

Hepatic encephalopathy (HE)

When the liver affects the brain





Preface

You are suffering from severe liver disease or a connection between the liver circulation and the main venous circulation (porto-systemic shunt) and therefore have a high risk of developing **hepatic encephalopathy** (HE) or have already been diagnosed with HE and would therefore like to find out about this condition.

You or your family members may have noticed physical and/or mental changes in you that you or they cannot yet understand or place. This can all be very frightening for those affected and their loved ones.

**«Before I was diagnosed with HE,
we did not know about it and its
warning symptoms. But now we are
confident that we can assess the
situation earlier and act accordingly.»**

61 year old female patient

This brochure is intended to answer possible questions about HE for patients and their family members, and explain what HE can mean in everyday life and what should be considered.

Those terms printed in **bold** in this brochure are explained in more detail in the glossary at the end.

Please note that this brochure is not intended to replace consultations with healthcare professionals. If you have any questions or concerns, also regarding your underlying disease, please contact your attending physician.

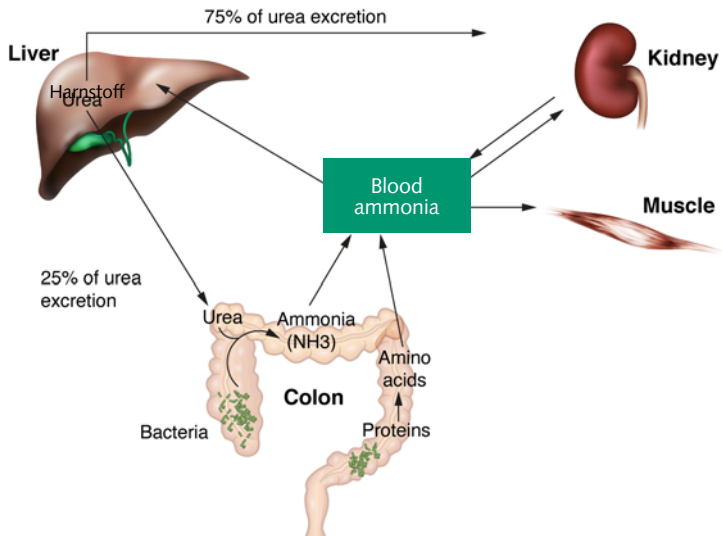
What does your brain have to do with your liver?

HE is a serious complication that may arise from advanced liver disease. In HE there is a temporary loss of brain function, which is characterised by a combination of mental and physical symptoms. In HE the liver can no longer filter enough toxins from the blood.

A healthy **liver** detoxifies the blood and thus helps to break down any toxins produced in the body. This includes the toxin **ammonia**, which is produced by bacteria in the intestine.

«I didn't realise that the liver had something to do with my brain.»

55 year old female patient



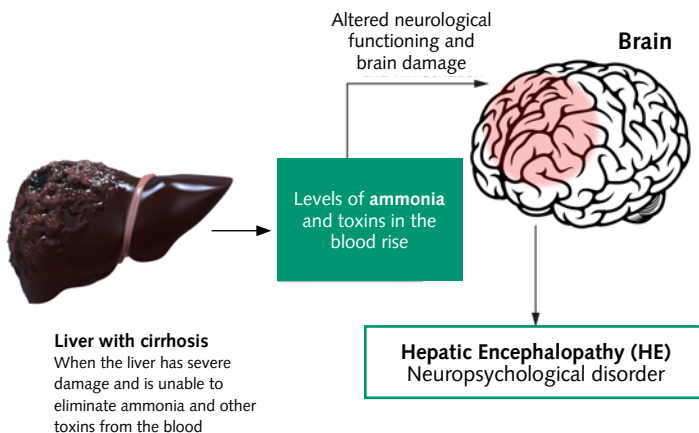
Ammonia production and detoxification by the liver

Once damaged, the liver can no longer filter toxins from the blood. This means that waste products, which are produced, for example, by digesting food or medication, are no longer filtered and broken down by the liver, or only to an inadequate degree. Instead, the accumulated toxins (e.g. ammonia) reach the brain via the bloodstream, where, once they exceed a certain level, they cause damage that impairs thinking and acting.

Toxins that accumulate in the blood and enter the brain lead to HE.

Patients with severe liver disease, such as cirrhosis of the liver, may develop HE. HE is by no means a rare secondary disease. About 20%–50% of patients with **liver cirrhosis** developed HE.

HE can develop in patients suffering from advanced liver damage.



Liver Dysfunction and HE

How can you recognize a HE?

HE symptoms can be physical, mental or a combination of both. They may be mild at first and worsen over time, but they may also appear suddenly. The course of the disease often includes periods of deterioration followed by improvement. The phases with deterioration are called episodes. In many cases, the early symptoms of HE go unnoticed, as they usually appear gradually and are difficult to differentiate. Moderate and severe symptoms become more evident for patients and their family members.

Symptoms of mild stages include:

- Shortened attention span
- Difficulty in concentration
- Changes in personality, e.g., euphoria or fears
- Forgetfulness, difficulty in thinking
- Poor judgment
- Changes in sleeping habits, e.g., sleeping more during the day

Symptoms of moderate and severe HE include:

- Inertia, indifference
- Marked personality change
- Inappropriate behaviour
- Disorientation, confusion
- Motor/coordination problems
- Trembling of hands
- Daze

«I just had a funny feeling. In my daily routine I suddenly had trouble with normal things such as opening a shampoo bottle or zipping up a jacket.»

63 year old male patient

HE is a serious complication that, if left untreated, may result in coma and permanent brain damage. In later stages HE can be life-threatening. Therefore it is crucial to detect and treat HE as early as possible.



Difficulty in concentration & forgetfulness are symptoms of mild stages



Hand shaking and disorientation are symptoms of moderate-severe HE stage

«I have noticed that I cannot do a lot of things anymore or do them right.»

48 year old male patient

How is HE treated?

Trigger of an HE episode

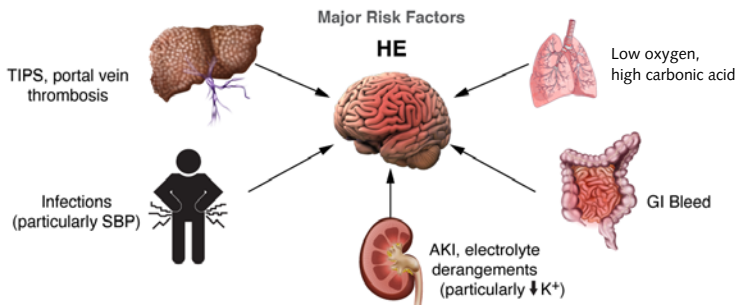
The primary goal is HE prevention. Each episode damages your brain (e.g., the ability to think and remember things).

What are some known triggers of HE?

- Infections (e.g., fever / cough / diarrhoea / burning sensation when urinating / markedly reddened wounds)
- Gastrointestinal bleeding (e.g., black stools (tarry stools))
- Incorrectly dosed dehydration medication (e.g., sudden marked increase / decrease in abdominal girth, unusually fast increase / decrease in body weight on the scales)
- Electrolyte disorders (e.g., caused by diarrhoea or dehydration medication)
- Constipation

In case there is an HE episode nevertheless, it is important to know that it can be treated. How quickly you will recover from HE depends on your underlying disease and the severity of the HE episode. Treatment depends on various aspects. Special attention is paid to what may have caused the onset of HE.

Not only can the prescribed medications contribute to improving the acute phase of HE, but they also help prevent new HE episodes. The medications support your brain in recovering from HE and its symptoms.



Major Risk Factors leading to the development of HE

Medication management

The first step when treating an episode of HE is to identify any factors that may have caused it. Then specific measures are initiated (e.g., adjustment of drug dosage).

The two drugs most commonly prescribed and their effects are detailed below.

Lactulose/lactitol

Even if you slowly feel better after starting the therapy, you must continue treatment; discontinuing the prescribed treatment may result in another HE episode.

Duphalac® (lactulose) and Importal® (lactitol)

Duphalac® and Importal® change the acidity in your intestine such that certain bacteria cannot grow as well. They also inhibit the growth of bacteria that produce ammonia. Furthermore, Duphalac® and Importal® will soften your stool and make you have more frequent bowel movements. This is necessary so that the toxins are eliminated from your body and do not accumulate in your brain via the bloodstream. The basic dosage of Duphalac® or Importal® will be prescribed by your attending physician. The maximum daily dose of Duphalac® is 135 ml and of Importal® 1.05 ml/kg body weight.

What Duphalac® and Importal® will do for you

The desired effect is achieved if you have soft bowel movements 2–3 times a day (soft bowel movement, without heavy pressing ≠ diarrhoea). Various factors, such as diet, stress, oral intake of sweeteners and medication, affect your digestion and thus also the number and consistency of your bowel movements. Therefore, you may need to adjust the Duphalac® dosage from time to time to meet the targeted 2–3 soft stools per day.

Goal of lactulose/lactitol treatment

Your goal should be 2–3 soft bowel movements every day. You and/or your family members will have to adjust the Duphalac® or Importal® dosage to reach this goal. If you are uncertain, please contact your family doctor or attending physician.

What if you have less than 2–3 bowel movements a day?

If your stools suddenly become a little firmer or you do not reach the target of 2–3 bowel movements, take an additional dose of Duphalac® or Importal®.

What if you have liquid or even watery stools more than 3 times a day?

If you have liquid to watery stools (= diarrhoea) more than 3 times a day, make sure that you drink enough liquid (e.g., water or tea). Fluid loss in diarrhoea can be dangerous for you. All the more so, since this can trigger an HE episode in your case. Contact your family doctor or attending physician if you have diarrhoea (more than 3 times liquid stool per day), and reduce Duphalac® or Importal® by one dose (only as long as you have diarrhoea).

What if you have no bowel movement / are constipated one day?

If you have not had a bowel movement for 12 hours, take an additional dose of Duphalac® or Importal® immediately. If you notice that you have not had a bowel movement for 3 days, contact your family doctor or attending physician immediately so that he can adjust your treatment.

Adverse effects of lactulose/lactitol

What are the adverse effects of Duphalac® (lactulose) and Importal® (lactitol)?

Some patients report side effects when taking Duphalac® or Importal®. Mostly it is abdominal pain (light abdominal pain), flatulence (winds) and nausea. If you suffer from these or other symptoms that make it difficult for you to take Duphalac® or Importal®, contact your attending physician so that a suitable solution can be found for you. Under no circumstances should you discontinue Duphalac® or Importal® by yourself without consulting your attending physician.

«I had been told that bowel movement is important, but with this nausea that was almost always present, I just couldn't take Duphalac® anymore. I thought, well, no bowel movement in 2–3 days for once is not so bad..., that will be just fine...»

55 year old female patient

If you cannot take your medication for any reason, such as nausea, contact your family doctor or attending physician. You must also contact your family doctor or attending physician if you wish to stop or change taking a medication.

Goal: Preventing an(other) HE episode.

Rifaximin

Xifaxan® (Rifaximin)

There are several antibiotics for treating HE. Xifaxan® stops the growth of certain intestinal bacteria that produce toxins during the digestion of food. Not every patient with HE is treated with antibiotics. Should you require Xifaxan®, it will be prescribed for you by your attending physician.

The usual daily dose is 1 Xifaxan® film-coated tablet taken twice daily. These tablets can be taken either with or between meals.

What Xifaxan® will do for you?

You have been prescribed Xifaxan® to prevent a (renewed) HE episode from occurring. Xifaxan® stops the growth of bacteria in the intestine that produce the toxins which would otherwise reach the brain via the bloodstream. This way, Xifaxan® protects your brain against bacterial toxins from the intestine. Xifaxan® remains in the intestine and only passes into the body in minute quantities.

What are the adverse effects of Xifaxan®?

When treated with Xifaxan®, your urine may appear somewhat reddish. This is absolutely normal. Most patients tolerate Xifaxan® well. But adverse effects can occur when taking antibiotics. Patients report the following adverse effects: Nausea and vomiting, stomach pain, dizziness, diarrhoea (>3 watery stools per day), tiredness (fatigue), headache.

The goal of Duphalac®/ Importal® and Xifaxan® is to reduce the formation and absorption of toxins such as ammonia and to eliminate the toxins present with the bowel movements.

Complementary and alternative medicine

Today, complementary treatment is often used alongside mainstream medicine to alleviate symptoms and provide holistic support for the body. Some of these complementary or alternative medications and therapies are digested by the liver and therefore are not suitable for patients with liver problems. They can damage your liver even further. In order for us to ensure that the therapy and/or medication you have chosen does not negatively affect your health or medical treatment, you should discuss any therapies and medication you are planning to pursue or take with your attending physician.



In case of adverse effects you should contact your attending physician.

What else you need to know about treatment in acute cases

In case of a moderate or major HE episode, you will probably be hospitalised to protect you from subsequent damage and to optimally adjust your treatment. Nursing measures will also be initiated to support your recovery (e.g., close monitoring, positioning measures, supporting you eating and drinking, etc.).

This phase of the disease in particular can be especially stressful for family members.

Dear family members, please contact the responsible nursing professional. We will inform you about the treatment procedure at all times and will gladly involve you in the care of your family members.

What you can do in your daily routine to avoid HE episodes

By taking an active role and paying close attention to yourself and your body, you can help avoid an(other) HE episode. The following recommendations are specific to HE. For general information regarding your underlying disease, please ask your attending physician.

Watch your diet (see figure)

- Eat a protein snack (e.g., yogurt or cottage cheese) 1 hour before you go to bed. Your body digests proteins well while you sleep.
- We recommend that you eat several smaller meals instead of three large meals a day. This avoids long periods of fasting and your body receives a steady supply of nutrients.

- Consume more such **proteins** as dairy products and vegetables instead of meat products (e.g., dried beans, peas, lentils, unsalted nuts, unsalted peanut butter, etc.)
- Avoid dehydration and drink enough water (check your body weight every 2–3 days)

Get moving in your daily routine

Walk wherever and whenever you can. For example, get off the bus one stop earlier or later, take the stairs instead of the elevator.

Move your arms and legs several times a day in small, simple and repetitive motions (e.g., move your arms in circles next to your body forward, backward, simultaneously, in turns, or paint circles on the floor with the tip of your foot) Keep yourself active throughout the day as much as possible and avoid long periods of sitting down.

«I found out that a healthy diet, exercise and adequate fluid intake are important measures to avoid HE.»

65 year old patient



Diet chart for patients with HE

Be a teetotaler in your illness

Since alcohol is processed by your liver, it can be dangerous for anyone with liver disease. Even small amounts of alcohol can cause problems in pre-existing liver disease. Despite its name, non-alcoholic beer still has an alcohol content (although very low) and should be avoided as well.

Stop smoking and refrain from illegal substances

Patients with liver disease have a compromised immune system and are more susceptible to infections, among other things. We therefore recommend that you stop smoking, for example, to help avoid respiratory tract infections. Smoking also increases the risk of developing various types of cancer, including liver cancer.

Any illegal substance (marijuana, cocaine, heroin, etc.) is strictly prohibited.

Avoid sleep medications

Since patients with liver disease react more strongly to the effects of sleep medications, these should be avoided and only taken in consultation with your attending liver specialist.

When and where you have to report symptoms

It is likely that the people around you will notice your HE symptoms before you will. It is therefore vital that people close to you know about possible symptoms.



Talk to family members and friends about possible symptoms so they can take action, if necessary.

If you have been diagnosed with HE before and feel that your condition has worsened or changed, please make an appointment with your family doctor or attending physician as soon as possible. Decide what you should do next.

- No bowel movement for 3 days
- Diarrhoea for 3 days with dehydration; may be accompanied by thirst and dizziness
- Marked drowsiness, fatigue
- Do you find it difficult to be attentive or to concentrate?
- Have you become more forgetful?



If you or your family members notice symptoms/alterations in you, take an extra dose of Duphalac®.

If you or your family members notice any of these symptoms, ask someone to take you to the hospital emergency room or call the emergency number 144.

- Do you have fever of 38.0°C or higher, especially with chills?
- Have you noticed black stools? (tarry stools)
- Have you noticed bright red blood in your stools?
- Has your handwriting changed or do you have difficulties with other fine motor skills, e.g., when zipping up your jacket, tying your shoe laces?
- Do you experience difficulties with actions or movements, do you have difficulty walking?
- Do you feel or appear to be indifferent, apathetic?
- Have you become more forgetful?
- Are you sometimes confused, disoriented, do you not know where you are or what day of the week it is?
- Have you been told that you have changed, are behaving inappropriately (e.g., uninhibited, diminished sense of shame)?
- Do your hands tremble?
- Is your speech blurred?
- Do you experience new fears or anxiety?
- Has your day-night rhythm changed?
- Increased drowsiness or fatigue?

Have you been discharged from hospital after being hospitalised for an HE episode? If so, please use the monitoring checklist on the next page. At least once a week, checkmark all symptoms you are suffering from at that time and note the date of observation.

In order to discuss the course of your symptoms, bring the monitoring checklist with you to your doctor or attending physician at your next follow-up.

Symptoms checklist

Date		Week 1	Week 2	Week 3	Week 4	Week 5
Mental health complaints	Confusion					
	Forgetfulness					
	Poor judgment					
	Increased nervousness					
	Not knowing where you are					
	Unusual behaviour					
	Personality changes					
Physical complaints	Breath with sweet or musty smell					
	Changes in sleep pattern					
	Changes in your handwriting					
	Difficulties with fine motor skills					
	Trembling hands					
	Blurred speech					
	Slowed movements					

Topics I should discuss with my attending physician

- Am I allowed to drive a car?
- Am I allowed to travel? If so where, and what do I have to consider?
- Do I need to refresh or complement my vaccinations?
- I will contact my attending physician when I have an appointment with the dentist to extract / operate on a tooth, as a short prophylactic course of antibiotics may be indicated.

For my family members it may be important to know...

- ... which symptoms to look out for and what to do when noticing these symptoms
- ... who has an emergency key for my apartment / how to get access to my apartment in case of an emergency
- ... whether and where I have a living will / what my will is regarding further medical treatment

If necessary, ask your attending physician about support options.

- Ordering medication / medication delivery service
- Support offers
 - For example, Spitex for sorting medication, blood sugar measurement, personal hygiene, security/control, relief for your family members etc.
 - Meals on wheels
 - Domestic help
- Help with taking medication (e.g. Post-Its, alarm clocks, apps, etc.)
- Sharing experiences, raising disease awareness:
www.swisshepa.org
<https://liverfoundation.org/hepatic-encephalopathy-patientsadvice>

Are you affected by **cirrhosis of the liver**? We will gladly provide you with our «Patient Information Brochure on Cirrhosis of the Liver». If you are interested, please ask your attending physician or go to our website listed on the last page of this brochure.

Glossary

Antibiotics (Rifaximin, Xifaxan®)	Special antibiotics reduce the number of bacteria in the intestine.
Ammonia	Toxic substance produced by the breakdown of proteins and amino acids in the body, but also produced by certain intestinal bacteria. High levels in the blood can damage the brain.
Diarrhoea	Liquid, watery bowel movements more than 3 times daily.
Proteins	As structural materials for cells and various tissues (muscles, organs), they provide the basic building blocks for the body. Proteins are difficult for the body to store. Therefore a steady supply via food is necessary to build up and regenerate your body substance.
Hepatic encephalopathy	Changes in the brain that may occur in patients with advanced liver disease due to high levels of toxins in the brain.
Liver	Among other things, it is responsible for filtering toxins from our blood, producing certain hormones, and releasing as well as storing energy from food.
Liver cirrhosis	Healthy liver cells have been damaged and replaced by scar tissue.

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Legal notice

This brochure «Hepatic Encephalopathy (HE) – Information for Patients and Family Members» was compiled in a collaborative effort with an internal project group comprising patients, physicians and nursing professionals. Text passages contributed by patients are marked in bold.

For better readability, only one gender form is used in this brochure. Thereby, the other gender is included in each case.

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