Hepatitis B virus was discovered as a consequence of a population study designed to identify inherited immunologic traits in humans (Blumberg, 1977; Blumberg et al., 1984). Beginning in 1955, with the introduction of the starch gel electrophoresis method by Smithies (1955), it became clear that there were a large number of inherited biochemical polymorphism of human serum proteins. Allison and Blumberg (1961) postulated that if any of these polymorphisms, involved antigenic proteins, patients who received even a small number of transfusions would be likely to be exposed to proteins or other biochemical entities which they themselves had not inherited or acquired but which were present in the donors' blood. If this was to happen the transfused patient might develop a precipitating antibody against this "Foreign" protein and the antisera so formed could be used to detect the polymorphic protein system.

The above mentioned hypothesis was tested by using the serum from transfused patients as a reagent in agar gel immunodiffusion experiments (Allison and Blumberg, 1961). Blumberg and Colleagues (1961, and 1962) soon identified a previously unknown polymorphism of the serum low density lipoproteins (termed the Ag system) which has proved to be of interest in genetics,
diseases' studies, and forensic medicine. After the initial discovery the hypothesis that serum protein polymorphisms could be identified by the transfused patients technique continued to be tested and a new precipitin system that was distinctly different from the first was detected (Blumberg et al, 1964 and 1965). The initial reaction was between the serum of a transfused haemophilia patient from New York city and an Australian aborigine. The antigenic material present in the aborigine was termed "Australia Antigen" (Au) and a series of studies to determine the biologic significance of the unusual constituents were designed.

Further field studies were done to describe the distribution of the antigen in human population (Blumberg et al, 1965). From the studies, data were collected from which hypothesis could be generated. Australia antigen was very rare in the United States and northern European population (Prevalence about 0.1 per cent) but common in tropical and Asian groups (Prevalence 5-15 per cent) (Blumberg et al, 1965; 1966). Blumberg and colleagues (1965) also found Australia antigen to be common in patients with leukaemia, an observation which arouse as a consequence of systematic studies of the distribution of the Australia antigen in a variety of diseases.
From the Australia antigen - leukaemia disease association, the hypothesis was made that patients who were likely to develop leukaemia were also likely to have Australia antigen (Blumberg et al, 1967). A series of population with a high likelihood of developing leukaemia were identified and tested. These included persons with Down syndrome who were known to have much greater risk of developing leukaemia in childhood than the general population (Miller et al, 1966). The prediction was fulfilled in that more than 30 per cent of uninstitutionalized persons with Down syndrome were found to have Australia antigen in their blood (Blumberg et al, 1967 and 1968).

At about the time of this discovery (1966) a series of observations were made which directed attention to the possibility that Australia antigen might be associated with a hepatitis virus (Blumberg, 1977). The most important of these, in retrospect, was the case of JB, a patient with Down syndrome (Blumberg et al, 1984). In the original series of studies on people with Australia antigen, its presence or absence appeared to be a persistent characteristic (Blumberg et al, 1965, 1966). JB did not have Australia antigen in his serum in the initial analysis. Contrary to expectation, Australia antigen was found in his blood on subsequent examination. Concomitant with the appearance of Australia antigen, JB developed enzyme elevation and hepatitis was diagnosed on
liver biopsy. A hypothesis was made that Australia antigen was associated with a hepatitis virus. This hypothesis was tested with another series of epidemiologic studies (Blumberg, 1967; 1968 and 1969).

It was found that Australia antigen was more common in patients with acute and chronic hepatitis than in healthy people or patients with other diseases (Blumberg et al., 1967; 1968 and 1969). These observations were soon confirmed by Okochi and Murakami (1968) and later by others (Prince et al., 1968). From these population studies, a biologic model was formulated, namely that Australia antigen, was or was on, a virus which could cause hepatitis (Bayer et al., 1968). This model was tested by a series of experimental laboratory studies. Eventually the virus particle was isolated by column separation ultracentrifugation and enzymatic digestion of remaining serum proteins. It was visualised under the electron microscope (Bayer et al., 1968; 1970) and its transmission by transfusion (Goeke et al., 1959 and 1970) and animal inoculation was shown (London et al., 1970 and 1973). Thomas and Blumberg did not test hypothesis that Australia antigen was associated with a particular type of hepatitis (i.e. serum or infectious). Thomas and Blumberg approach was to perform cross sectional studies to elucidate the relationship of Australia antigen to the various clinical forms of hepatitis. Other workers were more direct. Prince (1968) reported the
presence of an antigen in serum (SH antigen) that he said was specific for serum hepatitis. He found serum hepatitis antigen in 6 of 8 cases of post-transfusion or postinoculation hepatitis during the pre-clinical or early clinical phase of disease, but not in the blood of five patients with infectious hepatitis. Shortly thereafter, Prince stated that serum hepatitis antigen and Australia antigen were identical (Prince, 1968).

An experimental approach was taken by Krugman and colleagues (1967). In order to learn more about the biology, etiology and prevention of viral hepatitis beginning in 1955, they induced hepatitis in children residing in an institution for the mentally retarded (Krugman et al, 1967). By 1968, they had distinguished two infectious sera, MS-1 and MS-2, collected during two episodes of hepatitis which occurred in a single patient. Inoculation of MS-1 regularly produced a short incubation disease (Krugman et al, 1967). Gile et al (1969) reported that MS-2 contained Australia antigen, MS-1 did not (Gile et al, 1969). Furthermore, almost all children inoculated with MS-2 developed Australia antigen in their blood about the time of occurrence of hepatitis. None of the recipients of MS-1 acquired Australia antigen. These studies demonstrated the specificity of the association of Australia antigen with one type of hepatitis and also strongly supported the hypothesis
that Australia antigen was part of the infectious agent which caused the disease.

The importance of detection of Australia antigen in blood donor lies in the fact that some of the patients suffering from hepatitis B become chronic carriers, since they may be immunologically deficient. They are apparently normal individuals with Australia antigen in their sera without any clinical or biochemical abnormalities of liver functions. Hence the main significance lies in screening of professional and voluntary blood donors and reducing the incidence of direct transmission.