare instances, late-delayed radiation myelopathy has been noted to improve clinically and on imaging. However, in most cases, deficits persist or progress. Patients may present with weakness and sensory loss in the legs and a paraparesis and sensory level are confirmed on examination; another presentation is with Brown-Sequard syndrome. Problems with bladder and bowel control are also possible. MRI of the spinal cord may show increase signal at the level affected and even contrast enhancement . Although anticoagulation and hyperbaric oxygen are used occasionally, corticosteroids are the most commonly used therapy that may result in improvement.

| **Complication** | **Typical drugs causing complication** | **Clinical syndrome** | **Treatment and prevention** | **Prognosis** |
| --- | --- | --- | --- | --- |
| Peripheral and  cranial  neuropathy | Vinca alkaloids (tubulin  binding) vincristine,  vinblastine | Sensorimotor neuropathy  (axonal) | Drug withdrawal | Usually good with  discontinuation |
|  | Platinum compounds (DNA  crosslink formation) (cisplatin,  carboplatin, oxaliplatin) | Sensory neuropathy;  vestibulo-cochlear toxicity  with cisplatin (hearing loss,  dizziness, ataxia, vertigo) | Amifostine, carbamazepine to treat  oxaliplatin neuropathy; calcium  gluconate, magnesium sulfate, and  oxcarbazepine prophylaxis for  oxaliplatin neuropathy | Variable for  cisplatin; good  with treatment  for oxaliplatin |
|  | Taxanes: paclitaxel, docetaxel  (inhibition of microtubule  function) | Sensory neuropathy  (numbness, tingling) | Vitamin E and N-acetyl carnitine | Good with drug  discontinuation |
|  | Macrolide antibiotic:  ixabepilone (tubulin binding) | Sensory neuropathy  (numbness, tingling) | Discontinue drug or reduce dose | Good with  treatment |
|  | Thalidomide (antiangiogenesis) | Sensory neuropathy |  |  |
|  | Bortezomib (proteosome  inhibitor) | Distal sensory axonal  neuropathy | Discontinue drug/reduce dose | Good with treatment |
| Stroke | Bevacizumab; imatinib | Hemorrhagic or ischemic  stroke (rare) | Discontinue drug | Variable |
| Seizures | Cisplatin (DNA crosslinks);  cytosine arabinoside  (pyrimidine antimetabolite) | Seizures | Discontinue drug/reduce dose | Good with drug  discontinuation |
|  | Cyclophosphamide | Seizures | Discontinue drug/reduce dose | Good with drug  discontinuation |
|  | Nelarabine (purine nucleoside  analog) | – | Discontinue drug/reduce dose | Good with drug  discontinuation |
| Myelopathy | Cisplatin (DNA crosslinks);  Ara-C (pyrimidine antimetabolite);  MTX (dihydrofolate  reductase inhibitor) | Lhermitte’s sign with  cisplatin; motor, sensory  and bowel/bladder  dysfunction with Ara-C and  MTX. | Discontinue drug/reduce dose | Good with  treatment (drug  discontinuation) |
| Aseptic  meningitis | MTX (dihydrofolate reductase  inhibitor) | Headache, neck stiffness,  back pain and fever  following intrathecal  injection. | Discontinue drug and reduce dose;  corticosteroids | Usually good |
| Encephalopathy | Ifosfamide (alkylating agent) | Confusion, hallucinations,  drowsiness | Discontinue drug; benzodiazepines  may hasten recovery | Good with drug  withdrawal |
|  | Methotrexate (dihydrofolate  reductase inhibitor) | Acute mental status change,  seizures within 24 hours of  high-dose i.v administration | Discontinue drug | Good with drug  withdrawal |
| Cerebellar  syndrome | Cytosine arabinoside  (pyrimidine antimetabolite) | Ataxia, nystagmus, and  dysarthria | Prevention with avoidance of high-dose | Variable; may or  may not reverse  completely |

**Peripheral Nerve Involvement: Plexus and Individual Nerve Damage from Radiation Therapy**

The brachial and lumbosacral plexi may also be involved in the radiation fields for treatment of breast and lung cancers and pelvic tumors respectively. As with CNS involvement, the tempo of the injury helps predict the prognosis. Thus, early-delayed brachial plexopathy occurring in the first few months after treatment usually improves whereas late-delayed injury is a progressive, disabling disorder. In both cases, sensorimotor deficits in the limb supplied by the plexus are typical. EMG and nerve conduction studies are helpful, especially in helping distinguish brachial plexopathy of the late-delayed type from tumor recurrence with infiltration of the plexus. Myokymic discharges on EMG and the absence of severe pain favors radiation damage as the likely diagnosis. Neuroimaging with dedicated MRI of the plexus may show a mass involving the plexus; nonuniform, asymmetric diffuse, or focal enlargement especially eccentric masses with contrast enhancement favor neoplastic infiltration. In postradiation plexopathy, a more uniform symmetric swelling of the plexus is noted. In difficult cases, plexus biopsy may be necessary. Treatment of radiation-induced plexopathy includes steroids and pain management combined with physical therapy.

**Nervous System Complications from Chemotherapy**

Chemotherapy agents can result in toxicity to the nervous system. Peripheral neuropathy is the most common complication noted with a variety of chemotherapy agents.

**Ara-C—cytosine arabinoside; MTX—methotrexate**.

This table is not comprehensive of all neurotoxic agents used in cancer therapy and their complications. It is meant to provide examples of some of the most common neurologic toxicities seen with cancer therapy and the common agents causing such toxicity. The reader is referred to comprehensive texts on this subject. Some chemotherapy drugs cause more than one type of neurotoxicity (eg, cisplatin may cause peripheral and cranial neuropathies, seizures, and myelopathy). Neurotoxicity may be seen with newer agents and is not restricted to conventional chemotherapy. Neurotoxicity may be exacerbated by the administration of more than one neurotoxic drug or by combination with radiation. The best example of the latter is methotrexate leukoencephalopathy, commonly seen as a delayed complication of high-dose or intrathecal methotrexate with radiation administered before or during such therapy. This syndrome has been seen in adults treated for primary CNS lymphoma and children treated for leukemia with such combinations. Gradual cognitive dysfunction and frank dementia may develop in such cases although neurologic stabilization is seen in some patients.

**Peripheral Neuropathy**

Conventional chemotherapy agents such as vinca alkaloids, platinum compounds, and taxanes are well known to cause neuropathy syndromes. However, some newer agents such as bortezomib, a proteosome inhibitor, are also associated with this complication. The presentation of chemotherapy-induced neuropathy depends on the offending agent and type of neuropathy induced, duration of treatment, and patient-related factors. In sensory neuropathies, numbness, tingling, and pain in the extremity is typical. Investigation with EMG/NCS is not strictly necessary in most cases but is done occasionally when the presentation is atypical (eg, worsening of symptoms with withdrawal of chemotherapy). In axonopathies, a decrease in the amplitude of action potentials and prolonged latencies are noted. Demyelination results in delayed conduction velocities. Among prevention strategies for chemotherapy-induced neuropathy, perhaps the most obvious is the limitation in cumulative drug dosing with drugs such as thalidomide or the vinca alkaloids. However, there are chemotherapy-specific strategies, such as the use of magnesium and calcium salt infusions to limit oxaliplatin neuropathy. Other examples of specific treatments, as well as a list of nervous system complications of chemotherapy, are provided in.

**Neurologic Complication of Stem Cell Transplantation**

The regimen used in stem cell transplantation (SCT) for treatment of cancers such as leukemias and lymphomas has been associated with neurologic complications such as seizures, encephalopathy, and stroke. In addition, severe immunosuppression associated with this treatment may result in severe infections of the nervous system. Allogeneic stem cell transplantation was associated with neurologic complications in 18% of patients at day100 after transplant in a series of patients treated for malignant and nonmalignant disease]. Seizures may occur with high-dose busulfan conditioning SCT regimens and benzodiazepine prophylaxis has been advocated in such cases. The occurrence of seizures in this setting has been reported as high as 37%. Encephalopathy may have multiple causes in SCT patients. The chemotherapy agents used are the commonest offenders and ifosfamide, melphalan, and etoposide may all be associated with this complication. Stroke occurring as a complication of therapy for cancer has been discussed. The severe bone marrow suppression with thrombocytopenia in SCT makes this population high-risk for intracerebral hemorrhage. Hemorrhage can also be a result of septic emboli to the brain caused by opportunistic infections in this population.

**Infections**

Infections include opportunistic infections with bacteria, viruses, fungi, and parasites. Aspergillus fumigatus is the most common fungal infection in such cases and Toxoplasma gondii is the most common parasite to result in CNS infection. Viruses of the herpes group are very neurotropic and may result in skin eruptions from sensory nerve involvement, as well as encephalitis. JC virus reactivation, a consequence of treatment- or disease-related immunosuppression, results in progressive multifocal leukoencephalopathy with a very poor prognosis.

**Conclusions**

Cancer can involve the nervous system directly or through the toxic effects of treatment. Additionally, cancer can have effects on the immune system and the coagulation system that result in paraneoplastic syndromes and cerebrovascular disease, respectively. The immunosuppressant effect of cancer and its treatments may result in opportunistic infections of the nervous system.

Source

Giglio, P. and Gilbert, M.R. (2010) ‘Neurologic Complications of Cancer and its Treatment’, Curr Oncol Rep, 12(1), pp. 50–59. Available at: <https://doi.org/10.1007/s11912-009-0071-x> (Accessed: 12 June 2025).

**Mitochondrial Diseases**

**Overview**

A magnified mitochondria within a human cell affected by a mitochondrial disease. Mitochondrial diseases are genetic conditions that affect how mitochondria function in your body.

**What is mitochondrial disease?**

Mitochondrial diseases are a group of conditions that affect how mitochondria work in your body. Mitochondria make energy in your cells. When mitochondria aren’t able to produce enough energy that your body needs, it affects how your organs function. Mitochondrial diseases can affect almost any part of your body, including the cells of your:

• Brain.

• Nerves.

• Muscles.

• Kidneys.

• Heart.

• Liver.

• Eyes.

• Ears.

• Pancreas.

**What are mitochondria?**

You may hear mitochondria called “the powerhouse of the cell.” Mitochondria are an energy factory. The job of mitochondria is to process oxygen and convert substances from the foods you eat into energy. Mitochondria exist in nearly every cell in the human body. Mitochondria produce 90% of the energy our bodies need to function.

**What are the types of mitochondrial disease?**

There are many types of mitochondrial diseases. Some of the most common include:

• Mitochondrial encephalopathy, lactic acidosis and stroke-like episodes (MELAS) syndrome.

• Leber hereditary optic neuropathy (LHON).

• Leigh syndrome.

• Kearns-Sayre syndrome (KSS).

• Myoclonic epilepsy and ragged-red fiber disease (MERRF).

**How common is mitochondrial disease?**

An estimated 1 in 5,000 people has a genetic mitochondrial disease. It’s common for mitochondrial diseases to receive a misdiagnosis due to the number and type of symptoms and organ systems involved, so this number may be underestimated.

**Symptoms and Causes**

**What are the symptoms of mitochondrial disease?**

Symptoms of mitochondrial diseases vary based on the type and location of the affected cells. They can range from mild to severe and could include:

• Poor growth.

• Muscle weakness, muscle pain or a low muscle tone.

• Vision and/or hearing loss.

• Developmental delays or issues with cognitive development.

• Diarrhea or constipation.

• Unexplained vomiting.

• Acid reflux and/or swallowing difficulties.

• Seizures.

• Migraines.

• Respiratory (breathing) problems.

• Fainting.

Symptoms of mitochondrial diseases can be present at birth, but they can also arise at any age. A healthcare provider usually detects symptoms affecting more than one organ or organ system at the same time. Symptoms of the same disease can vary from person to person, even among family members.

**What causes mitochondrial disease?**

A lack of energy production from mitochondria in your cells causes mitochondrial disease. Mitochondria are responsible for producing energy within your body. When your mitochondria don’t receive the instructions they need from your body’s DNA to make energy, it can damage your cells or cause them to die early. This affects how your organs and organ systems function, which leads to symptoms of the condition.

**How does someone get a mitochondrial disease?**

Mitochondrial diseases are genetic. You can inherit these conditions from your biological family in an autosomal dominant or autosomal recessive pattern. This means that you can get a changed (mutated) gene that causes this condition from one or both of your biological parents respectfully. Some cases can occur randomly (de novo) without any history of the condition in your biological family. Certain cases of mitochondrial disease have a mitochondrial inheritance. This occurs when the mitochondria contain their own DNA. Mitochondrial conditions caused by mutations in the mitochondrial DNA are exclusively inherited from the child's mother.

**Can other conditions cause mitochondrial diseases?**

Yes. Mitochondrial dysfunction occurs when mitochondria don’t work as well as they should due to another disease or condition. Many conditions can lead to secondary mitochondrial dysfunction, including:

• Alzheimer’s disease.

• Muscular dystrophy.

• Type 1 diabetes.

• Multiple sclerosis (MS).

• Cancer.

If you have secondary mitochondrial dysfunction, you don’t have a genetic mitochondrial disease.

**What are the risk factors for mitochondrial disease?**

You’re more at risk of developing a mitochondrial disease if it runs in your biological family history or if you have a condition that causes secondary mitochondrial dysfunction. Mitochondrial disease affects both adults and children.

**What are the complications of mitochondrial disease?**

Mitochondrial diseases affect how your organs function. It can cause the following complications:

• Increased risk of infection.

• Strokes.

• Pancreatic failure.

• Parathyroid failure.

• Diabetes.

• Liver failure.

• Cardiomyopathy.

• Kidney disease.

• Dementia.

• Gastrointestinal conditions.

• Drooping eyelid (ptosis).

Complications can be life-threatening.

**Diagnosis and Tests**

**How is a mitochondrial disease diagnosed?**

A healthcare provider will diagnose a mitochondrial disease after a series of examinations and tests that may include:

• A review of your medical and family history.

• A complete physical examination.

• A neurological examination.

• A metabolic examination that includes blood and urine tests and, if needed, a cerebrospinal fluid test (spinal tap).

• DNA testing.

Other tests, depending on your symptoms and the affected areas of your body, might include:

• Magnetic resonance imaging (MRI) or spectroscopy (MRS) for neurological symptoms.

• Retinal exam or electroretinogram (ERG) for vision symptoms.

• Electrocardiogram (EKG) or echocardiogram for symptoms that affect your heart.

• Audiogram for hearing symptoms.

• Electroencephalogram (EEG) for seizures and related brain issues.

More advanced testing could include biochemical testing, which looks for changes in body chemicals involved in energy making. A healthcare provider may perform a biopsy where they take a sample of skin and/or muscle tissue to examine it under a microscope.

**Are mitochondrial diseases difficult to diagnose?**

Yes. Because mitochondrial diseases affect so many different organs and tissues of your body, and you may have many different symptoms, mitochondrial diseases can be difficult to diagnose. There’s no single laboratory test that can diagnose a mitochondrial disease. This is why a referral to a medical facility with physicians who specialize in these diseases is critical to making the diagnosis.

**Management and Treatment**

**How is a mitochondrial disease treated?**

Treatment for a mitochondrial disease varies based on the type and your symptoms. Treatment could include:

• Taking medications to reduce symptoms, like medications to prevent seizures.

• Taking vitamins or supplements, like riboflavin, coenzyme Q10 and carnitine.

• Changing your diet (nutrition) and exercising.

• Physical therapy, occupational therapy or speech therapy.

• Wearing assistive devices like hearing aids.

There’s no cure for mitochondrial disease. Treatment focuses on preventing life-threatening complications. Treatment that works for one person may differ from what works to treat someone else with the same condition.

**Are there side effects of the treatment?**

Talk to your healthcare provider about side effects before starting treatment. They’ll discuss the side effects of your treatment specifically and what you should look out for. Each type of treatment comes with its own possible side effects.

**Outlook / Prognosis**

**What is the life expectancy for mitochondrial disease?**

Your healthcare provider can give you the best advice on your life expectancy after a mitochondrial disease diagnosis. Your outlook depends on your symptoms, affected organs and general health. Some affected children and adults have the same expected lifespan as someone who doesn’t have this condition. Others might experience drastic changes in their health over a very short period of time. Some may have occasional flare-ups of symptoms throughout their lives. Although there’s no cure for mitochondrial diseases, research is ongoing to learn more.

**Prevention**

**Can mitochondrial disease be prevented?**

There’s no known way to prevent mitochondrial diseases. If you have a mitochondrial disease, you can avoid situations that can make your symptoms worse like:

• Exposure to extreme cold and/or heat.

• Skipping meals.

• Not getting enough sleep.

• Stress.

A healthcare provider may suggest you conserve (save) your energy to avoid using up all of your body’s energy in a short period of time.

**Source**

Cleveland Clinic (2023) Mitochondrial Diseases: Causes, Symptoms & Treatment. Available at: <https://my.clevelandclinic.org/health/diseases/15612-mitochondrial-diseases> (Accessed: 12 June 2025).

**A. Paediatric & Developmental Neurological Disorders**

**1. Autism Spectrum Disorder (Neurological** **Aspects)**

Autism spectrum disorder is a condition related to brain development that affects how people see others and socialize with them. This causes problems in communication and getting along with others socially. The condition also includes limited and repeated patterns of behavior. The term "spectrum" in autism spectrum disorder refers to the wide range of symptoms and the severity of these symptoms. Autism spectrum disorder includes conditions that were once thought to be separate — autism, Asperger's syndrome, childhood disintegrative disorder and a form of widespread developmental disorder that isn't specified. Autism spectrum disorder begins in early childhood. Over time, it can cause difficulty functioning in society. For example, people with autism spectrum disorder may have problems being social or when in school or at work. Often children show symptoms of autism within the first year of life. A small number of children with the condition appear to develop as expected in the first year. Then between 18 and 24 months of age, they may lose some skills and develop autism symptoms. There is no cure for autism spectrum disorder. But getting treatment early, during the preschool years, can make a big difference in the lives of many children with the condition.

**Symptoms**

Some children show signs of autism spectrum disorder in early infancy, such as less eye contact, not responding to their names or not being interested in caregivers. Other children may not develop as expected for the first few months or years of life. Then they suddenly become withdrawn or aggressive or lose the language skills they had before. Signs usually are seen by ages 2 to 3 years old. Some people in the mild range on the autism spectrum may have more symptoms that aren't noticed early on. They may not be diagnosed until middle to late childhood, when there is a greater need to communicate and be social. Sometimes a diagnosis is made for the first time in adulthood, though symptoms were likely present during childhood. Each child with autism spectrum disorder is likely to have a unique pattern of behavior that depends on whether symptoms are mild, moderate or severe. Some children with autism spectrum disorder have trouble learning, and some have signs of lower than usual intelligence. Other children with the condition have usual to high intelligence. These children learn quickly but have trouble communicating, applying what they know in everyday life and adjusting to social situations.Because each child can have a unique mix of symptoms, sometimes it can be hard to tell how severe the condition is. It's generally based on how severe the symptoms are and how much those symptoms affect a child being able to function. Below are some common signs shown by people who have autism spectrum disorder.

**Social communication and interaction**

People with autism spectrum disorder may have problems getting along with others and communicating. They may have a mix of these and other symptoms:

* Don't respond to their name, or they don't seem to hear at times.
* Don't want to be cuddled or held and prefer to play alone, retreating into their own worlds.
* Have poor eye contact and have no expression on their faces.
* Don't speak or have delayed speech or lose the ability to say words or sentences as they could before.
* Can't start a conversation or keep one going, or only start one to make requests or label items.
* Speak with an unusual tone or rhythm and may use a singsong voice or robotlike speech.
* Repeat words or phrases word for word but don't know how to use them.
* Don't seem to understand simple questions or directions.
* Don't show emotions or feelings and don't seem to be aware of how others feel.
* Don't point at or bring objects to share interest.
* Are passive, aggressive or disruptive when interacting with others.
* Have a hard time figuring out what it means when people have different looks on their faces, position their bodies differently or speak in different tones of voice.

**Patterns of behavior**

People with autism spectrum disorder may have limited, repetitive patterns of behavior, interests or activities, including a mix of these and other signs:

* Make the same movement over and over again, such as rocking, spinning or hand-flapping.
* Do activities where they could hurt themselves, such as biting or head-banging.
* Create specific routines or rituals and become upset at even small changes.
* Aren't coordinated and may be clumsy, or they move in patterns that aren't usual, such as walking on toes.
* Have unusual, stiff or exaggerated body language.
* Are fascinated by details of an object, such as the spinning wheels of a toy car, but they don't know what the object is for or how it works.
* Are sensitive to light, sound or touch but may not be affected by pain or temperature.
* Don't mimic others or take part in make-believe play.
* Fixate on an object or activity with unusual intensity or focus.
* Prefer specific foods, such as eating only a few foods or not wanting to eat foods with certain textures.

As they get older, some children with autism spectrum disorder interact more with others and show fewer disturbances in behavior. Some, usually those with the least severe problems, eventually may lead typical or nearly typical lives. But others continue to have trouble with language or social skills. And the teenage years can bring more behavioral and emotional challenges.

**Causes**

Autism spectrum disorder has no single known cause. Since the condition is complex and symptoms and severity vary, there could be many causes. Both genetics and the environment may play a role.

* **Genetics.** Several genes seem to be involved in autism spectrum disorder. For some children, autism spectrum disorder can be related to a genetic condition, such as Rett syndrome or fragile X syndrome. For other children, genetic changes, also known as mutations, may raise the risk of autism spectrum disorder. Still other genes may affect the way that the brain develops or brain cells communicate. Or those genes may affect how severe symptoms are. While some genetic changes seem to be inherited, others aren't.
* **Environmental factors.** Researchers are exploring whether factors such as viral infections, medicines, complications during pregnancy or air pollutants play a role in causing autism spectrum disorder.

**No link between vaccines and autism spectrum disorder**

One of the greatest controversies in autism spectrum disorder centers on whether there is a link between the condition and childhood vaccines. Many well-done research studies show no link between autism spectrum disorder and any vaccines. In fact, the original study that started the debate years ago was retracted due to poor design and questionable research methods.

When your child doesn't get vaccines, your child and other children could catch and spread viruses that cause serious diseases. These diseases include whooping cough, also known as pertussis, as well as measles, mumps and others.

**Risk factors**

The number of children diagnosed with autism spectrum disorder is rising. It isn't clear whether this is due to better ways to diagnose and report the condition, a real increase in the number of children with the condition, or both. Autism spectrum disorder affects children of all races and nationalities. But certain factors raise a child's risk, including:

* **Your child's sex.** Boys are about four times more likely to be diagnosed with autism spectrum disorder than girls are. While boys may get autism spectrum disorder more often than girls, it's possible that some girls aren't diagnosed.
* **Family history.** Families who have one child with autism spectrum disorder have a higher risk of having another child with the condition. Sometimes parents or relatives of a child with autism spectrum disorder may have minor problems being social or communicating, or they may show certain behaviors typical of the condition.
* **Other conditions.** Children with certain medical conditions have a higher risk of autism spectrum disorder or symptoms similar to autism. Examples include fragile X syndrome, an inherited condition that causes intellectual disability; tuberous sclerosis, a condition in which benign tumors develop in the brain; and Rett syndrome, a genetic condition that almost always occurs in girls and causes slowing of head growth, intellectual disability and loss of purposeful hand use.
* **Early birth.** Babies born before 26 weeks of a parent's pregnancy may have a higher risk of autism spectrum disorder.
* **Parents' ages.** There may be a connection between children born to older parents and autism spectrum disorder. But more research is needed to show this link.

**Complications**

Because people with autism spectrum disorder often have a hard time interacting socially, communicating or behaving, this can lead to problems with:

* School and learning.
* Getting a job.
* Not being able to live on their own.
* Being isolated socially.
* Stress within the family.
* Being a victim and being bullied.

**Prevention**

There's no known way to prevent autism spectrum disorder. But many studies have been done to see if taking folic acid and other vitamins before and during pregnancy can lower the risk of having a baby with autism spectrum disorder. A review of studies on what are known as prenatal vitamins shows no clear answer. This is due to the quality of the research. More high-quality studies are needed. Getting diagnosed and treated early is most helpful in improving behavior, skills and language development. But getting treatment is helpful at any age. Though children usually don't outgrow autism spectrum disorder symptoms, they may learn to function well.

**Diagnosis**

Your child's healthcare professional looks for signs of developmental delays at regular well-child checkups. If your child shows any symptoms of autism, you'll likely be referred to a specialist who treats children with autism spectrum disorder for an evaluation. This specialist could be a child psychiatrist or psychologist, a pediatric neurologist, or a developmental pediatrician. Because autism spectrum disorder symptoms and how severe they are can vary widely, it may be hard to make a diagnosis. There is no specific medical test to diagnose autism spectrum disorder. Instead, a specialist may:

* Observe your child and ask how your child has developed or changed over time in terms of interacting socially, communicating and behaving.
* Give your child tests covering hearing, speech, language, level of development, and social and behavioral issues.
* Present structured social and communication interactions to your child and score the performance.
* Include other specialists in coming up with a diagnosis.
* Recommend genetic testing to figure out whether your child has a genetic condition such as Rett syndrome or fragile X syndrome

**Treatment**

There is no cure for autism spectrum disorder, and there is no one-size-fits-all treatment. Treatment seeks to support your child's learning, development and behavior. Getting treated early, during the preschool years, can help your child learn critical social, communication, functional and behavioral skills. The range of home-based and school-based treatments for autism spectrum disorder can be overwhelming, and your child's needs may change over time. Your healthcare professional can recommend options and help find resources in your area. If your child is diagnosed with autism spectrum disorder, talk with experts about creating a treatment strategy and build a team of health professionals to meet your child's needs.

Treatment options may include:

* **Behavior and communication therapies.** Many programs address the range of social, language and behavioral difficulties linked with autism spectrum disorder. Some programs focus on reducing challenging behaviors and teaching new skills. Other programs focus on teaching children how to act in social situations or communicate better with others. Applied behavior analysis can help children learn new skills and adapt these skills to many situations by motivating them with rewards.
* **Educational therapies.** Children with autism spectrum disorder often respond well to highly structured educational programs. Successful programs usually include a team of specialists and various activities to improve social skills, communication and behavior. Preschool children who get intensive, individualized behavioral treatments often show good progress.
* **Family therapies.** Parents and other family members can learn how to play and interact with children who have autism in ways that support social interaction skills, manage challenging behaviors, and teach daily living skills and communication.
* **Other therapies.** Depending on your child's needs, speech therapy to make communication skills better, occupational therapy to teach activities of daily living, and physical therapy to make movement and balance better may help. A psychologist can recommend ways to manage problem behavior.
* **Medicines.** Medicine can't make the core signs of autism spectrum disorder better, but specific medicines can help control symptoms. For example, certain medicines may be prescribed if your child is hyperactive. Sometimes healthcare professionals prescribe antipsychotic medicines to treat severe behavioral symptoms. Or they may prescribe antidepressants for anxiety. Keep all healthcare professionals updated on any medicines or supplements your child takes. Some medicines and supplements can affect how one medicine acts with another, causing dangerous side effects.

**Managing other medical and mental health conditions**

In addition to autism spectrum disorder, children, teenagers and adults also can have:

* **Medical health issues.** Children with autism spectrum disorder also may have medical issues such as epilepsy, sleep disorders, limited food preferences or stomach problems. Ask your child's healthcare professional how to best manage these conditions together.
* **Problems with transition to adulthood.** Teens and young adults with autism spectrum disorder may have a hard time understanding body changes. Also, social situations become more complex during the teen years, and there may be less tolerance for individual differences. Behavior also may be challenging at this time.
* **Other mental health conditions.** Teens and adults with autism spectrum disorder often have other mental health conditions, such as anxiety disorders; depression; attention-deficit-hyperactivity disorder, also known as ADHD; and substance misuse. Your healthcare professional, mental health professional, and community advocacy and service organizations can help.
* **Behavioral health concerns.** In addition to autism spectrum disorder, your child could be irritable or aggressive and may not pay attention. Your child also could be hyperactive, have sudden outbursts or try self-harm. Work with your healthcare professional, mental health professional and other team members to look for a cause, such as pain, distress or frustration, and to manage these challenges if they occur.

**Treatment**

**Alternative medicine**

Because autism spectrum disorder can't be cured, many parents seek alternative or complementary therapies. But there's little or no research on these therapies to show whether they're helpful. And some alternative treatments could be dangerous. Talk with your child's healthcare professional about whether research supports any therapy that you're thinking about for your child.

Examples of complementary and alternative therapies that may offer some benefit when used along with proven treatments include:

* **Creative therapies.** Some parents choose to include art or music therapy along with educational and medical therapies. Doing so can make a child less sensitive to touch or sound.
* **Sensory-based therapies.** Therapists may use brushes, squeeze toys, trampolines and other materials to stir the senses, such as touch, balance and hearing. But research has not proved that these therapies work. It's possible that they may help when used with other treatments.
* **Melatonin.** Research shows that melatonin could help with sleep issues related to autism spectrum disorder when taken as directed. But it's important to work on developing healthy sleep habits first.
* **Massage.** While massage may be relaxing, there isn't enough evidence to show that it improves symptoms of autism spectrum disorder.
* **Pet or horse therapy.** Pets can give your child a companion and a fun time. But more research is needed to determine whether being with animals improves symptoms of autism spectrum disorder.

Some complementary and alternative therapies may not be harmful, but there's no evidence that they help. Some also may be costly and hard to carry out. Examples of these therapies include:

* **Vitamin supplements and probiotics.** Although not harmful when used in the usual amounts, there is no evidence they help autism spectrum disorder symptoms. Also, supplements can be costly. Talk with your healthcare professional about vitamins and other supplements and the right dose for your child.
* **Acupuncture.** This therapy has been used to improve autism spectrum disorder symptoms, but research doesn't show that it works.

Some complementary and alternative treatments aren't proved to help, and they could be dangerous. Examples of complementary and alternative treatments that aren't recommended for autism spectrum disorder include:

* **Special diets that limit nutrients.** There's no evidence that special diets effectively treat autism spectrum disorder. And for growing children, restrictive diets can mean that children won't get enough nutrients. If you decide to pursue a restrictive diet, work with a registered dietitian to create a proper meal plan for your child that has all the needed nutrients.
* **Chelation therapy.** This treatment is said to remove mercury and other heavy metals from the body, but there's no known link between these metals and autism spectrum disorder. Research doesn't support that chelation therapy works, and it can be very dangerous. In some cases, children treated with chelation therapy have died.
* **Hyperbaric oxygen treatments.** Hyperbaric oxygen involves breathing oxygen inside a pressurized chamber. This treatment has not been shown to be effective in treating autism spectrum disorder symptoms, and the U.S. Food and Drug Administration (FDA) has not approved it for this use.
* **Intravenous immunoglobulin (IVIg) infusions.** There is no evidence that using IVIg infusions improves autism spectrum disorder symptoms. The FDA has not approved immunoglobulin products for this use.
* **Other treatment claims.** Treatments that may not be safe or are not proved to help include CBD oil, secretin, antifungal therapy, and clay baths that supposedly remove toxins.

**Source**

<https://www.mayoclinic.org/diseases-conditions/autism-spectrum-disorder/symptoms-causes/syc-20352928>

<https://www.mayoclinic.org/diseases-conditions/autism-spectrum-disorder/diagnosis-treatment/drc-20352934>

2. ADHD- Attention-deficit/hyperactivity disorder

Attention-deficit/hyperactivity disorder, also called ADHD, is a long-term condition that affects millions of children. It often continues into adulthood. ADHD includes a mix of ongoing problems. These can include having a hard time paying attention, being hyperactive and being impulsive. Children with ADHD also may have low self-esteem and troubled relationships and do poorly in school. Symptoms sometimes lessen with age. Some people never completely outgrow their ADHD symptoms but they can learn strategies to be successful. While treatment won't cure ADHD, it can help a great deal with symptoms. Besides giving education about ADHD, treatment can involve medicines and behavior therapies. Early diagnosis and treatment can make a big difference in results.

**Symptoms**

The main features of ADHD include not paying attention and being hyperactive and impulsive. ADHD symptoms usually start before age 12. In some children, they can be seen as early as 3 years of age. ADHD symptoms can be mild, moderate or severe. Symptoms need to be seen in two or more settings, such as at home and at school. The symptoms cause problems with development and daily life and may continue into adulthood. ADHD occurs more often in boys than in girls. Behaviors can be different in boys and girls. For example, boys may be more hyperactive and girls may tend to quietly not pay attention.

There are three types of ADHD:

* **Predominately inattentive.** In this type, most symptoms fall under inattention. This means having trouble focusing and staying on a task. It also includes trouble getting and staying organized.
* **Predominately hyperactive and impulsive.** In this type, most symptoms involve being hyperactive and impulsive. Hyperactive means being too active and having too much energy. It may include disruptive behavior. Being impulsive means acting without thinking ahead about the results or effects of behavior.
* **Combined.** This type is a mix of inattentive symptoms and hyperactive and impulsive symptoms. The person meets the criteria for both predominately inattentive and predominately hyperactive and impulsive types of ADHD.

**Inattentive symptoms**

A child who shows a pattern of inattention may often:

* Fail to pay close attention to details or make careless mistakes in schoolwork.
* Have trouble staying focused in tasks or play.
* Seem not to listen, even when spoken to directly.
* Have a hard time following through on instructions and not finish schoolwork or chores.
* Have trouble organizing tasks and activities.
* Stay away from or not like tasks that need focused mental effort, such as homework.
* Lose items needed for tasks or activities, for example, toys, school assignments, pencils.
* Be easily distracted by other things, thoughts or activities rather than finishing a task.
* Forget to do some daily activities, such as forgetting to do chores.

**Hyperactive and impulsive symptoms**

A child who shows a pattern of hyperactive and impulsive symptoms may often:

* Fidget with or tap hands or feet, or squirm in the seat.
* Have a hard time staying seated in the classroom or in other situations.
* Be on the go, in constant motion.
* Run around or climb in situations when it's not proper.
* Have trouble playing or doing an activity quietly.
* Talk too much.
* Blurt out answers, interrupting the questioner.
* Have trouble waiting for a turn.
* Interrupt others' conversations, games or activities.

**Typical development versus ADHD**

Most healthy children are inattentive, hyperactive or impulsive at one time or another. It's typical for preschoolers to have short attention spans and not be able to stick with one activity for long. Even in older children and teenagers, attention span often depends on the level of interest. The same is true of hyperactivity. Young children are naturally energetic. They often are still full of energy long after they've tired their parents. And some children just naturally have a higher activity level than others do. Children should never be classified as having ADHD just because they're different from their friends or siblings. Children who have problems in school but get along well at home or with friends may likely have a concern other than ADHD. The same is true of children who are hyperactive or inattentive at home but whose schoolwork and friendships aren't affected.

**Causes**

While the exact cause of ADHD is not clear, research efforts continue. Factors that may be involved in the development of ADHD include genetics, the environment or central nervous system conditions at key moments in development.

**Risk factors**

Risk factors for ADHD may include:

* Having a blood relative, such as a parent or sibling, with ADHD or another mental health condition.
* Being around environmental toxins such as lead, which is found mainly in paint and pipes in older buildings.
* Being born to a parent who used recreational drugs, alcohol or tobacco during pregnancy.
* Being born too early, also called premature birth.

**Complications**

ADHD can make life hard for children. Children with ADHD:

* Often have trouble in the classroom, which can lead to failing grades and being judged by other children and adults.
* Tend to have more accidents and injuries of all kinds than do children who don't have ADHD.
* Tend to have poor self-esteem.
* Are more likely to have trouble interacting with and being accepted by peers and adults.
* Are at higher risk of alcohol and drug misuse and other behavior that can cause problems with the law.
* Have a higher risk of suicidal thoughts and suicide.
* Have sleep disorders.

**Conditions often linked with ADHD**

ADHD does not cause other mental health or developmental problems. But children with ADHD are more likely than others to also have conditions such as:

* **Oppositional defiant disorder.** This condition is generally defined as a pattern of negative, defiant and hostile behavior toward people who are in authority.
* **Conduct disorder.** This involves antisocial behavior such as stealing, fighting, destroying property, and harming people or animals.
* **Disruptive mood dysregulation disorder.** This involves irritability and problems handling frustration.
* **Learning disabilities.** These can include problems with reading, writing, understanding and communicating.
* **Substance use disorders.** This involves misuse of drugs, alcohol, marijuana or nicotine.
* **Anxiety.** This results in constant worry and nervousness that affect daily life.
* **Obsessive-compulsive disorder, also called OCD.** OCD is a pattern of unwanted thoughts and fears that lead to repetitive behaviors. These get in the way of daily activities and cause a lot of distress.
* **Mood disorders.** These include depression and bipolar disorder. Bipolar disorder includes depression and manic behavior.
* **Autism spectrum disorder.** This condition is related to brain development. It impacts how a person thinks of and socializes with others.
* **Tic disorders.** These conditions involve repetitive movements or unwanted sounds, called tics, that can't be easily controlled.

**Prevention**

To help lower your child's risk of ADHD:

* **During pregnancy,** avoid anything that could harm your baby's development before birth. For example, don't drink alcohol, use drugs or smoke cigarettes.
* **Protect your child from exposure to pollutants and toxins,** including cigarette smoke and lead paint.
* **Limit screen time.** Although still not proved, it may be a good idea for young children to limit TV, video games and other screen time.

**Diagnosis**

In general, a diagnosis of attention-deficit/hyperactivity disorder is made if the core symptoms of ADHD start early in life — before age 12 — and create major problems at home and at school on an ongoing basis. There's no specific test for ADHD. An evaluation can help find out whether symptoms are related to ADHD or another problem. Making a diagnosis will likely include:

* **A medical exam.** This can help rule out other possible causes of symptoms.
* **Information gathering.** This includes reviewing any current medical conditions, personal and family medical history, and school records.
* **Interviews or surveys.** These may include information from family members, teachers or other people who know your child well, such as caregivers, babysitters and coaches. This information can show how your child behaves in different situations.
* **ADHD rating scales.** These help collect and evaluate information about your child.

**Diagnosing ADHD in young children**

Signs of ADHD can sometimes be noticed in preschoolers or even younger children. But diagnosing the condition in very young children is harder. That's because developmental conditions such as language delays can be mistaken for ADHD. Children preschool age or younger suspected of having ADHD are more likely to need evaluation by a specialist, such as a psychologist or psychiatrist, speech pathologist, or developmental pediatrician.

**Other conditions with symptoms like those of ADHD**

Some medical conditions or their treatments may cause symptoms much like those of ADHD. Examples include:

* Learning or language delays.
* Mood disorders such as depression.
* Anxiety disorders.
* Seizure disorders.
* Vision or hearing conditions.
* Autism spectrum disorder.
* Medical conditions or medicines that affect thinking or behavior.
* Sleep disorders.
* Brain injury.

**Treatment**

Standard treatments for ADHD in children include medicines, behavior therapy, counseling and education services. These treatments can lessen many of the symptoms of ADHD, but they don't cure it. Treatment also can help prevent some complications caused by ADHD. It may take some time to find what works best for your child.

**Stimulant medicines**

Stimulant medicines, also called psychostimulants, are currently the most prescribed medicines for ADHD. Stimulants appear to boost and balance levels of brain chemicals called neurotransmitters. The medicines help lessen the symptoms of inattention and hyperactivity. They can sometimes help in a short period of time.

Examples of stimulant medicines include:

* **Amphetamines.** These include dextroamphetamine (Dexedrine Spansule), dextroamphetamine-amphetamine (Adderall XR, Mydayis) and lisdexamfetamine (Vyvanse).
* **Methylphenidates.** These include methylphenidate (Concerta, Ritalin, others), dexmethylphenidate (Focalin) and dexmethylphenidate-serdexmethylphenidate (Azstarys).

Stimulant medicines are available in short-acting and long-acting forms. Long-acting patches of methylphenidate (Daytrana) or dextroamphetamine (Xelstrym) are available. They can be worn on the hip.

The right dose varies from child to child, so it may take time to find what works for your child. And the dose may need to be adjusted if side effects occur or as your child matures. Ask your healthcare professional about possible side effects of stimulant medicines.

**Stimulant medicines and certain health risks**

Some research suggests that using ADHD stimulant medicines with certain heart problems may be a concern. Weight and growth may be affected. Also, the risk of certain mental health symptoms may be higher when using stimulant medicines.

* **Heart conditions.** Stimulant medicines may cause a rise in blood pressure or heart rate. But the higher risk of serious side effects or sudden death is still not proved. The healthcare professional evaluates your child for any heart condition or family history of heart disease before prescribing a stimulant medicine. The healthcare professional also monitors your child when stimulant medicines are used.
* **Appetite changes, weight loss and slowed growth.** Stimulant medicines can affect appetite and cause weigh loss. These medicines also can slightly affect height growth.
* **Mental health conditions.** Stimulant medicines may rarely raise the risk for agitation or irritability. Uncommonly, manic symptoms or losing touch with reality can happen. Contact your child's healthcare professional right away if your child has sudden new or worsening behavior or sees or hears things that aren't real while taking stimulant medicine.

**Source**

<https://www.mayoclinic.org/diseases-conditions/adhd/symptoms-causes/syc-20350889>

<https://www.mayoclinic.org/diseases-conditions/adhd/diagnosis-treatment/drc-20350895>

3. **Spina bifida**

Spina bifida is a condition that occurs when the spine and spinal cord don't form properly. It's a type of neural tube defect. The neural tube is the structure in a developing embryo that later becomes the baby's brain and spinal cord and the tissues that enclose them. Typically, the neural tube forms early in pregnancy and closes by the 28th day after conception. In babies with spina bifida, a portion of the neural tube doesn't close all the way. This affects the spinal cord and bones of the spine.

**Types**

**Spina bifida occulta**

Occulta means hidden. Spina bifida occulta is the mildest and most common type. This type of spina bifida results in a small separation or gap in one or more of the bones of the spine, called vertebrae. Many people who have spina bifida occulta don't know they have it. It may be found during an imaging test such as an X-ray that is done for another reason.

**Myelomeningocele**

Myelomeningocele is the most serious type. It also is known as open spina bifida. The spinal canal is open along several vertebrae in the lower or middle back. Part of the spinal cord, including the spinal cord's protective covering and spinal nerves, push through this opening at birth, forming a sac on the baby's back. Tissues and nerves usually are exposed. This makes the baby prone to dangerous infections. This type also may cause loss of movement in the legs, and bladder and bowel dysfunction.

**Meningocele**

This is a rare type of spina bifida. In this type, a sac of spinal fluid bulges through an opening in the spine. No nerves are affected and the spinal cord isn't in the fluid sac. Babies with meningocele may have some minor trouble with functioning, including with the bladder and bowels.

**Symptoms**

Symptoms of spina bifida vary by type and from one person to another.

* **Spina bifida occulta.** Typically, there aren't any symptoms of spina bifida occulta because the spinal nerves aren't involved. But you can sometimes see symptoms on the newborn's skin above the small gap in the spine. You might see a tuft of hair, a small dimple or a birthmark. Sometimes, these skin marks can be symptoms of a spinal cord issue that can be found with MRI or a spinal ultrasound in a newborn.
* **Meningocele.** This type may affect bladder and bowel function.
* **Myelomeningocele.** In this most serious type of spina bifida, the spinal canal remains open along several vertebrae in the lower or middle back. The membranes and part of the spinal cord or nerves protrude at birth, forming a sac. Tissues and nerves usually are exposed, though sometimes skin covers the sac. Babies with this type of spina bifida may have trouble with bladder and bowel function. They also may experience weakness or lack of movement in the legs. Babies may have a buildup of fluid in the brain called hydrocephalus that can put pressure on brain tissue

**Causes**

The cause of spina bifida is not known. It's thought that a combination of genetic, nutritional and environmental risk factors causes the condition. This includes having a family history of neural tube defects and getting too little folate, also known as vitamin B-9, during pregnancy.

**Risk factors**

Spina bifida is more common among Hispanic people and white people. Also, female babies are affected more often than male babies. Although healthcare professionals and researchers don't know why spina bifida occurs, they have identified some risk factors:

* **Too little folate in the pregnant person's body.** Folate, the natural form of vitamin B-9, is important to the development of a healthy baby. Folic acid is the synthetic form that's found in supplements and fortified foods. If folate levels are too low, it's known as a deficiency. Folate deficiency increases the risk of spina bifida and other conditions that affect the neural tube.
* **Family history of neural tube defects.** Having one child with a condition that affects the neural tube slightly increases the chance of having another baby with the same condition. The risk increases even more if two previous children have been affected by the condition.

Also, being born with a neural tube defect increases the chance of giving birth to a child with spina bifida. However, most babies with spina bifida are born to parents with no known family history of the condition.

* **Some medicines.** Taking anti-seizure medicines such as valproic acid during pregnancy increases the risk of having a baby with spina bifida. This might happen because the medicines interfere with the body's ability to use folate and folic acid.
* **Diabetes.** Having diabetes that is not well controlled before becoming pregnant increases the risk of having a baby with spina bifida.
* **Obesity.** Obesity at the time of pregnancy also is associated with an increased risk of spina bifida.
* **Increased body temperature.** Some evidence suggests that increased body temperature in the early weeks of pregnancy may increase the risk of spina bifida. A high core body temperature can be caused by a fever or by using a sauna or hot tub.

**Prevention**

You can greatly reduce your risk of having a baby with spina bifida or other neural tube defects by taking folic acid supplements. Begin taking the supplements at least one month before becoming pregnant and continue taking them through the first trimester of pregnancy.

**Get folic acid first**

Having enough folic acid in your body by the early weeks of pregnancy is critical to prevent spina bifida. But many people don't discover that they're pregnant until this time. For this reason, experts recommend that all people of childbearing age take a supplement of 400 micrograms (mcg) of folic acid a day.

It's also helpful to eat foods that contain folate or have had folic acid added to them, known as fortification. Foods that are fortified with folic acid include:

* Enriched bread.
* Pasta.
* Rice.
* Some breakfast cereals.

Folic acid may be listed on food packages as folate, which is the natural form of folic acid found in foods.

**Planning pregnancy**

Adults who are planning pregnancy or who could become pregnant need to get 400 to 800 mcg of folic acid a day.

The body doesn't absorb folate as easily as it absorbs folic acid, and most people don't get the recommended amount of folate through diet alone. Vitamin supplements that include folic acid are necessary to prevent spina bifida. It's also possible that folic acid may help lower the risk of other conditions that may be present at birth. These conditions include a cleft lip, a cleft palate and some heart conditions.

It's also a good idea to eat a healthy diet that includes foods rich in folate or fortified with folic acid. This vitamin is present naturally in many foods, including:

* Beans and peas.
* Citrus fruits and juices.
* Egg yolks.
* Cow's milk.
* Avocados.
* Dark green vegetables, such as broccoli and spinach.

**When higher doses are needed**

If you have spina bifida or if you've previously given birth to a child with spina bifida, you need extra folic acid before you become pregnant. If you're taking anti-seizure medicines or you have diabetes, you also may benefit from a higher dose of this B vitamin. Check with your healthcare professional before taking additional folic acid supplements.

**Diagnosis**

Tests before the birth of a baby, known as prenatal screening, can check for spina bifida and other conditions. The tests aren't perfect. Some people who have positive blood tests have babies without spina bifida. Even if the results are negative, there's still a small chance that spina bifida is present. Talk with your healthcare professional about prenatal testing, its risks and what the results mean.

**Blood tests**

Spina bifida can be screened with blood tests during pregnancy, but typically the diagnosis is made with an ultrasound exam.

* **Maternal serum alpha-fetoprotein (MSAFP) test.** For the MSAFP test, a sample of blood is drawn and tested for alpha-fetoprotein (AFP). This is a protein produced by the baby. It's typical for a small amount of AFP to cross the placenta and enter the pregnant parent's bloodstream. But high levels of AFP suggest that the baby may have a neural tube defect such as spina bifida. However, high levels of AFP don't always occur in spina bifida.
* **Test to confirm high AFP levels.** Varying levels of AFP can be caused by other factors such as a wrong estimate of the unborn baby's age or the presence of multiple babies. You may need a follow-up blood test to confirm the results. If levels of AFP are still high, you need further evaluation, including an ultrasound exam.
* **Other blood tests.** Your healthcare professional may perform the MSAFP test with two or three other blood tests. These tests screen for other conditions, such as trisomy 21 syndrome, also known as Down syndrome. They are commonly done with the MSAFP test.

**Ultrasound**

An ultrasound is the most accurate way to diagnose spina bifida in your baby before delivery. During pregnancy, an ultrasound may be done in the first 11 to 14 weeks of pregnancy, known as the first trimester. Or it may be done at 18 to 22 weeks, known as the second trimester. Spina bifida can be more accurately diagnosed during the second trimester ultrasound exam. This exam is crucial to identify and rule out conditions that may be present at birth. An advanced ultrasound can detect symptoms of spina bifida, such as an open spine or features in the baby's brain. Sometimes ultrasound also can help your healthcare professional see how serious spina bifida is.

**Amniocentesis**

If the prenatal ultrasound confirms the diagnosis of spina bifida, your healthcare professional may request a test cal led amniocentesis. During this test, a needle is used to remove a sample of fluid from the amniotic sac that surrounds the baby. This exam may be important to rule out genetic diseases. Talk to your healthcare professional about the potential risks of amniocentesis. There's a slight risk of loss of the pregnancy.

**Treatment**

Spina bifida treatment depends on how serious the condition is in your baby. Spina bifida occulta often doesn't need any treatment at all, but other types of spina bifida do.

**Surgery before birth**

Nerve function in babies with spina bifida can get worse if it's not treated. Prenatal surgery for spina bifida, also known as fetal surgery, takes place before the 26th week of pregnancy. Surgeons open the pregnant person's stomach and then the womb, also known as the uterus. The unborn baby's spinal cord is repaired. Then the surgeon closes the uterus and stomach. Sometimes this procedure can be done less invasively with a special surgical tool called a fetoscope. Instruments are inserted into the uterus through tiny ports to perform surgery on the unborn baby. Research suggests that children with spina bifida who have fetal surgery may have less disability and be less likely to need crutches or other walking devices. Fetal surgery also may lower the risk of hydrocephalus. Ask your healthcare professional whether this procedure may be right for you. Ask about the potential benefits. Also ask about the risks to you and your baby, such as premature delivery and other complications. It's important to have a comprehensive evaluation to determine whether fetal surgery can be done. This specialized surgery should only be done at a healthcare facility with experienced fetal surgery experts, a multispecialty team and neonatal intensive care. Typically, the team includes a fetal surgeon, a pediatric neurosurgeon, a maternal-fetal medicine specialist, a fetal cardiologist and a neonatologist.

**Cesarean birth**

Many babies with myelomeningocele tend to be in a feet-first position, known as breech. Cesarean birth may be a safer way to deliver if your baby is breech or has a large cyst or sac.

**Surgery after birth**

Myelomeningocele requires surgery to close the opening in the baby's back within 72 hours of birth. Early surgery can help lower the risk of infection associated with the exposed nerves. It also may help protect the spinal cord from more trauma. During the procedure, a neurosurgeon places the spinal cord and exposed tissue inside the baby's body and covers them with muscle and skin. At the same time, the neurosurgeon may place a shunt in the baby's brain to control hydrocephalus.

**Source**

<https://www.mayoclinic.org/diseases-conditions/spina-bifida/symptoms-causes/syc-20377860>

<https://www.mayoclinic.org/diseases-conditions/spina-bifida/diagnosis-treatment/drc-20377865>

4. **Rett Syndrome**

Rett syndrome is a rare genetic neurological and developmental disorder that affects the way the brain develops. This disorder causes a progressive loss of motor skills and language. Rett syndrome primarily affects females. Most babies with Rett syndrome seem to develop as expected for the first six months of life. These babies then lose skills they previously had — such as the ability to crawl, walk, communicate or use their hands. Over time, children with Rett syndrome have increasing problems with the use of muscles that control movement, coordination and communication. Rett syndrome can also cause seizures and intellectual disabilities. Unusual hand movements, such as repetitive rubbing or clapping, replace purposeful hand use. Although there's no cure for Rett syndrome, potential treatments are being studied. Current treatment focuses on improving movement and communication, treating seizures, and providing care and support for children and adults with Rett syndrome and their families.

**Symptoms**

Babies with Rett syndrome usually are born after an uncomplicated pregnancy and delivery. Most infants with Rett syndrome seem to grow and behave as expected for the first six months. After that, signs and symptoms start to appear. The most pronounced changes generally occur at 12 to 18 months of age, over a period of weeks or months. Symptoms and their severity vary greatly from child to child.

The main signs and symptoms include:

* **Slowed growth.** Brain growth slows after birth. Smaller than usual head size (microcephaly) is sometimes the first sign that a child has Rett syndrome. As children get older, there is delayed growth in other parts of the body.
* **Loss of movement and coordination abilities.** The first signs often include reduced hand control and a decreasing ability to crawl or walk. At first, this loss of abilities occurs rapidly, and then it continues more gradually. Eventually muscles become weak or stiff, with unusual movement and positioning.
* **Loss of communication abilities.** Children with Rett syndrome typically begin to lose the ability to speak, to make eye contact and to communicate in other ways. They may become disinterested in other people, toys and their surroundings. Some children have rapid changes, such as a sudden loss of language. Over time, children may gradually regain eye contact and develop nonverbal communication skills.
* **Unusual hand movements.** Children with Rett syndrome usually develop repetitive, purposeless hand movements, which differ from child to child. Hand movements may include hand-wringing, squeezing, clapping, tapping or rubbing.

Other signs and symptoms can include:

* **Unusual eye movements.** Children with Rett syndrome tend to have unusual eye movements, such as intense staring, blinking, crossed eyes or closing one eye at a time.
* **Breathing problems.** These include breath holding, rapid breathing (hyperventilation), forcefully blowing out air or saliva, and swallowing air. These problems tend to occur during waking hours. Other breathing disturbances such as shallow breathing or short periods of stopping breathing (apnea) can occur during sleep.
* **Irritability and crying.**Children with Rett syndrome may become increasingly agitated and irritable as they get older. Periods of crying or screaming may begin suddenly, for no apparent reason, and last for hours. Some children may experience fears and anxiety.
* **Other unusual behaviors.** These may include, for example, sudden, odd facial expressions and long bouts of laughter, hand licking, and grasping of hair or clothing.
* **Intellectual disabilities.** Loss of skills may be connected to losing the ability to think, understand and learn.
* **Seizures.** Most people who have Rett syndrome experience seizures at some time during their lives. Multiple seizure types may occur and are associated with changes on an electroencephalogram (EEG).
* **Sideways curvature of the spine (scoliosis).** Scoliosis is common with Rett syndrome. It typically begins between 8 and 11 years of age and progresses with age. Surgery may be required if the curvature is severe.
* **Irregular heartbeat.** This is a life-threatening problem for many children and adults with Rett syndrome and can result in sudden death.
* **Sleep disturbances.** Problems with sleep patterns can include irregular sleep times, falling asleep during the day and being awake at night, or waking in the night with crying or screaming.
* **Other symptoms.** A variety of other symptoms can occur, such as a decreased response to pain; small hands and feet that are usually cold; problems with chewing and swallowing; problems with bowel function; and teeth grinding.

**Stages of Rett syndrome**

Rett syndrome is commonly divided into four stages:

* **Stage 1: Early onset.** Signs and symptoms are subtle and easily overlooked during the first stage, which starts between 6 and 18 months of age. Stage 1 can last for a few months or a year. Babies in this stage may show less eye contact and start to lose interest in toys. They may also have delays in sitting or crawling.
* **Stage 2: Rapid deterioration.** Starting between 1 and 4 years of age, children lose the ability to perform skills they previously had. This loss can be rapid or more gradual, occurring over weeks or months. Symptoms of Rett syndrome occur, such as slowed head growth, abnormal hand movements, hyperventilating, screaming or crying for no apparent reason, problems with movement and coordination, and a loss of social interaction and communication.
* **Stage 3: Plateau.** The third stage usually begins between the ages of 2 and 10 years, and it can last for many years. Although problems with movement continue, behavior may slightly improve, with less crying and irritability, and there may be some improvement in hand use and communication. Seizures may begin in this stage and generally don't occur before the age of 2.
* **Stage 4: Late motor deterioration.** This stage usually begins after the age of 10 and can last for years or decades. It's marked by reduced mobility, muscle weakness, joint contractures and scoliosis. Understanding, communication and hand skills generally remain stable or improve slightly, and seizures may occur less often.

**Causes**

Rett syndrome is a rare genetic disorder. Classic Rett syndrome, as well as several variants (atypical Rett syndrome) with milder or more-severe symptoms, occur based on several specific genetic changes (mutations). The genetic changes that cause Rett syndrome occur randomly, usually in the MECP2 gene. Very few cases of this genetic disorder are inherited. The genetic changes appear to result in problems with the protein production critical for brain development. However, the exact cause is not fully understood and is still being studied.

**Rett syndrome in males**

Because males have a different chromosome combination from females, males who have the genetic changes that cause Rett syndrome are affected in devastating ways. Most of them die before birth or in early infancy. A very small number of males have a different genetic change that results in a less destructive form of Rett syndrome. Similar to females with Rett syndrome, these males are likely to live to adulthood, but they're still at risk of a number of intellectual and developmental problems.

**Risk factors**

Rett syndrome is rare. The genetic changes known to cause the disease are random, and no risk factors have been identified. In a very small number of cases, inherited factors — for instance, having close family members with Rett syndrome — may play a role.

**Complications**

Complications of Rett syndrome include:

* Sleep problems that cause significant sleep disruption to the person with Rett syndrome and family members.
* Difficulty eating, leading to poor nutrition and delayed growth.
* Bowel and bladder problems, such as constipation, gastroesophageal reflux disease (GERD), bowel or urinary incontinence, and gallbladder disease.
* Pain that may accompany problems such as gastrointestinal issues or bone fractures.
* Muscle, bone and joint problems.
* Anxiety and problem behavior that may hinder social functioning.
* Needing lifelong care and assistance with activities of daily living.
* Shortened life span. Although most people with Rett syndrome live into adulthood, they may not live as long as the average person because of heart problems and other health complications.

**Prevention**

There's no known way to prevent Rett syndrome. In most cases, the genetic changes that cause the disorder occur spontaneously. Even so, if you have a child or other family member with Rett syndrome, you may want to ask your health care provider about genetic testing and genetic counselling.

**Diagnosis**

Diagnosing Rett syndrome involves careful observation of your child's growth and development and answering questions about medical and family history. The diagnosis is usually considered when slowing of head growth is noticed or loss of skills or developmental milestones occurs. For a diagnosis of Rett syndrome, other conditions with similar symptoms must be ruled out.

**Evaluating other causes for the symptoms**

Because Rett syndrome is rare, your child may have certain tests to determine whether other conditions are causing some of the same symptoms as Rett syndrome. Some of these conditions include:

* Other genetic disorders
* Autism spectrum disorder
* Cerebral palsy
* Hearing or vision problems
* Metabolic disorders, such as phenylketonuria (PKU)
* Disorders that cause the brain or body to break down (degenerative disorders)
* Brain disorders caused by trauma or infection
* Brain damage before birth (prenatal)

What tests your child needs depends on specific signs and symptoms. Tests may include:

* Blood tests
* Urine tests
* Imaging tests such as magnetic resonance imaging (MRI) or computerized tomography (CT) scans
* Hearing tests
* Eye and vision exams
* Brain activity tests (electroencephalograms, also called EEGs)

**Core symptoms**

Diagnosis of classic Rett syndrome includes these core symptoms, which may start to show up anytime from 6 to 18 months of age:

* Partial or complete loss of purposeful hand skills
* Partial or complete loss of spoken language
* Walking problems, such as difficulty walking or not being able to walk
* Repetitive purposeless hand movements, such as hand-wringing, squeezing, clapping or tapping, putting hands in the mouth, or washing and rubbing movements

Additional symptoms that typically occur with Rett syndrome can support the diagnosis.

Guidelines for diagnosis of atypical Rett syndrome may vary slightly, but the symptoms are the same, with varying degrees of severity.

**Genetic testing**

If your child's health care provider suspects Rett syndrome after evaluation, genetic testing (DNA analysis) may be needed to confirm the diagnosis. The test requires drawing a small amount of blood from a vein in your child's arm. The blood is then sent to a lab, where the DNA is examined for clues about the cause and severity of the disorder. Testing for changes in the MEPC2 gene confirms the diagnosis. Genetic counseling can help you understand gene changes and their effects.

**Treatment**

Although there is no cure for Rett syndrome, treatments address symptoms and provide support. These may improve the potential for movement, communication and social participation. The need for treatment and support doesn't end as children become older — it's usually necessary throughout life. Treating Rett syndrome requires a team approach.

Treatments that can help children and adults with Rett syndrome include:

* **Regular medical care.** Management of symptoms and health problems may require a multispecialty team. Regular monitoring of physical changes such as scoliosis, gastrointestinal (GI) issues and heart problems is needed.
* **Medications.** Though medications can't cure Rett syndrome, they may help control some signs and symptoms that are part of the disorder. Medications may help with seizures, muscle stiffness, or problems with breathing, sleep, the GI tract or the heart.
* **Physical therapy.** Physical therapy and the use of braces or casts can help children who have scoliosis or require hand or joint support. In some cases, physical therapy can also help maintain movement, create a proper sitting position, and improve walking skills, balance and flexibility. Assistive devices such as a walker or wheelchair may be helpful.
* **Occupational therapy.** Occupational therapy may improve purposeful use of the hands for activities such as dressing and feeding. If repetitive arm and hand movements are a problem, splints that restrict elbow or wrist motion may be helpful.
* **Speech-language therapy.** Speech-language therapy can help improve a child's life by teaching nonverbal ways of communicating and helping with social interaction.
* **Nutritional support.** Proper nutrition is extremely important for healthy growth and for improved mental, physical and social abilities. A high-calorie, well-balanced diet may be recommended. Feeding strategies to prevent choking or vomiting are important. Some children and adults may need to be fed through a tube placed directly into the stomach (gastrostomy).
* **Behavioral intervention.** Practicing and developing good sleep habits may be helpful for sleep disturbances. Therapies may help improve problem behaviors.
* **Support services.** Early intervention programs and school, social and job-training services may help with integration into school, work and social activities. Special adaptations may make participation possible.

**Source**

<https://www.mayoclinic.org/diseases-conditions/rett-syndrome/symptoms-causes/syc-20377227>

<https://www.mayoclinic.org/diseases-conditions/rett-syndrome/diagnosis-treatment/drc-20377233>

5. **Neurogenetic Disorders**

**Down Syndrome**

Down syndrome is a genetic condition caused when an unusual cell division results in an extra full or partial copy of chromosome 21. This extra genetic material causes the developmental changes and physical features of Down syndrome. The term "syndrome" refers to a set of symptoms that tend to happen together. With a syndrome, there is a pattern of differences or problems. The condition is named after an English physician, John Langdon Down, who first described it. Down syndrome varies in severity among individuals. The condition causes lifelong intellectual disability and developmental delays. It's the most common genetic chromosomal cause of intellectual disabilities in children. It also commonly causes other medical conditions, including heart and digestive system problems. Better understanding of Down syndrome and early interventions can greatly improve the quality of life for children and adults with this condition and help them live fulfilling lives.

**Symptoms**

Each person with Down syndrome is an individual. Problems with intellect and development are usually mild to moderate. Some people are healthy while others have serious health issues such as heart problems that are present at birth. Children and adults with Down syndrome have distinct face and body features. Though not all people with Down syndrome have the same features, some of the more common features include:

* Flattened face and small nose with a flat bridge.
* Small head.
* Short neck.
* Tongue that tends to stick out of the mouth.
* Upward slanting eyelids.
* Skin fold of the upper eyelid that covers the inner corner of the eye.
* Small, rounded ears.
* Wide, small hands with a single crease in the palm and short fingers.
* Small feet with a space between the first and second toes.
* Tiny white spots on the colored part of the eye called the iris. These white spots are called Brushfield's spots.
* Short height.
* Poor muscle tone in infancy.
* Joints that are loose and too flexible.

Infants with Down syndrome may be average size, but typically they grow slowly and remain shorter than other children the same age.

**Developmental delays**

Children with Down syndrome take longer to reach developmental milestones, such as sitting, talking and walking. Occupational therapy, physical therapy, and speech and language therapy can help improve physical functioning and speech.

**Intellectual disabilities**

Most children with Down syndrome have mild to moderate cognitive impairment. This means that they have problems with memory, learning new things, focusing and thinking, or making decisions that affect their everyday life. Language and speech are delayed. Early intervention and special education services can help children and teens with Down syndrome reach their full potential. Services for adults with Down syndrome can help support living a full life.

**Causes**

Human cells usually contain 23 pairs of chromosomes. One chromosome in each pair comes from the sperm, the other from the egg. Down syndrome results from an unusual cell division involving chromosome 21. This unusual cell division results in an extra partial or full chromosome 21. This extra genetic material changes how the body and brain develop. It is responsible for the physical features and developmental problems of Down syndrome.

Any one of three genetic changes can cause Down syndrome:

* **Trisomy 21.** About 95% of the time, Down syndrome is caused by trisomy 21. This means the person has three copies of chromosome 21, instead of the usual two copies. The extra chromosome 21 is in all cells in the body. Trisomy 21 results from an unusual cell division during the development of the sperm cell or the egg cell.
* **Mosaic Down syndrome.** This is a rare form of Down syndrome. People with mosaic Down syndrome have only some cells with an extra copy of chromosome 21. This mosaic of typical and changed cells is caused by an unusual cell division after the egg has been fertilized by the sperm.
* **Translocation Down syndrome.** In a small number of people, Down syndrome can occur when a part of chromosome 21 becomes attached, also called translocated, onto another chromosome. This can happen before or at conception. The person has the usual two copies of chromosome 21, but also has extra genetic material from chromosome 21 attached to another chromosome.

**Is it inherited?**

Most of the time, Down syndrome is not passed down in families. The condition is caused by a random unusual cell division. This can happen during the development of the sperm cell or the egg cell or during early development of the baby in the womb. Translocation Down syndrome can be passed from parent to child. But only a small number of children with Down syndrome have translocation and only some of them inherited it from one of their parents. Either parent may have a balanced translocation. The parent has some rearranged genetic material from chromosome 21 on another chromosome, but no extra genetic material. This means the parent has no signs of Down syndrome, but can pass an unbalanced translocation on to children, causing Down syndrome in the children.

**Risk factors**

Some parents have a greater risk of having a baby with Down syndrome. Risk factors include:

* **Older age.** Chances of giving birth to a child with Down syndrome goes up with age because older eggs have a greater risk of unusual chromosome division. The risk of having a child with Down syndrome increases after a pregnant person is 35 years of age. But most children with Down syndrome are born to pregnant people under age 35 because they have far more babies.
* **Being carriers of the genetic translocation for Down syndrome.** Either parent can pass the genetic translocation for Down syndrome on to their children.
* **Having had one child with Down syndrome.** Both parents who have one child with Down syndrome and parents who have a translocation themselves are at higher risk of having another child with Down syndrome. A genetic counselor can help parents understand the risk of having a second child with Down syndrome.

**Complications**

Health concerns that result from having Down syndrome can be mild, moderate or severe. Some children with Down syndrome are healthy, while others may have serious health problems. Some health concerns may become more of a problem as the person gets older.

Health concerns can include:

* **Heart problems.** About half the children with Down syndrome are born with some type of heart condition that is present at birth. These heart problems can be life-threatening and may require surgery in early infancy.
* **Problems with the digestive system and digesting food.** Stomach and intestinal conditions occur in some children with Down syndrome. These may include changes in the structure of the stomach and intestines. There is a higher risk of developing digestive problems, such as intestinal blockage, heartburn called gastroesophageal reflux disease (GERD) or celiac disease.
* **Problems with the immune system.** Because of differences in their immune systems, people with Down syndrome are at higher risk of developing autoimmune disorders, some forms of cancer and infectious diseases such as pneumonia.
* **Sleep apnea.** Soft tissue and spinal changes can lead to blockage of the airways. Children and adults with Down syndrome are at greater risk of obstructive sleep apnea.
* **Being overweight.** People with Down syndrome are more likely to be overweight or obese compared with the general population.
* **Spinal problems.** In some people with Down syndrome, the top two vertebrae in the neck may not line up as they should. This is called atlantoaxial instability. The condition puts people at risk of serious injury to the spinal cord from activities that bend the neck too far. Some examples of these activities include contact sports and horseback riding.
* **Leukemia.** Young children with Down syndrome have a higher risk of leukemia.
* **Alzheimer's disease.** Having Down syndrome greatly raises the risk of developing Alzheimer's disease. Also, dementia often occurs at an earlier age than in the general population. Symptoms may begin around age 50.
* **Other problems.** Down syndrome also may also be linked with other health conditions, such as thyroid problems, dental problems, seizures, ear infections, and hearing and vision problems. Conditions such as depression, anxiety, autism and attention-deficit hyperactivity disorder (ADHD) also may be more common.

**Life expectancy**

Over the years, there have been advances in healthcare for children and adults with Down syndrome. Because of these advances, children born today with Down syndrome are likely to live a longer life than in the past. People with Down syndrome can expect to live more than 60 years, depending on how severe their health problems are.

**Prevention**

There's no way to prevent Down syndrome. If you're at higher risk of having a child with Down syndrome or you already have one child with Down syndrome, you may want to talk with a genetic counselor before becoming pregnant.

A genetic counselor can help you understand your chances of having a child with Down syndrome. The counselor also can explain the prenatal tests that are available and help explain the pros and cons of testing.

**Diagnosis**

The American College of Obstetricians and Gynecologists recommends offering the option of screening tests and diagnostic tests for Down syndrome to all who are pregnant, no matter what age.

* **Screening tests** can suggest the likelihood or chances that you're carrying a baby with Down syndrome. But these tests can't tell for sure whether your baby has Down syndrome.
* **Diagnostic tests** can tell for sure whether your baby has Down syndrome.

**Screening tests during pregnancy**

Screening for Down syndrome is offered as a routine part of care before the baby's birth, called prenatal care. Although screening tests can only tell your risk of carrying a baby with Down syndrome, they can help you make decisions about the need for diagnostic tests.

Screening tests include the first trimester combined test and the integrated screening test. The first trimester means about the first three months of pregnancy.

**The first trimester combined test**

The first trimester combined test is done in two steps. These include:

* **Blood test.** This blood test measures the levels of pregnancy-associated plasma protein-A (PAPP-A) and the pregnancy hormone known as human chorionic gonadotropin (HCG). Levels of PAPP-A and HCG outside the standard range may indicate a problem with the baby.
* **Nuchal translucency screening test.** During this test, an ultrasound is used to measure a specific area on the back of your baby's neck. When certain conditions caused by chromosome changes are present, more fluid than usual tends to collect in this neck tissue.

Using your age and the results of the blood test and the ultrasound, your healthcare professional or genetic counselor can estimate the risk that your baby has Down syndrome.

**Integrated screening test**

The integrated screening test is done in two parts during the first and second trimesters of pregnancy. The results are combined to estimate the risk of your baby having Down syndrome.

* **First trimester.** Part one includes a blood test to measure PAPP-A and an ultrasound to measure nuchal translucency.
* **Second trimester.** The quad screen measures your blood level of four substances present in pregnancy: alpha fetoprotein, estriol, HCG and inhibin A.

**Cell-free DNA testing**

A small amount of DNA is released from the placenta into a pregnant person's bloodstream. This cell-free DNA in the blood can be examined for the extra chromosome 21 material of Down syndrome. For those at risk of having an infant with Down syndrome, the test can be done starting at 10 weeks of pregnancy. If the test is positive, diagnostic testing is usually needed to confirm that the baby has Down syndrome.

**Diagnostic tests during pregnancy**

If your screening test results are positive or uncertain, or you're at high risk of having a baby with Down syndrome, you might consider more testing to confirm the diagnosis. Your healthcare professional can help you weigh the pros and cons of these tests.

Diagnostic tests that can identify Down syndrome include:

* **Chorionic villus sampling (CVS).** In CVS, cells are taken from the placenta. The cells are used to look at the baby's chromosomes. This test is usually done in the first trimester, between 10 and 14 weeks of pregnancy. The risk of pregnancy loss, called a miscarriage, from a CVS is very low.
* **Amniocentesis.** A sample of the amniotic fluid surrounding the baby in the womb is withdrawn through a needle inserted into the mother's uterus. This sample is then used to look at the chromosomes of the baby. This test is usually done in the second trimester, after 15 weeks of pregnancy. This test also carries a very low risk of miscarriage.

Couples who are being treated for infertility through in vitro fertilization (IVF) who know that they are at increased risk of passing on certain genetic conditions to their children may choose to have the embryo tested for genetic changes before it's implanted in the womb.

**Diagnostic tests for newborns**

A physical exam is usually enough to identify Down syndrome in an infant in the first 24 hours after birth. If your healthcare professional thinks that your infant has Down syndrome, your healthcare professional orders a test called a chromosomal karyotype to confirm the diagnosis. Using a sample of blood, this test looks at your child's chromosomes. If there's an extra full or partial chromosome 21 in all or some cells, the diagnosis is Down syndrome.

**Treatment**

Early intervention for infants and children with Down syndrome can make a major difference in improving their quality of life. Because each child with Down syndrome is unique, treatment will depend on your child's needs. Also, as your child gets older and enters different stages of life, your child may need different care or services. For people with Down syndrome, ongoing services, including healthcare, education and life skills support, are important throughout life. Getting routine medical care and treating issues when needed can help keep a healthy lifestyle.

**Team care**

If your child has Down syndrome, you'll likely rely on a team of specialists that can provide medical care and help your child develop skills as fully as possible. Depending on your child's needs, your team may include some of these experts:

* Primary care pediatrician to coordinate and give routine childhood care.
* Pediatric heart specialist called a cardiologist.
* Pediatric digestive system specialist called a gastroenterologist.
* Pediatric specialist in treating hormone-related conditions called an endocrinologist.
* Developmental pediatrician.
* Pediatric nervous system specialist called a neurologist.
* Pediatric ear, nose and throat (ENT) specialist.
* Pediatric eye doctor called an ophthalmologist.
* Hearing professional called an audiologist.
* Speech and language therapist called a speech-language pathologist.
* Physical therapist.
* Occupational therapist.

You'll need to make important decisions about your child's treatment, services and education. Build a team of healthcare professionals, teachers and therapists you trust. These professionals can help find resources in your area and explain state and federal programs for children and adults with disabilities. You may find it helpful to look for a developmental pediatrician, a specialist with expertise about Down syndrome. Also, some areas have a child Down syndrome specialty clinic that offers a range of services in one place. These experts give special attention to needs and issues that are more common in people with Down syndrome. They can work together with your primary care professional.

**Adults with Down syndrome**

As your child with Down syndrome becomes an adult, healthcare needs can change. Besides general health screenings recommended for all adults, ongoing healthcare includes evaluation and treatment for conditions that are more common in adults with Down syndrome. You may choose to visit an adult Down syndrome specialty clinic, if available.

Conditions common in adults with Down syndrome include:

* Vision and hearing problems.
* Dental issues.
* Low thyroid levels called hypothyroidism.
* Diabetes.
* Celiac disease and GERD.
* Heart disease, stroke and high cholesterol.
* Obesity.
* Sleep apnea.
* Mood and behavior changes.
* Alzheimer's disease.
* Bone problems, such as spine problems, arthritis and osteoporosis.

In addition to meeting health needs, caring for your adult loved one with Down syndrome includes planning for current and future life needs, such as:

* Living arrangements.
* Social and recreational opportunities.
* Support programs and jobs.
* Financial support.
* Guardianship.

**Source**

<https://www.mayoclinic.org/diseases-conditions/down-syndrome/symptoms-causes/syc-20355977>

<https://www.mayoclinic.org/diseases-conditions/down-syndrome/diagnosis-treatment/drc-20355983>

**B. Autonomic Nervous System Disorders**

**1. Dysautonomia/ Autonomic Dysfunction**

For children and young adults with autonomic dysfunction (AD) and postural orthostatic tachycardia syndrome (POTS), a holistic treatment approach is important to improving functionality and quality of life. We provide multidisciplinary care in the Autonomic Dysfunction (AD) Clinic at Johns Hopkins All Children’s Hospital in St. Petersburg, Florida. Our clinic is one of the only pediatric AD clinics in the Southeastern United States. The autonomic nervous system (ANS) regulates many of our automatic processes, such as blood pressure, breathing, digestion, and other functions we do not consciously think about. It also helps us feel and process sensations like hunger, happiness, anxiety and temperature. Autonomic dysfunction (sometimes called dysautonomia) describes a general state where the ANS is not functioning and communicating between organ systems as expected. Postural orthostatic tachycardia syndrome (POTS) is one of several disorders that fall into the category of autonomic dysfunction. Patients with AD can experience inappropriate heart rates, stomach problems, brain fog, fatigue, dizziness, lightheadedness, temperature intolerance, and other symptoms. Mood disturbances like anxiety and depression, and attention issues, such as ADHD, are also common in AD. AD and POTS can be difficult to diagnose. We have the expertise to recognize and appropriately diagnose our patients so they can receive the care that best meets their needs.

**What causes autonomic dysfunction?**

We’ve found through our experience and research that there is rarely a singular cause of autonomic dysfunction. This is part of what can make diagnosis and treatment challenging. Anything that causes dysregulation to the autonomic nervous system, such as an infection, an autoimmune response, and/or a traumatic life event, can lead to AD. Additionally, disruption to other organ systems or bodily processes, including emotional disruption, can put stress on the autonomic nervous system and make it more susceptible to dysregulation.

**How is postural orthostatic tachycardia syndrome (POTS) diagnosed?**

Postural orthostatic tachycardia syndrome (POTS) is one of the most well-known disorders of the autonomic nervous system. In youth, specific criteria are needed for diagnosis including an increase in heart rate of 30-40 beats per minute during performance of orthostatic vital signs (changing positions from lying to sitting to standing) without a significant decrease in blood pressure. However, diagnosis of POTS requires more than just identification of an increase in heart rate with position change. Individuals with POTS will also have abnormalities in other organ systems the autonomic nervous system is involved in regulating. Notably, patients do not have to have a diagnosis of POTS to experience challenging and impairing symptoms of AD.

**Treatment**

**Consistent hydration and salt**

Consistent and adequate fluid and salt intake has been shown to help with many of the common AD symptoms, such as dizziness and fainting (syncope). We work with patients to set goals for daily fluid (water and electrolytes) intake, as well as salt (sodium) intake, which can be achieved by adding it to food or using salt supplements, such as tablets or electrolyte additives.

**Physical activity**

An individually appropriate exercise regimen performed consistently has been proven to be an essential part of re-integrating the ANS and cardiovascular system, and increasing cardiovascular conditioning is one of the strongest predictors of long-term symptom improvement. Our exercise physiologist works with our patients to develop exercise plans that are right for them.

**Mental wellness**

Many individuals with AD deal with anxiety or other mood disturbance. For some, the mood disturbance was present before other symptoms of AD and for others, the mood challenges may have developed due to living with the complex symptoms of AD. Unfortunately, some individuals with AD and POTS have been told their symptoms are solely due to anxiety or depression. We know this to not be true; however, untreated or under treated mood disturbance will make it difficult to significantly improve ANS functioning and will often worsen symptoms of AD and POTS. We know that the psychological mind and physical body do not operate independently of each other, so coping activities are critical to adjusting to and managing symptoms.

**Additional treatments as needed**

Once these strategies have been implemented, we may add supplemental therapies, such as medications, that can be helpful in reducing specific symptoms, depending on the patient’s individual needs. It is also important to identify other sources of abnormal input into the autonomic nervous system from other organ systems. Conditions like anemia, thyroid disease, autoimmune disorders, chronic infections, and sleep disorders can stimulate the ANS in abnormal ways, resulting in development of symptoms similar to those of autonomic dysfunction and POTS. Over time, if some of these conditions are not identified and addressed, they can result in changes to how the ANS functions and processes signals. Our team monitors patients for signs of these conditions and can provide referrals to related specialists at Johns Hopkins All Children’s as needed.

**Source**

<https://www.hopkinsmedicine.org/all-childrens-hospital/services/heart-institute/heart-institute-programs-and-services/pediatric-cardiology-services/autonomic-dysfunction-clinic>

**2. Postural Orthostatic Tachycardia Syndrome (POTS)**

Postural orthostatic tachycardia syndrome (POTS) is a blood circulation disorder characterized by two factors:

* A specific group of symptoms that frequently occur when standing upright
* A heart rate increase from horizontal to standing (or as tested on a tilt table) of at least 30 beats per minute in adults, or at least 40 beats per minute in adolescents, measured during the first 10 minutes of standing

POTS is diagnosed only when orthostatic hypotension is ruled out and when there is no acute dehydration or blood loss. Orthostatic hypotension is a form of low blood pressure: 20mm Hg drop in systolic or a 10mm Hg drop in diastolic blood pressure in the first three minutes of standing upright.

**What does POTS stand for?**

* Postural: related to the position of your body
* Orthostatic: related to standing upright
* Tachycardia: increased heart rate
* Syndrome: a group of symptoms

**Why does heart rate increase excessively with POTS?**

In most patients with POTS, the structure of the heart itself is normal. POTS symptoms arise from a combination of the following:

* Lower amount of blood in the circulation
* Excessive pooling of blood below the level of the heart when upright
* Elevated levels of certain hormones such as epinephrine (also known as adrenaline since it is released by the adrenal glands) and norepinephrine (mainly released by nerves).

When we stand, gravity pulls more blood into the lower half of the body. In a healthy person, to ensure that a sufficient amount of blood reaches the brain, the body activates several nervous system responses. One such response is releasing hormones that help tighten blood vessels and cause a modest increase in heart rate. This leads to better blood flow to the heart and brain. Once the brain is receiving enough blood and oxygen, these nervous system responses settle back to normal. In people with POTS, for unclear reasons that may differ from person to person, the blood vessels don’t respond efficiently to the signal to tighten. As a result, the longer you are upright, the more blood pools in the lower half of your body. This leads to not enough blood returning to the brain, which can be felt as lightheadedness (faintness), brain fog and fatigue. As the nervous system continues to release epinephrine and norepinephrine to tighten the blood vessels, the heart rate increases further. This may cause shakiness, forceful or skipped heartbeats, and chest pain. Some people with POTS can develop hypotension (a drop in blood pressure) with prolonged standing (more than three minutes upright). Others can develop an increase in blood pressure (hypertension) when they stand.

**Types and Causes of POTS**

The causes of POTS vary from person to person. Researchers don’t entirely understand the origins of this disorder. The classification of POTS is the subject of discussion, but most authorities recognize different characteristics in POTS, which occur in some patients more than others. Importantly, these characteristics are not mutually exclusive; person with POTS may experience more than of these at the same time:

**Neuropathic POTS** is a term used to describe POTS associated with damage to the small fiber nerves (small-fiber neuropathy). These nerves regulate the constriction of the blood vessels in the limbs and abdomen.

**Hyperadrenergic POTS** is a term used to describe POTS associated with elevated levels of the stress hormone norepinephrine.

**Hypovolemic POTS** is a term used to describe POTS associated with abnormally low levels of blood (hypovolemia).

**Secondary POTS** means that POTS is associated with another condition known to potentially cause autonomic neuropathy, such as diabetes, Lyme disease, or autoimmune disorders such as lupus or Sjögren’s syndrome.

**What are the symptoms of postural orthostatic tachycardia syndrome?**

POTS symptoms vary from person to person and may include:

* Severe and/or long-lasting fatigue
* Lightheadedness with prolonged sitting or standing that can lead to fainting
* Brain fog: trouble focusing, remembering or paying attention
* Forceful heartbeats or heart palpitations (a feeling of the heart pounding or skipping a beat)
* Nausea and vomiting
* Headaches
* Excessive sweating
* Shakiness
* Intolerance of exercise or a prolonged worsening of general symptoms after increased activity
* A pale face and purple discoloration of the hands and feet if the limbs are lower than the level of the heart

POTS symptoms typically get worse:

* In warm environments, such as a hot bath or shower, a hot room or on a hot day
* In situations involving a lot of standing, such as waiting for a bus or when shopping
* If fluid and salt intake have not been adequate, such as after skipping a meal

POTS symptoms may also get worse when you get a common cold or an infection. In severe cases, POTS symptoms can prevent a person from being upright for more than a couple of minutes. This can greatly affect all aspects of personal, school, work and social life.

**How is POTS diagnosed?**

POTS diagnosis can be complicated because the symptoms can affect a wide range of organ systems, and the most bothersome symptom for each patient may differ. In most instances, symptoms have been present for months before the diagnosis is made. Your doctor will perform a physical exam, order bloodwork and arrange a standing test or a head-up tilt table test to confirm POTS.

**Tilt Table Test for POTS**

During the tilt table test, you are secured on a table while lying flat. Then the table is raised to an almost upright position. Your heart rate, blood pressure and often blood oxygen and exhaled carbon dioxide levels are measured during this test.

You might have POTS if you meet all three of these criteria:

* Your body produces an abnormal heart rate response to being upright
* Your symptoms worsen when upright
* You don’t develop orthostatic hypotension in the first three minutes of testing

**Other POTS Tests**

In some cases, other tests are warranted. They may include:

* Valsalva maneuver to test the response of the autonomic nerves that control the heart.
* Quantitative sudomotor axon reflex test (QSART) to measure response of the autonomic nerves responsible for regulating sweating.
* Although less common, your physician may also schedule an MRI and other imaging tests to rule out tumors or other abnormalities.

**Similar Conditions**

Many conditions share the same symptoms as POTS. POTS can complicate any other chronic health condition, from asthma to inflammatory bowel disease. The vast majority of adolescents and young adults with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) have POTS or related forms of orthostatic intolerance. The intensity of the fatigue, exercise intolerance and other symptoms are greater in those with ME/CFS and POTS than in those with POTS alone. Another condition similar to POTS is inappropriate sinus tachycardia, in which the resting heart rate is usually above 100 beats per minute. Fibromyalgia patients, those with gastrointestinal motility disorders (such as irritable bowel syndrome), excessive sweating (hyperhidrosis) and many other conditions can also develop POTS.

**How is POTS treated?**

Treatment for POTS should be tailored to each individual, because the symptoms and underlying conditions may vary widely. Although there is no known cure for POTS, the condition can be managed in most patients with diet, exercise and medications.

**Postural Orthostatic Tachycardia Syndrome Diet**

The foundation of treating POTS is to drink fluids frequently throughout the day. For most POTS patients, the goal is at least 64-80 ounces (about 2-2.5 liters) a day. You would also need to increase your intake of salty foods and add more salt to your diet with a saltshaker or salt tablets. These dietary modifications help keep water in the bloodstream, which helps more blood reach the heart and the brain. Certain foods or drinks can have an adverse effect on POTS symptoms in some patients. For example, alcohol almost always aggravates POTS. It diverts blood away from the central circulation to the skin and increases loss of fluids through urine. Caffeine can make some people more nervous and lightheaded, but for some it can help improve constriction of blood vessels. Your regular physician or POTS specialist can help you determine how your diet and certain medications could be helping or hindering your treatment.

**Exercise for Postural Orthostatic Tachycardia Syndrome**

Physical therapy can make a difference for some people with POTS. Because sometimes POTS symptoms can worsen with exercise, physical therapy has to start slowly and advance based on your tolerance rather than a rigid plan. As your blood circulation improves with medications and diet, the exercise intensity may be gradually increased. The goal is to retrain the autonomic nervous system to allow for more exercise, which then helps increase the blood volume. Those who can’t stand upright may start exercising in a horizontal or reclined position. Aquatic therapy may work for some POTS patients due to the water creating pressure around the body. Many experts find that manual physical therapy that addresses issues with nerve tightness and range of motion works as a bridge to build better tolerance of exercise.

**POTS Medications**

While no single medication is effective for everyone with POTS, most people with frequent symptoms affecting their quality of life need some form of medication. The search for the right medication or combination of medications requires patience and persistence on the part of both physicians and patients. These medications may focus on:

* Improving blood volume
* Helping the kidneys retain sodium (e.g., fludrocortisone)
* Reducing heart rate or blocking the effect of adrenal hormones on the heart (e.g., beta blockers)
* Improving blood vessel constriction (e.g., midodrine)

**Source**

<https://www.hopkinsmedicine.org/health/conditions-and-diseases/postural-orthostatic-tachycardia-syndrome-pots>

C. **CLASSIC CREUTZFELDT-JAKOB DISEASE**

• Classic CJD is a quick-moving, always fatal disease that occurs worldwide.

• It affects the brain and causes dementia and other problems.

• CJD mostly occurs in older adults.

• There is no treatment or cure.

• It usually leads to death within a year from when symptoms begin.

**Overview**

CJD is caused by a prion, a type of infectious protein. Prions trigger normal proteins in the body to misfold, leading to CJD. CJD causes dementia and other neurologic problems. Once symptoms begin, it can lead to death in months to a year. Classic CJD occurs worldwide in older adults, with the average age in the late 60s. Very few cases occur in people who are younger than 30 years old. CJD occurs worldwide with an estimated rate of about one to two illness per one million population members per year. In recent years in the United States, about 500-600 cases have been reported per year.

**Types**

There are three main types of CJD infection:

**Sporadic**

The vast majority of all CJD cases reported (about 85 percent) are called sporadic. These types of cases occur when prion proteins already in the body misfold for some unknown reason. The result is disease that breaks down the brain's functions. Some cases are fatal within a few months of the first symptoms, and most are fatal within a year.

**Familial**

About 5-15 percent of CJD cases occur because the person has inherited a mutation in the prion protein gene. A person with CJD with a first-degree relative (parent, sibling, or child) who also has the disease would have familial CJD.

**Iatrogenic**

Iatrogenic cases are caused by contact with prions in a healthcare setting or due to biological products. There have been six known CJD cases caused by surgical or medical equipment contaminated with prions is used on another patient.

People who received prion-contaminated human growth hormone prior to 1978 may also develop iatrogenic CJD. Even 50 years later, cases are still being identified.

Finally, cases can occur in people who receive a transplant of specific materials. These include corneal (eye) grafts or dura mater (a membrane in the brain and spinal cord) grafts. If the donor had CJD that was not discovered before the donation, recipients can contract CJD.

**How it affects your body**

People with CJD suffer from dementia. Other symptoms may include trouble walking, sudden jerky movements, and visual disturbances. CJD patients usually die within one year following the onset of symptoms.

**Testing and diagnosis**

Healthcare providers can diagnose an illness as a suspect case based on:

• Symptoms and course of illness

• Tests of a person's spinal fluid

• Magnetic Resonance Imaging (MRI), a brain scan

• EEG, a test of electrical activity in the brain.

The only way to confirm CJD is through testing brain tissue from a biopsy or an autopsy.

**Treatment and Prognosis**

Classic CJD is always fatal, usually within a few months. There is unfortunately no therapy that will slow or stop the progression of disease. So, treatment involves supportive care to make the patient more comfortable.

**Similar diseases**

Though they have very similar names, CJD and variant CJD (vCJD) are not the same disease. Both are prion diseases. However, variant CJD is tied to eating meat from cows infected with bovine spongiform encephalopathy (sometimes called Mad Cow Disease). CJD, sometimes called "classic CJD" to avoid confusion, mostly occurs sporadically. Unlike variant CJD, classic CJD is not caused by any other prion disease.

In general, classic CJD affects people older than 55 while vCJD cases were younger, with an average age of 28. Classic CJD progresses much more quickly, causing death in an average of 4-5 months, while vCJD averages more than a year.

**Source**

Centers for Disease Control and Prevention (2024) Classic Creutzfeldt-Jakob Disease. Available at: https://www.cdc.gov/creutzfeldt-jakob/about/index.html (Accessed: 12 June 2025).

**CREUTZFELDT-JAKOB DISEASE**

**Prevention**

Creutzfeldt-Jakob disease (CJD) is a rare and fatal condition that affects the brain. It causes brain damage that worsens rapidly over time.

**Symptoms of CJD**

Symptoms of CJD include:

• loss of intellect and memory

• changes in personality

• loss of balance and co-ordination

• slurred speech

• vision problems and blindness

• abnormal jerking movements

• progressive loss of brain function and mobility

Most people with CJD will die within a year of the symptoms starting, usually from infection.

This is because the immobility caused by CJD can make people with the condition vulnerable to infection.

**What causes CJD?**

CJD appears to be caused by an abnormal infectious protein called a prion. These prions accumulate at high levels in the brain and cause irreversible damage to nerve cells.

While the abnormal prions are technically infectious, they're very different from viruses and bacteria.

For example, prions aren't destroyed by the extremes of heat and radiation used to kill bacteria and viruses, and antibiotics or antiviral medicines have no effect on them.

**Types of CJD**

There are 4 main types of CJD.

**Sporadic CJD**

Sporadic CJD is the most common type.

The precise cause of sporadic CJD is unclear, but it's been suggested that a normal brain protein changes abnormally ("misfolds") and turns into a prion. Most cases of sporadic CJD occur in adults aged between 45 and 75. On average, symptoms develop between the ages of 60 and 65. Despite being the most common type of CJD, sporadic CJD is still very rare, affecting only 1 or 2 people in every million each year in the UK. In 2020, there were 131 recorded deaths from sporadic CJD in the UK.

**Variant CJD**

Variant CJD (vCJD) is likely to be caused by consuming meat from a cow that had bovine spongiform encephalopathy (BSE, or "mad cow" disease), a similar prion disease to CJD. Since the link between variant CJD and BSE was discovered in 1996, strict controls have proved very effective in preventing meat from infected cattle entering the food chain. But the average time it takes for the symptoms of variant CJD to occur after initial infection (the incubation period) is still unclear. The incubation period could be very long (more than 10 years) in some people, so those exposed to infected meat before the food controls were introduced can still develop variant CJD. The prion that causes variant CJD can also be transmitted by blood transfusion, although this has only happened 5 times in the UK. In 2020, there were no recorded deaths from variant CJD in the UK.

**Familial or inherited CJD**

Familial CJD is a very rare genetic condition where one of the genes a person inherits from their parent (the prion protein gene) carries a mutation that causes prions to form in their brain during adulthood, triggering the symptoms of CJD. It affects about 1 in every 9 million people in the UK. The symptoms of familial CJD usually first develop in people when they're in their early 50s. In 2020, there were 6 deaths from familial CJD and similar inherited prion diseases in the UK.

**Iatrogenic CJD**

Iatrogenic CJD is where the infection is accidentally spread from someone with CJD through medical or surgical treatment. For example, a common cause of iatrogenic CJD in the past was growth hormone treatment using human pituitary growth hormones extracted from deceased individuals, some of whom were infected with CJD. Synthetic versions of human growth hormone have been used since 1985, so this is no longer a risk. Iatrogenic CJD can also occur if instruments used during brain surgery on a person with CJD aren't properly cleaned between each surgical procedure and are reused on another person. But increased awareness of these risks means iatrogenic CJD is now very rare. In 2020, there was 1 death from iatrogenic CJD in the UK caused by receiving human growth hormone before 1985.

**How CJD is treated**

There's currently no cure for CJD, so treatment aims to relieve symptoms and make the affected person feel as comfortable as possible. This can include using medicine such as antidepressants to help with anxiety and depression, and painkillers to relieve pain. Some people will need nursing care and assistance with feeding.

**Symptoms-Creutzfeldt-Jakob disease**

The pattern of symptoms can vary depending on the type of Creutzfeldt-Jakob disease (CJD). In sporadic CJD, the symptoms mainly affect the workings of the nervous system (neurological symptoms) and these symptoms rapidly worsen in the space of a few months. In variant CJD, symptoms that affect a person's behaviour and emotions (psychological symptoms) will usually develop first. These are then followed by neurological symptoms around 4 months later, which get worse over the following few months. Familial CJD has the same sort of pattern as sporadic CJD, but it often takes longer for the symptoms to progress – usually around 2 years, rather than a few months. The pattern of iatrogenic CJD is unpredictable, as it depends on how a person became exposed to the infectious protein (prion) that caused CJD.

**Initial neurological symptoms**

Initial neurological symptoms of sporadic CJD can include:

• difficulty walking caused by problems with balance and co-ordination

• slurred speech

• numbness or pins and needles in different parts of the body

• dizziness

• vision problems, such as double vision

• hallucinations (seeing or hearing things that aren't really there)

**Initial psychological symptoms**

Initial psychological symptoms of variant CJD can include:

• severe depression

• withdrawal from family, friends and the world around you

• anxiety

• irritability

• difficulty sleeping (insomnia)

**Advanced neurological symptoms**

Advanced neurological symptoms of all forms of CJD can include:

• loss of physical co-ordination, which can affect a wide range of functions, such as walking, speaking and balance (ataxia)

• muscle twitches and spasms

• loss of bladder control (urinary incontinence) and bowel control (bowel incontinence)

• blindness

• swallowing difficulties (dysphagia)

• loss of speech

• loss of voluntary movement

**Advanced psychological symptoms**

Advanced psychological symptoms of all forms of CJD include:

• loss of memory, which is often severe

• problems concentrating

• confusion

• feeling agitated

• aggressive behaviour

• loss of appetite, which can lead to weight loss

• paranoia

• unusual and inappropriate emotional responses

**Final stages**

As the condition progresses to its final stages, people with all forms of CJD will become totally bedridden. They often become totally unaware of their surroundings and require around-the-clock care. They also often lose the ability to speak and can't communicate with their careers. Death will inevitably follow, usually either as a result of an infection, such as pneumonia, or respiratory failure, where the lungs stop working and the person is unable to breathe. Nothing can be done to prevent death in these circumstances. Advancements in end of life care (the treatment of incurable conditions) mean that people with CJD often have a peaceful death.

**Causes-Creutzfeldt-Jakob disease**

Creutzfeldt-Jakob disease (CJD) is caused by an abnormal infectious protein in the brain called a prion. Proteins are molecules made up of amino acids that help the cells in our body function. They begin as a string of amino acids that then fold themselves into a 3-dimensional shape. This "protein folding" allows them to perform useful functions within our cells. Normal (harmless) prion proteins are found in almost all body tissues, but are at the highest levels in brain and nerve cells. The exact role of normal prion proteins is unknown, but it's thought they may play a role in transporting messages between certain brain cells. Mistakes sometimes occur during protein folding and the prion protein can't be used by the body. Normally, these misfolded prion proteins are recycled by the body, but they can build up in the brain if they aren't recycled.

**How prions cause CJD**

Prions are misfolded prion proteins that build up in the brain and cause other prion proteins to misfold as well. This causes the brain cells to die, releasing more prions to infect other brain cells. Eventually, clusters of brain cells are killed and deposits of misfolded prion protein called plaques may appear in the brain. Prion infections also cause small holes to develop in the brain, so it becomes sponge-like. The damage to the brain causes the mental and physical impairment associated with CJD, and eventually leads to death. Prions can survive in nerve tissue, such as the brain or spinal cord, for a very long time, even after death.

**Types of CJD**

The different types of CJD are all caused by a build-up of prions in the brain. But the reason why this happens is different for each type.

**Sporadic CJD**

Even though sporadic CJD is very rare, it's the most common type of CJD, accounting for around 8 in every 10 cases. It's not known what triggers sporadic CJD, but it may be that a normal prion protein spontaneously changes into a prion, or a normal gene spontaneously changes into a faulty gene that produces prions. Sporadic CJD is more likely to occur in people who have specific versions of the prion protein gene. At present, nothing else has been identified that increases the risk of developing sporadic CJD.

**Variant CJD**

There's clear evidence that variant CJD (vCJD) is caused by the same strain of prions that causes bovine spongiform encephalopathy (BSE, or "mad cow" disease). In 2000, a government inquiry concluded that the prion was spread through cattle that were fed meat-and-bone mix containing traces of infected brains or spinal cords. The prion then ended up in processed meat products, such as beef burgers, and entered the human food chain. Strict controls have been in place since 1996 to prevent BSE entering the human food chain, and the use of meat-and-bone mix has been made illegal. It appears not everyone who's exposed to BSE-infected meat will go on to develop vCJD. Almost all definite cases of vCJD occurred in people with a specific version (MM) of the prion protein gene, which affects how the body makes a number of amino acids. It's estimated up to 4 in 10 of the UK population have this version of the gene. Cases of vCJD peaked in the year 2000, in which there were 28 deaths from this type of CJD. There have been no confirmed deaths from 2017 to 2020. Some experts believe that the food controls have worked and further cases of vCJD will continue to decline, but this doesn't rule out the possibility that other cases may be identified in the future. It's also possible for vCJD to be transmitted by blood transfusion, although this is very rare and measures have been put in place to reduce the risk of it happening. We don't know how many people in the UK population could develop vCJD in the future and how long it'll take for symptoms to appear, if they ever will. A study published in October 2013 that tested random tissue samples suggested around 1 in 2,000 people in the UK population may be infected with vCJD, but show no symptoms to date.

**Familial or inherited CJD**

Familial or inherited CJD is a rare form of CJD caused by an inherited mutation (abnormality) in the gene that produces the prion protein. The altered gene seems to produce misfolded prions that cause CJD. Everyone has 2 copies of the prion protein gene, but the mutated gene is dominant. This means you only need to inherit 1 mutated gene to develop the condition. So if 1 parent has the mutated gene, there's a 50% chance it will be passed on to their children. As the symptoms of familial CJD don't usually begin until a person is in their 50s, many people with the condition are unaware that their children are also at risk of inheriting this condition when they decide to start a family.

**Iatrogenic CJD**

Iatrogenic CJD (iCJD) is where the infection is spread from someone with CJD through medical or surgical treatment. Most cases of iatrogenic CJD have occurred through the use of human growth hormone to treat children with restricted growth. Between 1958 and 1985, thousands of children were treated with the hormone, which at the time was extracted from the pituitary glands (a gland at the base of the skull) of human corpses. A minority of those children developed CJD, as the hormones they received were taken from glands infected with CJD. Since 1985, all human growth hormone in the UK has been artificially manufactured, so there's now no risk. But a small number of people exposed before 1985 are still developing iCJD. A few other cases of iCJD have occurred after people received transplants of infected dura mater (tissue that covers the brain) or came into contact with surgical instruments that were contaminated with CJD. This happened because prions are tougher than viruses or bacteria, so the normal process of sterilising surgical instruments had no effect. Once the risk was recognised, the Department of Health tightened the guidelines on organ donation and the reuse of surgical equipment. As a result, cases of iCJD are now very rare.

**BSE ('MAD COW' DISEASE)**

Bovine spongiform encephalopathy (BSE), also known as "mad cow" disease, is a relatively new disease that first occurred in the UK during the 1980s. One theory about why BSE developed is that an older prion disease that affects sheep, called scrapie, may have mutated. The mutated disease may have then spread to cows that were fed meat-and-bone mix from sheep containing traces of this new mutated prion.

**Is CJD contagious?**

In theory, CJD can be transmitted from an affected person to others, but only through an injection or consuming infected brain or nervous tissue. There's no evidence that sporadic CJD is spread through ordinary day-to-day contact with those affected or by airborne droplets, blood or sexual contact. But in the UK, variant CJD has been transmitted on 5 occasions by blood transfusion.

**Diagnosis-Creutzfeldt-Jakob disease**

A diagnosis of Creutzfeldt-Jakob disease (CJD) is usually based on medical history, symptoms and a series of tests. A neurologist (a doctor who specialises in conditions of the nervous system) will carry out the tests to rule out other conditions with similar symptoms, such as Alzheimer's disease, Parkinson's disease, or a brain tumour. The only way to confirm a diagnosis of CJD is to examine the brain tissue by carrying out a brain biopsy or, more commonly, after death in a post-mortem examination of the brain.

**Tests for CJD**

A clinical neurologist will rule out other conditions with similar symptoms. They'll also check for some common signs of CJD by carrying out the following tests:

• an MRI brain scan – uses strong magnetic fields and radio waves to produce a detailed image of the brain, and can show up abnormalities particular to CJD

• an EEG – records brain activity and may pick up abnormal electrical patterns seen in sporadic CJD

• a lumbar puncture – a procedure where a needle is inserted into the lower part of the spine to draw out a sample of cerebrospinal fluid (which surrounds your brain and spinal cord) so it can be tested for a certain protein that indicates you may have CJD

• a prototype blood test for variant CJD has also been developed by the prion unit at the Medical Research Council (MRC) and is available through the National Prion Clinic

• tonsil biopsy – a small piece of tissue can be taken from the tonsils and checked for the abnormal prions found in variant CJD (they're not present in other types of CJD)

• genetic test – a simple blood test to find out whether you have a mutation (fault) in the gene that produces normal protein; a positive result may indicate familial (inherited) prion disease

Brain biopsy

During a brain biopsy, a surgeon drills a tiny hole into the skull and removes a small piece of brain tissue using a very thin needle.

It's carried out under general anaesthetic, which means the person will be unconscious during the procedure.

As a brain biopsy carries the risk of causing brain damage or seizures (fits), it's only performed in a few cases where there's a concern that someone doesn't have CJD but some other treatable condition.

**Treatment-Creutzfeldt-Jakob disease**

There's no proven cure for Creutzfeldt-Jakob disease (CJD), but clinical studies are under way at the National Prion Clinic to investigate possible treatments.

At present, treatment involves trying to keep the person as comfortable as possible and reducing symptoms with medicines.

For example, psychological symptoms of CJD, such as anxiety and depression, can be treated with sedatives and antidepressants, and muscle jerks or tremors can be treated with medicines like clonazepam and sodium valproate.

Any pain experienced can be relieved using powerful opiate-based painkillers.

Advance directive

Many people with CJD draw up an advance directive (also known as an advance decision).

An advance directive is where a person makes their treatment preferences known in advance in case they can't communicate their decisions later because they're too ill.

Issues that can be covered by an advance directive include:

• whether a person with CJD wants to be treated at home, in a hospice, or in a hospital once they reach the final stages of the condition

• what type of medicines they'd be willing to take in certain circumstances

• whether they'd be willing to have a feeding tube if they were no longer able to swallow food and liquid

• whether they're willing to donate any of their organs for research after they die (the brains of people with CJD are particularly important for ongoing research)

• if they lose lung function, whether they'd be willing to be resuscitated by artificial means – for example, by having a breathing tube inserted into their neck

Your care team can provide more advice about making an advance directive.

Treating symptoms of CJD

• treating ataxia (loss of physical co-ordination)

• treating urinary incontinence (loss of bladder control)

• bowel incontinence (loss of bowel control)

• treating dysphagia (swallowing difficulties)

• dystonia (muscle spasms and stiffness)

• blindness or vision loss

Care and support in the advanced stages of CJD

As CJD progresses, people with the condition will need significant nursing care and practical support.

As well as help with feeding, washing and mobility, some people may also need help peeing. A tube inserted into the bladder to drain urine (a catheter) is often required.

Many people will also have problems swallowing, so they may have to be given nutrition and fluids through a feeding tube.

It may be possible to treat someone with CJD at home, depending on the severity and progression of their condition.

Caring for someone with CJD can be distressing and difficult to cope with, so many carers prefer to use the specialist services of a hospital or hospice.

Prevention-Creutzfeldt-Jakob disease

Although Creutzfeldt-Jakob disease (CJD) is very rare, the condition can be difficult to prevent.

This is because most cases occur spontaneously for an unknown reason (sporadic CJD) and some are caused by an inherited genetic fault (familial CJD).

Sterilisation methods used to help prevent bacteria and viruses spreading also aren't completely effective against the infectious protein (prion) that causes CJD.

But tightened guidelines on the reuse of surgical equipment mean that cases of CJD spread through medical treatment (iatrogenic CJD) are now very rare.

There are also measures in place to prevent variant CJD spreading through the food chain and the supply of blood used for blood transfusions.

Protecting the food chain

Since the link between bovine spongiform encephalopathy (BSE, or "mad cow" disease) and variant CJD was confirmed, strict controls have been in place to stop BSE entering the human food chain.

These controls include:

• a ban on feeding meat-and-bone mix to farm animals

• the removal and destruction of all parts of an animal's carcass that could be infected with BSE

• a ban on mechanically recovered meat (meat residue left on the carcass that's pressure-blasted off the bones)

• testing on all cattle more than 30 months old (experience has shown that infection in cattle under 30 months of age is rare, and even cattle that are infected haven't yet developed dangerous levels of infection)

Blood transfusions

In the UK, there have been 5 cases where variant CJD has been transmitted by blood transfusion.

In each case, the person received a blood transfusion from a donor who later developed variant CJD.

3 of the 5 recipients went on to develop variant CJD, while the other 2 recipients died before developing variant CJD but were found to be infected following a post-mortem examination.

It's not certain whether the blood transfusion was the cause of the infection, as those involved could have contracted variant CJD through dietary sources.

Nevertheless, steps were taken to minimise the risk of the blood supply becoming contaminated.

These steps include:

• not allowing people potentially at risk from CJD to donate blood, tissue or organs (including eggs and sperm for fertility treatments)

• not accepting donations from people who have received a blood transfusion in the UK since 1980

• removing white blood cells, which may carry the greatest risk of transmitting CJD, from all blood used for transfusions

Source

NHS (2024) Creutzfeldt-Jakob disease (CJD) - Prevention. Available at: https://www.nhs.uk/conditions/creutzfeldt-jakob-disease-cjd/prevention/ (Accessed: 12 June 2025).

**PARANEOPLASTIC SYNDROMES**

Overview

What is a paraneoplastic syndrome?

A paraneoplastic syndrome is a set of signs and symptoms that can occur when you have cancer. The symptoms develop when a malignant tumor causes changes in your body that aren’t directly caused by the cancer itself. The tumor may secrete a hormone or protein that affects a particular body system. Often with paraneoplastic syndromes, your immune system releases antibodies to destroy the tumor. During this process, the antibodies also damage healthy cells (autoimmune response). Paraneoplastic syndromes can affect multiple body systems and organs, including your nervous system, endocrine system (hormones), kidneys, bones, joints, skin and blood, etc. Often, the symptoms of a paraneoplastic syndrome are the first signs of cancer.

**Who is affected by paraneoplastic syndromes?**

You’re more likely to have a paraneoplastic syndrome if you’re middle-aged or older and you have lung, lymphatic, ovarian or breast cancer. The same factors that increase your cancer risk can increase your chances of developing a paraneoplastic syndrome.

**How common are paraneoplastic syndromes?**

About 8% to 20% of people with cancer develop paraneoplastic syndromes.

**What cancers are associated with paraneoplastic syndromes?**

Anyone with a cancerous tumor can develop a paraneoplastic syndrome. The types of cancer most commonly associated with paraneoplastic syndromes are:

• Breast cancer.

• Stomach cancer.

• Leukemia.

• Lymphoma.

• Lung cancer (especially small-cell lung cancer).

• Ovarian cancer.

• Pancreatic cancer.

• Prostate cancer.

• Kidney cancer.

• Testicular cancer.

**Symptoms and Causes**

**What causes paraneoplastic syndromes?**

Some cancerous tumors secrete substances, like hormones or proteins, that cause certain organs in your body to work atypically. As a result, you may experience symptoms that wouldn’t occur without the tumor. These substances can permanently damage an organ or system without treatment. Often, paraneoplastic syndromes occur because your body’s immune system mistakenly harms healthy tissue. Your immune system makes a substance called antibodies. Antibodies protect you from disease by identifying and destroying abnormal cells, like cancer cells. Sometimes, the signals get crossed, and antibodies attack healthy cells and tissue instead, causing symptoms associated with a paraneoplastic syndrome.

**What are the symptoms of paraneoplastic syndromes?**

Symptoms of paraneoplastic syndromes vary depending on the organ systems affected. In more than half of cases (60%), people experience symptoms before receiving a cancer diagnosis. Identifying a paraneoplastic syndrome early can help your healthcare provider diagnose cancer in its early stages when it’s easiest to treat.

Common symptoms of a paraneoplastic syndrome include:

• Fever.

• Loss of appetite and weight.

• Night sweats.

Paraneoplastic syndromes that affect particular organs or body systems may cause system-specific symptoms. Nervous system Paraneoplastic syndromes affecting your central nervous system (brain, spinal cord) and your peripheral nervous system (nerves outside of your brain and spinal cord) may cause:

• Dizziness.

• Double vision.

• Speech difficulty.

• Memory loss.

• Seizures.

• Muscle weakness.

• Reduced reflexes, sensation or coordination.

• Loss of feeling in your arms and legs.

Endocrine system

Paraneoplastic syndromes affecting your endocrine system may cause:

• Fatigue.

• High blood pressure.

• Muscle weakness.

• Nausea and vomiting.

• Unexplained weight gain.

Joints, bones and muscles (rheumatologic)

Paraneoplastic syndromes affecting your joints, bones, muscles and connective tissue may cause:

• Arthritis.

• Joint pain, swelling or stiffness.

Skin

Paraneoplastic syndromes affecting your skin may cause:

• Itching.

• Flushing (redness).

• Thickened skin.

• Benign (noncancerous) skin growths.

What are the types of paraneoplastic syndromes?

There are several paraneoplastic syndromes, including those that affect your nervous system, endocrine system, joints, blood, skin, kidneys, etc.

Nervous system paraneoplastic syndromes

Examples include:

• Cerebellar degeneration.

• Dysautonomia.

• Encephalitis.

• Encephalomyelitis.

• Lambert-Eaton myasthenic syndrome (LEMS).

• Myasthenia gravis (MG).

• Myelopathy.

• Neuromyotonia.

• Opsoclonus-myoclonus syndrome.

• Neuropathy (peripheral neuropathy).

• Stiff-person syndrome.

Endocrine system paraneoplastic syndromes

Examples include:

• Cushing’s syndrome.

• Hypercalcemia.

• Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH).

Rheumatic paraneoplastic syndromes

Examples include:

• Eosinophilic fasciitis.

• Erythromelalgia.

• Hypertrophic osteoarthropathy.

• Palmar fasciitis.

• Paraneoplastic polyarthritis.

Blood paraneoplastic syndromes

Examples include:

• Paraneoplastic erythrocytosis.

• Paraneoplastic thrombocytosis.

Skin paraneoplastic syndromes

Examples include:

• Acanthosis nigricans.

• Dermatomyositis.

• Leukocytoclastic vasculitis.

• Paraneoplastic pemphigus.

• Sweet syndrome.

• Paraneoplastic glomerulonephritis is a paraneoplastic syndrome that affects your kidneys.

**Diagnosis and Tests**

**How are paraneoplastic syndromes diagnosed?**

Your healthcare provider will diagnose paraneoplastic syndromes with a medical history, physical exam and several tests.

• Neurological exam: Paraneoplastic syndromes often affect your nervous system, impacting your brain and muscle function. Your provider may ask you to perform specific tasks to check how your nervous system functions. They’ll want to judge any change in your abilities related to strength, memory and coordination.

• Imaging: Your provider may use imaging tests such as CT scans, MRIs and ultrasounds to look for a tumor that may be causing symptoms.

• Blood tests: Blood tests can reveal suspicious findings that suggest a tumor or that confirm you have antibodies linked to paraneoplastic syndromes. Blood tests can also help your provider rule out other conditions that may be causing your symptoms, like an infection, a hormone disorder or a metabolic disorder.

• Spinal tap: In some instances, your provider may perform a spinal tap (lumbar puncture) to test your cerebrospinal fluid for signs of antibodies attacking healthy cells. During a spinal tap, your provider inserts a needle into your lower back to withdraw a fluid sample. Later, your healthcare provider will test the liquid for antibodies.

**Management and Treatment**

**How are paraneoplastic syndromes managed or treated?**

Your healthcare provider will treat the underlying cancer that’s causing your symptoms. They’ll also work to manage your symptoms to decrease any damage to your body’s organs or systems. Therapies used to manage paraneoplastic syndromes include:

• Corticosteroids: Medications, such as cortisone or prednisone, that reduce inflammation (swelling).

• Immunosuppression: Drugs that decrease your body’s immune response. The drug therapies your provider prescribes will be tailored to your paraneoplastic syndrome.

• Intravenous immunoglobulin: Treatment that destroys the harmful antibodies causing the syndrome. During the procedure, your provider gives you a shot of healthy antibodies that destroy the harmful ones.

• Plasmapheresis: A procedure that decreases the number of antibodies by removing plasma (liquid) from your blood. The plasma contains the antibodies that damage healthy tissue.

• Physical and speech therapy: Muscle exercises that can help improve functions like speech and movement. You may need this therapy if you have a neurological paraneoplastic syndrome.

**Outlook / Prognosis**

**What can I expect if I have a paraneoplastic syndrome?**

Your prognosis mostly depends on your cancer. In some instances, paraneoplastic syndromes cause mild, temporary symptoms. In others, paraneoplastic syndromes cause severe symptoms that must be managed long-term.

Talk to your healthcare provider about how your stage of cancer and response to treatment will affect your prognosis.

**What complications are associated with paraneoplastic syndromes?**

You may experience a broad range of complications, some of which are minor and some that may be more serious or even life-threatening without treatment. Your healthcare provider will discuss potential complications and treatment options with you.

**Source**

Cleveland Clinic (2022) Paraneoplastic Syndromes: Symptoms, Types & Treatment. Available at: <https://my.clevelandclinic.org/health/diseases/17938-paraneoplastic-syndromes> (Accessed: 12 June 2025).

**Neurologic Complications of Cancer and its Treatment**

The central nervous system (CNS) and peripheral nervous system (PNS) are very susceptible to cancer and its treatment. The most direct involvement of the nervous system manifests in the development of primary brain and spinal cord tumors. Many cancers exhibit a propensity toward spread to the CNS, and brain metastases are common problems seen in malignancies such as lung, breast, and melanoma. Such spread may involve the brain or spine parenchyma or the subarachnoid space. In the PNS, spread is usually through direct infiltration of nerve roots, plexi, or muscle by neighboring malignancies. In some cases, cancer has sudden, devastating effects on the nervous system: epidural spinal cord compression or cord transection from pathologic fractures of vertebra involved by cancer; increased intracranial pressure from intracranial mass lesion growth and edema; and uncontrolled seizure activity as a result of intracranial tumors (status epilepticus), which are neuro-oncologic emergencies. The best known indirect or remote effects of cancer on the nervous system are the neurologic paraneoplastic syndromes. Cancer can also result in a hypercoagulable state causing cerebrovascular complications. Treatment of cancer can have neurologic complications. The commonest of these complications are radiation-induced injury to the brain, spine, and peripheral nerves and chemotherapy-induced peripheral neuropathy. The suppressant effect of cancer and its treatment on the body’s immune system can result in infectious complications within the nervous system.

**Introduction**

Cancer often affects the nervous system and may result in significant neurologic morbidity and mortality. These effects may be direct—with direct cancer involvement of the brain, spine, or peripheral nervous system (PNS)—or indirect as in paraneoplastic neurologic syndromes. Treatment of cancer can also damage the nervous system. This article discusses the effects of systemic cancers and their treatment on the nervous system, although the complications of primary brain and spine tumors are not discussed.

**Epidemiology**

Cancer takes a huge toll on the human race. In 2009, it was estimated that almost 1.5 million new cases of cancer would be diagnosed in the United States, resulting in more than half a million deaths . Many of these patients are expected to develop complications in sites distant to the original tumor location. The nervous system is very susceptible to such complications. In a prospective evaluation in a large cancer center, slightly less than half (45.2%) of more than 800 cancer patients seen in neurologic consultation during a 6-month period had metastases to the nervous system .

**Direct Cancer Complications**

**Brain Metastases**

Metastases to the brain from systemic malignancies are the most common direct form of nervous system involvement by cancer. It is estimated that in the United States as many as 200,000 cases of brain metastases (BMs) are diagnosed each year . The most common cancers resulting in BMs are lung, breast, and melanoma. BMs are rare in prostate cancer and quite uncommon in cancers of the female reproductive tract . Gastrointestinal cancers and hematologic malignancies are less likely to result in parenchymal brain metastases. Leukemia and lymphoma are more likely to result in leptomeningeal metastases. Most brain metastases develop in the cerebral hemispheres (80%) in accordance with higher blood flow to the supratentorial compartment .

**Clinical Presentation and Diagnosis**

Seizures, headaches, and focal neurologic deficits, depending on location, usually lead to the diagnosis of brain metastases. Examination may reveal focal neurologic deficits such as focal weakness, numbness, or language problems. Head CT scans will reveal single or multiple discreet areas of contrast enhancement and associated vasogenic edema. Brain MRI may uncover metastases too small for CT resolution and prove more effective in defining size and location of lesions.

**Treatment**

Treatment of brain metastases includes symptomatic therapy for seizures and vasogenic edema. Although there are several anticonvulsants available, nonenzyme-inducing newer generation anticonvulsants are tolerated better and pose less risk of drug–drug interactions than older enzyme-inducing agents. Examples of nonenzyme-inducing anticonvulsants include levetiracetam, lacosamide, and pregabalin. Although seizure prophylaxis is still used, no evidence supports this practice. However, hemorrhagic metastases are more likely to cause seizures and prophylaxis may be prudent in these situations. Vasogenic edema is treated with corticosteroids, usually dexamethasone. Depending on the degree of vasogenic edema and the presence or absence of mass effect, midline shift, and herniation of brain structures, high doses of corticosteroids (dexamethasone 12–24 mg daily) may be necessary. Short-term complications include hyperglycemia, psychoses, and weight gain. Once patients are controlled on symptomatic therapy, more directed therapy for the metastastic lesions is planned. The most important modalities of treatment are surgery and radiation therapy. Chemotherapy has a modest role in the management of this cancer complication. Radiation therapy includes whole brain radiation therapy (WBRT) and stereotactic radiosurgery (SRS). The best treatment for patients with BMs depends on several factors. Age, performance status, and the presence of systemic metastatic disease emerged as the most important factors in a recursive portioning analysis (RPA) of the Radiation Therapy Oncology Group (RTOG) trials that demonstrated benefit from WBRT . The prognostic classes from this analysis were defined as follows. RPA class I is characterized by younger than 65 years old and Karnofsky Performance Status greater than 70; no extracranial disease and primary tumor not progressive; and median survival of 7.1 months. RPA class II is characterized by patients other than those in RPA class I or III and median survival of 4.2 months. RPA class III is characterized by Karnofsky Performance Status less than 70 and median survival of 2.3 months. Tumor histology and number of brain metastases are also important factors in determining treatment. The following guidelines apply given current available data. WBRT is indicated in RPA class I and II patients with single metastasis after surgical resection and as palliative therapy in patients with a poor performance status (RPA class III). WBRT may also be used in RPA class I and II patients with multiple metastases but emerging data indicate that SRS alone as a first-line intervention may be preferable in these patients given the early development of cognitive dysfunction with WBRT .

**Leptomeningeal Metastases**

The largest autopsy series to date indicates that 8% of patients with cancer have leptomeningeal seeding at autopsy. This complication is seen mostly in small cell lung cancer , breast cancer , and melanoma. In hematologic and lymphoid malignancies, non-Hodgkin’s lymphoma (NHL) and acute nonlymphocytic leukemia account for most cases.

**Clinical Presentation, Pathophysiology, and Diagnosis**

Patients present with evidence of spinal cord or nerve root involvement, cranial neuropathies, or symptoms and signs referable to the cerebral hemispheres Patients may present with limb weakness, pain referable to the involved nerve roots or bladder, and bowel disturbances in spine and sacral root involvement. Examination confirms weakness, sensory loss, and changes in deep tendon reflexes. Cranial nerve VI, III, and IV dysfunction result in diplopia and optic nerve involvement causes visual blurring. The fifth cranial nerve is also involved in some cases. Extraocular nerve abnormalities or facial sensory deficits are present. Multiple cranial neuropathies in a patient with cancer are highly indicative of leptomeningeal metastases (LM).

**Cerebral Symptoms**

Cancer cells gain access to the cerebrospinal fluid (CSF) in three ways. The most common route is hematogenous, but direct extension from cancer sites contiguous to the central nervous system (CNS) and entry via perineural and perivascular spaces is also possible . The diagnosis of LM should be confirmed with CSF examination. This study also helps exclude other causes of cerebral, cranial nerve, and spinal/nerve root dysfunction in patients with cancer such as chronic (opportunistic) infections. The presence of malignant cells in the CSF is diagnostic; additionally high protein, low glucose, elevated opening pressures, and increased white cell count support the diagnosis when cytology is negative. A repeat CSF analysis increases the yield in such cases and should be performed. Flow cytometry and polymerase chain reaction techniques are useful in cases of NHL with suspected lymphomatous meningitis . Before CSF analysis, neuroimaging should be performed. MRI of the brain and entire spine is indicated in such cases to help stage the extent of LM and guide management. LM is often associated with increased intracranial pressure and concomitant parenchymal metastatic disease with mass effect. In such cases, a lumbar puncture (LP) for CSF analysis may be contraindicated. MRI imaging may demonstrate LM enhancement, which may be linear or more nodular. Cranial nerve enhancement, especially in the presence of cranial neuropathies, is highly indicative of LM disease. MRI sensitivity is low (<50%) although it is considered more sensitive than CT. CSF flow analysis in patients with LM is another important diagnostic and prognostic tool. Abnormal CSF flow is common in LM and 111indium-diethylenetriamine pentaacetic acid or 99Tc macroaggregated albumin tracers may be used to define the extent and location of such disturbances.

**Treatment**

Treatment is palliative, and the patient and family should be made aware of this fact, as well as of prognostic implications. Surgery, radiation, and chemotherapy play a role, as the multidisciplinary care of these patients is very important. Patients with LM may require ventriculoperitoneal shunting for hydrocephalus. Surgery is also required for placement of Ommaya reservoirs for administration of intrathecal chemotherapy. Radiation therapy may have significant palliative value in patients with LM. Radionuclide studies may demonstrate CSF flow abnormalities. Radiation therapy to areas of CSF block has been shown to be of benefit . Patients who have cerebral LM and concomitant brain metastases are treated with WBRT. Finally, focused radiation to bulky tumor involving the spine can help stabilize or improve neurologic function. Chemotherapy has shown activity in LM, especially lymphomatous and leukemic meningitis. The responses and palliation seen with chemotherapy in solid tumors are less robust but some benefit can also be derived in these cases. Most commonly, chemotherapy is administered via an Ommaya reservoir. DepoCyt (Enzon; New Brunswick, NJ) is considered the drug of choice for such administration. DepoCyt is sustained-release cytarabine (a liposomal formulation) and has shown benefit in patients with lymphomatous meningitis and solid tumor LM . In lymphomatous meningitis, Glantz et al. demonstrated high response rates and better quality of life when liposomal cytarabine was compared with standard cytarabine. In solid tumors, the response rates noted to DepoCyt were similar to what had been reported for methotrexate administration . However, the less-frequent administration of DepoCyt compared with methotrexate was felt to benefit the patient. This drug is also less toxic to the CNS than methotrexate. Direct spinal fluid injection of methotrexate, cytarabine, thiotepa, etoposide, topotecan, and rituximab have all been used in patients with LM. Chamberlain provided a very recent and comprehensive review on this subject.

**Spine Metastases**

Spine metastases are common in cancer patients. The most common form of involvement is metastases to the bone of the spine with or without encroachment on the epidural space. This represents up to 98% of cases of spine metastases. Metastases to the parenchyma of the spinal cord are uncommon. Epidural spinal cord compression (ECSS) is a consequence of metastases to the vertebral bone with encroachment on the epidural space. Cancers most likely to result in ESCC are breast, lung, and prostate cancer, but NHL, melanoma, and adenocarcinoma of unknown primary were also noted in ESCC in a retrospective series of patients . The pathophysiology mainly involves hematogenous dissemination of cancer cells to the vertebral body.

**Clinical Presentation and Diagnosis**

The presenting features of ESCC depend on the level of involvement but pain is essentially universal in such patients. Pain may be reflective of nerve root involvement and have radicular or axial features. Thoracic spine involvement is most common so that mid-back pain, bilateral lower extremity weakness, and sensory disturbances tend to be the most common presenting symptoms. Patients may also develop bowel and bladder symptoms. Such dysfunction may be very prominent in compression occurring at the level of the conus medullaris or cauda equina. The diagnosis of ESCC is clinical. However, neuroimaging is required to confirm the level of compression, assess for the presence of other levels of bone and epidural involvement, and determine the presence of LM. Chamberlain and Kormanik [27] found involvement at more than one level in 29% of cases within their series. In the occasional patient who cannot undergo MRI, CT or CT myelography can also be diagnostic.

**Treatment**

Supportive care includes high-dose steroid therapy, usually with dexamethasone to reduce edema. This often helps with pain control and stabilization and improvement of neurologic function. We usually use immediate intravenous administration of 10 mg of dexamethasone followed by 6 mg every 4 hours. Pain control is very important and specific pain therapy besides corticosteroids is almost always necessary. For definitive therapy, early liaison with a radiation oncologist and a neurosurgeon are key to success. The neurosurgeon may use vertebroplasty or kyphoplasty for pain relief in collapsed vertebrae, corpectomy to resect tumor in the vertebral body and decompress the spine (anterior decompression), or a laminectomy (posterior decompression). Radiation therapy is the most common therapeutic modality available to patients with ESCC and may be the only source of palliation for patients who are not surgical candidates. The various radiation therapy modalities include stereotactic radiotherapy, intensity modulated radiotherapy (IMRT), and conventional external beam radiation therapy. Conventional fractionated external beam radiation therapy is most commonly administered. Radiation therapy is administered one level above and below the site of compression to reduce the risk of recurrence from epidural tumor extension. Success with radiation is highly dependent on tumor histology (eg, melanoma and renal cell carcinoma are radioresistant).

**Peripheral Nervous System Metastases**

The peripheral nervous system may be directly involved by cancer. Metastases to individual nerves is rare; more commonly noted is direct infiltration or compression of nerve roots, plexi (cervical, brachial, or lumbosacral), individual nerves, or muscles.

**Clinical Presentation and Diagnosis**

Cancer may infiltrate a nerve plexus causing pain and sensorimotor deficits in one limb. Examination in such cases may reveal evidence of partial or complete injury to the plexus. In the case of the lumbosacral plexus, injury to the entire plexus from infiltrating neoplasm is seen in 18% of cases, upper plexus involvement (L1-L4) is seen in 31% and the lower plexus (L4-S1) in 51%. Patients with extensive lumbosacral plexus involvement would have weakness of thigh flexion, eversion and adduction, as well as leg extension. Sensory loss over the genitoinguinal region, thigh, and medical aspect of the lower leg as well as loss of the patellar reflex would also be expected signs in such cases. Similarly, involvement of the cervical or brachial plexus by cancer may cause typical findings on examination; the reader is referred to comprehensive texts on this subject. Weakness or numbness may also result from individual nerve involvement. Metastases to a nerve are rare but involvement of nerves from bone, soft tissue, or CSF metastases is not. The numb chin syndrome (NCS) caused by malignant infiltration of the mental or inferior alveolar nerve is one example. Patients present with orofacial numbness involving the chin or lower lip. The most common cause is bone involvement by cancer and nerve compression, although some cases are associated with leptomeningeal metastases . Appropriate diagnostic studies such as a Panorex radiograph of the jaw and cerebrospinal analysis often determines the etiology.

Neuroimaging with MRI is the diagnostic modality of choice for most cases of tumor-related compression neuropathy or plexopathy. It may show direct infiltration of a nerve plexus or a mass compressing an individual nerve. Neuroimaging of plexus lesions may be difficult to interpret, especially when previous radiation therapy to the area (eg, brachial plexus) raises the possibility of radiation plexopathy. In such cases, electrodiagnostic studies with electromyography and nerve conduction studies may be very helpful. This differential is discussed later under nervous system complications from radiation therapy (see below). Treatment of PNS involvement by cancer includes steroids and analgesics to reduce pain. Pain relief may be accomplished using tricyclic or other antidepressants such as duloxetine as well as anticonvulsants. Pregabalin and gabapentin are often the first choices. More definitive therapy includes both radiation and chemotherapy, depending on the underlying histology and site of involvement.

**Indirect Complications of Cancer**

**Paraneoplastic Syndromes**

Neurologic paraneoplastic syndromes (NPNS) are disorders caused by cancer without direct infiltration, metastases, or compression of the CNS or PNS structure involved as determined by clinical presentation. The mechanism is autoimmune and recognition of these syndromes is very important as it may lead to an early cancer diagnosis. Additionally, these syndromes are treatable by control of the underlying malignancy and immunomodulatory therapies. A classic paraneoplastic syndrome, Lambert-Eaton myasthenic syndrome, is discussed and summarized, along with other well-recognized syndromes,

Pathology and clinical presentation of the paraneoplastic syndromes

| **Paraneoplastic Syndrome** | **Antibody** | **Clinical presentation** | **Usual cancer association** | **Pathology** | **Treatment**[**a**](https://pmc.ncbi.nlm.nih.gov/articles/PMC3637950/#TFN1) |
| --- | --- | --- | --- | --- | --- |
| Paraneoplastic  cerebellar  degeneration | Anti-Hu, anti-  Yo, anti-Tr,  anti-Ri | Gait disturbance,  nausea, dizziness,  diplopia | SCLC, ovarian,  breast,  Hodgkin’s  lymphoma | Purkinje cell loss,  dentate, and olivary  nuclei degeneration | Plasmapheresis and  IVIg |
| Paraneoplastic  limbic encephalitis | Anti-Hu, anti-  Ma-2, anti-  NMDAR | Seizures, memory loss,  insomnia | SCLC | Loss of neurons, limbic  microglial  proliferation,  perivascular and  interstitial  inflammation | Corticosteroids and  IVIg or plasma  exchange |
| Paraneoplastic  encephalomyelitis  and associated  paraneoplastic  phenomena | Anti-Hu, anti-  CV-2/  CRMP5, anti-  Ma proteins,  anti-NMDAR | Brainstem: diplopia,  dysphagia, dysarthria;  autonomic: orthostatic  hypotension,  arrhythmias | SCLC, thymoma,  testicular (germ  cell), non-SCLC,  ovarian terato-  mas |  | Plasma exchange, IVIg  or cyclophosphamide  (for anti-CV2/  CRMP5 and anti-  NMDAR) |
| Paraneoplastic stiffman  syndrome | Anti-  amphiphysin | Generalized rigidity | Breast, SCLC | Motor neurons and  interneurons anterior  horn cell loss | IVIG, benzodiazepines |
| Paraneoplastic  sensorimotor  neuropathy | ? | Motor and sensory loss  in extremities | Multiple, usually  advanced | Axonal degeneration or  demyelination | Corticosteroids, IVIg |
| Paraneoplastic  sensory  neuronopathy | Anti-Hu | Sensory loss (limbs,  trunk, face) | SCLC | Neuronal degeneration | Steroids |
| Paraneoplastic  opsoclonusmyoclonus | ? | Falls, ataxia,  opsoclonus, | Neuroblastoma  (children),  SCLC (adults) |  | Corticosteroids, IVIg,  ACTH; adults: IVIg |
| Lambert-Eaton  myasthenic  syndrome | Anti P/Q-type  VGCC | Weakness, fatigue,  autonomic  dysfunction | SCLC | P/Q type VGCC  antibody | Immunotherapy, 3,4-  DAP, pyridostigmine,  guanidine |
| Polymyositis and  dermatomyositis  [ | ? | Proximal myopathy,  neck flexion  weakness, eyelid rash  in DM | Ovarian, breast,  lung,  gastrointestinal | Immune-mediated  vasculopathy, muscle  necrosis with elevated  creatine kinase | Corticosteroids, IVIg  and chemotherapy  (eg, azathioprine) |
| Myeloma associated  sensorimotor  neuropathy | ? | Neuropathy (sensory,  sensori-motor) | Multiple myeloma |  | None specific |

Refers to specific treatment modalities. In most cases treatment of the underlying tumor is usually the most effective treatment of the paraneoplastic syndrome.

ACTH—adrenocorticotropic hormone; CRMP5—collapsin response mediator protein 5; IVIg—intravenous immunoglobin; NDMR—N-methyl-D-aspartate receptor; SCLC—small cell lung cancer; VGCC—voltage-gated calcium channel.

**LAMBERT-EATON MYASTHENIC SYNDROME**

Patients with small cell lung cancer (SCLC) sometimes present with a neuromuscular syndrome consisting of fluctuating weakness, fatigue, and autonomic dysfunction caused by a defect in acetylcholine release from the presynaptic terminal at the neuromuscular junction. In turn, this is caused by antibodies to presynaptic voltage-gated calcium channels (VGCC). Examination confirms limb (especially lower extremity) weakness and hyporeflexia. Electromyography (EMG)/NCS show a decremental response to low-frequency repetitive nerve stimulation and an incremental response to higher frequency stimulation. Detection of VGCC antibodies in the presence of such findings should prompt an aggressive search for an underlying malignancy, usually SCLC. Treatment includes 3,4-diaminopyridine to improve acetylcholine release, pyridostigmine, and guanidine. Immunomodulatory therapy with intravenous Ig and plasmapheresis, as well as long-term steroid therapy, may also be necessary .

**Cerebrovascular Complications of Cancer**

**Ischemic Stroke**

Cancer patients are at risk for cerebrovascular complications for three reasons: 1) cancer and its treatment result in disorders of coagulation; 2) cancer may directly affect blood vessels; and 3) infections in individuals who are immunocompromised may result in secondary stroke . Cancer induces a hypercoagulable state. Tumors produce procoagulant factors, such as tissue factor and cancer procoagulant, and interaction of these with the host blood vessels result in abnormal clotting. Additionally, there is some downregulation of anticoagulant pathways, activated protein C resistance, or an imbalance between tissue factor expression and tissue factor plasminogen inhibitor . The normal coagulation balance tips in favor of a hypercoagulable state resulting in localized thrombosis or even a chronic disseminated intravascular coagulation (DIC) in cancer patients. As recently reviewed by Rogers, there are two thrombotic syndromes in cancer that may result in cerebrovascular disease: nonbacterial thrombotic endocarditis (NBTE) and cerebral intravascular thrombosis without NBTE. Graus et al. described nonbacterial thrombotic endocarditis as the most common cause of stroke in cancer patients. This complication—often seen in patients with lung or gastrointestinal mucin-producing adenocarcinoma—results from cardiac vegetations that embolize to main cerebral arteries, often the middle cerebral. As a result, patients present with typical stroke symptoms such as aphasia, focal weakness, and numbness. Heparin has been recommended in such cases, as well as consideration for valve replacement if the patient is felt to have a reasonable prognosis. In non-NBTE cerebral thrombosis, the process of thrombosis is more widespread and affects smaller blood vessels than in NBTE cases; heparin is also recommended in such cases. Because the process is multifocal, more generalized presentations (eg, encephalopathy) than in NBTE are common. There are also documented cases of embolic stroke from tumor cell embolization and tumors can cause direct compression of blood vessels, especially venous sinuses. In such cases, direct management of the tumor is the only therapy possible. Venous sinus thrombosis occurring in cancer patients is yet another manifestation of hypercoagulability. Diagnosis is confirmed with magnetic resonance venography and this complication is treated with anticoagulation.

**Hemorrhagic Stroke**

Intracranial blood may be seen in patients with hemorrhagic metastases. Melanoma, lung cancer, and renal cell cancer are the most likely metastatic histologies to be hemorrhagic. Such cases may present with seizures, headache, and are diagnosed and managed in a similar manner to nonhemorrhagic metastases. The occurrence of a consumptive coagulopathy (DIC) may result in intracranial hemorrhage in hematologic malignancy.

**Neurologic Complications of Cancer Treatment**

**Nervous System Complications from Radiation Therapy**

The central and peripheral nervous system may be affected by radiation therapy. In the brain and spinal cord this is believed to be caused by a combination of vascular damage and damage to glia, mainly oligodendrocytes. The timing of radiation complications has led to a classification of such injury and this is helpful in predicting reversibility. During or immediately after radiation therapy, patients may develop acute injury, usually manifest mainly by headache, nausea, and vomiting. Injury to capillaries and leakage with edema are the likely mechanism and this injury is steroid-responsive. Complications occurring beyond a month and up to 6 months from completion of radiation therapy are termed early-delayed injury. In these cases, patients may develop drowsiness, fatigue, and cognitive problems (somnolence syndrome). In addition, patients may also develop brain MRI changes suggestive of tumor progression. These changes are reversible and improvement may be hastened by steroids. Conversely, late injury is associated with permanent diffuse white matter changes (leukoencephalopathy), focal areas of necrosis, and cognitive impairment. This is irreversible and the most severe forms result in a severe dementia and, ultimately, death. The most important risk factors in the development of leukoencephalopathy and cognitive impairment are older age, radiation dose, brain volume receiving radiation, and combination with chemotherapy . The combination of radiation therapy with methotrexate for treatment of primary CNS lymphoma is the best example of this; very severe forms of leukoencephalopathy may be seen in patients treated with such combinations especially when methotrexate is administered concomitantly with radiation. Radiation-induced cognitive impairment presents a spectrum of severity ranging from mild impairment to frank dementia . Neuroimaging shows white matter abnormalities and in cases associated with dementia, significant atrophy may be noted. There are no effective therapies although psychostimulants have been advocated for the attention and memory problems associated with mild to moderate cognitive dysfunction . Focal areas of necrosis in the brain raise concern about possible tumor progression because the appearance can be very similar with heterogenous enhancement and lesional areas consistent with necrosis. Surgery may be necessary when such areas are symptomatic and to exclude tumor progression requiring further treatment.

**Spinal Cord Injury**

In the spinal cord, radiation-induced damage may be early-delayed, which is almost always reversible and late-delayed, which is more likely to be permanent . Because the former improves spontaneously, specific treatment is not really necessary. Leung et al. noted Lhermitte’s sign in 121 (10.3%) of 1171 nasopharyngeal carcinoma patients treated with radiation. They also noted that median development time for such signs was 3 months and that it was more likely to happen when the dose to the cervical cord exceeded 48.9 Gy. In rare instances, late-delayed radiation myelopathy has been noted to improve clinically and on imaging. However, in most cases, deficits persist or progress. Patients may present with weakness and sensory loss in the legs and a paraparesis and sensory level are confirmed on examination; another presentation is with Brown-Sequard syndrome. Problems with bladder and bowel control are also possible. MRI of the spinal cord may show increase signal at the level affected and even contrast enhancement . Although anticoagulation and hyperbaric oxygen are used occasionally, corticosteroids are the most commonly used therapy that may result in improvement.

| **Complication** | **Typical drugs causing complication** | **Clinical syndrome** | **Treatment and prevention** | **Prognosis** |
| --- | --- | --- | --- | --- |
| Peripheral and  cranial  neuropathy | Vinca alkaloids (tubulin  binding) vincristine,  vinblastine | Sensorimotor neuropathy  (axonal) | Drug withdrawal | Usually good with  discontinuation |
|  | Platinum compounds (DNA  crosslink formation) (cisplatin,  carboplatin, oxaliplatin) | Sensory neuropathy;  vestibulo-cochlear toxicity  with cisplatin (hearing loss,  dizziness, ataxia, vertigo) | Amifostine, carbamazepine to treat  oxaliplatin neuropathy; calcium  gluconate, magnesium sulfate, and  oxcarbazepine prophylaxis for  oxaliplatin neuropathy | Variable for  cisplatin; good  with treatment  for oxaliplatin |
|  | Taxanes: paclitaxel, docetaxel  (inhibition of microtubule  function) | Sensory neuropathy  (numbness, tingling) | Vitamin E and N-acetyl carnitine | Good with drug  discontinuation |
|  | Macrolide antibiotic:  ixabepilone (tubulin binding) | Sensory neuropathy  (numbness, tingling) | Discontinue drug or reduce dose | Good with  treatment |
|  | Thalidomide (antiangiogenesis) | Sensory neuropathy |  |  |
|  | Bortezomib (proteosome  inhibitor) | Distal sensory axonal  neuropathy | Discontinue drug/reduce dose | Good with treatment |
| Stroke | Bevacizumab; imatinib | Hemorrhagic or ischemic  stroke (rare) | Discontinue drug | Variable |
| Seizures | Cisplatin (DNA crosslinks);  cytosine arabinoside  (pyrimidine antimetabolite) | Seizures | Discontinue drug/reduce dose | Good with drug  discontinuation |
|  | Cyclophosphamide | Seizures | Discontinue drug/reduce dose | Good with drug  discontinuation |
|  | Nelarabine (purine nucleoside  analog) | – | Discontinue drug/reduce dose | Good with drug  discontinuation |
| Myelopathy | Cisplatin (DNA crosslinks);  Ara-C (pyrimidine antimetabolite);  MTX (dihydrofolate  reductase inhibitor) | Lhermitte’s sign with  cisplatin; motor, sensory  and bowel/bladder  dysfunction with Ara-C and  MTX. | Discontinue drug/reduce dose | Good with  treatment (drug  discontinuation) |
| Aseptic  meningitis | MTX (dihydrofolate reductase  inhibitor) | Headache, neck stiffness,  back pain and fever  following intrathecal  injection. | Discontinue drug and reduce dose;  corticosteroids | Usually good |
| Encephalopathy | Ifosfamide (alkylating agent) | Confusion, hallucinations,  drowsiness | Discontinue drug; benzodiazepines  may hasten recovery | Good with drug  withdrawal |
|  | Methotrexate (dihydrofolate  reductase inhibitor) | Acute mental status change,  seizures within 24 hours of  high-dose i.v administration | Discontinue drug | Good with drug  withdrawal |
| Cerebellar  syndrome | Cytosine arabinoside  (pyrimidine antimetabolite) | Ataxia, nystagmus, and  dysarthria | Prevention with avoidance of high-dose | Variable; may or  may not reverse  completely |

**Peripheral Nerve Involvement: Plexus and Individual Nerve Damage from Radiation Therapy**

The brachial and lumbosacral plexi may also be involved in the radiation fields for treatment of breast and lung cancers and pelvic tumors respectively. As with CNS involvement, the tempo of the injury helps predict the prognosis. Thus, early-delayed brachial plexopathy occurring in the first few months after treatment usually improves whereas late-delayed injury is a progressive, disabling disorder. In both cases, sensorimotor deficits in the limb supplied by the plexus are typical. EMG and nerve conduction studies are helpful, especially in helping distinguish brachial plexopathy of the late-delayed type from tumor recurrence with infiltration of the plexus. Myokymic discharges on EMG and the absence of severe pain favors radiation damage as the likely diagnosis. Neuroimaging with dedicated MRI of the plexus may show a mass involving the plexus; nonuniform, asymmetric diffuse, or focal enlargement especially eccentric masses with contrast enhancement favor neoplastic infiltration. In postradiation plexopathy, a more uniform symmetric swelling of the plexus is noted. In difficult cases, plexus biopsy may be necessary. Treatment of radiation-induced plexopathy includes steroids and pain management combined with physical therapy.

**Nervous System Complications from Chemotherapy**

Chemotherapy agents can result in toxicity to the nervous system. Peripheral neuropathy is the most common complication noted with a variety of chemotherapy agents.

**Ara-C—cytosine arabinoside; MTX—methotrexate**.

This table is not comprehensive of all neurotoxic agents used in cancer therapy and their complications. It is meant to provide examples of some of the most common neurologic toxicities seen with cancer therapy and the common agents causing such toxicity. The reader is referred to comprehensive texts on this subject. Some chemotherapy drugs cause more than one type of neurotoxicity (eg, cisplatin may cause peripheral and cranial neuropathies, seizures, and myelopathy). Neurotoxicity may be seen with newer agents and is not restricted to conventional chemotherapy. Neurotoxicity may be exacerbated by the administration of more than one neurotoxic drug or by combination with radiation. The best example of the latter is methotrexate leukoencephalopathy, commonly seen as a delayed complication of high-dose or intrathecal methotrexate with radiation administered before or during such therapy. This syndrome has been seen in adults treated for primary CNS lymphoma and children treated for leukemia with such combinations. Gradual cognitive dysfunction and frank dementia may develop in such cases although neurologic stabilization is seen in some patients.

**Peripheral Neuropathy**

Conventional chemotherapy agents such as vinca alkaloids, platinum compounds, and taxanes are well known to cause neuropathy syndromes. However, some newer agents such as bortezomib, a proteosome inhibitor, are also associated with this complication. The presentation of chemotherapy-induced neuropathy depends on the offending agent and type of neuropathy induced, duration of treatment, and patient-related factors. In sensory neuropathies, numbness, tingling, and pain in the extremity is typical. Investigation with EMG/NCS is not strictly necessary in most cases but is done occasionally when the presentation is atypical (eg, worsening of symptoms with withdrawal of chemotherapy). In axonopathies, a decrease in the amplitude of action potentials and prolonged latencies are noted. Demyelination results in delayed conduction velocities. Among prevention strategies for chemotherapy-induced neuropathy, perhaps the most obvious is the limitation in cumulative drug dosing with drugs such as thalidomide or the vinca alkaloids. However, there are chemotherapy-specific strategies, such as the use of magnesium and calcium salt infusions to limit oxaliplatin neuropathy. Other examples of specific treatments, as well as a list of nervous system complications of chemotherapy, are provided in.

**Neurologic Complication of Stem Cell Transplantation**

The regimen used in stem cell transplantation (SCT) for treatment of cancers such as leukemias and lymphomas has been associated with neurologic complications such as seizures, encephalopathy, and stroke. In addition, severe immunosuppression associated with this treatment may result in severe infections of the nervous system. Allogeneic stem cell transplantation was associated with neurologic complications in 18% of patients at day100 after transplant in a series of patients treated for malignant and nonmalignant disease]. Seizures may occur with high-dose busulfan conditioning SCT regimens and benzodiazepine prophylaxis has been advocated in such cases. The occurrence of seizures in this setting has been reported as high as 37%. Encephalopathy may have multiple causes in SCT patients. The chemotherapy agents used are the commonest offenders and ifosfamide, melphalan, and etoposide may all be associated with this complication. Stroke occurring as a complication of therapy for cancer has been discussed. The severe bone marrow suppression with thrombocytopenia in SCT makes this population high-risk for intracerebral hemorrhage. Hemorrhage can also be a result of septic emboli to the brain caused by opportunistic infections in this population.

**Infections**

Infections include opportunistic infections with bacteria, viruses, fungi, and parasites. Aspergillus fumigatus is the most common fungal infection in such cases and Toxoplasma gondii is the most common parasite to result in CNS infection. Viruses of the herpes group are very neurotropic and may result in skin eruptions from sensory nerve involvement, as well as encephalitis. JC virus reactivation, a consequence of treatment- or disease-related immunosuppression, results in progressive multifocal leukoencephalopathy with a very poor prognosis.

**Conclusions**

Cancer can involve the nervous system directly or through the toxic effects of treatment. Additionally, cancer can have effects on the immune system and the coagulation system that result in paraneoplastic syndromes and cerebrovascular disease, respectively. The immunosuppressant effect of cancer and its treatments may result in opportunistic infections of the nervous system.

Source

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**Mitochondrial Diseases**

**Overview**

A magnified mitochondria within a human cell affected by a mitochondrial disease. Mitochondrial diseases are genetic conditions that affect how mitochondria function in your body.

**What is mitochondrial disease?**

Mitochondrial diseases are a group of conditions that affect how mitochondria work in your body. Mitochondria make energy in your cells. When mitochondria aren’t able to produce enough energy that your body needs, it affects how your organs function. Mitochondrial diseases can affect almost any part of your body, including the cells of your:

• Brain.

• Nerves.

• Muscles.

• Kidneys.

• Heart.

• Liver.

• Eyes.

• Ears.

• Pancreas.

**What are mitochondria?**

You may hear mitochondria called “the powerhouse of the cell.” Mitochondria are an energy factory. The job of mitochondria is to process oxygen and convert substances from the foods you eat into energy. Mitochondria exist in nearly every cell in the human body. Mitochondria produce 90% of the energy our bodies need to function.

**What are the types of mitochondrial disease?**

There are many types of mitochondrial diseases. Some of the most common include:

• Mitochondrial encephalopathy, lactic acidosis and stroke-like episodes (MELAS) syndrome.

• Leber hereditary optic neuropathy (LHON).

• Leigh syndrome.

• Kearns-Sayre syndrome (KSS).

• Myoclonic epilepsy and ragged-red fiber disease (MERRF).

**How common is mitochondrial disease?**

An estimated 1 in 5,000 people has a genetic mitochondrial disease. It’s common for mitochondrial diseases to receive a misdiagnosis due to the number and type of symptoms and organ systems involved, so this number may be underestimated.

**Symptoms and Causes**

**What are the symptoms of mitochondrial disease?**

Symptoms of mitochondrial diseases vary based on the type and location of the affected cells. They can range from mild to severe and could include:

• Poor growth.

• Muscle weakness, muscle pain or a low muscle tone.

• Vision and/or hearing loss.

• Developmental delays or issues with cognitive development.

• Diarrhea or constipation.

• Unexplained vomiting.

• Acid reflux and/or swallowing difficulties.

• Seizures.

• Migraines.

• Respiratory (breathing) problems.

• Fainting.

Symptoms of mitochondrial diseases can be present at birth, but they can also arise at any age. A healthcare provider usually detects symptoms affecting more than one organ or organ system at the same time. Symptoms of the same disease can vary from person to person, even among family members.

**What causes mitochondrial disease?**

A lack of energy production from mitochondria in your cells causes mitochondrial disease. Mitochondria are responsible for producing energy within your body. When your mitochondria don’t receive the instructions they need from your body’s DNA to make energy, it can damage your cells or cause them to die early. This affects how your organs and organ systems function, which leads to symptoms of the condition.

**How does someone get a mitochondrial disease?**

Mitochondrial diseases are genetic. You can inherit these conditions from your biological family in an autosomal dominant or autosomal recessive pattern. This means that you can get a changed (mutated) gene that causes this condition from one or both of your biological parents respectfully. Some cases can occur randomly (de novo) without any history of the condition in your biological family. Certain cases of mitochondrial disease have a mitochondrial inheritance. This occurs when the mitochondria contain their own DNA. Mitochondrial conditions caused by mutations in the mitochondrial DNA are exclusively inherited from the child's mother.

**Can other conditions cause mitochondrial diseases?**

Yes. Mitochondrial dysfunction occurs when mitochondria don’t work as well as they should due to another disease or condition. Many conditions can lead to secondary mitochondrial dysfunction, including:

• Alzheimer’s disease.

• Muscular dystrophy.

• Type 1 diabetes.

• Multiple sclerosis (MS).

• Cancer.

If you have secondary mitochondrial dysfunction, you don’t have a genetic mitochondrial disease.

**What are the risk factors for mitochondrial disease?**

You’re more at risk of developing a mitochondrial disease if it runs in your biological family history or if you have a condition that causes secondary mitochondrial dysfunction. Mitochondrial disease affects both adults and children.

**What are the complications of mitochondrial disease?**

Mitochondrial diseases affect how your organs function. It can cause the following complications:

• Increased risk of infection.

• Strokes.

• Pancreatic failure.

• Parathyroid failure.

• Diabetes.

• Liver failure.

• Cardiomyopathy.

• Kidney disease.

• Dementia.

• Gastrointestinal conditions.

• Drooping eyelid (ptosis).

Complications can be life-threatening.

**Diagnosis and Tests**

**How is a mitochondrial disease diagnosed?**

A healthcare provider will diagnose a mitochondrial disease after a series of examinations and tests that may include:

• A review of your medical and family history.

• A complete physical examination.

• A neurological examination.

• A metabolic examination that includes blood and urine tests and, if needed, a cerebrospinal fluid test (spinal tap).

• DNA testing.

Other tests, depending on your symptoms and the affected areas of your body, might include:

• Magnetic resonance imaging (MRI) or spectroscopy (MRS) for neurological symptoms.

• Retinal exam or electroretinogram (ERG) for vision symptoms.

• Electrocardiogram (EKG) or echocardiogram for symptoms that affect your heart.

• Audiogram for hearing symptoms.

• Electroencephalogram (EEG) for seizures and related brain issues.

More advanced testing could include biochemical testing, which looks for changes in body chemicals involved in energy making. A healthcare provider may perform a biopsy where they take a sample of skin and/or muscle tissue to examine it under a microscope.

**Are mitochondrial diseases difficult to diagnose?**

Yes. Because mitochondrial diseases affect so many different organs and tissues of your body, and you may have many different symptoms, mitochondrial diseases can be difficult to diagnose. There’s no single laboratory test that can diagnose a mitochondrial disease. This is why a referral to a medical facility with physicians who specialize in these diseases is critical to making the diagnosis.

**Management and Treatment**

**How is a mitochondrial disease treated?**

Treatment for a mitochondrial disease varies based on the type and your symptoms. Treatment could include:

• Taking medications to reduce symptoms, like medications to prevent seizures.

• Taking vitamins or supplements, like riboflavin, coenzyme Q10 and carnitine.

• Changing your diet (nutrition) and exercising.

• Physical therapy, occupational therapy or speech therapy.

• Wearing assistive devices like hearing aids.

There’s no cure for mitochondrial disease. Treatment focuses on preventing life-threatening complications. Treatment that works for one person may differ from what works to treat someone else with the same condition.

**Are there side effects of the treatment?**

Talk to your healthcare provider about side effects before starting treatment. They’ll discuss the side effects of your treatment specifically and what you should look out for. Each type of treatment comes with its own possible side effects.

**Outlook / Prognosis**

**What is the life expectancy for mitochondrial disease?**

Your healthcare provider can give you the best advice on your life expectancy after a mitochondrial disease diagnosis. Your outlook depends on your symptoms, affected organs and general health. Some affected children and adults have the same expected lifespan as someone who doesn’t have this condition. Others might experience drastic changes in their health over a very short period of time. Some may have occasional flare-ups of symptoms throughout their lives. Although there’s no cure for mitochondrial diseases, research is ongoing to learn more.

**Prevention**

**Can mitochondrial disease be prevented?**

There’s no known way to prevent mitochondrial diseases. If you have a mitochondrial disease, you can avoid situations that can make your symptoms worse like:

• Exposure to extreme cold and/or heat.

• Skipping meals.

• Not getting enough sleep.

• Stress.

A healthcare provider may suggest you conserve (save) your energy to avoid using up all of your body’s energy in a short period of time.

**Source**

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**Treatments & Drug Information**

**Common Medications:**

* Sumatriptan (Imitrex): For acute migraines; side effects: chest tightness.
* Levetiracetam (Keppra): Antiseizure; side effects: drowsiness, mood changes.
* Dopamine agonists (e.g., Pramipexole): For Parkinson’s; side effects: hallucinations.

**Procedures/Therapies:**

* Botox Injections: For chronic migraines/spasticity.
* Deep Brain Stimulation (DBS): For Parkinson’s tremor.
* IV Thrombolytics (tPA): Emergency stroke treatment.

**5. Prognosis, Risk Factors, Prevention**

**Chronic Condition Management:**

* Epilepsy: 70% achieve seizure control with medication.
* Stroke: FAST recognition (Face, Arms, Speech, Time) improves outcomes.

**Prevention:**

* **Stroke:** Control hypertension, quit smoking.

Neuropathy: Manage diabetes, limit alcohol.

**Predefined Q&A Sets**

**Q:** *"What’s the difference between a seizure and epilepsy?"* **A:** *"A seizure is a single event; epilepsy is ≥2 unprovoked seizures."*

**Q:** *"Can migraines cause brain damage?"* **A:** *"No, but chronic migraines may increase stroke risk."*

**Q:** *"Is Parkinson’s disease hereditary?"* **A:** *"Most cases are sporadic, but 15% have genetic links."*

**Doctor-Patient Conversations (De-identified)**

**Example 1:**

* **Patient:** *"My hands shake when I’m stressed. Could it be Parkinson’s?"*
* **Neurologist:** *"Essential tremor is more likely. Let’s check for resting tremors."*

**Example 2:**

* **Patient:** *"How long does a lumbar puncture take?"*
* **Neurologist:** *"About 30 minutes. You’ll lie on your side, and we’ll numb the area first."*

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