Hepatitis B vaccination in HIV-infected patients: a survey of physicians and patients participating in the Aquitaine cohort

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SUMMARY

In France, HIV-infected (HIV+) patients are frequently coinfected with hepatitis B virus (HBV) or at risk for this infection. Physicians and their patients should be more committed to HBV prevention than the average population.

Aims — To gain insight into the attitude towards HBV and its vaccination in HIV+ patients from the Aquitaine Cohort and their attending physicians in France.

Methods — A cross-sectional survey based on self-administered questionnaires was performed from November 2002 to June 2003. It targeted 198 physicians from the clinical group on AIDS epidemiology (Groupe d’Épidémiologie Clinique du SIDA en Aquitaine, GECSA) or participating in medical HIV networks in southwestern France, and 512 patients from the cohort. Questions concerned the following items for the physicians: HBV status, prescription of HBV serology and vaccination (frequency, type, schedule), risk factors assessed, reasons for non-vaccination; and for the patients: HBV status, information received, risk factors, attitude towards vaccination.

Results — 93% of physicians and 22% of patients stated they were vaccinated against HBV. HBV serological status was reported to be systematically ascertained by 75% of physicians, but post-vaccinal testing was only prescribed by 23% of them. The main reasons for not prescribing more often HBV vaccine were forgetting (79%), difficulty to identify subjects at risk (44%) and being afraid of post-vaccinal complications (32%). Thirty percent of patients reported not to have received any information on HBV vaccination. Overall, 44% considered not to be at risk of infection but 82% of them had been confronted with at least one risk. The main reasons for not having been vaccinated were mostly worry about AIDS (70%), not having been asked by physician (65%) or afraid of complications (58%); nonetheless, 42% of patients were willing to be vaccinated.

Conclusions — Results from this survey underline the need for specific health actions to be undertaken concerning hepatitis B vaccination in HIV+ patients as well as their health care providers.

RÉSUMÉ

Vaccination contre l’hépatite B chez les malades infectés par le virus de l’immunodéficience humaine : enquête chez les médecins et les malades de la cohorte aquitaine

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En France, les malades infectés par le virus de l’immunodéficience humaine (VIH) sont fréquemment co-infectés par le virus de l’hépatite B (VHB). Les médecins et les malades devraient être particulièrement attentifs à la prévention de la contamination par ce virus.

Objectifs — Évaluer l’attitude vis-à-vis du VHB et de la pratique de la vaccination chez les médecins et les malades infectés par le VIH de la cohorte Aquitaine.

Méthodes — Une enquête transversale, basée sur deux auto-questionnaires, a été menée entre novembre 2002 et juin 2003. Cent quatre vingt dix médecins du Groupe d’Épidémiologie Clinique du SIDA en Aquitaine (GECSA) et des réseaux VIH de la région ont été interrogés ainsi que 512 malades de la cohorte. Les questionnaires explorait pour les médecins, la détermination du statut VIH, la prescription de la sérologie et de la vaccination (fréquence, type de vaccin, schéma), et pour les malades, le statut VIH, l’information reçue, les facteurs de risque de contamination, l’attitude vis-à-vis de la vaccination.

Résultats — 93 % des médecins et 22 % des malades déclaraient être vaccinés. 75 % des médecins disaient évaluer le statut sérologique des malades au moins une fois, mais 23 % d’entre eux seulement disaient avoir prescrit un dosage post-vaccinal des anticorps. Les principales raisons invoquées pour ne pas davantage pratiquer cette vaccination étaient : l’oubli (79 %), la difficulté à identifier les malades à risque (44 %), et la crainte d’effets secondaires (32 %). Parmi les malades, 30 % n’avaient pas reçu d’information sur le vaccin contre le VHB. Globalement, 44 % ne se considéraient pas à risque, alors que 82 % avaient été exposés à un ou moins un facteur de risque. Les principales raisons invoquées pour l’absence de vaccination étaient la préoccupation plus importante pour l’infection par le VIH (70 %), la non proposition par leur médecin (65 %) ou la crainte d’effets secondaires (38 %). Cependant, parmi ceux qui se disaient non vaccinés, 42 % accepteraient de l’être.

Conclusion — Des campagnes d’information et de sensibilisation ciblées sont nécessaires chez les malades infectés par le VIH ainsi que chez leurs médecins.
Introduction

Hepatitis B is a major public health problem throughout the world with two million persons infected by the virus [1]. Among these infected persons, 350 million have chronic disease [2] with a risk of progression to cirrhosis and hepatocellular carcinoma [3, 4]. In metropolitan France, endemic hepatitis B virus (HBV) infection is low; the prevalence of HBV carriers in the general population is to the order of 0.2 to 0.5%. The prevalence of chronic carriers is however much higher in certain populations such as persons infected with the human immunodeficiency virus (HIV) where the prevalence of HBV reaches 10% [5].

HIV infection modifies the natural course of HBV infection in several ways: i) progression to chronic HBV infection is more frequent in co-infected patients [6], ii) patients who do not eliminate HBs antigens have less effective clearance of HBe antigens [7, 8] and their plasma load of HBV is higher [7-9], iii) progression to cirrhosis appears to be accelerated [9, 10], and iv) hepatitis B can be reactivated after reappearance of anti-HBs antibodies [11, 12]. The disease is more severe in HIV+ patients co-infected with HBV, increasing the risk of death [13, 14].

Hepatitis B vaccination is the most effective preventive measure against HBV infection and associated complications [15-17]. In France, since marketing approval in 1981, hepatitis B vaccination was first proposed for health care personnel then selected patient groups at a high risk of infection. In 1995, it was considered that vaccination of subjects at risk was insufficient to halt propagation of HBV in France. France thus integrated hepatitis B vaccination as a routine vaccination schedule proposed for infants and adolescents. However, in 1998, the French Ministry of Health suspended hepatitis B vaccinations in school prevention programs after certain studies suggested there could be a relationship between the vaccination and the development of central demyelinating events [18]. During the last ten years, the safety of hepatitis B vaccination has been questioned often with some suggesting a cause and effect relationship between vaccination and the advent of diverse secondary effects including chronic fatigue syndrome, diabetes, rheumatoid arthritis, demyelinating neurological diseases, and acute lymphoblastic leukemia [19-22]. Furthermore, more general problems with vaccinal safety concern the presence of other additives including aluminum or thimerosal. This has contributed to growing concern in the public opinion, reinforcing the negative attitude towards hepatitis B vaccination. In 2001, among the 38 European countries engaged in a program of universal vaccination of infants, France had one of the lowest coverage rates (27.4%) with an overall coverage, all ages considered together, of 30-40% [23].

Our knowledge of perception of risk of HBV infection and vaccination practices is limited in the HIV+ population, a specific target population for vaccination. The purpose of this survey was to gain insight into the attitude towards HBV and its vaccination in HIV+ patients from the Aquitaine Cohort and their attending physicians.

Patients and methods

Study populations and surveys

The Aquitaine Cohort was initiated in 1987 by the GECSA (Groupe d’Epidémiologie Clinique du SIDA en Aquitaine) a study group on AIDS epidemiology in the Aquitaine region in southwestern France. This prospective hospital cohort includes all HIV+ patients, irrespective of the stage of infection, followed regularly at the Bordeaux University Hospitals and four other hospitals in the Aquitaine region. All patients consent to their enrolment in the cohort. At each consultation, the attending physician completes a standardized chart consigning epidemiological, clinical, biological and therapeutic data for later computer processing. Patients are scheduled for follow-up visits in accordance with each physician’s practices. In December 2001, at the time when the present survey was designed, 6110 patients had been enrolled in the cohort, including 2508 patients who had been seen at least once during the preceding year.

Two parallel cross sectional surveys were conducted starting late in 2002: a “physician” survey and a “patient” survey. The physician survey concerned all practitioners (N = 33) with infectious diseases or internal medicine consultations in the GECSA-participating hospitals attended by HIV+ patients and also all general practitioners participating in HIV networks in southwestern France (Bordeaux, Dax and Côte Basque: N = 63, 56 and 40 physicians respectively) or in charge of HIV outpatient clinics in five general hospitals (Agen, Libourne, Pau, Périgueux, Villeneuve-sur-Lot, N = 6). Thus a total of 198 physicians participated in the survey.

The patient survey was conducted with a sample of patients attending consultations at the Bordeaux University Hospitals. The sample for this study was drawn from the population of 2508 patients with an active GECSA file who had consulted at least once in 2001. The estimated number of subjects needed to achieve an accuracy of ±5% and an alpha risk of 5% for a frequency attitude of 50%, i.e. 335 subjects, was determined from this population. Anticipating a non-response rate of 35%, 512 had to be included, i.e. 20% of the patients with an active GECSA file, stratified by center. The necessary sample size was not calculated for the physician survey since all GECSA or network participating physicians were to be contacted. The analysis was limited to physicians who had HIV+ patients attending their consultations.

Data collected

Data were collected with self-administered questionnaires. The physician questionnaire was sent by mail and included 19 items concerning the physician’s anti-HBV vaccinal status, mode of HBV serology prescriptions, and vaccination practices (frequency, type of vaccine used, vaccinal schedule), type of patients for whom vaccine was prescribed, and any reasons for not prescribing vaccination.

The physicians delivered the patient questionnaire to their patients during consultations. The patients completed the questionnaire without assistance (medical or other) immediately after the consultation. The patient questionnaire included 20 items designed to determine the patient’s knowledge of risk factors for HBV infection, and the patient’s attitude concerning hepatitis B vaccination. The questionnaires were returned in anonymous envelopes.

The surveys were conducted from November 2002 to April 2003 for the physician questionnaire and from January to June 2003 for the patient questionnaire.

Responses were processed with Epilinfo and data were analyzed with SAS software, v8.02 (SAS Institute Inc, Cary, NC, USA).

Results

Physician survey

Among the 198 physicians who received questionnaires, 23 participating in the GECSA and 75 participating in HIV networks responded, giving a response rate of 69.7% and 45.5% from these two sources respectively or an overall rate of 49.5%.

Responding physicians were predominantly male (78.6%) with median age of 47 years (age range 31-65 years). Nine physicians (9/97) stated they were not themselves vaccinated against HBV. GECSA participating physicians saw a median twelve HIV+ patients per week. Among the physicians participating in HIV networks, 32 had not seen any HIV+ patients in consultation during the last months, the others saw three patients per week. Because of this distribution, the results from the HIV-network physicians were noted for 43 physicians.

Among the 64 responding physicians, the large majority stated they delivered information concerning hepatitis B vaccination often (45.3%) or sometimes (34.3%), irrespective of the HIV serology of the patients. This information was delivered "always" for only 18.8%. Conversely, for HIV+ patients, information appeared to be delivered more regularly (always: 33.8%, often 33.9%, sometimes 30.8%). Only one physician (1.5%) responded "never" delivering this information.

Prescriptions for hepatitis B vaccine were equivalent for HIV+ and HIV- patients for 45% of physicians, more often among HIV-patients for 33% and more often among HIV+ patients for 22%.

At the patient’s first consultation, physicians checked HBV serology in HIV+ patients always for 75.4%, sometimes for 12.3% and never for 1.5%. Three network physicians stated they were not concerned by this question (4%). Physicians followed the HIV+ patient’s HBV serology after the first consultation at least once a year for 22.6%, rarely for 64.5%, and never for 9.7%. Two physicians responded they were not concerned by this question.

The different reasons for prescribing hepatitis B vaccine are presented in table I according to the patients’ profile. The main reasons for vaccination were: HBV+ partner (81.3%), use of intravenous drugs (76.9%), multiple partners (67.2%), partners co-infected by the hepatitis C virus (61.5%).

The most frequently prescribed vaccines were Genhevac B® (Aventis Pasteur) (21.5%), Engerix B® (GlaxoSmithKline) (18.5%) or one or other of these two (27.7%). Only two physicians prescribed HB Vax DNA® (Pasteur Mérieux MSD) and only one a combination anti-HBV anti-HBA vaccine (Twinrix®, GlaxoSmithKline); 27.7% of physicians stated they had no preference.

For the vaccinal schedule, 73.4% used two injections one month apart, followed by a booster at six months (M0, M1, M2, M6). The other physicians used an accelerated schedule (three injections, M0, M1, M2 (14.1%)), or the same schedule with a booster at six months, (M0, M1, M2, M6 (12.5%)).

Post-vaccinal assay of anti-HBs antibodies was proposed by 56.9% of physicians (always: 23.1%; often 33.8%) and sometimes by 30.8% and never by 12.3%.

Sixty-five percent of the physicians stated they took into consideration the immunological status of the HIV+ patient assessed from the CD4 cell count before prescribing hepatitis B vaccination. Vaccination was carried out by 85.7% of physicians if the CD4 count was > 500/mm3, and by 22.5% if the CD4 count was < 200/mm3.

Reasons for not prescribing more vaccinations were: forgetting as the main reason for 78.9%, difficulty in identifying non-protected patients for 43.9%, worry about adverse effects for 31.6%, and worry about inefficacy for 14%. In general, 10.5% of responders were not convinced about hepatitis B vaccination.

**Patient survey**

Four hundred twenty-four patients responded to the patient questionnaire for a response rate of 82.8%. Most responders (78.9%) were men and median age was 42 years (range 20-78). Women were younger than men, median ages 39 years and 42 years respectively (P = 0.001).

Sixty-four percent of patients stated they had discussed hepatitis B at least once with their physician; 43.5% considered they had no risk of infection, 33.1% considered they did have a risk and 23.4% did not know. The notion of risk varied with gender. For men 52.8% considered they had a risk of HBV infection compared with 27.4% of women (P = 0.005).

Factors of HBV infection to which the patients considered they were exposed are given in table II. The most frequently cited by patients were: homosexuality (49.6%), multiple sexual partners (28.7%), tattooing or piercing (22.9%), use of intravenous drugs (17.5%). Among the patients who were intravenous drug users, 76% stated they shared injection material. Both genders appeared to recognize the risk of tattooing and piercing in equal proportions while more men were aware of other risk factors. Among men, 98% stated they had sexual intercourse with persons of the same sex (P < 0.001), 87.9% stated they had multiple sexual partners (P < 0.001), and 65.7% stated they were intravenous drug users (P = 0.002). Globally, 82.3% of patients stated they had been exposed to at least one risk of injection, a proportion which was higher in men (86.8%) than women (67.8%) (P < 0.001).

Sixty-five percent stated they had been informed about vaccination against hepatitis B, 32% had not been and 3% did not know whether or not they had been informed. For 59%, informa-

| Table I. – Frequency of prescription of HBV vaccination according to the physician’s assessment of the patient’s risk of infection. |
| Fréquences des motifs de prescription du vaccin contre le VHB chez des patients VIH+. |

<table>
<thead>
<tr>
<th>Physicians prescribing HBV vaccination</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>always</td>
<td>often</td>
</tr>
<tr>
<td>New patient, no prior contact with HBV</td>
<td>25</td>
</tr>
<tr>
<td>(37.9)</td>
<td>(25.8)</td>
</tr>
<tr>
<td>Patient co-infected with HCV*</td>
<td>18</td>
</tr>
<tr>
<td>(27.7)</td>
<td>(33.8)</td>
</tr>
<tr>
<td>Patient with a prison history</td>
<td>15</td>
</tr>
<tr>
<td>(24.2)</td>
<td>(19.4)</td>
</tr>
<tr>
<td>Patient with HBV+ partner</td>
<td>44</td>
</tr>
<tr>
<td>(68.8)</td>
<td>(12.5)</td>
</tr>
<tr>
<td>Patient using intravenous drugs</td>
<td>34</td>
</tr>
<tr>
<td>(52.3)</td>
<td>(24.6)</td>
</tr>
<tr>
<td>Patient with several sexual partners (≥ 2)</td>
<td>24</td>
</tr>
<tr>
<td>(37.5)</td>
<td>(29.7)</td>
</tr>
<tr>
<td>Patient envisaging reproduction</td>
<td>21</td>
</tr>
<tr>
<td>(33.3)</td>
<td>(17.5)</td>
</tr>
<tr>
<td>Patient envisaging acupuncture, piercing or tattooing</td>
<td>19</td>
</tr>
<tr>
<td>(29.7)</td>
<td>(17.2)</td>
</tr>
</tbody>
</table>

*hepatitis C virus
tion about vaccination had been delivered by the attending physician in the unit where they had received the questionnaire. For the others, this information had been delivered by their primary care physician, another hospital physician, or the occupational medicine physician.

Forty-eight percent of patients stated they had received this information more than one year before, 29% less than three months before, and 8% between 3 and 12 months before. Fifteen percent could not remember when.

Among the 413 responders, 22% had been vaccinated against HBV, 70% knew they had not been and 8% were unaware of their vaccinal status. Reasons patients cited for not being vaccinated were: predominant worry about HIV infection (70.1%), vaccination not proposed by physician (65%), worry about adverse effects (57.6%), notion of prior infection (50.7%), feeling of not being at risk of infection (39.9%).

Among patients who stated they were not vaccinated against HBV, 42% had a favorable opinion about this vaccination, 30% were opposed to it, and 28% had no opinion.

**Discussion**

This survey provides two types of information. The medical data provide insight into hepatitis B vaccination practices among practitioners involved in management of HIV+ patients in southwestern France. Patients also provided information concerning their perception of hepatitis B vaccination and of risk factors for HBV infection.

In France, as in other low endemic areas, HBV infection generally occurs during adulthood, mainly via sexual contact or parenteral contamination [24]. Transmission via blood transfusion has practically disappeared and mother-child transmission has greatly decreased due to systematic search for HBs antigen during pregnancy. Certain practices, such as tattooing and piercing, could however be a mode of contamination on the rise [25].

Vaccination is clearly the most effective prevention against HBV infection. The recent recommendations issued by the French Public Health Superior Council are in favor of systematic vaccination of all children before the age of 13 years, favoring vaccination of infants and groups at risk [26]. These recommendations confirm those promulgated by the hepatitis B consensus conference held in September 2003 by the National Health Accreditation and Evaluation Agency (ANAES, Agence Nationale d'Accréditation et d'Evaluation en Santé) and INSERM (Institut National de la Santé et de la Recherche Médicale) [27]. The pertinence of these strategies has been recently confirmed [28].

Special vaccination strategies are recommended for HIV-infected subjects [29]: systematic search for markers of HBV infection (HBs antigen, anti-HBs and anti-HBc antibodies) in all HIV-positive patients; vaccination of all HIV+ persons without any marker of HBV infection; anti-HBs titer for vaccination patients with booster vaccination if titer is too low (< 10 mU/mL).

Approximately 90-95% of healthy adults develop a protective level of anti-HBs antigens after vaccination [1, 30]. HIV infection can dampen response to vaccination. This response varies from 24 to 55% depending on the series reported [31-35] and is lower in individuals with low CD4 cell counts (< 500/mm³) [33]. There are however preliminary results suggesting that using more injections, 3 to 6, can increase the response rate to 90% [33].

Drugs most widely used for the treatment of hepatitis B are alpha interferon, lamivudine, adefovir and, more recently, teno-

<table>
<thead>
<tr>
<th>Table II. – Exposure to risk factors of HBV infection, patient questionnaire.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facteurs de risque de contamination par le virus de l’hépatite B chez les patients ayant répondu à l’enquête.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patients exposed N (%)</th>
<th>yes</th>
<th>no</th>
<th>don’t know</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>At birth, mother infected with HBV</td>
<td>4 (1.0)</td>
<td>348 (83.0)</td>
<td>67 (16.0)</td>
<td>419</td>
</tr>
<tr>
<td>Living with an HBV-positive person</td>
<td>64 (15.2)</td>
<td>244 (58.1)</td>
<td>112 (26.7)</td>
<td>420</td>
</tr>
<tr>
<td>Direct contact with human blood</td>
<td>94 (22.8)</td>
<td>284 (68.8)</td>
<td>35 (8.4)</td>
<td>413</td>
</tr>
<tr>
<td>Contact with human blood products</td>
<td>29 (6.9)</td>
<td>380 (91.0)</td>
<td>9 (2.1)</td>
<td>418</td>
</tr>
<tr>
<td>Hemophilia, renal dialysis, or transfusion before 1975</td>
<td>23 (5.5)</td>
<td>391 (93.5)</td>
<td>4 (1.0)</td>
<td>418</td>
</tr>
<tr>
<td>Tattooing or piercing</td>
<td>96 (22.9)</td>
<td>324 (77.1)</td>
<td>--</td>
<td>420</td>
</tr>
<tr>
<td>Imprisonment</td>
<td>35 (8.3)</td>
<td>384 (91.7)</td>
<td>--</td>
<td>419</td>
</tr>
<tr>
<td>HBV-positive sexual partner</td>
<td>56 (13.5)</td>
<td>166 (39.9)</td>
<td>194 (46.6)</td>
<td>416</td>
</tr>
<tr>
<td>Same-sex sexual intercourse</td>
<td>207 (49.6)</td>
<td>210 (50.4)</td>
<td>--</td>
<td>417</td>
</tr>
<tr>
<td>Multiple sexual partners( &gt; 5 )</td>
<td>115 (28.7)</td>
<td>286 (71.3)</td>
<td>--</td>
<td>401</td>
</tr>
<tr>
<td>Use of intravenous drugs</td>
<td>72 (17.5)</td>
<td>334 (81.3)</td>
<td>5 (1.2)</td>
<td>411</td>
</tr>
</tbody>
</table>
Poor perception of the risk of infection is apparent not only in patients but also in physicians since they stated they had difficulty in identifying patients at risk. In our survey, 44% of patients considered they were not at risk of infection, yet among the patients who were not vaccinated, 82% were exposed to at least one risk factor. Concerning the poor awareness of risk, it has been demonstrated that health care personnel do not systematically evaluate risks related to sexual activity and use of intravenous drugs and thus fail to inform the patients about hepatitis B and anti-HBV vaccination. The lack of sufficient evaluation would be related to limited time for consultation, a certain lack of experience in approaching personal subjects with patients, desire to preserve the patient’s private life, and incomplete responses [46, 51]. Institution of information programs and specific vaccination campaigns might thus compensate for deficient medical information and improve diffusion of information to HIV+ patients since 30% of patients considered they had not been informed.

In our survey, among the patients stating they were not vaccinated, 30% were opposed to vaccination, 42% were favorable, and 28% had no opinion. This refusal of vaccination could be modified with targeted information from primary care physicians [47]. Factors affecting such a change in attitude include patient awareness of the risk of HBV infection, their knowledge of the beneficial effect of vaccination, and the positive attitude of health care personnel in regard to the vaccine [52].

The concern about potential adverse effects of vaccination, expressed by both patients and physicians, should be addressed specifically since epidemiological evidence has failed to demonstrate to date any cause and effect relationship between hepatitis B vaccination and such adverse effects except for one publication showing an association between HBV vaccination and multiple sclerosis [18, 53-60]. The association demonstrated in that study reached statistical significance when vaccinations performed during the three years preceding the first signs of multiple sclerosis were taken into consideration [60]. It is generally accepted that the hepatitis B vaccine is safe [61]. The beneficial effect of vaccination in at-risk adults appears superior to any potential risk associated with vaccination [28].

In conclusion, our survey demonstrated that despite medical practices of information and vaccination, awareness of the risk of HBV infection and vaccinal coverage remain insufficient among HIV-positive patients. Information campaigns targeted on this at-risk population are thus necessary in addition to reinforced education of the medical community concerning the usefulness of hepatitis B vaccination. Overall long-term care for HIV-infected patients whose disease has become chronic must include care for the risk of HBV co-infection and its prevention.

REFERENCES


HIV and Hepatitis B vaccination


Appendix — GECSA

Scientific Council : Prs J. Beylot, M. Dupon, M. Le Bras, J.L. Pellegrin, JM. Ragnaud and R. Salamon; Scientific Coordination: Prs F. Dabis and G. Chêne, Dr R. Thiebaut; Medical Coordination: Drs N. Bernard, D. Lacoste, D. Malvy, P. Mercié and D. Neau, Prs M. Dupon, J.F. Moreau, P. Morlat, J.L. Pellegrin and J.M. Ragnaud; Data processing and analysis: Dr S. Lawson-Ayayi, E. Balestre, V. Lavignolle ; Equipe technique : M.J. Blaizeau, M. Decoin, S. Delveaua, A.M. Formaggio, S. Labarrère, B. Uwamaliya, G. Palmer, D. Touchard, D. Dutot, F. Pereira, B. Boulant; Participating hospital units (practitioners): Centre Hospitalier Universitaire de Bordeaux : Pr J. Beylot (Pr P. Morlat, Drs N. Bernard, M. Bonarek, F. Bonnet, D. Lacoste, C. Nouts), Pr P. Couzigou, Pr H. Fleury (Pr ME. Lafon, Drs B. Masquelier, I. Pellegrin), Pr M. Dupon (Dr M. Dutronc, G. Cipriano, S. Lafarie), Pr J.L. Pellegrin (Prs P. Mercié, JF. Viallard, Drs C. Cipriano, S. Tchamgoué), Pr M. LeBras (Drs F. Djossou, D. Malvy, JP. Pivotaud), Pr J.F. Moreau (Dr JL. Taupin), Pr J.M. Ragnaud (Drs D. Chambon, C. De La Taille, H. Dutronc, D. Neau, A. Ochoa), Hôpital de Dax : Dr M. Loste (Dr L. Caunègre); Hôpital de Bayonne: Drs F. Bonnal (Drs S. Farbos, M. Ferrand, MC. Gemain); Hôpital de Libourne: Dr J. Ceccaldi.

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