



Congenital Disorders of Glycosylation (CDG)

Learn All You Can About Congenital Disorders of Glycosylation (CDG)

Finding out your child has a rare genetic disorder like CDG can be hard. Learning more about CDG can help you care for your child and make plans for the future.

Read this resource to learn about the disorder, medical terms you are likely to hear, causes, symptoms, and how the disorder may be diagnosed and treated. Also learn about the health care providers who may be a part of your child's care over time. Talk to your child's health care team at any time if you have questions.



This resource includes some wise words from a parent of a child with CDG.

Understanding CDG

Congenital disorders of glycosylation (CDG) is a large group of rare, inherited disorders that affect a complex process in the body called glycosylation. Most children who have CDG have neurological issues and symptoms, developmental problems, growth delays and problems with organs not working like they should.

Congenital means that CDG is a condition that happens at or before birth.

Notice that “disorders” is plural. This is because CDG is not just one disorder, but rather, a group of disorders. There are many types. Which type your child has depends on which body system is affected.

About glycosylation

Glycans are sometimes called “sugar trees,” “antennas” or “sugar chains” by health care providers. They are built from sugar “building blocks.”

When some people hear sugar, they think of blood sugar, blood glucose or diabetes. This is not the case with glycans, which are not used for burning calories.

Glycosylation is the process of creating, changing and attaching these sugar building blocks to proteins and lipids.

- When the sugar building blocks attach to proteins, they are called “*glycoproteins*.”
- When the sugar building blocks attach to lipids, they are called “*glycolipids*.”

When someone has CDG, his or her body cannot properly add or attach the sugar building blocks to proteins or lipids. Every single system in the body needs the process of glycosylation to work right so the body can function normally. This is why people with CDG have many health problems — because many body systems are affected by glycosylation not working correctly.

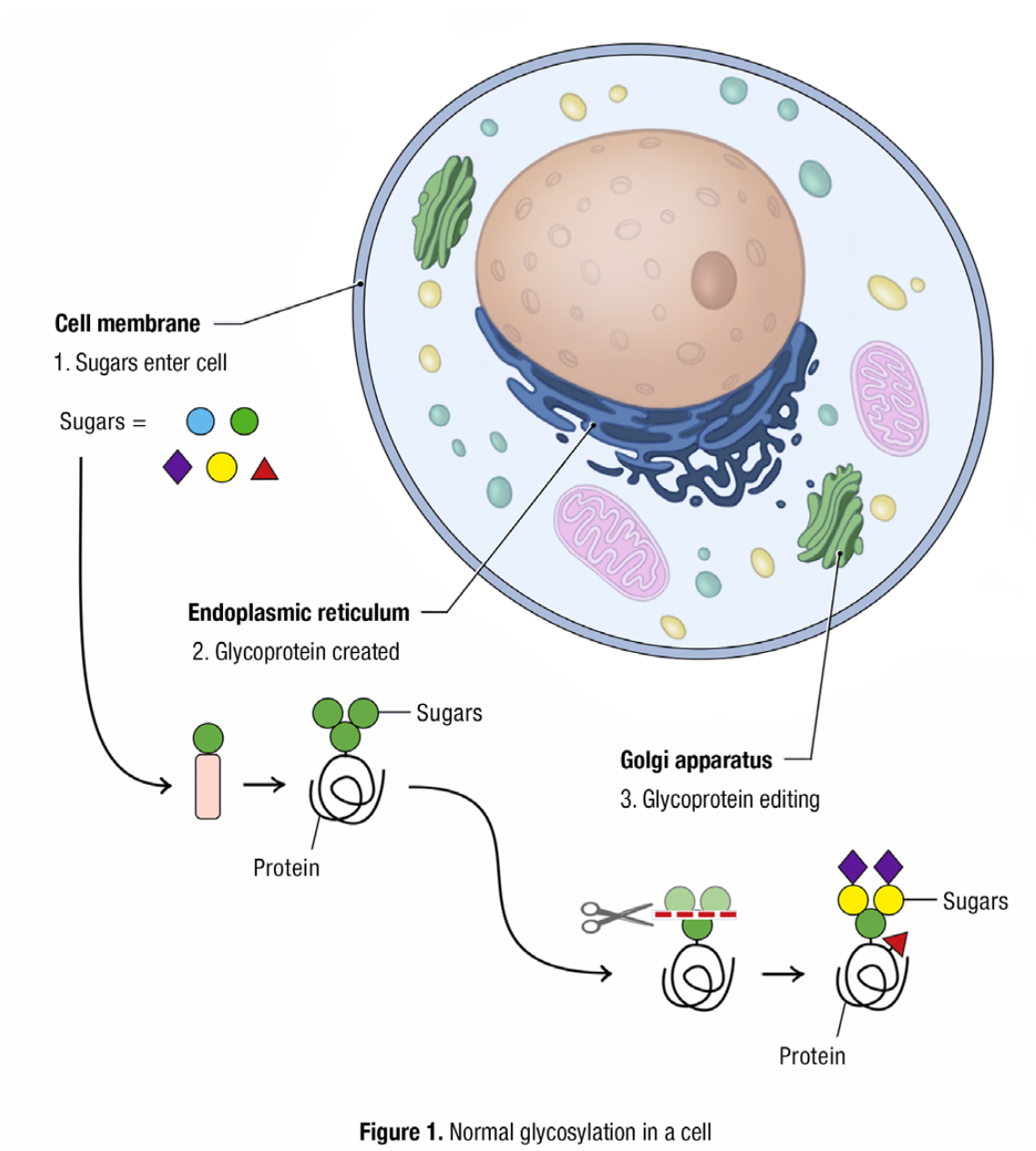


Figure 1. Normal glycosylation in a cell

Your Child's Health Care Team

Depending on your child's unique needs, he or she may need care from many medical specialists.

Over time, your child may have many appointments with his or her care team. After your child has been seen the first time, each provider usually recommends when the next follow-up visit will be.

Your child's health care team may include:

- A medical genetics specialist.
- Genetic counselors.
- A primary care pediatrician.
- Nurse practitioners and special nurses.
- Neurologists.
- Physical therapists (PT).
- Occupational therapists (OT).
- Speech language pathologists.
- Registered dietitians.
- Gastroenterologists.
- Endocrinologists.
- Cardiologists.
- Vision specialists, called ophthalmologists.

Depending on your child's unique health concerns, the team may also include:

- Liver specialists, called hepatologists.
- Coagulation and blood disease specialists, called hematologists.
- Orthopedic specialists.
- Infectious disease physicians, called immunologists.
- Hearing specialists, called audiologists.
- Ear, nose and throat specialists.
- Financial representatives.
- Social workers.

Your child's health care team works together to provide supportive care for your child and help him or her make the most of his or her abilities. Know that you and your child are the most important members of this team.



"Build a health care team you trust, a team that understands the complexity of your child's health, that listens to others, that understands the rarity of your child's disease and knows that your CDG child is unlike most kids, that your child will present symptoms in a way that a typical child would not. Find a team of doctors that will fight for the answers, be thorough and compassionate."

Symptoms of CDG

Symptoms vary depending on the type and sub-type your child has. They also vary among family members with the same type. Symptoms can range from mild to severe.

CDG can affect every body system. Which symptoms and complications your child has depends on which systems are affected.

Because the condition is very rare, only a few people have each type and sub-type. This makes it hard for health care providers to have a complete list of symptoms. Not everyone has every symptom.

Some children have serious medical conditions which can be life-threatening. Your child may be in the hospital often and for long stays.

Neurological problems

- Developmental delays, such as talking and walking later than others
- Cognitive impairment
- Seizures
- Poor balance and coordination problems, called ataxia
- Slurred speech, called dysarthria
- Crossed eyes, called esotropia

Growth problems

- Feeding difficulties leading to slow weight gain, called failure to thrive
- Delays in getting taller or gaining weight

Problems related to your child's organs not working as they should

- Gastrointestinal symptoms, such as throwing up and diarrhea
- Liver problems
- Heart problems

Endocrine problems

- Decreased thyroid hormone activity, called hypothyroidism
- Low blood sugar due to high insulin levels, called hypoglycemia or hyperinsulinism
- Growth hormone deficiency

Skeletal and joint problems

- Curvature of the spine, called scoliosis
- Joint problems

Hematologic problems

- Blood clotting problems, such as increased bleeding
- Increased risk of forming blood clots, called thrombosis

General problems

- Severe or long-lasting infections
- Swelling of the skin and fluid collection around the organs

"Do not compare your child to others, even ones who do not have CDG."

Cause of CDG

To understand the cause of CDG, it can help to understand some basic concepts about genes and heredity.

What are genes?

Most people have 46 chromosomes in all their cells. Each chromosome is made up of a long chain of a chemical called deoxyribonucleic acid (DNA).

A gene is a section of one of these DNA chains. See Figure 2.

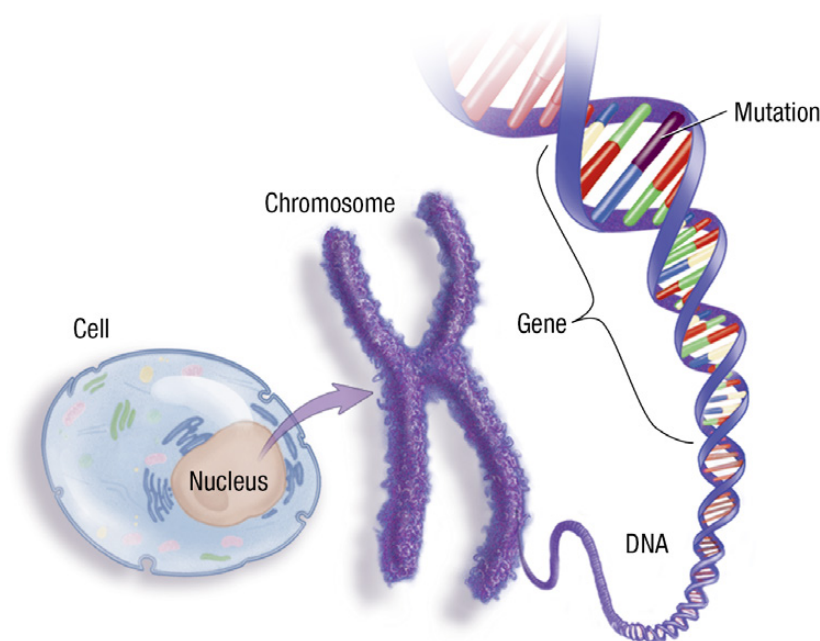


Figure 2. Each cell has chromosomes in its nucleus. Chromosomes are long chains of DNA that contain genes.

Everyone is unique because of their genes. Genes are like an instruction book that tells your cells how to work. For example, genes determine everything from your eye color to your blood type to your height.

CDG is caused by mistakes or changes in genes. Health care providers used to call these mutations. They are now called pathogenic genetic variants.

Pathogenic genetic variants are like words in a sentence that are spelled wrong or are in the wrong order. The sentence cannot be read correctly when this happens. Inherited genetic variants pass from a parent to a child. At birth, they are in every cell of a child's body. Genetic variants can be inherited from either the mother or the father.

Pathogenic genetic variants can keep cells from doing their work correctly, which can lead to genetic diseases like CDG. Genes determine how well the process of glycosylation works in your body. There are over 400 genes in the human genome that have a role in the process of glycosylation.

How CDG Types Are Named

Currently, over 150 types of CDG have been identified with new types being identified all the time. CDG types are grouped based on the sugar building blocks affected.

Children diagnosed with the same type usually have the same medical problems, but not always.

The largest CDG group is called the “N-linked” group. The N-linked group is divided into two types: type I and type II.

- In type I, sugar chains are missing.
- In type 2, sugar chains are incomplete or incorrect.

Health care providers used to name the types based on the pattern of the sugar building blocks, but that system became confusing.

Now providers use a system of naming the type using the official abbreviation of the name of the affected gene followed by “-CDG.” For example, one type is PMM2-CDG and another is PGM1-CDG.

Diagnosing CDG

CDG is usually diagnosed when your child is a baby. To diagnose CDG, your child's health care provider does a thorough physical exam and talks to you about your and your family's medical history.

Children with CDG are often mistakenly diagnosed with other conditions. This is because their symptoms are similar to symptoms of other conditions. Some are mistakenly diagnosed with cerebral palsy or other neurological or genetic disorders. An important part of diagnosis is ruling out other conditions.

Your child's health care provider may order these tests:

- Genetic testing, which is the most reliable way to diagnose CDG. Genetic testing can also determine the type.
- Blood tests to check for many things, including missing sugar building blocks on hormone proteins, coagulation factors, transport proteins, and elevated liver enzymes (ALT and AST).
- A transferrin glycosylation test, which is used to check for missing or incomplete sugar chains. Transferrin glycosylation results are often normal in many children with CDG. Special laboratory tests might be needed.



Additional tests

Depending on symptoms or problems your child has, you may be referred to specialists for tests of other conditions that are often associated with CDG.

Your child may have imaging exams done, such as liver ultrasounds, X-rays and MRI scans. Results of these can be used by your child's provider to plan treatment.

Overview of Treatment

Although there is currently no cure for CDG, there are many treatments and therapies available to help your child. The goal of these treatments is to treat the symptoms and the problems caused by the condition. This type of treatment is called supportive therapy.

Supportive therapy may include:

Physical therapy — A physical therapist (PT) can work with your child to develop muscle training and exercises that may help your child's strength, flexibility, balance, motor development, and mobility.

Speech therapy — Speech-language pathologists can help improve your child's ability to speak clearly or to communicate using sign language.

Occupational therapy — Occupational therapists (OT) can develop an exercise program for your child that includes stretching, strengthening, and functional use of the upper extremities.

A special diet — There are two CDG types where a diet that includes a special sugar supplement can help improve most symptoms.

- For the type called MPI-CDG, mannose can help.
- For the type called PGM1-CDG, galactose can help.

Other treatment may include:

- Seizure management.
- Nutrition care including tube feeding, if needed.
- Heart medication.
- Hormone supplements to treat growth problems.
- Antibiotics to treat or prevent infection.
- Organ transplants.

Next Steps

The next step for you is to learn more information about how your child's condition may be treated. You can also learn about how to help your child have the best life possible.

Talk to your child's health care team about next steps in your CDG journey.

"Love for your child will carry you through even on the hardest days. Your life may no longer be the same, but the feelings of gratitude for this special child will far outweigh the feelings of stress on tough days ahead. The tears of confusion and sadness will eventually change to tears of joy."

Terms You May Hear or Read About CDG

Medical conditions can be complicated. Genetic conditions are especially complicated. CDG is even more so.

Here is a list of terms you are likely to read or hear. Understanding these terms can help you have good conversations with your child's health care provider.

Autosomal — Humans have 23 pairs of chromosomes. One pair determines which sex a person is. The other 22 are called autosomes.

Carrier — A person who has the gene for a condition or trait that can be passed on to his or her children.

Chromosomes — Any of the DNA-containing structures located in the nucleus of cells that contain all or most of the genes in an organism.

Congenital — Term used to describe a condition someone has from birth.

Enzymes — Complex proteins produced by cells that cause biochemical reactions.

Enzyme assay — A test that is done to measure a protein's activity to determine how efficient the protein is in biochemical reactions.

Failure to thrive — Term used to describe when a child does not gain weight as he or she should.

Gene — A coding sequence in the DNA. A specific mistake in a gene causes a specific disease.

Gene variant — Changes in the DNA code in a specific gene.

Genetic code — A DNA code written using four letters: A, T, C, and G.

Genetic — Relating to or caused by genes.

Glycoproteins — Sugar blocks attached to proteins.

Glycolipids — Sugar blocks attached to lipids.

Metabolism — The process by which your body converts what you eat and drink into energy.

Mutations — This term was previously used by providers to describe a mistake in genetic code. The new term used is pathogenic genetic variant.

Oligosaccharides — Sugar blocks assembled in a chain.

Pathogenic genetic variant — Mistake in the DNA code in a specific gene. This used to be called a mutation.

Prognosis — The anticipated or expected plan for healing or recovery.

This material is for your education and information only. This content does not replace medical advice, diagnosis or treatment. New medical research may change this information. If you have questions about a medical condition, always talk with your health care provider.