



Liddle syndrome

Liddle syndrome is an inherited form of high blood pressure (hypertension). This condition is characterized by severe hypertension that begins unusually early in life, often in childhood, although some affected individuals are not diagnosed until adulthood. Some people with Liddle syndrome have no additional signs or symptoms, especially in childhood. Over time, however, untreated hypertension can lead to heart disease or stroke, which may be fatal.

In addition to hypertension, affected individuals can have low levels of potassium in the blood (hypokalemia). Signs and symptoms of hypokalemia include muscle weakness or pain, fatigue, constipation, or heart palpitations. The shortage of potassium can also raise the pH of the blood, a condition known as metabolic alkalosis.

Frequency

Liddle syndrome is a rare condition, although its prevalence is unknown. The condition has been found in populations worldwide.

Causes

Liddle syndrome is caused by mutations in the *SCNN1B* or *SCNN1G* gene. Each of these genes provides instructions for making a piece (subunit) of a protein complex called the epithelial sodium channel (ENaC). These channels are found at the surface of certain cells called epithelial cells in many tissues of the body, including the kidneys, where the channels transport sodium into cells.

In the kidney, ENaC channels open in response to signals that sodium levels in the blood are too low, which allows sodium to flow into cells. From the kidney cells, this sodium is returned to the bloodstream (a process called reabsorption) rather than being removed from the body in urine.

Mutations in the *SCNN1B* or *SCNN1G* gene change the structure of the respective ENaC subunit. The changes alter a region of the subunit that is involved in signaling for its breakdown (degradation) when it is no longer needed. As a result of the mutations, the subunit proteins are not degraded, and more ENaC channels remain at the cell surface. The increase in channels at the cell surface abnormally increases the reabsorption of sodium (followed by water), which leads to hypertension. Reabsorption of sodium into the blood is linked with removal of potassium from the blood, so excess sodium reabsorption leads to hypokalemia.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Other Names for This Condition

- pseudoaldosteronism
- pseudoprimary hyperaldosteronism

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
[/primer/testing/geneticTesting](#)
- Genetic Testing Registry: Pseudoprimary hyperaldosteronism
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0221043/>

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22Liddle+syndrome%22>

Other Diagnosis and Management Resources

- Merck Manual for Health Care Professionals
<https://www.merckmanuals.com/professional/genitourinary-disorders/renal-transport-abnormalities/liddle-syndrome>

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Hypertension
<https://medlineplus.gov/ency/article/000468.htm>
- Encyclopedia: Hypokalemia
<https://medlineplus.gov/ency/article/000479.htm>
- Health Topic: Fluid and Electrolyte Balance
<https://medlineplus.gov/fluidandelectrolytebalance.html>

Genetic and Rare Diseases Information Center

- Liddle syndrome
<https://rarediseases.info.nih.gov/diseases/7381/liddle-syndrome>

Additional NIH Resources

- National Institutes of Diabetes and Digestive and Kidney Diseases: The Kidneys and How They Work
<https://www.niddk.nih.gov/health-information/kidney-disease/kidneys-how-they-work>

Educational Resources

- American Heart Association: What is High Blood Pressure?
<https://www.heart.org/en/health-topics/high-blood-pressure/the-facts-about-high-blood-pressure/what-is-high-blood-pressure>
- KidsHealth from Nemours: High Blood Pressure (Hypertension)
<https://kidshealth.org/en/parents/hypertension.html>
- MalaCards: liddle syndrome 1
https://www.malacards.org/card/liddle_syndrome_1
- MalaCards: liddle syndrome 2
https://www.malacards.org/card/liddle_syndrome_2
- Merck Manual Home Health Edition: Alkalosis
<https://www.merckmanuals.com/home/hormonal-and-metabolic-disorders/acid-base-balance/alkalosis>
- Merck Manual Home Health Edition: Sodium
<https://www.merckmanuals.com/home/hormonal-and-metabolic-disorders/electrolyte-balance/overview-of-sodium-s-role-in-the-body>
- Orphanet: Liddle syndrome
https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=526

Patient Support and Advocacy Resources

- National Kidney Foundation
<https://www.kidney.org/>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28Liddle+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+2880+days%22%5Bdp%5D>

Catalog of Genes and Diseases from OMIM

- LIDDLE SYNDROME 1
<http://omim.org/entry/177200>

Medical Genetics Database from MedGen

- Pseudoprimary hyperaldosteronism
<https://www.ncbi.nlm.nih.gov/medgen/67439>

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