

## **This Week's Citation Classic**

**London W T, DiFiglia M, Sutnick A I & Blumberg B S.** An epidemic of hepatitis in a chronic-hemodialysis unit: Australia antigen and differences in host response. *N. Engl. J. Med.* 281:571-8, 1969.[Inst. for Cancer Res., Fox Chase, and Dept. Nephrology, Jefferson Med. Coll. Hosp., Philadelphia, PA]

**This paper made two new points: 1) Australia antigen, a marker of hepatitis B virus, was prevalent in patients treated in a chronic hemodialysis unit; 2) the infected patients had a mild, persistent, anicteric hepatitis whereas staff members exposed to the same virus contracted an acute, icteric, transient illness. This demonstrated the essential role of the host immune response in the clinical manifestations of the hepatitis. [The SO® indicates that this paper has been cited over 230 times since 1969.]**

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"In 1968, Blumberg, Sutnick, and I were in need of human antibodies to what was then called Australia antigen. This antigen, now called hepatitis B surface antigen (abbreviated HBsAg), is the outer coat of the hepatitis B virus. Our best sources of antibody had been patients who had received many blood transfusions. Therefore, in collaboration with P.J. McKenna, we began screening serum from patients at Thomas Jefferson University Hospital who had received five or more blood transfusions. Of the first 39 patients tested, we were surprised to find six whose blood contained Australia antigen, not the antibody to it. On investigation it turned out that five of the six were patients with end-stage renal disease who were being treated in the hospital's chronic hemodialysis unit. Since there were only nine patients receiving hemodialysis, we knew that we had stumbled on to an interesting situation. At that time, Marion DiFiglia was a fellow on the nephrology service. She told us about

several cases of viral hepatitis among staff members, but she was unaware of hepatitis problems among the patients. This observation became the major focus of our investigation and the subsequent paper.

"Ultimately, we found that eight of the nine hemodialysis patients were HBsAg(+), and the one HBsAg(-) patient was only tested once before she died. At autopsy she had evidence of mild chronic hepatitis. Six of the 15 staff members developed hepatitis, and the two that we were able to test were HBsAg(+). Laboratory studies confirmed DiFiglia's initial clinical observation. The dialyzed patients had a chronic anicteric illness without symptoms of hepatitis, whereas the staff members had acute hepatitis with high serum bilirubin levels and markedly elevated serum transaminase levels. We hypothesized that the differences in response to the virus infection were due to impairment of the immune systems of the patients with chronic renal disease. From this we concluded that it was the immune response to the infection, rather than replication of the virus, which caused liver damage and the clinical signs and symptoms of hepatitis.

"After our paper was published, many investigators in the United States and Europe reported similar findings. I think it was the great prevalence of silent hepatitis B infections in dialysis units that led to the numerous citations of our paper. Following our initial report, we began a long-term study of patients and staff in chronic hemodialysis units in Philadelphia, which still continues, and has resulted in several interesting findings.<sup>1,2</sup>

"The hepatitis B vaccine, which should be available shortly, will most likely be administered to the patients and staff of hemodialysis units. My guess is that hepatitis B infection will be eliminated from dialysis units within 15 years of the discovery of the problem."

1. **London W T, Drew J S, Lustbader E D, Werner B G & Blumberg B S.** Host responses to hepatitis B infection in patients in a chronic hemodialysis unit. *Kidney Int* 12:51-8. 1977.
2. **London W T & Drew J S.** Sex differences in response to hepatitis B infection among patients receiving chronic dialysis treatment. *Proc. Nat. Acad. Sci. US* 74:2561-3. 1977.