STUDY OF ANTIBODIES TITRES (Anti HbsAg) AND HEPATITIS-B SURFACE ANTIGEN (HBs Ag) CARRIER STATES AFTER HEPATITIS-B VACCINATION [Recombinant Merck vaccine. {2.5 μ gm/0.5 ml}] IN EGYPTIAN CHILDREN 3-4 YEARS OF AGE.

THESIS

Submitted for Partial Fulfillment of

THE MASTER DEGREE

IN

PEDIATRICS.

Presented by

MAHMOUD MOHAMED EL-GHONAMY.

M.B., B.Ch

(Alexandria University)

UNDER SUPERVISION OF

Prof. Dr. NANCY ABDEL AZIZ SOLIMAN,

Professor of Pediatrics,

Faculty of Medicine,

Ain Shams University.

Prof. Dr. IMAM ZAGHLOUL IMAM,

EX. Chairman of VACSERA, AGOUZA,

Consultant NAMRU3.

Maj. Gen. Dr. MAHMOUD SHAKER IBRAHIM,

Head of Central Laboratories,

Melitary Medical Academy.

Faculty of Medicine

Ain Shams University

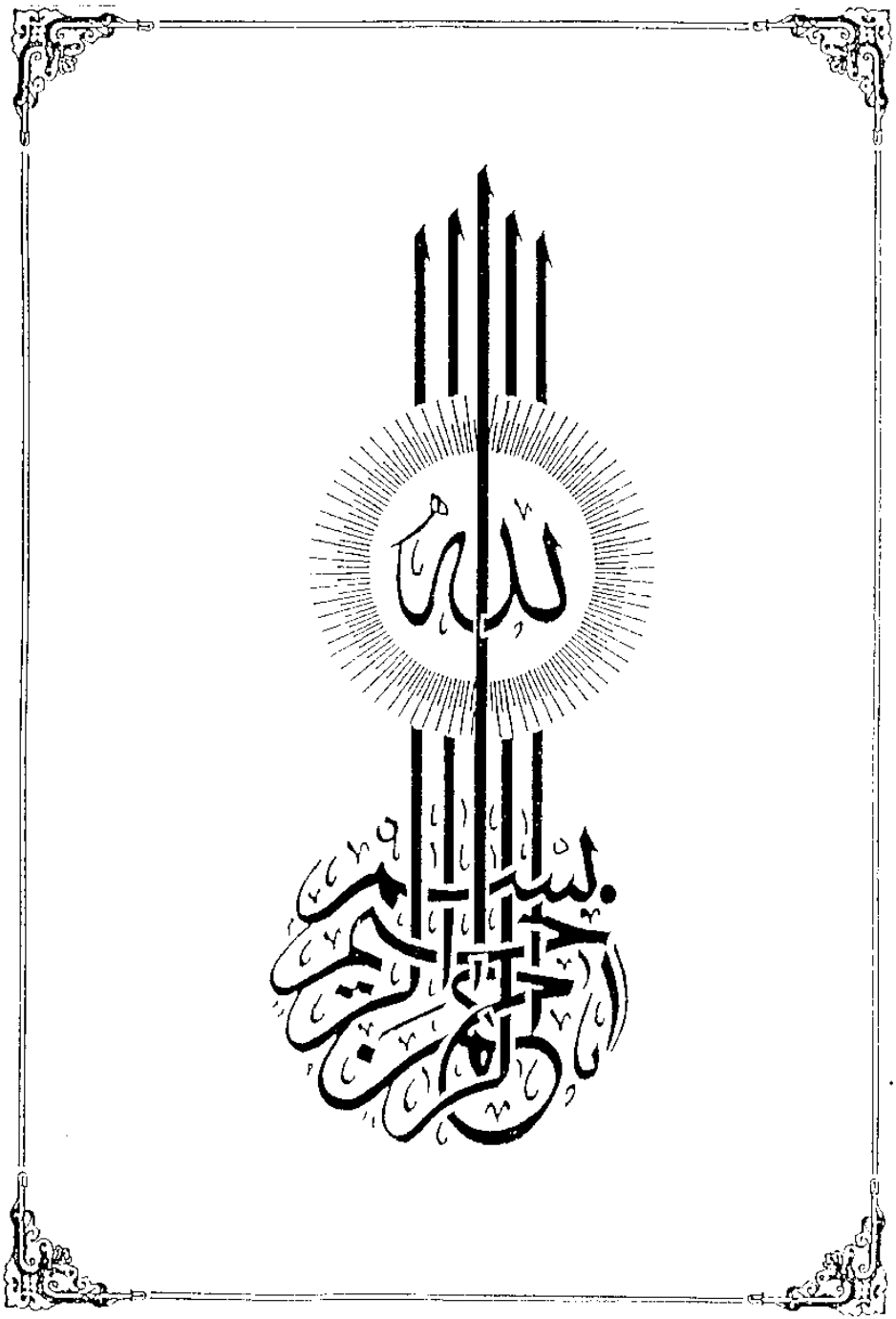
1998.

Examiners

Prof. Dr. Nancy Abdel Aziz Soliman,
Professor of Pediatrics,
Faculty of Medicine,
Ain-Shams University

Prof. Dr. Fouad Badrawy,
Professor of Pediatrics,
Faculty of Medicine,
Ain-Shams University.

Prof. Dr. Moustafa Fathy,
Professor of Pediatrics,
Faculty of Medicine,
Zagazig University.



Abbreviation

AAP	American Academy of Pediatrics.
DPT	Diphtheria, Pertussis, Tetanus.
ELISA	Enzyme Linked Immuno Sorbant Assay
FDA	Food and Drug Administration.
HBcAg	Hepatitis B core antigen.
HBeAg	Hepatitis B envelope antigen.
HBIG	Hepatitis B immune-globulins.
HBsAg	Hepatitis B surface antigen.
HBV	Hepatitis B virus.
HIV	Humman Immuno-defficiency virus.
MS&D	Merck Sharp & Dome.
OD	Optimal Density
PEM	Protein Energy Malnutrition.
WHO	World Health Organization.

Introduction

Hepatitis is a major health problem worldwide. The viruses of hepatitis A, hepatitis B, and at least three other viruses causing hepatitis that are neither A nor B have been identified. They are designated hepatitis viruses C, D and E. Other unidentified viruses may also cause hepatitis. In addition, cytomegalovirus, Epstein-Barr virus, rubella virus and enteroviruses may cause hepatitis(Brunell, 1995).

Hepatitis B virus (HBV) infection has an impact on blood transfusion services which emphasizes its importance. Its association with progression to chronic liver disease and subsequent development of cirrhosis and hepatocellular carcinoma are of utmost importance (Hollinger et al., 1989).

In addition, infection with HBV may be followed by a persistent carrier state (Tong et al., 1988).

Aim of the work

The aim of the present work is to:-

1. Study the antibodies titres (anti-HBs-Ag) after mass vaccination of infants (2-6 months of age) with recombinant Merck vaccine (2.5 µgm/0.5 ml) in children 3-4 years of age.
2. Detect HBs-Ag carrier states.

Hepatitis B infection

Clinical picture and Transmission of HBV infection:-

The clinical picture of hepatitis B is variable. The mildest attack is without symptoms and is marked only by a rise in serum transaminases levels. Alternatively, patients may still be anicteric but suffer from gastro-intestinal and influenza-like symptoms. Such patients are likely to remain undiagnosed unless there is a clear history of exposure to hepatitis B or blood transfusion. Increasing grades of severity are then encountered ranging from the icteric hepatitis from which recovery is usual to fulminant fatal hepatitis (Krugman et al., 1979).

The major sources for spread of HBV infection are either apparently healthy chronic carriers or patients with acute hepatitis B (Balisteri, 1988). HBV most commonly spreads through the parenteral route. Other major mechanisms of transmission are close personal contact involving salivary exchange, sexual contact or vertical transmission from mothers to

offsprings (Raufman et al., 1981). Transplanted organ can serve as vectors of HBV infection (Balisteri 1988).

Renal dialysis patients and personnel have a hig rate of HBV infection particularly those patients o renal dialysis who are immunosuppressed an on contracting the disease become chroni carriers (Knight et al., 1970). HBV may be present i the saliva of infected individuals but in small amount so that transmission may occur via bites but no through indirect oral exposure (i.e. shared toys (Balisteri, 1988).

In endemic areas the acquisition of HBV infectio in childhood is an important mode of transmission Perinatal HBV transmission from asymptomatic carrie mothers to infants represents the major route of sprea in hyperendemic areas(Chow et al., 1989).

The frequency of HBV transmission is high (75%) when the acute type of HBV infection occurs in the third trimester of pregnancy or near the time o

delivery and low when hepatitis occurs in the first two trimesters of pregnancy (Schweitzer et al., 1973; Delaphane et al., 1983).

Maternal-neonatal transmission of HBV may occur during the process of delivery, post partum transmission and transplacental transmission in utero may also occur. Transmission appears to occur mainly at or around the time of delivery, so that most of infected children are found to develop HBV infection three to six months after birth (Dupuy et al., 1978).

Schweitzer et al. (1973), stated that HBV infection of neonates was negative after birth and then they became seropositive for hepatitis B surface antigen (HBsAg) between 34 and 94 days of age. It has been suggested that oral ingestion of HBsAg positive blood is a possible route of infection (Krugman et al., 1970).

Postpartum transmission of HBV infection may infrequently occur by other routes since HBsAg has

been found in saliva, breast milk, urine and stool (Schweitzer et al., 1973).

Hepatitis B markers in individuals with HBV infection:-

The system of markers of HBV infection is composed of three distinct antigens and their corresponding antibodies. Hepatitis B surface antigen (HBsAg) is the primary marker of acute HBV infection (Deinhardt, 1980). The second antigen, hepatitis B core antigen (HBcAg) is not detectable in serum, but can be found in the nuclei of hepatocytes of infected individuals (Zuckerman et al., 1974). Hepatitis B envelope antigen (HBeAg) is detectable only in (HBsAg) positive serum and its presence correlates with number of viral particles and infectivity of serum (Shikata et al., 1977). The antibodies corresponding to HBV surface, core and envelope antigens are present in the serum. The detection of anti-HBs in serum signifies immunity to HBV either as a result of active infection or in response to immunization with HBV vaccine. Anti HBcore is easily detectable during the

acute icteric phase of infection and it persists during convalescence and is usually life long. The IgM class antibody to HBcAg develops during the acute stage of infection, persists for 4-6 months and then disappears (Lemon et al., 1981).

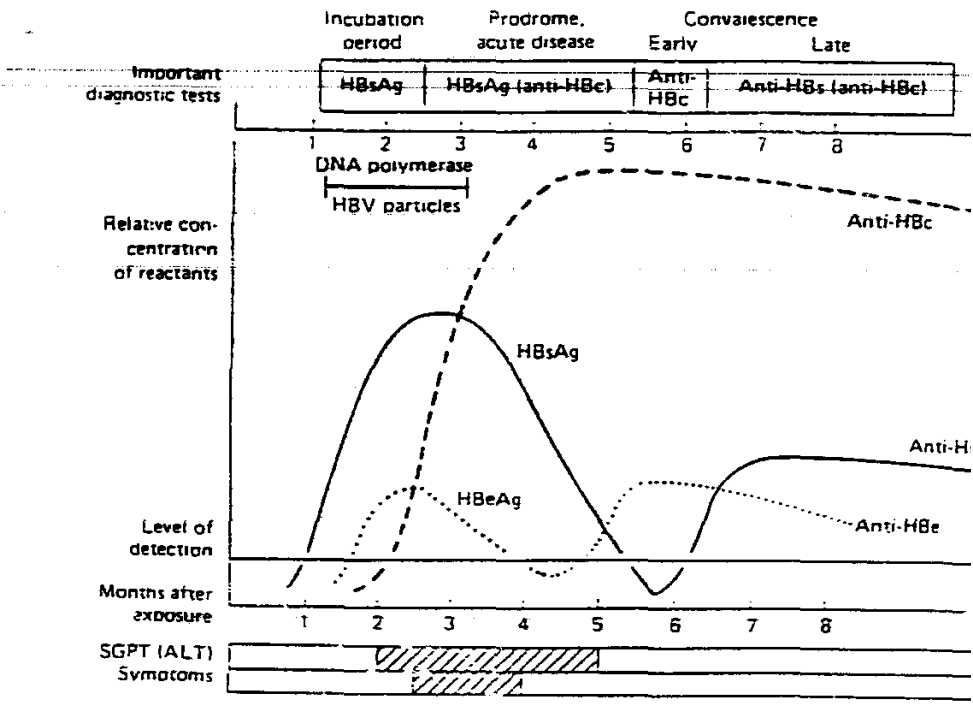


Fig. (1): Serological and clinical patterns observed during acute HBV infection
(Quoted from Bonino, 1986)

The interpretation of serological serum markers of HBV is shown in the following table (Quoted from Hoofnagle, 1983).

Table I: Serodiagnostic patterns in hepatitis B infection.

attern	HBsAg	IgM anti-HBc	IgG anti-HBc	Anti-HBs	Interpretation(s)
I	+	-	-	-	Early acute HBV infection before anti-HBc response
II	+	+	- or +	-	Early acute HBV infection, because IgM antibody to HBcAg is positive, the onset is within 4-6 months IgG antibody usually appears shortly after IgM, and, therefore, both are usually positive when IgM antibody is present.
III	-	+	+	- or +	Recent acute HBV infection (within 4-6 months) with resolution, i e. HBsAg has already disappeared. Anti-HBs usually appears within a few weeks or months of HBsAg disappearance.
IV	+	-	+	-	HBV infection, onset probably at least 6 months in the past because IgM anti-HBc has disappeared. Probably chronic HBV carrier.
V	-	-	+	+	Past HBV infection (recovered).

Table I: ***Continued***

Pattern	HBsAg	IgM anti-HBc	IgG anti-HBc	Anti-HBs	Interpretati
VI	+	-	+	+	Occasional pro chronic HBV in especially with advanced disease
VII	-	-	+	-	Long after r from acute infe "Low HBsAg carrier state.
VIII	-	-	-	+	Responder to immunization HBsAg recipi hepatitis B globulin or lon HBV infection.