



## Smith-Lemli-Opitz syndrome

Other Names: RSH syndrome

*Smith-Lemli-Opitz syndrome is a rare multisystem genetic syndrome caused by an inability of the body to make adequate amounts of cholesterol. It is caused by mutations in the DHCR7 gene which makes the protein called 7-dehydrocholesterol reductase.*

### Characteristics of Smith-Lemli-Opitz syndrome

First described as the “RSH syndrome” after the initials of the first three patients, the syndrome is now better known as “Smith-Lemli-Opitz syndrome” (SLOS) after the names of the three geneticists who first described it. SLOS is a rare multisystem genetic syndrome caused by an inability of the body to make adequate amounts of cholesterol. Cholesterol is essential for normal development; it plays an important role in protecting nerve cells, aiding in digestion, as well as making certain hormones. Individuals with SLOS are not able to make enough cholesterol that is needed for normal growth and development.

In addition to pre- and post-natal growth restriction (growth problems before and after birth), microcephaly (small head size), and intellectual disability, many different birth defects have been described in SLOS. The most common include: cleft palate (a split in the roof of the mouth), polydactyly (extra fingers or toes), 2-3 toe syndactyly (webbing between 2nd and 3rd toes), heart defects, genital anomalies, and a distinctive facial appearance. Individuals with SLOS may also have autism spectrum disorder, sensory hypersensitivity and self-injurious behaviors. The signs and symptoms seen in SLOS are highly variable within families as well as between other unrelated, affected individuals.

### Diagnosis/Testing

Most individuals with SLOS have changes or mutations in a gene called DHCR7. This gene makes the 7-dehydrocholesterol reductase enzyme which is responsible for the last biochemical step in making cholesterol (i.e., it converts a substance called 7-dehydrocholesterol to cholesterol). Mutations in the DHCR7 gene cause the enzyme to not work properly. This results in a deficiency of cholesterol and a buildup of 7-dehydrocholesterol. Biochemical testing (i.e., looking for a buildup of 7-dehydrocholesterol in serum) can also be done to diagnose SLOS.

If a pregnancy is known to be at risk for SLOS, chorionic villus sampling (CVS) or amniocentesis can be used for prenatal diagnosis. There are also two screening tests available during pregnancy – maternal urinary steroid testing, and maternal serum screening.

### Management/Surveillance

The deficiency of cholesterol, as well as excess cholesterol precursors (e.g., 7-dehydrocholesterol) contributes to the features seen in SLOS. Therefore the treatment goals have been to increase cholesterol production by cholesterol supplementation, and to decrease the accumulation of the precursors by statin treatment. Many of the birth defects seen in SLOS require surgical repair. Individuals with SLOS are at increased risk for complications during anesthesia (e.g., difficulties with airway management, existing heart and lung problems, and the potential need of sedation to control aggression before and after surgery). Photosensitivity (sensitivity to sunlight) is common in SLOS. Many children cannot tolerate any exposure to sunlight while others can tolerate varying periods of exposure if properly clothed and

protected with a UVA- and UVB-protection sunscreen.

### **Mode of inheritance**

SLOS is inherited in an autosomal recessive pattern. This means that an individual has to inherit two DHCR7 mutations (i.e., one from each parent) to be affected with SLOS. If both parents are carriers of a DHCR7 mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with SLOS.

### **Risk to family members**

Parents of a child with SLOS are carriers of SLOS. If a sibling of a child with SLOS is unaffected, he/she has a 2 in 3 (66%) chance of being a carrier of SLOS.

### **Special considerations**

None

### **Resources**

Smith-Lemli-Optiz/RSH Foundation

<http://www.smithlemliopitz.org/>

Genetics Home Reference: Smith-Lemli-Opitz syndrome

<http://ghr.nlm.nih.gov/condition/smith-lemli-opitz-syndrome>

Learn.Genetics: Smith-Lemli-Opitz syndrome

<http://learn.genetics.utah.edu/content/disorders/whataregd/slos/>

### **References**

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