MAYO CLINIC

PATIENT EDUCATION

GPI Anchor Disorders: A Subtype of Congenital Disorders of Glycosylation (CDG)

BARBARA WOODWARD LIPS
PATIENT EDUCATION CENTER

Mayo Clinic Children's Center

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Infectious Diseases
Medical Genetics
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Nephrology
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Transgender Clinic
Transitions Program
Transplant Center
Travel Clinic
Vascular Malformations
Velo-Pharyngeal Insufficiency Clinic
Voiding Clinic
Weight Management Clinic

Learn All You Can About Your Child's Condition

GPI anchor disorders are a subtype of a rare genetic condition called congenital disorders of glycosylation, also called CDG. Finding out your child has a rare genetic condition like GPI anchor disorders can be hard. You probably have many questions and you may feel overwhelmed. Your child's health care team is here to help.

Read this resource to learn about the condition and medical terms you are likely to hear. Read about the causes, symptoms and how the condition is 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. Learning more about the condition can help you care for your child and make plans for the future.

The quotes you see throughout this resource were provided by the mother of two daughters who have GPI anchor disorders. She has shared her wise words and special story to help you on your journey as the parent of a child with this condition.

Understanding CDG

To understand GPI anchor disorders, it can help to first learn about CDG.

Congenital disorders of glycosylation (CDG) are a large group of rare, inherited disorders. These disorders affect a complex process in the body called glycosylation.

Most children who have CDG have neurological and 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 a group of disorders. There are many subtypes. The subtype a child has depends on which body system is affected.

GPI anchor disorders is one of those subtypes. Within GPI anchor disorders, there are also many more subtypes.

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.

See Figure 1 for how glycosylation works in someone who does not have CDG.

"Rely on your health care team for information. Don't put too much effort into medical research online because much of what's out there is outdated and doesn't capture the capabilities of our children. Each child will write his or her own story."

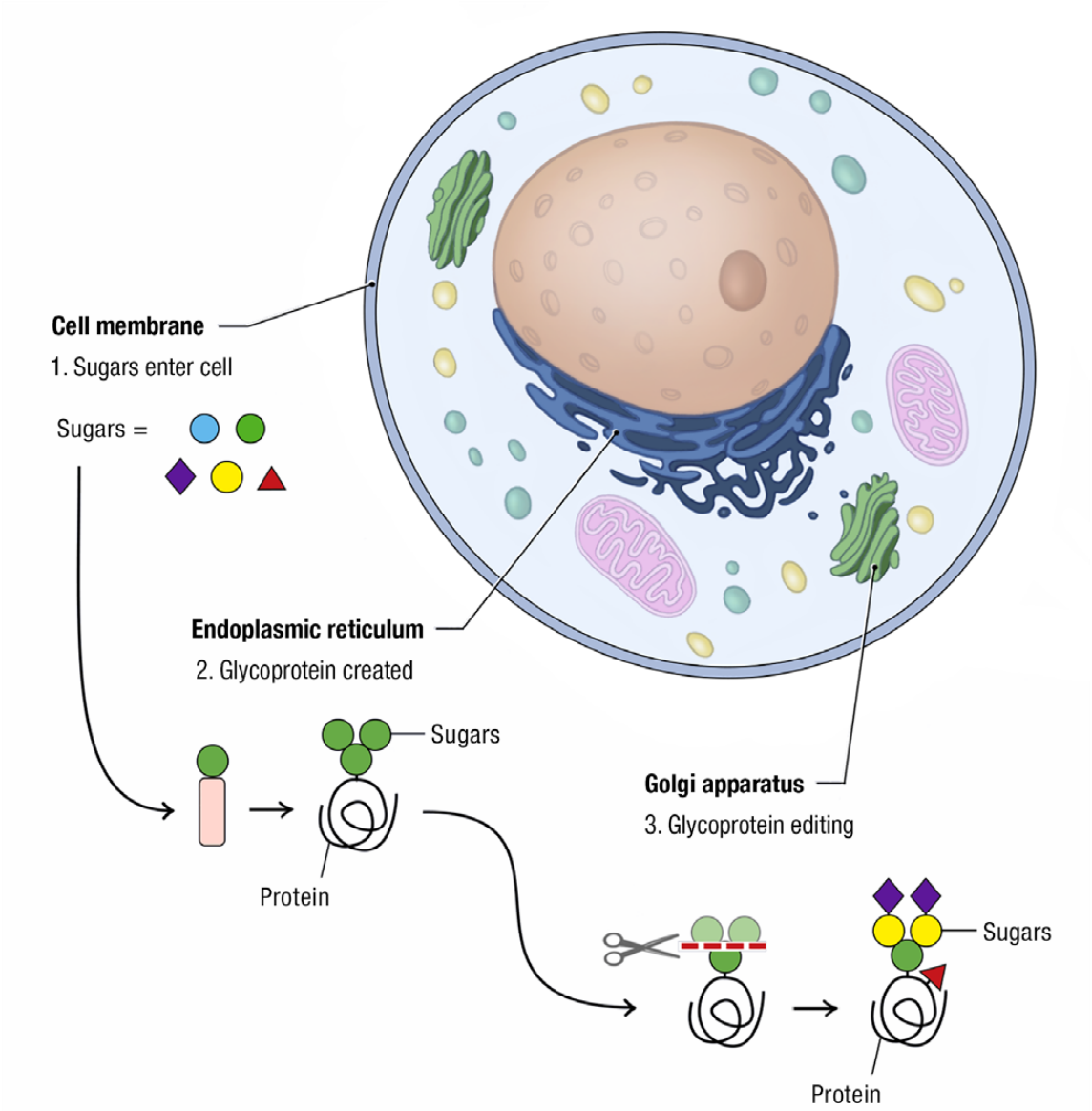

Figure 1. How glycosylation works in someone who does not have GPI anchor disorders or any subtype of CDG

Every single system in the body needs the process of glycosylation to work right so the body can function as it should. This is why people who have CDG have many health problems. Many body systems are affected by glycosylation not working correctly.

"This is a difficult diagnosis and the uncertainty can feel unbearable, but there is a community of families who can provide unconditional love and encouragement."

Understanding GPI Anchor Disorders

A glycolipid is made from sugar building blocks and fat. GPI (glycosylphosphatidylinositol) is a glycolipid anchor. The GPI anchor is responsible for attaching some proteins to the outside of the cell surface membrane.

When the GPI anchor does not form as it should, proteins are not able to stay anchored to the cell membrane. The proteins attached to the GPI anchor have several important roles. See Figure 2.

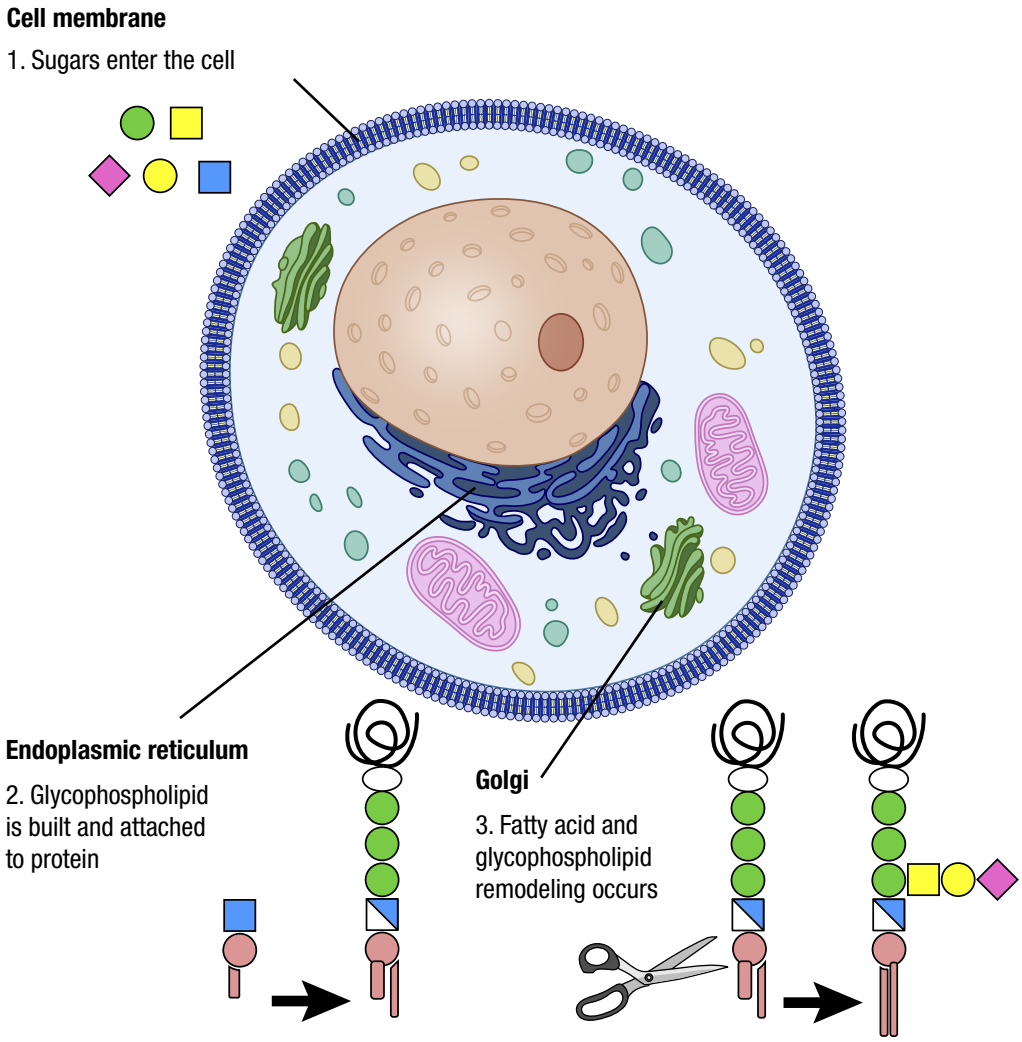

Figure 2. Glycosylation in a cell with healthy GPI anchor synthesis

GPI anchor disorders is one of the rarest subtypes of CDG. All subtypes of GPI anchor disorders are named for a specific step in the genetic pathway. They are named using letters. For example, some subtypes are PIGA-CDG, PIGB-CDG and PIGC-CDG.

Symptoms of GPI Anchor Disorders

Symptoms can vary between each child with GPI anchor disorders. Symptoms are even different among family members with the same type. Symptoms can range from mild to severe.

GPI anchor disorders can affect every system in the body. Which symptoms and complications your child has depends on which systems are affected. Because it is so rare, it is hard for health care providers to have a complete list of symptoms. Not everyone with the condition has every symptom.

Some children have serious medical conditions caused by GPI anchor disorders that can be life-threatening. Your child may often be in the hospital, sometimes for long stays.

Neurological problems

- Developmental delays, such as talking and walking later than others
- Cognitive impairment
- Seizures
- Low muscle tone
- Poor balance and coordination problems
- Slurred speech or no speech
- Crossed eyes
- Rapid eye movement
- Cortical visual impairment or delayed visual maturation
- Hearing loss

Growth and feeding problems

- Feeding difficulties leading to slow weight gain
- Poor swallowing ability

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

- Gastrointestinal symptoms, such as throwing up, diarrhea and constipation
- Congenital heart defects
- Frequent respiratory infections
- Stiffening of the heart muscles
- Calcification of the kidneys or kidney cysts
- Liver problems

Endocrine problems

- Decreased thyroid hormone activity
- Low blood glucose levels

Muscle, bone, teeth and joint problems

- Teeth problems and a high-arched palate
- Joint problems
- Fingers or toes that do not form as they should
- High levels of a bone enzyme called alkaline phosphatase

Hematologic problems

- Increased risk of forming blood clots

Other problems

- Severe or long-lasting infections
- Dry skin

Your Child's Health Care Team

Your child may need care from many medical specialists. Over time, your child may have many appointments with different members of the 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 the following:

- 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 (SLP)
- Registered dietitians
- Gastroenterologists
- Endocrinologists
- Cardiologists
- Vision therapists
- Ophthalmologists
- Orthotist

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

- Hepatologists
- Nephrologists
- Hematologists
- Audiologists
- Otolaryngologists
- Financial representatives
- Social workers

Members of your child's health care team work together to provide care and support. They help your child develop each ability to the highest level that can be reached. You and your child are the most important members of this team.

"Be an advocate for your child. We as parents know and understand more about our kids than most doctors. CDG kids don't act medically like other kids."

Cause of GPI Anchor Disorders

To understand the cause of GPI anchor disorders, it helps to understand genes and heredity.

About genes

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

A gene is a section of one of these DNA chains. See Figure 3.

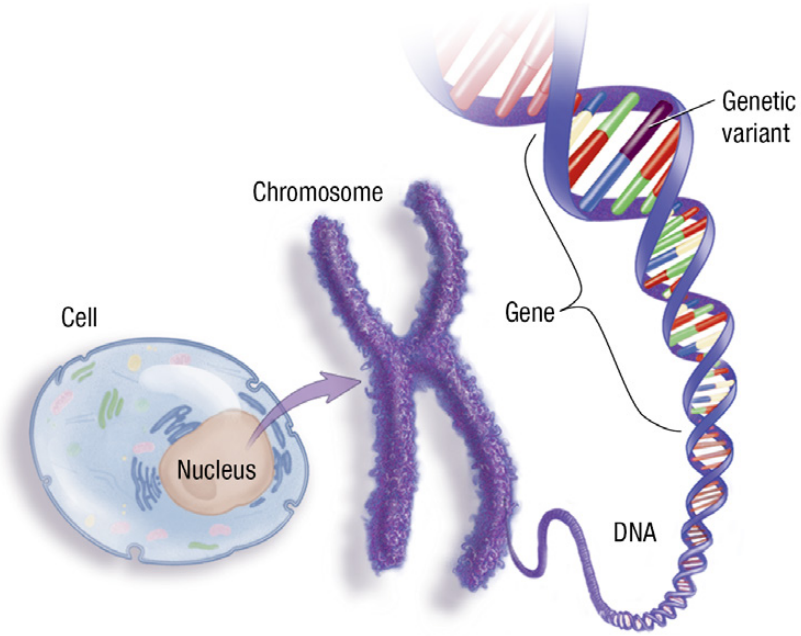

Figure 3. Each cell has chromosomes in its nucleus. Chromosomes are long chains of DNA that contain genes.

Everyone is unique because of individual 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.

GPI anchor disorders are 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.

About paroxysmal nocturnal hemoglobinuria (PNH)

If you search on the internet for information about the gene variant that causes GPI anchor disorders, you may get information about a condition called paroxysmal nocturnal hemoglobinuria (PNH). This is because PNH has been linked to the PIGA genes and different types of genetic variants in the PIGA gene can also cause the GPI anchor disease called PIGA-CDG.

PNH is not a CDG. PNH is a blood disease in which a person's own body attacks and destroys red blood cells. This is a very different condition from GPI anchor disorders.

Diagnosing GPI Anchor Disorders

GPI anchor disorders are usually diagnosed when your child is a baby. To make a diagnosis, 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 GPI anchor disorders 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. At this time, genetic testing is the only way to diagnose GPI anchor disorders.

Additional tests your health care team may request

Depending on symptoms or problems your child has, you may be referred to specialists for tests of other conditions that are often associated with GPI anchor disorders. Some of these tests are done to learn more to help manage the symptoms of the condition.

Your child may have the following tests:

- Imaging exams, such as abdominal ultrasounds, X-rays and MRIs.
- Electrocardiogram (ECG) to check heart function
- Electroencephalogram (EEG) to determine seizure activity
- Blood test to measure vitamin B6 metabolites
- Blood tests for elevated liver enzymes such as alkaline phosphatase, ALT and AST
- Other special blood tests, such as measuring the GPI anchored proteins on the surface of blood cells

"The diagnosis can be overwhelming and take a long time to process. I feel like it took a year for us to work through it."

Overview of Treatment and Supportive Services

Although there is currently no cure for GPI anchor disorders, 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 exercises that may help your child's strength, flexibility, balance, motor development and mobility.

Speech therapy — Speech-language pathologists (SLP) can help improve your child's ability to speak clearly or to communicate. Speech therapy may help your child communicate using sign language, picture systems or talking devices.

Occupational therapy — Occupational therapists (OT) can help develop fine motor skills that support self-feeding, writing, balance and coordination.

Other treatment may include:

- Seizure management.
- Nutrition including tube feeding if needed.
- Heart medication.
- Hormone supplements to treat growth problems.
- Antibiotics to treat or prevent infection.
- Special diet, such as a ketogenic diet to control seizures.
- Supplements for vitamin deficiencies, such as vitamin B6.

Supportive services may include:

Durable medical equipment companies (DME) — DME companies help supply wheelchairs, hospital beds, walkers, ventilators, oxygen, standers, special adaptive bikes and other home monitoring equipment. DME companies require prescriptions from your health care team to provide this equipment.

Home infusion companies — Infusion companies can supply tube feeding supplies necessary to feed your child. Sometimes DME companies also supply tube feeding supplies.

Orthotic services — An orthotist is a health care provider who fits children for special braces recommended by physical therapists to support mobility.

Other supportive services — States can provide financial and social service assistance to help care for a child with GPI anchor disorders. Check with local government and county agencies to see what services may be available to your family.

Also, social media can be a useful resource to connect with other families who have children with GPI anchor disorders.

"These kids have joy and a perspective we can all learn from."

A Message From a Parent

I am the mom of three children. Two of them are little girls who have GPI anchor disorders. With my oldest daughter, I began to suspect something was wrong when she was very little. She seemed behind in her development. My husband and I did not have genetic testing done at that time.

We had a second child, a little boy, and he developed normally. Then when I got pregnant again, I worried whether this child would be OK. After she was born, I noticed something wrong with her vision. Her eyes didn't seem to track well. Our doctor ordered neurological and genetic testing. This is when we got a clear diagnosis on both our daughters: GPI anchor disorders. I had never heard of this condition!

I tried to learn more about the condition by searching on the internet. I joined some social media groups and learned about specialists who treat this condition. The specialist connected us with other doctors around the world so I could learn more.

My oldest daughter communicated using sign language until she was 4 years old. Then she started talking verbally. She has large motor problems and uses a walker. She can't stand up without help, but she can crawl and pull up. My youngest daughter is verbally limited. She uses sign language too.

Yes, my girls have GPI anchor disorders — but there is so much more to them! My oldest is spunky, determined, shy in front of others and loved by all at her school. I call her "my little mommy" because she loves housework and always wants to help. She's so sweet. My youngest has this beautiful brown curly hair. She is a spitfire! She's got such sass.

My advice to other parents of children with GPI anchor disorders and any subtype of CDG is to appreciate all that goes into loving a child with special needs. Although times will be tough, there is so much joy in everyday victories.

Once the shock of the diagnosis wears off, you will quickly realize you have been given a gift to appreciate deeply that others may never understand. I distinctly remember how grateful I was when my son, who doesn't have CDG, was able to stand without assistance. I was overjoyed! It was a simple milestone, but one that made me realize just how much other parents take for granted what should be celebrated.

Build a support network by joining social media groups for the condition. It can help you connect with others around the world. Build a stronger local support network as there will be days when you need hands to help. Use services offered to you locally. Contact the county's health department to find out about support services that are available to your child and family. Connect with your school district to see what is available to your child even before he or she is old enough to attend school.

My hope for my daughters is they continue to live their lives being true to themselves and profoundly impacting others around them.

Terms You May Hear or Read About GPI Anchor Disorders

Medical conditions can be complicated and genetic conditions are especially complicated.

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.

Ataxia — Poor balance and coordination.

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.

Dysphagia — Poor swallowing ability.

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.

Esotropia — Crossed eyes.

Failure to thrive — Term used to describe when a child does not gain weight and grow 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 lipids.

Hypothyroidism — Decreased thyroid hormone.

Hypotonia — Low muscle tone.

Ichthyosis — Dry skin.

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.

Nystagmus — Rapid eye movement.

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.

Restrictive cardiomyopathy — Stiffening of the heart muscle.

Thrombosis — Increased risk of forming blood clots.

"The path life has taken is nowhere near what I expected, but the gratitude and appreciation I've been given is by far a gift I wouldn't trade for the world. My kids continually show me how to appreciate the small things in life."

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BARBARA WOODWARD LIPS PATIENT EDUCATION CENTER

Mrs. Lips, a resident of San Antonio, Texas, was a loyal Mayo Clinic patient of more than 40 years and a self-made business leader who significantly expanded her family's activities in oil, gas and ranching. Upon her death in 1995, Mrs. Lips paid the ultimate compliment by leaving her entire estate to Mayo Clinic. By naming the Barbara Woodward Lips Patient Education Center, Mayo honors her generosity, her love of learning, her belief in patient empowerment and her dedication to high-quality care.

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