## This Week's Citation Classic **OCTOBER 17, 1988**

Prince A M. Prevalence of serum-hepatitis-related antigen (SH) in different geographic regions. Amer. J. Trop. Med. Hyg. 19:872-9, 1970. [Laboratory of Virology, New York Blood Center, and Department of Pathology, New York Hospital-Cornell Medical Center, New York, NY]

A gel diffusion assay for what is now termed hepatitis B virus specific antigen was used to assess the prevalence of the hepatitis B virus carrier state in seven African, four South American, and two Asian countries. The prevalences found were 8 to 100 times higher than those of New York blood donors. [The SCI® indicates that this paper has been cited in over 140 publications.]

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This paper emerged out of an exciting phase of hepatitis B virus (HBV) research. Evidence was at last at hand indicating the existence of an HBV specific antigen (HBsAg) that could be detected by relatively insensitive assays in the serum of persons with acute or chronic carrier type infections with this virus.<sup>1,2</sup> At the time this study was done, we called this the serum hepatitis-related antigen (SH), while B.S. Blumberg and his group called it the Australia antigen.<sup>3</sup>

It thus became possible to systematically study the geographic distribution of infection with this virus. Blumberg's studies had already indicated unusually high prevalences in populations in Africa and the Amazon region of South America.<sup>3,4</sup>

I therefore wrote to everyone whom I knew who had access to sera from different tropical regions in Africa, Asia, and South America. Particularly helpful were the Medical Mission Sisters of Philadelphia, who requested and received the cooperation of their colleagues in the field, and the World Health Organization (WHO) serum reference banks. In this way we accumulated 2,238 sera from 13 countries in tropical regions of the world.

Our finding that the populations sampled had an 8- to 100-fold higher prevalence of chronic HBV carriers than did blood donors in New York has been abundantly confirmed,5 but remains unexplained even today. Our speculation that bloodsucking insects might play a role seemed to be strengthened by our finding of HBsAg in mosquitoes caught in the wild;6 however, we have been unable to show transmission by this route in chimpanzee experiments (unpublished).

The actual prevalences reported in this paper were considerable underestimates, as was recognized in the paper, due to the use of the very insensitive Ouchterlony assay, which was then the only one available. With today's ELISA and radioimmunoassays, two- to fourfold higher prevalences would be observed.

The frequency with which this unsophisticated paper has been cited reflects the extraordinary importance of HBV infection in tropical regions of the world, the ease with which HBV infections can be studied, and the consequent large number of publications on HBV infection prevalence, which has been reported from every country.

Bull. NY Acad. Med. 44:1566-86, 1968. (Cited 340 times.)

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<sup>1.</sup> Prince A M. An antigen detected in the blood during the incubation period of serum hepatitis. Proc. Nat. Acad. Sci. USA 60:814-21, 1968. (Cited 800 times.) [See also: Prince A M. Citation Classic. (Barrett J T, ed.) Contemporary classics in the life sciences. Volume 1: cell biology. Philadelphia: ISI Press, 1986. p. 160.]

<sup>2.</sup> Prince A M, Hargrove R L, Szmuness W, Cherubin C E, Fontana V J & Jeffries G H. Immunological distinction

between infectious and serum hepatitis. N. Engl. J. Med. 282:987-91, 1970. (Cited 235 times.)

<sup>3.</sup> Blumberg B S, Sutnick A I & London W T. Hepatitis and leukemia: their relation to Australia antigen.

<sup>4.</sup> Blumberg B S, Melartin L, Guinto R A & Werner B. Family studies of a human serum isoantigen system (Australia antigen). Amer. J. Hum. Genet. 18:594-608, 1966. (Cited 165 times.)

<sup>5.</sup> Sobeslavsky O. HBV as a global problem. (Vyas G N, Conen S N & Schmid R, eds.) Viral hepatitis.

Philadelphia: Franklin Institute Press, 1978. p. 347-56. (Cited 35 times.)

<sup>6.</sup> Prince A M, Metselaar D, Kafuko G W, Mukwaya L G, Ling C M & Overby L R. Hepatitis B antigen in wild-caught mosquitos in Africa. Lancet 2:247-50, 1972. (Cited 100 times.)