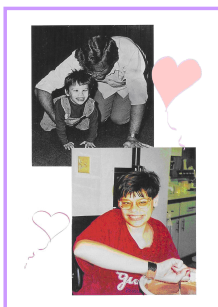


What is CDG

Congenital Disorders of Glycosylation (CDG), formerly known as Carbohydrate-deficient glycoprotein syndrome, are a group of disorders caused by the defective synthesis of N-linked oligosaccharides. These oligosaccharides are assembled in a specific order to create different sugar chain patterns on proteins in every cell. Because of the important biologic functions of these oligosaccharides for protein stability and cell communication, incorrect synthesis may result in multi-system involvement.

Clinical Presentation

Clinical presentations seen in infancy range from significant neurologic impairment with multiple organ system involvement to hypoglycemia and protein losing enteropathy with normal childhood development. Today, the clinical spectrum of CDG is expanding with milder and more severe features being recognized, still many cases are not diagnosed. CDG is often misdiagnosed. CDG-1A patients are sometimes mistaken for having inherited mitochondrial disorders or ataxic cerebral palsy.



Physicians should suspect CDG in children who present with the following signs and symptoms:

- hypotonia
- failure to thrive
- developmental delay
- hepatopathy
- coagulopathy
- esotropia
- seizures
- cerebellar hypoplasia

At a later age, adolescence or adulthood, affected individuals may have these additional clinical features:

- ataxia
- dysarthria
- absent puberty in females
- retinitis pigmentosa
- progressive scoliosis
- joint contractures

Key U.S. Research Contacts

Donna Krasnewich, MD, Ph.D.
Deputy Clinical Director, NHGRI
NIH/NHGRI/MGB
Building 10 CRC, Room 3-2551
10 Center Drive, MSC-1205
Bethesda, MD. 20892-1205
Phone: 302-402-8255
FAX: 301-496-7157
Email: dkras@codon.nih.gov

Hudson Freeze, Ph.D.
Professor of Glycobiology, Director,
Glycobiology and Carbohydrate
Chemistry Program
The Burnham Institute
10901 N. Torrey Pines Road
La Jolla, CA. 92037
Phone: 858-646-3142
Email: Hudson@burnham.org

Where to Get Help & Information

The CDG Family Network is a nonprofit organization founded to:

- Exchange information about CDG with families and physicians.
- Identify individuals with CDG.
- Raise awareness among the medical community and general public.
- Encourage medical research
- The CDG Family network sponsors family conferences, newsletters, a parent contact list, an e-mail list, and a website.



**The CDG
Family Network**

Attn: Cynthia Wren-Gray,
P.O. Box 860847,
Plano, Texas, 75074
Phone: 800-250-5273
Web: www.cdgs.com

Your contribution is tax-deductible and will be gratefully acknowledged by The CDG Family Network. Our Federal Tax Identification Number is #02-0491935.

Congenital Disorders of Glycosylation (CDG)



**The CDG
Family Network
Physician Information**

If a child presents with unexplained delayed development, seizures, stroke like episodes, or has cerebellar hypoplasia OR hypoglycemia and gastrointestinal symptoms CDG should be considered.

"Discovery is seeing what everybody else has seen, and thinking what nobody has thought."

- Albert Szent-Gyorgi

Scope of the Disorders

Congenital Disorders of Glycosylation (CDG) result from defects in the assembly, transfer, and processing of N-linked oligosaccharides. The CDGs are divided into groups I and II. Defective genes are lettered in chronological order of their discovery. Type I CDGs are defined by mutations in steps leading to the assembly and transfer of the lipid linked oligosaccharide chain (LLO) from the carrier lipid to potential N-glycosylation sites on newly synthesized proteins in the ER. Approximately 40 genes are needed to carry out the first stage. Type II CDG defects are defined as those that involve the sequential, highly ordered removal and, addition of individual sugars on protein-bound N-linked sugar chains. More than 20 additional genes are required for this stage. All the CDGs are autosomal recessive disorders.

Laboratory Diagnosis

Fortunately, most CDG patients can be diagnosed by a simple blood test to analyze the glycosylation status of transferring (Tf). Abnormal Tf is detected by isoelectric focusing, or by electrospray ionization-mass spectrometry. Once CDG is diagnosed, further testing is required to determine the type of CDG.

Mayo Medical Laboratories

Request: Carbohydrate Deficient Transferrin, serum.
 Test Code 82414, CPT Code 82373
 Will detect all known CDG-I types, many CDG-x.
 Will not detect: CDG-IIb, CDG IIc, CDG-IIf. Test may need to be rerun if done less than 2 weeks of age.
 Phone: 1-800-533-1710 Fax: 1-507-284-4542
 E-mail: mml@mayo.edu
 Web: www.mayoreferenceservices.org/mrs/index.asp

Treatment

There is no specific medicine to treat CDG, except for CDG-Ib and some CDG-IIc patients. Current treatment for CDG patients is supportive therapy and treatment of symptoms and sequelae. The effective therapy for CDG-Ib is oral mannose. CDG-Ib presents with protein-losing enteropathy, coagulopathy and liver disease without neurological involvement. These patients have significant gastrointestinal problems, but are neurologically and intellectually normal. Fucose supplements have been used to treat patients with CDG-IIc who have a defective GDP-Fucose transporter. Infections cease and health improves. Unfortunately, fucose does not improve or reverse the developmental delay.

Known Deficiency by Type

Type	Enzyme Defect (Gene Name)	Key Features
CDG-Ia	Phosphomannomutase II (PPM2)	Developmental delay, hypotonia, esotropia, lipodystrophy, cerebellar hypoplasia, stroke-like episodes, seizures
CDG-Ib	Phosphomannose Isomerase (MPI)	Hepatic fibrosis, protein losing enteropathy, coagulopathy, hypoglycemia
CDG-Ic	Glucosyltransferase I Dol-P-Glc: Man9GlcNAc2-PP-Dol Glucosyltransferase (ALG6)	Moderate developmental delay, hypotonia, esotropia, epilepsy
CDG-Id	Dol-P-Man: Man5GlcNAc2-PP-Dol Mannosyltransferase (ALG3)	Profound psychomotor delay, optic atrophy, acquired microcephaly, iris colobomas; hypsarrhythmia
CDG-Ie	Dol-P-Man Synthase I GDP-Man: Dol-P- Mannosyltransferase (DPM1)	Profound psychomotor delay, severe developmental delay, optic atrophy, epilepsy, hypotonia, mild dysmorphism, coagulopathy
CDG-If	MPDU1/Lec35 (MPDU1)	Short stature, ichthyosis, psychomotor retardation, pigmentary retinopathy
CDG-Ig	Dol-P-Man: Man7GlcNAc2PP-Dol Mannosyltransferase (ALG12)	Hypotonia, facial dysmorphism, psychomotor retardation, acquired microcephaly. Frequent infections
CDG-Ih	Glucosyltransferase II Dol-P-Glc: Glc1Man9GlcNAc2-PP-Dol Glucosyltransferase (ALG8)	Hepatomegaly, protein-losing enteropathy, renal failure, hypoalbuminemia, edema, ascites
CDG-Ii	Mannosyltransferase II GDP-Man: Man1GlcNAc2-PP-Dol Mannosyltransferase (ALG2)	Normal at birth; developmental delay, hypomyelination, intractable seizures, iris colobomas, hepatomegaly, coagulopathy

Known Deficiency by Type

Type	Enzyme Defect (Gene Name)	Key Features
CDG-Ij	UDP-GlcNAc: dolichol phosphate N-acetylglucosamine 1-phosphate transferase (DPAGT1)	Severe developmental delay, hypotonia, seizures, microcephaly, exotropia
CDG-Ik	Mannosyltransferase I GDP-Man: GlcNAc2-PP-Dol Mannosyltransferase (ALG1)	Severe psychomotor retardation, hypotonia, acquired microcephaly, intractable seizures, fever, coagulopathy, nephrotic syndrome, early death
CDG-Il	Mannosyltransferase Dol-P-Man: Man6 and 8GlcNAc2-PP-Dol Mannosyltransferase (ALG9)	Severe microcephaly, hypotonia, seizures, hepatomegaly
CDG-IIa	GlcNAc-Transferase 2 (GnT II) (MGAT2)	developmental delay, dysmorphism, stereotypies, seizures
CDG-IIb	Glucosidase I (GLS1)	Dysmorphism, hypotonia, seizures, hepatomegaly, hepatic fibrosis (death at 2.5 months)
CDG-IIc	GDP-Fucose Transporter (SLC35C1/FUCT1)	Recurrent infections, persistent neutrophilia, developmental delay, microcephaly, hypotonia (normal Tf)
CDG-IId	b1,4 galactosyltransferase (B4GALT1)	Hypotonia (myopathy), spontaneous hemorrhage, Dandy-Walker malformation
CDG-IIe	Conserved oligomeric Golgi complex subunit 7 (COG7)	Fatal in early infancy; dysmorphism, hypotonia, intractable seizures, hepatomegaly, progressive jaundice, recurrent infections, cardiac failure.
CDG-IIf	CMP-Sialic acid transporter (SLC35A1)	Thrombocytopenia, no neurologic symptoms, normal Tf, abnormal platelet glycoproteins