



## What is GRACILE syndrome?

GRACILE syndrome is an inherited disease characterized by poor fetal growth, iron overload, liver damage, and death in infancy. It involves defects in a protein that research suggests most likely involves energy production in cells and iron metabolism. Symptoms associated with GRACILE syndrome may be attributed, at least in part, to iron accumulation, mainly in the liver.<sup>1,2</sup> GRACILE syndrome is also known as Fellman syndrome.<sup>2</sup>

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

GRACILE is an acronym for the symptoms of the syndrome, which may include<sup>1</sup>:

- **G**rowth **R**etardation during pregnancy
- **A**minoaciduria (high levels of amino acids in the urine)
- **C**holestasis (build up of bile in the liver)
- **I**ron overload (high levels of iron in the body, especially the liver)
- **L**actic acidosis (high levels of lactic acid in the body)
- **E**arly death, within the first days of life or by four months of age

There have been reports of affected individuals with hypotonia (low muscle tone) and seizures.<sup>1</sup>

There is no cure for GRACILE syndrome. Treatment includes supportive care for symptoms.<sup>2</sup>

## How is GRACILE syndrome inherited?

GRACILE syndrome is an autosomal recessive disease caused by mutations in the *BCS1L* gene.<sup>1</sup> An individual who inherits one mutation in the *BCS1L* gene is a “carrier” and is not expected to have related health problems. An individual who inherits two copies of the c.232A>G (p.S78G) mutation in the *BCS1L* gene, one from each parent, is expected to be affected with GRACILE syndrome.<sup>2</sup> *BSC1L* mutations can also cause Bjornstad syndrome, Leigh syndrome, and mitochondrial complex III deficiency.<sup>3</sup>

If both members of a couple are carriers, 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 GRACILE syndrome?

GRACILE syndrome occurs primarily in individuals of Finnish descent. In Finland, the incidence is at least 1 in 47,000, with a carrier frequency of approximately 1 in 110.<sup>1</sup>

Having a relative who is a carrier or is affected can also 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.

## 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?

- Genetics Home Reference: <http://ghr.nlm.nih.gov/gene/BCS1L>

### References

1. Visapää I et al. GRACILE syndrome, a lethal metabolic disorder with iron overload, is caused by a point mutation in *BCS1L*. *American Journal of Human Genetics*. 2002; 71: 863-876.
2. Fellman V. The GRACILE syndrome, a neonatal lethal metabolic disorder with iron overload. *Blood Cells, Molecules, and Diseases*. 2002; 29(3): 444-450.
3. BCS1L. Genetics Home Reference. Available at: <http://ghr.nlm.nih.gov/gene/BCS1L> Accessed May 16, 2012.

