Meretoja disease

Guide for patients, their family and nursing staff

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Cover photo: Corneal build-up in a patient with Meretoja disease. amyloid accumulation in the cornea causes blurred lines (CLA= corneal lattice area amyloidosis). From K.M. Saari, ed. Ophthalmology, 6th edition. Kandidaattikustannus Oy, Helsinki 2011.

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Foreword

The purpose of this guide is to provide information about Meretoja disease, its symptoms and treatment for patients, relatives and caregivers. Due to its rarity, Meretoja disease is poorly understood by both patients and healthcare professionals, and there is no previous guide to the disease. We hope this guide will be useful for anyone interested in Meretoja disease!

The content of the guide has been compiled from a wide range of experts and studies. At the end of the guide, you will find contact i nformation to find out more about the disease and how to live with it. The patient guide is a thesis of the nursing studies at Diakonia University of Applied Sciences and we have made it in cooperation with the Finnish Amyloidosis Association.

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Secretary of the association

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What is Meretoja disease?

Meretoja disease, or hereditary gelsolinium amyloidosis (PGA), is an age-related disease that most commonly appears with eye, nerve and skin symptoms. Meretoja disease was described by Finnish ophthalmologist Jouko Meretoja, MD, in 1969. Meretoja disease is one of about 40 hereditary diseases specific to Finland, the so-called Finnish disease heritage. In Finland, there are an estimated 1000 patients with the disease. The disease is inherited in an autosomal, or gender-independent, manner. You get the disease when you get a faulty disease gene from one of your parents.

Originally, Meretoja disease was found to be most prevalent in Häme and Kymenlaakso. The disease has also been reported in other parts of Europe, North and South America and Asia. The disease is also known as: Kymenlaakso disease, Finnish hereditary amyloidosis, familial amyloidosis Finnish type, familial amyloid polyneuropathy IV, amyloidosis V and corneal lattice amyloidosis (CLA) type II.

What causes the disease?

Meretoja disease is an inherited gelsolin protein metabolism disorder. Gelsolin is a protein found inside cells, in many different tissues and secreted into the blood. In Meretoja disease, a defect in the gelsolin gene leads to a structural defect in gelsolin. As a result, the normal cleavage of gelsolin in the body is disrupted and the abnormal gelsolin fragments begin to form difficult-to-cleave amyloid. This gelsolinium amyloid accumulates mainly in the walls of blood vessels, outside cells and in the basement membranes of various organs, causing the symptoms of Meretoja disease.

The child of a person with Meretoja disease is equally at risk of either having the disease or not. Anyone who does not inherit the disease gene is free of the disease, as are his or her descendants. If the disease gene is inherited from both parents, the disease is more severe and any child who inherits the disease gene will get Meretoja disease.

How is Meretoja disease diagnosed?

The incidence of Meretoja sickness varies from family to family, so it is usually known within the family. In this case, people who are able to inherit the disease from their parents are aware of the nature of the disease.

The clinical diagnosis of Meretoja disease is made based on an examination by an ophthalmologist. It is based on the finding of corneal degeneration, or CLD, in a biomicroscopic examination. It is characteristic of Meretoja disease, distinguishing it from other diseases. The disease rarely starts with neurological or skin symptoms. The accumulation of amyloid can be demonstrated by skin or muscle biopsy and subcutaneous fat aspiration. In Finland, studies have shown that the underlying cause of Meretoja disease is a mutation in the gelsolin gene c.640 G>A (previously known as G654A).

If you suspect a health problem is a sign of Meretoja disease, you can contact a health centre or occupational health service. Together with your doctor, you can plan the necessary tests depending on the symptom that has raised your concern. When you go to the doctor, it's a good idea to tell him or her about a family history of the disease. This preliminary information usually helps to speed up the diagnosis and the beginning of the necessary treatment.

If you have inherited a genetic defect in Meretoja disease, the disease will manifest itself at some point in your life. It is possible that someone at risk of getting sick may want to find out about their situation even before the symptoms of the illness have appeared. In this case, it's called predictive genetic testing. A prerequisite for predictive genetic testing is that the genetic defect in the family is known. If you wish to have this test, you should go to the Department of Clinical Genetics of the University Hospital for a discussion and an assessment of the need for sampling. From a blood sample, it is possible to find out if you have inherited the gene for the disease. However, the carrying of the genetic defect does not give a clearer indication of the symptoms to be expected and the exact age of onset cannot be predicted. Predictive genetic testing is only done for adults or those becoming adults having a risk to develop the disease. Knowing if you carry a genetic defect can be important, especially if you are planning to start a family. Genetic testing can also be done on a foetus in early pregnancy.

Examinations to find out the symptoms of Meretoja disease are carried out in public health care at the cost of a polyclinic fee. Hereditary counselling and any genetic

tests are also included in the polyclinic fee if they are covered by your municipality. You can apply for KELA reimbursement for the fees of a private doctor.

Symptoms of Meretoja disease

Meretoja disease is characterised by eye, nerve, skin and oral symptoms that increase with age. The first symptoms are noticed after about 20 years of age, for some people not until 30-40 years of age. However, the majority of patients are still in good health at the age of 60-70. Typical symptoms include eye symptoms, skin itching, dryness, numbness and tingling of the skin, and oral symptoms. Rarely, other symptoms and findings may also occur, such as arrhythmias and increased protein excretion in the urine.

Eye symptoms

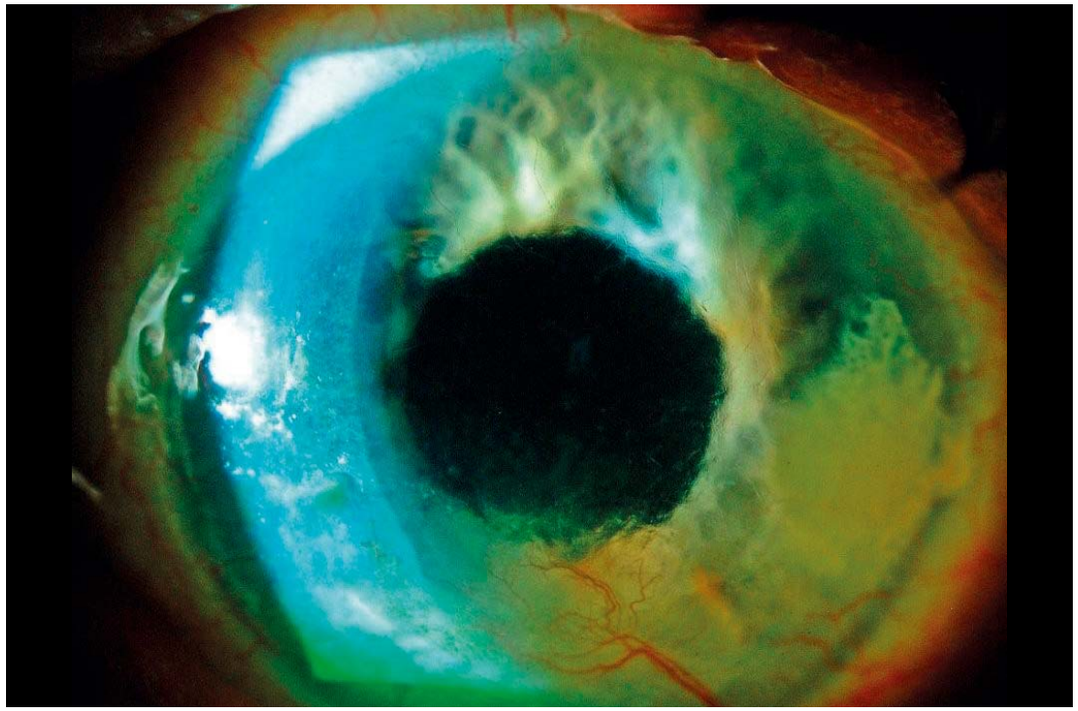
The first symptoms of Meretoja disease often appear as eye symptoms. The symptoms lead patients to see an optician or doctor, which is how many people with Meretoja disease have been diagnosed. The disease causes a reticular degeneration of the cornea of the eye, which progressively causes loss of vision, dryness, itching, irritation, inflammation, and sensitivity to sun and dust.

Dry eye is the most common eye symptom and occurs in people of all ages. Due to the reduced corneal sensation, the patient does not feel dryness in the eyes and the use of moisturising drops may be limited. The outward turning of the lower eyelid dries the eye, because as the eyelid widens, the eye evaporates more tear fluid.

Cataracts and glaucoma become more common after the age of 60 in people with Meretoja disease.

In cataracts, the lens of the eye becomes cloudy, preventing light from reaching the retina and causing vision loss. Scotopic vision (twilight vision) is particularly impaired in cataracts because the eyes cannot distinguish contrasts. The opacification of the lens affects the scattering of light and causes photosensitivity.

Glaucoma is a disease that can cause damage to the nerve fibre layer of the retina, the papillae and the visual field. The disease is diagnosed when the doctor examines the eye pressure, optic nerve head, nerve fiber layer, visual field and ventricular angle.



Reticular corneal lattice degeneration in a patient with Meretoja's disease (corneal lattice amyloidosis CLA II) is visible as pale, streaky formations at the top of the image. Biomicroscopic image by Seppo Lemberg, HYKS Eye Clinic. Kiuru-Enari S. and Haltia M. Duodecim. 2010,126:1162-71.

Symptons in the nervous system

Neurological problems often start around the age of 40. Neurological symptoms typically present as a slowly increasing neuropathy of the facial nerve, i.e. a nerve dysfunction. The facial nerve is responsible for the functions of facial muscles and expressions. Neuropathy typically starts in the upper parts of the facial nerve and later spreads to the lower branches. The first sign may be difficulty in frowning. Gradually, the eyelids begin to droop, which later causes visual impairment. As the symptoms progress, it may become difficult to smile and swallow. Some may develop atrophy of the tongue as a result of hypoglossal nerve dysfunction. Some patients may also experience thickening of the tongue. Speech can also become slurred.

Symptoms slowly worsen with age. Later on, you may also experience other brain nerve symptoms, such as facial tics or hearing loss due to a deficiency in auditory

nerve function. Peripheral nervous system symptoms are usually mild, such as numbness and tingling in hands and legs. Sometimes peripheral neuropathy can present as carpal tunnel syndrome in the wrist, which means numbness, muscle weakness and pain in the thumb, index and middle finger areas.

People over 70 years of age may experience balance and gait problems, limb weakness and mild autonomic nervous system dysfunction such as impaired sweating, low blood pressure, dizziness and constipation. Meretoja disease does not cause dementia.

Symptoms in the skin area

The skin symptoms associated with Meretoja disease begin around the age of 50. The skin dries out easily, causing itching and bruising, abraison and sores from even minor injuries.

Cutis laxa, or abnormal loosening of the skin, is very characteristic of Meretoja disease. The skin loosens on the face, scalp, back, elbows, knees and hands. Facial laxity and sagging skin change the appearance and affect facial expressions. Skin sagging leads to premature ageing of facial features. Because the facial changes are easily noticeable and the symptoms are similar, older people with Meretoja disease are surprisingly alike. Cutis laxa can result in a reduced field of vision and difficulty in speaking and using the mouth, causing significant inconvenience to patients.

Loose skin on the upper limb of a 67-year-old patient with Meretoja disease. Source: Kiuru-Enari Sari, HYKS Neurology Clinic

Problems in the mouth and teeth

Meretoja disease involves a variety of oral and dental problems. Dry mouth is common and can easily cause oral infections and discomfort. Dry mouth is caused by a drooping lower lip, which allows saliva to dry out of the open mouth. Dehydration is also caused by a decrease in saliva secretion due to atrophy of the salivary glands. Its symptoms include a metallic taste in the mouth and atypical tooth decay. Salivary gland samples from people with Meretoja disease have shown amyloid accumulation and inflammatory changes, as well as more yeast growth in the mouth than normal. Reduced salivation predisposes to fungal infections, with symptoms including a red and scarred area of the mucous membrane or tongue and sometimes a white coating in the mouth. A fungal infection can also be found under dentures, as this is a favourite breeding ground for fungi. If you suspect a fungal infection, you should consult your dentist.

Treatment of Meretoja disease

There is no specific treatment for Meretoja disease, which is treated symptomatically.

Eye care

Regular and continuous daily management of eye symptoms has a major impact on the patient's quality of life and on maintaining the clarity of the cornea. When outdoors, it is advisable to wear skin-tight goggles, and sometimes plastic surgery to correct the outward turning of the lower eyelid edges may be necessary. Important measures to protect the eyes include moisturising the eyes, protecting them from wind, dust and glare, and cleaning the eyelids to prevent infection. Individually packaged, additive-free drops should be used to moisten the eyes. Sometimes the treatment for eye symptoms can be a corneal transplant.

The only treatment for cataracts is surgery. If your eyesight gets worse, you should see a doctor, who will refer you to a specialist if necessary. Surgery is often performed using ultrasound, which means the wound size is very small and healing is fast.

The key to treating glaucoma is to lower the pressure in the eye, which can be done with medication, laser therapy or surgery. Pressure relief can help prevent damage to the structure and function of the eye.

Most people with Meretoja disease benefit from regular follow-up with an ophthalmologist, especially to take into account corneal problems and the possibility of developing glaucoma.

Facial surgery and treatment of neurological symptoms

People with Meretoja disease are covered by public health care for facial functional symptoms. This means that patients can get a referral from their doctor to a plastic surgeon for an assessment of the help that surgical procedures can provide. The plastic surgeon will assess the need and timing of the surgery. Due to the progressive nature of Meretoja disease, procedures may sometimes be needed over a number of years, and it is therefore sometimes best to wait for symptoms to progress before starting surgical treatment. The face of a person with Meretoja disease can undergo a wide range of corrective procedures, such as eyebrow or forehead lift, eyelid correction, face lift, and various types of eyelid and mouth support. The most common problems after surgery are dry eyes, haematoma and swelling. It is important that the operating surgeon is aware of the disease and takes it into account in his or her treatment decisions. There are usually no problems with tissue healing as such.

The development of neurological disorders cannot be prevented but a neurologist can help with the symptoms. If a person with Meretoja disease has a loss of consciousness, it is important to remember that in addition to the neurological causes, there are sometimes arrhythmias associated with the disease, in which case a cardiologist can often help. Symptoms of carpal tunnel syndrome, such as numbness and weakness in the hands, can be relieved in many patients by nerve root release surgery. Vitamin B can be used to relieve neurological symptoms and magnesium for muscle cramps.

It is a good idea to know and take into account Meretoja disease before surgery, as the tissue in a person with the disease is usually more fragile than normal and haemorrhages can occur more easily.

Skin care

The most effective treatment for dry, oxidised and itchy skin is liposuction. Dry skin sufferers don't

need to avoid washing, as showering, bathing and swimming help the skin to restore water levels to normal. However, after a shower, bath or swim, the skin should be immediately lubricated with a base cream or moisturiser to maximise water absorption. Among the different types of creams, you should choose the one that suits you best, based on your own preferences. Some creams can increase the evaporation of water through the skin, drying it out even more. If necessary, the pharmacy staff can help you choose the creams you need.

Sun and light therapy can relieve symptoms. In summer, the benefits of the sun's ultraviolet rays can also be enjoyed in the shade. Stress lowers the threshold for itching and can make symptoms worse. Surgical treatment for skin problems can include face, forehead and eyelid lift surgery.

Mouth and teeth care

The key to caring for your mouth and teeth is to keep your mouth moist. If you suffer from dry mouth, your dentist can measure your saliva secretion. Reduced saliva production significantly increases the risk of tooth decay.

In addition to regular dental check-ups, the key to preventing tooth decay is careful dental care at home. Careful dental care includes brushing your teeth twice a day and daily cleaning of the spaces between your teeth. The toothbrush should be soft-bristled to prevent wear at the tooth neck. An electric toothbrush is more effective at removing plaque and the smaller brush head makes it easier to get to the hard spots. There is a wide range of toothbrushes and interdental cleaning aids to suit different hand motor skills.

For toothpaste, choose a fluoride-based, non-foaming paste, as foam causes irritation of the mucous membranes for many people. Cleaning can be enhanced with mouthwash, which should contain fluoride and be alcohol-free, as alcohol dries out the mucous membranes. Dentures must also be cleaned every morning and evening and rinsed after every meal. They should be deep cleaned every week or month, as needed. Xylitol gum and fluoride tablets available from pharmacies can also help prevent teeth decay.

Dry mouth is an uncomfortable problem, even if saliva secretion is not reduced. Increasing chewing, and adding wholemeal bread and raw grits to the diet, for example, can help to get the salivary glands to produce more saliva. Chewing xylitol gum has the same effect, but should be used in moderation for its laxative effects. You should drink enough fluid, preferably water or milk (1-1.5 litres) per day. Sweet juices and large amounts of coffee should be avoided. Many sugar-free drinks are also acidic and are therefore not recommended for drinking.

Many medicines can cause dry mouth as a side effect. You can ask your doctor if there are alternatives to this medicine. You can buy sucking tablets from the pharmacy to treat dry mouth, but not all of them are of significant benefit. A mouthwash for dry mucous membranes is also available from the pharmacy, but home-made cooking and olive oils also work. They can be dabbed on the mucous membranes of the mouth, especially on the cheeks and inner lips. There are also plenty of commercial products for dry mouth, and you can try them to find the right one for you.

Living with Meretoja disease

The severity of Meretoja disease has a major impact on the extent to which it interferes with everyday life. Mild symptoms may not interfere much with daily life, while more advanced symptoms may cause more problems. It is good to recognise the limitations caused by your illness so that you can adapt your lifestyle accordingly. It is important to maintain good general fitness, but excessive physical and mental strain should be avoided. You have to listen to your body and act accordingly to what feels good.

The biggest practical problems are usually related to the condi-

Oral and dental care

Toothpaste: Salutem, Bioténe, BioXtra, Emmelle
Mouthwash: Bioténe, BioXtra, Paroex chlorhexidine mouthwash.

Chewing tablets with fluoride
Additional fluoride also from mouthwash: Meridol, Elmex

tion of the eyes, skin and mouth. However, it is possible to get some relief with various treatments. It is important to note that although Meretoja disease may make it difficult to pursue a hobby, for example, it is not a barrier to a full and rich life. Meretoja disease has no effect on fertility or any negative impact on child intake in general. It does not affect your education, career or financial situation.

If a close relative has Meretoja disease, you can already prepare for it yourself because of its high heritability. The initial symptoms of Meretoja disease often do not appear until adulthood, so in addition to public health care, occupational health care also plays a role in the detection and treatment of Meretoja disease. The Finnish Amyloidosis Association has people with the disease who can provide new contacts, experiences and peer support for living with the disease. Meretoja disease is usually a fairly slow-moving disease, so people with it have many years of full life ahead of them.

The Finnish Amyloidosis Association

The Finnish Amyloidosis Association SAMY is an association of patients with Meretoja disease. The aim of the association is to provide information and act as a link for patients in various treatment and rehabilitation options. It also aims to support and promote research into the disease by providing a patient network for researchers.

People with Meretoja disease can join the Finnish Amyloidosis Association in writing or via the association's website by e-mail. Below you will find the contact details of the association.
Telephone: 045 8774 411 Tuesdays 18 - 20
www.suomenamyloidoosiyhdistys.fi/information-in-english/
samy@suomenamyloidoosiyhdistys.fi

Peer support

One of the key contributions of the Finnish Amyloidosis Association is peer support. Peer support groups meet in main regions where the disease appears. The activities will also be expanded whenever new, regional demand for them arises.

Peer support groups are informal, mainly self-directed, low-threshold regional actors. All groups decide independently on their meeting schedules, venues and any visitors, lectures, visits, etc. to be included in the meetings.

The group meetings are open to all patients and their family members interested in Meretoja disease and the challenges it brings to everyday life. Welcome to join us.

Suomen Amyloidoosiyhdistys ry

Contact details of the groups

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Kotka region:
Mervi Rossi, phone 044-5604066,
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Pirkanmaa region:
Pirkko Keskisaari,
phone 040 5193863
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Useful links

Kela : ***www.kela.fi***
Federation of the Visually Impaired: ***www.nkl.fi***
Disability Federation: ***www.invalidiliitto.fi***
Patients' rights: ***www.valvira.fi***
Patient compensation: ***www.pvk.fi***
Deduction for tax disability: ***www.vero.fi***
Pension insurance: ***www.kela.fi, www.etk.fi, www.tela.fi***
Access to care: ***www.stm.fi, www.kunnat.fi***
Heredity advice: ***www.vaestoliitto.fi***
Heredity clinics:
Helsinki and Uusimaa Hospital District (HUS) 050 432 7111
Kuopio University Hospital (KUH) 017-1721 48
Oulu University Hospital (OYS) 08-3153 218
Tampere University Hospital (TAYS) 03-3116 5507
Turku University Hospital (TYKS) 02-3131 390
Folkhälsans genetics programme:
https://www.folkhalsan.fi/en/knowledge/research/genetics/

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TUETTU VEIKKAUKSEN TUOTOILLA