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Mevalonate Kinase Deficiency (MKD), or Hyper IGD Syndrome

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1. WHAT IS MKD

1.1 What is it?

Mevalonate kinase deficiency is a genetic disease. It is an inborn error of the body’s chemistry. Patients suffer from recurrent bouts of fever, accompanied by a variety of symptoms. These include painful swelling of lymph nodes (especially in the neck), skin rash, headache, sore throat, ulcers in the mouth, abdominal pain, vomiting, diarrhoea, joint pain and joint swelling. Severely affected individuals can develop life-threatening fever attacks in infancy, developmental delay, impaired vision and kidney damage. In many affected individuals, a blood component, immunoglobulin D (IgD), is elevated, giving rise to the alternative name of "hyper IgD periodic fever syndrome".

1.2 How common is it?

The disease is a rare entity; it affects people of all ethnic groups but is more common among the Dutch. The frequency of the disease, even in the Netherlands, is very low. Fever attacks start before the age of six years in the vast majority of patients, usually in infancy. Mevalonate kinase deficiency affects both boys and girls equally.

1.3 What are the causes of the disease?

Mevalonate kinase deficiency is a genetic disease. The responsible gene is called MKD. The gene produces a protein, mevalonate kinase.

Mevalonate kinase is an enzyme, a protein that enables a chemical reaction that is required for normal health; this reaction is the conversion of mevalonic acid to phosphomevalonic acid. In patients, both available copies of the MVK gene are damaged, resulting in insufficient activity of the mevalonate kinase enzyme. This results in accumulation of mevalonic acid, which will appear in the urine during fever flares. Clinically, the result is recurrent fever. The worse the mutation in the MVK-gene, the more severe the disease tends to be. Although the cause is genetic, fever attacks can sometimes be provoked by vaccinations, viral infections, injury or emotional stress.

1.4 Is it inherited?

Mevalonate kinase deficiency is inherited as an autosomal recessive disease. This means that to have mevalonate kinase deficiency, an individual needs two mutated genes, one from the mother and the other from the father. Hence, both parents are generally carriers (a carrier has only one mutated copy but not the disease) and not patients. For such a couple, the risk of having another child with mevalonate kinase deficiency is 1:4.

1.5 Why does my child have the disease? Can it be prevented?

The child has the disease because it has mutations in both copies of the gene that produces mevalonate kinase. The disease cannot be prevented. In very severely affected families, antenatal diagnosis can be considered.

1.6 Is it infectious?

No, it is not.

1.7 What are the main symptoms?

The main symptom is fever, often starting with shaking chills. Fever lasts about 3-6 days and recurs at irregular intervals (weeks to months). The bouts of fever are accompanied by a variety of symptoms. These may include painful swelling of lymph nodes (especially in the neck), skin rash, headache, sore throat, ulcers in the mouth, abdominal pain,

vomiting, diarrhoea, joint pain and joint swelling. Severely affected individuals can develop life-threatening fever attacks in infancy, developmental delay, impaired vision and kidney damage.

1.8 Is the disease the same in every child?

The disease is not the same in every child. Moreover, the type, duration and severity of attacks may be different each time, even in the same child.

1.9 Is the disease in children different from the disease in adults?

As patients grow up, the fever attacks tend to become fewer and milder. However, some disease activity remains in most if not all affected individuals. Some adult patients develop amyloidosis, which is organ damage due to abnormal protein deposition.