To The Editor,

Journal of BMC Infectious Diseases

Please refer to your e-mail regarding our manuscript entitled "Immune responses in patients with HIV infection after vaccination with recombinant Hepatitis B virus vaccine". We observe that some very relevant comments have been made by the referees. I enclose below my comments and reply to queries raised in the context of our paper. Necessary changes have now been made as desired by the referee. I hope that you will now find the paper in order.

With best wishes,
Yours sincerely,
Neelam Pasricha

Comments by the authors
General comments:
It is a very painstaking study from a resource-constrained part of India where the patient drop out rate is very high because of the ignorance of the masses affected by disease. This study is also different from those of the west where most patients are put on antiretroviral therapy as and when indicated. In this situation, however, these patients could not afford HAART treatment during the study hence the data of immune response is not modified by therapy and ideal for a logical interpretation. National AIDS control organization has only recently started free antiretroviral treatment for a very limited number of patients in some centers in India.

Specific comments:
Abstract-The patients have been regrouped into high and low CD4 counts as desired by the referee. The comment is justified.

Introduction-The term background has been replaced by "Introduction". It was an inadvertent silly error. Necessary changes have also been made in the introduction and the term co-infection replaced by the details of the markers.

(Changes:
1st para: 3rd sentence onwards, new sentences added
3rd para: Addition: "which are crucial.........response")
The rationale for assessing the T cell functions has been mentioned in the text. In fact T cells offer help to B cells to form antibodies and since our aim was to get at the root cause of low titers, this investigation was very relevant. Vast data is available regarding severely compromised TH1 response in HIV but this alone could not fully explain the low antibody titers. On the other hand, there is a controversy in the literature regarding TH2 response, which governs the antibody response. Several authors reported an increase in TH2 response. Our data, however, illustrates that even TH2 type of response is also severely compromised. This could further compromise the antibody response.

Methods- The illustration in the method section has been shifted as figure 1.

Results-The increase in CD4+, CD8+ and CD3+ cells after vaccination was a consistent and a clear cut finding in our studies. The investigators have used flowcytometry in clinical practice for nearly 15 years. Since most patients in this study did not have severe opportunistic infections and only a fraction of the peripheral T cells are actually infected with HIV, rise of CD4 cell number may not be unexplainable. It is well documented that any vaccine can trigger immune activation. Further, there is no clear-cut study till date, which has proven beyond doubt that the viral copy number increases substantially after vaccination. The only study of Rey et al (Vaccine 2000, 18:1161-65) observed a significant rise of HIV viral load in a small number of cases but the rise was transient. The authors also concluded that the effects on viral load are limited. We do agree that there are too many tables and figures. We have therefore deleted 10/13 figures. If we omit the remaining 3 tables also, it might jeopardize the authenticity of the data. But the authors are open to further suggestions.

Discussion:
We are grateful to the referees for giving the latest valuable references on this very important issue. The main references about HBV/HCV published in 2005, i.e. multi center studies (no 34, 35) have been included in the discussion. Some additional comments have been made in discussion with 3 relevant references (30-32) while three of the old references (18, 19 and 26) have been omitted. Other minor mistakes have also been corrected as far as possible.