

## This Week's Citation Classic

Almeida J D, Rubenstein D & Stotl E J. New antigen-antibody system in Australia-antigen-positive hepatitis. *Lancet* 2:1225-7, 1971. [Dept. Virology, Royal Postgrad. Med. Sch., London, and Clinical Res. Ctr., Northwick Park Hosp., Harrow, Middlesex, England]

The paper reported that the double shelled Dane particle of what is now hepatitis B antigen, but which was then Australia antigen, could be degraded by detergents to reveal an internal component that was antigenically distinct from the surface of the particle. [The SC<sup>®</sup> indicates that this paper has been cited in over 345 publications since 1971.]

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"It has been said that Columbus, sailing in the wrong direction and using a false premise, nevertheless discovered America. The authors of this paper must admit that what happened to them had a certain similarity to his situation. The group included one electron microscopist and two tissue culture experts who had decided to have an attempt at the difficult task of growing the virus of hepatitis B in culture. Incidentally, over ten years later this still has not been achieved. Based on the fact that some viruses, for example, the reoviruses, have a higher infectivity for tissue culture if they are degraded with enzymes, it was felt that it might be possible to degrade the so-called Australia antigen with enzymes, and/or detergents, making available the essential nucleic acid. One year earlier, David Dane and his co-workers<sup>1</sup> had described a double shelled particle present in Australia antigen preparations that had much better viral characteristics than the smaller spheres and tubules of such preparations. This particle was later termed the Dane particle.

"We started with a preparation rich in Dane particles and subjected it to several degradative procedures. The end products of these experiments were always checked in the electron microscope by the negative staining technique as well as being inoculated onto a wide range of tissue cultures. Luckily, since one of my major interests is the visualisation of the interaction between virus and antibodies, we were able to recognise that Dane particles split with detergent released an inner component that became covered with antibody that must have been present in the original serum. Almost immediately we dropped the tissue culture aspect of the work that had yielded no positive results and turned our attention to this new phenomenon. It didn't take long to establish that sera positive for hepatitis B antigen always had antibody to this internal component or core, and that this system was quite distinct from the other antigenic components.

"The paper has been much quoted because it suggested that the Dane particle had the characteristics of other compound viruses such as the herpes group. It focused the attention of the biochemists on the inner component as the likely location for the viral nucleic acid, an assumption that turned out to be true. It also gave rise to the terminology that is still employed: that the outer covering of the Dane particle would be surface antigen, or HBsAg, and the inner component, the core antigen, or HBcAg.<sup>2</sup>

"One final comment about this paper is that the three authors took great pleasure in their work and whenever possible saw the funny side of things. For example, the micrograph that is figure 1 of the paper was carefully arranged so that there is a hepatitis B antigen cross marking a Western style grave at the foot."

1. Dane D S, Cameron C H & Briggs M. Virus-like particles in serum of patients with Australia antigen-associated hepatitis. *Lancet* 1:695-8, 1970.
2. Dienstag J L. Hepatitis viruses: characterization and diagnostic techniques. *Yale J. Biol. Med.* 53:61-9, 1980.