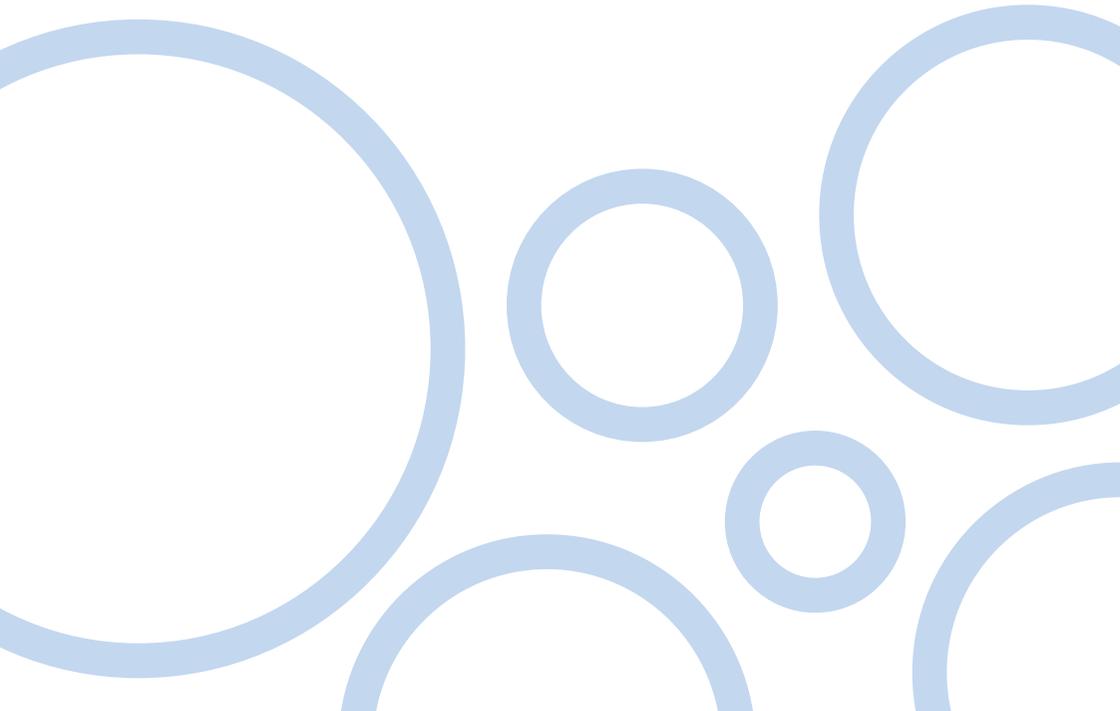




HAM/TSP

Your guide to HTLV-
Associated Myelopathy/
Tropical Spastic Paraparesis

Information for patients, relatives and carers



What you need to know about HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP)

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What is HAM/TSP?

HAM/TSP is an inflammation of the spinal cord that can cause nerve damage in patients infected with human T-lymphotropic virus type 1 (HTLV-1 - please see leaflet on HTLV-1).

The condition is caused by the immune system trying to remove HTLV-1 infection from the body. HTLV-1 is a virus that infects a group of cells known as lymphocytes, which are a part of the immune system responsible for recognizing and fighting infection. When lymphocytes encounter HTLV-1 they release chemicals called cytokines. When cytokines are released in the spinal cord, this can lead to nerve damage. The nerves are ‘innocent bystanders’ caught up in the immune system’s fight against the virus.

History of HAM/TSP

The term TSP originates from the Caribbean, where it has been used for many decades. The cause of the condition was unknown until 1985, when evidence of HTLV-1 infection was found in the blood of the majority of patients with TSP in Martinique (an island in the eastern Caribbean Sea).

At around the same time neurologists in Japan found that patients with a specific pattern of neurological symptoms were infected with HTLV-1. They called this condition HTLV-1-associated myelopathy (HAM).

It was later discovered that TSP and HAM are in fact the same conditions, and the names have now been combined.

Who is likely to be affected?

The likelihood of developing HAM/TSP varies across the globe. For example, in the UK, about three out of every 100 people infected with HTLV-1 (also known as carriers) will develop HAM/TSP at some stage in their life. There are similar rates of the condition (between two and seven out of every 100 carriers) in Africa, the Caribbean, South America and the USA. HAM/TSP is less common in Japanese carriers of HTLV-1.

Factors that may contribute to the development of HAM/TSP include the following:

- **Gender** – women infected with HTLV-1 are more likely to develop the condition than men (three women to every two men)
- **Time or route of infection** – for example, you are less likely to develop HAM/TSP if you have been infected with HTLV-1 virus as an adult rather than as a child
- **The amount of virus in the blood** (known as proviral load) – the risk increases if more than 1% of lymphocytes are infected
- **Immune system genetics** – certain genetic variations seem to increase protection against HAM/TSP while others may lower it

How does HAM/TSP develop?

Most patients who develop HAM/TSP will have been infected with HTLV-1 for months, years or even decades. We do not know what triggers the development of the condition.

What are the symptoms?

Symptoms of HAM/TSP usually occur for the first time between 30 and 50 years of age, but they may also occur at any time after childhood. It is very rare for the condition to develop in childhood.

The earliest symptoms of HAM/TSP are often mild. They are similar to the symptoms of a number of other more common diseases or may be attributed to getting older, which can delay the correct diagnosis. The symptoms include the following:

- Stiffness or weakness of the legs
- Problems with the bladder and bowel movements
- Impotence
- Lower back pain

Stiffness/weakness of legs

Symptoms you may experience could be:

- **Weakness:** Difficulty moving your legs. You may need help with walking and need a walking stick or a frame. You may find it difficult to climb stairs.
- **Stiffness:** Your legs may feel stiff, heavy or difficult to move.
- **Spasms:** Your leg muscles may cramp involuntarily, when you are sitting still or lying down. The weakness and stiffness can lead to frequent slips, trips and falls.

Bladder problems or backache are often the first symptoms to appear.

The most common **bladder problems** are:

- **Frequency**, which is feeling the need to go to the toilet more often than usual (more than every two or three hours)
- **Urgency**, which is the need to pass an often small amount of urine with very little warning
- **Nocturia**, which is having to get up to go to the toilet more than once a night
- **Incontinence**, which is the unintentional passing of urine

These symptoms are usually due to an ‘overactive’ bladder, which is when the bladder tries to empty suddenly and unpredictably before it is full.

In some patients with HAM/TSP the bladder may be ‘underactive’ (‘floppy’ bladder) or partially paralysed. This means that these patients have a very weak urge or no urge to empty the bladder, even when it is full. Urine that is trapped in the bladder may become infected, causing cystitis (infection of the bladder). This can lead to fever and feeling generally unwell, and sometimes to infection of the kidneys (pyelonephritis). If your bladder becomes too full, your doctor will recommend that a catheter (tube) is inserted into your bladder to help empty it and protect your kidneys from damage.

Sometimes the ring of muscles that controls when the bladder opens does not relax when the bladder tries to empty. If this happens, you may experience an urge to pass urine, but be unable to empty your bladder completely.

Please see the ‘How your bladder works’ leaflet for more information on bladder function.

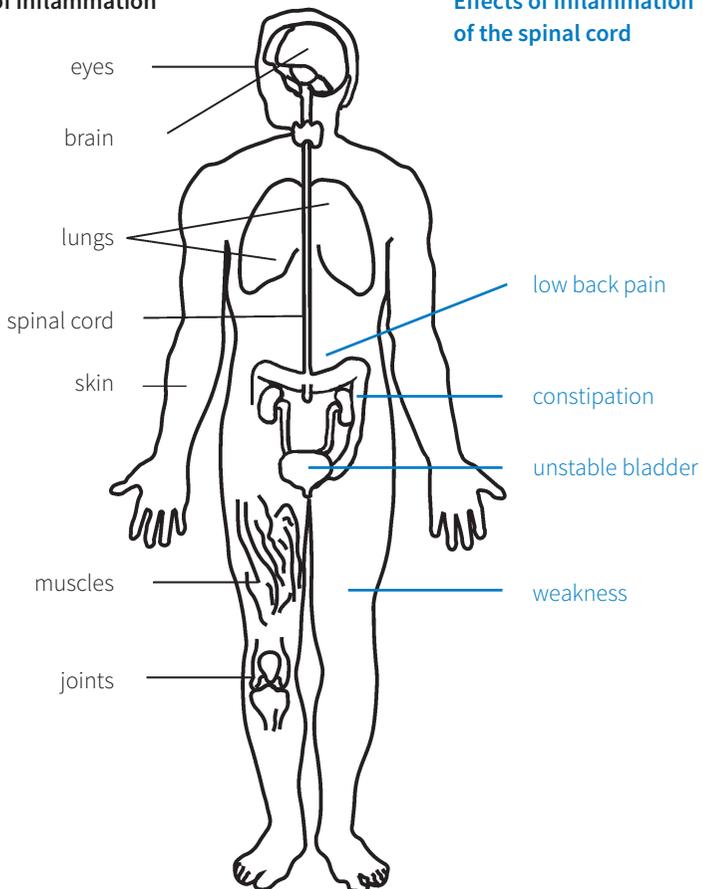
Your **bowel function** can slow down if you have HAM/TSP, resulting in constipation.

Inflammation of the nerves can cause pain, especially in the **lower back** (lumbar spine) but also in the buttocks and backs of the legs.

Men with HAM/TSP may complain of **impotence** (erectile dysfunction). This is normally due to inflammation affecting the nerves responsible for maintaining sexual function.

Primary sites of inflammation in HAM/TSP

Effects of inflammation of the spinal cord



Your doctor may not be able to diagnose HAM/TSP until the nerves that carry instructions from the brain to the leg muscles are affected, causing weakness in the legs. When this happens, you may notice that your legs are stiff and that you often trip, and you may find it difficult to climb up or down stairs, or get out of a low chair. The weakness in the legs mostly affects the hips and the knees rather than the ankles. The nerves responsible for feeling in the legs are not usually affected, especially at the start.

How is HAM/TSP diagnosed?

Your doctor will make a diagnosis by:

- Recognising the pattern of symptoms
- Identifying HTLV-1 infection (based on the presence of HTLV-1 antibodies in the blood)
- Ruling out other conditions, especially pressure on the spinal cord

Your doctor may also want to confirm the diagnosis by:

- Detecting HTLV-1 antibodies in the fluid that surrounds the brain and spinal cord, called cerebrospinal fluid (CSF)
- Measuring the amount of HTLV (proviral load) in the blood and CSF

What tests and investigations help with the diagnosis

A number of tests are needed to diagnose HAM/TSP and to exclude other conditions with similar symptoms. These include blood tests, CT and MRI scans and lumbar puncture. Some patients may also need electromyography, nerve conduction studies and ultrasound scans.

Blood tests

Evidence of HTLV-1 antibodies is essential but not enough to make a diagnosis of HAM/TSP. It is also helpful to find out what the proviral load (the amount of virus) in the blood is.

Your doctor will recommend other blood tests to rule out other possible conditions.

CT and MRI scans

CT and MRI scans provide detailed images of the spinal cord and the brain, showing areas of inflammation. They help to exclude other conditions and any cause of pressure on the spinal cord, for example a prolapsed (slipped) disc.

A CT scan, or computed tomography scan, is a kind of three-dimensional X-ray. It can detect a wide range of brain and spinal cord disorders.

An MRI scan, or magnetic resonance imaging scan, uses a magnetic field and very-high-frequency radio waves to produce high-quality pictures that show more detail than a CT scan.

Lumbar puncture (spinal tap)

A lumbar puncture is a way to sample cerebrospinal fluid (CSF) for testing. It is done by inserting a fine needle into the fluid-filled space below the end of the spinal cord to draw out a CSF sample.

Examination of the CSF gives information about the degree of inflammation in the spinal cord in patients with HAM/TSP. It can also help exclude other infections or causes of inflammation. Detecting HTLV-1 antibodies and checking the HTLV-1 proviral load in the CSF can be important steps in making the right diagnosis.

Electromyography (EMG)

This test measures electrical activity in the muscles at rest and during contraction. It helps diagnose diseases that damage muscle tissue, nerves or the junctions between muscle and nerve.

Nerve conduction studies

This type of test measures the speed at which signals travel through the nerves to the brain and back. This helps to work out whether symptoms are caused by a disease that is affecting muscle tissue or nerves.

Ultrasound scans

These scans use high-frequency sound waves to produce real-time images of the inside of the body. Radiation (X-rays) is not involved. Ultrasound is a useful way of examining many organs, including the heart, liver, gallbladder, spleen, kidneys and bladder. In patients with HAM/TSP it is used to check the bladder, especially its capacity and its ability to empty completely.

What is the natural course of HAM/TSP?

The natural course of HAM/TSP varies from person to person, but most changes usually occur during the first couple of years after the first symptoms develop. From then on, the condition either stabilizes or worsens slowly.

The level of disability also differs from patient to patient. Some patients have very mild disability that does not interfere with their lives too much. Up to half of all patients with HAM/TSP may eventually need to use a wheelchair. However, it can take many years before this is necessary.

How can it be treated?

Although there is no cure for HAM/TSP, there are a number of treatments available that can help reduce the severity of the condition. There are two approaches to treatment:

- ‘Symptomatic’ treatments to relieve symptoms such as bladder problems, constipation, impotence, back pain or stiffness of the legs.
- Direct treatments to target the underlying cause of the condition (the inflammation in the spinal cord caused by HTLV-1 infection).

Symptomatic treatments

Some medications can improve symptoms caused by an **overactive bladder**, such as frequency, urgency and nocturia. If you also experience pain when passing urine and/or have a fever or feel generally unwell, this may be a sign of bladder infection. This will require antibiotic treatment.

If you suffer from a **'floppy' bladder**, your doctor may recommend you are given an 'in-and-out' catheter (tube) that you can use to empty your bladder yourself when needed (intermittent self-catheterisation).

If you are **constipated**, it may be best to start with changing your diet to increase the amount of fibre you eat. Your doctor will prescribe you laxatives, suppositories or enemas if required.

Treatment to manage your **pain** may include:

- Painkillers, such as paracetamol or codeine
- Anti-inflammatory medications such as ibuprofen
- Specialised drugs for nerve pain
- Injection of local anaesthetics or steroids
- Different physical methods, such as physiotherapy

Painful spasms and stiffness of the legs can be treated with medications such as baclofen.

Physiotherapy can help improve your ability to walk and increase your physical strength. It can also reduce muscle stiffness through stretching and strengthening exercises, and through providing walking aids. Social services may need to assess your home environment to ensure that it is suitable and safe, and that it meets your needs.

Direct treatments

Steroids

Corticosteroids, drugs used in many inflammatory conditions like asthma and arthritis, are commonly used to reduce inflammation in the spinal cord in HAM/TSP. Your doctor will recommend how best to use this treatment. Most frequently this is given into the vein over one hour on three consecutive days. In some patients, lower doses are given by mouth over a period of weeks to years. Long-term steroid use has a number of potential side effects which your doctor will discuss with you if steroids are prescribed.

Biological anti-inflammatory agents

A number of other medications can be prescribed to dampen down the immune response in HAM/TSP. These drugs, which have proven benefit in a wide range of other inflammatory conditions, are chosen based on our understanding of how HAM/TSP develops and to avoid the side effects of steroids. Because of its rarity in high-resource countries, there have been few clinical trials in HAM/TSP.

Research into which anti-inflammatory agents are best for the treatment of HAM/TSP is ongoing.

Antiviral drugs

To date drugs that target the virus have not been successful in reducing the viral load in HTLV-1 infection.

However, a recent study from Japan has shown that some patients with HAM/TSP improved following treatment with an agent that allows the immune system to kill HTLV-1 infected cells. This drug, an anti-CCR4 monoclonal antibody, is not yet available in the UK.

Am I at risk of developing any other conditions if I have HAM/TSP?

Patients with HAM/TSP may also develop other inflammatory conditions such as:

- Uveitis (inflammation of the eye)
- Arthritis (inflammation of one or more joints)
- Alveolitis (inflammation of lung tissue) or bronchiectasis (damage to the airways)
- Polymyositis (inflammation of muscle)
- Keratoconjunctivitis (inflammation of the cornea and conjunctiva in the eye)
- Infectious dermatitis (inflammation of the skin)

HTLV research at Imperial College Healthcare NHS Trust

At the HTLV clinic at St Mary's Hospital we have an active research programme that has the following aims:

- To find out how different factors (such as the immune system, or genetic or lifestyle factors) may influence why some patients with HTLV infection develop HAM/TSP and some do not
- To learn about the body's response to the virus and how it may prevent or cause disease
- To develop effective treatments for HAM/TSP

Summary

HAM/TSP is a chronic inflammation of the spinal cord caused by a virus called HTLV-1. Early diagnosis of HAM/TSP is important to enable prompt use of treatments that may stop or slow down the disease progression.

HAM/TSP is diagnosed by:

- Recognising the pattern of your symptoms
- Diagnosing HTLV-1 infection by an antibody test
- Confirming the presence of HTLV-1 in your CSF
- Ruling out any other diseases that may cause similar symptoms

Although there is currently no cure for HAM/TSP, many treatments are available to relieve your symptoms. We are also investigating new treatments that target the underlying cause of HAM/TSP.

If you have HAM/TSP, a multidisciplinary team will care for you, including a neurologist, infection specialist, physiotherapist and a clinical nurse specialist.

Where to find HTLV services in the UK

The National Centre for Human Retrovirology is situated on the ground floor of the Winston Churchill Wing at St Mary's Hospital, London.

You are advised to travel, if possible, by public transport when visiting the clinic. Car parking is very limited and you may find it difficult to find a place to park near the hospital. Disabled parking is available on Winsland Street. The nearest tube station is Paddington (Bakerloo, District, Circle and Hammersmith & City lines), which is also a railway station. Buses that stop on Praed Street are numbers 7, 15, 23, 27 and 36.

If you or your family wish to know more about HTLV, ATL, HAM/TSP, or participate in research, please contact:

The National Centre for Human Retrovirology

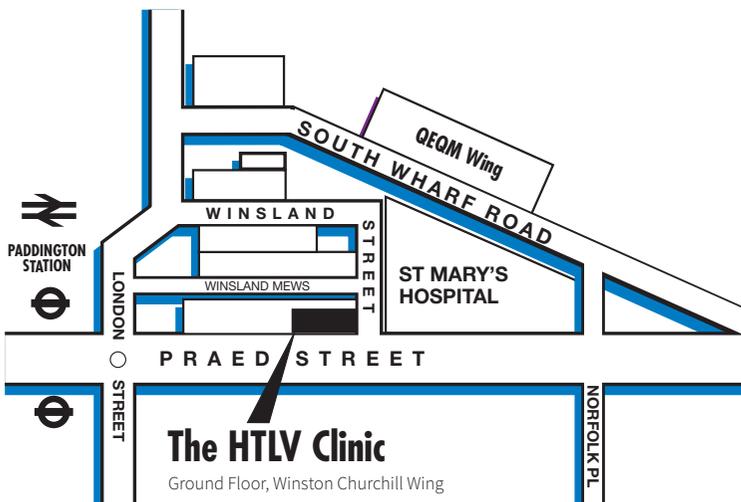
Ground floor, Winston Churchill Wing

St Mary's Hospital, Praed Street, London W2 1NY

Tel: 020 3312 6604 Fax: 020 3312 6123

Email: imperial.htlv@nhs.net

More information can be found at: www.htlv1.eu



There are also HTLV Clinics in Birmingham, Manchester and York
– see addresses and contact details below:

Manchester HTLV Clinic

Pennine Acute NHS Trust, Department of Infectious Diseases,
North Manchester General Hospital, Crumpsall, Manchester M8 5RB
Tel: 0161 720 2734 Fax: 0161 720 2680

Birmingham HTLV Clinic

University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital Birmingham, 3rd Floor East Block,
Main Drive, Edgbaston, Birmingham B15 2TH
Tel: 0121 371 6954 Fax: 0121 371 6981

York HTLV Clinic

York Teaching Hospitals NHS Foundation Trust
Monkgate Health Centre, 31 Monkgate, York YO31 7WA
Tel: 01904 725423 Fax: 01904 725157