



Greenberg dysplasia

Greenberg dysplasia is a severe condition characterized by specific bone abnormalities in the developing fetus. This condition is fatal before birth.

The bones of affected individuals do not develop properly, causing a distinctive spotted appearance called moth-eaten bone, which is visible on x-ray images. In addition, the bones have abnormal calcium deposits (ectopic calcification). Affected individuals have extremely short bones in the arms and legs and abnormally flat vertebrae (platyspondyly). Other skeletal abnormalities may include short ribs and extra fingers (polydactyly). In addition, affected fetuses have extensive swelling of the body caused by fluid accumulation (hydrops fetalis). Greenberg dysplasia is also called hydrops-ectopic calcification-moth-eaten skeletal dysplasia (HEM), which reflects the condition's most common features.

Frequency

Greenberg dysplasia is a very rare condition. Approximately ten cases have been reported in the scientific literature.

Causes

Mutations in the *LBR* gene cause Greenberg dysplasia. This gene provides instructions for making a protein called the lamin B receptor. One region of this protein, called the sterol reductase domain, plays an important role in the production (synthesis) of cholesterol. Cholesterol is a type of fat that is produced in the body and obtained from foods that come from animals: eggs, meat, fish, and dairy products. Cholesterol is necessary for normal embryonic development and has important functions both before and after birth. Cholesterol is an important component of cell membranes and the protective substance covering nerve cells (myelin). Additionally, cholesterol plays a role in the production of certain hormones and digestive acids. During cholesterol synthesis, the sterol reductase function of the lamin B receptor allows the protein to perform one of several steps that convert a molecule called lanosterol to cholesterol.

LBR gene mutations involved in Greenberg dysplasia lead to loss of the sterol reductase function of the lamin B receptor, and research suggests that this loss causes the condition. Absence of the sterol reductase function disrupts the normal synthesis of cholesterol within cells. This absence may also allow potentially toxic byproducts of cholesterol synthesis to build up in the body's tissues. Researchers suspect that low cholesterol levels or an accumulation of other substances disrupts the growth and development of many parts of the body. It is not known, however, how a disturbance of cholesterol synthesis leads to the specific features of Greenberg dysplasia.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- chondrodystrophy, hydropic and prenatally lethal type
- Greenberg skeletal dysplasia
- HEM dysplasia
- HEM skeletal dysplasia
- hydrops - ectopic calcification - moth-eaten skeletal dysplasia
- moth-eaten skeletal dysplasia

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
[/primer/testing/geneticTesting](#)
- Genetic Testing Registry: Greenberg dysplasia
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C2931048/>

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22Greenberg+skeletal+dysplasia%22>

Other Diagnosis and Management Resources

- Lurie Children's Hospital of Chicago: Fetal Skeletal Dysplasia
<https://www.luriechildrens.org/en/specialties-conditions/fetal-skeletal-dysplasia/>

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Hydrops Fetalis
<https://medlineplus.gov/ency/article/007308.htm>
- Health Topic: Bone Diseases
<https://medlineplus.gov/bonediseases.html>

Genetic and Rare Diseases Information Center

- Greenberg dysplasia
<https://rarediseases.info.nih.gov/diseases/8754/greenberg-dysplasia>

Educational Resources

- Cedars-Sinai Medical Center: Skeletal Dysplasia
<https://www.cedars-sinai.edu/Patients/Health-Conditions/Skeletal-Dysplasia.aspx>
- MalaCards: greenberg dysplasia
https://www.malacards.org/card/greenberg_dysplasia
- Orphanet: Greenberg dysplasia
https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=1426

Patient Support and Advocacy Resources

- The Compassionate Friends
<https://www.compassionatefriends.org/>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28greenberg+skeletal+dysplasia%5BTIAB%5D%29+OR+%28hydrops--ectopic+calcification--moth-eaten+skeletal+dysplasia%5BTIAB%5D%29+OR+%28greenberg+dysplasia%5BTIAB%5D%29+OR+%28moth-eaten+skeletal+dysplasia%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

Catalog of Genes and Diseases from OMIM

- GREENBERG DYSPLASIA
<http://omim.org/entry/215140>

Sources for This Summary

- Clayton P, Fischer B, Mann A, Mansour S, Rossier E, Veen M, Lang C, Baasanjav S, Kieslich M, Brossuleit K, Gravemann S, Schnipper N, Karbasyian M, Demuth I, Zwerger M, Vaya A, Utermann G, Mundlos S, Stricker S, Sperling K, Hoffmann K. Mutations causing Greenberg dysplasia but not Pelger anomaly uncouple enzymatic from structural functions of a nuclear membrane protein. *Nucleus*. 2010 Jul-Aug;1(4):354-66. doi: 10.4161/nucl.1.4.12435. Epub 2010 May 21.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/21327084>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3027044/>
- Duband-Goulet I, Courvalin JC. Inner nuclear membrane protein LBR preferentially interacts with DNA secondary structures and nucleosomal linker. *Biochemistry*. 2000 May 30;39(21):6483-8.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/10828963>
- Silve S, Dupuy PH, Ferrara P, Loison G. Human lamin B receptor exhibits sterol C14-reductase activity in *Saccharomyces cerevisiae*. *Biochim Biophys Acta*. 1998 Jun 15;1392(2-3):233-44.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/9630650>
- Trajkovski Z, Vrcakovski M, Saveski J, Gucev ZS. Greenberg dysplasia (hydrops-ectopic calcification-moth-eaten skeletal dysplasia): prenatal ultrasound diagnosis and review of literature. *Am J Med Genet*. 2002 Sep 1;111(4):415-9.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12210303>

- Tseng LC, Chen RH. Temporal control of nuclear envelope assembly by phosphorylation of lamin B receptor. *Mol Biol Cell*. 2011 Sep;22(18):3306-17. doi: 10.1091/mbc.E11-03-0199. Epub 2011 Jul 27.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/21795390>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3172257/>
 - Waterham HR, Koster J, Mooyer P, Noort Gv Gv, Kelley RI, Wilcox WR, Wanders RJ, Hennekam RC, Oosterwijk JC. Autosomal recessive HEM/Greenberg skeletal dysplasia is caused by 3 beta-hydroxysterol delta 14-reductase deficiency due to mutations in the lamin B receptor gene. *Am J Hum Genet*. 2003 Apr;72(4):1013-7. Epub 2003 Feb 28.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12618959>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1180330/>
-

Reprinted from Genetics Home Reference:

<https://ghr.nlm.nih.gov/condition/greenberg-dysplasia>

Reviewed: February 2012

Published: September 10, 2019

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services