



PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 69362

Title: Viral hepatitis: Past, present, and future

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00863327

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Full Professor

Reviewer's Country/Territory: Taiwan

Author's Country/Territory: United States

Manuscript submission date: 2021-06-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-06-28 03:37

Reviewer performed review: 2021-06-28 10:22

Review time: 6 Hours

Scientific quality	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

It is an interesting review article discussing latest clinical information and organizational guidelines for hepatitis viruses including Hepatitis A, B, C, D, E, and G, focusing on epidemiology and natural history of infection and clinical course as well as prevention/diagnosis/treatment. Furthermore, for each hepatitis virus, the authors bring known information together with current investigations to target on future directions. In particular, in Hepatitis B virus, there is a “Future Therapies Under Investigation” section discussing the novel direct-acting antiviral therapies such as gene editing via clustered regularly interspaced short palindromic repeats (CRISPR-Cas9) technology with the potential to promote a true cure. The manuscript is well written in English and directly relevant to the clinical application. There are only minor suggestions as follows. 1. Table 1 lacks the title, and there is no explanation of abbreviations like HBIG, IVDU, etc. 2. A Conclusion section is needed at the end of this manuscript.



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Reviewer’s code: 03550401

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Reviewer’s Country/Territory: China

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
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SPECIFIC COMMENTS TO AUTHORS

This manuscript systematically introduces Epidemiology, Natural History of Infection & Clinical Course, Prevention, Diagnosis, and Treatment of hepatitis A, B, C, D, E, G. Furthermore, the author introduced the future therapies under Investigation including CRISPR-CAS-9, siRNA, ASO in the hepatitis B virus infection, and the application of hepatitis C positive donors in solid organ transplantation. Overall, this article is very interesting and useful in virus hepatitis, but I hope that the author can add more of his own views on the prevention and diagnosis of viral hepatitis in the manuscript, in addition, they should summarize at the end of the manuscript and put forward his own opinions and prospects. Minor comments

1. Punctuation is missing in several places in the manuscript.
2. In the section of hepatitis A virus, the references are too old and needs to be updated accordingly. Such as the author cited a reference of 2006, to explain the risk factors related to death from Fulminant HAV (14. Taylor, R. M. et al. Fulminant hepatitis A virus infection in the United States: Incidence, prognosis, and outcomes. *Hepatology* 44, 1589–1597 (2006)), newer reference should be cited (A Model to Predict 1-Month Risk of Transplant or Death in Hepatitis A-Related Acute Liver Failure. *Hepatology*. 2019 08; 70 (2), 621-629.), and the paragraph needed to be updated.
3. The author indicated that hepatitis B was mainly transmitted via exposure to infected blood or bodily fluids, the most common being intravenous drug injection, sexual contact or vertical transmission, but in endemic areas, vertical transmission between mother and child and horizontal transmission among young children are the most common routes of HBV infection, we recommend that the author add the route of vertical transmission between mother and child.
4. In section Natural History of Infection & Clinical Course of HBV, the sixth paragraph. We feel that this description is



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unreasonable“current antivirals can help clear HBsAg”,because until today antiviral drugs cannot effectively eliminate HBsAg. 5. The author indicated that chronic hepatitis B has four distinct phases, but did not find a complete introduction to the 4 stages in this section. 6. Because HCV infection can remain asymptomatic for years, and during this time many infections go undiagnosed while patients suffer from sustained liver damage; but the author have not introduced the the diagnosis of HCV infection, 7. Please write the title consistently “Natural History of Infection & Clinical Course” and “Natural History of Infection & Clinical Course.