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Prevalence of Antibodies to Hepatitis C Among Recently Treated Leprosy Patients in Senegal Parallels Those in Normal Populations

TO THE EDITOR:

Recent reports focused on a higher prevalence of hepatitis C (HCV) antibodies (Abs) in leprosy patients than in matched uninfected individuals ([3, 5]). Having followed a 175-patient cohort under field conditions, we do not confirm a higher carriage of hepatitis C among leprosy patients in Sénégal, and we suggest that the high levels previously observed might rather be associated with epidemiological conditions within the populations studied.

Infection with *Mycobacterium leprae* is accompanied by a profound alteration of cellular immunity leading to the different aspects of the leprosy spectrum. Little is known about the exact influence of the lack of T-cell immunity observed in leprosy and the susceptibility to viral infections. In this line, we investigated the seroprevalence to HCV using sequentially 2 third-generation ELISAs (Ortho HCV 3.0®; Chiron Corp., Emeryville, California, U.S.A.; Murex anti-HCV version III, Templehill, England) and an immunoblot assay (Ortho RIBA 3.0.®; Chiron). Genotyping of positive HCV sera was carried out using an ELISA revealing circulating antibodies to recombinant NS4 proteins (Murex HC02) ([1]). Two other markers of viral infection were also examined, i.e., the presence of hepatitis B virus antigen (HBs Ag) and HIV antibodies using commercially available kits; Monolisa® and Elavia mixte®, respectively (Sanofi-Pasteur, Marne la Coquette, France).

Subjects consisted of 147 newly diagnosed patents and 28 previously treated (monotherapy) patients entering a new survey for the efficacy of a fully supervised, intermittent, single-dose poly-antibiotherapy. Enrollment was done from March to December 1995; patients received full information regarding this investigation and an initial blood sample was taken at the time of the enrollment visit. During the survey, serum was kept in a dry sterile tube at 4°C (for approximately 12 hr) in the field and then frozen at –20°C until further assays.

A similar prevalence of the viral markers was found in sera from leprosy patients and a normal population. The HIV antibody prevalence reported here is in line with previous studies conducted on West African populations ([2, 6]). Secondly, the HBs antigen carriage found in this study was not higher than that found in recent determinations

THE TABLE. *Characteristics of the cohort of leprosy patients and results of the screening for antibodies to HIV and HCV and for HbS antigen.*

	Patients		Type of leprosy		Positive serology		
	No.	Mean age	PB[a]	MB[a]	HIV-1	HCV	HbS Ag
Males	103	31	50 (48.5%)	53 (51.5%)	1	1[b]	16 (15.5%)
Females	72	31	40 (55.6%)	32 (44.4%)	1	0	8 (11.1%)
Total	175	31 (6–65)	90 (51.4%)	85 (48.6%)	2 (1.1%)	1 (0.6%)	24 (13.7%)

[a] PB = paucibacillary; MB = multibacillary.
[b] PB leprosy (clinically BT).

that we carried out in the control population belonging to a matched study of hepatitis cases (19% of HBs$^+$) (Renaudineau, Y. and Raphenon, G. Manuscript in preparation).

In addition, in contrast to data from others ([3, 5]), we did not find a higher level of prevalence of HCV in this leprosy population. Two explanations can be proposed: first, the use of third-generation ELISAs leads to more accurate results and probably eliminates false positives; second, the patients enrolled in this study did not live in conditions favoring transmission of HCV (such as observed in leprosarium) associated with promiscuity and/or with poor sanitary conditions ([4, 5]). As a matter of fact, using the third-generation techniques, a relatively low frequency was found recently in a cohort of Senegalese patients suffering from liver diseases (2 out of 67; the HCV$^+$ patients had hepatocarcinoma) as compared to a control population (6 of 943 blood donors). In addition, the HCV antibody-positive leprosy patient was from serotype 2, which is the main circulating serotype since it is found in 80% of the confirmed HCV$^+$ serologies in our overall studies (Renaudineau, Y. and Raphenon, G. Manuscript in preparation).

Taken together, our results suggest that anergy or disorders of the immune system which accompany leprosy are not associated with chronic carriage of hepatitis C when epidemiological conditions for *M. leprae*-infected patients do not favor hepatitis C transmission.

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Dormancy, Drug Resistance or Dependency; Some Thoughts to Ponder

TO THE EDITOR:

This study, using the mouse foot pad method, was aimed at investigating *Mycobacterium leprae* persistors in the skin and nerves of leprosy patients and their sensitivity to drugs after a fixed duration of the World Health Organization-recommended multidrug treatment (WHO/MDT). Certain observations were intriguing and persuasive.

Secondary resistance to dapsone (DDS) (0.01 g%) and rifampin (0.001 g%) were recorded in two of the multibacillary cases treated and released from WHO/MDT. It was noted, however, that in both patients the percentages of takes (in second passage, mice to mice) were higher in the presence of DDS. Both were 80% as compared to untreated mice of 60% and 16.6%, respectively (The Table), and the average fold increases/foot pad of *M. leprae* were 10 times more in DDS-treated mice, suggesting that these organisms grew better in the presence of 0.01 g% DDS given by oral feeding.

A reconfirmation of the results was sought in these two patients. A second skin biopsy was obtained from each patient 3 years after release from treatment (RFT). The bacterial index (BI) of these biopsies were: Patient CS had a BI of 5+ and a morphological index (MI) of 1%; patient DS had a BI of 4.5+ and a MI of 1%.

Inocula were appropriately diluted to give 1×10^4/0.03 ml and injected into the foot pads of normal Swiss white mice, and a direct test for sensitivity to the same concentration of DDS (0.01 g%) and a higher concentration of rifampin (0.03 g%) was carried out.

Contrary to our expectations, both inocula showed no recordable count in the foot pads of mice at 6, 7, 8 and 12 months. However, significant counts were obtained at 16 months in both of the control groups of mice. The percentage take in patient CS was 80% (4/5); in patient DS, 67% (4/6). Only inocula from patient CS showed growth in the foot pads of drug-treated mice (percentage take with DDS 0.01 g% = 25% (1/4); with rifampin 0.03 g% = 33% (2/6), thus confirming resistance to both DDS and rifampin using highest concentrations.

Since there were no mice left, further harvests and confirmation of growth could not be carried out. Nevertheless, these cumulative data have raised several questions.

Results from the first part of the study indicate that there was a subpopulation of *M. leprae* that were not only refractory to DDS but grew better in the presence of DDS (? DDS dependence) and a doubtful rifampin resistance considering the concentration of rifampin used in this test was only 0.001 g%.

Three years after RFT, the second biopsies obtained from the same patients, in spite of showing a good BI and 1% MI, failed to show a normal growth pattern. Since the harvests were carried out at regular intervals beginning from month 6, the