Cutis laxa

Cutis laxa is a disorder of connective tissue, which is the tissue that forms the body’s supportive framework. Connective tissue provides structure and strength to the muscles, joints, organs, and skin.

The term "cutis laxa" is Latin for loose or lax skin, and this condition is characterized by skin that is sagging and not stretchy (inelastic). The skin often hangs in loose folds, causing the face and other parts of the body to have a droopy appearance. Extremely wrinkled skin may be particularly noticeable on the neck and in the armpits and groin.

Cutis laxa can also affect connective tissue in other parts of the body, including the heart, blood vessels, joints, intestines, and lungs. The disorder can cause heart problems and abnormal narrowing, bulging, or tearing of critical arteries. Affected individuals may have soft out-pouchings in the lower abdomen (inguinal hernia) or around the belly button (umbilical hernia). Pouches called diverticula can also develop in the walls of certain organs, such as the bladder and intestines. During childhood, some people with cutis laxa develop a lung disease called emphysema, which can make it difficult to breathe. Depending on which organs and tissues are affected, the signs and symptoms of cutis laxa can range from mild to life-threatening.

Researchers have described several different forms of cutis laxa. The forms are often distinguished by their pattern of inheritance: autosomal dominant, autosomal recessive, or X-linked. In general, the autosomal recessive forms of cutis laxa tend to be more severe than the autosomal dominant forms. In addition to the features described above, some people with autosomal recessive cutis laxa have delayed development, intellectual disability, seizures, and problems with movement that can worsen over time.

The X-linked form of cutis laxa is often called occipital horn syndrome. This form of the disorder is considered a mild type of Menkes syndrome, which is a condition that affects copper levels in the body. In addition to sagging and inelastic skin, occipital horn syndrome is characterized by wedge-shaped calcium deposits in a bone at the base of the skull (the occipital bone), coarse hair, and loose joints.

Frequency

Cutis laxa is a rare disorder. About 200 affected families worldwide have been reported.

Causes

Cutis laxa can be caused by mutations in several genes, including ATP6V0A2, ATP7A, EFEMP2, ELN, and FBLN5. Most of these genes are involved in the formation and function of elastic fibers, which are slender bundles of proteins that provide strength and flexibility to connective tissue throughout the body. Elastic fibers allow the skin to
stretch, the lungs to expand and contract, and arteries to handle blood flowing through
them at high pressure.

The major component of elastic fibers, a protein called elastin, is produced from the
ELN gene. Other proteins that appear to have critical roles in the assembly of elastic
fibers are produced from the EFEMP2, FBLN5, and ATP6V0A2 genes. Mutations in any
of these genes disrupt the formation, assembly, or function of elastic fibers. A shortage
of these fibers weakens connective tissue in the skin, arteries, lungs, and other organs.
These defects in connective tissue underlie the major features of cutis laxa.

Occipital horn syndrome is caused by mutations in the ATP7A gene. This gene
provides instructions for making a protein that is important for regulating copper levels
in the body. Mutations in the ATP7A gene result in poor distribution of copper to the
body’s cells. A reduced supply of copper can decrease the activity of numerous copper-
containing enzymes that are necessary for the structure and function of bone, skin,
hair, blood vessels, and the nervous system. The signs and symptoms of occipital horn
syndrome are caused by the reduced activity of these copper-containing enzymes.

Inheritance Pattern

Cutis laxa can have an autosomal dominant, autosomal recessive, or X-linked
recessive pattern of inheritance.

When cutis laxa is caused by ELN mutations, it has an autosomal dominant inheritance
pattern. Autosomal dominant inheritance means one copy of the altered gene in each
cell is sufficient to cause the disorder. Rarely, cases of cutis laxa resulting from FBLN5
mutations can also have an autosomal dominant pattern of inheritance.

Researchers have described at least three forms of autosomal recessive cutis laxa,
which result from mutations in several different genes. Autosomal recessive inheritance
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.

Occipital horn syndrome has an X-linked recessive pattern of inheritance. It results
from mutations in the ATP7A gene, which is located on the X chromosome. The X
chromosome is one of the two sex chromosomes. In males (who have only one X
chromosome), one altered copy of the gene in each cell is sufficient to cause the
condition. In females (who have two X chromosomes), a mutation would have to occur
in both copies of the gene to cause the disorder. Because it is unlikely that females will have two altered copies of this gene, males are affected by X-linked recessive disorders much more frequently than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Other Names for This Condition
- dermatolysis
- dermatomegaly

Diagnosis & Management

Genetic Testing Information
- What is genetic testing? [link]
- Genetic Testing Registry: Cutis laxa with osteodystrophy [link]
- Genetic Testing Registry: Cutis laxa, autosomal dominant [link]
- Genetic Testing Registry: Cutis laxa, autosomal recessive [link]
- Genetic Testing Registry: Cutis laxa, X-linked [link]

Research Studies from ClinicalTrials.gov
- ClinicalTrials.gov [link]

Other Diagnosis and Management Resources
- GeneReview: ATP6V0A2-Related Cutis Laxa [link]
- GeneReview: ATP7A-Related Copper Transport Disorders [link]
- GeneReview: EFEMP2-Related Cutis Laxa [link]
- GeneReview: FBLN5-Related Cutis Laxa [link]
- MedlinePlus Encyclopedia: Colon Diverticula (image) [link]
• MedlinePlus Encyclopedia: Emphysema (image)
  https://medlineplus.gov/ency/imagepages/17055.htm

• MedlinePlus Encyclopedia: Hernia
  https://medlineplus.gov/ency/article/000960.htm

Additional Information & Resources

Health Information from MedlinePlus

• Encyclopedia: Colon Diverticula (image)
  https://medlineplus.gov/ency/presentations/100158_2.htm

• Encyclopedia: Emphysema (image)
  https://medlineplus.gov/ency/imagepages/17055.htm

• Encyclopedia: Hernia
  https://medlineplus.gov/ency/article/000960.htm

• Health Topic: Connective Tissue Disorders
  https://medlineplus.gov/connectivetissuedisorders.html

Genetic and Rare Diseases Information Center

• Cutis laxa
  https://rarediseases.info.nih.gov/diseases/6227/cutis-laxa

• Occipital horn syndrome

Additional NIH Resources

• National Institute of Arthritis and Musculoskeletal and Skin Diseases: Heritable Disorders of Connective Tissue
  https://www.niams.nih.gov/health-topics/heritable-disorders-connective-tissue

Educational Resources

• MalaCards: cutis laxa
  https://www.malacards.org/card/cutis_laxa

• Merck Manual Consumer Version

• Orphanet: Acquired cutis laxa
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=228285

• Orphanet: Cutis laxa
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=209
Patient Support and Advocacy Resources

- Cutis Laxa Internationale
  http://www.cutislaxa.org/en/
- Cutis Laxa Research Study, University of Pittsburgh
  http://cutislaxa.pitt.edu/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/cutis-laxa/
- Resource list from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/connect.html

Clinical Information from GeneReviews

- ATP6V0A2-Related Cutis Laxa
  https://www.ncbi.nlm.nih.gov/books/NBK5200
- ATP7A-Related Copper Transport Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK1413
- EFEMP2-Related Cutis Laxa
  https://www.ncbi.nlm.nih.gov/books/NBK54467
- FBLN5-Related Cutis Laxa
  https://www.ncbi.nlm.nih.gov/books/NBK5201

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Cutis%20Laxa%5BMAJR%5D%29+AND+%28cutis+laxa%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- CUTIS LAXA, AUTOSOMAL DOMINANT 1
  http://omim.org/entry/123700
- CUTIS LAXA, AUTOSOMAL DOMINANT 2
  http://omim.org/entry/614434
- CUTIS LAXA, AUTOSOMAL DOMINANT 3
  http://omim.org/entry/616603
- CUTIS LAXA, AUTOSOMAL RECESSIVE, TYPE IA
  http://omim.org/entry/219100
- CUTIS LAXA, AUTOSOMAL RECESSIVE, TYPE IB
  http://omim.org/entry/614437
- CUTIS LAXA, AUTOSOMAL RECESSIVE, TYPE IC
  http://omim.org/entry/613177
• CUTIS LAXA, AUTOSOMAL RECESSIVE, TYPE IIA
  http://omim.org/entry/219200
• CUTIS LAXA, AUTOSOMAL RECESSIVE, TYPE IIB
  http://omim.org/entry/612940
• CUTIS LAXA, AUTOSOMAL RECESSIVE, TYPE IIIA
  http://omim.org/entry/219150
• CUTIS LAXA, AUTOSOMAL RECESSIVE, TYPE IIIB
  http://omim.org/entry/614438
• CUTIS LAXA, NEONATAL, WITH MARFANOID PHENOTYPE
  http://omim.org/entry/614100
• OCCIPITAL HORN SYNDROME
  http://omim.org/entry/304150

Medical Genetics Database from MedGen
• Autosomal recessive cutis laxa type IA
• Cutis laxa
• Cutis laxa with osteodystrophy
• Cutis laxa, acquired type
• Cutis laxa, autosomal dominant
• Inherited cutis laxa

Sources for This Summary
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  Mefford HC, Smith RJH, Stephens K, editors. GeneReviews® [Internet]. Seattle (WA): University of
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301586
• Kaler SG. Metabolic and molecular bases of Menkes disease and occipital horn syndrome. Pediatr
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10463276
Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24443027

Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23954411
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Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23154624

Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301755

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