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In 2017, the European Association for the Study of the Liver (EASL) released updated guidelines for hepatitis B virus (HBV) infection [122] and for HBV vaccination. [123, 124] In 2018, the EASL released updates for the management of decompensated cirrhosis [125] and hepatocellular carcinoma (HCC). [126] Recommendations from these guidelines are outlined below. All patients with e antigen (HBeAg)-positive or -negative chronic hepatitis B, defined by HBV DNA above 2,000 IU/mL, alanine aminotransferase (ALT) greater than the upper limit of normal (ULN), and/or at least moderate liver necroinflammation or fibrosis, should be treated. Patients with compensated or decompensated cirrhosis need treatment with any detectable HBV DNA level and regardless of ALT levels. Patients with HBV DNA >20,000 IU/ml and ALT greater than two times the ULN should start treatment regardless of the degree of fibrosis. Patients with HBeAg-positive chronic HBV infection, defined by persistently normal ALT and high HBV DNA levels, may be treated if they are older than 30 years regardless of the severity of liver histologic lesions. Patients with HBeAg-positive or HBeAg-negative chronic HBV infection and a family history of hepatocellular carcinoma (HCC) or cirrhosis and extrahepatic manifestations can be treated even if typical treatment indications are not fulfilled. Clinicians should vaccinate against chronic HBV in all unvaccinated adults at risk for infection, including the following: Adults at risk by sexual exposure (sex partners of hepatitis B surface antigen [HBsAg]-positive persons, sexually active persons who are not in a mutually monogamous relationship, persons seeking evaluation or treatment for a sexually transmitted infection, and men who have sex with men). Adults at risk by percutaneous or mucosal exposure to blood (adults who are recent or current users of injection drugs; household contacts of HBsAg-positive persons; residents and staff of facilities for developmentally disabled persons; incarcerated, healthcare, and public safety workers at risk for exposure to blood or blood-contaminated body fluids). Adults with chronic liver disease, including but not limited to hepatitis C virus infection, cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, and an ALT or aspartate aminotransferase (AST) level greater than twice the upper limit of normal. Adults with end-stage renal disease, including those receiving predialysis care, hemodialysis, peritoneal dialysis, and home dialysis. Adults with human immunodeficiency virus (HIV) infection. Pregnant women who are at risk for HBV infection during pregnancy (eg, having more than 1 sex partner during the previous 6 months, having been evaluated or treated for a sexually transmitted infection, recent or current injection drug use, or having an HBsAg-positive sex partner). International travelers to regions with high or intermediate levels of endemic HBV infection. Any adult seeking protection from HBV infection. Clinicians should screen (HBsAg, antibody to hepatitis B core antigen [anti-HBc], and antibody to hepatitis B surface antigen [anti-HBs]) for HBV in high-risk persons, including persons born in countries with 2% or higher HBV prevalence, men who have sex with men, persons who inject drugs, HIV-positive persons, household and sexual contacts of HBV-infected persons, persons requiring immunosuppressive therapy, persons with end-stage renal disease (including hemodialysis patients), blood and tissue donors, persons infected with hepatitis C virus, persons with elevated ALT levels (≥19 IU/L for women and ≥30 IU/L for men), incarcerated persons, pregnant women, and infants born to HBV-infected mothers. Clinicians should provide or refer all patients identified with HBV (HBsAg-positive) for posttest counseling and hepatitis B–directed care. In patients with decompensated cirrhosis, the etiologic factor, should be removed, particularly alcohol consumption and hepatitis B or C virus infection, as this strategy is associated with decreased risk of decompensation and increased survival. Strategies based on targeting abnormalities in the gut-liver axis by antibiotic administration (ie, rifaximin), improving the disturbed systemic circulatory function (ie, long-term albumin administration), decreasing the inflammatory state (ie, statins), and reducing portal hypertension (ie, beta blockers) have shown potential benefit to decrease cirrhosis progression in patients with decompensated cirrhosis. A diagnostic paracentesis is recommended in all patients with new-onset grade 2 or 3 ascites, or in those hospitalized for worsening of ascites or any complication of cirrhosis. Neutrophil count and culture of ascitic fluid (bedside inoculation blood culture bottles with 10 mL fluid each) should be performed to exclude bacterial peritonitis. A neutrophil count above 250 cells/μL is required to diagnose spontaneous bacterial peritonitis (SBP). Ascitic total protein concentration should be performed to identify patients at higher risk of developing SBP. The serum ascites albumin gradient (SAAG) should be calculated when the cause of ascites is not immediately evident, and/or when conditions other than cirrhosis are suspected. Cytology should be performed to differentiate malignancy-related from non-malignant ascites. Since the development of grade 2 or 3 ascites in patients with cirrhosis is associated with reduced survival, liver transplantation (LT) should be considered as a potential treatment option. A moderate restriction of sodium intake (80–120 mmol/day, corresponding to 4.6–6.9 g of salt) is recommended in patients with moderate, uncomplicated ascites. This is generally equivalent to a no-added-salt diet with avoidance of pre-prepared meals. Adequate nutritional education of patients on how to manage dietary sodium is also recommended. Diets with a very low sodium content (< 40 mmol/day) should be avoided, as they favor diuretic-induced complications and can endanger a patient’s nutritional status. Patients with the first episode of grade 2 (moderate) ascites should receive an anti-mineralocorticoid drug alone, starting at 100 mg/day with stepwise increases every 72 hr (in 100 mg steps) to a maximum of 400 mg/day if there is no response to lower doses. In patients who do not respond to anti-mineralocorticoids, as defined by a body weight reduction of less than 2 kg/wk, or in patients who develop hyperkalemia, furosemide should be added at an increasing stepwise dose from 40 mg/day to a maximum of 160 mg/day (in 40 mg steps). Patients with long-standing or recurrent ascites should be treated with a combination of an anti-mineralocorticoid drug and furosemide, the dose of which should be increased sequentially according to the response. Torasemide can be given in patients exhibiting a weak response to furosemide. During diuretic therapy, a maximum weight loss of 0.5 kg/day in patients without edema and 1 kg/day in patients with edema is recommended. Once ascites has largely resolved, the dose of diuretics should be reduced to the lowest effective dose. In patients presenting with gastrointestinal (GI) hemorrhage, renal impairment, hepatic encephalopathy, hyponatremia, or alterations in serum potassium concentration, these abnormalities should be corrected before starting diuretic therapy. In these patients, cautious initiation of diuretic therapy and frequent clinical and biochemical assessments should be performed. Diuretic therapy is generally not recommended in patients with persistent overt hepatic encephalopathy. Diuretics should be discontinued if severe hyponatremia (serum sodium concentration < 125 mmol/L), acute kidney injury (AKI), worsening hepatic encephalopathy, or incapacitating muscle cramps develop. Furosemide should be stopped if severe hypokalemia occurs (< 3 mmol/L). Anti-mineralocorticoids should be stopped if severe hyperkalemia occurs (>6 mmol/L). Albumin infusion or baclofen administration (10 mg/day, with a weekly increase of 10 mg/day up to 30 mg/day) is recommended in patients with muscle cramps. Large volume paracentesis (LVP) is the first-line therapy in patients with large ascites (grade 3 ascites), which should be completely removed in a single session. LVP should be followed with plasma volume expansion to prevent postparacentesis circulatory dysfunction (PPCD). In patients undergoing LVP greater than 5 L of ascites, plasma volume expansion should be performed by infusing albumin (8 g/L of ascites removed), as it is more effective than other plasma expanders, which are not recommended for this setting In patients undergoing LVP less than 5 L of ascites, the risk of developing PPCD is low. However, it is generally agreed that these patients should still be treated with albumin because of concerns about use of alternative plasma expanders. Nonsteroidal anti-inflammatory drugs should not be used in patients with ascites because of the high risk of developing further sodium retention, hyponatremia, and AKI. Repeated LVP plus albumin (8 g/L of ascites removed) is recommended as first-line treatment for refractory ascites. Diuretics should be discontinued in patients with refractory ascites who do not excrete >30 mmol/day of sodium under diuretic treatment. Antibiotic prophylaxis is recommended in cirrhotic patients with acute GI bleeding because it reduces the incidence of infections and improves control of bleeding and survival. Treatment should be initiated on presentation of bleeding and continued for up to 7 days. Ceftriaxone (1 g/24 hr) is the first choice in patients with decompensated cirrhosis, those already on quinolone prophylaxis, and in hospital settings with high prevalence of quinolone-resistant bacterial infections. Oral quinolones (norfloxacin 400 mg bid) should be used in the remaining patients. Vaccination against hepatitis B reduces the risk of HCC and is recommended for all newborns and high-risk groups. In patients with chronic hepatitis, antiviral therapies leading to maintained HBV suppression in chronic hepatitis B and sustained viral response in hepatitis C are recommended, since they have been shown to prevent progression to cirrhosis and HCC development. Once cirrhosis is established, antiviral therapy is beneficial in preventing cirrhosis progression and decompensation. Furthermore, successful antiviral therapy reduces but does not eliminate the risk of HCC development. Antiviral therapies should follow the EASL guidelines for management of chronic hepatitis B and C infection. Coffee consumption has been shown to decrease the risk of HCC in patients with chronic liver disease. In these patients, coffee consumption should be encouraged. Diagnosis of HCC in cirrhotic patients should be based on noninvasive criteria and/or pathology. In noncirrhotic patients, diagnosis of HCC should be confirmed by pathology. Noninvasive criteria can only be applied to cirrhotic patients for nodule(s) ≥1 cm, in light of the high pretest probability and are based on imaging techniques obtained by multiphasic computed tomography (CT), dynamic contrast-enhanced magnetic resonance imaging (MRI), or contrast-enhanced ultrasound (CEUS). Diagnosis is based on the identification of the typical hallmarks of HCC, which differ according to imaging techniques or contrast agents (arterial phase hyperenhancement (APHE) with washout in the portal venous or delayed phases on CT and MRI using extracellular contrast agents or gadobenate dimeglumine, APHE with washout in the portal venous phase on MRI using gadoxetic acid, APHE with late-onset (>60 s) washout of mild intensity on CEUS). Because of their higher sensitivity and the analysis of the whole liver, CT or MRI should be used first. Fluorodeoxyglucose (FDG)-positron emission tomography (PET) scan is not recommended for early diagnosis of HCC because of the high rate of false-negative cases. In patients at high risk of developing HCC, nodule(s) less than 1 cm in diameter detected by ultrasound should be followed at ≤4-month intervals in the first year. If there is no increase in the size or number of nodules, surveillance could be returned to the usual 6-month interval thereafter. In cirrhotic patients, diagnosis of HCC for nodules of ≥1 cm in diameter can be achieved with noninvasive criteria and/or biopsy-proven pathologic confirmation. Repeated bioptic sampling is recommended in cases of inconclusive histologic or discordant findings, or in cases of growth or change in enhancement pattern identified during follow-up, but with imaging still not diagnostic for HCC. Staging systems for clinical decision making in HCC should include tumor burden, liver function, and performance status. Multiphasic contrast-enhanced CT or MRI is recommended for assessment of response after resection, locoregional, or systemic therapies. Perioperative mortality of liver resection (LR) in cirrhotic patients should be less than 3%. LR is recommended for a single HCC lesion of any size and in particular for tumors >2 cm, when hepatic function is preserved, and when sufficient remnant liver volume is maintained. Tumor vascular invasion and extrahepatic metastases are an absolute contraindication for liver transplantation in HCC. Thermal ablation with radiofrequency is the standard of care for patients with BCLC (Barcelona Clinic Liver Cancer) 0 and A tumors not suitable for surgery. Thermal ablation in single tumors 2 to 3 cm in size is an alternative to surgical resection based on technical factors (location of the tumor) and hepatic and extrahepatic patient conditions. In patients with very early stage HCC (BCLC-0), radiofrequency ablation in favorable locations can be adopted as first-line therapy even in surgical patients. Ethanol injection is an option in some cases where thermal ablation is not technically feasible, especially in tumors < 2 cm. Combination atezolizumab and bevacizumab is first-line systemic therapy for HCC. For patients with contraindications to this regimen or with progression of disease on this regimen, alternative first-line/second-line therapy with sorafenib or lenvatinib can be offered. Sorafenib was previously the standard first-line systemic therapy for HCC. It is indicated for patients with well-preserved liver function (Child-Pugh A) and with advanced tumors (BCLC–C) or earlier stage tumors progressing upon or unsuitable for locoregional therapies. Lenvatinib has been shown to be non-inferior to sorafenib. It is indicated for patients with well-preserved liver function (Child-Pugh A class), with good performance status, and with advanced tumors – BCLC-C without main portal vein invasion or tumors progressing upon or unsuitable for locoregional therapies. Following first-line therapy with either sorafenib or lenvatinib or in patients who did not have access to atezolizumab-bevacizumab, second-line therapy with regorafenib, cabozantinib, nivolumab (with or without ipilimumab), or pembrolizumab can be offered. [127] Outcome of COVID-19 in Patients With Autoimmune Hepatitis: An International Multicenter Study. Efe C, Dhanasekaran R, Lammert C, Ebik B, Higuera-de la Tijera F, Aloman C, Rıza Calışkan A, Peralta M, Gerussi A, Massoumi H, Catana AM, Torgutalp M, Purnak T, Rigamonti C, Gomez Aldana AJ, Khakoo N, Kacmaz H, Nazal L, Frager S, Demir N, Irak K, Ellik ZM, Balaban Y, Atay K, Eren F, Cristoferi L, Batıbay E, Urzua Á, Snijders R, Kıyıcı M, Akyıldız M, Ekin N, Carr RM, Harputluoğlu M, Hatemi I, Mendizabal M, Silva M, Idilman R, Silveira M, Drenth JPH, Assis DN, Björnsson E, Boyer JL, Invernizzi P, Levy C, Schiano TD, Ridruejo E, Wahlin S. Efe C, et al. Hepatology. 2021 Jun;73(6):2099-2109. doi: 10.1002/hep.31797. Hepatology. 2021. PMID: 33713486 Free PMC article. AASLD develops evidence-based practice guidelines and practice guidances which are updated regularly by a multi-disciplinary panel of experts, including hepatologists, and include recommendations of preferred approaches to the diagnostic, therapeutic, and preventive aspects of care. Acute Liver Failure, Management Acute-on-Chronic Liver Failure and the Management Alcohol-Associated Liver Disease Ascites, Spontaneous Bacterial Peritonitis and Hepatorenal Syndrome, Management Autoimmune Hepatitis, Management Drug, Herbal, and Dietary Supplement-induced Liver Injury Hemochromatosis, Management Hepatic Encephalopathy Hepatitis B, Chronic Hepatitis C, Guidance Hepatocellular Carcinoma, Management Liver Biopsy Liver Transplantation, Evaluation of the Adult Patient Liver Transplantation, Evaluation of the Pediatric Patient Long-Term Management of the Adult Liver Transplant AASLD strives to review and update its practice guidelines every five (5) years, as necessary. Users are cautioned that in the interim, scientific and medical developments may supersede or invalidate, in whole or in part, specific recommendations in any guideline. A guideline is considered to be "inactive" if it has not been updated by AASLD in at least five (5) years, and for this reason particular care must be exercised in placing reliance on an inactive guideline. AASLD commissions and provides financial support for the formulation and production of practice guidelines/guidances by volunteer experts. Financial support from commercial entities or the pharmaceutical industry is not accepted for the development of AASLD practice guidelines. As a library, NLM provides access to scientific literature. Inclusion in an NLM database does not imply endorsement of, or agreement with, the contents by NLM or the National Institutes of Health. Learn more: PMC Disclaimer | PMC Copyright Notice . Author manuscript; available in PMC: 2019 Apr 1. Published in final edited form as: Hepatology. 2018 Apr;67(4):1560–1599. doi: 10.1002/hep.29800 This AASLD 2018 Hepatitis B Guidance is intended to complement the AASLD 2016 Practice Guidelines for Treatment of Chronic Hepatitis B (1) and update the previous hepatitis B virus (HBV) guidelines from 2009. The 2018 updated guidance on chronic hepatitis B (CHB) includes (i) updates on treatment since the 2016 HBV guideline (notably the use of tenofovir alafenamide) and guidance on (ii) screening, counseling, and prevention; (iii) specialized virologic and serologic tests; (iv) monitoring of untreated patients; and (v) treatment of hepatitis B in special populations, including persons with viral coinfections, acute hepatitis B, recipients of immunosuppressive therapy, and transplant recipients. The AASLD 2018 Hepatitis B Guidance provides a data-supported approach to screening, prevention, diagnosis, and clinical management of patients with hepatitis B. It differs from the published 2016 AASLD guideline which conducted systematic reviews and used a multidisciplinary panel of experts to rate the quality (level) of the evidence and the strength of each recommendation using the Grading of Recommendations Assessment, Development and Evaluation system in support of guideline recommendations (1–4). In contrast, this guidance document was developed by consensus of an expert panel, without formal systematic review or use of the Grading of Recommendations Assessment, Development, and Evaluation system. The 2018 guidance is based upon the following: (i) formal review and analysis of published literature on the topics; (ii) World Health Organization guidance on prevention, care, and treatment of persons with CHB (5); and (iii) the authors’ experience in acute hepatitis B and CHB. Intended for use by health care providers, this guidance identifies preferred approaches to the diagnostic, therapeutic, and preventive aspects of care for patients with CHB. As with clinical practice guidelines, it provides general guidance to optimize the care of the majority of patients and should not replace clinical judgement for a unique patient. This guidance does not seek to dictate a “one size fits all” approach for the management of CHB. Clinical considerations may justify a course of action that differs from this guidance. Since the publication of the 2016 AASLD Hepatitis B Guideline, tenofovir alafenamide (TAF) has been approved for treatment of CHB in adults. Tenofovir alafenamide joins the list of preferred HBV therapies, along with entecavir, tenofovir disoproxil fumarate (TDF), and peginterferon (peg-IFN) (Tables 1 and 2) (6–16) (section: Updated Recommendations on the Treatment of Patients With Chronic Hepatitis B). Approved Antiviral Therapies in Adults and Children Drug Dose in Adults1 Use in Children1 Pregnancy Category2 Potential Side Effects2 Monitoring on Treatment3 Preferred Peg-IFN-α-2a(adult)IFN-α-2b(children) 180 mcg weekly ≥1 yeardose: 6 million IU/m2 three times weekly4 C Flu-like symptoms, fatigue, mood disturbances, cytopenia, autoimmune disorders in adults, anorexia and weight loss in children Complete blood count (monthly to every 3 months)TSH (every 3 months)Clinical monitoring for autoimmune, ischemic, neuropsychiatric, and infectious complications Entecavir 0.5 mg daily5 ≥2 yearsdose: weight-based to 10–30 kg; above 30 kg: 0.5 mg daily5 C Lactic acidosis (decompensated cirrhosis only) Lactic acid levels if there is clinical concernTest for HIV prior to treatment initiation Tenofovir dipovoxil fumarate 300 mg daily ≥12 years B Nephropathy, Fanconi syndrome, osteomalacia, lactic acidosis Creatinine clearance at baselineIf at risk for renal impairment, creatinine clearance, serum phosphate, urine glucose and protein at least annuallyConsider bone density study at baseline and during treatment in patients with history of fracture or risks for osteopeniaLactic acid levels if there is clinical concernTest for HIV prior to treatment initiation Tenofovir alafenamide 25 mg daily -- There are insufficient human data on use during pregnancy to inform a drug-associated risk of birth defects and miscarriage Lactic acidosis Lactic acid levels if clinical concernAssess serum creatinine, serum phosphorus, creatinine clearance, urine glucose, and urine protein prior to initiating and during therapy in all patients as clinically appropriateTest for HIV prior to treatment initiation Non-Preferred Lamivudine 100 mg daily ≥2 yearsdose: 3 mg/kg daily to max 100 mg C PancreatitisLactic acidosis Amylase if symptoms are presentLactic acid levels if there is clinical concernTest for HIV prior to treatment initiation Adefovir 10 mg daily ≥12 years C Acute renal failureFanconi syndromeLactic acidosis Creatinine clearance at baselineIf at risk for renal impairment, creatinine clearance, serum phosphate, urine glucose, and urine protein at least annuallyConsider bone density study at baseline and during treatment in patients with history of fracture or risks for osteopeniaLactic acid levels if clinical concern Telbivudine 600 mg daily -- B Creatine kinase elevations and myopathyPeripheral neuropathyLactic acidosis Creatine kinase if symptoms are presentClinical evaluation if symptoms are presentLactic acid levels if there is clinical concern Efficacy of Approved First-Line Antiviral Therapies in Adults with Treatment-Naïve Chronic Hepatitis B and Immune-Active Disease (Not Head-to-Head Comparisons) HBeAg Positive Peg-IFN1 Entecavir2 Tenofovir Disoproxil Fumarate2 Tenofovir Alafenamide3 % HBV DNA suppression (cutoff to define HBV DNA suppression)4 30–42 (