High-Flux Membranes Are Not Permeable to Hepatitis B Virus-DNA

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Dear Sir,

High-flux membranes have been found to be permeable to HBsAg [1] in contrast to cellulose membranes [2]. Backfiltration from inoculated dialysate has been proposed as a possible route of transmission of hepatitis B virus (HBV) in dialysis patients [1]. As HBV-DNA, rather than HBsAg, is the marker of infectivity, we have investigated whether AN69 membranes are permeable to HBV-DNA.

Fifteen HBsAg-positive patients were investigated. Renal replacement therapy consisted of hemodialysis in 9 and hemofiltration in 6 patients. AN69 dialyzers were used. Blood was investigated for HBeAg, anti-HBe (ELISA, Abbott Laboratories, North Chicago, Ill.) and HBV-DNA [molecular hybridization according to the method described by Shimizu et al. [3]. Dialysate and ultrafiltrate were tested for HBsAg after 5-fold concentration, while HBV-DNA was determined after phenol extraction from 2.5 ml as well as from 25 ml of fluid. All 9 hemodialysis patients were HBeAg-positive; HBV-DNA could be demonstrated in blood of 7 patients. Of the hemofiltration patients, 6 were HBeAg-positive and 1 anti-HBe-positive; all were negative for HBV-DNA in blood. HBsAg was not found in the dialysate or ultrafiltrate of any patient, nor could HBV-DNA sequences be demonstrated in these fluids. The difference between cellulose and high-flux membranes is a greater permeability in the latter to larger molecules, notably in the range of 5,000-50,000 daltons [4]. As the molecular weight of HBsAg is 24,000 daltons

[5], it is to be expected that it can be demonstrated in the dialysate during treatment with high-flux membranes but not with cellulose membranes. The molecular weight of the full-length HBV-DNA can be estimated to be about 2,000,000 daltons, while an intact HBV virion (Dane particle) has a diameter of 42 nm. Therefore, it cannot pass into the dialysate. The absence of HBsAg in the dialysate or ultrafiltrate was unexpected, although others also failed to demonstrate this in all seropositive patients [1]. The sieving coefficient for HBsAg must have been lower than was estimated by the molecular weight. In this study we could not demonstrate HBV-DNA sequences in dialysate, making infectivity unlikely. However, overt

blood leaks, but also leaks which allow passage of particles smaller than erythrocytes but larger than 42 nm may result in infectivity of the dialysate or ultrafiltrate [6]. This may be important in dialysis machines with a recirculating single pass dialysate system, as the dialysis solution of the subsequent patients may become contaminated. Handling of dialysate or the compartments of a dialysis machine has to be considered a contamination risk.

References

Moynot A, Dubreuil P, Daniel F, Pillot J: Dialysis membrane permeability to HBsAg; in European Dialysis and Transplant Association – European Renal Association: Book of Abstracts, 1990, p 152.

Andrew R, Harihan S, Saha V, John JT, Kiruba-karan MG, Shastry JCM: Biochemical evaluation of ultrafiltrate in dialysis-dependent HBsAg-positive patients. *Nephron* 1988; 49:88. Shimizu Y, Ida S, Matsukara T, Yuasa T: Determination of hepatitis B virus DNA in serum by molecular hybridization. *Microbiol Immunol* 1984;28:1117-1123.

Samtleben W, Gurland HJ: Plasma exchange: Principles and practice; in Maher JF (ed): Replacement of Renal Function by Dialysis. Dordrecht, Kluwer Academic Publishers, 1989, pp 46(M74).

Van Ditzhuijsen TJM, Kuijpers LPC, Koens MJ, Rijntjes PJM, van Loon AM, Yap SH: Hepatitis B pre-S1 and pre-S2 proteins: Clinical significance and relation to hepatitis B virus DNA. *J Med Virol* 1990;32:87-91. Snyderman DR, Bryan JA, London WT, Werner B, Bregman D, Blumberg BS, Gregg MB: Transmission of hepatitis B associated with hemodialysis: Role of malfunction (blood leaks) in dialysis machines. *J Infect Dis* 1976; 134:562-570.

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