Clinical and Experimental HEPATOLOGY

Clin Exp HEPATOL 2025; 11, 1: 1–8
DOI: https://doi.org/10.5114/ceh.2025.148265
Received: 28.07.2024, **Accepted:** 09.09.2024, **Published:** 31.03.2025

Review paper

Recommended vaccinations for patients with chronic liver diseases

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Abstract

Patients with chronic liver diseases, particularly those with liver cirrhosis, are more vulnerable to severe superinfections compared to the general population. They face an increased risk of liver function decompensation and mortality when contracting viral or bacterial infections. Vaccination is crucial in mitigating these risks, yet its efficacy in this patient group may be limited. Despite the safety of vaccines, their effectiveness in individuals with chronic liver diseases remains constrained. A significant challenge is the inadequate implementation of vaccination protocols, often due to insufficient communication and recommendations from physicians, including hepatologists, and the high cost of vaccines.

Key words: vaccinations, immunization, chronic liver disease.

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Introduction

The population of patients with chronic liver disease (CLD) is highly heterogeneous in terms of liver disease severity, etiology, and comorbidities. This group primarily includes patients chronically infected with hepatitis B virus (HBV) and hepatitis C virus (HCV), those with metabolic dysfunction-associated steatotic liver disease (MASLD), with alcohol-related liver disease (ALD), drug-induced liver injury (DILI), and autoimmune and genetic liver diseases. In each of these groups, patients with compensated or decompensated cirrhosis, often complicated by hepatocellular carcinoma (HCC), should be distinguished by the severity of their liver disease. A special subpopulation is liver transplant patients who remain on immunosuppressive therapy. People with CLD are at significant risk of liver disease decompensation or deterioration from most viral or bacterial infections. Mortality from bacterial infections among cirrhotic patients is 3.75 times higher than in the general population (38% vs. 10%) [1-3].

Immunization plays a key role in the prevention of many infectious diseases, which is particularly important for patients at risk of severe disease. In addition, vaccination provides population protection, leading to a reduction in disease incidence (e.g., measles) and the elimination of certain pathogens (e.g., smallpox virus). This article is intended as a reminder of the importance of the implementation of recommended vaccinations in this subpopulation of patients.

Recommendations for vaccination, including for specific groups of patients according to age or disease burden, are published by the US Advisory Committees on Immunization Practices (ACIP). The American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL) are the authorities on this issue.

Patients with CLD, especially those with cirrhosis, should be treated as immunocompromised patients. This group of patients has an increased risk of both acquiring infections and suffering from severe ones. Simultaneously, the effectiveness of vaccination decreases as liver disease progresses. The complex pathomechanism referred to as cirrhosis-associated

immune dysfunction (CAID) involves multiple pathophysiological components of immunodepression mechanisms:

- decrease in complement activity,
- impaired macrophage function,
- abnormal synthesis of immunoglobulins,
- dysfunction of the reticuloendothelial system,
- reduction in the number of memory and helper CD4 cells and depletion of T lymphocytes.

These disorders result from the loss of active liver mass, liver blood supply disorders, metabolic abnormalities, impaired protein synthesis and loss, malnutrition, splenomegaly, and changes in gut microbiota [4].

Inactivated vaccines are preferred over live attenuated ones, but despite the immunosuppression associated with cirrhosis, there is no contraindication to the use of live attenuated vaccines in most CLD patients. Exceptions to this are patients undergoing liver and other organ transplantation, patients on intensive immunosuppressive therapy, those undergoing and three months after chemotherapy, and patients taking high doses of immunosuppressive drugs for the treatment of autoimmune liver disease (more than two weeks of treatment with prednisone > 20 mg/day, methotrexate > 0.4 mg/kg/week, azathioprine > 3 mg/kg/day). General contraindications are the same as in the general population (e.g., allergies to vaccine components, acute infectious disease, exacerbation of chronic disease). It is recommended that vaccination be performed early in the course of liver disease to achieve an optimal immune response.

Clinical data indicate that vaccination does not cause liver damage or acute liver failure, cholestasis, increased aminotransferases, impaired protein production, or plasma dyscrasias.

Unfortunately, overall vaccination coverage for those with CLD remains poor. This is a consequence of the high cost of vaccines, the lack of reimbursement for them, and insufficient information provided by doctors caring for liver disease patients concerning the benefits of vaccination and its safety [3].

A study evaluating vaccination rates in 700 patients with chronic liver disease under the care of general practitioners and specialized facilities indicated that patients under the care of general practitioners were more likely to be vaccinated against influenza and pneumococcus. In contrast, in a group of patients from specialized centers (gastroenterology and hepatology) susceptible to hepatitis A virus (HAV) or HBV infection, vaccination against these viruses was more frequently completed [5].

It is advised that communication between the GP and the specialist caring for the patient should be improved to streamline the implementation of vaccinations. Providing specific recommendations regarding vaccinations for a given patient, including the recommended intervals and location of vaccinations, can significantly improve vaccination rates in this group.

With this article, we would like to draw attention to the need to update knowledge concerning vaccination among hepatologists, and, thus, its implementation in this particular group of patients under our care.

Hepatitis B virus (HBV) vaccination

The ACIP recommends HBV vaccination for all patients with CLD with or without cirrhosis who have not yet been vaccinated [2].

Despite these recommendations, the percentage of CLD patients vaccinated against hepatitis B is low (30%) [6].

The superimposition of acute hepatitis B on existing cirrhosis or less advanced liver disease can lead to sudden decompensation, the development of acute-on-chronic liver failure (ACLF), and an increased risk of death. In addition, patients with HBV/HCV co-infection have an increased risk of HCC, and liver recipients have an increased risk of rejection of the transplanted organ.

Patients with latent HBV infection (anti-HBc total positive, anti-HBs positive or negative, HBs antigen negative) are not recommended to be vaccinated against hepatitis B. On the other hand, the importance of prophylaxis of reactivation of HBV infection with entecavir or tenofovir in the case of chemotherapy, immunosuppressive, or biologic treatment is emphasized.

Hepatitis B vaccines which contain recombinant HBs antigens fall into the category of "killed" (inactivated) vaccines. In patients with CLD, the hepatitis B vaccine should be administered according to the standard schedule (0, 1, 6 months) or in an accelerated schedule of 0, 7, 21 days, 12 months, or 0, 1, 2, 12 months. Several studies among patients with cirrhosis, liver transplantation, and toxic or metabolic liver damage have found a lower response to vaccination compared to the general population (> 90%). In the literature, seroconversion after a three-dose course of vaccination among patients with cirrhosis was in the range 16-79% [7, 8].

Hepatitis B vaccination has been available worldwide for four decades, and vaccination programs vary from country to country. Still, vaccination rates among adults are not optimal, limiting further reduction of hepatitis B infections.

Vaccination is recommended for adults who have not been vaccinated but are susceptible to infection,

and who, due to their lifestyle or occupation, are at risk of infection associated with damage to tissue continuity or through sexual contact:

- people traveling to hepatitis B endemic areas (HbsAg prevalence > 2%),
- people infected with HCV,
- patients with chronic liver disease,
- diabetics,
- people living with HIV,
- people engaging in risky sexual behavior,
- men having sexual relations with men,
- partners of HBV-infected persons,
- intravenous drug addicts,
- residents and employees of facilities for people with developmental disabilities,
- health and public safety workers,
- people undergoing dialysis,
- and all previously unvaccinated children and adults, especially the elderly [9].

In Poland, vaccination is mandatory and free of charge for adults in medical professions at risk of infection, persons particularly exposed to infection as a result of contact with an HBV-infected person, dialysis patients, and/or patients with progressive chronic kidney disease with glomerular filtration rate (GFR) < 30 ml/min/1.73 m^2, HCV-infected persons, and persons before or after hematopoietic stem cell transplantation, solid organ transplantation, and splenectomy [10].

Hepatitis A virus (HAV) vaccination

The ACIP recommends HAV vaccination for every patient with chronic liver disease [2].

Individuals with liver disease are not at increased risk of HAV infection; however, they are at increased risk of death from HAV infection (28-35% depending on the publication), decompensation, and exacerbation of ACLF [11, 12].

Serologic testing for HAV before vaccination is not recommended but can be considered in some situations to reduce the costs associated with vaccinating people who are already immune. This applies to people who were born or have lived for a long time in areas of the world with high or moderate hepatitis A endemicity. There is no contraindication to vaccinating a person who has undergone natural infection or received previous doses of the vaccine.

Vaccines contain inactivated virus and are recommended not only for patients with chronic liver disease but also for people traveling to countries with high and intermediate endemicity, those employed in food production and distribution, disposal of municipal waste and liquid waste, and maintenance of equipment used for this purpose, as well as those who engage in risky sexual contacts and use drugs [10]. In contrast, CDC guidelines for U.S. residents recommend routine vaccination for children aged 12-23 months and booster vaccination for children and adolescents aged 2-18 who have not previously received the hepatitis A vaccine at any age, in addition to recommending vaccination for adults at risk of infection (those living in a homelessness crisis center, drug users, and men who have sex with men) and those at risk of a more severe course of infection, i.e., patients living with HIV and liver disease.

The vaccines are well tolerated, with minimal mild side effects. The vaccination regimen involves the administration of two doses into the shoulder muscle at an interval of 6-36 (60) months (depending on the Summary of Product Characteristics – SPC), and preferably between six and 12 months [13, 14]. The ACIP does not recommend routine testing of antibody titers after immunization in immunocompetent individuals [15].

In patients with thrombocytopenia and coagulation disorders, subcutaneous (s.c.) administration is acceptable due to the risk of bleeding after intramuscular (i.m.) administration.

This vaccination is also recommended for people who are not immunized after contact with people with acute hepatitis A, as part of post-exposure prophylaxis (PEP) as soon as possible up to 14 days after exposure; in countries with access to immunoglobulin, PEP can be considered. Combined vaccines (A + B) are not recommended in these situations [15].

Patients with CLD are best vaccinated before decompensation of liver function occurs, due to reduced vaccination efficacy in those with advanced disease (seroconversion is in the range 49-66% vs. 95% overall among patients with liver disease vs. 98% in the general population) [16, 17].

Clinical observations have not confirmed the greater efficacy of combination vaccines against HAV and HBV compared to uncombined preparations. Combined vaccination against HAV and HBV is implemented in a three-dose schedule: 0, 1, 6 months or an accelerated four-dose one: 0, 7, 21 days + 12 months.

Vaccination against tetanus, diphtheria, and pertussis

ACIP guidelines recommend booster vaccinations against tetanus, diphtheria, and pertussis every ten years for all adults, including patients with CLD [18].

The full cycle of vaccinations and booster doses is carried out as part of mandatory childhood and early adolescent immunization programs. In subsequent adulthood, booster doses should be given every ten years.

An adult over 18 years of age who has never previously received a primary vaccination series against tetanus, diphtheria or pertussis should be vaccinated with the following regimen: one dose of Tdap (tetanus, diphtheria, acellular pertussis), followed by one dose of Td or Tdap at least four weeks later and a third dose of Td or Tdap 6 to 12 months later (Tdap can be replaced by any dose of Td, but is preferred as the first dose), Td or Tdap then every ten years [10, 18].

In the event of an injury, a booster dose may be required earlier if more than five years have passed since the last dose. If the patient is planning to travel to a country where polio occurs, we recommend the combination vaccine DTaP.

Chronic liver disease itself is a major burden on the body. An additional infection, especially one such as whooping cough (pertussis), which can cause a long-term cough, weakness, and other symptoms, can significantly worsen the patient's health. Given the significant increase in whooping cough cases in 2024, this vaccination should be especially recommended for individuals with CLD.

Vaccination against measles, mumps, and rubella

A combination vaccine against measles, mumps, and rubella is mandatory in childhood; it is implemented within the Polish vaccination program in a two-dose regimen and in many countries, including the U.S., according to ACIP recommendations.

Recommendations in adulthood for patients with CLD are those for the general population. One should consider vaccinating people who have never been vaccinated or have only been given one dose of vaccine, especially against measles, given the increase in measles cases worldwide in recent years.

The vaccine is a live vaccine, so it is important to be aware of general contraindications to its use, such as status after liver or other solid organ transplantation, up to 3 months after chemotherapy, high doses of azathioprine (more than 3 mg/kg dose), disseminated cancer, and high-dose steroid therapy (> 14 days).

Influenza vaccination

Influenza vaccination is recommended by the ACIP for all patients with CLD

The goals of seasonal influenza virus vaccination are to reduce transmission of the influenza virus, reduce hospitalizations and deaths, and reduce the risk of post-influenza complications such as pneumonia, respiratory failure, exacerbation of chronic respiratory conditions, exacerbation of heart failure, and myocarditis. In patients with CLD, vaccination also helps prevent decompensation of liver function, exacerbation of liver failure, and increased susceptibility to bacterial superinfection. In addition, vaccination protects individuals at risk of complications, reduces costs associated with treating influenza and its complications, and reduces costs directly related to absenteeism from work and lost productivity.

Due to the millions of cases of illness each year worldwide, the number of patients hospitalized due to influenza virus infection is very high, with a mortality rate of 650,000 cases per year. The number of deaths among patients with cirrhosis is 3-4 times higher than among patients without cirrhosis [19, 20]. The influenza virus is cosmopolitan and occurs seasonally during the fall and winter, which in the northern hemisphere occurs from October to April, and in the southern hemisphere from May to September. Three types of the virus cause disease in humans: types A, B, and C. Type A is divided into subtypes depending on the structure of the surface proteins: N-neuraminidase and H-hemagglutinin, e.g., H1N1 or H3N2.

Influenza virus infection occurs via the droplet route, and the course of the disease can range in symptoms from a mild cold (headache, fever, muscle aches) to ear infections, laryngitis, and coughing.

A live attenuated intranasal vaccine against influenza is not recommended for CLD due to the lack of clinical trials in this patient group.

An inactivated quadrivalent vaccine produced several months before the flu season is recommended. Every year, vaccination should be received a few weeks before the expected disease season. The composition of the vaccine is determined annually based on the WHO Global Influenza Surveillance and Response System report, which matches the respective surface antigens of the different A and B virus strains. Thus, the vaccine protects against four strains of influenza virus (two strains of A and two strains of B). Immunity after the vaccine administration develops within 2-3 weeks and persists for 6-12 months.

The effectiveness of the vaccine in a healthy population is about 90% (although it is not always possible to match the composition of the vaccine to the predominant strain of influenza virus in any given area and season). A meta-analysis of 12 studies evaluating efficacy and seroconversion after vaccination in patients with CLD showed that the seroconversion rate for the A/H1N1 strain was 80% and for the B strain was 87%. There was no effect on mortality reduction in the subgroups of vaccinated and unvaccinated cirrhotic

patients; however, a 27% reduction in hospitalizations was observed [21]. The vaccine is well tolerated, and the most common mild post-vaccination symptom is erythema at the vaccination site, a symptom that is not more common among patients with CLD than among controls.

COVID-19 vaccination

All patients with liver disease should be vaccinated against COVID-19 [22].

Patients with liver disease have about a three-fold higher risk of COVID-19-related death than those without liver disease, and the risk increases up to five-fold in patients with cirrhosis. In addition, 20-50% of patients with cirrhosis are more likely to develop complications or decompensation of liver function, such as ascites, encephalopathy, spontaneous peritonitis, esophageal variceal bleeding, or ACLF [23]. Currently, the predominant SARS-CoV-2 variants are much less pathogenic.

Most scholarly liver disease societies recommend that patients with chronic liver disease and those who have undergone liver transplantation receive a full COVID-19 vaccination and a booster dose.

Candidates for liver transplantation should, if possible, receive the COVID-19 vaccine before transplantation or three months after transplantation of this organ [24].

Vaccines are generally well tolerated, with the most common side effect being pain at the injection site. Documented serious side effects are very rare.

A recent prospective study of patients with cirrhosis or chronic liver disease who received two doses of mRNA-based vaccines showed adequate seroconversion rates (97% and 88-96%, respectively) [25].

Respiratory syncytial virus (RSV) vaccination

Patients with chronic liver disease receiving immunosuppressive therapy after liver transplantation represent a subgroup of patients predisposed to severe respiratory syncytial virus (RSV) infection. The course of this disease can range from mild cold symptoms to bronchitis, bronchiolitis, bronchopneumonia, shortness of breath, respiratory failure, and heart disorders. RSV infection increases the risk of hospitalization, mechanical ventilation, cardiovascular events (acute coronary syndrome, cardiac arrhythmias, exacerbation of cardiac failure), and death. Unfortunately, there is no causal treatment.

A breakthrough in the prevention of RSV infection came in 2023 when the European Medicines Agency (EMA) approved two RSV vaccines used in a one-dose regimen:

- recombinant with adjuvant; containing F-glycoprotein and adjuvant ASO1E to stimulate specific CD4 lymphocyte response, RSVPreF3 OA; recommended for the elderly: > 60 years of age,
- recombinant, containing glycoprotein F subtypes A and B in the pre-fusion conformation of RSVpreF; recommended for the elderly (over 65 years of age) and as effective passive protection for infants in the first six months of life through vaccination of pregnant women between 24 and 36 weeks of pregnancy [26, 27].

Currently, the results of registration clinical trials of vaccines are available, but further studies of the so-called *real life* and on particular subgroups of patients, e.g., after solid organ transplantation, are needed [28, 29]. The favorable safety profile of the vaccines has been confirmed. The formulations had a higher number of adverse vaccine reactions (AVRs) than the placebo, but these were mainly typical local and systemic AVRs of mild-to-moderate severity that resolved without treatment within a few days.

However, it appears that CLD patients over 60 years of age who are in the risk group for severe RSV infection may benefit from such vaccination.

On 21 June 2023, ACIP issued recommendations to consider vaccination against RSV among those over the age of 60. The decision to vaccinate a patient should be based on a discussion between the physician providing care and the patient [30].

Vaccination against shingles

The incidence of shingles among patients with CLD is low, but slightly higher than in the general population. The development of shingles is the result of reactivation of the varicella-zoster virus (VZV) after a previous case of chickenpox. VZV remains latent in the ganglion cells of the medulla and cranial nerve ganglia and is reactivated in the presence of favorable factors such as immunosuppression [31]. Risk factors predisposing to the development of shingles are:

- age over 50,
- cancers,
- autoimmune diseases,
- status after organ transplantation and bone marrow stem cell transplantation,
- chemotherapy, radiation therapy,
- immunomodulatory and immunosuppressive treatment,

- HIV infection and other acquired and congenital immunodeficiencies.

An inactivated, recombinant, adjuvanted two-dose zoster vaccine (RZV) is available for administration two months apart (the acceptable interval between doses is 1-6 months). This formulation was registered in 2017 by the US Food and Drug Administration (FDA) while in European countries it was registered by the European Medicines Agency (EMA) in 2018. Vaccination is recommended for people over the age of 50 and those over the age of 18 with an increased risk of contracting shingles; this is to prevent shingles and shingles neuralgia in people who have contracted chickenpox in the past. It is not necessary to test for a history of chickenpox before vaccination. The vaccine does not protect against contracting chickenpox.

Studies on the vaccine have shown:

- > 90% efficacy against herpes zoster in all groups ≥ 50 years,
- 91.2% efficacy in those aged ≥ 50 years and 88.8% in those aged ≥ 70 years against shingles neuralgia [32, 33].

The most commonly reported adverse reactions after vaccine administration are injection-site pain, muscle aches, fatigue, and headache.

Another herpes zoster vaccine contains live attenuated Oka VZV (live zoster vaccine – LVZ) and has been registered since 2006 in the United States for adults over the age of 60. However, LVZ is not recommended for use with patients suffering from chronic liver diseases [34].

Recombinant herpes zoster vaccination is recommended by the ACIP for CLD patients over the age of 50 and liver recipients and liver transplant recipients aged > 18 years [2].

Pneumococcal vaccination

Pneumococcal vaccination is recommended for patients with liver disease

Invasive pneumococcal disease (IPD) can manifest as sepsis, bacteremia, pneumonia, neuro- infection, or spontaneous bacterial peritonitis (SBP). The risk of invasive pneumococcal disease is two times higher among patients with CLD, especially after age 60, and mortality is high [35]. *Streptococcus pneumoniae* is the most common bacterial cause of pneumonia in this group of patients and the third most common cause of SBP after *Escherichia coli* and *Klebsiella* [36].

In recent years, the availability of pneumococcal vaccines has been variable. The ACIP guidelines should be adapted to the current vaccine market situation in a given country.

Three basic pneumococcal vaccines are available in the world:

- 13-valent conjugated vaccine (PCV13),
- 20-valent conjugated vaccine (since 2023, PCV20),
- 23-valent polysaccharide vaccine (PPSV23).

The latest ACIP recommendations, updated in 2023, consider different variations in vaccination schedules based on previous vaccinations and the preparations available in the country. These recommendations vary according to patient age groups and comorbidities, as shown in Tables 1 and 2 [37].

The effectiveness of the above vaccinations in hepatology patients is poorly studied, and clinical trials have been conducted on small numbers of patients. Implementation of pneumococcal vaccination in this patient group remains low (in one study, published in 2005, 39% of patients under the care of family physicians and 19% in specialized care were vaccinated) [5].

Table 1. Recommendations for pneumococcal vaccination for adults aged 19-64 years, additionally burdened by chronic conditions, i.e., alcoholism, chronic heart disease, chronic liver disease, chronic lung disease, including chronic obstructive pulmonary disease, emphysema, and asthma, smoking, or diabetes

Vaccination history	Vaccine available PCV20	Vaccines available PCV13 and PPSV23
No	1 dose of PCV20	First of all, PCV13, and after at least one year, PPSV23
PPSV23	After at least one year, administer one dose of PCV20	After at least one year, administer one dose of PCV13
PCV13	After at least one year, administer one dose of PCV20	After at least one year, administer one dose of PPSV23 It is essential to check the current recommendations when the patient reaches the age of 65 years or older
PCV13 and PPSV23	No additional vaccination doses It is essential to check the current recommendations when the patient reaches the age of 65 years or older	

Table 2. Pneumococcal vaccination recommendations for adults aged ⩾ 65 years with or without additional conditions (chronic renal failure, congenital or acquired lack of spleen, congenital or acquired immunodeficiency, generalized malignancy, HIV infection, Hodgkin's disease, iatrogenic immunosuppression (including diseases requiring treatment with immunosuppressive drugs such as long-term systemic corticosteroids and radiation therapy), leukemia, lymphoma, multiple myeloma, nephrotic syndrome, sickle cell anemia or other hemoglobinopathies, and solid organ transplantation)

Vaccination history	Without or with underlying diseases, ⩾ 65 years of age	Without underlying diseases, ⩾ 65 years of age	With underlying diseases, ⩾ 65 years of age
	Vaccine available PCV20	Vaccines available PCV13 and PPSV23	Vaccines available PCV13 and PPSV23
No	1 dose of PCV20	First of all, PCV13, and after at least one year, PPSV23	Administer a single dose of PCV13, then ⩾ 8 weeks after PCV13 administration, administer a single dose of PPSV23
PPSV23	After at least one year, administer one dose of PCV20	At least one year after PPSV23 vaccination, administer one dose of PCV13	Administer a single dose of PCV13 ⩾ 1 year after the last dose of PPSV23
PCV13	After at least one year, administer one dose of PCV20	At least one year after PCV13 vaccination, administer one dose of PPSV23	Administer a single dose of PPSV23 ⩾ 8 weeks after the last dose of PCV13
PCV13 and PPSV23 in any order, no additional dose of PPSV23 at age ⩾ 65 years	After at least 5 years from the last dose of PCV13 or PPSV23, administer one dose of PCV20	Administer a single dose of PPSV23 ⩾ 1 year after the last dose of PCV13 or ⩾ 5 years after the last dose of PPSV23	Administer a single dose of PPSV23 ⩾ 8 weeks after the last dose of PCV13 or ⩾ 5 years after the last dose of PPSV23
PCV13 and PPSV23 in any order and PPSV23 taken at age ⩾ 65 years	Physicians should work with patients to decide whether to administer a single dose of PCV20 to adults aged ⩾ 65 years who have already received PCV13 at any age and PPSV23 at age ⩾ 65 years. The interval should be ⩾ 5 years since the last dose of PCV13 or PPSV23	Not applicable	Not applicable

Other vaccinations

The vaccinations associated with travel medicine, recommended or mandatory for travelers arriving from other climate zones, are subject to the general rules of vaccination. Patients with liver disease should be offered a full pre-departure consultation with a specialist in travel medicine, who considers not only vaccine prophylaxis but also other aspects of preparing for a trip to tropical areas.

Vaccination against monkeypox or *Human papillomavirus* (HPV) is not routinely recommended to all adults, including patients with liver disease. The decision to administer such vaccinations should be taken on an individual basis, considering additional risk factors and epidemic situations.

Meningococcal and *Haemophilus influenzae* vaccinations are not included according to the ACIP for patients with CLD due to a lack of recommendations. However, for patients who are scheduled for splenectomy, such vaccinations should be considered.

Summary

In conclusion, prophylactic vaccination against various infectious diseases is extremely important for people with chronic liver disease (CLD), as it reduces the risk of mortality, complications, treatment failure, and exacerbation of the underlying disease. The main problem at present is the implementation of these vaccinations, mainly due to the lack of adequate communication and recommendations from attending physicians, including hepatologists, and the cost of the vaccines, which prevents many patients from taking advantage of this important form of prevention.

Disclosures

This research received no external funding.
Institutional review board statement: Not applicable.
The authors declare no conflict of interest.

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