

Gamma-glutamyl cysteine synthetase deficiency -GCS- This is a rate-limiting enzyme in glutathione biosynthesis, and necessary for normal RBC survival. GCS deficiency is an autosomal recessive genetic disorder associated with chronic haemolytic anaemia and neurological disease.

What causes the disease and how common is it?

This is a genetic disease. It is linked to mutations of the GCS gene, encoding the GCS enzyme. These mutations lead to reduced GCS activity. An individual can be heterozygous for the disorder (healthy carrier) when only one of the GCS genes is mutated, or homozygous or compound heterozygote (affected individual) when the two GCS genes are mutated. Up to now only nine families with this enzymopathy have been described.

What are the most frequent symptoms if I have the disease?

The common clinical manifestation is chronic haemolytic anaemia of variable intensity. Drug- and infection-induced hemolytic crises may occur. In approximately half of the patients the hemolytic anaemia is associated with neurological dysfunctions.

Which treatment must I follow if I have the disease?

Supportive measures such as red cell transfusions in case of severe anaemia. In some cases spleen removal (splenectomy) may improve the anaemia and thereby patient's clinical situation.

What is the risk of passing the condition on to my children?

Two people who carry each one copy of one of the mutated GCS gene have a 25 percent risk of having a child affected by the disorder at each pregnancy. The risk of having a child who is a healthy carrier of the disorder is 50 percent at each pregnancy, and the risk that a child will not have the disorder and will not be a carrier is 25 percent. Ask for genetic counselling to get a complete explanation.