

# 2023

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# Year in Review

**CLDF**

*Chronic Liver Disease Foundation*

*Unparalleled expertise,  
unprecedented access*

# Letter from the President

The Chronic Liver Disease Foundation (CLDF), a distinguished not-for-profit educational organization, proudly commemorates its 22nd anniversary. Guided by an all-volunteer board of trustees, the CLDF has consistently excelled in the field, offering outstanding educational programs covering comprehensive updates on liver disease.

A recent highlight in liver education is the evolution of the Liver Connect meeting. Following the success of the 3rd annual Liver Connect Conference, which educated over 550 live attendees and 999 virtual learners to date, we eagerly anticipate the 4th Annual CLDF Liver Connect Conference to be held in Scottsdale, Arizona, in April.

As the flagship educational CLDF conference, Liver Connect showcases worldwide experts, delivering cutting-edge educational presentations in an interactive format. Distinguished hepatologists spearhead educational content development, including emerging data from recent publications and congress abstracts, influencing current diagnostic and management approaches. Specialized sessions centered on NASH, cirrhosis, HBV-HDV, and women with liver disease deliver the most up-to-date and crucial information in these areas.

As an organization, the CLDF continues to provide state-of-the-art education to all stakeholders. Live events, broadcasts, and enduring webcasts grant healthcare providers nationwide the opportunity to learn from esteemed specialists. Practical clinical guidelines and algorithms offer valuable insights for managing patients. The collaboration of ambassadors and advisors in guiding educational initiatives has solidified the CLDF's position as an unparalleled organization for over two decades.

The dedication and expertise of our program staff, CME-accredited providers, and network of collaborators have propelled the organization through another thriving year of impactful initiatives in 2023. The CLDF remains committed to delivering exceptional education in 2024, thanks to the unwavering support and contributions of all involved.

Our heartfelt gratitude extends to everyone who has contributed to making the CLDF the outstanding entity it has become.

Sincerely,

Zobair M. Younossi, MD, MPH

President and Chairman, CLDF Board of Trustees

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Marcelo Kugelmas, MD	

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# *2023 Programs*

**Cholestatic Liver Disease**

**Cirrhosis**

**Hepatorenal Syndrome**

**HCC**

**NAFLD/NASH**

**Pediatric Liver Disease**

**Viral Hepatitis**



# 3<sup>RD</sup> ANNUAL LIVER C-CONNECT CONFERENCE

12 live activities  
12.75 CME AMA PRA credits

Educated over  
**550** live  
attendees and  
**>1,000** virtual  
learners to date.



Accredited by



Presented by



# HCV Webcast and Podcast

## HCV 101 – Confidently Treat HCV in any Setting

*Anthony Martinez, MD & Tipu V. Khan, MD*

**ACCESS PODCAST**



*June 2023*

## HCV Elimination Starts With You: A Call to Action for all Healthcare Providers

*Pierre M. Gholam, MD & Marina Roytman, MD*

**VIEW WEBCAST**



*June 2023*

# NASH to PATHway Treatment

Friday, January 6, 2023

This activity is jointly provided by Medical Education Resources and the Chronic Liver Disease Foundation



Supported by an educational grant from Novo Nordisk, Inc.



## Faculty



**Michael Charlton, MBBS, FRCP**  
University of Chicago  
Chicago, Illinois, USA



**Rohit Loomba, MD, MHSc**  
University of California San Diego  
San Diego, California, USA



**Maru E. Rinella, MD**  
University of Chicago  
Chicago, Illinois, USA

This symposium reviewed the pathophysiology, risk factors, clinical consequences, and guidelines for diagnosing and treating NAFLD/NASH.

Relevant advances and challenges in diagnosing and treating NASH and liver fibrosis, including the latest NASH screening guidelines.

Novel agents in development for the treatment of NASH were highlighted during this enlightening symposium.



# Introducing Recent HRS-AKI Advances into **Clinical Care**



Marcelo Kugelmas, MD



Nikolaos T. Pylsopoulos, MD, PhD

**VIEW NOW**

***Introducing Recent HRS-AKI  
Advances into Clinical Care***

*Nikolaos T. Pylsopoulos, MD, PhD  
Marcelo Kugelmas, MD*

[https://chronicliverdisease.org/webcasts/special\\_event/HRS-AKI-Sympo23/](https://chronicliverdisease.org/webcasts/special_event/HRS-AKI-Sympo23/)

# 2023 NEW ADVANCES IN HRS/AKI

CLINICAL UPDATE AND EXPERT  
RECOMMENDATIONS

This activity is jointly provided by Medical Education Resources  
and the Chronic Liver Disease Foundation.



Supported by an educational grant from Mallinckrodt Pharmaceuticals.

This ongoing series defines the prevalence, manifestations, and pathophysiology of Hepatorenal Syndrome (HRS) and reviews the diagnosis and management of Acute Kidney Injury in cirrhosis. The program discussions encompass updated HRS guidelines and recommendations, treatment goals in HRS, and the unmet treatment needs for HRS in the United States.

30

Meetings across the US

20

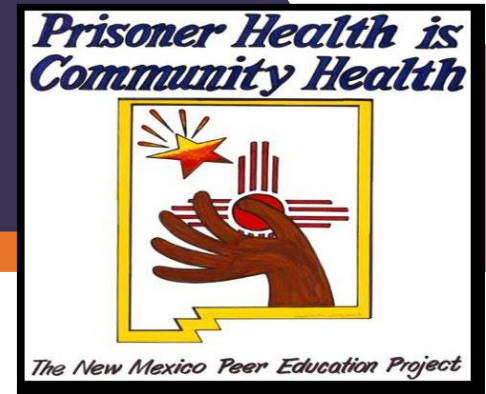
CLDF faculty participants

718

Attendees educated

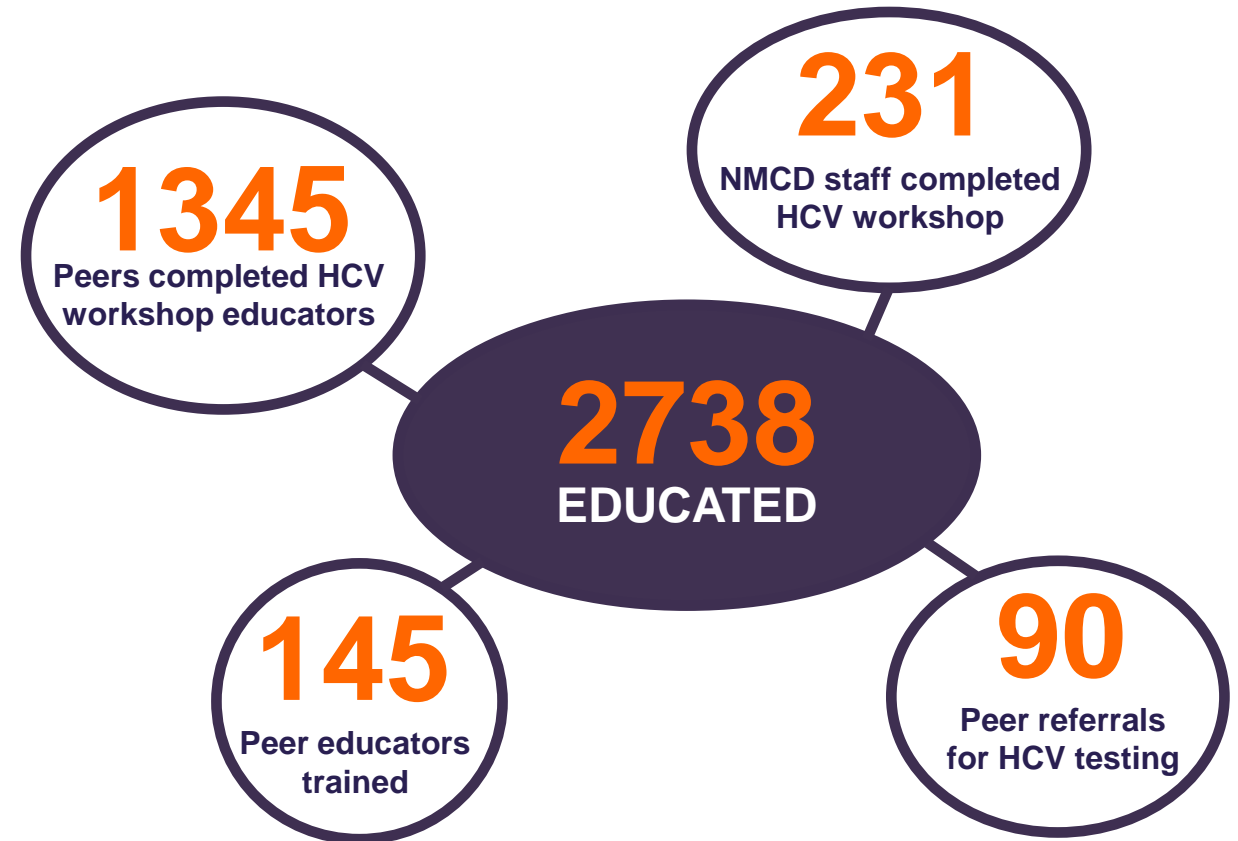


# 2023 Highlights CLDF & Project ECHO Collaboration Accomplishments:



The CLDF and The New Mexico Peer Education Project (NMPEP), continued collaborating with Project ECHO at the University of New Mexico Health Sciences Center and the New Mexico Corrections Department, leveraging the ECHO Model to make a powerful and lasting intervention in prison community health.

Supported by an educational grant from AbbVie.



# CLDF Education Portal

## Online Tools – Featured Resources

**CLDF**  
Chronic Liver Disease Foundation

# HEADLINE VIEWS™

Recently Published Abstracts  
on Chronic Liver Disease

Headline Views™ is a free service of CLDF for Healthcare Professionals.

Published December 2023

Improving Outcomes in Hepatorenal Syndrome - Acute Kidney Injury with Early Diagnoses and Implementation of Approved Treatment Regimens

**ACCESS NOW**

Credit Designation:  
1.0 AMA PRA Category 1 Credit™

**NEW FEATURES & UPDATED RESOURCES!**

**CLDF HCC CARE CASCADE DECISION SUPPORT TOOL**

NOVEMBER 2023 **LEARN MORE**

*Gastroenterology & Hepatology, Volume 19, Issue 9*  
*Published September 2023*

IMPROVING THE MANAGEMENT OF HEPATORENAL SYNDROME-ACUTE KIDNEY INJURY USING AN UPDATED GUIDANCE AND A NEW TREATMENT PARADIGM

**VIEW NOW**

**PUBLISHED JULY 2023**  
*American Journal of Health-System Pharmacy*

EXPERT PERSPECTIVES FOR THE PHARMACIST ON FACILITATING AND IMPROVING THE USE OF ALBUMIN IN CIRRHOSIS

**VIEW NOW**

**PUBLISHED JUNE 2023**  
*Digestive Disease and Sciences*

DIAGNOSIS AND MANAGEMENT OF HEPATITIS DELTA VIRUS INFECTION

**VIEW NOW**

HCV Elimination Starts With You: A Call to Action for all Healthcare Providers

*Pierre M. Gholam, MD & Marina Roylman, MD*

**VIEW WEBCAST**

June 2023

**HCV 101 – Confidently Treat HCV in any Setting**

*Anthony Martinez, MD & Tipu V. Khan, MD*

**ACCESS PODCAST**

June 2023

**PUBLISHED MAY 2023**  
*Hepatology Communications*

WILSON DISEASE: A SUMMARY OF THE UPDATED AASLD PRACTICE GUIDANCE

**VIEW NOW**

**VIEW NOW**

**An Up-To-Date Algorithm for the Treatment of PBC**

*Published in The American Journal of Gastroenterology Feb 2023*

Addressing Health Outcomes and Rising Costs in the Management of Chronic Liver Disease/Cirrhosis

June 2022

**VIEW NOW**

**VIEW NOW**

**Interactive Expert Perspectives from CLDF on the AASLD Guidelines, HRS**

Chronic Liver Disease Foundation

# LIVER CONNECT

National Annual Conference

**LEARN MORE**

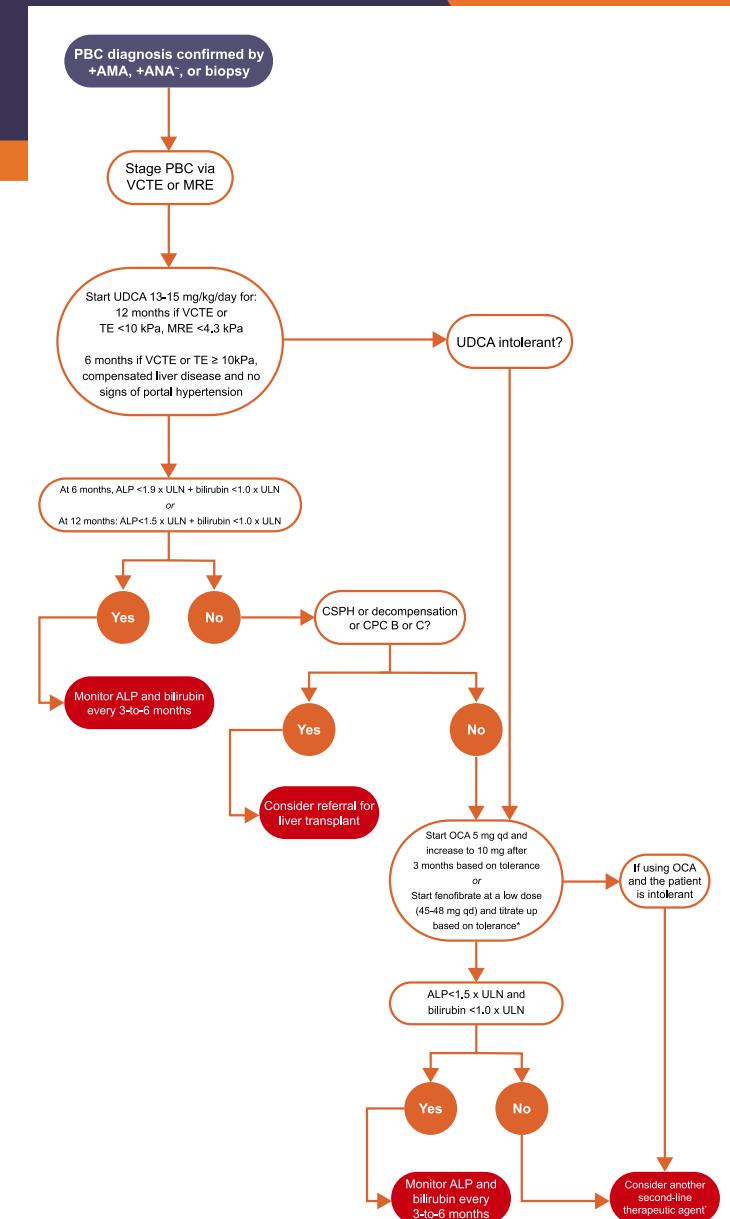


# An Up-To-Date Algorithm for the Treatment of PBC

Published in the American Journal of Hepatology Feb 2023

The key features of the algorithm include new guidance-informed suggestions for staging PBC using noninvasive testing (NIT), earlier assessment of lower thresholds to gauge ursodeoxycholic acid (UDCA) response after initiation of therapy, possible earlier initiation of second-line therapy with obeticholic acid (OCA) at lower levels of alkaline phosphatase (ALP) or bilirubin, avoidance of OCA in patients with cirrhosis complicated by portal hypertension or liver decompensation, and the safety and durability of response with long-term OCA therapy and off-label use of fibrates.

Unrestricted education grant supported by Intercept



# HCC Care Cascade Decision-Support Tool

**NEW FEATURES &  
UPDATED RESOURCES!**

**CLDF HCC CARE CASCADE  
DECISION SUPPORT TOOL**

**NOVEMBER 2023**

**LEARN MORE**

[https://www.chronicliverdisease.org/disease\\_focus/hcc.cfm?dstate=hcc&sec=Algorithm](https://www.chronicliverdisease.org/disease_focus/hcc.cfm?dstate=hcc&sec=Algorithm)

Supported by educational grants from AstraZeneca and Exelixis, Inc.

## HCC Care Cascade

➤ Clinical Question

### HCC Care Cascade in Adults

? What is your clinical question?

Screening Guidance

LI-RADS Interpretation & Follow Up Recommendation

Staging & Treatment Guidance

Search for Liver Transplant Centers and associated Services, Providers, Treatments, Clinical Trials, Contact and Referral Information, Insurance Coverage

Search for Industry Sponsored Patient Assistance Programs

Useful HCC Calculator/Resource Center

# *Publications*

# The use of current knowledge and non-invasive testing modalities for predicting at-risk non-alcoholic steatohepatitis and assessing fibrosis

## Liver International

Feb.  
2023

Received: 1 December 2022 | Revised: 7 February 2023 | Accepted: 20 February 2023  
DOI: 10.1111/liv.15555

**REVIEW**

### The use of current knowledge and non-invasive testing modalities for predicting at-risk non-alcoholic steatohepatitis and assessing fibrosis

Marcelo Kugelmas<sup>1</sup> | Mazen Nouredin<sup>2</sup> | Nadege Gunn<sup>3</sup> | Kimberly Brown<sup>4</sup> | Zobair Younossi<sup>5</sup> | Manal Abdelmalek<sup>6</sup> | Naim Alkhoury<sup>7</sup>

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**KEYWORDS:** At-risk, non-alcoholic steatohepatitis, non-invasive testing

**1 | INTRODUCTION**

Non-alcoholic fatty liver disease (NAFLD) is defined as the presence of steatosis in  $\geq 5\%$  of hepatocytes, without significant alcohol consumption or other known causes of steatosis.<sup>1</sup> NAFLD is subdivided into two primary subtypes, the fairly benign non-alcoholic fatty liver (NAFL) and the more severe, progressive form termed

**3 | NITs TO DETERMINE FIBROSIS STAGE AND PREDICT MAJOR ADVERSE LIVER OUTCOMES (MALOs) IN NAFLD**

**3.1 | Staging fibrosis in NAFLD**

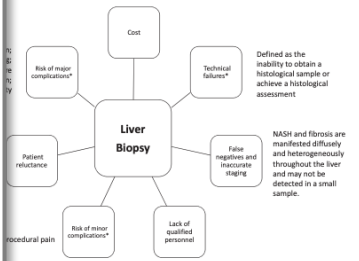
One of the necessary steps in assessing patients with NAFLD and NASH is to determine their fibrosis stage.<sup>30</sup> Given that liver biopsies are impractical given the large number of NAFLD patients and are associated with many other limitations (Figure 1), several NITs are becoming widely used for this purpose. A brief review of wet NITs is provided in Table 1,<sup>31-37</sup> and a detailed overview of dry NITs is presented in Table 2.<sup>38</sup>

With regard to wet NITs, the Fibrosis-4 index (FIB-4) and NAFLD fibrosis score (NFS) (Table 1) are the most extensively utilized. FIB-4 and NFS have been highlighted in the AASLD guidance document as 'clinically useful tools for identifying patients with NAFLD with

and/or NAS  $\geq 4$ ) must be identified early in the disease course.<sup>12</sup> In the USA, approximately 4.5 million people might have advanced fibrosis related to NASH<sup>43</sup> but unfortunately, go unrecognized. Most patients with end-stage liver disease secondary to NASH have died. This is related to the lack of available liver transplantation. This is related to the lack of available liver transplantation. This is related to the lack of available liver transplantation.

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with liver biopsies. In a systematic review and meta-analysis of 30 studies that report complications resulting from 64 356 percutaneous liver biopsy procedures in patients with chronic liver disease, the incidence of major complications was 2.44% (95% CI: 0.85–6.75), including hospitalization in 0.65% (95% CI: 0.38–1.11), major bleeding in 0.48% (95% CI: 0.22–1.06), moderate/severe pain in 0.34% (95% CI: 0.08–1.37) and with mortality in 0.01% (95% CI: 0.00–0.11). Approximately, 1 in 10 patients experienced post-procedural pain or other minor complications. Technical failure, which is the inability to obtain a histological sample or achieve a histological assessment, may occur in approximately 1% of liver biopsy procedures.<sup>39</sup>

**3.6 | MRI (MAST) score**

The NITs detail but do not include commonly used pre-clinical trials. N which incorporate proven better respectively, to external validation cohorts was alanine aminotransferase concentrations. patients whose NIS4 value was having at-risk NASH (ruled out sensitivity, 63.0% (95% CI: 57.8–68.2) (95% CI: 72.5–82.4), whereas 100% (95% CI: 83.1–90.3) specificity, and a positive predictive value of 0.2. The authors concluded that non-invasively rule in or rule out alcoholic risk factors and suspected

**3.7 | Multicenter**

iron-corrected rich biomarkers to clinical trial participants with

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# Wilson disease: A summary of the updated AASLD Practice Guidance

## Hepatology Communications

May  
2023

**REVIEW**

**OPEN**

### Wilson disease: a summary of the updated AASLD Practice Guidance

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**Abstract**  
 Wilson disease (WD) is caused by autosomal variants affecting the *ATP7B* gene on chromosome 13, resulting in alterations in physiological copper homeostasis and copper accumulation. Excess copper clinically manifests in many organs, most often in the central nervous system and liver, ultimately causing cirrhosis and death. Often considered a pediatric or young adult disease, WD actually affects patients of all ages, and aging patients need to be regularly managed with long-term follow-up. Despite over a century of advances in diagnosis and treatment, WD is still associated with diagnostic challenges and considerable disability and death, in part due to delays in diagnosis and limitations in treatment. Standard-of-care treatments are considered generally effective when the diagnosis is timely but are also limited by efficacy, safety concerns, multiple daily dosing, and adherence. This expert perspective review seeks to facilitate improvements in the awareness, understanding, diagnosis, and management of WD. The objectives are to provide a full overview of WD and streamline updated diagnosis and treatment guidance, as recently published by the American Association for the Study of Liver Diseases, in a practical way for clinical use.

**INTRODUCTION**  
 Wilson disease (WD) is a pediatric and adult liver disease first described in 1912 by Kinneir Wilson as "progressive lenticular degeneration."<sup>1</sup> WD is a genetic disease of copper metabolism<sup>2</sup> that demonstrates an autosomal recessive pattern of inheritance. Excess copper accumulates in various body tissues and, if left untreated, may cause several systemic manifestations, including central nervous system dysfunction, acute/chronic liver disease, cirrhosis, and ultimately, death. Despite over a century of significant advances in "progressive lenticular degeneration,"<sup>1</sup> WD is a genetic disease of copper metabolism<sup>2</sup> that demonstrates an autosomal recessive pattern of inheritance. Excess copper accumulates in various body tissues and, if left untreated, may cause several systemic manifestations, including central nervous system dysfunction, acute/chronic liver disease, cirrhosis, and ultimately, death. Despite over a century of significant advances in diagnosis and treatment, WD is still associated with considerable disability and death. Several factors may contribute to this, including the rarity of the disease; multisystemic involvement; clinical heterogeneity, which is reflected until their acute clinical associated with WD typically nonimmune (Coombs negative) coagulopathy, ascites, pruritus, altered ratios of alkaline phosphatase (<1.4) and aspartate aminotransferase (>2.2), and dysfunction.<sup>3,26</sup> Without liver rates of ALF due to WD

**Abbreviations:** AE, adverse event; APL, autoimmune hepatitis; ALF, acute liver failure; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; AASLD, American Association for the Study of Liver Diseases; INR, international normalized ratio; KF, Kayser-Fleischer; MCV, mean corpuscular volume; NCC, nonceruloplasmin copper; qd, once-daily; UWD/RS, United WD Rating Scale; WD, Wilson disease; WBC, white blood cell count.

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**WILSON DISEASE**

**TABLE 2** WD diagnostic recommendations for patients presenting to hepatology/gastroenterology practices

Neurological: Dysarthria, Dysphagia and excessive salivation, Declining performance at work or school, Rigidity and intention tremors, Gait disturbance, chorea, and rigidity, Mask-like face and rhus nodules, Migraine headaches, Insomnia, Seizures.

Psychiatric: Mood or behavior changes, Depression, Anxiety.

Ocular: Kayser-Fleischer (KF) rings, Sunflower cataracts.

Cardiac: Cardiomyopathy, Arrhythmias, Atrial fibrillation.

Renal: Fanconi syndrome (aminoaciduria, phosphaturia, mucopolysacchariduria, and defective urinary acidification), Muscle weakness secondary to hypokalemia, Hypouricemia, Nephrolithiasis.

Hematologic: Coombs-negative hemolysis, Spherocytosis, Hematuria, Hemoglobinuria, Thrombocytopenia and leukopenia with hyperplasia.

Hepatic: Asymptomatic (normal) or symptomatic (elevated liver enzymes), Liver disease with hepatocellular signs or cholestatic/cholelithiasis of liver failure.

Manifestations of WD impact on several organ systems.<sup>3,20-24</sup> Abbreviation: WD, Wilson disease.

ected until their acute clinical associated with WD typically nonimmune (Coombs negative) coagulopathy, ascites, pruritus, altered ratios of alkaline phosphatase (<1.4) and aspartate aminotransferase (>2.2), and dysfunction.<sup>3,26</sup> Without liver rates of ALF due to WD

al manifestations of WD are characteristically manifest at <20 or later. A less common but sic of WD is the "face of the im MRI), comprising increased [8] However, this is only found neurological presentation.<sup>20</sup> commonly include Kayser-ich are usually seen as a peripheral cornea caused by copper on the inner surface of net membrane.<sup>28</sup> KF rings are patients with neurological d absent in ~60% of patients [13,29,30] Sunflower cataracts, in newly diagnosed patients, are considered a very rare manifestation of WD. These cataracts resemble a sunflower with thin, centralized opacification located under the anterior capsule, and secondary opacifications arranged in ray-like structures around it. Sunflower cataracts do not affect visual acuity and are typically reversible after treatment.<sup>29</sup>

Sex-specific considerations

Three studies on patients with WD, detailed in Table 1, [44-46] consistently found that hepatic symptoms are slightly more predominant in female patients (57%), whereas neurological symptoms are more predominant in male patients (60%).<sup>44-46</sup> Female patients with WD are more likely to develop ALF than male

Copper parameters	Histological features	Differential diagnosis
• Low or mildly low ceruloplasmin (between 14 and 20 mg/dL)	Normal liver histology	Not applicable
• Mildly increased 24 h urinary excretion of copper (>40 µg/24 h)		
• Increased NCC		
• Increased hepatic copper (> 75 µg/g)		
• Low or normal ceruloplasmin	Acute or chronic inflammatory infiltrate	
• Increased 24 h urinary excretion of copper (> 100 µg/24 h)		
• Increased NCC		
• Increased hepatic copper (> 250 µg/g)		
• Low ceruloplasmin (< 14 mg/dL)	Hepatocyte steatosis, mainly macrovesicular	
• Increased 24 h urinary excretion of copper (> 100 µg/24 h)		
• Increased NCC		
• Increased hepatic copper (> 250 µg/g)		
• Low or very low ceruloplasmin (< 5 mg/dL)	• Bridging fibrosis • Cirrhotic nodules	
• Increased 24 h urinary excretion of copper (> 100 µg/24 h)		
• Increased NCC		
• Increased hepatic copper (> 250 µg/g)		
• Thrombocytopenia		
• Increased INR		
• ALP: total bilirubin <4 and AST: ALT > 2.2	• Hepatocyte necrosis • Acute inflammatory infiltrates	
• Low or elevated ceruloplasmin		
• Increased NCC		
• Increased 24 h urinary excretion of copper (> 100 µg/24 h)		
• Increased hepatic copper (> 250 µg/g)		
• Hemolysis indicated by decreased haptoglobin levels, Coombs negative hemolytic anemia (high reticulocyte count and MCV)		
• Low hemoglobin may be present if hemolysis occurs.		
• Low WBC and thrombocytopenia develop in those with hyperplasia due to portal hypertension		
• Increased INR		

meeting classic descriptions of WD, g systems may aid in establishing /D diagnosis. Prognostic scoring ip to determine the potential for al therapy for WD.

ore is useful in facilitating The arithmetic scoring system and biochemical findings and has hildren and adults.<sup>51,63</sup> Prognostic used to predict when patients with therapy. The first of these scoring zore score, which is based on serum aminotransferase, and prothrombin Index supersedes the Nazer om it by including white blood cell in, and international normalized in time).<sup>53</sup> AASLD guidance can be

consulted for recommendations on t diagnostic and prognostic scoring s

**Treatment**

1. All patients with a newly establish WD should be initiated on lifelong for WD Figure 2.<sup>13</sup>

The primary treatment of WD is cop involves pharmacotherapy through copper or blockade of copper absorp Failure to comply with lifelong therapy recurrent or new symptoms (including psychiatric as well as hepatic), if ultimately, liver transplantation or th

**WILSON DISEASE**

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# Diagnosis and Management of Hepatitis Delta Virus Infection

## Digestive Disease and Sciences

June  
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REVIEW

## Diagnosis and Management of Hepatitis Delta Virus Infection

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### Abstract

Hepatitis D virus (HDV) depends on hepatitis B virus (HBV) to enter and exit hepatocytes and to replicate. Despite this dependency, HDV can cause severe liver disease. HDV accelerates liver fibrosis, increases the risk of hepatocellular carcinoma, and hastens hepatic decompensation compared to chronic HBV mono-infection. The Chronic Liver Disease Foundation (CLDF) formed an expert panel to publish updated guidelines on the testing, diagnosis, and management of hepatitis delta virus. The panel group performed network data review on the transmission, epidemiology, natural history, and disease sequelae of acute and chronic HDV infection. Based on current available evidence, we provide recommendations for screening, testing, diagnosis, and treatment of hepatitis D infection and review upcoming novel agents that may expand treatment options. The CLDF recommends universal HDV screening for all patients who are Hepatitis B surface antigen-positive. Initial screening should be with an assay to detect antibodies generated against HDV (anti-HDV). Patients who are positive for anti-HDV IgG antibodies should then undergo quantitative HDV RNA testing. We also provide an algorithm that describes CLDF recommendations on the screening, diagnosis, testing, and initial management of Hepatitis D infection.

**Keywords** Hepatitis D virus · HDV Co-infection · HDV superinfection · HDV screening · Hepatitis delta virus

### Introduction

Hepatitis D virus (HDV) is a hepatotropic virus that causes acute and chronic liver disease [1]. HDV is variously described as a “satellite virus,” an “incomplete virus” or “defective virus” because it can only complete its life cycle with the aid of the hepatitis B virus (HBV) [2]. HDV

Calvin Pan, Robert Gish, Ira M. Jacobson, Ke-Qin Hu, Heiner Wedemeyer, and Paul Martin have contributed equally to this work.

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### History, and Clinical

percutaneously and, to a lesser extent with infectious blood and by sharing needles with an high sexual exposure. HDV can be salivally of infected individuals mucosal membranes or through hygiene objects such as razors or nly rare, HDV can be transmitted mother to fetus in utero or appear to accumulate in breast infect newborns during breast

ngle-stranded, circular, of approximately 1700 nucleotides or “satellite” RNA virus that replicates only in hepatocytes and replicates in two forms, the small (s) HDV antigen, encapsulated by does not encode its own poly-RNA polymerase II of the host contains an antigenomic RNA, copy of the genomic RNA [2]. is abundant and not assembled HDV, which is produced in s) HDV. L-HDAG is critical HDV subviral prior to release

enter hepatocytes in the same the hepatocyte, the HDV DV antigens are produced, and is formed. Replication can pro- V, though HBV must provide a using of HBsAg, for complete HDV assembly, release, and transmission [31]. Farnesylation of L-HDAG with an isoprenoid 15-C lipid moiety (a form of a process referred to as “prenylation”) facilitates

the interaction of the riboprotein with HBsAg on the viral surface. Without the HBV glycoprotein envelope, the ribonucleoprotein complex cannot exit the cell and infect other hepatocytes [7, 22]; however, replication-competent HDV RNA can be transferred between cells during hepatocellular mitosis [23].

HBV-infected cells produce about 10,000-fold more HBsAg than that required for assembly of HBV virions [24]. The empty envelopes are present in substantial quantities in the circulation and re-enter hepatocytes. Additionally, HDV can be packaged and transmitted via truncated HBsAg from naturally integrated HBV [25]. Thus, even when HBV replication is undetectable, there are still sufficient amounts of empty glycoprotein envelopes to coat HDV ribonucleoprotein complexes and subsequently permit release of virions and infect other hepatocytes [24].

### Clinical Manifestations and Outcomes of HDV Infection

Symptoms of acute hepatitis D typically first appear 3–7 weeks after initial HDV infection [26]. Initial signs and symptoms of acute hepatitis D are nonspecific and include fever, fatigue, loss of appetite, nausea, and vomiting. Serum levels of serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) increase dramatically as HDV replication is at its most active. Initial symptoms are often followed by an icteric phase. Nausea and fatigue persist and may worsen in the icteric phase, but abate in the third phase of acute infection, the convalescent phase.

While the clinical manifestations of acute HDV infection are largely indistinguishable from those of other etiologies of acute viral hepatitis, patients with HDV tend to have more severe disease and therefore worse outcomes (Table 1 [17, 27–31]). Nearly half of patients with HDV infection have cirrhosis at the time of diagnosis [6]. Of patients with chronic HDV superinfection, cirrhosis, and liver failure occur in 70%–80% within 5–10 years and in 15% within 1–2 years, respectively [32–34]. A 28-year follow-up study of patients with chronic HDV infection in Italy found that liver failure was the cause of death in 59% of patients [30]. The estimated, adjusted five-year probability for hepatic

**Table 1** Risks associated with chronic hepatitis delta infection

Clinical sequelae	Increased relative risk vs. HBV mono-infection
Cirrhosis [28, 31]	2.3 to 2.58
Hepatocellular carcinoma [17, 27, 29, 30]	1.43 to 9.3
Liver decompensation [29, 30]	2.2 to 3.17
Liver transplantation [28]	1.93
Mortality [29, 30]	2.0 to 7.88

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**Table 2** HDV Screening Recommendations in Patients with Hepatitis B

Organization	Year	Screening Recommendation
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3239

patients with HBV infection. “Other causes of chronic liver disease should be systematically looked for, including coinfections with HDV, HCV and HIV. Comorbidities, including alcoholic, autoimmune, and metabolic liver disease with steatosis or steatohepatitis should be assessed.”

patients with HBV infection. “Co-morbidities, including alcoholic, autoimmune, metabolic or steatohepatitis and other causes of chronic liver disease should be systematically screened for in patients with HDV, HCV and HIV.”

HDV screening should be performed for all patients with HBV infection. “Other causes of chronic liver disease should be systematically looked for, including coinfections with HDV, HCV and HIV. Comorbidities, including alcoholic, autoimmune, and metabolic liver disease with steatosis or steatohepatitis should be assessed.”

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# Expert perspectives for the pharmacist on facilitating and improving the use of albumin in cirrhosis

## American Journal of Health-System Pharmacy

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### CLINICAL REVIEW

## Expert perspectives for the pharmacist on facilitating and improving the use of albumin in cirrhosis

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**Purpose:** Albumin, the most abundant and arguably most important protein in the human body, plays a unique role in decompensated cirrhosis because its structure and function are quantitatively and qualitatively affected. A literature review was performed to provide insights into albumin use. The manuscript was developed using a multidisciplinary approach; 2 hepatologists, a nephrologist, a hospitalist, and a pharmacist, who are all members of or work closely with the Chronic Liver Disease Foundation, collaborated to write this expert perspective review.

**Summary:** Cirrhosis represents the potential end in the spectrum of all chronic liver diseases. Decompensated cirrhosis, defined by the overt manifestation of liver failure (eg, ascites, hepatic encephalopathy, variceal bleeding), is the infection point associated with increased mortality. Human serum albumin (HSA) infusion serves an important role in the treatment of advanced liver disease. The benefits of HSA administration in patients with cirrhosis are widely accepted, and its use has been advocated by several professional societies. However, inappropriate HSA use can lead to significant adverse patient events. This paper discusses the rationale for the administration of HSA in the treatment of complications of cirrhosis, analyzes the data on the use of HSA in cirrhosis, and streamlines practical recommendations set forth in published guidance.

**Conclusion:** Use of HSA in clinical practice needs to be improved. The objective of this paper is to empower pharmacists to facilitate and improve the use of HSA in patients with cirrhosis at their practice sites.

**Keywords:** albumin, ascites, cirrhosis, hepatorenal syndrome, spontaneous bacterial peritonitis, terlipressin

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Cirrhosis is defined as the histological development of regenerative nodules surrounded by fibrous bands in response to chronic liver injury that leads to portal hypertension and end-stage liver disease.<sup>1</sup>

Resulting from numerous etiologies (eg, chronic viral infection, alcohol- and non-alcohol-related liver disease, hereditary diseases), cirrhosis represents the end in the spectrum of chronic liver diseases (CLDs)<sup>2</sup> and afflicts 10% to 20% of patients with CLD within 10 to 20 years of diagnosis.<sup>3</sup> In 2018, the Centers for Disease Control and Prevention estimated that 4.5 million adults in the US had been diagnosed with CLD.<sup>4</sup> Liver disease accounts for approximately 2 million deaths each year worldwide, half of which are attributed to cirrhosis. The natural history of cirrhosis is characterized by compensated cirrhosis, a period of disease associated with normal or nearly normal liver function, followed by decompensated cirrhosis, when clinical signs and symptoms of hepatic dysfunction such as jaundice, ascites, hepatic encephalopathy (HE), hepatorenal syndrome (HRS), and variceal hemorrhage are observed.

Albumin is the most abundant and arguably most important plasma protein in the human body.<sup>5</sup> As liver disease progresses to decompensated cirrhosis, quantitative, qualitative, and functional changes to albumin occur,

contributes to increased serum bile acid concentrations.<sup>6</sup> Clinical outcomes in cirrhosis have been shown to correlate with reduced albumin concentrations. The Child-Turcotte-Pugh score (also known as the Child-Turcotte-Pugh score) is used as a guide to predict mortality in patients with cirrhosis. The scoring system divides patients into 3 categories: (A) patients with good hepatic function (5 to 6 points); (B) those with moderately impaired hepatic function (7 to 9 points); and (C) those with advanced hepatic dysfunction (10 to 15 points). Albumin levels are considered to be one of the essential clinical measures of the synthetic function of the liver and, as such, are part of this scoring system; albumin levels above 3.5 g/dL are equal to 1 point, 2.8 to 3.5 g/dL are equal to 2 points, and less than 2.8 g/dL are equal to 3 points.<sup>7</sup>

In healthy individuals, a small proportion of albumin exists as mixed disulfide compounds known as human nonmercaptalbumin 1 (HNA1), and an even smaller fraction is found in a highly oxidized form known as human nonmercaptalbumin 2 (HNA2).<sup>8</sup> In advanced liver disease, increases are observed in the abundance of the irreversibly oxidized form of albumin known as human nonmercaptalbumin (HNA).<sup>9</sup> One study found that the plasma levels of HNA2 are closely related to survival in decompensated cirrhosis and acute-on-chronic liver failure (ACLF), with a strong correlation of HNA2 with 30- and 90-day mortality. Increased concentrations of HNA1 and HNA2 correlate closely with Model for End-Stage Liver Disease score, bilirubin concentration, international normalized ratio, and C-reactive protein concentration.<sup>10</sup> In a larger study (N = 2,376 patients hospitalized for cirrhosis but without HE), decreased serum albumin levels were potentially associated with higher risk of overt HE (odds ratio [OR] = 0.878, 95% confidence interval [CI] = 0.834-0.924) and death from overt HE (OR = 0.864, 95% CI = 0.771-0.967).<sup>11</sup>

### VIEW

### HUMAN SERUM ALBUMIN IN CIRRHOSIS

In a study, 161 patients (91%) administered HSA had serum albumin values of <3.5 g/dL, while in only 38% of patients were these values <2.5 g/dL. In the majority of cases, HSA was administered to increase oncotic pressure, improve renal function, or to provide energy malnutrition. The new Italian Ministry of Health recommendations did not influence how albumin was prescribed. A total of 156 bottles were ordered. The number of patients in different wards were close to normal (2.5 and 2.8 g/dL, respectively). The HSA doses requested by the wards were 2.0 times higher than expected. The HSA doses requested by the wards were 2.0 times higher than expected. The HSA doses requested by the wards were 2.0 times higher than expected. The HSA doses requested by the wards were 2.0 times higher than expected.

**Findings**

- In the study, 161 patients (91%) administered HSA had serum albumin values of <3.5 g/dL, while in only 38% of patients were these values <2.5 g/dL.
- In the majority of cases, HSA was administered to increase oncotic pressure, improve renal function, or to provide energy malnutrition.
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and Drug Administration for HRS-AKL the past in the US and Canada, clinicians defaulted to the off-label use of these drugs in combination with HSA.<sup>12</sup> However, elsewhere, terlipressin—a vasopressin analog that exerts vasoconstrictive activity via selective V1 and V2 agonism—is approved for HRS-AKL.<sup>13</sup> In fact, in late 2022, terlipressin became the first drug to be approved in the US, in combination with yperonic (25% HSA) solution, for the treatment of HRS-AKL.<sup>14</sup> According to European Association for the Study of Liver Diseases<sup>15</sup> and AASLD guidelines (Table 2),<sup>16</sup> terlipressin, when combined with 25% HSA, is the treatment of choice for HRS-AKL.<sup>17</sup> Terlipressin was demonstrated to be safe and effective for treatment of RS-AKL in the phase 3 CONFIRM study, which analyzed 300 patients with cirrhosis and HRS-AKL (formerly termed HRS-1) and in which patients received terlipressin (n = 199) or placebo (n = 101) in a blinded manner; patients were administered 1 mg of terlipressin or placebo intravenously for 2 minutes every 5.5 to 6.5 hours. It was strongly recommended that all patients receive HSA (1 g per kilogram of body weight to a maximum of 100 g on day 1 and 20 to 40 g per day thereafter). On day 4, patients with a serum creatinine level that had decreased by less than 30% from the baseline level received a minimum of 10 doses of terlipressin or placebo could receive 2 mg every 6 hours, except those with coronary artery disease, circulatory overload, pulmonary edema, or bronchospasm. The primary endpoint of verified HRS reversal—defined as 2 consecutive serum creatinine measurements of 1.5 mg/dL or less at least 2 hours apart up to day 14 and survival without renal replacement therapy for at least an additional 10 days of HRS—was reported in 32% of patients in the terlipressin group and 17% of patients in the placebo group (P = 0.006).<sup>17</sup> The recommendations from the US package insert for terlipressin are detailed in Table 3.<sup>18</sup> With the approval of

### CLINICAL REVIEW

### HUMAN SERUM ALBUMIN IN CIRRHOSIS

Table 3. Terlipressin US Package Insert Recommendations<sup>18</sup>

Prescribing parameter	Description
Boxed warning	<b>Warning: serious or fatal respiratory failure.</b> Terlipressin may cause respiratory failure. Patients with volume overload or with ACLF or oxygen saturation (eg, SpO <sub>2</sub> ) before initiating terlipressin. Do not initiate terlipressin in patients experiencing hypoxia or respiratory distress. Monitor patients for hypoxia using continuous pulse oximetry and regular clinical assessments. Actively prevent and adjust terlipressin therapy as appropriate.
Indications	To improve kidney function in adults with hepatorenal syndrome.
Contraindications	In patients experiencing hypoxia or worsening respiratory or ongoing coronary, peripheral, or mesenteric ischemia.
Warnings and precautions	<b>Serious or fatal respiratory failure.</b> Monitor patients for cyanosis, oxygen desaturation, and respiratory distress. Actively prevent and adjust terlipressin therapy as appropriate. <b>Not for use in liver transplantation.</b> Terlipressin-related mortality in liver transplantation is not known. <b>Ischemic events.</b> Terlipressin is a vasoconstrictor and can cause peripheral, coronary, or mesenteric ischemia that may require dose interruption or discontinuation. <b>Embryo-fetal toxicity.</b> Terlipressin may cause fetal harm. Females of reproductive potential of the potential hazard should be advised to avoid pregnancy during treatment.
Adverse reactions	The most common adverse reactions (≥10%) include abdominal pain, diarrhea, and dyspnea.
Abbreviation: ACLF, acute-on-chronic liver failure.	

and Drug Administration for HRS-AKL the past in the US and Canada, clinicians defaulted to the off-label use of these drugs in combination with HSA.<sup>12</sup> However, elsewhere, terlipressin—a vasopressin analog that exerts vasoconstrictive activity via selective V1 and V2 agonism—is approved for HRS-AKL.<sup>13</sup> In fact, in late 2022, terlipressin became the first drug to be approved in the US, in combination with yperonic (25% HSA) solution, for the treatment of HRS-AKL.<sup>14</sup> According to European Association for the Study of Liver Diseases<sup>15</sup> and AASLD guidelines (Table 2),<sup>16</sup> terlipressin, when combined with 25% HSA, is the treatment of choice for HRS-AKL.<sup>17</sup> Terlipressin was demonstrated to be safe and effective for treatment of RS-AKL in the phase 3 CONFIRM study, which analyzed 300 patients with cirrhosis and HRS-AKL (formerly termed HRS-1) and in which patients received terlipressin (n = 199) or placebo (n = 101) in a blinded manner; patients were administered 1 mg of

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# Improving the Management of Hepatorenal Syndrome–Acute Kidney Injury Using an Updated Guidance and a New Treatment Paradigm

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## Improving the Management of Hepatorenal Syndrome–Acute Kidney Injury Using an Updated Guidance and a New Treatment Paradigm

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**Abstract:** Cirrhosis, or advanced scarring of the liver, represents the end stage of chronic liver disease and is associated with high morbidity and mortality. Hepatorenal syndrome–acute kidney injury (HRS-AKI), a condition causing functional and progressive kidney failure, is a complication of cirrhosis that contributes to its high mortality rate. In the United States, the standard-of-care treatments for HRS-AKI have historically been suboptimal. Recently, terlipressin became the first drug approved for HRS-AKI in the United States, and the American Association for the Study of Liver Diseases updated its guidance document on HRS diagnosis and management. Clinical practice guidelines and guidance documents have a variable effect on physician behavior owing to a lack of awareness, familiarity, and education. The implementation of standardized order sets can improve guidance adherence and the quality of care delivered by encouraging data-driven treatment administration, especially for new therapies. This review seeks to facilitate improvements in the management of HRS-AKI by discussing early HRS-AKI interventions, which will streamline diagnosis and treatment in a practical way for clinical use, and how to incorporate new treatments into patient care to improve survival in this subset of patients. Finally, these recommendations are integrated into a sample order set developed by members of the Chronic Liver Disease Foundation and experts in the management of HRS-AKI.

### Keywords

Cirrhosis, hepatorenal syndrome–acute kidney injury, terlipressin, diagnosis, treatment

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*and Lisa D. Pedicone, PhD, MEd.*

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**Current management of hepatorenal syndrome and the potential of terlipressin in patients with cirrhosis and acute kidney injury.** *Ann Intern Med.* 2022;176(10):1461-1465.

**Prognosis of acute kidney injury and liver disease: a prospective cohort study.** *Am J Kidney Dis.* 2022;179(1):109-119.

**Terlipressin in cirrhosis: pathogenesis and treatment.** *Am J Kidney Dis.* 2022;179(1):109-119.

**Diagnosis and management of hepatorenal syndrome.** *Am J Kidney Dis.* 2022;179(1):109-119.

**The hepatorenal syndrome patient health record.** *Curr Ther Res Clin Exp.* 2022;179(1):109-119.

**Acute-on-chronic liver failure: an update.** *N Engl J Med.* 2022;386(10):1183-1192.

**Diagnosis, evaluation, and management of acute kidney injury and liver disease: a prospective cohort study.** *Am J Kidney Dis.* 2022;179(1):109-119.

**Diagnostic and prognostic value of the acute kidney injury and liver disease patient health record.** *Curr Ther Res Clin Exp.* 2022;179(1):109-119.

**Why don't physicians follow clinical research?** *JAMA.* 1999;282(15):1958-1962.

**CRK.** News in pathophysiology.

LOFTUS ET AL

in dose is difficult to determine. Therefore, patients risk of pulmonary edema and fluid overload secondary to albumin-induced increases in plasma oncotic pressure (25%) human albumin solution dose of infusion should be adjusted according to the patient's volume status,<sup>33,34</sup> which requires evaluation after hyperoncotic (25%) human albumin solution dose indicates signs of cardiopulmonary dysfunction and status (eg, blood pressure, pulse, oxygenation, oxygen requirements, respiratory rate, development of peripheral edema, vital weights, inputs, and outputs). Patients with HRS-AKI, the additive effects provided by vasoconstrictors and hyperoncotic (25%) human albumin infusion are thought to improve outcomes compared with either agent alone,<sup>35</sup> although this further complicates the adverse event profile. Close monitoring for these side effects is recommended,<sup>36</sup> and 8-hour albumin stopping rule is included in the order set as a checkpoint for a committed benefit. The first clinical sign of cardiovascular overload (ie, dyspnea, jugular venous distention, and increased blood pressure), the infusion must be slowed or immediately stopped, and furosemide can be considered for volume management. Data indicate that a rise in mean arterial pressure (MAP) during vasoconstrictor or albumin therapy is associated with better kidney function.<sup>36</sup> The intent of a prespecified target of MAP increases improve renal outcomes in HRS-AKI.<sup>37</sup> However, Zuckerman and colleagues concluded, the minimum required elevation to achieve a beneficial effect for kidney function remains speculative and would require a prospective study for confirmation.<sup>37</sup> Importantly, all patients with HRS-AKI, including those who respond to vasoconstrictors, should be considered for liver transplant evaluation, given the high term mortality in this patient population. In candidates for transplant, the use of RRT is indicated in cases (resolving renal function, electrolyte disturbances, or rising volume overload unresponsive to vasoconstrictors). HRS-AKI requiring RRT is a severe liver failure, a marker of the likelihood of further deterioration of organ dysfunction that may not necessarily be reversed by the provision of RRT.<sup>38</sup> Therefore, in those who are not transplant candidates, determining when to initiate RRT involves defining the goals with the patients and their families,<sup>39</sup> with the understanding that without liver transplant and without significant chance of renal recovery, continuous RRT is considered futile owing to the high mortality rate and risk of renal recovery, high risk of complications (eg, infection), and more prolonged hospitalizations.<sup>39</sup> Concomitantly, the decision to start RRT in these patients is

**Table 5. A Sample HRS Order Set: HRS-AKI Diagnosis**

Test	Order
Serum blood tests	CMP
	Uric acid
	sCr
Hemoglobin	Hemoglobin
	Total protein
	Urine
Urine	Urine analysis
	Urine specific gravity
	Urine sodium
	Urine urea nitrogen
Fractional excretion of sodium	Fractional excretion of sodium
	Fractional excretion of urea
Microbiology	Urine culture
	Blood culture
Diagnostic paracentesis	Paracentesis
	Chest radiograph
Imaging	Ultrasound bladder
	Chest radiograph
Risk factor management	Withdraw n drugs (NSAIDs, diuretics, etc)
	Reduce or discontinue volume
Albumin challenge	Administer 25% human albumin solution 1 g (maximum 6 g/day) until 1-2 mL/min adequate urine achieved (or by improvement in hemodynamic parameters) (function of 2 days)

AKI, acute kidney injury; CMP, complete metabolic panel; NSAIDs, nonsteroidal anti-inflammatory drugs.

### TREATING HEPATORENAL SYNDROME–ACUTE KIDNEY INJURY

resulting in early diagnosis, followed by timely treatment with approved effective medical therapy.<sup>1</sup> In late 2022, terlipressin (Terlipres, Mallinckrodt), a vasopressin analogue that exerts vasoconstrictive activity via selective vasopressin 1 and 2 receptors, was approved in the United States for the treatment of HRS-AKI in combination with hyperoncotic (25%) human albumin solution.<sup>5</sup> In addition, the American Association for the Study of Liver Diseases (AASLD) recently published an updated guidance document focusing on the diagnosis and management of HRS-AKI.<sup>6</sup> Prompt universal adoption of this standard of care is key to reducing morbidity and mortality for HRS-AKI in the United States. However, in various therapeutic areas including cirrhosis,<sup>11</sup> clinical practice guidelines have demonstrated limited impact on physician behavior.<sup>12</sup> Factors negatively affecting the adoption of society guidelines include limited physician awareness and familiarity with the guidelines<sup>13</sup> as well as inadequate processes to inform clinicians about the existence of these guidelines.<sup>14</sup> Implementation of standardized order sets in cirrhosis and its complications can limit the variability in clinical practice and improve overall timeliness and effectiveness of treatment. Prompt universal adoption of this standard of care is key to reducing morbidity and mortality for HRS-AKI in the United States.

This expert perspective review seeks to facilitate improvements in the management of HRS-AKI, and discusses early HRS-AKI interventions to streamline the diagnosis and treatment guidance in a practical way for clinical use, as well as recommends how to incorporate this guidance into clinical practice. Finally, the new treatment and updated guidance will be integrated into a sample order set developed by the authors, who are experts in the management of HRS-AKI and are members of or work closely with the Chronic Liver Disease Foundation (CLDF), a nonprofit 501(c)(3) educational organization dedicated to raising awareness of liver disease.

### A Review of Hepatorenal Syndrome–Acute Kidney Injury

Previously, HRS was classified by the International Club of Ascites as either type 1 (or HRS-1), a rapid deterioration of renal function, often because of a precipitating event) or type 2 (or HRS-2, moderate and stable or slowly progressive renal dysfunction, often without an obvious precipitant), but now the International Club of Ascites delineates HRS-1 and HRS-2 according to the presence or absence of AKI, respectively. HRS-1 is now termed HRS-AKI; the new definition encourages clinicians to initiate the treatment of patients early, even when increases in serum creatinine (sCr) are small. Specifically, HRS-AKI is defined as an absolute increase in

sCr of at least 0.3 mg/dL within 48 hours or an increase within the previous 3 months. HRS-AKI occurs in the absence of hypovolemia or significant abnormalities in kidney histology.<sup>15</sup> A diagnosis of HRS-AKI requires that all other causes for AKI be ruled out and that there is no current or recent treatment with nephrotoxic medication. HRS–non-AKI, or NAKI, is diagnosed in a context of subacute or chronic renal dysfunction, specifically in a patient with cirrhosis and a glomerular filtration rate less than 60 mL/min/1.73 m<sup>2</sup> for longer than 3 months in whom other causes have been excluded or in the context of acute kidney disease, defined as a renal dysfunction that does not meet the criteria for AKI and lasts less than 90 days.<sup>15</sup>

A 2015 examination of National Health and Nutrition Examination Survey data found that the prevalence of cirrhosis in the United States was 633,323 adults, or 0.3% of the population. However, this is likely an underestimate because many patients remain undiagnosed, particularly patients who have compensated disease and are asymptomatic.<sup>16</sup> The estimated annual incidence for HRS type 1 (now termed HRS-AKI) in the United States ranges from 9000 patients to more than 35,000 patients.<sup>15,17</sup> In patients with decompensated cirrhosis with ascites, the probability of developing HRS ranges between 8% and 20% per year and increases to 40% at 5 years. An estimated 35% to 40% of patients with end-stage liver disease and ascites will develop HRS.<sup>18</sup> HRS-AKI is potentially reversible with treatment; without treatment, the consequences of HRS-AKI include irreversible renal failure, with mortality rates approaching 100% at 3 months after diagnosis.<sup>19</sup> More recent publications have analyzed evolving trends in HRS-AKI (Table 1).<sup>20-24</sup> HRS contributes to hospitalizations of patients with cirrhosis, and these hospitalizations confer significant health care burdens.<sup>25</sup> High mortality rates and hospital readmissions were attributed to inconsistencies in hospital-based HRS treatment strategies and called for greater disease awareness and more effective treatment options.<sup>7</sup> Conversely, earlier diagnosis,<sup>26</sup> the implementation of the protocolized management of HRS,<sup>27</sup> and better utilization of health care resources<sup>28</sup> ameliorated outcomes.

The poor prognosis of cirrhotic patients with HRS-AKI and previously inadequate therapies prompted the need to develop new treatments. Liver transplantation is the gold standard for treating HRS-AKI, as it corrects the underlying liver failure. However, many patients with HRS-AKI are ineligible for a liver transplant or will expire before receiving one. Moreover, patients with significant kidney injury prior to liver transplant may demonstrate worse long-term posttransplant outcomes. Renal replacement therapy (RRT) may bridge patients to liver



# Improving Outcomes in Hepatorenal Syndrome–Acute Kidney Injury With Early Diagnoses and Implementation of Approved Treatment Regimens Gastroenterology & Hepatology

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**Improving Outcomes in Hepatorenal Syndrome–Acute Kidney Injury With Early Diagnoses and Implementation of Approved Treatment Regimens**

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**IMPROVING OUTCOMES IN HEPATORENAL SYNDROME–ACUTE KIDNEY INJURY**

Key Questions Surrounding HSA Administration

Question	Recommendation
When to administer HSA	Correcting albumin based on fluid status is more important than achieving goal serum albumin levels. HSA use should be guided by functional (volume status, treatment response) rather than quantitative laboratory value endpoints <sup>44,45</sup>
When to administer HSA	<ul style="list-style-type: none"> <li>Because it is difficult to identify the optimum HSA dose, the most common AEs of HSA administration are pulmonary edema and fluid overload</li> <li>Pulmonary edema is precipitated by HSA-induced increases in plasma volume, especially when infused rapidly<sup>44</sup></li> </ul>
How to administer HSA	<ul style="list-style-type: none"> <li>The HSA dose and rate of infusion should be adjusted according to the patient's volume status,<sup>44,45</sup> which requires evaluation after each HSA dose<sup>44</sup></li> <li>Evaluation should include signs of cardiopulmonary dysfunction and fluid status after each dose of HSA: blood pressure, pulse, oxygenation, escalating oxygen requirements, respiratory rate, development of peripheral edema, and renal function<sup>44</sup></li> <li>Volume overload can also be determined via chest radiograph or bedside echocardiography</li> <li>Upon the first clinical sign(s) of cardiovascular overload (headache, dyspnea, jugular venous distention, increased blood pressure), the infusion must be slowed or stopped immediately<sup>44</sup> and diuretics can be considered for volume management<sup>44</sup></li> <li>Clinicians should also be mindful of the sodium content in HSA preparations, which is included for isotonicity. As a result, hypernatremia occurs in patients administered HSA over several days, and this may contribute to the development of pulmonary edema<sup>44</sup></li> </ul>
When to stop HSA	HSA must be used with caution in conditions where hypervolemia and its consequences could represent a special risk to the patient, such as pulmonary hypertension with right heart failure, congestive heart failure, pulmonary edema, renal insufficiency, and chronic kidney disease <sup>44,45</sup>
When to stop HSA	In patients with HRS-AKI, the additive effects provided by vasoconstrictors and HSA infusion provide benefits, but this may further complicate the AE profile. These patients should be closely monitored for the possible development of side effects of vasoconstrictors and HSA, including ischemic complications and pulmonary edema <sup>44</sup>
When to stop HSA	Assessing intravascular volume status by measuring the inferior vena cava diameter and percent collapsibility with inspiration using conventional ultrasound machines or at bedside using point-of-care ultrasound could be a useful tool in guiding HSA infusion <sup>44</sup>

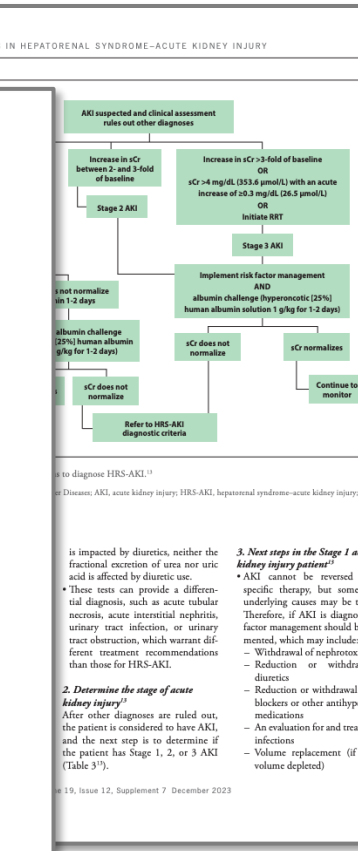
Key Questions Surrounding HSA Administration

When to administer HSA

When to stop HSA

When to stop HSA

When to stop HSA



**IMPROVING OUTCOMES IN HEPATORENAL SYNDROME–ACUTE KIDNEY INJURY**

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# AASLD Abstracts 2023 – Advisors Review

## 115 Abstracts Reviewed on 9 topics

*Alcohol Liver Disease*

*HCC and Liver Transplant*

*NAFLD/NASH*

*Cholestatic Liver Disease*

*HCV*

*Pediatric Liver Disease*

*Complications of Cirrhosis*

*HBV/HDV*

*Varices*

# 61 Live Independent Reviewers



### Complications of Cirrhosis

Abstract No.	Title	Grade
210 (Oral)	HIGH DOSES OF ALBUMIN INCREASES MORTALITY AND COMPLICATIONS IN TERLIPRESSIN TREATED PATIENTS WITH CIRRHOSIS: INSIGHTS FROM THE ATTIRE TRIAL	A
Abstract No.	Title	Grade
211 (Oral)	ALBUMIN DOSING WITH TERLIPRESSIN FOR THE TREATMENT OF HRS-AKI: A DOUBLE-EDGED SWORD	A
223 (Oral)	MEAN ARTERIAL PRESSURE: A TARGET FOR ACUTE KIDNEY INJURY RESPONSE REGARDLESS OF ACUTE KIDNEY INJURY TYPE	A
224 (Oral)	IMPROVED MEAN ARTERIAL PRESSURE FROM BASELINE TO THE END OF TREATMENT WITH TERLIPRESSIN IS ASSOCIATED WITH HEPATORENAL SYNDROME REVERSAL: A POOLED ANALYSIS OF 3 PHASE III STUDIES	A

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