

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.
[Bland-Sutton Inst., Middlesex Hosp., London, England]

Virus-like particles 42 nm in diameter were found in the blood of three patients infected with hepatitis B virus. These particles were thought to be complete virions and the much more numerous 22 nm particles and long forms excess virus-coat material. [The SC P® indicates that this paper has been cited over 455 times since 1970.]

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"In 1965 at the Queen's University, Northern Ireland, I started a research programme which aimed at identifying human hepatitis viruses by electron microscopy (EM). Conventional methods of isolating and growing viruses in tissue culture or small laboratory animals had been unsuccessful for hepatitis and I thought that EM and negative staining techniques had developed to the stage where they could be used by virologists in rather the same way as light microscopy was used by bacteriologists. As a first step Moya Briggs and I looked at as many different morphological types of viruses as we could using negative staining and concentrating on the recognition of viruses in unpurified preparations.

"This work was brought to an end by a move to the Middlesex Hospital, London, in 1966. We did not start again until 1969 when a hematologist friend, J.W. Stewart, persuaded me to test some of his patients for the mysterious 'Australia antigen'¹ This antigen was found in the blood of patients with hepatitis B virus infections in the form of spherical 22 nm diameter particles which were often present in enormous numbers A few long forms of the antigen which were 22

nm wide might also have been present. The antigen particles did not contain nucleic acid and therefore could not be conventional virions. Some people even doubted whether Australia antigen was specifically related to hepatitis B virus.

"One of the first blood samples we were given was from a hemophiliac patient who complained of feeling 'liverish.' Colin Cameron demonstrated Australia antigen by immunodiffusion and we then looked at it by EM Among the enormous numbers of the small round and long antigen particles described by others we saw just a few quite different, larger particles with inner cores. They looked like virions and it was a simple matter to show that in other Australia antigen positive blood samples there were small numbers of these larger 42 nm diameter particles which had a core surrounded by an outer coat Cameron showed that they were denser than the other particles and might therefore contain nucleic acid In appearance and also immunologically the outer coat of the 42 nm particles seemed to be made of the same material as the much more numerous small round and long particles. We suggested that the 42 nm particle was the infective virus and that the other particles consisted of surplus coat material. This explanation of Australia antigen was later reinforced when our friend June Almeida demonstrated the immunological specificity of core antigen,² and DNA and DNA polymerase were found to be associated with cores.

"Hepatitis B research has been something of a growth industry in recent years and many papers have been published. When mention has been made of the virus particle our paper has often been quoted. The 42 nm particle was christened the Dane particle, but I never discovered whether the person who originally referred to it in this way was a well-wisher who thought we were right or someone who hoped we were wrong."

- Blumberg B S, Alter H J & Visnich S.A** new antigen in leukemia sera.
J. Amer. Med. Ass. 191:541-6, 1965.
[Citation Classic. *Current Contents/Life Sciences* (51):14, 17 December 1979.]
- Almeida J D, Rubenstein D & Scott E J.** New antigen-antibody system in Australia-antigen-positive hepatitis. *Lancet* 2:1225-7, 1971.