Acute hepatitis B virus infection despite previous immunization in the context of recent HIV-1 infection

Landrum et al. [1] report high rates of hepatitis B virus (HBV) infection in patients immunized against HBV after HIV infection in a large military cohort. They found that, in fully vaccinated patients, a hepatitis B surface antibody (HBsAb) titre of 10 IU/l or greater was more widely associated with a reduced but ongoing risk of HBV infection compared with those with a HBsAb titre less than 10 IU/l. They did not report the median HBsAb titre in the group that developed HBV infection and it is therefore unclear whether there is a threshold of postvaccination HBsAb titre that reduces the risk of subsequent HBV infection. Also, the authors could not assess whether vaccine escape could be an explanation for postvaccination HBV infection, most commonly as a result of mutations with loss of the ‘a’ determinant of HBV surface antigen (HBsAg) [2–5]. We report a case of acute HBV infection in the context of recent HIV-1 infection despite previous immunization and high HBsAb titres.

A 30-year-old man presented with lethargy, rash, weight loss and lymphadenopathy after unprotected sexual intercourse with a casual male partner. HIV antibody testing was positive for HIV-1 infection (negative 18 months previously) with significant immunodeficiency [CD4+ T cells 190 × 10^6/l (5%)] and immune activation with 85% of CD8+ T cells expressing CD38. The HBsAb titre was 130 IU/l at HIV diagnosis (after a complete immunization course in the period between HIV-negative and positive tests) and hepatitis A and C antibodies were not detected. There was no clinical or biochemical evidence of hepatitis or serological evidence of past natural HBV infection [hepatitis B core antibody (HbcAb) and HBsAg negative]. At review 3 months later, marked liver enzyme derangement was present (alanine aminotransferase 1292 U/l, aspartate aminotransferase 1292 U/l). At this time, HbcAb, hepatitis B e antigen and HBsAg were positive (Abbott axsym mEIA test; Abbott Laboratories, Abbott Park, Illinois, USA). The HBV DNA viral load was above 200 000 copies/ml and the HBsAb titre was zero (Fig. 1). Acute hepatitis A, hepatitis C, syphilis, toxoplasmosis, EBstein–Barr virus and cyto-megalovirus infections were excluded. PCR sequence analysis of the HBV envelope region showed no changes associated with vaccine escape [6]. Treatment for HBV was commenced using adefovir 10 mg daily and famciclovir 500 mg t.i.d. The liver enzymes normalized after 12 weeks of treatment. HBV DNA was undetectable after 24 weeks of therapy and seroconversion to HBsAb was documented (titre > 1000 IU/l). As he was persistently immunodeficient [CD4 220 × 10^6/l (5%)], treatment was changed to lamivudine, tenofovir and lopinavir/ritonavir.

Why did this patient develop HBV infection despite adequate vaccination? This patient was relatively young and was not receiving antiretroviral therapy (ART) at the time of HBV acquisition. These factors were associated with acquisition of HBV in previously vaccinated persons with HIV in the study by Landrum et al. [1]. Mutations in the virus that allow vaccine escape were excluded by viral sequencing and testing for unrecognized prior HBV infection was negative. Hyporesponsiveness and anergy associated with excessive immune activation induced by HIV may have prevented primed anti-HBV T cells from responding appropriately [7,8]. Alternatively, reductions in CD4 T cell help due to HIV-induced T cell loss may have resulted in loss of protective anti-HBV responses. Importantly, this patient experienced HBV infection persistently.
We treated HBV infection with dual therapy (with agents that are less likely to select for HIV resistance) to maximize HBV suppression prior to the initiation of combination ART with the aim of preventing the development of immune restoration disease [9]. It is uncertain whether the anti-HBV treatment affected the outcome in our patient, and note that patients with HBsAb titres above 101U/l, in the study by Landrum et al. [1], who developed HBV infection were less likely to develop chronicity. In conclusion, wild-type HBV infection may occur in immunodeficient HIV-infected, HBV-vaccinated patients despite high HBsAb titres.

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References


First report of abacavir associated with hypoglycemia

The nucleoside reverse transcriptase inhibitor abacavir has not previously been associated with hypoglycemia but there are reports in the literature with hyperglycemia [1].

We describe a 41-year-old woman diagnosed with HIV infection in 2000. She was started on Combivir (zidovudine/lamivudine) and nelfinavir in 2001 when her CD4 cell count was 197 cells/mm³. She responded to this treatment with undetectable viral loads and an appropriate rise in CD4 cell counts. She was diagnosed with diabetes mellitus in February 2007 when her random blood glucose was 27.3 mmol/l requiring insulin treatment. In November 2007, it was felt zidovudine was contributing to her chronic anemia (hemoglobin 112 g/l). Her HLA-B*5701 test was negative and the decision was made to change to Kivexa (abacavir/ lamivudine) and continue on nelfinavir. No other medication changes were made and she denied any herbal medication use. Ten days following the change, she reported symptomatic and documented hypoglycemic episodes (glucose nadir: 1.8 mmol/l) for 2 days despite frequent snacks every 2–4 h. Her exogenous insulin was discontinued but she continued to experience hypoglycemia. Investigations revealed a normal serum insulin level, C-peptide, thyroid-stimulating hormone, serum and urine cortisol, adrenocorticotropic hormone stimulation test, growth hormone levels, and cyclic citrullinated peptide antibody (Table 1). Her insulin autoantibody level was elevated (12 μU/ml). MRI of the abdomen revealed no evidence of insulinomas or other abnormalities. Although lamivudine has been associated with grade III or IV hypoglycemia [2], we felt that this was unlikely to be the cause given the long-term treatment with lamivudine. We were concerned about the newly initiated abacavir. In March 2008, her abacavir was discontinued and replaced with tenofovir, whereas she remained on lamivudine and nelfinavir. Her hypoglycemic episodes resolved 4 days after discontinuing abacavir. She continues to remain euglycemic despite lack of insulin or oral hypoglycemic medications. At her last...
follow-up visit, her viral load remained undetectable and her CD4 cell count was 920 cells/mm$^3$ (34%).

Abacavir has been in clinical use for the treatment of HIV since the late 1990s [3]. It has been proven to have a low adverse event profile in individuals who are HLA-B*$^5701$ negative [4]. This is the only case of abacavir-associated hypoglycemia in our clinic and, to our knowledge, the first reported case in the literature. Given the temporal relationship of hypoglycemic episodes with the addition of abacavir and resolution following its discontinuation, it is difficult to implicate another cause. As we cannot postulate a biological mechanism for this reaction, we realize the need to be vigilant of other patients who may experience similar symptoms.

Acknowledgements

Contributed to patient care are O.E.L., K.K., and M.L.B. O.E.L., K.K., and M.L.B analyzed the data. O.E.L. wrote the paper. O.E.L., K.K., and M.L.B edited the manuscript. All authors read and approved the final manuscript.

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### References


### Table 1. Laboratory values near the time of treatment with abacavir.

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>CD4 cell count (cells/mm$^3$)</td>
<td>700–1100</td>
<td>879</td>
<td>588</td>
<td>ND</td>
<td>ND</td>
<td>714</td>
<td>ND</td>
<td>920</td>
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<tr>
<td>CD4 cell%</td>
<td>38–46</td>
<td>33</td>
<td>33</td>
<td>ND</td>
<td>ND</td>
<td>37</td>
<td>ND</td>
<td>34</td>
</tr>
<tr>
<td>VL (copies/ml)</td>
<td>&lt;40</td>
<td>&lt;40</td>
<td>&lt;40</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>179</td>
</tr>
<tr>
<td>WBC (×10$^9$/l)</td>
<td>4.5–11</td>
<td>5.3</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>6.0</td>
<td>ND</td>
<td>6.8</td>
</tr>
<tr>
<td>Cr (µmol/l)</td>
<td>35–97</td>
<td>85</td>
<td>59</td>
<td>ND</td>
<td>ND</td>
<td>67</td>
<td>66</td>
<td>55</td>
</tr>
<tr>
<td>Glucose (mmol/l)</td>
<td>3.6–6.0</td>
<td>25.1</td>
<td>ND</td>
<td>2.3</td>
<td>4.8</td>
<td>4.8</td>
<td>3.7</td>
<td>4.0</td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>4.0–6.0</td>
<td>10.2</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>6.3</td>
<td>4.4</td>
<td>ND</td>
</tr>
<tr>
<td>Insulin level (µU/ml)</td>
<td>&lt;140</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Insulin autoantibody (µU/ml)</td>
<td>&lt;5</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>C-peptide (µmol/l)</td>
<td>298–2350</td>
<td>ND</td>
<td>ND</td>
<td>513</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
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<tr>
<td>TSH (mU/l)</td>
<td>0.4–4.2</td>
<td>1.43</td>
<td>ND</td>
<td>2.04</td>
<td>ND</td>
<td>1.43</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Cortisol (A.M.) (nmol/l)</td>
<td>140–690</td>
<td>314</td>
<td>ND</td>
<td>293</td>
<td>274</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>24h urine free cortisol (nmol/day)</td>
<td>50–250</td>
<td>ND</td>
<td>ND</td>
<td>48</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>ACTH (A.M.) (µg/l)</td>
<td>&lt;10</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>ACTH stimulation test (µg/l)</td>
<td>Peak &gt;550</td>
<td>ND</td>
<td>ND</td>
<td>6.4</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
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<tr>
<td>Basal GH (µg/l)</td>
<td>0–5</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>279</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>30min GH (µg/l)</td>
<td>0–5</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>638</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>60min GH (µg/l)</td>
<td>0–5</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>560</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>GH (µg/l)</td>
<td>0–5</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>0.3</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>CCP IgG (units)</td>
<td>0–5</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
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<tr>
<td>HAART medications</td>
<td>NFN, AZT, 3TC, NFN, ABC, 3TC, NFN, ABC, 3TC, NFN, ABC, 3TC, NFN, TDF, 3TC, NFN, TDF, 3TC, NFN, TDF, 3TC</td>
<td></td>
<td></td>
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</table>

3TC, lamivudine; ABC, abacavir; ACTH, adrenocorticotropic hormone; AZT, zidovudine; CCP, cyclic citrullinated peptide; GH, growth hormone; HAART, highly active antiretroviral therapy; Hb, hemoglobin; HbA1C, glycosylated hemoglobin; ND, not done; NFN, nelfinavir; TDF, tenofovir; TSH, thyroid-stimulating hormone; VL, viral load; WBC, white blood cell count.
AIDS education programs miss target

I was interested to read the recent article, ‘Effectiveness of HIV prevention for youth in sub-Saharan Africa: systematic review and meta-analysis of randomized and nonrandomized trials’ [1].

One of the reasons the AIDS education programs reviewed in the above article may have failed to reduce the incidence of HIV or other sexually transmitted infections among youth in sub-Saharan Africa is that none of them explained how long-term concurrent or overlapping partnerships amplify the sexual transmission of HIV in this region. Such information could help young people understand why they need to adopt such harm-reduction strategies as abstinence, monogamy/partner reduction or consistent, correct condom use, even if they have very few trusted, long-term sexual partners, or even only one.

There is growing evidence that HIV rates are high in parts of East and Southern Africa not because people there are typically ‘promiscuous’ in the sense of having many casual partners, but because they are more likely than people in other regions of the world to have a small number of longer-term partnerships that may overlap for months or years. If such behavior is relatively frequent, this could theoretically give rise to a stable network of sexual partnerships that serves as a virtual superhighway for HIV [2–4]. Long-term concurrent relationships often involve strong social, emotional and economic ties, making behavior change particularly difficult. However, AIDS education programs do a disservice to young people by neglecting to raise awareness about the risks associated with long-term concurrency, as none of those listed in the review by Michielsen et al. [1] did.

In 2005, I visited an AIDS education program in South Africa, sponsored by a distinguished US university. Topics covered included AIDS knowledge, contraception, sexually transmitted infections, abstinence, sexual rights, gender violence, and responsible relationships, all crucial elements of any comprehensive program. However, concurrent partnerships were never mentioned, nor was monogamy – even temporary monogamy – or the need for partner reduction or the complexity of using condoms consistently and correctly, even in long-term relationships with someone you think must be ‘safe’, but who may nevertheless be at risk because s/he is linked up through just one other partner to a wider network of concurrent partnerships.

Afterwards I interviewed about 15 students (aged 14–17 years) who had been through the entire program, many of whom indicated they were sexually active. Several boys bragged that they had two, three or four girlfriends. When I asked the girls whether it bothered them that their boyfriends had other girlfriends, they said it did not. ‘When he’s with me, he with me,’ was a typical response.

This may have been youthful bravado, and it is possible the students were not actually having as much sex as they claimed. However, a small study of recent graduates (aged 18–24 years) of schools in the area where the program was operating found that among young people with at least one partner, 21 of 23 of young men, and half of young women, had at least one concurrent sexual partnership, with overlap durations of 8.5 and 17 months, respectively [5].

The students I met may likewise have soon put into practice the highly risky behaviors they described to me – if they had not done so already. It is unfortunate that their AIDS education program did not give them a chance to think about it first, or warn them about the risks they were taking.

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Concurrency and the limited effectiveness of behavioural interventions on sexual risk behaviour of youth in sub-Saharan Africa

In our manuscript ‘Effectiveness of HIV prevention for youth in sub-Saharan Africa: systematic review and meta-analysis of randomized and nonrandomized trials’ we reviewed 28 interventions aimed to reduce sexual risk behaviour of youth in sub-Saharan Africa [1]. Of eight outcome variables studied (five behavioural and three biological outcomes), only condom use at last sex among men was found to be significantly influenced by the interventions (relative risk = 1.46; 95% confidence interval = 1.31–1.64).
Helen Epstein, in her commentary to this review [2], posits that the lack of inclusion of concurrency in these HIV prevention programmes may account for their failure. In the studies reviewed, detailed information on the interventions was often lacking and concurrency might well have been left out. Although the majority of evaluations assessed the number of sexual partners (lifetime or in the last weeks/months), only five included outcome measures related to multiple partnerships, with only one having an adequately specific indicator of concurrency [3]. The measures used include: multiple partners in the last 6 months [4], multiple regular partnerships in the last 3 months [5], multiple sexual partners during the last 3 months [6], sticking to one partner as a prevention method [7] and ongoing nonprimary partners (makhwapheni) since last interview [3]. The study of Visser [6] in South Africa surprisingly showed that the number of learners who had multiple sexual partners during the last 3 months increased in both the intervention and control groups from pretest to posttest and in the experimental group this increase was statistically significant. By contrast, the intervention led to a reduction in multiple regular partnerships in the study in Zambia by Agha and Van Rossem [5], and Kim [7] reported that an intervention in Zimbabwe led to more youths sticking to one partner. A second study of Visser [4] did not detect a change in the number of partners, whereas Jewkes et al. [3] did not specifically report changes in nonprimary partners. One study assessed perceptions towards men having concurrent partnerships, asking respondents their opinion on the statement ‘Men need to have more than one sexual partner, often at the same time’. No effect was noted in the intervention arm [8]. Finally, in another study, the intervention group did not have an increased awareness that ‘not having multiple partners’ was a prevention method for HIV transmission [9]. Overall, in these evaluations, as elsewhere, there is marked variation in how long-term concurrency is measured [10]. Hopefully, the recent UNAIDS consultation on concurrent sexual partnerships will assist in standardizing these indicators [11].

Mostly, the researchers dichotomized relationships as being either with a ‘steady’ or ‘casual’ partner, the latter being portrayed as considerably more risky and promiscuous. This distinction and the significance placed on it complicate HIV prevention efforts and is alluded to by Helen Epstein: an undue focus on the dangers of casual partnering alone risks conveying a message that long-term steady relationships are safe. In reality, they may well be most hazardous.

Though there is much evidence that concurrency is important in HIV transmission dynamics, there is much uncertainty about the portion of HIV infections attributable to this factor [10,12,13]. In our view, the projects failed not only because of a lack of focus on concurrency, but more importantly because they were often poorly implemented. Implementation difficulties were pervasive across studies and manifested as: refusal of teachers to talk about condoms, resource constraints and nonadherence to project design. In addition, interventions lacked grounding in conceptual frameworks of behaviour change. Moreover, notwithstanding the inherent complexities of behavioural research, overall, we could not detect a clear progression in the design of interventions, where subsequent interventions build upon the previous.

Ultimately, it is possible that some interventions were doomed from the outset, simply because it is immensely difficult to alter individuals’ sexual behaviour in the presence of static community norms. Even the two most well elaborated interventions and rigorous evaluations, including biological outcomes [3,14] resulted in small behaviour changes and no changes in HIV or pregnancy incidence. Jewkes et al. [3] did report a reduction in herpes simplex virus 2, but the only positive sexual behaviour change detected was a reduction in transactional sex in men. As Helen Epstein infers, long-term relationships – and we would add all types of sexual relationships – are difficult to alter through knowledge, raising awareness and skills learning, owing to the underlying social, emotional and economic dimensions of sex, which vary markedly between settings. Interventions, thus far, perhaps were not sufficiently cognisant of local community norms, be it concerning concurrency, condom use or other behaviours. Changing these community norms will require more than a behavioural intervention targeting individual youth; a shift in paradigm may be necessary, perhaps from a focus on the individual to a scenario of greater community responsibility.

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References

Pandemic influenza vaccine in adult HIV-1-infected patients

International [1] and national [2] guidelines suggest that a single shot of adjuvanted vaccine is sufficient to protect immunosuppressed HIV-infected patients aged less than 60 years from the H1N1 pandemic influenza in the season 2009–2010.

Bickel and co-workers [3] report a low seroconversion rate (69%) 21 days after vaccination with a split virion, AS03 adjuvanted pandemic H1N1 vaccine containing 3.75 μg antigen in a cohort of 160 HIV-infected patients and suggest the need to investigate whether a second dose of the vaccine will increase the seroconversion rate.

Here, we report our preliminary experience on immunogenicity of a single-shot monovalent MF59-adjuvanted influenza A/California/2009(H1N1) surface-antigen vaccine containing 7.5 μg of hemagglutinin in HIV-infected outpatients attending the Department of Infectious Diseases – L Sacco University Hospital, Milan (Italy).

Among 496 HIV-infected patients, vaccinated according to guidelines defined by Italian Ministry of Health in the period October to December 2009, 253 consenting patients were evaluated for anti-H1N1 antibody titers measured by hemagglutination-inhibition assay (HIA) on day 0 and after vaccine [median time 21 days, interquartile range (IQR) 21–26 days].

Patients included in this analysis (75 women and 177 men) had a mean age of 46.65 ± 9.5 years, a median time from the HIV diagnosis of 12.15 ± 7.8 years and were mainly on highly active antiretroviral therapy (HAART) regimens (90.56%). They had experienced a mean of 4.2 ± 3.6 antiretroviral treatments, had a mean CD4 cell count of 569.7 ± 265.9 cells/μl and a mean viral load of 1.9 ± 0.78 log_{10} copies/ml with a suppressed viremia in 82.05% of the cases.

On baseline evaluation 67 (26.48%) had HIA titers of at least 1 : 40; this high rate of prevaccine protective antibody titers could be explained by the late vaccine distribution when the pandemic wave has already reached the peak in Italy (reported on November/December 2009) [4]. Seroconversion, defined as HIA titer of at least 1 : 40 and a four-fold increase in H1N1 antibody titers from baseline, was achieved in 209/253 (82.61%), with the overall proportion of patients with titers of at least 1 : 40 being 92.49% (234/253). Antibody titers, expressed as geometric means, increased from a median value of 5 (IQR 5–40) to 160 (IQR 80–320) (Mann–Whitney test P < 0.0001).

Immuno-virological and clinical characteristics of seroconverters or of patients who generated protective titers antibody responses for natural infection and/or vaccine are compared with nonseroconverters or patients with antibody titers less than 1 : 40 (Table 1).

Patients with a longer lasting infection (>2 years) had a higher probability of seroconversion compared to those with a recent diagnosis of HIV infection [odds ratio (OR) 3.79 with 95% confidence interval [CI] 1.44–10.01]. Sex, age, number of previously experienced antiretroviral regimens, mean CD4 and HIV viral load, class of CD4, having a suppressed HIV viral load, being on/off HAART, did not affect the seroconversion rate.

Higher CD4 cells were observed in patients with antibody titers of at least 1 : 40 and patients with CD4 cells more than 500/μl showed a 6.35 (95% CI 1.42–28.44)-fold higher probability of a protective titer of anti-H1N1 antibodies.
Table 1. Immuno-virological and clinical characteristics of seroconverters or patients with antibody titers of at least 1:40 compared to nonseroconverters or patients with antibody titers less than 1:40 within 21 days after vaccination.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Seroconverters (n=209)</th>
<th>Nonseroconverters (n=234)</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>HIA titer ≥ 1:40 (OR 95% CI)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>HIA titer &lt; 1:40</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex (women/men)</td>
<td>61/148</td>
<td>14/29</td>
<td>0.71</td>
</tr>
<tr>
<td>Age (mean + SD)</td>
<td>47.02 ± 21.13</td>
<td>47.02 ± 21.13</td>
<td>0.97</td>
</tr>
<tr>
<td>Years since HIV diagnosis (mean + SD)</td>
<td>13.67 ± 6.23</td>
<td>13.67 ± 6.23</td>
<td>0.95</td>
</tr>
<tr>
<td>CD4 cells/ml</td>
<td>517.7 ± 169.4</td>
<td>517.7 ± 169.4</td>
<td>0.48</td>
</tr>
<tr>
<td>CD4 class (&gt;500/&lt;500 cells/ml)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV Viral Load log_{10} copies/ml</td>
<td>4.32 ± 1.6</td>
<td>4.32 ± 1.6</td>
<td>0.32</td>
</tr>
<tr>
<td>HAART (on/off)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ARV, antiretroviral; CI, confidence interval; HAART highly active antiretroviral therapy; OR, odds ratio.</td>
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</tbody>
</table>

Considering both the naturally and/or vaccine-induced protective titers (≥1:40 measured on day 21) and only the vaccine-induced seroconversion rate, our preliminary results show that a single-shot monovalent influenza A(H1N1)2009 MF59-adjuvanted vaccine generates antibody responses possibly associated with protection within 21 days in successfully HAART-treated HIV-infected adults, with rates comparable to those achieved in healthy adults [5], and at a higher rate than those reported by Bickel and co-workers [3]. How long protective antibody titers can be detected after one single vaccine injection in HIV-infected patients is under evaluation.

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