The morphologic structure, antigenic composition, DNA size and structure, DNA polymerase activity and biologic properties of HBV distinguish this agent from all previously known human viruses. DNA containing viruses which appear to be phylogenetically related to human HBV (Summer, 1981) as determined by ultrastructural criteria, circular DNA with large single strand regions, cohesive ends and approximately 3000-3300 base pairs, DNA polymerase activity circulating surface antigen particles and ability to induce persistent infection have been discovered in the eastern world chuck (Mornotanax) (Summers et al., 1978; Werner et al., 1979), the California ground squirrel (Spermophilus buchevi) (Marian et al., 1980b) and the pekin duch (Anus domesticus) (Peitelson et al., 1981). Woodchuck hepatitis virus, infection is associated with the development of chronic hepatitis and hepatocellular carcinoma (Popper et al., 1981, Summers et al., 1978) and may serve as a key model in the study of the pathogenesis of other disorders which also are associated with persistent HBV infection in human beings.

Further study of this new class of HBV type virus may provide information about the biology of infection and virus host interactions which are critical to a complete understanding of human HBV. The virus of
hepatitis B (HBV) is present in the sera of infected patients often at a very high level. Associated with it are three antigen antibody systems (Ag, Ab), the detection of which can be employed singly or in combination as markers for current or past infection. The presence of hepatitis B surface antigen (HBsAg) denotes current infection and as such is the most useful single marker for identifying the potentially infectious patients. It is a complex antigen released from infected hepatocytes and exists in serum as three morphological forms. The bulk of serum HBsAg comprises excess virus coat antigen in the form of small 22nm particles and filament. The HBV particles (Dow Canison and Briggs, 1970) are 42 nm in diameter and have an outer coat of HBsAg. Inside this coat is a 27 nm core resembling a conventional small virus which carries with it the circular DNA genome and attendant DNA polymerase.

HBsAg carries a major antigen 'a' which is common to all HBV strains. In addition, two pheno-typic antigens d or Y and W or 'r' are present (Le Bouvier, 1971), while these do not confirm any other particular attributes on the virus, they are useful for epidemiologists as they breed true. In other words, an a d r infection in a surgeon can only have arisen from an 'adr' source. This can be of great help. After recovery from an infection, most patients produce
antibody to HBsAg, anti HBs, the specificity of which is directed mostly to the common 'a' determinant. In some patients it may be months or some times even longer before serum anti-HBs can be detected. Anti-HBs denotes past infection and immunity to further infection.

The 27 nm nucleocapsid (core) of the human HBV contains the viral genome; circular, double stranded DNA, comprising about 3200 base pairs, with a large but variable single stranded region, and specific discontinuities or nicks which confer cohesive ends on the molecule (Sattler and Robinson, 1979). In studies of a human hepatocellular carcinoma cell line (PLC/PRF/5) which produces HBsAg and in which produces HBsAg and in which HBV genomes are integrated into host DNA, it has been suggested that integration occurs at the nicked cohesive end region (Edman et al., 1980). A protein molecule is covalently bound to the 5' end of the complete DNA strand but its function is uncertain (Gurlich and Robinson, 1980). The DNA polymerase associated with the HBV nucleocapsid is believed to repair the gap in the short DNA strand by lengthening its 3' end. In addition to HBV specific DNA polymerase, the nucleocapsid of HBV is also associated with the protein kinase activity (Albin and Robinson, 1980). The kinase serves to phosphorylate the major polypeptide of the core.
TYPICAL CLINICAL AND LABORATORY FEATURES OF

ACUTE VIRAL HEPATITIS TYPE B.

JANODICE.

↑ALT.

HBsAg.

ANTI HBC.

WEEKS AFTER EXPOSURE.
Cloning of the HBV genome, a major technological advance in the study of HBV, has been reported by several laboratories (Borrel et al., 1979; Charnay et al., 1979; Sninsky et al., 1979; Valenzuela et al., 1979). Restriction endonuclease cleavage maps of the cloned HBV genome has been constructed and the nucleotide sequences have been established.

Different antigenic subtypes of HBV have yielded distinct restriction endonuclease cleavage sites for cloned DNA (Price et al., 1980), but the restriction patterns of clones derived from the same source are similar (Swinsky et al., 1979). These observations suggest homogeneity of the HBV genome in any given infected individual. Regions of the genome coding for the major polypeptides of the surface and core antigens of HBV have been identified appear to be present on the same DNA molecule, and recombinant plasmids which direct the synthesis of these peptides have been developed (Edman et al., 1981). RNA transcripts specific for the surface antigen sequencies of HBV, DNA has been demonstrated (Adman et al., 1988). A detailed review of present knowledge of the genetic organisation of HBV is available (Tiollais et al., 1981).

Following the successful cloning of HBV in bacterial plasmids, it became feasible to introduce the clones HBV DNA or its fragments into mammalian cell lines (Hirschman et al., 1980; Narurty et al., 1981). These models are likely to provide information about
mechanism of intracellular HBV infection and replication which cannot be achieved by further characterisation of HBV DNA per se. The Hela cell model is of particular interest (Hirschman et al., 1980). When Hela cells were exposed to cloned HBV DNA which had been excised from a plasmid and recircularised, they showed cytopathic changes, and, 11-14 days after subculture, produced both the surface and the core antigen of HBV. Furthermore, 42 nm HBV-like particles, as well as smaller, 20 nm particles resembling surface antigen, particles were detected in the culture media of the Hela cells transfected with cloned HBV DNA. These data suggest that this widely available cell line is suitable for studies of the production in intact HEV as well as synthesis of its gene products (Raymond S Koff, 1983).

Another approach to further understanding of the biology of HBV has been the establishment of the tissue culture cell line (PLC/PRF/5) derived from hepatocellular carcinoma in a Mozambican carrier of the hepatitis B surface Ag. This hepatocellular carcinoma cell line shows typical epithelial cell growth and retains the ability to produce surface antigen which is identical to that isolated from HBV carriers (Skelly et al., 1979). The cells exhibit many of the functions of hepatocytes, e.g. they secrete liver specific proteins such as alpha fetoprotein and form solid tumours when transplanted into athymic nude mice (Bassendine et al., 1980). Although
Components of the Hepatitis B Virus.

Virion of HBV.

Surface antigen particles.

The antigen and antibody markers of hepatitis B.
PLC/PRF/5 cells do not produce the core of Ag of HBV or intact infectious HBV particles (Daemer et al., 1980), and only RNA transcripts specific for surface Ag have been detected (Edman et al., 1980), molecular hybridization with cloned HBV DNA probes indicate the presence of complete or nearly complete sequences of HBV DNA (Brechet et al., 1980; Chakraborty et al., 1980; Marion et al., 1980 'a'). Restriction fragment hybridization studies indicated that most, if not all, of the viral DNA in infected cells is integrated into host DNA (Brechet et al., 1980; Chakraborty et al., 1980; Marion et al., 1980). Several copies (3-4) of HBV DNA are present per haploid cell DNA equivalent and 3-6 specific integration sites have been identified. Other cell lines, also derived from human hepatocellular carcinomas, and which secrete the surface antigen of HBV have been established (Knowles et al., 1980) and provides experimental models for further investigation. These exciting techniques may be crucial to the search for knowledge of the mechanism underlying persistent production of HBV products following infection and to understanding the oncogenicity of HBV in human beings (Raymonds Koff, 1983).

The nucleocapsid or core of HBV contains two immunologically reactive materials the hepatitis B core Ag (HBcAg), and Hepatitis Be antigen (HBeAg) which appears to be interrelated but distinct from the hepatitis B surface antigen (HBsAg) of the HBV envelope.
HBCAg and HBeAg have been detected in the nucleus of hepatocytes of patients with persistent HBV infection (Yoshi-sawa et al., 1979). HBCAg is also present in the nucleus of acutely infected patients. It was detected in liver biopsy specimens in 3 of 24 patients with acute hepatitis B (Mathisen et al., 1973). Six of these 24 had HBSAg on the surface of their hepatocytes. HBCAg is not readily detected in the serum of infected patients because antibody (HBCAg) is invariably present and marks the presence of HBCAg. However, separation of anti HBC from HBV particles permits identification of HBCAg in the sera of the patients with persistent HBV infection (Rezzetto et al., 1981). HBeAg has been identified in HBSAg positive sera exclusively although there is one, unconfirmed report of HBeAg positivity in the absence of HBSAg (Tabor et al., 1980b).

A variable number of constituent polypeptides have been isolated from HBV cores. HBCAg is believed to comprise a major polypeptide weighing 19000 daltons with 183-185 amino acids as determined by the Nucleotide sequences of the HBV genome coding for its production. (Tissailais et al., 1981). HBeAg can be released from the inside of HBV cores, after treatment with detergent Sodium Dodecyl Sulphate (Taka hashi et al., 1979). Two polypeptides with weight of 19000-45000 daltons were identified; both had HBeAg activity. In other studies degradation of core particles resulted in the antigen
conversion of HBeAg to HBeAg (Ohori et al., 1980). These studies suggested that the antigenic determinants of HBeAg and HBeAg reside on different protein structure of the same 19000 dalton polypeptide. Whether this polypeptide is immunogenic and can raise antibodies against HBeAg and HBeAg remains to be determined (Raymond S. Koff, 1983). The relationship of the 19000 dalton polypeptide to the three antigenic components of HBeAg now recognised (Murphy et al., 1978), also remain uncertain (Blancy et al., 1980).

All individuals acutely infected with HBV become HBeAg positive. HBeAg in serum is detected shortly after the appearance of HBsAg and in most instances, disappears while HBsAg is still present (Krugman et al., 1979). In persistently infected HBsAg carriers, prevalence of HBeAg is variable but independent of sex, race, and HBsAg antigenic sub-type (Szmuness et al., 1981a), since a steadily increasing proportion of carriers clear HBeAg with time, older carriers are less likely to be HBeAg positive than younger once. The presence of HBeAg appears to incite active viral replication, an abundance of intact HBV particles, and an increased risk of infectiousness in number of epidemiological settings (Forzillo et al., 1979). It remains an excellent, if imperfect markers of potential infectivity and may have clinical value in assessment of patient with HBV associated chronic hepatitis (Hoofnagle et al., 1981). In
addition, HBcAg may play a role in immunopathogenesis of the immune complex mediated membranous glomerulonephritis associated with HBV infections (Ito et al., 1981).

HBsAg is the most extensively studied of the known antigen of HBV. Infected hepatocyte synthesize HBsAg in excess of that required for the envelope of HBV. A large number of 20-22 nm HBsAg particles appear in the circulation and HBsAg is detectable on the surface of hepatocytes. The small, non-infectious HBsAg, particles are immunogenic and because they induce antibodies which are protective, they have served as the source for an effective, safe, commercially available vaccine against HBV (Szmuness et al., 1981b). Biochemical characterization of HBsAg has disclosed the presence of number of polypeptides, some of which are glycosylated (Shiraishi et al., 1980). Although isolated polypeptide have varied in size, major component have molecular weight of 22000-23000 and 27000 daltons; different degrees of aggregation and glycosylation may be responsible for the observed heterogeneity. Solubilization of partially purified 22 nm HBsAg particles in sodium dodecyl sulphate, in the absence of reducing agents, yielded a polypeptide measuring 49000 daltons (Mishra et al., 1980). This polypeptide was split, on incubation in reducing conditions, into two polypeptides with molecular weight identical to that of major polypeptides. The 49000 daltons peptide was immunogenic and
retained the common and sub type determinants of the source HBsAg particles (Raymond S Koff, 1983).

From nucleotide sequencing studies, an amino acid sequence of 226 residues has been suggested for one of the major HBsAg polypeptides. Chemically synthesized peptide corresponding to these amino acid sequences have been prepared, they have been shown to elicit antibodies to both native HBsAg and the major HBsAg polypeptides (Lerner et al, 1981).

Antigenic sub determinants of HBsAg coded for by the genome HBV are useful as epidemiological tools in tracing infection and serves as markers of population migration patterns. The hepatitis B vaccine prepared from HBsAg subtype ad particles confers cross protection (Zammess et al, 1981b). The rare occurrence of HBsAg of different subtypes in the same individual may reflect double infection by different HBV's or exchange of DNA sequences between HBV of different subtypes (Hess et al, 1979).

The association of human serum proteins and purified preparation of HBsAg has been extensively studied. A species specific receptor for polymerized human albumin has been demonstrated on HBsAg particles (Imai et al, 1979), on individual HBsAg polypeptides (Kosanu - Matin et al, 1980), in the cytoplasm of HBsAg containing hepatocyte, 'Thung and Garber, 1981a), in PLC/PRF/5 cells and their media in tissue culture,
(Thung and Garber, 1981a), and on HBsAg particles produced by these cells (Ionescu-Matiu et al., 1980). The association of polymerized human albumin with the surface of hepatocyte and the receptor on HBsAg of the intact HBV particle may be an important determinant in the attachment of HBV to hepatocytes. However, the precise role of this system and its interaction with antibodies to polymerized human albumin (Hung and Garber et al., 1981b), and the complement sub component, C1q (Milich et al., 1981), are the subjects of continuing investigation.

There is wide global variation in the prevalence of the carrier. In UK blood donors it is between 0.1 and 0.2 percent. It ranges from about 5 percent in Mediterranean countries to as high as 10% or more in the countries of south east Asia (Sobaslavsky, 1978). One consequence of the high prevalence of carriers in those countries is the high incidence of chronic liver disease, cirrhosis and hepatoma. The higher prevalence of severe liver disease amongst carriers in many Mediterranean countries contrast with the relatively benign course of HBsAg carriage in Britain and may be due to the co-passage in these countries of another hepatic virus like agent - The delta agent (Rizzetto et al., 1977).

The carrier state is not static, it evolves with time and, at the outset, the markers present in the serum will (except for the absence of anti HBCAg) be very similar to those of an early acute infection.
However, unlike the acute infection, where events occur with a time course measurable in weeks or months, the carrier state evolves over years or decades (Tedder, 1983).

It is possible to divide carriers broadly into two groups - on the basis of their HBeAg/Anti-HBe status. Early in the carrier state the patient will have the circulating HBeAg. Serum from such patients is known to be infectious where small volume inoculation accidents have occurred (Alter et al., 1976). These patients also have high level of circulating HBsAg, DNA polymerase and tend to have mildly elevated serum transaminases (Barbora et al., 1978). They are known to be infectious for perinatal (Okada et al., 1976) and horizontal (Shikata et al., 1977). Transmission some time after the beginning of the carrier state, the patient will seroconvert from HBeAg to anti-HBe. It will usually take years for this to occur (Miyakawa and Mayumi, 1978) although it may some time happen after a few months.

The delta agent antigen is distinct from the known antigens of the nucleocapsid and surface of HBV, and antibody to delta antigen is unrelated to known antibodies induced by HBV infection. The delta antigen was initially detected by immunofluorescent techniques in the nucleus of hepatocyte of patients with persistent HBV infection (Canese et al., 1979). Antibody to delta antigen could be detected in the sera of HBsAg carriers in the various parts of the world, although the
prevalence is highest in Italy (Rizzetto et al., 1979). The delta antigen has been partially characterized as a 68000 dalton protein (Rizzetto et al., 1980a) which in the serum of infected chimpanzees and humans is associated as an internal component, with a 35 to 37 nm subpopulation of HBsAg particles and a RNA molecules smaller than that of known RNA viruses (Bonino et al., 1981; Rizzetto et al., 1980c). Delta agent is transmissible to chimpanzees (Rizzetto et al., 1980b). Because delta results in chronic infections only in the presence of persistent HBsAg and may be transmitted by superinfection or co-infection of HBsAg carriers, it is believed to be a defective pathogenic agent requiring the helper function of HBV replication for its synthesis. The pathogenicity of infection with the delta agent is still incompletely understood but appears to be inversely related to the extent of productive HBV replication; HBsAg carriers with diminished HBV synthesis appears to be an increased risk of developing chronic delta infection (Smedele et al., 1981).

In addition to its presence in blood, HBsAg in blood vessel walls has been identified in body fluids and secretions in glomeruli, but not in the faeces of HBV infected individuals (Peinman et al., 1979). Intact infectious HBV particles are present in the liver and blood and also have been demonstrated, by experimental transmission to nonhuman primates in semen and saliva
(Scott et al., 1980). Whether HBsAg and HBV are simply deposited from the circulation or reflect HBV replication in the testes or salivary glands is unknown. The presence of HBsAg in bile is consistent with the notion of hepatic replication of HBV but replication of HBV in extrahepatic sites has yet to be established (Raymond S. Koff, 1983). The presence of HBsAg in pure pancreatic juice (Hoefs et al., 1980) and the identification of both HBsAg and HBeAg in the cytoplasm of pancreatic acinar cells is intriguing (Shimoda et al., 1981).

HBsAg may be detected in blood as early as six days after parenteral exposure to HBV (Krugman et al., 1979) in most infected patients HBsAg appears considerably later (1 to 3 months) but usually before the onset of biochemical evidence of hepatic injury. Blood obtained during the incubation period, before either HBsAg becomes detectable or serum aminotransferase levels are elevated has been shown to be infectious (Rinker and Galambos, 1981). The detection of HBeAg, by a widely available radioimmuno essay (Mushahwar et al., 1981), does not add to the diagnostic specificity of HBsAg. Antibody to HBeAg (Anti-HBe) appears immediately after HBeAg disappears and may remain detectable for a protracted period (Krugman et al., 1979). Mushahwar et al., 1981). Early in the course of HBV infection, concomitantly with or near the time of appearance of HBsAg, all patients develop anti-HBc. It may be the only detectable marker in the period between the
disappearance of HBsAg and appearance of measurable antibody to HBsAg (Anti HBs) (Raymond Sl Koff, 1983).

The combination of tests for HBsAg and anti HBC permits the detection, without exception, of all acute HBV infections but does not distinguish between acute and chronic infection. Anti HBC may be detectable for years following acute infection (Krugman et al., 1979), and is present in HBsAg carriers with or without chronic hepatitis. High titres of IgM anti HBC are almost invariably present in acute HBV infection and may persist for several months to 1 to 2 years, and occasionally longer, after clearance of HBsAg (Kryger et al., 1981; Lemon et al., 1981). IgM anti HBC is also present in many HBsAg carriers but in lower titres than following acute infection (Kryger et al., 1981). Quantitative assessment of IgM anti HBC may help in distinguishing between patients with acute hepatitis B and HBsAg carriers with acute Non A, Non B hepatitis. IgM anti HBC in carriers is believed to indicate continuing HBV infection and it may be useful in identifying low level carriers who are infectious (Raymond S. Koff, 1983).

Since screening of the blood and blood products for HBsAg has been widely adopted the classical mode of blood borne transmission i.e. transfusion, is now responsible for only a minor fraction of HBV infections. In high risk regions, maternal infant and intrafamilial spread appears to be responsible for perpetuation of HBV infection and its association with the development chronic liver disease and primary hepatocellular carcinoma (Beasley et al.,
Maternal infant transmission involves carrier women, women with acute hepatitis B in the third trimester and mothers with acute hepatitis B during the first five weeks after delivery (Tong et al., 1981). The high frequency of HBV transmission, when acute hepatitis B occurs in the early post partum period suggests that close contact between mother and infant may play a more important role than previously believed. The precise mode of transmission is ill defined. Oral secretions, e.g. saliva, which may contain intact HBV particles (Scott et al., 1980), appear to have a low infectivity potential but may play a role under intense exposure conditions. The exchange of vehicles contaminated with oral secretions may be responsible for intra-familial clusters of HBV infection among children (Leichtner et al., 1981). Similarly, transmission of HBV in class rooms, from carrier children to classmates (Oleske et al., 1980), may involve physical transfer of virus to oral mucosal surfaces. The frequency of spread of HBV in schools may depend on the numbers of carriers and susceptibles and their class room behaviours (Raymond S. Keff, 1983).

The presence of HBV in semen (Scott et al., 1980) and HBsAg in menstrual discharge (Inaba et al., 1979) and the documentation of transmission between spouses (Inaba et al., 1979; Fazzillo et al., 1979), support a venereal mode of transmission. The extra ordinary high risk of HBV infection in homosexual men, confirmed in the hepatitis B
vaccine studies (Szmuness et al., 1980b), indicates remarkable efficiency of intimate sexual contact in transmitting HBV. The total prevalence of HBV markers, in homosexual, was 68% in baseline studies (Raymonds Koff et al., 1983) designed to identify susceptibles. During the two year follow up period 26% of the susceptibles who received placebo developed evidence of HBV infection (Szmuness et al., 1981b). Inoculation with shared contaminated needles may lead to HBV infection in illicit drug users and accidental percutaneous inoculation with contaminated needles is responsible for some instances of Nosocomial hepatitis B. Contamination of environmental surfaces with infected blood (Lauer et al., 1979), may contribute to the occurrence of HBV transmission in clinical laboratories and haemodialysis units in which exposure to blood is common place. Transmission of HBV by infected health care workers to their patients is infrequent but transfer of HBV from minor laceration and inapparent breaks in the integrity of the skin of the hands may be responsible for outbreaks involving infectious oral surgeons and dentists (Hodler et al., 1981).

The notion that haematophagous arthropods play a role in HBV transmission is supported by the persistence of HBsAg in bed bugs as long as six weeks after a single meal of HBsAg positive blood (Ogston et al., 1979). Epidemiological evidence for arthropod borne transmission is absent. Similarly faecal oral spread and our breaks
of hepatitis B due to ingestion of faecally contaminated food and water not documented (Raymond S Koff et al., 1983).

Shiff (1975) and Zuckerman (1978) have reported that following HBV infection, HBsAg usually disappear within 9 to 12 weeks. All cases with complications following HBV infection are associated with persistent antigenemia though a vast majority of carriers are asymptomatic. Antigenaemia is also common in patients with leukaemia, leprosy, down syndrome, Hodgkin's disease, chronic renal failure on dialysis and in I/V drug addicts. Hepatitis B infection in males and during childhood is also followed by a higher carriers rate (Zuckerman, 1979).

The estimated number of HBsAg carriers in the world is 20 to 125 million (Zuckerman, 1978). One to two percent of voluntary blood donors in USA are HBsAg carriers. In tropical countries the carrier states is much more common up to 20% being reported by Zuckerman, (1978).

In India the incidence of carrier state of Australia antigen in healthy adult male and female voluntary blood donors has been reported to be 2.2% and 1.3% respectively (Pal et al., 1973). High incidence of antigen in blood donors has also been reported by other workers from different parts of the country (Sahgal and Aikat, 1970; and Dutta and Mohammad, 1972).

Blumberg et al. (1968) reported 2.3% positivity of HBsAg among 127 serum samples of south Indian origin by immune-electro-immunoassay (IEO). There is no
remarkable difference of carrier rates amongst healthy population of North and South India. The prevalence of HBsAg is definitely higher in Indians than in Americans (0.1 to 0.2%) and Denis population (Gocke et al, 1969; Bunke et al, 1971). In tropical countries the incidence is 0.2 to 0.5% and in South east Asia as high as 20% in certain endemic areas (Blumberg et al, 1970). In Greek population the incidence is 0.8 to 1.8 percent, which is similar to that in India (Blumberg, et al, 1970).

In a study conducted on pregnant women attending the antenatal clinic for routine check up at Trivandrum 2.6% of them had Australia antigen (Shanmugam and Raj-Sekharan, 1982), whereas in pregnant woman of Kerala an incidence of 3% was recognised; the cord sera were also found to be positive in 1.7%. For Australia antigen in Bombay (Shanmugam and Raj-Shekharian, 1982). In Lahore 9.3% of the women were reported to be HBsAg positive during pregnancy. They are carriers and continuous to show the same antigenemic state, until 6 months or more after delivery. The persistent carrier rates of HBsAg among symptomatic mothers was found to be very high ranging from 66.1% to 100% in Finland, UK, USA and Senegal (Summows et al, 1973; Tapp et al, 1976 and Ukkonen, 1980).

Recently Darzo et al (1978) reported that 8% of children of HBsAg carrier mothers from Asian communities (India, Pakistan, Bangla Desh) are HBsAg carriers.
The risk of serum hepatitis from blood transfusions, varies from 10 to 70 fold depending upon the source of blood (Allen, 1972). The hepatitis which followed HBsAg positive blood transfusion also have been reported to be severe (Cocke and Kavey, 1969). Prior experience of frequency of HBsAg in blood donors of New Delhi was 2.73% in 1973 (Shama et al., 1973) which increased to 3.9% in 1975 (Pastakia et al., 1975). Incidence of Australia antigen increased at alarming rate until 1970 in large cities mostly because of practice of needle sharing by parental drug users. The sale of blood by indigents to commercial blood banks had resulted in increased infectivity to those who received commercially prepared blood products (Ashcavai and Peters, 1971).

In some cities the incidence of clinical hepatitis acquired from a blood transfusion had been as high as 20 per 1000 units of blood. Although two thirds of patients contracting hepatitis had developed subclinical disease only (Grady, 1970; Taswell et al., 1970 and Allen et al., 1972). Pooling of blood products obviously increase the risk of transmitting the agent and storage of plasma for 6 months at room temperature is not effective in completely inactivating the agents (Redkar et al., 1968).

Blood fibrinogen carries a particularly high risk of transmitting hepatitis B (Boeve et al., 1969).

Viral hepatitis type B has a worldwide distribution and transmission takes place by parenteral
infections. The virus is also present in saliva (Brodersen et al., 1974; Plainson et al., 1975 and Villarezos et al., 1974). Tears, ascitic fluid sneez droplets and blood sucking insect (Zebe et al., 1972; Prince et al., 1972) and rarely in urine (Villarezos et al., 1974) menstrual fluid (Darani and Gerbar, 1974) involved kissing (Villarezos et al., 1974 and Prince et al., 1972), bitting (Macquarri et al., 1974) razors and tooth brush (Mahley, 1975).

Study from different parts of the world (Blumberg et al., 1968; Okochi Murakami, 1968; Wright et al. 1969 and Fox et al., 1969) have high lighted the difference in the incidence of Australia antigen in viral hepatitis. 50% of acute hepatitis in the USA is caused by HBV (Australia antigen) (Purcell et al., 1978), 23.6% of cases endemic hepatitis in India are HBsAg positive (Joshi et al., 1977 and Dutta et al., 1977).

The incidence of HBsAg in acute and non epidemic viral hepatitis has been widely variable in India. An incidence of 44% was reported from North India (Sehgal and Aikat, 1970), 22.6% from Delhi Cantt (Dutta and Mohammed, 1972), 22% in Patient admitted to naval hospital, Bombay (Gupta, 1973), 23% at Military Hospital Chandigarh and 10% in Non fulminant hepatitis at Chandigarh (Pal et al., 1973).

Western workers reported higher incidences (Gecke and Kavey, 1969) with 83% positivity within x
12 days of infection. Ringert (1971) reported 100% positivity rate in such cases within 10 days of infection and 53% after 20 days of infection, whereas an incidence of 40% was recorded by Nelson et al (1971) and 33% by Smith et al. (1973). There is variation in positivity in tubercular and non tubercular patients; Tubercular patients had 44.62% positivity within 8 to 14 days of hepatitis.

Sixty five to seventy five per cent of mothers who have hepatitis B, in their late pregnancy or during the immediate postpartum period transmit HBsAg to their children. Whereas the rate of transmission is only 3.5 to 5 percent in asymptomatic carriers. Severity of hepatitis transmitted to offsprings is greater when mother is asymptomatic (Wands et al, 1979).

Turner et al (1968) reported the incidence of the HBsAg positivity in the nurses and technicians who were heavily jaundiced and the hepatitis associated antigen was also seen in the person who handles the haemodialysis Unit without having jaundice sera strongly positive for HBsAg contain as many as $10^{12}$ to $10^{13}$ particles per ml. Radioimmunoassay (RIA) is the best technique to demonstrate HBsAg (Hoofnagle, 1979). HBsAg appears in the serum usually 4 to 6 weeks after the initial infections, the range is 12 days to 24 weeks (Shiff, 1975 and Holland et al, 1975). The level of HBsAg peaks and falls before the the patient is clinically ill. Therefore, it is important
to test for Australia antigen as soon as the diagnosis of hepatitis is clinically suspected (Holland et al., 1975). In general the antigen is present at the lower concentration during the acute phase and disappears during convalescence in an uncomplicated case. Anti HBsAg detected in children exposed to HBsAg with subsequent and more pronounced rise. The anti HBsAg titre suggest an anamnestic response. People with an anamnestic reaction don't develop biochemical and clinical evidence of acute hepatitis. These anti bodies persist for at least one year or may be life long. HBsAg appears 2 weeks to 2 months after the disappearance of HBsAg (Hoofnagle, 1979).

Pal et al (1973) observed that the incidence of Australia antigen is significantly high in cases of fulminating hepatitis and all the positive cases had fatal outcome and they had definite history of parenteral infection. However, Redker (1975) reported that the incidence of acute fulminating hepatitis is only one or two percent after acute viral hepatitis infection and it is more common following HBV infection but may also follow HAV infection.

The concept that acute viral hepatitis might in some instances lead to chronic hepatitis and/or cirrhosis is old one and is derived largely from autopsy data from serial biopsy studies in which the sequence of changes have been observed (Howard and Watson, 1947). Ruggieri et al (1947), Ratnofd and Patakay (1955), Graig et al.
(1955) and MacDonald and Mallong (1958). The frequency of Australia antigen in patients of chronic active hepatitis has been reported by several workers from different countries (Wright et al, 1969; Maccarato et al, 1969; Blumberg et al, 1970 and Prince et al, 1970). The incidence was 25 percent in United State in 1969 and 67 percent in 1970; 34% in Italy and 26% in Great Britain. These findings suggested that frequency of Australia antigen is more in these countries. But other reports from the Great Britain, Denmark, Australia and Chili suggested that Australia antigen is present in lower proportion of chronic active hepatitis in these countries (Prince et al, 1970) and Wright et al, 1970). However, it has not been determined whether these discrepancies represent variations in immunological technique or a true geographic variation in frequency of SH antigen in these conditions.

Sherlock et al (1970) and Nelson et al (1971) found that serial biopsy specimen of the patients who undergo from the acute viral hepatitis to cirrhosis of the liver were having persistent antigenemia. Australia antigenemia has been shown to be associated with 25 to 30 percent of patients with chronic hepatitis. Progression from hepatitis to cirrhosis with hepatoma has been recorded in an Australia antigen positive case (Pal et al, 1973).
It has been recognised that the large percentage of patients with chronic active hepatitis who have negative LE cell preparation who lack smooth muscles antibodies and have circulating HBsAg in their sera (Gitnick et al., 1969; Wright et al., 1963). About 1-3% of patients with viral hepatitis which are ill enough for hospitalization, will develop chronic hepatitis, which may be lead to cirrhosis. However, Kedeker (1975) has suggested that if initial hepatitis is fulminated patient rarely developed chronic hepatitis. Moslay (1975) reported that in chronic active hepatitis the HBsAg titre are usually low with marked fluctuations in contrast to the asymptomatic carrier where HBsAg titre are often very high. Clearance of HBsAg in a very good prognostic sign regardless of histology while Nelson (1971) reported that in 253 patients who are admitted in the copenhagen Hospital, 113 were australian antigen positive for one to 13 weeks average 4.5 weeks. Australia antigen persisted for more than 13 weeks. In 11 of the 253 patients 8 (4.3%) of them developed clinical and biochemical signs of chronic hepatitis and they were diagnosed as chronic aggressive hepatitis and 2 of them has chronic persistant hepatitis histologically.

The incidence of Australia antigen in cases of chronic persisting hepatitis as reported by different workers from different countries (Fox et al., 1969). Guadía (1976), Krasnitsky (1970) and Vischer (1970) have been markedly variable ranging from 0.14% to 5.3% by agar gel diffusion method (Alfred and Prince, 1971).
Chronic active hepatitis B often progress to cirrhosis an epidemiological associations between a high incidence HBsAg antigenemia and macronodular cirrhosis in certain tropical countries has been reported by William (1975). Significantly greater frequency of Australia antigen, than present in control proportion has been observed by most of the authors in cases of cryptogenic cirrhosis and post necrotic cirrhosis in different countries (Okochi and Murakami, 1968; Fox et al., 1969; Golke et al., 1969; Fobar et al., 1970; Prince et al., 1970 and Reinick and Nordenfelt, 1970).

In India Kelkar et al. (1977) reported 34% positivity of Australia antigen in patients of cirrhosis by IEOB method. Pal et al. (1973) reported 28% positiveness of australia antigen in post necrotic cirrhosis while other workers have reported that the incidence of Australia antigen in liver cirrhosis was low at Bombay (Baxi, 1972). Wright et al. (1969) have observed 4% positiveness of Australia antigen in post necrotic cirrhosis.

The frequency of Australia SH antigen in cases of alcoholic cirrhosis to be significantly lower suggesting that this may be an etiologically lower distinct entity (Alfred and Prince, 1971). In primary biliary cirrhosis an antigen which appeared to be similar to or identical with SH was found in 9 out of 10 cases studied by Kroh et al. (1970) and in one out of three cases reported by Passerato et al. (1969); while others could not detect Australia antigen in such cases (Fox et al.,

The frequency of Australia antigen in Indian childhood cirrhosis has been studied by Chandra (1970) who reported Australia antigen positivity in 20% cases.

More than 60% of all primary carcinomas of the liver occur in patients with pre-existing cirrhosis and more than 40% of autopsied cases of cirrhosis in Africa have co-existing carcinoma. Studies on the prevalence of Australia antigen carrier, state in cases of primary liver cancer are thus of special interest (Alfred and Prince, 1971).

The etiology of liver cell carcinoma is not known but recent research on the role of alpha toxin and hepatitis B virus strongly suggested that they may be involved, it is well known that liver cell carcinoma arises more often in cirrhotic liver. The frequency of liver cell carcinoma in various part of the world may differ by as much as 100 folds. In Europe and the United States the frequency varies from 0.1 to 0.7% of all autopsies. In portions of south east Asia, where the incidence of carcinoma is low usually between 4 to 6% rarely 10% of patients with cirrhosis eventually develop carcinoma of liver. This contrasts with some areas of Africa where the frequency is about 40% of all men with cirrhosis (Anderson, 1977). A higher familial incidence
of HBsAg positive liver cell carcinoma has been reported from Japan where the family members without carcinoma had an unusually high incidence of PVHB, CAVHB and active viral hepatitis B (Ohbayashi, 1976).

Various workers (Fox et al, 1969; Smith and Blumberg, 1969; Hadziyahnis et al, 1970; Prince et al, 1970; Vogal et al, 1970) from all over the world reported the frequency of 0 to 40% of Australia antigen in primary carcinoma liver. The maximum frequency was reported in Sangal 42% by (Prince et al, 1970 and Vogal et al, 1970). From all over the world reported the frequency of 40% by Vogal et al, 1970 and 31% in France, while minimum frequency of Australia antigen by Prince et al, 1970 in USA (2 to 4% Hong Kong 5%, East Africa 0% and UK 5%) (Fox et al, 1969).

Anderson (1977) also reported that in Losanges the incidence of hepatocellular carcinoma increased over the past 30 years both in the cirrhotic and non cirrhotic liver. The percentage of cases in which HBsAg can be demonstrated in liver tissue has also increased and is currently found in sera of 20% of non alcoholic cirrhosis. Patients who developed cirrhosis and 30% with all patients with hepatocellular carcinoma. According to Smith and Blumberg (1969) the incidence of HBsAg was high in the hepatocellular carcinoma. There is high incidence of hepatocellular carcinoma in areas of world,
where the prevalence rate of HBs antigenemia is high. In Taiwan 90% hepatocellular carcinoma of HBsAg positive (William, 1975). Younger patients with hepatocellular carcinoma show HBsAg in malignant cells. Kaw et al (1979) reported that HBsAg and HBeAg was reported in 61.6% and 90% of patients with HCC respectively. Szmuness et al (1975) have reported that approximately 1 out of 500 of HBsAg carrier developed HCC (Hepato-cellular carcinoma).