INCIDENCE OF DELTA ANTIBODY IN HEPATITIS B SURFACE ANTIGEN POSITIVE SCHISTOSOMAL PATIENTS

T H E S I S

Submitted in Partial Fulfilment of
Master Degree in Tropical Medicine

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1989

بسم الله الرحمن الرحيم

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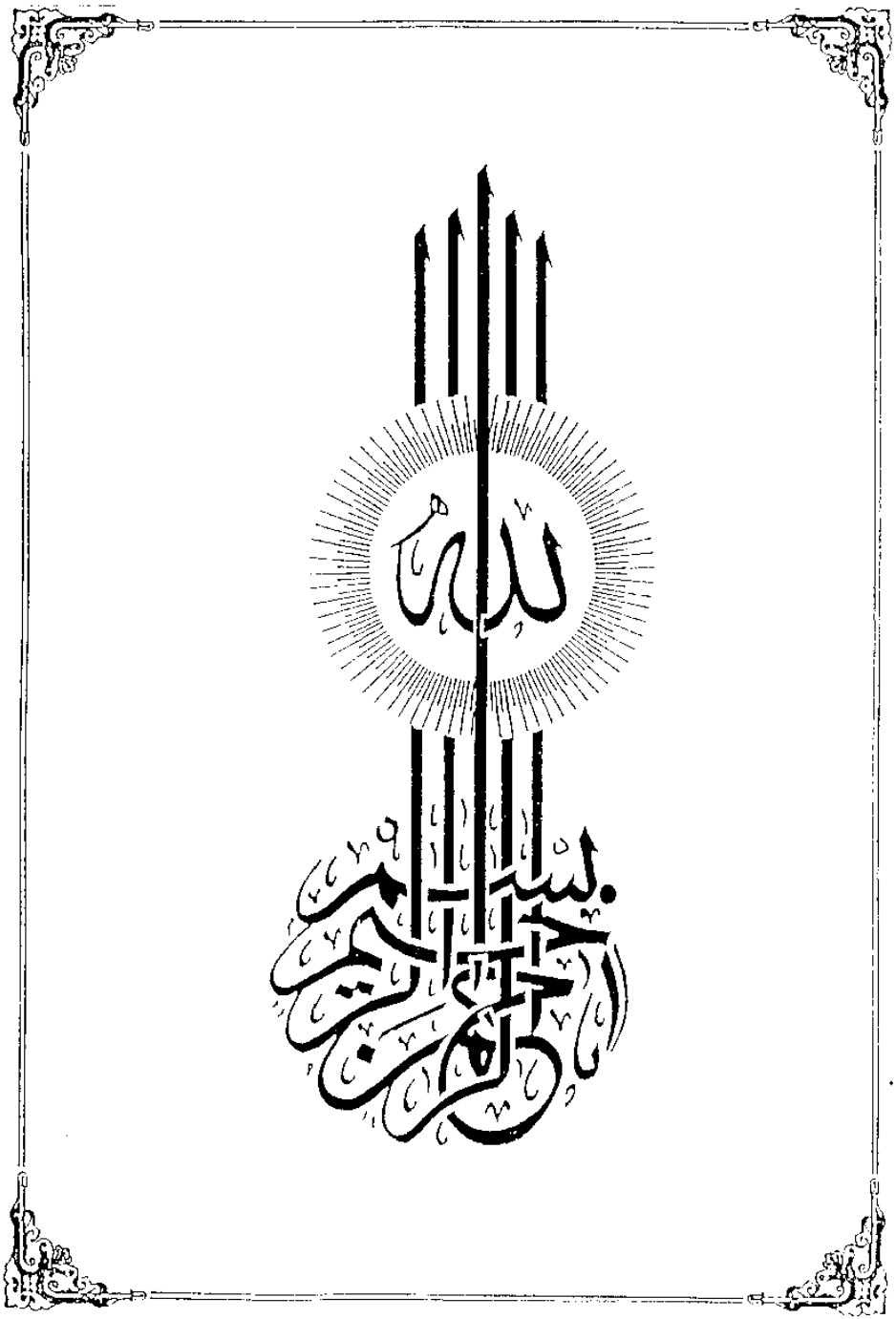

This research project is carried out under grant No. 82013 by foreign relation co-ordination unit of the Supreme Council of Universities.

This grant is in pursuiently university linkage project grant No. 263-0118 dated 28 September 1980 between Government of A.R.E and U.S.A.

ACKNOWLEDGMENT

I would like to express my deepest gratitude to Prof. Nooman Mohamed Hasseb, Professor and Head of Tropical Medicine Department, Ain Shams University, for his most kind help and advice throughout this work.

I am deeply indebted to Prof. Mohamed Ali Madwar, Professor of Tropical Medicine, Ain Shams University. His meticulous supervision, kind advice and great effort were invaluable. He has gratefully given me a lot of his time and experience.

I would like to express my sincere indebt and gratitude to Dr.Maha El Tahawy lecturer of Clinical Pathology, Ain Shams University for her most appreciable advice and help throughout this work. My gratitude to her is greater than I could put in words.

Many thanks also goes to Prof. Mohssen Gadallah, Professor of Public Health, Ain Shams University, for his great help and support during preparing this thesis.

I am also grateful to Dr. Mohssen Mustafa, Lecturer of Parsitology, Zagazeg University, for his kind help and cooperation in the practical part of the study.

To all staff members of Tropical Medicine, Ain Shams University, who freely cooperated to make the work possible, I must record my sincer gratitude.

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INTRODUCTION

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AIM OF WORK

antibody in hepatitis B surface antigen positive schistosomal patients in an attempt to define the role played by schistosomiasis on the presence of delta antibody.

REVIEW OF LITERATURE

PART (I): HEPATITIS DELTA VIRUS (HDV)

PART (II): ASSOCIATION OF HEPATITIS B INFECTION AND SCHISTOSOMIASIS

PART (I): HEPATITIS DELTA VIRUS (HDV)

HISTORICAL NOTE

While studying liver biopsies from patients who were seropositive for the hepatitis B surface antigen (HBsAg) by direct immunofluorescence, it was noted that an antiserum against the hepatitis B core antigen (HBcAg) as well as staining specimens in which core particles could be demonstrated by the electron microscope (EM), also reacted with additional biopsies which did not contain core particles (at electron microscope) and were negative with other reference antisera against HBcAg.

When the EM core positive and core negative specimens were tested with several HBsAg positive sera, it soon became apparent that some sera reacted with either one or the other liver substrate; this suggested that there were two distinct nuclear antigenic specificities.

The identification of this new antigen and of its antibody as an immunological system independent of other known reactions associated with the HB virus was reported in this communication provisionally, it was called δ. (Rizzetto et al., 1977).

Studies have shown that the new pathogen has an RNA genome smaller than all known RNA animal viruses (Rizzetto et al., 1980a).

The unique feature of the delta antigen is its dependency on a replicating hepatitis B virus (Redeker, 1983).

Anti-delta was found only in HBsAg positive sera with a highest incidence in patients with liver disease; an inverse correlation was noted between its titre and that of HBcAb, one antibody usually excludes the other (Rizzetto et al., 1977).

A sensitive solid-phase radioimmunoassay for anti-delta has been developed by using human liver obtained at necropsy as a source of antigen. Sera from HBsAg - positive patients and HBsAg-negative controls from different geographical regions of the world were analysed for anti-delta by this radioimmunoassay. Anti-delta antibody was detected in persistently high titres in 19.1% and 2.6% of sera from patients with chronic hepatitis and asymptomatic chronic carriers, respectively, and was not detected in the sera of HBsAg-negative controls. Anti-delta antibody appeared transiently and in low titres in 4.8% of sera from patients with acute type B hepatitis. The presence and persistence of anti-delta antibody seem to be associated with chronic HBV infection and the development of progressive liver damage (Rizzetto et al., 1979).

STRUCTURE AND NOMENCLATURE

1. Structure of Hepatitis Delta Virus:

Hepatitis delta virus (HDV) is 36-nm spherical particle containing an RNA of 1.750 bases and a specific antigen (delta antigen) (HDAg). HBV infected cells overproduce the viral envelope protein (hepatitis B surface antigen (HBsAg) and this surplus material is utilized by HDV, which apparently has no envelope protein of its own. (Bonino et al., 1986).

The particle in which the RNA is sequestered is organized to prevent hydrolysis of the nucleic acid by circulating RNAse.

This protective effect is probably responsible for persistence of the RNA in serum, and infectivity is presumably maintained by the integrity of the particle (Hoyer et al., 1983).

Size chromatography appears to be an efficient procedure for purifying HDV-associated particles from the majority of serum proteins and any anti-HD. In combination with density centrifugation it was also able to remove the HBsAg particles which did not contain HDAg. Surprisingly, these HBsAg particles contained a subfraction of unusual size (32nm) and density (1.23g/ml) in addition to the well known particles of 20 nm and 1.20g/ml. The significance of

these particles is unknown. Their occurrence is probably, not related to the HDV infection (Bonino et al., 1986).

A. The Delta Antigen:

HDAg from serum is precipitated by an antibody to HBsAg (anti-HBs), and it is only detected after removal of HBsAg envelope with detergents.

By size chromatography and by density centrifugation hepatitis delta antigen (HDAg) was detected at a column elution volume corresponding to 36-nm particles and banded at density of 1.25 g/ml. Two proteins of 27 and 29 Kilodaltons which specifically bound antibody to HDAg but not HBV-specific antibodies were detected in the interior of the 36nm particle. Since these proteins were structural components of HDAg and were most likely coded for by HDV, they were designated P27d and P29d (Bonino et al., 1986).

The prevalence of antibody to delta Ag (antidelta) in human population and transmission experiments in chimpanzees indicated that delta Ag represents a marker of a transmissible and pathogenic agent (delta agent) that requires the helper functions of HBV for its expression (Rizzetto et al., 1980c, Raimondo et al., 1982).

B. Hepatitis B Virus Derived Envelope:

The protein composition of the HDAg containing particles were analysed by immunoblotting with HDAg, HBsAg,