

## Donohue syndrome

### Description

Donohue syndrome is a rare disorder characterized by severe insulin resistance, a condition in which the body's tissues and organs do not respond properly to the hormone insulin. Insulin normally helps regulate blood sugar levels by controlling how much sugar (in the form of glucose) is passed from the bloodstream into cells to be used as energy. Severe insulin resistance leads to problems with regulating blood glucose levels and affects the development and function of organs and tissues throughout the body.

Severe insulin resistance underlies the varied signs and symptoms of Donohue syndrome. Individuals with Donohue syndrome are unusually small starting before birth, and affected infants experience failure to thrive, which means they do not grow and gain weight at the expected rate. Additional features that become apparent soon after birth include a lack of fatty tissue under the skin (subcutaneous fat); wasting (atrophy) of muscles; excessive body hair growth (hirsutism); multiple cysts on the ovaries in females; and enlargement of the nipples, genitalia, kidneys, heart, and other organs. Most affected individuals also have a skin condition called acanthosis nigricans, in which the skin in body folds and creases becomes thick, dark, and velvety. Distinctive facial features in people with Donohue syndrome include bulging eyes, thick lips, upturned nostrils, and low-set ears. Affected individuals develop recurrent, life-threatening infections beginning in infancy.

Donohue syndrome is one of a group of related conditions described as inherited severe insulin resistance syndromes. These disorders, which also include Rabson-Mendenhall syndrome and type A insulin resistance syndrome, are considered part of a spectrum. Donohue syndrome represents the most severe end of the spectrum; most children with this condition do not survive beyond age 2.

### Frequency

Donohue syndrome is estimated to affect less than 1 per million people worldwide. Several dozen cases have been reported in the medical literature.

### Causes

Donohue syndrome results from mutations in the *INSR* gene. This gene provides

instructions for making a protein called an insulin receptor, which is found in many types of cells. Insulin receptors are embedded in the outer membrane surrounding the cell, where they attach (bind) to insulin circulating in the bloodstream. This binding triggers signaling pathways that influence many cell functions.

The *INSR* gene mutations that cause Donohue syndrome greatly reduce the number of insulin receptors that reach the cell membrane or disrupt the function of these receptors. Although insulin is present in the bloodstream, without functional receptors it cannot exert its effects on cells and tissues. This severe resistance to the effects of insulin impairs blood glucose regulation and affects many aspects of development in people with Donohue syndrome.

[Learn more about the gene associated with Donohue syndrome](#)

- INSR

## **Inheritance**

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**

- Donohue's syndrome
- Leprechaunism
- Leprechaunism syndrome

## **Additional Information & Resources**

### Genetic Testing Information

- Genetic Testing Registry: Leprechaunism syndrome (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0265344/>)

### Genetic and Rare Diseases Information Center

- Leprechaunism (<https://rarediseases.info.nih.gov/diseases/6885/index>)

### Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (<https://rarediseases.org/>)

## Clinical Trials

- ClinicalTrials.gov ([https://clinicaltrials.gov/search?cond=%22Donohue syndrome%22](https://clinicaltrials.gov/search?cond=%22Donohue%20syndrome%22))

## Catalog of Genes and Diseases from OMIM

- DONOHUE SYNDROME (<https://omim.org/entry/246200>)

## Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28Donohue+syndrome%5BTIAB%5D%29+OR+%28leprechaunism%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D%29%29>)

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