Chapter 1

Introduction
1. INTRODUCTION

The term viral Hepatitis is commonly used for several clinically similar diseases that are etiologically and epidemiologically distinct (Fransis et al., 1982). Viral Hepatitis is generally referred to the infection of the liver caused by a group of hepatotrophic viruses. The incidence of viral hepatitis amongst the general population varies widely in different parts of the world. The clinical, epidemiological, pathological and immunological attributes of viral hepatitis share many clinical features despite their remarkably different etiologies. The viruses of hepatitis include multiple unrelated hepatitis viruses, called Hepatitis A virus (HAV), Hepatitis B virus (HBV), Hepatitis C virus (HCV), Hepatitis D virus (HDV), Hepatitis E virus (HEV), Hepatitis F virus (HFV), Hepatitis G virus (HGV), Transfusion Transmitted virus (TTV), etc. These viral agents have a dichotomous mode of epidemiological transmission viz. enteric for HAV and HEV, which do not establish persistent infection and parenteral for HBV, HCV, HDV and HGV which tend to establish persistent infection or chronic carrier state.

Hepatitis B is a serious, but preventable disease of the liver, caused by hepatitis B virus, a small dsDNA virus that belongs to the family of Hepadnaviridae. Hepatitis B infection is the major health problem all over the world. The disease is highly variable. Acute Hepatitis B viral infection can either be mild and self-limiting or it can cause fatal fulminant or sub fulminant hepatic failure in a small percentage of people. The more serious consequence of HBV infection is the progression to chronic liver diseases namely cirrhosis of the liver and hepatocellular carcinoma. There are presently about 350 million chronic carriers of HBV in the world population. It is estimated that 75-100 million of them will die of liver cirrhosis and/or hepatocellular carcinoma. The probability of developing the carrier state following HBV infection is greatest in the early life and decreases with increasing
age. Up to 90% of babies born to carrier mothers may become carriers and they are at a very high risk of developing chronic liver disease at a younger age. In India it is estimated that there are 43 million carriers of Hepatitis B infection, about 10% of the world population. There is no specific and consistently effective treatment for the disease till date. Though some success has been had in treating chronic infections, however, long-term treatment is required but proves costly and is unavailable to the vast majority of victims. All major world authorities, therefore, agree that the most effective approach to reducing the burden of HBV is prevention through vaccination. Prevention of the disease through vaccination alone plays a significant role in eradicating this dreadful disease. The discovery in 1964, by Blumberg and by Prince of the surface antigen of Hepatitis B virus present in the blood of human carrier of the infection opened the door to the development of hepatitis B vaccine. Currently there are two types of Hepatitis B vaccines available.

- Plasma derived vaccine.
- Recombinant DNA vaccine, Yeast / Mammalian cell derived

The first generation is plasma-derived vaccines and the second generation is the recombinant vaccines. The first HBV vaccine for routine use became available in 1981 in the United States and the recombinant yeast derived vaccine is available since 1986 in USA. The first genetically engineered vaccine produced in India is Shanvac B manufactured by Shantha Biotechnics Pvt Ltd., made available in 1998. Now there are a few more vaccines that are developed and available in India. The global advisory group of the Expanded Program on Immunization (EPI) and the World Health Organization (WHO) recommended inclusion of hepatitis B vaccination in all nation immunization program beginning in 1997 to reduce the incidence of new carriers by eight percentage. Over 500 million individuals have received the HBV vaccine globally.
In 1993 WHO had recommended that, HBV vaccination be included in the Expanded Program on Immunization (EPI) of all countries with a high prevalence rate of HBV by 1995. The remaining countries should adopt this program by 1997. Introduction and implementation of Universal vaccination has shown a significant reduction in HBV carrier rates among children from 10% to less than 1%. In Thailand hepatitis B vaccination was given simultaneously with other EPI vaccines, which resulted in a significant reduction of carrier rates from 6% to 0.23%. They are expecting virtual eradication of HBV infection.

The current recommendation from the Advisory committee on Immunization Practices (ACIP) and American Academy of Pediatrics (AAP) is Universal immunization of infants. The policy of Universal immunization in infants has been found to be cost effective on our country. In fact, in the long-term, it has been calculated to cost less per case prevented, than a policy of screening and vaccinating only high risk new born. The adoption of HBV vaccination in EPI by 1995 was first recommended by Indian Academy of Pediatrics (IAP), which was followed by the resolution from Indian Society of Gastroenterology and Indian Association for the study of Liver (INASL).

There are several practical problems associated with the introduction of Universal HBV vaccination in our country. Firstly the high cost of vaccine has hampered the inclusion of this vaccine in EPI. Till recently the vaccine needed to be imported which adds to the exchequer. Now, with the availability of indigenous vaccines the cost of the vaccines has come down. The universal immunization at birth is not feasible in the Indian context; given that only a small proportion of birth occurs in the hospitals and others are inaccessible. To individual families that can afford the vaccine, the option of immunization should be offered.
Currently there are many types of recombinant vaccines developed in India. However there is not much documented evidence of the efficacy of these vaccines. Hence the present study was planned to document the efficacy of an indigenous recombinant DNA hepatitis B vaccine Genevac B manufactured by the Serum institute of India, Pune, India. A comparison was made by conducting clinical trials in adults, adolescents and new borns with the different dosage regimens and different schedules of immunization with the different HBV vaccines available in the country.