The Dutch College of General Practitioners (NHG) Practice Guideline
This NHG Practice Guideline is a translation of the Dutch guideline. It is specifically written for Dutch general practitioners in the Dutch environment. The advice which is given may therefore not be in accordance with the views of general practitioners in other countries.

NHG Practice Guideline 'Viral hepatitis and other liver disorders'
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This practice guideline replaces the NHG Practice Guideline 'Blood tests if liver disorders are suspected' (Huisart Wet 1992;35:78-82). The recommendations and the scientific basis have been updated. The most important changes are:
- Recommendations have been added for further diagnosis of liver disorders when indicated, with emphasis on the diagnosis of viral hepatitis, if suspected.
- Recommendations have been added for the management and prevention of viral hepatitis.
- Recommendations concerning neonatal jaundice and glandular fever have been removed. For information about these disorders, see the NHG Practice Guidelines 'Pregnancy and childbirth' and 'Acute sore throat'.

INTRODUCTION
The NHG Practice Guideline 'Viral hepatitis and other liver disorders' provides guidance for the diagnosis of suspected viral hepatitis and a few other liver disorders. The standard provides guidance for the management and prevention of viral hepatitis and discusses liver damage due to alcohol or pharmaceuticals.
Diagnostic studies for a possible liver disorder is indicated in patients with:
- jaundice
- generalized malaise together with suspicion of viral hepatitis
- because the patient is in a risk group for this disorder, or
- because there has been a risk contact
Neonatal jaundice is not covered by this practice guideline but is discussed in the NHG Practice Guideline 'Pregnancy and childbirth'.1 The diagnosis of prehepatic jaundice (haemolytic anaemia, Gilbert's syndrome) and posthepatic jaundice (cholelithiasis, cholecystitis, cholangitis, or bile duct obstruction due to a malignancy) are discussed briefly in this practice guideline. For patients with general malaise but no indication of a liver disorder in the history and examination, requesting blood tests for liver disorders is not worthwhile. Blood tests for liver disorders are not necessary for patients with glandular fever. Guidelines for the diagnosis and management of this disorder are described in the NHG Practice Guideline 'Acute sore throat'.2 As liver metastases are rarely the first manifestation of a carcinoma, there is no place for blood tests for liver function disorders to detect liver metastases in patients who are not known to have a carcinoma.
The total incidence of liver disorders is about 1 per 1,000 patients per year. The prevalence is 2-3 per 1,000 patients per year. Figures for liver damage due to alcohol and pharmaceuticals are not known. The incidence of viral hepatitis in general practice is 0.1 per 1,000 patients per year and the prevalence is 0.5-1 per 1,000 patients per year.3 In the Netherlands the main causes of viral hepatitis are the hepatitis A, B, and C viruses.4 5 Hepatitis D and E rarely occur.6 The practice guideline is therefore limited to the management of hepatitis A, B, and C. It is expected that due to immigration and the increase in international passenger traffic, the incidence and prevalence of hepatitis A and B in particular will increase.7 As a result, the general practitioner will be increasingly confronted with questions about the detection and prevention of viral hepatitis.
Background
Jaundice is the clinical manifestation of an elevated bilirubin concentration in the blood. There are three forms:
- Prehepatic jaundice occurs when the glucuronic acid-forming capacity of the liver is exceeded and part of the unconjugated bilirubin continues to circulate in the blood. Neonatal jaundice is a prehepatic form of jaundice, as is jaundice due to haemolytic anaemia or Gilbert's syndrome.\(^8\)
- Hepatic jaundice (parenchymatous jaundice) follows a viral infection or toxic damage that leaves the liver unable to convert and excrete all of the bilirubin it receives.
- Posthepatic jaundice occurs due to biliary obstruction caused by cholelithiasis, cholecystitis, cholangitis, or malignancies such as a pancreatic or biliary carcinoma.

Viral hepatitis
There is no difference in clinical symptoms among the acute form of hepatitis A, B, and C. Three phases are distinguished: a prodromal phase (tiredness, reduced appetite, fever, pain in the area of the liver), an icteric phase (jaundice, emaciation, and tiredness, in which the fever largely disappears), and a recovery phase.\(^9\)

Hepatitis A
Hepatitis A is particularly prevalent in children of school age. In young children the disease is usually subclinical. From the age of 5 years onwards the probability of clinical manifestation is greater than 75%.\(^10\) Infection occurs via the faecal-oral route. The average incubation period is 28 days. A patient is infectious from one week before to one week after the onset of jaundice.\(^11\) The recovery from hepatitis A is complete and complications are rare.\(^12\)

Hepatitis B
Hepatitis B is particularly prevalent in adults and is often subclinical.\(^13\) Infectious sources are blood or body fluids containing blood or virus, such as semen and vaginal fluid of infected persons. Infection takes place mainly by means of blood-blood contact.\(^14\) The incubation period is 2-3 months. Infectiousness begins about 6 weeks before the onset of clinical signs and persists until the hepatitis B antigen disappears from the body.\(^15\) In 5-10% of adults, acute hepatitis B progresses to a chronic form. About half of these persons develop liver cirrhosis within 10 years and about 10% of those with liver cirrhosis develop a liver cell carcinoma.\(^16\)

Hepatitis C
Hepatitis C is particularly prevalent in adults and is usually subclinical.\(^17\) The routes of infection are the same as for hepatitis B.\(^18\) The incubation period is about 2 months. Infectiousness begins about 11 weeks before the onset of possible symptoms. Chronic hepatitis develops in about 80-85% of infected persons.\(^19\) The risk groups and risk contacts for hepatitis A, B, and C are given in table 1.

Table 1. Risk groups and risk contacts for viral hepatitis
<table>
<thead>
<tr>
<th>Hepatitis A</th>
<th>Risk groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Family members, care providers, partners of patients with hepatitis A</td>
</tr>
<tr>
<td></td>
<td>Residents and staff of care homes for the mentally handicapped</td>
</tr>
</tbody>
</table>
Homosexual men with changing oro-anal sexual contacts
- Travellers, especially children, to areas where hepatitis A is endemic

**Hepatitis B**
- Risk groups
  - Intravenous drug users (past or present)
  - Persons working in the health care sector
  - Children of hepatitis B-positive mothers
  - Persons with changing sexual partners
  - Residents of homes for the mentally handicapped
- Risk contacts
  - Needle-prick accidents
  - Non-sterile procedures such as tattoos, piercing, and acupuncture
  - Sexual contact with a hepatitis B patient

**Hepatitis C**
- Risk groups
  - As for hepatitis B*
  - First-generation immigrants
- Risk contacts
  - Blood transfusion or organ transplantation, needle-prick accident, dialysis, or endoscopy before 1992*

*Transmission occurs via blood-blood contact. The risk of hepatitis C transmission via sexual contact is negligible.

**Liver damage due to alcohol abuse**
Alcohol abuse can eventually lead to liver damage. A fatty liver develops initially and can be reversed by reducing or stopping alcohol use. Continued alcohol abuse can lead to alcoholic hepatitis and in 15% of cases to liver cirrhosis.

**Liver damage due to pharmaceuticals**
Many pharmaceuticals, including as NSAIDs, antimycotics, and antituberculotics, can cause liver damage, which can be manifested in various ways and in varying degrees of severity. Liver cell damage, cholestasis, and combinations of the two are the most prevalent. Liver damage can be manifested clinically as jaundice as well as by general extrahepatic symptoms such as fever and rash. Liver enzyme levels can be slightly elevated, as in patients taking anticonvulsant drugs or statins. Liver damage can be the result of a direct toxic effect or a hypersensitivity reaction. Liver damage due to direct toxicity occurs with predictable regularity and is dose dependent, whereas hepatitis due to a hypersensitivity reaction is unpredictable, occurs less frequently, and is dose independent.

**DIAGNOSTIC GUIDELINES**
The general practitioner considers the possibility of a liver disorder in patients with:
- jaundice
- general malaise and a reason to suspect viral hepatitis:
  - because they belong to a risk group for this disorder, or
  - because there has been a risk contact

Persons with an increased risk of viral hepatitis (risk groups) or one or more contacts for which an increased risk of viral hepatitis transmission exists (risk contacts) are detailed in table 1.

**History**
The general practitioner enquires about:
duration and progression of the complaints
fever
problematic use of alcohol
medicines, especially those mentioned above
colic pains in the upper right half of the abdomen
weight loss
hepatitis B or C in the past

Physical examination
The general practitioner carries out the following examination:
inspection of the sclerae for jaundice
percussion and palpation of the liver and gall bladder area (enlarged, painful liver, peritoneal irritation)

Supplementary investigations
Jaundice together with colicky pain in the upper right half of the abdomen, with or without fever, raises suspicion of cholelithiasis, cholecystitis, or cholangitis (hence extrahepatic jaundice). During the physical examination, palpation of the upper abdomen elicits pain and the peritoneum may be sensitive. Jaundice without pain (‘silent jaundice’) together with emaciation can indicate a malignancy. The patient is referred, after ultrasonography if necessary.

If viral hepatitis is suspected the general practitioner requests laboratory determination of ALAT, gGT, and hepatitis serology. This applies to patients with:
jaundice without suspicion of gall bladder or bile duct disease or a malignancy (see above)
general malaise with suspicion of viral hepatitis, because
the patient is in a risk group for this disorder, or
there as been a risk contact for viral hepatitis (see table 1), or
there has been a previous episode of hepatitis B or C

The appropriate serological tests are listed in table 2.

In children the most probable cause is hepatitis A. Hence serology for hepatitis A is requested first and if it is negative, then serology for hepatitis B and/or C.
In adults the general practitioner selects hepatitis serology on the basis of the risk group or risk contacts. If the results are negative, the investigation can be extended to other forms of hepatitis.

Table 2. Serological tests for viral hepatitis

<table>
<thead>
<tr>
<th>Hepatitis</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>IgM anti-HAV</td>
</tr>
<tr>
<td>B</td>
<td>HBsAg (26)</td>
</tr>
<tr>
<td></td>
<td>IgM anti-HBc, if HBsAg is negative in a patient who until recently was icteric (27)</td>
</tr>
<tr>
<td>C</td>
<td>Anti-HCV *</td>
</tr>
</tbody>
</table>

*In acute hepatitis C anti: HCV can be negative in the first few months. Recent hepatitis C infection may then be demonstrated by the presence of HCV-RNA

Evaluation
In a patient with jaundice, normal ALAT and gGT, and no abnormalities in hepatitis
serology, the jaundice is prehepatic and probably due to haemolytic anaemia or Gilbert's syndrome. Discussion of further diagnostic studies for these diseases is beyond the scope of this practice guideline.

- In a patient with suspected viral hepatitis, the serological results are interpreted as follows:
  - **Hepatitis A** is confirmed by the presence of IgM anti-HAV and excluded if it is absent.
  - **Hepatitis B** is confirmed by the presence of HBsAg. If HBsAg is absent but if IgM anti-HBc is present, there is a recently-healed acute hepatitis B. If both virus markers are absent, hepatitis B is excluded.
  - **Hepatitis C** is confirmed by the presence of anti-HCV. If anti-HCV is absent, a recent hepatitis C infection cannot be completely excluded but may be demonstrated by the presence of HCV RNA.
  - If **serology for viral hepatitis is negative and ALAT and gGT are elevated** (>1.5 times the upper limit of normal), possible causes are:
    - **liver damage due to pharmaceuticals**: A moderate increase in ALAT and gGT often accompanies use of pharmaceuticals. If ALAT and gGT increase progressively or ALAT rises above 100 U/l, the pharmaceutical suspected of causing the increase should be stopped, if possible,²⁸
    - **liver damage due to alcohol abuse**: For management see the NHG Practice Guideline 'Problematic alcohol use',²¹
    - **other liver disorders**, such as haemochromatosis²⁹ or autoimmune hepatitis: Discussion of diagnostic studies is beyond the scope of this practice guideline.
  - Patients with jaundice and suspected cholelithiasis, cholecystitis, cholangitis, or a pancreatic or biliary malignancy are referred with or without prior ultrasonography.

**MANAGEMENT GUIDELINES FOR VIRAL HEPATITIS**

There is a compulsory declaration in cases of viral hepatitis A, B, and C.³⁰ The general practitioner can request the municipal health service to take steps to prevent others from becoming infected.

**Information**

The general practitioner explains that viral hepatitis is a contagious viral infection of the liver. For hepatitis A the clinical course is almost always favourable. Tiredness, sometimes serious and prolonged (several months), is one of the symptoms, but strict bed rest is not necessary. During the acute phase the use of pharmaceuticals which are metabolized or eliminated by the liver should be avoided. Specific dietary recommendations are not necessary, although in the recovery period there may be an intolerance for fat and alcohol. The moderate use of alcohol in this phase does not affect recovery, but in patients with chronic hepatitis C, alcohol use should be strictly avoided because it increases the risk of permanent liver damage.³¹

The general practitioner makes the following recommendations to prevent the infection of others:

- **Patients with hepatitis A**. Advise strict hygiene until one week after the onset of jaundice.³² Advise the patient to stay at home during this period and not go to work or school.³³
- **Persons in the immediate environment of a patient with hepatitis A**. Advise strict hygiene until one week after the onset of jaundice or until the administration of immunoglobulin (passive immunization) has taken place. Passive immunization is indicated for persons in the immediate environment of the patient if they have never
been infected with hepatitis A. This provides direct protection. Passive immunization is no longer necessary 2 weeks or more after the last risk contact.\textsuperscript{34}

- **Patients with hepatitis B or C.** Advise a patient with hepatitis B not to have unsafe sexual contacts with non-vaccinated persons. The chance of hepatitis C transmission by means of sexual contact is negligible. Advice should be given on how to avoid contact with blood from infected persons.\textsuperscript{35} No special precautions are necessary in normal social contacts at work, school, or in nurseries. In specific situations, there should be discussion between directly-responsible persons such as company doctors or the occupational health service and advisory experts. This is especially relevant if the infected person works in the health care sector or is a child with risk-behaviour such as biting.\textsuperscript{36} The same recommendations apply to persons revealed by screening to be HBsAg-positive.

- **Persons in the immediate environment of a person with hepatitis B or C.** Give recommendations aimed at preventing contact with blood from the patient and, if the patient has hepatitis B, avoiding unsafe sexual contacts unless vaccination has been obtained.

**Follow-up and referral**

- In patients with *acute hepatitis* A the general practitioner simply follows the clinical progress. Monitoring of liver function is not necessary.
- In patients with *acute hepatitis* B and demonstrable HBsAg, the serological test for HBsAg should be repeated 6 months later and if HBsAg is still found to be present, the patient has chronic hepatitis B.\textsuperscript{14}
- In patients with *hepatitis* C monitoring by the general practitioner is not required because these patients are referred.
- **Referral** to an internist or, if possible, a hepatologist is indicated in patients with:
  - suspected acute liver failure: confusion, reduced consciousness\textsuperscript{12}
  - chronic hepatitis B or hepatitis C, to determine eligibility for treatment with interferon and/or another antiviral treatment\textsuperscript{37,38}

**GUIDELINES FOR THE PREVENTION OF VIRAL HEPATITIS**

The prevention of viral hepatitis is undertaken in consultation with the municipal health service. The general practitioner follows the vaccination recommendations of the municipal health service. Passive immunization is the administration of immunoglobulin and active immunization is the administration of hepatitis A or hepatitis B vaccine.\textsuperscript{39} Active vaccination for the prevention of hepatitis C is not possible.

**Hepatitis A**

- **Vaccination**
  Persons in the risk groups (see table 1) should be advised to obtain active immunization if risk contacts are expected to continue. However, passive immunization should be advised for children <2 years of age, as well as for persons who expect to remain only a short time in an endemic area and for those who expect to enter an endemic area in the near future.\textsuperscript{40} The general practitioner also advises active immunization against hepatitis A for persons with chronic liver disease and those whose anticoagulant production is disrupted.\textsuperscript{41}

**Hepatitis B and C**

- **Vaccination**
Active immunization for hepatitis B is recommended for all persons in the risk groups (see table 1). Passive vaccination for hepatitis B is indicated:
- in neonates of HBsAg-positive mothers
- after a needle-prick accident
- in victims of sexual violence inflicted by a hepatitis B-infected person
- after unsafe sexual contact with a hepatitis patient

Vaccination against hepatitis C is not possible.

- **Prevention of vertical transmission of hepatitis B virus**
  If a pregnant woman is HBsAg-positive, the neonate should receive passive immunization immediately post-partum. Active immunization is provided subsequently at the health centre.
  The general practitioner receives a report from the municipal health service about a positive HBsAg screening test. He decides whether it is a chronic hepatitis or a recent infection (IgM anti-HBc-positive) and then treats the patient as indicated in the section 'Management guidelines for viral hepatitis: follow-ups and referral'.

- **Prevention and management after contact with possibly infected blood**
  If possible, use disposable materials and dispose of them in the same manner as for other infected material. Non-disposable objects are cleaned with abundant soap and water. Clothing contaminated with infected blood must be washed using a full washing machine cycle. Skin contaminated with infected blood should be washed with abundant soap and water and then disinfected with 70% ethanol. The purpose of these measures is to reduce concentration of virus at the point of contact, especially by dilution. The general practitioner contacts the municipal health service within 24 hours for advice about additional prophylactic measures when blood-blood contact could have occurred.\(^\text{43}\)

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**note 1**

**note 2**

**note 3**
The incidence and prevalence figures are taken from recording projects in Dutch general practices.1-3

note 4
In 95% of cases, viral hepatitis is caused by a hepatitis virus such as hepatitis A, B, or C virus.¹ Other viruses which can cause hepatitis are: cytomegalovirus, Epstein-Barr virus, human immunodeficiency virus, herpes simplex virus, varicella zoster virus, adenovirus, and coxsackievirus.²


note 5
In the Netherlands about 900 cases of hepatitis A are reported each year (6 per 100,000 inhabitants).¹ For hepatitis B more than 230 cases per year are reported (about 1.5 per 100,000 inhabitants).¹,² No exact figures are available for the incidence and prevalence of hepatitis B in the general population. Estimates are based on the notification of acute cases to the Dutch Health Inspectorate and the screening of pregnant women and new blood donors for HBsAg, which has been carried out in the Netherlands since 1989. In 1988 the incidence of acute hepatitis B among intravenous drug users was 90 per 100,000.² The prevalence of chronic hepatitis B was estimated at 5 per 1,000 residents. The screening of pregnant women since 1989 has revealed a prevalence of 4.5 per 1,000 and in donors a prevalence of 0.6 per 1,000. In mental health care institutions, the prevalence of chronic hepatitis B is 39 per 1,000 and a quarter of the residents have at sometime had a hepatitis B infection.²


note 6
Hepatitis D only occurs as a coinfection or superinfection of hepatitis B. Hepatitis E is an 'imported disease' in the Netherlands and from a clinical and epidemiological viewpoint is comparable to hepatitis A. It is endemic in Asia, Africa, and Latin America. Both hepatitis D and E are rare in the Netherlands and are therefore not discussed in this practice guideline. This also applies to hepatitis G, about which very little is known at present.

note 7
Each year the number of notifications for hepatitis A in children increases during the months of August and September. This increase is caused by notifications for children of non-Dutch parents, who have acquired the infection while on holiday in their parents' home country, particularly in Morocco and Turkey. After this brief peak, there is an increase in notifications for children and adults with secondary infections acquired in the Netherlands as a consequence of contact with the above children.¹ A study in the cities of Amsterdam, Utrecht, Rotterdam, and The Hague revealed that children who had spent the summer holidays in a country where hepatitis A is endemic were the most important importers of hepatitis A into the Netherlands.²

2. Van Gorkum J, Leentvaar-Kuijpers A, Kool JJ, Coutinho RA. Jaarlijkse epidemie van hepatitis A in verband gebracht met reisgedrag van kinderen van immigranten in de vier grote steden [Annual epidemics of hepatitis A in four large cities related to

note 8
Gilbert's syndrome is not a disease but a genetic condition which results in less efficient conjugation of bilirubin in the liver. As a result, the bilirubin level is slightly elevated, varying from 20 to 50 µmol/l. The syndrome is usually discovered during young adulthood, e.g., due to a period of mild jaundice, and is not associated with complaints.


note 9
The clinical manifestations of acute hepatitis begin with a prodromal stage lasting 3-10 days, in which there is malaise, tiredness, reduced appetite, and fever. Nausea and vomiting can also occur during this phase, as well as pain in the upper right half of the abdomen, a rash, and arthralgia. This is followed by the icteric stage, which is associated with jaundice, elevated temperature, the characteristic dark urine and sometimes pale (acholic) faeces. Pruritus due to the cholestasis also occurs frequently in this phase. The acute phase generally lasts for 1-3 weeks. However, particularly in adults, the jaundice, as well as the malaise and tiredness, can persist for several months. There is often an intolerance for fat, alcohol, and tobacco during this phase.

note 10
The duration and seriousness of the clinical course of hepatitis A generally increase with age. In the 1980s an American study of hepatitis A found that the course was symptomatic in 16% children up to 2 years of age, in 50% of those 3-4 years old, and 80% of those aged 5 years and older.1,2


note 11
Transmission of the hepatitis A virus is predominantly via the faecal-oral route, including oro-anal sexual contacts. Infection can also occur by drinking contaminated water that has not been boiled or food, especially from contaminated water, such as prawns or shellfish.1-3 Infectiousness is strongly correlated with the concentration of the virus in the faeces or in the infected food. The highest concentration of the virus in the faeces of the patient occurs from 2-3 weeks before the onset of the disease until 1-2 weeks later.1,4 The period of infectiousness is particularly toward the end of the incubation period and in the first week after the onset of jaundice, but anicteric, subclinical patients are also infectious.2,3

A rare complication of acute viral hepatitis is acute liver failure, which occurs within 12 weeks after the start of the icteric phase and is characterized by encephalopathic symptoms. Leebeek et al. described 2 patients in the Netherlands with acute liver failure due to a hepatitis A infection, one requiring a liver transplant. The risk of a hepatitis A infection with a serious clinical outcome is increased in persons with chronic liver disorders and it also increases with age.


note 13
The occurrence of clinical symptoms in hepatitis B infection is also age-dependent. Less than 5% of the infections in children <5 years of age are symptomatic, while in adults 30-50% are.


note 14
The route of transmission can be horizontal or vertical. Horizontal transmission of hepatitis B virus occurs most often via parenteral administration of blood or blood products, or via sexual contact in which damaged skin or mucosa is exposed to blood-containing body fluids (semen, vaginal fluid). There is no transmission via saliva and although transmission can occur through a bite wound, the importance of this risk is unknown. Vertical transmission of hepatitis B is primarily via perinatal blood contact, from mother to child. In both horizontal and vertical transmission, infectiousness is highly dependent on the concentration of virus particles in the body fluid involved. The concentration in the blood is usually high if the infected person is HBsAg-positive. The probability of infection when horizontal transmission occurs can be up to 40% and by vertical transmission it can be up to 90%.


note 15
Complete recovery from hepatitis B is signalled by seroconversion, i.e., the disappearance of HBsAg, which is accompanied by the appearance of anti-HBs. This also marks the end of infectiousness. The infection is considered to be chronic if HBsAg persists for >6 months.

note 16
Fattovich et al. followed 105 patients with chronic hepatitis for 1 to 16 years. Liver cirrhosis
had developed in 20% of the patients after 5 years and in 50% after 10 years.\textsuperscript{1} A hepatocellular carcinoma developed in about 10% of the patients with liver cirrhosis due to chronic hepatitis B.\textsuperscript{2}

\begin{enumerate}
\end{enumerate}

\textbf{note 17} \hspace{1em}
A hepatitis C infection is usually subclinical, regardless of age; only 20-30% of those infected have complaints and only 10-15% develop jaundice.\textsuperscript{1,2}

\begin{enumerate}
\end{enumerate}

\textbf{note 18} \hspace{1em}
The route of infection by hepatitis C is virtually the same as for hepatitis B, by means of blood-blood contact.\textsuperscript{1-4} Since 1992, blood donors have been tested for hepatitis C, which virtually rules out the risk of transmission via a blood transfusion. The risk of vertical transmission (intra-uterine or perinatal) and of transmission within the family or by sexual contact is small and scarcely plays a role in the dissemination of the disease.\textsuperscript{1,5,6} Follow-up studies were carried out during 15 years in the children and partners (monogamous relationships) of 161 women who became infected in 1978 and 1979 with the hepatitis C virus via contaminated anti-D immunoglobulin. The vertical transmission was very low (1.3%). None of the partners developed any signs of hepatitis C infection.\textsuperscript{5}

\begin{enumerate}
\item Di Bisceglie AM. Hepatitis C. Lancet 1998;351:351-5.
\item Everhart JE. Risk for Non-A, Non-B (type C) hepatitis through sexual or household contact with chronic carriers. Ann Intern Med 1990;112:544-5.
\item Ledda C. Preventing the spread of viral hepatitis. Am Fam Physician 1993;8:1479-86.
\end{enumerate}

\textbf{note 19} \hspace{1em}
A hepatitis C infection results in chronic hepatitis in 80-85% of cases.\textsuperscript{1,2} In 20-30% of patients with chronic hepatitis, liver cirrhosis develops within 10-20 years.\textsuperscript{2-6} After 20 years, a hepatocellular carcinoma has developed in 2-7% of cases.\textsuperscript{5} In its report, the Health Council of the Netherlands advises approaching persons in risk groups so that they can be tested for hepatitis C. The general practitioner can undertake contacting three groups by means of case finding:

- persons who received an incidental transfusion of blood or a blood product before 1992
persons who have had tattoos, piercings, or other non-sterile procedures (8-30% anti-HCV-positive)

- former drug users, including non-injectors, 10% of whom are anti-HCV-positive

Persons in the remaining risk groups are usually seen regularly by other organizations or care providers.\(^2\) The work group does not endorse this advice but is of the opinion that the professional group must first determine whether such preventative tasks are necessary. Furthermore, with regard to hepatitis C, case-finding is scarcely effective because the general practitioner is far from adequately informed about past blood transfusions or drug use. Treatment possibilities are still limited and weighing up the pros and cons of treatment is a complex issue.


**note 20**

No reports have been found of good scientific research on the predictive value in general practice of complaints, symptoms, and characteristics associated with liver disorders, or of the results of the laboratory tests usually employed. Hence, no scientifically-justified guidelines can be formulated for the history, physical examination, and supplementary investigations for confirming or excluding a liver disorder, or for differentiating various liver disorders. Accordingly, only a global outline for the diagnosis is provided. The predictive value of jaundice for the existence of a liver disorder will be high and that for other complaints and symptoms will be low.

**note 21**


**note 22**

The risk of hepatitis A is increased in:

- partners or carers of hepatitis A patients and those living in the same house\(^1-3\)
- staff and residents of day-care centres and care homes for the mentally handicapped\(^1-3\)
- persons with oro-anal sexual contacts\(^2-4\)
- travellers to areas where hepatitis A is endemic, especially if hygiene and sanitation are inadequate, and especially children of immigrants from endemic areas who go on holiday to their land of origin and persons subsequently in the vicinity of these
children.1-5 An overview of 8,800 new cases of hepatitis A in the United States in 1993 found that in 50% of the patients the source of infection could not be traced.6


note 23
In 1996, the Health Council of the Netherlands published an advisory report on hepatitis B compiled by a committee of experts in the fields of epidemiology, microbiology, internal medicine, and liver diseases. The risks groups listed in table 1 are taken from this advisory report, in which data on the prevalence of hepatitis B and the vaccination status of the risk groups are given.


note 24
At the request of the minister of Health, Welfare and Sport, an advisory report was compiled in 1997 concerning the detection and treatment of hepatitis C, previously termed ‘non-A, non-B post-transfusion hepatitis’. The most important conclusion of this report is discussed in note 19.


note 25
ALAT (alanine-aminotransferase, SGPT) and ASAT (aspartate-aminotransferase, SGOT) are transaminases which are active in the liver as well as in other tissues. ALAT is found primarily in hepatocytes and to a lesser extent in the skeleton, myocardium, kidney, and pancreas. ASAT is found in hepatocytes, cardiac and skeletal muscles, and to a lesser extent in other organs. Elevation of ALAT is the most specific indication of hepatocyte damage1 and measurement of ALAT is therefore used in this practice guideline. A slight increase in the ALAT concentration (to 1.5 times above the normal upper limit) often has no clinical significance in a patient who is not ill, and watchful waiting is justified.2 The enzyme gGT (γ-glutamyltransferase) occurs in hepatic cells, as well as in the pancreas, heart, kidney, and other organs. It is highly elevated when obstruction of the biliary tract is
present. It can be slightly elevated in the absence of liver damage, as a result of certain medicines, alcohol use, or steatosis and obesity. Alkaline phosphatase is present in the placenta, bone, and liver. In liver disorders, the alkaline phosphatase is a measure of the degree of obstruction of the biliary tract. However, it has a low-specificity and gGT is a better for this purpose.¹


note 26 ➣
For the clinical course of the viral markers of hepatitis B in the various stages of infection see table 3.¹


### Table 3. Clinical course of hepatitis B viral markers

<table>
<thead>
<tr>
<th>Infection stage</th>
<th>HBsAg</th>
<th>anti-HBs</th>
<th>IgG anti-HBc</th>
<th>IgM anti-HBc</th>
<th>HBe-Ag</th>
<th>anti-HBe</th>
<th>HBV DNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Late in incubation period</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>±</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Acute hepatitis</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+++</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Chronic infection, highly infectious</td>
<td>+</td>
<td>-</td>
<td>+++</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Chronic infection, scarcely infectious</td>
<td>+</td>
<td>-</td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>+</td>
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<td>Hepatitis, cured for &lt;6 months</td>
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<tr>
<td>Hepatitis, cured for &gt;6 months</td>
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<td>Post-vaccination</td>
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**HBsAg** hepatitis B surface antigen, previously termed the Australia antigen  
**anti-HBs** antibodies against HBsAg  
**IgG anti-HBc** antibodies of the IgG type against HbcAg (HbcAg: hepatitis B core antigen; core is the nucleus of the hepatitis B virus, in which the DNA is located)  
**IgM anti-HBc** antibodies of the IgM type against HbcAg  
**HBeAg** hepatitis B e antigen (‘early antigen’)  
**anti-HBe** antibodies against HBeAg
HBV DNA  hepatitis B viral DNA

note 27
During an acute infection, IgM anti-HBc can be demonstrated within 5 weeks after the appearance of HBsAg and disappears within 2-6 months. IgM anti-HBc is always present in the 'window phase' during the clearance of the hepatitis B virus—the interval during which HBsAg can no longer be demonstrated but anti-HBs has not yet disappeared from the blood. IgM anti-HBc identifies persons with an acute hepatitis B infection in whom HBsAg has become negative.1,2


note 28

note 29
Haemochromatosis is a metabolic disorder in which iron accumulates in various organs. The liver, pancreas, and heart are particularly affected. It is an autosomal recessive inherited disease. Ten percent of the European population are carriers and about 1 in 250 persons is a homozygote. The disease is only expressed in a fraction of the homozygotes, much less often in women than in men, probably because the blood lost during the menstrual cycle protects against iron accumulation. Tiredness in combination with joint complaints are early symptoms. The treatment consists of regular bloodletting.1 It has recently become possible to demonstrate the presence of the abnormal gene.2


note 30
The physician who diagnoses a case of viral hepatitis is legally required to notify the municipal health service within 24 hours. He should also do this when he has substantial reason to suspect that a patient has a viral hepatitis but the patient refuses to undergo the examinations and tests necessary to confirm the diagnosis. The notification should contain the following information:

- name, permanent address, present address, and date of birth of the infected person
- the infectious disease, first day of illness, vaccination status, use of prophylactic measures, possible source or place of infection, date on which viral hepatitis was diagnosed or suspected
- any professional involvement in handling food and drinks or in treatment, nursing, or caring for other persons in his immediate environment

Upon receipt of the notification, the municipal health service considers whether measures are required. Government Public Health Inspectorate. Infectious Diseases Act. SDU,. The Hague 1999.

note 31
Tozun et al. concluded that moderate use of alcohol during the recovery phase of acute hepatitis did not affect clinical progress. Patients with hepatitis A, B, and non-A non-B who previously used alcohol moderately were randomly assigned to either a group who continued alcohol use or a control group who stopped using alcohol throughout the study.
All of the patients entered the study at least 6 weeks after the onset of symptoms of hepatitis and thus after the acute phase. After 3 months no differences were observed between the two groups in terms of well-being, clinical symptoms, or liver function.\textsuperscript{1} However, the advisory report of the Health Council of the Netherlands recommends that persons with \textit{chronic} hepatitis C infection should be given strict advice to stop consuming alcohol or to limit it as much as possible in order to minimize progression of the disease.\textsuperscript{2} Studies have shown that in persons with persistent hepatitis C infection, alcohol consumption rapidly increases progression of the disease and the onset of cirrhosis.\textsuperscript{3}


\textbf{note 32} 
Hygienic measures for patients with hepatitis A:
- avoid contact with faeces
- wash hands after using the toilet and before preparing food, drying hands with disposable towels
- clean the toilet twice daily with 0.1% chlorine solution
- use disposable nappies for babies, and clean the baby-changing pad frequently and intensively

\textbf{note 33} 
This advice applies to children aged 4 years and over. Children with hepatitis A can be permitted to come to a crèche or day nursery. In view of the often asymptomatic course of the disease in children up to 4 years of age, refusing a single child will not prevent transmission. An exception is a child who returns from holiday with symptomatic hepatitis A and thus cannot have infected any other children yet.

\textbf{note 34} 
Passive immunization against hepatitis A provides an effective immune response in 90\% of those vaccinated. The duration of effectiveness of a standard dose is 4-6 months. Active immunization results in an adequate response in 95-100\% of cases, with a duration of protection of 1 year after the initial dose and more than 10 years after the second dose.

\textbf{note 35} 
Advise the patient to ensure that others avoid contact with objects which could have come in contact with his blood: toothbrushes, shaving equipment, needles, syringes, equipment for hand and foot care, bandages, sanitary towels, medical apparatus such as glucose meters. Take care with skin lesions such as small wounds, open eczema, and impetigo. There is no risk associated with communal use of cutlery, bathrooms, or clothes, or with normal tactile contact.\textsuperscript{1-5} No studies of the effectiveness of such measures were found.

note 36 ➡
Only very general guidelines were found in the literature for patients with hepatitis B or C who work in the health care sector. What a person is allowed to do depends on the nature of the work and in particular how invasive it is. Procedures involving risks should be established by experts for each department. HBeAg-positive persons should not undertake any risk-bearing interventions without consulting experts.

note 37 ➡
A meta-analysis of 16 randomized and controlled trials involving a total of 837 patients with chronic hepatitis B revealed seroconversion of HBsAg to anti-HBs in 7.8% of the patients treated with interferon a, compared with 1.8% of the controls, 6-12 months after completion of the treatment. These results concur with those of other studies. Interferon a is thus only effective in a small proportion of patients with a chronic hepatitis B infection.

note 38 ➡
Cooreman et al. discussed current treatment of hepatitis C in the acute phase. Antiviral treatment with interferon during the acute phase has been shown to be effective in preventing chronic carriers of hepatitis C and thus the onset of chronic hepatitis. Interferon a also inhibits replication of the hepatitis C virus. Three meta-analyses revealed a response in 44-51% of patients after 6 months of treatment with interferon, compared with 2-3% of controls. However, there was a relapse in more than half of the patients 3-12 months after the treatment was stopped. A permanent response was eventually confirmed in 17-21% of the patients treated.

note 39  
The work group follows the vaccination advice of the municipal health service because for both hepatitis A and B, effective vaccines are available with no more than moderate side effects.1,2


note 40  
Passive immunization is preferred for children <2 years of age, because active immunization may be ineffective if maternal antibodies are still present. Passive immunization is preferred for a short stay in an endemic area because it is less expensive and simpler than active immunization. This is also true for imminent departure, in addition to which active immunization is only effective after about 1 month.


note 41  

note 42  
Since 1989 there has been a guideline from the Chief Medical Inspectorate for Public Health: Prevention of hepatitis B in neonates.1 The guideline was reviewed in 1998.2 If the result of a screening test for HBsAg is positive during pregnancy, the general practitioner and the provincial vaccination administration (PEA) receive a copy. The neonate should preferably be given passive immunization within 2 hours after birth by administration of 300 IU HB Ig intramuscularly in the anterolateral side of the thigh. Subsequently, the person who has supervised the pregnancy issues a prescription for hepatitis B vaccine, which is administered at the health centre. The PEA is responsible for the administration and monitors the call-up for injections.

The risk of infection is initially estimated from the infectiousness of the source. If possible, the medical records of the person from whom the material originates are consulted and in case of doubt the person is requested to undergo tests for hepatitis B and C. If a probable or confirmed HBsAg-positive source is found, Post-Exposure Prophylaxis (PEP) is given. This consists of passive immunization within 48 hours after the exposure by administering 500 IU hepatitis B immunoglobulin (HBIg) to adults and 8 IU/kg HBIg to children. After passive immunization, active immunization should always be given with a hepatitis B vaccine. New guidelines were published recently with respect to possible infection with hepatitis C. Every month for 6 months the acceptor can be monitored by measuring ALAT. If it increases, a test for HCV RNA can be performed and if this is positive, interferon treatment can be given.