

Dear Editor,

Please find enclosed the edited manuscript in Word format.

Title: Three decades of Hepatitis B control with vaccination

Name of journal: World Journal of Hepatology

Manuscript NO.: 19465

Column: Editorial

Title: Hepatitis B vaccination - Past and future

Authors: Liliane C Meireles, Rui T Marinho and Pierre V Damme

The manuscript has been improved according to all the suggestions of reviewers:

1. Format has been updated
2. Small change in title was held
3. Revision has been made according to the suggestions of the reviewer (the changes are indicated by highlighting in yellow).

First Reviewer:“Hepatitis B virus has about 400,000,000 infected patients in the world, and one third of people once infected with HBV in the world.

Endemic areas of HBV are the developing countries mainly Asia and Africa. Therefore, prevention of HBV infection is unmet need in world health problem. Vaccination of HBV was developed about 30 years ago and improved by new biotechnology. Cost of vaccination become cheap, therefore, its cost-effectiveness is excellent. This review is

well written and compact. I recommend authors to add two issues.

1. Escape mutant for vaccine.
2. Add the result of Recent GWAS study for the response to vaccination.

(Hum Mol Genet 20:3893-3898. 2011)”

We would like to express our appreciation for your attention. Based on your suggestion, we added a small explanation about escape mutant for vaccine and a brief summary of the result of GWAS studies for the response to vaccination.

Second Reviewer: “I read with great interest the review paper by Meireles et al dealing with “Hepatitis B vaccination”. It is an interesting and well-written paper, which promotes the already established efficacy and safety of vaccination. Some minor comments are following: ? Page 3, line 79: according to WHO ? Page 3, line 80: correct WGO to WHO ? Studies from Mediterranean basin have shown routes of intrafamilial transmission of hepatitis B through folk remedies by using glass syringes in the past for medical purposes (Stefos et al, Eur J Intern Med 2009; Zervou et al, Eur J Gastroenterol Hepatol 2005). ? Page 4, line 136: delete “Immunisation” ? Page 4, line 142: correct HVB to HBV ? Page 5, line 155: “hepB” abbreviation is the first time mention in the paper without an explanation ? Page 6, lines 201-204: In this point, it should be mentioned that vaccination should be initiated shortly after the birth and absolutely before the completion of 1st year of live, in order to avoid early intrafamilial transmission (especially in endemic areas). One of the major errors from the

pediatricians is to postpone the hepB vaccination to the childhood. ? Page 7, line 225: I don't understand the meaning of "comproved". ? Page 8, lines 264-266: The authors have to provide recommendations and evidence regarding the efficacy of a second trial with hepB vaccination in subjects non-responders to initial vaccination program. ? Page 9, lines 301-302: Epidemiological data regarding prevalence of HBV among health care workers will be useful to emphasize the magnitude of the problem in this special population. ? Page 9, lines 303-305: The description of "vaccine-escape" phenomenon must be presented more comprehensive in the main-text of the paper (not just three line in the conclusion). Lazarevic in WJG 2014 (doi: 10.3748/wjg.v20.i24.7653) provides an detailed explanation of this phenomenon."

We would like to thank you for your insightful comments. Based on your comments all spelling and expression mistakes were corrected.

We emphasized the routes of intrafamilial transmission of HBV and the absolute need of vaccine administration before the completion of 1st year of live. We addressed the problem of unresponsiveness and we provide the recommendations of a second trial with HBV vaccination in persons unresponsive to a first series of three doses of vaccine. We highlight the importance of the greater prevalence of HBV among health care workers. We added a new paragraph in the manuscript, accordingly your revision, about the vaccine-escape phenomenon.

Sincerely yours,

Liliane Meireles, MD