



# *I. Hepatitis*

# 1. GENERAL INFORMATION

## WHAT IS HEPATITIS?

### 1.1 The most important information in brief

#### **Hepatitis (inflammation of the liver)\_\_\_**

Hepatitis is also often called jaundice. This is misleading because the yellowing of the skin is merely one of many symptoms of the disease, which does not occur with every form of hepatitis and can also be observed in the case of other diseases.

#### **Causes of hepatitis**

The most common cause of hepatitis in the industrialized countries is excessive alcohol consumption. Infection with hepatitis viruses is the second most common cause. Inflammation of the liver is occurring ever more commonly as the result of fatty deposits due to obesity and poor diet. Hepatitis cases are less commonly associated with infections with other microorganisms, which can also lead to hepatitis, especially in people with compromised immune systems. The hepatitis virus needs the cells of the human liver as a host.

#### **Progression forms of viral hepatitis**

An *acute infection* can often go unnoticed or may be associated with exhaustion, nausea, vomiting, and pain in the right upper abdomen.

A *chronic infection* can last for years and may lead to cirrhosis of the liver or liver cancer (hepatocellular carcinoma).

In the case of cirrhosis of the liver, the liver forms scar tissue to replace dead liver tissue (with increasing impairment of liver function). Advanced cirrhosis of the liver represents a severe disruption of liver function and can lead to various syndromes with highly diverse symptoms.

#### **Detection of viral infections**

In cases of suspected viral hepatitis the treating physician will initially make a simple primary diagnosis. This will include a blood test for the detection of antibodies, which the immune system has formed in response to the virus and/or the direct detection of viral components.

#### **Who should be tested for hepatitis?**

In general, hepatitis tests should be conducted on anyone exhibiting possible symptoms of the disease, such as yellowing of the skin, fatigue, and nausea. The infection rates for hepatitis diseases are high among drug users. The earlier an infection is discovered and treated, the better the chances of recovery.

#### **The different forms of viral hepatitis**

##### **Hepatitis A**

- *Route of transmission of the virus:* Through fecal contamination of water, food or people. Through oral and oral-anal sexual contact.
- *Progression:* Approx. 50-70 % of infected adults will develop symptoms of the disease (nausea, yellowing of the skin, etc.). The infection never becomes chronic and always leads to life-long immunity, i.e. it is not possible to become reinfected.
- *Treatment:* There is no accepted medicinal anti-viral treatment.
- *Vaccination:* The hepatitis A vaccination and the combination hepatitis A and B vaccination have been shown to be safe and effective.

### **Hepatitis B**

- *Route of transmission of the virus:* Through contaminated blood, through unprotected sexual intercourse, through the joint use of the same injection materials, through the joint use of the same shaving utensils, tooth brushes or tattooing equipment, as well as from infected mothers to their newborns (through the transfer of blood during birth, as well as percutaneous or permucosal absorption, i.e. through wounds of the skin or mucosa).
- *Progression:* Symptoms of acute hepatitis B occur in 50-70 % of adults, whereby the progression is different depending on age: babies infected at birth usually develop a chronic infection, which only occurs in 5-10 % of cases among adolescents and adults; however, such an infection can lead to cirrhosis of the liver or liver cancer. Immunity is only guaranteed if the person fully recovers from an infection. Liver failure is rare (in approx. 1 % of cases).
- *Treatment:* There are two types of anti-viral treatment: treatment with interferon (injection) or with anti-viral medications (tablets). The indication for each treatment and the chances of success depend on the person's current immune status.
- *Vaccination:* The hepatitis B vaccination is safe and effective (for adults 3 injections, for adolescents 2 injections).

### **Hepatitis C**

- *Route of transmission of the virus:* Chiefly through contaminated blood: through blood transfusions (prior to 1990), through injured skin (percutaneous) or injured mucosa (permucosal), e.g. through the joint use of the same shaving utensils, tooth brushes or tattooing equipment.
- *Progression:* Infections with the hepatitis C virus lead to acute hepatitis in only approx. 10-20 % of those affected, i.e. the disease usually progresses with no symptoms. Chronic inflammation occurs in 70-80 % of those affected, which in turn leads to cirrhosis of the liver in 5-50 % of those infected after 5-50 years, and some of these will develop liver cancer. *A reinfection is possible after successful treatment and recovery from the disease!* Fulminant hepatitis (rapid progression up to and including liver failure) is possible in cases of co-infections with hepatitis A and hepatitis B, which can be prevented with the corresponding vaccination(s).
- *Treatment:* The currently accepted medicinal anti-viral treatment is the combination of interferon (subcutaneous) and ribavirin with a 50-90 % chance of recovery, depending on the genotype of the virus.
- *Vaccination:* There is no vaccination available.

### **Hepatitis D**

The hepatitis D virus can only reproduce by using the viral envelope of the hepatitis B virus. As a result, hepatitis D only occurs in conjunction with a hepatitis B infection.

Transmission occurs through the same routes as with hepatitis A, especially through the fecal-oral route.

### **Hepatitis E**

Hepatitis E is rare in Switzerland and the other industrialized countries. People who have travelled to affected areas in Asia or Africa are especially at risk.

The hepatitis E virus behaves in a way that is similar to that of the hepatitis A virus and can cause similar illnesses. It is transmitted through the fecal-oral route and can lead to an acute but never to a chronic inflammation.

Table: Overview of the 5 forms of viral hepatitis

|                               | Hepatitis A   | Hepatitis B   | Hepatitis C   | Hepatitis D   | Hepatitis E   |
|-------------------------------|---|---|---|---|---|
| <b>Route of transmission</b>  | <b>oral</b><br>Fecal contamination of water, food or people | <b>percutaneous/per mucosal</b><br>Contaminated blood, unprotected sexual intercourse, from the mother to her newborn | <b>percutaneous/per mucosal</b><br>Contaminated blood                                   | <b>percutaneous/per mucosal</b><br>Like hep B and only found in conjunction with hep B (coinfection or superinfection)* | <b>oral</b><br>Like hep A                               |
| <b>Incubation time</b>        | 15-50 days  | 1-6 months  | 50 days-6 months  | 1-6 months  | 15-50 days  |
| <b>Progression</b>            | Symptoms in 50-70 % of those affected (nausea, etc.)        | Very different, depending on age  | Usually without symptoms, long-term effects are cirrhosis of the liver and liver cancer | Like hep B  | Like hep A; progression can be severe in pregnant women |
| <b>Acute hepatitis</b>        | Yes   | In 50-70 % of all infections in the adult age group   | Rare (in 5-10 % of those affected)  | Yes   | Yes   |
| <b>Chronic hepatitis</b>      | Never   | In 5 % of adults and 90 % of children during birth  | In 70-80 % of those affected  | Yes   | Never   |
| <b>Reinfection</b>            | No  | No  | Yes   | No  | No  |
| <b>Preventive vaccination</b> | Yes   | Adults 3/adolescents 2 injections; also protects against hep D  | No  | Yes. Vaccination against hep B also protects against hep D  | Yes   |
| <b>Treatment</b>              | No  | Anti-viral medications and interferon; varying success rates < 50 %   | Interferon and ribavirin; 50-90 % successful  | Interferon and anti-viral medications; low success rates  | No  |

\* When an infection with both viruses occurs at the same time or when a person with hepatitis B becomes infected with hepatitis D as well.

### Coinfections

A coinfection is a case in which several pathogens are simultaneously active. In the case of a coinfection with HIV/HBV and/or HIV/HCV and/or HIV/HBV/HDV the person has become infected with HIV as well as HBV and/or HCV and/or HDV. These combinations are quite common because HIV and some of the hepatitis viruses are transmitted through the same routes. Coinfections can also be described as those infections in which there are at least two hepatitis pathogens involved, e.g. HBV/HCV. The most common coinfection among drug users is HIV/HCV.

### 1.2 Structure and function of the liver

The liver, which is the largest internal organ of the human body, is located in the right upper abdomen directly below the diaphragm; it consists of a right and a left hepatic lobe and weighs 1,500-2,000 grams. Due to the fact that the liver itself is not sensitive to pain, liver diseases often go completely unnoticed. Only the exterior of the organ is

surrounded by a membrane that is sensitive to pain, such that any increase in size (due to an inflammation, for example) is expressed as tensional pain.

The liver is an organ that is very well supplied with blood. Although it only makes up about 4 % of total body weight, about 28 % of the blood in the body flows through it and it uses about 20 % of the body's total oxygen. The blood flows in from two main sources: blood vessels, transporting nutrient-rich blood from the intestines, and arteries of the greater blood circulation system from the heart. After flowing through the liver, the blood from both of these systems flows back into the greater blood circulation system to be distributed to the rest of the body through the heart.

As the most important metabolic organ of the human body, the liver is involved in a vast number of very different metabolic processes. It converts nutrients, such as fats, proteins, and sugars into building blocks for the body; it stores important substances produced by the body, such as sugars, vitamins, trace elements, and minerals, and supplies them to other organs. In addition to blood coagulation factors and enzymes, it also produces several hormones; in addition, it is also involved in the activation and decomposition of hormones. In order to absorb the fats from nutrients the liver produces approx. 600 ml of bile daily, which is stored in the gall bladder and released into the intestines. As a detoxification organ the liver breaks down toxins (alcohol!) and medications and eliminates them along with the bile.

Moreover, a healthy liver also has an enormous *ability to repair itself*, i.e. it can rapidly regenerate damaged or destroyed hepatic tissue.

### 1.3 What does hepatitis mean?

"Hepatitis" comes from hepar, the Greek word for the "liver" while the suffix "itis" always stands for "inflammation" in medical terminology. Thus, "hepatitis" (plural: hepatitises) is generally used to describe all forms of liver inflammations, but does not reveal anything about their cause or type.

Hepatitis is also often referred to as jaundice. This is misleading because the yellowing of the skin is merely one of many symptoms of the disease, which does not occur with every form of hepatitis and can also be observed in the case of other diseases.

#### **The various terms for the disease**

- *Acute infection*: Infestation of the body with microorganisms with or without signs of disease.
- *Acute illness (acute hepatitis)*: Infestation of the body with microorganisms with signs or symptoms of disease.
- *Chronic infection*: Condition following the acute infection or illness, when the microorganism continuously remains in the body (for longer than 6 months) with or without signs of disease.
- *Chronic illness*: Condition following the acute infection or illness, when the microorganism continuously remains in the body (for longer than 6 months) with symptoms or signs of disease.

## 1.4 Causes of hepatitis

The most common cause of hepatitis in the Western countries is *excessive alcohol consumption*. Alcohol causes direct harm to the liver, while the liver is the main organ responsible for breaking down alcohol in the human body. The threshold values for liver damage with regular alcohol consumption are 40-60 g and 20 g of pure alcohol daily in men and women, respectively. A standard glass holds 10 g of pure alcohol, which corresponds to 3 dl of beer, 1 dl of wine or 2 cl of spirits.

The second most common cause of hepatitis is infection with hepatitis viruses. Inflammation of the liver due to fatty changes is increasingly gaining significance in the industrialized countries. The main risk factors are obesity and elevated blood fat values due to poor diet.

Hepatitis cases are less commonly associated with infections due to other microorganisms, which can also lead to hepatitis, especially in people with compromised immune systems. Examples of these include cytomegalovirus (CMV), Epstein-Barr virus (EBV, which is the pathogen that causes infectious mononucleosis, i.e. Pfeiffer's disease), the varicella zoster virus (VZV, which causes chicken pox and shingles), and the herpes simplex virus (HSV). In such cases the inflammation of the liver is usually accompanied by the inflammation of other organs. Such combinations can be life-threatening in persons with compromised immune systems (e.g. persons infected with HIV). Pathogens, such as the yellow fever virus or the ebola virus, are hardly an issue for us; however, they can be of importance in connection with travel to Africa (Democratic Republic of Congo, Congo-Brazzaville, Sudan, Gabon, Ivory Coast or Uganda). Inflammations caused by bacteria can also lead to hepatitis; examples include: brucellosis (transmissible through milk), leptospirosis (transmissible through the urine of rats), and typhoid fever. Even protozoa can ultimately cause hepatitis. Usually other organs are also affected in such cases.

In rare cases hepatitis can also occur as a medication-related side effect, such as iron or copper deficiencies, or autoimmune phenomena, in which the immune system attacks the body's own cells.

This manual is chiefly concerned with hepatitides, which are caused by hepatitis viruses.

## 1.5 Progression forms of hepatitis

In the case of viral inflammations of the liver, a basic distinction is made between *acute infections* and *chronic infections*.

An *acute infection* can often go unnoticed (asymptomatic) or can be associated with exhaustion, nausea, vomiting, weight loss, and pain in the right upper abdomen. In rare cases fever may also occur. After about a week approximately one third of patients will experience jaundice with a yellowing of the ocular mucosa (sclericterus) and the skin (icterus). These symptoms usually clear up in two to six weeks. In rare cases acute liver failure may occur with a fatal outcome (fulminant progression).

The yellowing of the skin occurs as the result of a deficiency of bilirubin excretion. Bilirubin is a normal byproduct of the blood pigment (hemoglobin) and is normally excreted with the bile via the liver into the stool. If there is a disruption in the excretion of bilirubin

bin, then a portion of it is stored in the ocular mucosa and in the skin, while another portion is excreted via the kidneys. As a result, the urine will turn brown, while the stool will turn pale because it lacks bilirubin, which is otherwise responsible for giving the stool its brown color. Because there is a lack of biliary acid the absorption of fats through the intestinal cells is also disrupted, which may result in diarrhoea.

During this phase the patients will often feel considerably better than they did at the outset of the illness, even though they may still appear to be very ill. The risk of infection (infectivity) also goes down at this point; it is directly related to the number of viruses in the blood and/or stool.

A *chronic infection* (> 6 months) can last for years and may lead to *cirrhosis of the liver*. As liver function becomes increasingly impaired, the liver forms scar tissue to replace dead liver tissue. *Liver cancer* (hepatocellular carcinoma) may also develop.

However, only a portion of acute inflammations of the liver become chronic infections. This depends especially on the type of virus; e.g. hepatitis B results in a chronic infection in 5-10 % of adults; in the case of hepatitis C the figure is approx. 70-80 %.

Infections with the hepatitis B, C, and D viruses can become chronic with possible long-term effects. Under such circumstances it is very important to prevent or minimize any additional harmful influences as much as possible. Medications that are harmful to the liver (e.g. paracetamol = Panadol) and especially alcohol consumption should be kept to moderate and controlled levels. A patient's disposition, blood test results, and tissue pattern will not always match. Thus, for example, in the case of chronic hepatitis C a large number of viruses or large viral load (→ Chapter 1.2.4) may be measured from time to time, which is the expression of intensive virus replication, without any evidence of a pronounced inflammation of the liver in the analysis of the tissue. It is also possible that disposition and Laboratory test results are satisfactory even as the cirrhosis of the liver progresses.

*Advanced cirrhosis of the liver* means a severe disruption in liver function. It can lead to clinical pictures with varying symptoms. In addition to persistent fatigue, an increasing drop in performance capabilities, feelings of pressure and fullness in the stomach, as well as itchy skin in some cases, the following signs may occur:

- Decrease in musculature
- Small, spider-web-shaped blood vessels (spider angiomas) under the surface of the skin, especially around the cleavage.
- Redness on the surface of the hands and soles of the feet (palmar or plantar erythema)
- Yellowing of the skin
- Feminization in men. Men also form small amounts of female sex hormones in the adrenal cortex. These are rapidly broken down in a healthy liver. But this degradation process is impaired in a cirrhotic liver (surrounded by fibrous scar tissue), such that potent concentrations of female sex hormones gradually build up. This results in growth of the breast glands (gynecomastia), degeneration of the testicles (testicular atrophy) and changes in hair patterns (abdominal alopecia). In some cases erectile dysfunction (impotentia coeundi) may occur, also followed sometimes by infertility (impotentia generandi).
- Menstrual disorders in women, including a complete absence of menstruation (amenorrhoea).

- Peritoneal fluid excess (ascites) as the result of multiple pathological processes. Because the flow of blood from the hepatic portal vein through the liver is severely impaired, due to inflammatory and fibrous scar tissue changes within that organ, a high level of pressure is built up there (portal hypertension). This causes clear blood plasma (transudates) to be forced out of the portal vein into the open abdominal cavity. This process is facilitated by the fact that certain levels of blood proteins (albumins) are too low. A healthy liver produces sufficient amounts of albumins, which pull water into the blood vessels. However, a vicious cycle can occur, in which control processes due to hormones play a role, leading to a replacement of the forced out fluid within the circulatory system and maintenance of the portal hypertension. It is possible to administer medications that counter the development of portal hypertension (Propranolol). Certain medications are able to lower portal hypertension slightly (beta blockers and nitrates).
- Circulatory anastomoses: A very small blood vessel (esophagogastric junction) leads from the hepatic portal vein under the mucosa of the food pipe (esophagus) to the upper vena cava. This junction becomes severely expanded under portal vein pressure, resulting in esophageal varices. These varices can burst and lead to life-threatening hemorrhages.
- Blood coagulation disorders: The liver is no longer able to produce enough coagulation factors. In addition, portal hypertension leads to a swelling of the spleen, where the blood platelets are broken down rapidly. This results in a cumulative shortage of blood platelets. Both factors – shortage of coagulation factors and a drop in the number of platelets – increase the risk of hemorrhage.
- Hepatic encephalopathy (disease of the brain): Impairment of cognitive function can occur in some patients with portal hypertension. In some cases hepatic encephalopathy develops due to considerable impairment of liver function. Substances absorbed by the intestinal cells are no longer able to be modified or purified by the diseased liver or they make their way directly from the hepatic portal vein via the circulatory anastomoses into the circulatory system instead of being processed within the liver. Of special significance here is ammonia, which is formed during the break down of proteins by bacteria within the intestine and is converted into urea within the healthy liver. Ammonia increases the permeability of the cerebral vessels, such that blood plasma is leaked into the brain. This is the main cause of sudden death with liver failure. A chronic progression leads to a gradual dying off of the nerve cells (cerebral atrophy) with increasingly pronounced disorders. Memory and attention deficit disorders are followed by sleep disorders as well as restlessness and disorientation. The impairment of fine motor coordination, which becomes noticeable through changes in handwriting among other things, is followed by articulation problems, walking instability, involuntary rhythmic eye movements, and failure of the reflexes. Treatment is aimed especially at reducing the accumulation of ammonia. This is achieved by reducing the supply of proteins, regularly emptying the bowels (e.g. with lactulose) and reducing the number of bacteria in the intestines through treatment with antibiotics. Improvement does occur in the case of chronic forms, but the long-term prognosis tends to be unfavourable. Hemorrhaging in the gastrointestinal region, especially from the varices of the esophagus, can have a rapid deteriorative effect on hepatic encephalopathy.



Please note: Only a portion of infections with hepatitis viruses become chronic, and not all of these symptoms and accompanying effects will necessarily occur during chronic progression.

## THE FIVE HEPATITIS VIRUSES

### 1.6 Hepatitis viruses

Viruses can only infest very specific host organisms, which have certain features on the surface of their cells that enable the virus to dock. Hepatitis viruses need the human liver as a host. During infection the DNA of the virus is infiltrated into the cells. It influences the metabolism of the liver cell such that new viruses are produced.

The details on how damage occurs due to an infection with hepatitis viruses have not been determined for all of the known pathogens to date. Hepatitis A, B, C, D, and E differ in fundamental aspects, such as genetic structure, routes of transmission, riskiness or treatability.

### 1.7 Hepatitis A

#### **Route of transmission of the virus**

The hepatitis A virus (HAV) is transmitted via the fecal-oral route. The viruses are present in the feces of the infected person and the infection via the oral route occurs, for example, through oral-anal sexual practices, contaminated sex toys and joints, as well as through food, beverages, contaminated objects or body parts. During the incubation period, i.e. the timespan between the infection with the virus and the onset of the disease (with hepatitis A an average of 25-30 days) the virus is also detectable for a short time in the blood, which is why in very rare cases it is possible to transmit the disease via the blood route. An infected person is contagious from the second half of the incubation period (in other words, before the onset of the disease) up until one week following the onset of the disease.

Nowadays infections of this type occur most commonly while travelling in countries with low hygiene standards. Thus, hepatitis A is also often referred to as "traveller's hepatitis".

#### **Progression of the infection**

The incubation period is 15-50 days (average 25-30 days). The infection often progresses in small children with no symptoms, with acute hepatitis developing in only about 5 % of cases. By comparison, approx. 50-70 % of infected adults will develop symptoms of the disease (nausea, etc.). Fulminant hepatitis (rapid progression up to and including liver failure) is rare with pure hepatitis A infections (0.1 %), but is more common in combination with another form of hepatitis.

The infection never becomes chronic and always leads to life-long immunity.

#### **Diagnosis**

The detection of antibodies against the hepatitis A virus makes it possible to distinguish between a new infection (detection of immunoglobulin M; IgM) and immunity (detection of immunoglobulin G; IgG). The IgM antibodies can be detected 5-10 days following infection (in other words, prior to the development of symptoms) and then for about another 4-6 months.

**Incidence**

According to the reports received by the Swiss Federal Office of Public Health (FOPH) 250-350 cases of acute hepatitis A occurred annually in the years prior to 2000. Since 2001, the number of cases has dropped to less than 200 per year.

Due to the fact that only some of the infected persons will become acutely ill, the number of new infections each year is 2-4 times higher than the number of cases of acute hepatitis A. Injecting drug users used to be commonly affected; the numbers among this population group have gone down in recent years. Nowadays it is chiefly travellers to high-risk regions (Asia, Africa, Central and South America) who become infected.

**Treatment**

There is no accepted medicinal anti-viral treatment.

**Vaccination**

Whoever has been vaccinated against hepatitis A (2 doses; for the combined A/B vaccination: 3 doses) is protected for at least several years, but most probably for decades. The protection provided by the vaccination takes effect approx. 10-14 days after the first dosage of the vaccination (active immunization).

In addition to active immunization there is also passive immunization. This involves injecting a person with serum containing protective antibodies (immunoglobulins). But the duration of effect is only a few months. The administration of immunoglobulins within 7 days following contact with an infected person can prevent the onset of the disease in 85 % of cases. Following a possible at-risk situation, vaccination within the first 7 days is currently recommended with preference given to passive immunization. The hepatitis A vaccination introduced in 1992 and the combination hepatitis A and B vaccination introduced in 1997 have been shown to be highly effective and safe. In the case of drug users, anyone who is HAV Ab-negative (hepatitis A virus antibodies-negative) should be vaccinated. This is also applicable to any personnel coming into close contact with drug users.

**Prevention through hygiene**

The risk is especially high while travelling in at-risk countries. The following rules should be observed while there in order to avoid contact with infected feces and contaminated water:

Drink bottled beverages only; do not consume any ice cubes or ice cream; eat only fruits that you have peeled yourself; exercise caution when eating salads and raw seafood. Wash your hands with soap more often than you would at home, especially after each time you use the toilet. The virus can survive for a very long time. The virus can be killed by boiling potentially contaminated objects (20 min. at 85-90° or steaming them for 90 seconds) and foodstuffs (4 min. at 85-90°).

**1.8 Hepatitis B****Route of transmission of the virus**

The hepatitis B virus (HBV) is transmitted through contaminated blood and genital secretions (sperm and vaginal mucous). This occurs mainly during unprotected oral-genital or anal sexual intercourse, through the joint use of the same injection materials, and through the joint use of the same shaving utensils, tooth brushes, and tattooing equipment. Transmission is also possible from an infected mother to her newborn during childbirth. Infections through blood transfusions occur only in very rare cases in Switzerland because a policy of testing the blood for hepatitis B viruses (HBs antigens) has been in place for decades now.

Contaminated blood or secretions reach the blood circulation system with the prick of

a needle or through a wound or through the mucosa (unprotected sexual contact). An infected person is already contagious several weeks before the onset of the disease and remains so throughout its entire duration. The more viruses there are in the blood, the more contagious the carrier is.

### **Progression of the infection**

The incubation period is 1-6 months (60-90 days on average). Depending on the age of the person, the infection can lead to different symptoms (acute hepatitis B) and differing chronic progressions with corresponding outcomes.

In the case of newborns (transmission through the mother) and small children an infection will rarely if ever lead to an acute illness, but it will become chronic in 70-90 % of cases.

Infections among adolescents and adults lead to acute hepatitis in 20-50 % of cases and become chronic in 5-10 % of cases, regardless of whether or not an acute illness occurs. Following an infection duration of 5-50 years, a chronic hepatitis illness associated with cirrhosis of the liver and hepatocellular carcinoma may occur in 10-40 % of cases.

### **Diagnosis**

There are seven Laboratory tests for the detection of antibodies, viral proteins, primarily that of the HBsAg envelope, as well as viral DNA. These make it possible to distinguish between new infections, chronic infections, and immunity. The Laboratory tests show whether immunity has come about due to a vaccination or based on having successfully recovered from the disease. The HBsAg test result will be positive at 2 weeks following infection at the earliest, but normally after 5-9 weeks (in other words, prior to the occurrence of symptoms); in rare cases the result will not be positive until 6-9 months following an infection.

### **Incidence**

Between 1988-1995 the FOPH received reports of 350-500 cases of acute hepatitis B each year; between 1996-2000 there were only 200-250 cases reported each year. Since 2000 there have been fewer than 200 cases reported annually, whereby about 70 % involved men aged 25 to 29. Only a portion of infected persons became acutely ill and were thus reported to the FOPH. It is estimated that the number of unreported new infections is about 4-10 times higher (500-1000 persons per year).

While the most common reason for an infection used to be intravenous drug use, nowadays it is unprotected sexual contact (hetero- and homosexual). Even a single sexual encounter can result in an infection. In Switzerland it is estimated that approx. 20,000 people (1 person for every 200-400 inhabitants) suffer from chronic hepatitis B. A large number of them show no symptoms, while a smaller number suffer from cirrhosis of the liver or liver cancer.

### **Treatment**

Patients with chronic hepatitis B are usually treated with a medicinal regimen. There are currently two types of anti-viral substances available for treatment. On the one hand there is *pegylated interferon* (administered as a subcutaneous injection, once a week for a period of one year) and on the other hand there are *oral anti-viral* medications. Experienced specialists (in infectology, gastroenterology, hepatology or internal medicine) should establish the indication. Treatment requires continuous meticulous monitoring. At about 20-30 %, the likelihood of completely recovering from hepatitis B is considerably lower than that of hepatitis C. In cases where a complete cure is unsuccessful, the aim is to lower the viral load in the blood. This will stop the inflammatory processes underway in the liver and the associated damage to the liver. This treatment

goal is achieved in practically 100 % of patients. It should be mentioned here that there are also patients who have been shown to have hepatitis B in the blood, but who demonstrate no signs of inflammation of the liver. These patients do not have chronic hepatitis B, but instead are considered to be inactive hepatitis B surface antigen-positive (HBsAg+) carriers, who usually require no medicinal treatment.

### **Vaccination**

The hepatitis B vaccination is highly effective and safe. Children and adults receive 3 injections, while adolescents receive 2 injections at the adult dosage. The same is true for the combined A + B vaccination in children. There are approved combination vaccinations, e.g. against hepatitis A and B, but also combinations against hepatitis B and other pathogens.

Since 1982 the hepatitis B vaccination has been recommended for all at-risk groups and general vaccination campaigns have been conducted for all 11- to 15-year-olds in Switzerland since 1998.

*Drug users should always be encouraged and motivated to get vaccinated. An initial preventive dose of vaccination should be administered upon initial contact even without having any lab results available because this will greatly reduce the costs associated with tests and treatment. In the case of a positive anti-HBc result the person has already become infected and a vaccination is no longer necessary.*

Any personnel, who come into contact with drug users while on the job, should also be vaccinated against hepatitis B. In the case of high-risk situations, the administration of the vaccination and the immunoglobulins (active and passive immunization) within 24-48 hours following blood-to-blood contact with contaminated blood can protect against the illness (→Chapter II.1.7).

### **Testing within the blood donor service**

All donated blood and blood products have been tested for HBsAg since 1980 in Switzerland. Since then transfusion-related infections have been extremely rare. Based on the so-called diagnostic window the residual risk per donation is about 1:300,000. In the case of a person infected with hepatitis B the HBs antigen is not able to be detected until a few days after the infection took place.

### **Testing of pregnant women**

Since 1985 with restrictions and since 1996 with no restrictions the recommendation in effect within Switzerland has been to test all pregnant women for the HBs antigen with immediate vaccination (and passive immunization) of the newborn in cases where the mother is infected.

### **Prevention through hygiene**

The rules of safer sex (which are also applicable for the prevention of HIV infections) are to be strictly followed. It is also necessary to avoid sharing and exchanging potentially infected syringes and injection materials. Cuts, punctures, and scrapes with sharp instruments should also be avoided. This is especially applicable during drug use, but also in the case of receiving a tattoo, a piercing, and especially in the case of health treatments under insufficient hygienic conditions involving the injection of substances.

The virus can survive in the environment at room temperature for at least a week. Contaminated objects must therefore be carefully washed and potentially contaminated objects should not be shared (toothbrushes, razors, nail clippers, manicuring tools, etc.).

## 1.9 Hepatitis C

### **Route of transmission of the virus**

The hepatitis C virus (HCV) is most commonly transmitted through contaminated blood, which enters the body through a wound in the skin or mucosa. In most cases the infection will occur with the joint use of injection materials for intravenous drug use, in rarer cases while receiving a tattoo, and in exceptional cases due to the joint use of razors and toothbrushes. Hepatitis C, unlike hepatitis B, is not a sexually transmitted disease. Transmission from the mother to her newborn can occur during childbirth with a likelihood of approx. 5 %. Unlike in the developing countries, the risk of becoming infected through a blood transfusion in Switzerland is next to nil. The majority of infected persons and untreated cases are contagious within one or more weeks following the onset of the disease.

### **Testing within the blood donor service**

Testing of all donated blood and blood products for anti-HCV was introduced in Switzerland in 1990. The highly sensitive PCR method (→ below: Diagnosis) has been available since 1999. The current residual risk of infection through a transfusion is approx. 1-1.4 million per transfusion. This corresponds to approx. one case within 5-10 years for blood donated immediately following infection if the PCR results are still negative (diagnostic window).

### **Progression of the infection**

The incubation period is between 20 days and 6 months. The infection with the hepatitis C virus usually progresses without any symptoms and leads to acute hepatitis in only about 10-20 % of infected persons. However, it leads to a chronic infection in about 70-80 % of infected persons and chronic hepatitis will occur in 5-50 years in 5-50 % of infected persons. A portion of infected persons suffer from cirrhosis of the liver or hepatocellular carcinoma.

### **Diagnosis**

The first step is to test the blood for the presence of antibodies against the hepatitis C virus (screening test). A positive result must be confirmed through a more specific method (confirmation test). The diagnosis is not certain unless this test also turns out positive. The test for antibodies will show positive within 15 weeks (on average 7-8 weeks) following the infection or within 6 weeks following the onset of symptoms. Unlike the test for antibodies, the PCR method (polymerase chain reaction) can already detect the DNA of the virus 1-3 weeks following the infection. Thus, the PCR method must be conducted in cases of suspected acute or chronic infections even when the test for antibodies is negative.

### **Incidence**

According to reports received by the FOPH from Laboratories and physicians the number of cases of persons with hepatitis C stagnated at around 50-65 cases per year from 1992 to 2000. Starting in 2000 an increase of approx. 80-90 cases per year was observed. In 2002 alone 133 cases were discovered, many of them during a hepatitis C awareness campaign (more testing among drug users). In 2003 the number of cases dropped back down to 90. This tendency is supported by the numbers for the year 2006 with 65 cases.

As with hepatitis A and B, only a portion of the persons infected with hepatitis C will develop symptoms, such that the number of new infections can be assumed to be 5 to 10 times higher. It is estimated that the number of new infections is 300-1000 per year. Since the 80s the main group affected by new infections has been intravenous drug users (proportion: 60-80 %). Sixty per cent of these are men, most of them between the

ages of 25 and 29. Nevertheless, there are still a lot of people with chronic infections, who became infected through blood transfusions prior to the introduction of the corresponding tests for antibodies.

### **Chronic infection**

HCV infections can progress in many cases for years and even decades without any clinical symptoms. This enables us to estimate that only about half of the estimated 50,000–70,000 infected persons are aware of their infection.

### **Treatment**

The currently accepted medicinal anti-viral treatment is *the combination of pegylated interferon (injection) and ribavirin*. If the treatment is started as early as possible, then the chances of recovery are 50-90 %; however, the chances of recovery are more certain prior to the onset of cirrhosis. Treatment success depends mostly on the type of virus (genotype): Patients with genotype 1 and 4 are cured by the 48 week treatment in approx. 50 % of cases. Patients with genotype 2 or 3 only need 24 weeks of treatment and can expect the likelihood of their recovery to be approx. 85 %. The most significant side effects of the treatment are fatigue, fever, muscle and joint ache, blood count changes and depressive mood swings. Therefore, the treatment requires continuous meticulous monitoring. As with hepatitis B, patients with hepatitis C in the advanced stages of liver failure should also be evaluated with respect to a possible liver transplant procedure. This usually takes place at a medical centre associated with a university.

### **Prevention through hygiene**

Infections through potentially contaminated utensils (syringes, needles, spoons, filters, water), which have been shared while using drugs, must be avoided; the same is true for infections due to cuts, punctures, and scrapes with sharp instruments. This is especially applicable during drug use, but also in the case of receiving a tattoo, a piercing, and especially in the case of health treatments under insufficient hygienic conditions involving the injection of substances.

The most important measures include 24 hour access to free sterile injection materials for drug users, as well as compliance with all safer use rules while using drugs.

The hepatitis C virus is estimated to survive in the environment for up to several days. Therefore, when in doubt, all objects should be considered contaminated and handled accordingly (→ Chapter II.2, Rules of Use).

## **1.10 Hepatitis D**

The hepatitis D virus can only reproduce by using the viral envelope of the hepatitis B virus. In other words, any time there is a hepatitis D infection, there is a pre-existing hepatitis B infection as well.

The incubation period is 1-6 months. The vaccination against hepatitis B also protects against hepatitis D. The disease is rare in Switzerland, but it does play a role in association with coinfections.

### **1.11 Hepatitis E**

The hepatitis E virus (HEV) is transmitted via the fecal-oral route. The incubation period is 2 to 8 weeks. The virus behaves roughly the same way as the hepatitis A virus and can lead to similar clinical symptoms and an acute illness; but the infection never becomes chronic. The disease can have grave consequences for pregnant women.

Hepatitis E epidemics have occurred in recent years primarily in countries with low standards of hygiene. Hardly any cases of illness have occurred to date in Switzerland.

## **COINFECTIONS**

### **1.12 What are coinfections?**

A coinfection is a case in which several pathogens are simultaneously active. In the case of an HIV/HBV and/or HIV/HCV and/or HIV/HDV coinfection, the person has become infected with HIV as well as HBV and/or HCV and/or HDV, respectively. HIV/HCV coinfections are quite common among drug users, while the other combinations are rare. Basically, any diseases accompanied by a weakening of the immune system can adversely influence the progression of an infectious disease.

### **1.13 Coinfections with HIV**

HIV is the virus that can cause AIDS. The CD4 value is the number of certain helper cells in the blood. During the progression of an untreated HIV infection the number of CD4 helper cells in the blood is constantly reduced. The fewer CD4 cells there are in the blood, the more severe the damage is to the immune system.

An HIV infection is incurable. However, the infection can be kept under control for a very long time with antiretroviral treatments and it is possible to inhibit the progression of the immunodeficiency caused by the HIV. This has resulted in a pronounced improvement in the quality of life and life expectancy among those affected. The HI virus itself and the medications used for HIV treatment place an enormous burden on the liver over time. One consequence of this has been that liver failure is currently one of the most common causes of death among HIV patients. Such cases often involve viral hepatitis as well.

A question of considerable importance for persons with HIV infections concerns which vaccinations are necessary. Fundamentally, they should build up and maintain the protection provided by vaccinations early on. In cases where the results of blood serum tests show no HAV and HBV infection, vaccinations against hepatitis A and/or hepatitis B are indicated. If the immune system is compromised due to the HIV infection, then the success of a vaccination will be less certain than it otherwise would have been; in other words, under these conditions the immune system is often no longer able to produce enough protective antibodies. For this reason any patient with an existing HIV illness should be vaccinated as soon as possible before the immune system is further compromised. The inactive vaccinations against hepatitis A and B are safe even if the

immune system is compromised because both the active vaccination against hepatitis A as well as the vaccination against hepatitis B are created using killed microorganisms, consisting of inactivated HAV or genetically engineered components of HBV (HBs antigens).

The side effects caused by the vaccinations are no stronger than normal and the progression of the HIV infection is not adversely influenced, although a short-term increase in the HI viral load will be observed in the blood plasma.

The HIV/HCV coinfection is important for drug users because both infections can occur due to contaminated blood. Approx. 90 % of all HIV-positive drug users are also carriers of the hepatitis C virus. The two infectious diseases influence each other during progression and have a negative reciprocal effect on the chances of successful treatment. From the prognostic standpoint any coinfection with chronic hepatitis is unfavourable. If the chronic hepatitis is unable to be treated, then it can have a very negative effect on the quality of life.

Chronic hepatitis C in people with an HIV infection can be treated with pegylated interferon and ribavirin. Some of the same anti-viral medications are effective in the treatment of HIV/HBV coinfections.

#### **1.14 HIV and hepatitis A**

Hepatitis A does not progress as a chronic infection and is therefore only significant as a coinfection with HIV in people with pre-existing liver damage. Here, there is a risk of a progression to fulminant hepatitis. In addition, unlike hepatitis B and C, the route of infection for hepatitis A (mostly via the fecal-oral route) is not the same as with HIV. Hepatitis A is not treatable; the only measure for HIV patients is to get vaccinated for hepatitis A.

#### **1.15 HIV and hepatitis B**

Like chronic hepatitis B, this coinfection is much less commonly observed among drug users than chronic hepatitis C. In the case of patients with an HIV infection and advanced immunocompromised status hepatitis B commonly becomes chronic (in approx. 25 % of those affected).

A coinfection with HIV worsens the progression of a hepatitis B infection by speeding up the progression of the liver disease and raising the risk of liver failure to a level higher than the one associated with an HBV infection alone. The long-term intake of HIV medications (triple therapy) is a heavier burden on the liver of HBV/HIV coinfecting persons, such that a suppression of the hepatitis B virus using medications is especially indicated for such persons.

Individual substances used in a combination treatment against HIV are also effective against the hepatitis B virus. An HIV/HBV coinfection is treated with anti-viral medications (3TC, FTC, tenofovir), which are effective against both viruses. Thus, lamivudine (3TC) is used for both treatments and especially for coinfections as well. But both viruses are also able to develop resistances to these substances. Tenofovir is also effective



against HBV and HIV, but is currently approved for HIV treatment only. If there are no resistances to these two substances, then they are preferable for use in the treatment of HIV in HIV/HBV coinfecting persons.

The goal of HIV and HBV treatments is to suppress the viruses as much as possible. This results in treatments lasting many years. The main problem with such treatments is the development of resistances, especially in the case of hepatitis B therapy.

HIV-infected persons, who have never successfully recovered from an acute hepatitis B infection or are not suffering from chronic hepatitis B, are urgently recommended to get an active immunization against the hepatitis B virus.

### **1.16 HIV and hepatitis B/D**

The progression of hepatitis B determines the progression of hepatitis D. For this reason, HIV-infected persons, especially those with advanced immunocompromised status, are more likely to suffer from chronic progressions of hepatitis D. Hepatitis D seems to progress more severely when there is a simultaneous HIV infection present.

### **1.17 HIV and hepatitis C**

This is the most common coinfection among drug users and should be treated as early as possible.

Chronic hepatitis C in people with an HIV infection can be treated with pegylated interferon and ribavirin. The treatment of hepatitis C in persons with HIV is made difficult by the unfavourable reciprocal influence of both infections. In HIV-infected persons chronic hepatitis C progresses more rapidly and is more likely to result in liver failure than in persons not infected with HIV.

In the age of modern HIV treatments few people die of an HIV infection in the industrialized countries; among this small number of people one of the most common causes of death is liver failure as the result of an HCV infection. The more advanced the scarring of the liver is, the worse the prospects are that the hepatitis C will be treated successfully.

Therefore, every effort should be made to begin hepatitis C treatment as soon as possible.

The prospects for the successful treatment of hepatitis C in HIV-infected persons are between 40 and 80 %, depending on the hepatitis C genotype. This is slightly lower than the chances of recovery for persons not infected with HIV.

Persons with an advanced HIV infection have a higher HCV viral load than persons not infected with HIV. Therefore, a higher infectivity must be assumed with respect to the hepatitis C virus. This is also expressed, among other things, by the fact that HCV is more commonly transmitted from an HIV-infected mother to her newborn, than from a mother not infected with HIV.

In the case of HIV-infected drug users a single negative test for antibodies is not sufficient to rule out hepatitis C due to the fact that in approx. 10 % of cases there is a lack of antibodies against the virus. Thus, it becomes more pressing to perform an assay to quantify the hepatitis C virus RNA (PCR) (→Chapter I.2.4).

### **1.18 Hepatitis A and hepatitis C**

The risk of a coinfection can be countered with an active vaccination against the hepatitis A virus.

An HAV/HCV coinfection occurs when there is a hepatitis A infection on top of a pre-existing case of chronic hepatitis C. The inverse situation is not possible because hepatitis A does not progress chronically. Such a "super-infection" with hepatitis A and chronic hepatitis C can lead to an acute and dangerous progression of the hepatitis accompanied by liver failure. No specific treatment options exist. As a preventive measure, all patients with hepatitis C are urgently recommended to get vaccinated against hepatitis A and B.

### **1.19 Hepatitis B and hepatitis C**

This coinfection is rare. Sometimes it is not possible to find the component of the envelope of the hepatitis B virus (HBs antigen) in persons with chronic hepatitis C, even with existing chronic hepatitis B. It is suspected that the HCV inhibits HBV replication.

## 2. TESTS, COUNSELING & VACCINATION

### GET TESTED

#### 2.1 General information about hepatitis tests

The infection rates for hepatitis are high among drug users. The initial infection often goes unnoticed and there are no visible signs of the disease. Therefore, each drug user should be tested for hepatitis A, B and C, and in the case of negative results and ongoing risky behaviour, each drug user should be screened once annually (screening for antibodies). The tests can be used to detect the various categories of antibodies.

The test results provide information as to whether:

- there is an existing infection or the person has successfully recovered from an infection
- there is a cured infection or
- the person has been vaccinated (vaccination immunity)

There are basically two test methods in use:

- Detection of specific antibodies against the corresponding viruses
- Detection of viruses or their components (proteins or genetic material)

A hepatitis test should be conducted approx. 3 weeks at the earliest following exposure (at-risk situation). The results of tests conducted too early are unreliable.

In addition to these tests, liver function tests should also be performed on a regular basis. If the test results are above normal, then non-infectious causes need to be ruled out, such as damage due to alcohol or medications.

Viral hepatitis often progresses asymptotically, such that a person can be infected without ever feeling ill. If viral components are found in the blood itself, this means that the virus is active in the body. In such a case it is possible to infect other persons. If the tests for the detection of antibodies and viral components are combined, then it is possible to reach the following conclusions:

The infection has been cured or there is a chronic infection.

An immunity is assumed based on the presence of certain forms of antibodies in the case of hepatitis A and B for the following reasons: The person became infected in the past and the disease was cured or the person got vaccinated and is protected against new infections as a result. In the case of fully cured hepatitis C, however, the antibodies provide no protection against reinfection!

## 2.2 Who should get tested for hepatitis?

The following symptoms and situations require a complete medical examination, including hepatitis tests:

### **Hepatitis A**

In the case of:

- Yellowing of the skin, fatigue, nausea

The test for HCA antibodies is recommended for:

- Persons employed in the fields of wastewater handling and treatment
- Persons with high-risk sexual practices (especially oral-anal)
- Drug users who are hepatitis B carriers
- Patients with chronic liver diseases (especially hepatitis B) following serological testing.

### **Hepatitis B**

In the case of:

- Yellowing of the skin, fatigue, nausea
- High-risk sexual practices
- Non-specific complaints, skin problems, kidney- and joint-related complaints

The screening for hepatitis B antibodies is recommended for:

- Pregnant women
- Family members, including children, who live in the same household with an HBV-infected person
- Sexual partners of HBsAg-positive persons
- Employees of institutions, in which they have contact with drug users
- Persons from areas with a high prevalence of hepatitis B
- Intravenous drug users (including ex-users as well)
- Persons with seropositive HIV status

### **Hepatitis C**

In the case of:

- Yellowing of the skin
- Fatigue, nausea, joint-related complaints

The test for HCV antibodies is recommended for:

- Intravenous drug users, persons who snort or smoke drugs (including ex-users as well)
- Persons who received a blood transfusion prior to 1992
- Persons who received stored blood prior to 1987 (e.g. hemophiliacs)
- Persons with kidney insufficiency undergoing blood dialysis (artificial kidney)
- Sexual partners of persons infected with the hepatitis C virus
- Children of mothers infected with the hepatitis C virus
- Persons with seropositive HIV status
- Health care personnel following contact with blood (injury with contaminated sharps or other contaminated materials)

## 2.3 What do the test results show?

### Hepatitis A

- *Positive for IgM and IgG antibodies:*  
Acute or very recent infection (IgM are only detectable for 4-6 months following an infection).
- *Negative for IgM and positive for IgG antibodies:*  
Cured infection or presence of protection provided by vaccination.
- *Negative for IgM and IgG antibodies:*  
No contact with the virus to date and no protection provided by vaccination. Such persons should get vaccinated.

### Hepatitis B

- *Positive for HBs antigen (viral protein):*  
The virus is active in the body (acute or chronic infection). In such a case, a viral load determination (HBV DNA) and an HBe antigen test are performed to further clarify the diagnosis. If the results are positive for HBe antigen, then the patient has highly active chronic hepatitis B. It is worth noting here that there are also patients with hepatitis B viruses in their blood, but who show no signs of any inflammation of the liver. These patients do not have chronic hepatitis B, but instead are considered to be inactive hepatitis B surface antigen-positive (HBsAg+) carriers, who usually require no medicinal treatment.
- *Positive for HBc antibodies (screening test):*  
Current (or past) infection with the virus.
- *Positive for HBs antibodies:*  
Cured infection (even if positive for anti-HBc antibodies) or immune response to the corresponding vaccination (if negative for anti-HBc antibodies).
- *Negative for HBc and HBs antibodies:*  
No contact with the virus to date and no protection provided by vaccination; such persons should get vaccinated.

### Hepatitis C

- *Positive for anti-HCV antibodies:*  
Current (or past) infection with the virus (acute, chronic or cured).
- *Positive for HCV RNA (genetic material of the virus):*  
The virus is present in the body, i.e. there is an acute or chronic infection.

## 2.4 Laboratory analyses and microscopic examinations

### **Blood levels for the measurement of inflammation and function of the liver**

In addition to measuring the reaction of the body to the viruses (antibodies) and measuring for viral components themselves (antigens), liver function tests and other tests are performed.

On the one hand, this enables the activity of the inflammation to be assessed. The rise in liver enzymes (transaminases/transferases) indicate the degree of cellular destruction due to the inflammation. These tests primarily include ALT (alanine aminotransferase, formerly GPT: glutamate pyruvate transaminase) and AST (aspartate aminotransferase; formerly GOT: glutamate oxalacetate transaminase).

On the other hand, the function of the liver is able to be evaluated based on the following measurements:

- If the synthesizing capacity of the liver is reduced, then the blood plasma will contain reduced levels of ChE (cholinesterase) coagulation factors and in the case of severe impairment it will contain reduced levels of albumin (an important blood protein). Bilirubin will increase with impaired liver function because the liver is no longer able to break it down normally (→ Chapter 1.5)
- The functional capacity of the coagulation system is determined based on the prothrombin time or the INR value (determination of the effect of blood-thinning medications). Bile flow disorders are expressed by an increase in AP (alkaline phosphatase), among other things. A reduction in detoxification capacity in the case of well advanced cirrhosis of the liver is expressed as an increase in ammonia levels in the blood.

### **Viral load**

The measurement of the viral load in the blood plasma, i.e. the number of copies of viral DNA per milliliter of blood plasma, is performed using the polymerase chain reaction technique (PCR). Here DNA building blocks are copied. The sequence of their amino acids or their chemical reactions are characteristic of a certain pathogen.

The PCR diagnostic test is also of importance for monitoring treatment. If interferon is used (possibly in combination with another substance), the viral load is determined in order to monitor the efficacy of the treatment. The viral load can be negative due to a spontaneous recovery or within the framework of a favourable course of treatment.

### **Liver biopsy**

In cases of suspected chronic hepatitis a liver biopsy is sometimes performed. Here, a small piece of tissue is removed from the liver using a very thin needle. The analysis under the microscope enables the degree of severity of the inflammatory reaction to be determined, as well as the extent of the fibrous scar tissue surrounding the organ, among other things. In addition, it is also possible to detect any other adverse influences (e.g. due to alcohol).

Prior to the biopsy appointment the physician explains the procedure to the patient and an ultrasound scan is made of the liver. On the morning of the day of the biopsy appointment the patient does not eat anything. Using the ultrasound monitor for visualization, the physician determines the insertion path for the needle prior to performing the procedure. The skin is then disinfected and the insertion channel is anaesthetized with local anesthesia. During insertion the patient must not breathe so that the liver does not move. The biopsy is performed with a thin cannula, which is inserted into the liver to a depth of 4-5 cm. Using suction, a small sample of liver tissue is removed through the cannula and sent to the Laboratory for further analysis. The procedure usually does not hurt. In some cases the patient may experience a rapidly dissipating pain in the area of the insertion site or in the right shoulder.

The entire procedure lasts 5 to 10 minutes. Following the biopsy the patient is typically kept under observation for approx. 4 hours in order to ensure that any possible bleeding, a rare complication, is not overlooked.

After approx. 5-8 business days the test report from the lab becomes available; it provides information about the degree of severity of the liver damage and the cause of the damage.

### **Fibroscan®**

As an alternative to liver biopsy, the Fibroscan® technique is available for measuring the stiffness or elasticity of the liver. The device it uses looks like an ultrasound scanner.

This totally non-invasive examination procedure measures the fibrosis of the liver

through the placement of a probe between the costal arches on the right flank. The measuring principle of the Fibroscan® is based on a histological fact: The stiffer the liver, the more severe the fibrosis (abnormal increase in connective tissue). Therefore, the degree of severity of the fibrosis is able to be determined based on the stiffness of the liver. Here, a small vibration is generated on the surface of the skin which penetrates the liver.

The speed at which this audible vibration travels under the skin at a distance of 2 to 4 centimeters is tracked using ultrasound. The faster the vibration travels, the stiffer the liver and the more advanced the fibrosis. This measurement technique is non-invasive (i.e. it is not necessary to perform a surgical procedure or take a blood sample), involves no pain to the patient, and takes only about five minutes to complete. The Fibroscan® technique cannot be used in cases of fluid accumulation in the abdominal cavity (ascites) or morbid obesity, which make it impossible to measure elasticity. In practice the results of a high-quality liver biopsy do not always correlate with those of a Fibroscan. Specialists currently tend to recommend liver biopsies more than Fibroscan® procedures. Therefore, the latter should be performed on patients who refuse to have a liver biopsy and who are not contraindicated for a Fibroscan® (obesity with a BMI > 26, ascites, small and abnormally shaped liver).

## 2.5 Test results: comments and additional analyses

### **Hepatitis B**

In suspected cases of hepatitis B patients should always be tested for *HBs antigen (HBsAg)* and for *anti-HBs* and *anti-HBc antibodies*.

If the results are *HBsAg-positive*, then the patient has acute or chronic hepatitis B. It should be mentioned here that there are also patients who have been shown to have hepatitis B in the blood, but who demonstrate no signs of inflammation of the liver. These patients do not have chronic hepatitis B, but instead are considered to be inactive hepatitis B surface antigen-positive (HBsAg+) carriers.

If the results are *HBsAg-positive*, then the patient has acute or chronic hepatitis B. *The presence of anti-HBs antibodies* suggests an earlier case of hepatitis B that was cured. The anti-HBs antibodies are always present in cases of hepatitis B.

Following vaccination patients are *negative for anti-HBc antibodies* and *positive for anti-HBs antibodies*. The values make it possible to reach a conclusion about how the person has responded to the vaccination.

### **Hepatitis C**

If the HCV-Ab test turns out positive, then the HCV RNA (the genetic information of the HCV) must be qualitatively determined. The HCV occurs in four different genotypes (families of viruses). It is important to know the genotype and the viral count in order to provide skilled counseling and treatment. If the HCV RNA test turns out positive, then the genotype must be assayed and an HCV RNA quantitative assay must be performed. In accordance with our current state of knowledge, treatment success rates are 70-90 % for genotypes 2 and 3, and 50-70 % for genotype 1, and somewhat higher for the rare genotype 4.

### **Chronic hepatitis**

In cases of chronic hepatitis B or C, in which no treatment has been required (yet) or requested, annual liver function tests are recommended, as well as a liver biopsy every 5 years or, alternatively, an annual Fibroscan procedure.

## 2.6 Obligation to notify the authorities

Various contagious diseases are subject to the obligation to notify the authorities, in accordance with the Swiss Federal Law on the Control of Communicable Diseases. Notifications enable the outbreak of diseases to be detected early and provide for the ongoing review of the necessity and/or efficacy of preventive measures. Hepatitis A, B, and C are among the diseases subject to the obligation to notify the authorities. Test Laboratories are obligated to simultaneously report any positive tests to the Swiss Federal Office of Public Health (FOPH) and the competent Cantonal Surgeon General (Kantonsarzt); these authorities will then request more information with respect to possible routes of transmission from the physician(s) that ordered the test(s). Such information is considered to be a supplementary notification and is passed along from the Cantonal Surgeon General to the FOPH.

In the case of hepatitis A, B, and C these notifications also contain information on the names and addresses of the affected persons so that the Laboratories, physician(s), and hospitals can take any further necessary measures (such as a search for infected and exposed persons, etc.) This involves the following procedures:

1. In the case of hepatitis B and C the additional information is provided by the treating physician in order to determine whether the infection involved in the respective case is old or new. The information provided by the Laboratories do not enable such a determination.
2. In cases of suspected infections through blood transfusions a review is ordered to be performed in order to discover any contagious blood donor(s) and to destroy any related donated blood or blood products that may remain.
3. In the case of hepatitis B and C further tests are also ordered to be performed in suspected cases of transmission within a hospital or through hospital personnel. The same applies for hepatitis A in suspected cases of an infection due to contaminated water or foodstuffs.
4. Possible vaccination errors must be ruled out.
5. Possible post-exposure prophylactic measures can be ordered.

By providing the name of each patient it is also possible to avoid multiple listings of chronically ill people, who have sought treatment from different physicians. All of this information is protected by medical confidentiality and the Swiss Data Protection Act. The corresponding documents are destroyed once the cases have been cleared up.

## GET VACCINATED

### 2.7 Vaccination against hepatitis

There is both an active and a passive immunization against hepatitis A and B. There is no vaccination against hepatitis C to date. For more detailed information on the other aspects, see → Chapter II.3.1.



**Passive immunization**

Rarely used, *passive immunization* involves the administration of antibodies against the hepatitis A or the hepatitis B virus.

The advantage of passive immunization is the immediate protective effect. An immunization can even be effective following high-risk behaviours associated with a possible infection.

The disadvantage is the short duration of the protective effect, which lasts only a few months. The immune system of the immunized person has not learned how to produce its own antibodies to be delivered as needed. There is no vaccination against hepatitis C and no post-exposure prophylaxis.

**Active immunization**

*Active immunization* involves the injection of antigens. Here, inactivated pathogens or genetically engineered viral components are used to stimulate the immune system to produce antibodies against the virus. Active immunization can be used in most cases. The advantage lies in the fact that the immune system of the immunized person can continue to produce its own antibodies, whenever necessary.

The disadvantages include: The protection provided by the immunization does not take effect immediately because the body needs two to three weeks in order to produce antibodies.

However, in the case of hepatitis A, the incubation period (time from the infection to the onset of the disease) is longer than the time required by the body to build up the protection provided by the immunization, which is why it is still possible to administer an active immunization following high-risk situations in such cases.

In the case of hepatitis B the vaccination must be administered early enough prior to a high-risk situation (many people do not anticipate subjecting themselves to risk) and repeated at certain intervals in order to ensure long-term protection (twice for hepatitis A, three times for hepatitis B).

Combined hepatitis A and hepatitis B vaccinations do exist. They are usually administered at zero time, after one month, and after six months and have been shown to be highly effective ( $\geq 90\%$ ) and well tolerated. Although the vaccinations are recommended to be administered twice or three times, respectively, and at the intervals mentioned above, even a single vaccination reduces the risk of infection considerably.

In some cases individuals do not produce antibodies (in approx. 5-10 % of those receiving active immunizations) in response to the three-time application of the active hepatitis B immunization. These individuals are called non-responders. Nevertheless, almost 70 % of non-responders do begin producing antibodies when the immunization regimen is extended (by a maximum of 3 additional doses at intervals of 3-4 months).

In some cases the only way for these persons to acquire a certain amount of protection is through passive immunization. The vaccination is injected into the upper arm and, in the case of children, into the thigh. If active and passive immunizations are being administered simultaneously, then the left and right upper arms are used, or the right and left thighs, respectively. Anyone undergoing post-exposure prophylaxis (PEP), such as a person who has been stabbed with a potentially infected needle, will receive both the passive and the active immunizations against hepatitis B.

In addition to the immunizations there are also recommendations with respect to behaviour, which will considerably reduce the risk of transmission (→ Chapter II.2 Rules of Use).

In the interest of full disclosure it should be pointed out here that certain objections have been raised against vaccinations. Some of the arguments and responses include:

*"Non responders" live with a false sense of security by thinking that they are not infected.*

In the case of persons with high-risk behaviours it is possible to verify the development of antibodies following vaccination; should it be determined that antibodies are not being produced, then it is possible to establish whether or not the person is already infected (a chronic hepatitis B infection can be a reason for the lack of antibody production following vaccination).

*Vaccinations can mislead people into failing to protect themselves using other protective measures (protective measures against infection with the hepatitis viruses are also effective against HIV).*

In the case of the hepatitis B vaccination it is important to emphasize that this vaccination does not provide protection against any other viruses, especially HIV. The rules of safer use are always applicable! Compared with HIV, the hepatitis B virus is more widespread within the population and thus the risk of becoming infected is significantly greater. Therefore, it is worth it to get vaccinated, even when the normal preventive measures against HIV are being taken.

*There have been cases of multiple sclerosis following a hepatitis B vaccination.*

Cases of multiple sclerosis have in fact been identified at the same time as a hepatitis B vaccination. However, detailed studies were unable to prove a causal connection between the vaccination and the disease.

## **2.8 Vaccination against hepatitis A**

### **The vaccination is recommended for:**

- Drug users
- Any personnel coming into close contact with drug users or with persons from at-risk regions
- Travellers to endemic zones (→visit [www.safetravel.ch](http://www.safetravel.ch) for a list of corresponding countries)
- Children residing in Switzerland and originally from endemic areas, who are travelling to their home countries
- Men who have sex with men
- Persons with chronic hepatitis, especially hepatitis C
- HIV/HCV coinfecting persons

This vaccination has been covered by obligatory health insurance since 01 January 2008 for persons subject to higher risk; travellers are excluded from this coverage. In most cases the employee's costs are covered by the employer. It is recommended to check the list of medications covered by the health insurance funds.

## **2.9 Vaccination against hepatitis B**

The vaccination has been recommended for all 11- to 15-year-olds in Switzerland since 1998. The vaccination is preventive in nature in order to minimize the risk of infection with the onset of sexual activity. According to the data collected from obligatory notifications, sexual activity is highest between the ages of 20 and 24. The strategy has been

effective. The latest data show that considerably fewer cases of acute hepatitis B have been reported in 15- to 19-year-olds. The vaccination is recommended for the other age groups in the following situations:

**The vaccination is recommended for:**

- Health care personnel coming into contact with blood or possibly infected bodily fluids, soiled or contaminated objects, and infectious materials
- Social workers, prison and police personnel, coming into frequent contact with drug users
- Drug users
- Persons who frequently change sexual partners
- Persons living in the same household with or having sexual contact with virus carriers (HBs antigen)
- Persons originally from at-risk areas (Africa, Asia, Oceania, certain regions of South America) (→ visit [www.safetravel.ch](http://www.safetravel.ch) for a list of corresponding countries)
- Travellers to endemic zones who will come into close contact with the local population (extended stay or risky behaviours)
- Persons with reduced immunofunction (immunocompromised persons), patients with artificial kidneys (patients with hemolytic anaemia), hemophiliacs
- Persons with chronic hepatitis C
- Persons with HIV and HCV coinfections

This vaccination is covered by obligatory health insurance. The vaccination is also covered by most employers for qualified professionals working in the fields of medicine and social work.

## HEPATITIS AND PREGNANCY

### 2.10 Hepatitis B and pregnancy

The transmission of the virus from a pregnant woman with an acute or chronic infection to her unborn child usually takes place in most cases during the last trimester, especially during childbirth. There is a suspected risk of transmission through breast milk, but the results from the current research are still incomplete; however, this risk is low compared with the risk during the process of childbirth, even if HBs antigens are present in the breast milk.

Whether the child will indeed become infected depends on the concentration of the virus in the mother and the amount of the virus that is transmitted. If no immunoprophylactic measures are taken during childbirth, then the risk of transmission is 70-90 % in the case of HBeAg-positive mothers.

In the case of HBsAg-positive mothers the risk of transmission is 10-40 %. In the case of acute hepatitis B the risk of transmission is 60-70 % at the end of the pregnancy.

The biggest problem for infected children is the high rate of chronic hepatitis, which can later lead to cirrhosis of the liver or hepatocellular carcinoma.

Through the determination of HBs antigen in the mother during the final trimester of pregnancy it is possible to ascertain which women could potentially transmit the virus to their newborns. Within the first 12 hours directly following delivery the children of HBsAg-positive women receive a passive and an active hepatitis B immunization, which is repeated after four and six months. These immunizations provide the newborn with a 95 % chance of not becoming infected by its mother. The immunization of the child also enables it to be breastfed.

The risk of transmission to the child is considerably higher in the case of hepatitis B than with hepatitis C. However, by taking the measures described above it is possible to give birth to a child without infecting it.

### **2.11 Hepatitis C and pregnancy**

While a transmission of the hepatitis C viruses within the womb cannot be fully ruled out, it occurs only very rarely (in approx. 5 % of cases). However, hepatitis C is not a reason to dissuade a woman from getting pregnant or from taking extraordinary measures beyond the normal rules of hygiene during pregnancy and birth. A woman infected with hepatitis C can breastfeed her child as long as she has no open wounds on her nipples. There is no empirical proof of a connection between viral load during the process of childbirth and the risk of transmission. The same applies for both Caesarean section and vaginal birth.

One exception is an HIV/HCV coinfection. In such cases the risk of transmission of hepatitis C from the mother to the child is 8-30 % higher. The child is delivered by Caesarean section due to the HIV infection.