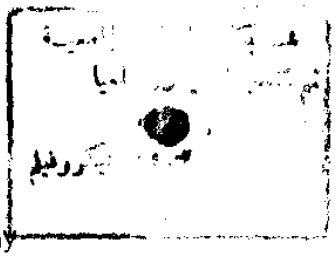
PREVENTION OF RH-HAEMOLYTIC DISEASE OF THE NEWBORN IN EGYPT



THESIS

Submitted for the Partial Fulfilment
for the M.S. Degree in Obstetrics and Gynaecology

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1989

ACKNOWLEDGEMENT

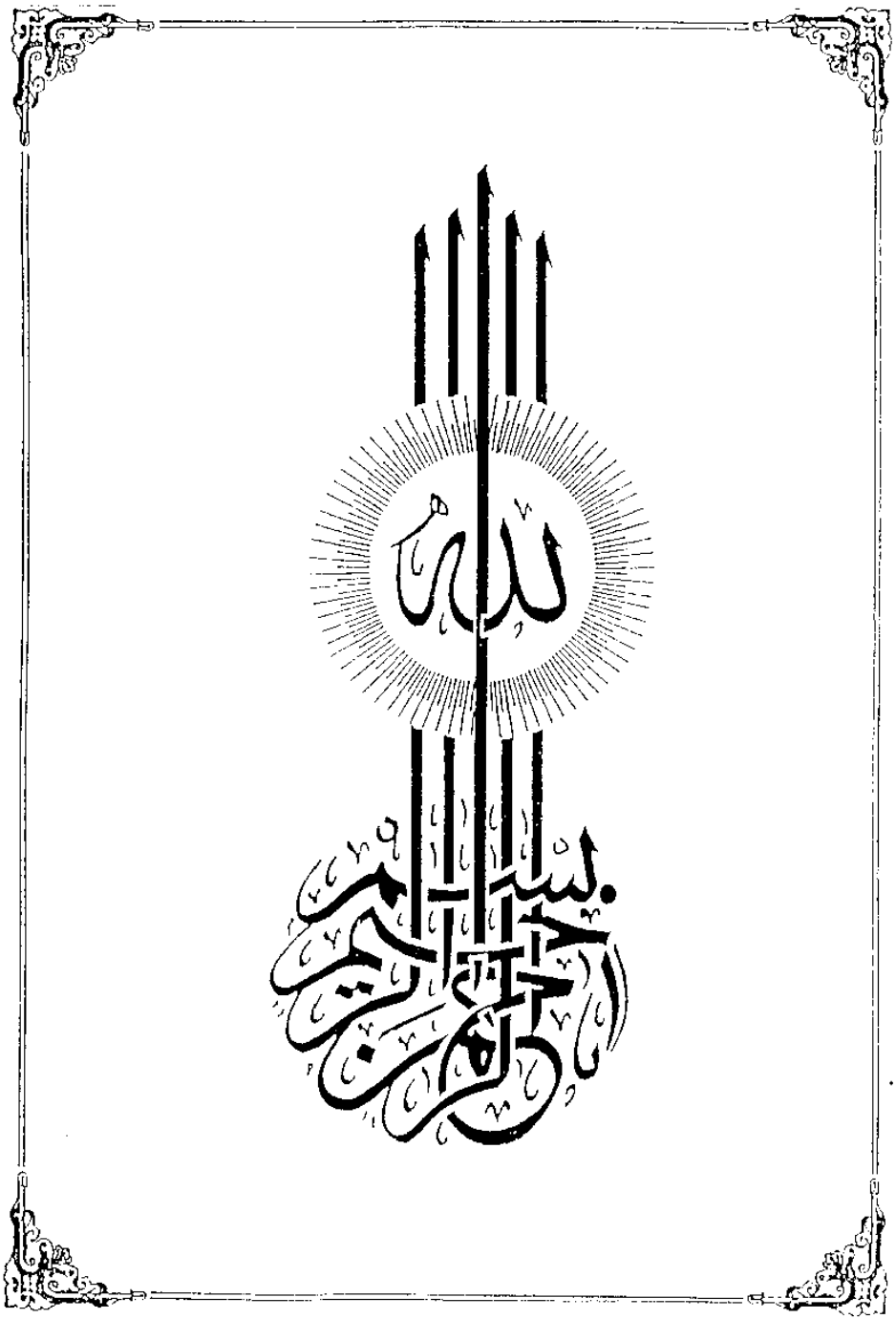
First and foremost thanks are due to GOD the most beneficent and Merciful.

I would like to express my sincere gratitude to Professor Dr. MOHAMED NABEGH AL MAHALLAWAY, Assistant Prof. of Obstetrics and Gynaecology Faculty of Medicine, Ain Shams University, for his kind supervision, continuous encouragement and maximum accuracy through the whole work.

I would like also to express my thanks to Dr. MAGDY MOHAMMED KAMAL, Lecturer of Obstetric and Gynaecology, Faculty of Medicine, Ain Shams University, for his valuable and honest assistance through the whole work.

I am indebted to Prof. Dr. RAGAA HASSAN ALI, Chairman of Board Directors of the Egyptian Organization for Biological and Vaccination Production, she offered me the opportunity to perform the practical part of this work.

I want to thank all workers in central blood bank in Ministry of Health, who helped me to do this work.



CONTENTS

AIM OF THE WORK

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The aim of the present thesis is not to repeat what has already been will written, nor to review the voluminous literature on this subject, but it is to explain all the prophylactic measures in prevention of Rh-haemolytic disease of the newborn in Egypt, as the useful indications, dosages, possible mechanisms of actions, the risks and causes of failure of the anti-D immunoglobulin will be discussed.

The prevalence of the foetuses at risk of haemolytic disease in Egypt will be estimated through the practical part of this thesis.

Future expectations and recommendation for the prophylactic measures against the Rh haemolytic disease of the newborn will also be presented.

REVIEW OF LITERATURE

HISTORICAL REVIEW

The first description of haemolytic disease of the newborn was in 1609, but no rational treatment was possible until the discovery early in this century of the ABO blood groups and later the Rh factor. Understanding the aetiology of this disorder improved clinical management and ultimately led to the development of a method of prevention *(Scott, 1982).*

In *1932, Diamond and Associates* demonstrated that icterus gravis anemia of newborn and hydrops foetalis were related and that erythroblastosis was common to all three disorders.

In *1940, Landsteiner and W*iener set out to determine whether the human red cell might contain specific inherited antigens other than AB and MN. First, they produced an anti-rhesus monkey red cell serum. By mixing the human red cells of members of a Caucasian population with their product, they found that about 85% of this population had red cells that were agglutinated by the serum and the remaining 15% were not.

The red cells that were agglutinated had an antigen in common with rhesus monkey red cells and had the term "Rh-antigen". Those who possess this antigen are classed Rh-positive while those whose red cells are not agglutinated are classed Rh-negative.

In *1941, Levine and associates*, demonstrated that iso-immunization of Rh-negative woman to Rh-antigen was the predominent cause of erythroblastosis foetalis.

In *1944, Halbrecht* suggested that neonatal jaundice occurring in the 24 hours of life, might be due to ABO incompatibility and referred the diseas as "Ictrus precox". His work followed Levine's discovery of Rh-system and after the identification of ABO blood groups 40 years earlier.

The thirty following Landsteiner and Wiener's work have witnessed the discovery of the complexities of Rh-blood system and the discovery of many other blood group systems such as Lewis blood group system, kell, kidd and also private antigen. Over sixty red cells antigens have been identified, *(Lowis.. 1982).*

Bevis, (1956) began reporting studies correlating bilirubin staining of amniotic fluid with foetal anaemia.

Liley in 1963, made the succesful development of intra-uterine transfusion to alleviate foetal an aemia.

Finn and associated, (1961) in England and *Freda and Corman, (1962)* in the United States established that Rh-isoimmunization could be prevented by the use of anti-Rh gamma globulin. Since 1968, the use of Rh-immunoglobulin for prevention became a wide public health program.

The British perinatal mortality survey of 1958 that as many as 4.3% of stillbirths and early neonatal deaths were then due to Rh-isoimmunization, *(Bulter and Bonham, 1963).* On the other hand, the perinatal mortality rate from this cause in the Scottish survey for 1977, was only 0.3 per thousand total births *(McIlwain et al., 1979).*

Whitfield (1983), demonstrated the managing of Rh-isoimmunization so, that it will be possible to maintain the necessary obstetric paediatric and laboratory expertise at only a few centers organized on a regional basis.

Nevertheless, every obstetrician, midwife and general practitioner participating in antenatal care must be alert to the importance of identifying the few new Rh(D) immunization cases that will still occur. They also should detect as early as possible, during pregnancy, the presence of any other irregular antibodies of the Rh or non Rh-systems.

PHYSIOLOGY OF BLOOD GROUPS

BLOOD TYPES

According to *Ganong (1979)* it is reported that, the membrane of human red cells contains a variety of antigens called agglutinogens. The most important and best known of these are the A and B agglutinogens. Individuals are divided into 4 major blood group types A, B, AB, O. On the basis of the agglutinogens present on their red cells.

Agglutinogens start to appear in the sixth week of foetal life. Concentration gradually rises and at birth it reaches one-fourth of the adult level. The adult level is reached at about puberty, *(Cheraskin and Langley, 1978).*

Antibodies against agglutinogens are called agglutinins. They may occur naturally (i.e be inherited), or they may be produced by exposure to the red cells of another individual. This exposure may occur via a transfusion, or during pregnancy, when foetal red cells cross the placenta and enter the maternal circulation, *(Ganong, 1979).*

Walter and Isreal, (1979) reported that antibodies to blood group antigens not possessed by the individual are termed alloantibodies and these are capable of reacting with the red cells of people of a different blood group, but do not react with the individual's own red cells.

A. ABO-BLOOD GROUP SYSTEM

Cheraskin and Langley, (1978) reported that, the A and B antigens are inherited as mendelian allelomorphs.

A and B being dominant, there are 4 major ABO blood groups. These groups are called O, A, B, AB.

Group A is subdivided into A_1 and A_2, group AB is also divisible into A_1B and A_2B. Approximately 75 - 80% of group A belong to the subgroup A_1 while, 60% of group AB belong to the subgroup A_1B. The remainder belong to subgroups A_2 and A_2B.

Guyton, (1967) described that splitting group A blood into the subtypes is usually unnecessary from the practical point of view because transfusion reaction between bloods of these subgroups have rarely occurred.

The finding of subgroups A1 and A2 suggests that there are four alleles, A_1, A_2, B and O leading to six phenotypes.

Phenotype (group)	Genotype (group)	Phenotype (Group)	Genotype (Group)	Phenotype (Group)	Genotype Group)
O	OO	A_2	A_2O	A_1B	A_1B
			A_2A_2		
A_1	A_1A_1	B	Bo	A_2B	A_2B
	A_1O		BB		
	A_1A_2				

Frequency of Blood Groups

Cheraskin and Langley, (1978) reported that a racial difference in the distribution of blood groups.

Group O has been found to be more common amongst Indian Tribes of America, a section of Australians and Africans, north, western Europeans, etc... People of America, west Europeans and west Asians have a higher frequency of group A where as group B is more common in central and south-east Asians.

Amongst Indians, group B is highest in north-east (25 - 30%) and lesser in south (20%).

Relative Frequency of the Different Blood Group

Guyton, (1967) reviewed the prevalence of the different blood types among white persons is approximately as following:

Type	Percent
O	47
A	41
B	9
AB	3

It is obvious from these percentages that the O and A genes occur frequently but the B gene is infrequent.

B. Rh-BLOOD GROUP SYSTEM

Landsteiner and Wiener. (1940 - 1941). immunized rabbits and guinea pigs with the red cells of a rhesus monkey. they resulting antiserum produced agglutination in a large portion of the human red cells studies. The responsible human blood antigen was called Rh. About 85% of Caucasians are Rh positive and 15% are Rh negative. There are several Rh antigens "Rh-positive", "Rh-negative" refers to the absence of the most important the D antigen.

According to *Pritchard et al. (1985).* they reported the racial differences of the Rh-blood group system. American, Indians, Chinese and other Asiatic peoples are almost all Rho(D) positive (99%). Among black Americans there is a lesser incidence of Rho(D) negative individuals (7 to 8%) than among white Americans (13%) of all racial and ethnic groups studied thus far. The Basques show the highest incidence of Rho(D) negative (34%).

PATHOGENESIS OF HAEMOLYTIC DISEASE OF THE NEWBORN

Red cell antigen are present by the sixth foetal week *(Mollison and Cutbush. 1959).* These foetal antigens can initiate antibody formation in the mother lanking it. This antibody (of IgG class) crosses the placental barrier and results in foetal RBcs haemolysis.

The role of the Rh antibody in classic erythroblastosis foetalis was first elucidated by *Levine and Kalzin, (1941).*

It is now recognized that the Rh antigen is a large protein molecule with several antigenic sites and that each of these antigens reflects a specific chemical or structural protein characteristic *(Avery and Taeusch, 1984).*

The antigen is not a single antigen but rather a group of antigens *(Walter & Isreal., 1979 and Rote, 1982).*

A. HAEMOLYTIC DISEASE DUE TO Rh (D) ANTIGEN

Nomenclature of Rh Blood Group

According to *Walter & Isreal (1979) and Rote (1982),* three systems of nomenclature for the Rh-antigens have been developed.