Nephronophthisis

Nephronophthisis is a disorder that affects the kidneys. It is characterized by inflammation and scarring (fibrosis) that impairs kidney function. These abnormalities lead to increased urine production (polyuria), excessive thirst (polydipsia), general weakness, and extreme tiredness (fatigue). In addition, affected individuals develop fluid-filled cysts in the kidneys, usually in an area known as the corticomedullary region. Another feature of nephronophthisis is a shortage of red blood cells, a condition known as anemia.

Nephronophthisis eventually leads to end-stage renal disease (ESRD), a life-threatening failure of kidney function that occurs when the kidneys are no longer able to filter fluids and waste products from the body effectively. Nephronophthisis can be classified by the approximate age at which ESRD begins: around age 1 (infantile), around age 13 (juvenile), and around age 19 (adolescent).

About 85 percent of all cases of nephronophthisis are isolated, which means they occur without other signs and symptoms. Some people with nephronophthisis have additional features, which can include liver fibrosis, heart abnormalities, or mirror image reversal of the position of one or more organs inside the body (situs inversus).

Nephronophthisis can occur as part of separate syndromes that affect other areas of the body; these are often referred to as nephronophthisis-associated ciliopathies. For example, Senior-Løken syndrome is characterized by the combination of nephronophthisis and a breakdown of the light-sensitive tissue at the back of the eye (retinal degeneration); Joubert syndrome affects many parts of the body, causing neurological problems and other features, which can include nephronophthisis.

Frequency

Nephronophthisis is found in populations worldwide. It occurs in an estimated 1 in 50,000 newborns in Canada, 1 in 100,000 in Finland, and 1 in 922,000 in the United States. Its incidence in other populations is unknown. Nephronophthisis is the most common genetic cause of ESRD in children and young adults.

Causes

Nephronophthisis has several genetic causes, which are used to split the condition into distinct types. Nephronophthisis type 1, which is the most common type of the disorder and one cause of juvenile nephronophthisis, results from changes affecting the \( NPHP1 \) gene. The proteins produced from \( NPHP1 \) and the other genes involved in nephronophthisis are known or suspected to play roles in cell structures called cilia. Cilia are microscopic, finger-like projections that stick out from the surface of cells and are involved in chemical signaling. Cilia are important for the structure and function of
many types of cells and tissues, including cells in the kidneys, liver, and brain and the light-sensitive tissue at the back of the eye (the retina).

The genetic mutations involved in nephronophthisis are thought to impair the structure or function of cilia in some way, which likely disrupts important chemical signaling pathways during development. Although researchers believe that defective cilia lead to the features of nephronophthisis, the mechanism remains unclear. It is unknown why some people with mutations in nephronophthisis-associated genes have only kidney problems, while others develop additional signs and symptoms.

**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**

- NPH
- NPHP

**Diagnosis & Management**

**Genetic Testing Information**

- What is genetic testing? /primer/testing/genetictesting
• Genetic Testing Registry: Nephronophthisis 14
• Genetic Testing Registry: Nephronophthisis 15
• Genetic Testing Registry: Nephronophthisis 16
• Genetic Testing Registry: Nephronophthisis 18

Research Studies from ClinicalTrials.gov
• ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22nephronophthisis%22

Other Diagnosis and Management Resources
• GeneReview: Nephronophthisis
  https://www.ncbi.nlm.nih.gov/books/NBK368475
• Merck Manual Consumer Version

Additional Information & Resources

Health Information from MedlinePlus
• Encyclopedia: End-Stage Kidney Disease
  https://medlineplus.gov/ency/article/000500.htm
• Encyclopedia: Thirst - Excessive
  https://medlineplus.gov/ency/article/003085.htm
• Encyclopedia: Urination - Excessive Amount
  https://medlineplus.gov/ency/article/003146.htm
• Health Topic: Kidney Cysts
  https://medlineplus.gov/kidneycysts.html
• Health Topic: Kidney Failure
  https://medlineplus.gov/kidneyfailure.html

Genetic and Rare Diseases Information Center
• Nephronophthisis
  https://rarediseases.info.nih.gov/diseases/206/nephronophthisis
Educational Resources

- Johns Hopkins Medicine: End Stage Renal Disease
  https://www.hopkinsmedicine.org/health/conditions-and-diseases/end-stage-renal-failure
- MalaCards: nephronophthisis
  https://www.malacards.org/card/nephronophthisis
- Orphanet: Nephronophthisis
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=655

Patient Support and Advocacy Resources

- Ciliopathy Alliance
  https://www.ciliopathyalliance.org/ciliopathies
- National Kidney Foundation
  https://www.kidney.org/

Clinical Information from GeneReviews

- Nephronophthisis
  https://www.ncbi.nlm.nih.gov/books/NBK368475

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Kidney+Diseases,+Cystic%5BMAJR%5D%29+AND+%28nephronophthisis%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

- NEPHRONOPHTHISIS 1
  http://omim.org/entry/256100
- NEPHRONOPHTHISIS 2
  http://omim.org/entry/602088
- NEPHRONOPHTHISIS 3
  http://omim.org/entry/604387
- NEPHRONOPHTHISIS 4
  http://omim.org/entry/606966
- NEPHRONOPHTHISIS 7
  http://omim.org/entry/611498
- NEPHRONOPHTHISIS 9
  http://omim.org/entry/613824
• NEPHRONOPHTHISIS 11  
  http://omim.org/entry/613550  
• NEPHRONOPHTHISIS 12  
  http://omim.org/entry/613820  
• NEPHRONOPHTHISIS 13  
  http://omim.org/entry/614377  
• NEPHRONOPHTHISIS 14  
  http://omim.org/entry/614844  
• NEPHRONOPHTHISIS 15  
  http://omim.org/entry/614845  
• NEPHRONOPHTHISIS 16  
  http://omim.org/entry/615382  
• NEPHRONOPHTHISIS 18  
  http://omim.org/entry/615862  

Sources for This Summary  
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22388554  
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9326933  
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21071979  
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2992643/  
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10712196  
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1288163/  
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20652329  
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4160028/  

Reprinted from Genetics Home Reference:  

Reviewed: September 2014  
Published: July 16, 2019