

What is Smith-Lemli-Opitz syndrome?

Smith-Lemli-Opitz syndrome is an inherited disease characterized by multiple birth defects and intellectual disability. Symptoms of Smith-Lemli-Opitz syndrome are attributed to the body's inability to produce cholesterol due to a deficiency of the enzyme 7-dehydrocholesterol reductase (7-DHC). Cholesterol production is essential for normal development since it is a component of most cells and is used in the production of some hormones and digestive acids.¹

What are the symptoms of Smith-Lemli-Opitz syndrome and what treatment is available?

Signs and symptoms of Smith-Lemli-Opitz syndrome range from mild, including minor physical anomalies and behavioral and learning disabilities, to severe, including life threatening birth defects and profound intellectual impairment. Intellectual disability typically falls in the moderate to severe range.¹ Signs and symptoms of Smith-Lemli-Opitz syndrome may include:²

- Intellectual disability
- Microcephaly (small head)
- Extra fingers
- Webbing between the toes
- Congenital heart defects
- Cleft palate
- Genital malformations
- Brain and kidney malformations
- Hypotonia (low muscle tone)
- Feeding problems
- Prenatal and postnatal growth retardation
- Cataracts
- Hearing loss
- Sensitivity to sun light
- Behavioral problems, including hyperactivity, irritability, sleep disturbances, and self-injury
- Miscarriage or stillbirth of affected pregnancies³

There is no cure for Smith-Lemli-Opitz syndrome. Surgical repair is available for some birth defects. Supplementation with cholesterol has been shown to improve growth and sensitivity to light; however it has not been shown to improve developmental and behavioral function.²

How is Smith-Lemli-Opitz syndrome inherited?

Smith-Lemli-Opitz syndrome is an autosomal recessive disease caused by mutations in the *DHCR7* gene. An individual who inherits one copy of a *DHCR7* gene mutation is a carrier and is not expected to have related health problems. An individual who inherits two *DHCR7* mutations, one from each parent, is expected to be affected with Smith-Lemli-Opitz syndrome.

If both members of a couple are carriers of a mutation in the same gene, the risk of having 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 Smith-Lemli-Opitz syndrome?

Smith-Lemli-Opitz syndrome has an estimated pregnancy incidence in all populations of 1 in 20,000 and a carrier frequency of 1 in 71. Smith-Lemli-Opitz syndrome occurs most commonly in the Caucasian population and is less common in individuals of Asian or African ancestry.³

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

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetic 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?

The Smith-Lemli-Opitz | RSH Foundation: <http://www.smithlempiopitz.org>

Genetic and Rare Diseases (GARD) Information Center: <https://rarediseases.info.nih.gov/gard/5683/smith-lemli-opitz-syndrome/resources/1>

National Organization for Rare Disorders (NORD): <http://rarediseases.org/rare-diseases/smith-lemli-opitz-syndrome/>

References

1. Genetics Home Reference. Smith-Lemli-Opitz. <http://ghr.nlm.nih.gov/condition/smith-lemli-opitz-syndrome>. Accessed March 8, 2012
2. GeneReviews. Smith-Lemli-Opitz Syndrome. <http://www.ncbi.nlm.nih.gov/books/NBK1143/>. Accessed 01/04/2012
3. Craig, W *et al.* Identifying Smith-Lemli-Opitz syndrome in conjunction with prenatal screening for Down syndrome. *Prenatal Diagnosis* 2006; 26:842-849.