

# Persistence of vaccine immunity against the hepatitis B virus and response to revaccination in vertically HIV-infected adolescents on highly active antiretroviral therapy\*

Persistência da imunidade vacinal contra o vírus da hepatite B e resposta à revacinação em adolescentes infectados pelo HIV por transmissão vertical em uso de terapia antirretroviral potente

Persistencia de la inmunidad vacunal contra el virus de la hepatitis B y respuesta a la revacunación en adolescentes infectados por el VIH por transmisión vertical en uso de terapia antirretroviral potente

Silvana Duarte Pessoa

Programa de Pós-Graduação em Pediatria e Ciências Aplicadas a  
Pediatria, Universidade Federal de São Paulo, São Paulo, São Paulo, Brasil

Maria Isabel de Moraes-Pinto

Laboratório de Pesquisa da Disciplina de Infectologia Pediátrica,  
Universidade Federal de São Paulo, São Paulo, São Paulo, Brasil

Regina Célia de Menezes Succi

Departamento de Pediatria, Universidade Federal de São Paulo, São  
Paulo, São Paulo, Brasil

**Introduction:** Children infected with the human immunodeficiency virus (HIV) present alterations both in their humoral and cellular immune responses. These changes might lead to an inefficient immune response against certain specific vaccine antigens and/or to an early reduction in the antibody levels considered protective after immunization. This low immune protection against vaccine antigens is due to a deficiency in the treatment of antigens, a failure in the generation of the immunologic memory and/or the quantitative and functional loss of T and B memory cells. In addition, the introduction of highly active antiretroviral therapy (HAART) leads to the suppression of viral replication and to a partial restoration of the immunologic function, including the immune response against vaccine antigens. Recent studies have demonstrated that only a low percentage of children vertically infected with HIV treated with HAART maintain levels of protective antibodies after the primary immunization against the hepatitis B virus (HBV); however, the factors associated with the persistence of protective antibodies after primary vaccination and with the response to revaccination have not been clarified. **Objective:** To evaluate the persistence of the levels of protective antibodies against HBV in adolescents vertically infected with HIV treated with HAART and their response to vaccination. **Material and Methods:** This study was approved by the Ethics Committee of the Universidade Federal de São Paulo (UNIFESP/EPM). It was performed in the AIDS pediatric outpatient facilities of the institution. From January 2006 to August 2007, 40 adolescents vertically infected with HIV (HIV group) were selected for a prospective, longitudinal, controlled and intervention study. Twenty-three healthy HIV-negative adolescents were selected as the control group. The inclusion criteria for the groups were as follows: 10-20 years of age, absence of a previous history of hepatitis B and full immunization against HBV at least four years before the beginning of this study. The exclusion criteria were blood and blood products transfusion up to six months before the beginning of the study, acute febrile disease seven days prior to inclusion in the study, previous history or serologic evidence of HBV infection (i.e., the presence of anti-HBc antibodies). Furthermore, all the adolescents of both groups had received three doses of the recombinant vaccine against hepatitis B in the primary immunization. The adolescents with anti-HBs antibody levels of < 10 mUI/mL were revaccinated against HBV with up to six doses over an interval of 30-60 days. The adolescents in the HIV group received a double dose of the recombinant vaccine against HBV (20 µg of Euvax-B<sup>®</sup>, LG Chemical Ltd., from Korea). The adolescents in the control group were revaccinated with a standard dose of the Brazilian recombinant vaccine against HBV (10 µg of Butang<sup>®</sup>, by Instituto Butantã de São Paulo, São Paulo). The maturation of lymphocytes was assessed by flow cytometry through the phenotypic profile. Statistical analysis was executed using SPSS version 12.0, with a significance level of  $p < 0.05$ . **Results:** In the beginning of the study, anti-HBs antibody levels  $\geq 10$  mUI/mL were observed in 18/40 (40.5%) of the HIV-infected adolescents and in 18/23 (78.3%) of the adolescents in the control group. The adolescents in the HIV group with anti-HBs  $\geq 10$  mUI/mL presented a higher percentage of TCD4<sup>+</sup> cells, a higher percentage of central memory and of naïve TCD8<sup>+</sup> cells and a lower immune activation. After revaccination, 18/12 (66.7%) adolescents in the HIV group

Translated by / Traduzido por / Traducido por :

André Monteiro Diniz

\* Summary of dissertation presented to the Pediatrics and Applied Sciences Post-graduation Program of the Universidade Federal de São Paulo, São Paulo State, Brazil.

presented anti-HBs antibody levels  $\geq 10$  mUI/mL. The adolescents who did not respond to the vaccination course presented with a lower percentage of TCD4+ cells, a higher immune activation and a detectable viral load. **Conclusion:** These findings suggest that a higher percentage of TCD4+ cells, a lower immune activation and a better control of the replication of the HIV might be associated with a better vaccine response against the HBV.

**Keywords:** Hepatitis B Vaccines; HIV; Antigens, CD38.

**Financial support:** Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) - 04/15934-0.

---

**Correspondence / Correspondência / Correspondencia:**

Regina Célia de Menezes Succi  
Universidade Federal de São Paulo  
Rua Pedro de Toledo, 928  
CEP: 04039-002 São Paulo-São Paulo-Brasil  
Tel.: 55 (11) 5085-0229 | Fax: 55 (11) 5572-8922  
E-mail: succi@picture.com.br

Received / Recebido em / Recibido en: 8/26/2010  
Accepted / Aceito em / Aceito en: 9/29/2010