PROGRESSION AND TREATMENT

HSPs are chronic, progressive diseases, although severity and the progression of the disease may vary greatly depending on the genetically defined form. Patients with uncomplicated HSP usually retain full strength and mobility of the upper extremities and have no difficulties speaking, chewing or swallowing. Although symptoms can be restricting, lifespan is not shortened by HSP.

Although, with exceptions, current treatment options don't target genetic causes, quality of life, course of the disease and prognosis can be improved by early detection of symptoms and specific associated disease risks. These can be addressed by physiotherapy, orthopedic measures, or symptomatic pharmacological treatment.

SELF-HELP GROUPS/USEFUL ADDRESSES

- Orphanet.
  The platform for rare diseases and orphan drugs.
  www.orpha.net

On our website you will find additional information on other clinical topics as well as organizational information. Visit us at www.mgz-muenchen.com

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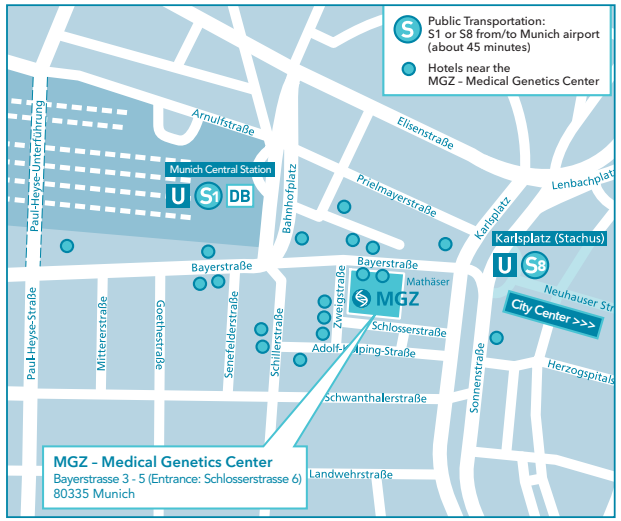

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Patient Information

HEREDITARY SPASTIC PARAPLEGIA (HSP)

Dear patient,

This booklet summarizes information about the basics of the disease, the hereditary aspects, as well as medical care.

HEREDITARY SPASTIC PARAPLEGIA

The group of hereditary spastic paraplegias (HSPs) includes various neurological diseases of genetic origin with the leading symptom of progressive spastic paralysis of the legs (= spastic paraplegias).

> ***Spasticity*** *refers to an increased intrinsic tension of the muscles, which usually presents itself with a decrease in muscle strength (= paresis) and increased reflexes. It is caused by damage to the motor pathways of the central nervous system (brain or spinal cord).*

For the patient, the disease is initially perceived as an unsteady gait or weakness of the legs while walking.

- HSPs are referred to as **"pure" or "uncomplicated"**, if symptoms are mainly limited to spastic paraplegia of the legs. However, this is often accompanied by a bladder disorder that can manifest as urge incontinence or difficulty emptying the bladder.
- By contrast, in **"complex" or "complicated" forms**, a wide variety of additional neurological symptoms can arise. These notably include disorders of the cerebellar function, which manifest as dizziness or unsteady gait (ataxia) or difficulty speaking (dysarthria).

Disease onset can occur from early childhood to later adulthood. A peak of disease onset is observed in infancy and around age 40, although this is also determined by the respective genetically determined sub-form of the disease.

The overall frequency (prevalence) of HSPs is estimated to be 1:10,000 (1 in 10,000 people affected by disease in the general population). It is therefore relatively common among the "rare diseases".

GENETIC CAUSES

The HSPs are diseases that are caused by a change in the genetic material.

> *The genetic material is present in every human being in the form of DNA molecules that, in certain sequences, form the so-called genes. The* ***genes*** *are the blueprint that underlies all processes in the human body. Pathological gene changes are called* ***mutations*** *or* ***pathogenic variants****.*

In case of HSPs, there are a variety of different genes whose alterations lead to genetically defined forms of HSP. These various sub-forms have heterogeneous biological causes and therefore differ with regard to frequency of occurrence, inheritance, disease-associated symptoms, and sometimes therapeutic approach.

INHERITANCE

> *The* ***DNA****, which is the genetic material of humans, forms two sets of 23 chromosomes each. One set of chromosomes is inherited from the mother, the other one from the father.*

The inheritance of HSPs depends on the genetically defined subtype of the individual patient. As many different subtypes exist, all modes of inheritance (autosomal dominant, autosomal recessive, X-linked or mitochondrial) are possible. The risk of disease occurrence in genetic relatives or offspring depends on the underlying inheritance and can differ greatly.

Genetically-induced HSP cannot be ruled out if there are no other affected family members.

If the family includes affected persons in several generations, this can indicate autosomal dominant inheritance. In this case, in about half of the cases, the most common form of HSP is present (SPG4), which results from genetic modification of the SPAST gene.

In the context of human genetic counseling - should the causative genetic change be identified – the mode of familial inheritance, as well as individual risk of having affected offspring can be determined, and possibilities for family planning can be discussed.

DIAGNOSIS

Even if a characteristic clinical presentation suggests an HSP, the diagnosis and delimitation of non-genetic differential diagnoses is made by a human genetic analysis from a blood sample. Only by detecting the underlying genetic change, can the disease be categorized as one of the numerous genetically determined forms of HSP.

However, as there are still scientifically unexplained genetic causes, it is not always possible to confirm the diagnosis genetically. Depending on the family history and the scope of the examination, this is possible in 30 - 70% of patients.