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Nephrotic syndrome

What is nephrotic syndrome?

Nephrotic syndrome is an inherited disorder characterized by progressive kidney disease with variable severity and age at onset.[1,2] Nephrotic syndrome type 1, *NPHS1*-related, is caused by a defect in the production of a protein called nephrin.[2] Nephrotic syndrome type 2, *NPHS2*-related, is caused by a defect in the production of a protein called podocin.[2] Both proteins are essential for normal kidney function. Signs and symptoms of nephrotic syndrome are attributed to the kidney's inability to maintain normal blood protein levels.[2] Nephrotic syndrome type 1 is also known as Finnish congenital nephrosis.[3]

What are the symptoms of nephrotic syndrome and what treatment is available?

Symptoms of nephrotic syndrome type 1 are usually present at birth or develop within the first year of life; however, some individuals may have childhood onset of symptoms.[5] Symptoms of nephrotic syndrome type 2 are usually first seen during childhood; however, some individuals may have earlier or later onset of symptoms. Nephrotic syndrome is typically a progressive disorder that is resistant to steroid treatment and results in end-stage renal disease within a few years of onset (type 1) or the first or second decade of life (type 2).[1] Atypical cases with milder symptoms and/or partial responsiveness to steroids have been reported.[1,4]

Signs and symptoms of nephrotic syndrome may include:[3,4]

- Proteinuria (high protein levels in urine)
- Hypoalbuminemia (low protein levels in the blood)
- Hyperlipidemia (high fat levels in the blood)
- Edema (swelling due to excessive fluid in body cavities)
- Resistance to steroid therapy
- Progression to end-stage kidney disease

Kidney transplant is typically curative; however, recurrence of kidney disease following transplant has been reported.[5]

How is nephrotic syndrome inherited?

Nephrotic syndrome is autosomal recessive disease caused by mutations in the *NPHS1* and *NPHS2* genes.[1] An individual who has one mutation in one of these genes is a carrier and is not expected to have related health problems. An individual who inherits two mutations in the same gene, one from each parent, is expected to be affected with nephrotic syndrome. For example, a child with two *NPHS1* mutations is expected to be affected with nephrotic syndrome, and a child with one *NPHS1* mutation and one *NPHS2* mutation is a carrier.

If both members of a couple are carriers of a mutation in the same gene, the risk for an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.

Who is at risk for nephrotic syndrome?

Nephrotic syndrome type 1, *NPHS1*-related, can occur in any race or ethnicity. It is particularly common in the Finnish and Maltese populations.[6,7] In the Finnish population, it has an incidence of approximately 1 in 8,200 and a carrier frequency of 1 in 45.[6] In the Maltese population, the incidence is approximately 1 in 1,900 with a carrier frequency at 1 in 22.[7]

Nephrotic syndrome type 2, *NPHS2*-related, can occur in any race or ethnicity. Its incidence and carrier frequency are unknown.[8]

Having a relative who is a carrier or who is affected can increase an individual's risk of being a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

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What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

What does a negative test result mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?

NephCure Kidney International: http://www.nephcure.org/

National Kidney Foundation: https://www.kidney.org/atoz/content/nephrotic

References

1. Caridi G, et al. Familial Forms of Nephrotic Syndrome. *Pediatric Neurology*. 2010; 25:241-252.
2. Tryggvason K, et al. Hereditary Proteinuria Syndromes and Mechanisms of Proteinuria. *The New England Journal of Medicine*. 2006; 354:1387-401.
3. Nephrotic Syndrome, Type 1; NPHS1. OMIM. Available at: http://www.omim.org/entry/256300. Accessed April 13, 2016.
4. Nephrotic Syndrome, Type 2; NPHS2. OMIM. Available at: http://www.omim.org/entry/600995. Accessed April 13, 2016.
5. Benoit G and Machuca E. Hereditary nephrotic syndrome: a systematic approach for genetic testing and a review of associated podocyte gene mutations. *Pediatr nephrol.* 2010; 25:1621-1632.
6. Huttunen, N. Congenital Nephrotic Syndrome of Finnish Type. *Archives of Disease in Childhood*. 1976: 51:344-348.
7. Koziel A, et al. Genotype/phenotype correlations of NPHS1 and NPHS2 mutations in nephrotic syndrome advocate a functional inter-relationship in glomerular filtration. *Hum Molec Genet.* 2002; 11(4): 379-388.
8. Franceschini N, et al. NPHS2 gene, nephrotic syndrome and focal segmental glomerulosclerosis: A HuGE review. *Genet Med*. 2006 Feb; 8(2): 63-75.