RH ISOIMMUNIZATION

THESIS

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By

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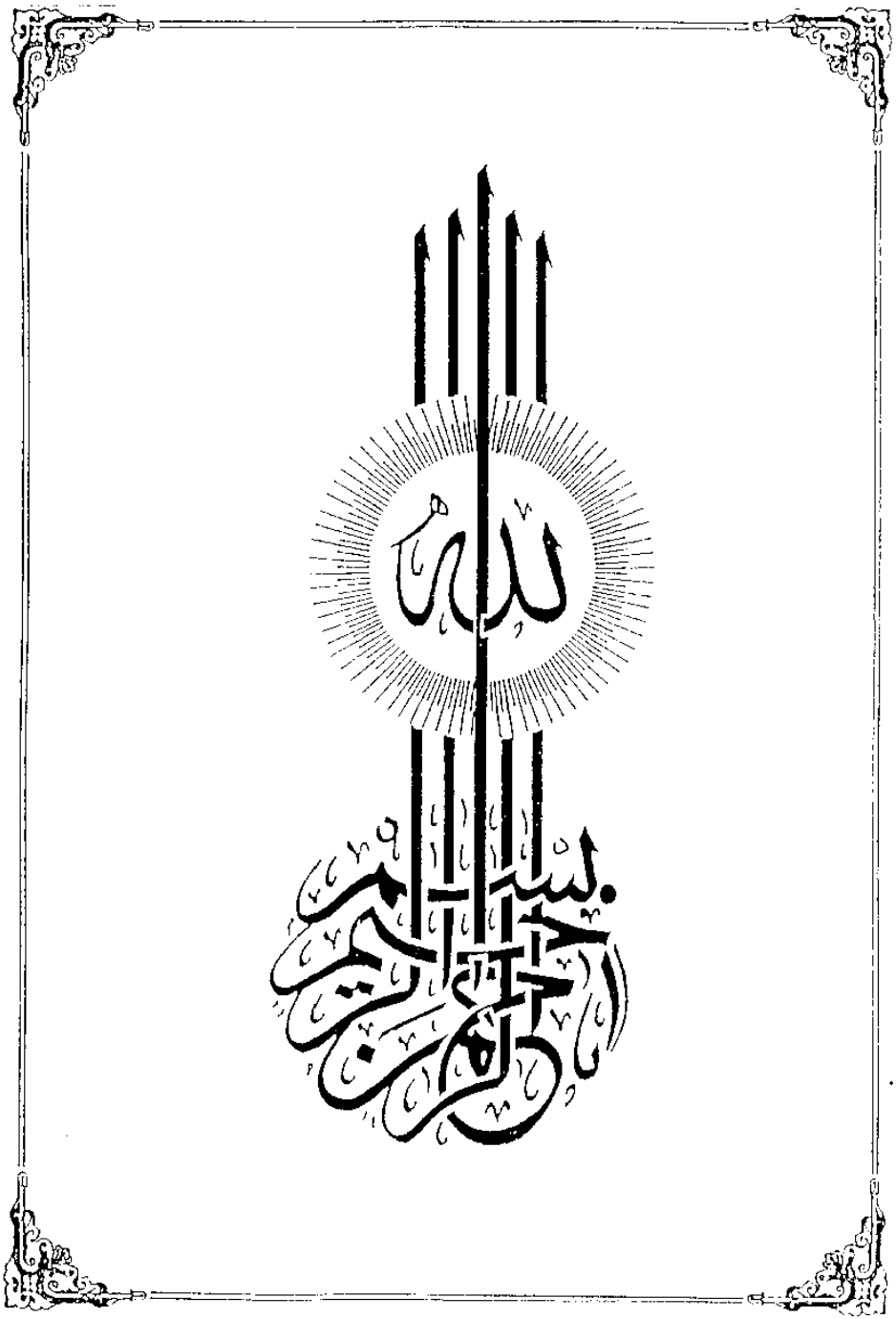

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C O N T E N T S

REVIEW OF THE LITERATURE

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Erythroblastosis fetalis (EBF) is a disease of the fetus and newborn, caused by an incompatibility of fetal and maternal blood. Usually the Rh-negative mother becomes immunized by an exposure to Rh-positive fetal erythrocytes during pregnancy or delivery, but occasionally immunization is due to an injection or transfusion of Rh-positive bliid. The maternal antibodies pass through the placenta to the fetal circulation where they react with the Rh-positive fetal erythrocytes, causing a hemolytic anemia. In severe cases the fetus dies in utero because of congestive heart failure secondary to hemolytic anemia. At delivery the fetus may show the massive swelling of hydrops fetalis.

Accounts of EBF have been traced as far back as 400 B.C. when Hippocrates described a syndrome which Ballantyne(3) accepted as the first report of hydrops fetalis.

According to pickles(18), the first clear-cut account of hydrops fetalis was given in 1641 by Felix plater(19), the famed Renaissance physician.

While there had been some knowledge of the clinical aspects of this disorder for many hundreds of years, its etiology was not discovered until relatively recently (1939-1940).

This discovery focused attention on the disease, and initiated great progress in its understanding and treatment.

Some of the major scientific events leading to modern knowledge of EBF are listed on the following pages:

1875 Orth[17] described kernicterus.

1892 Ballantyne[3] brought the disease into prominence by describing the clinical and pathologic criteria for the diagnosis of hydrops fetalis. He described edema, anemia, and enlargement of the liver, spleen, and placenta. In addition, he noted bilirubin staining of the amniotic fluid.

1912 Rautmann[22] was the first to use the term "erythroblastosis".

1932 Diamond et.al.[7] reported that hydrops fetalis, icterus gravis neonatorum, and anicteric anemia of the newborn were manifestations of the same disease process, EBF. They did not fetal-maternal incompatibility in the ABO blood groups in their patients.

1938 Darrow[6] concluded that the pathogenesis of EBF was based on the formation of a maternal antibody ageinst a component of fetal blood.

1938 Hellman[12] and Hertig reported the peculiar familial occurrence of EBF and noted its rarity among first-born.

1939 Levine and Stetson[15] described an atypical agglutinin in the blood of a woman who had just given birth to a stillborn macerated fetus and who subsequently incurred a transfusion reaction when transfused with apparently compatible blood.

They postulated that maternal immunization was the result of a fetal antigen inherited from the father and lacking in the mother.

1940 Landsteiner and Wiener[13] discovered the Rh antigen in red blood cells.

1946 Wallerstein[23] performed one of the first exchange transfusions for the treatment of an infant having EBF.

1950 Allen, Diamond[2] and vaughan demonstrated statistically that severe hyperbilirubinemia leads to kernicterus. They showed that exchange transfusion minimized the hyperbilirubinemia and reduced the frequency of kernicturus in their of 109 infants treated by exchange transfusion, kernicterus developed in only 1.

They clearly established the role of exchange transfusion in the treatment of EBF.

1953 Claireaux[5], cole, and Lathe showed that kernicterus was due to indirect (unconjugated) bilirubin.

1954 Allen[1], Diamond, and Jones proved the value of preterm delivery in decreasing the number of stillbirths due to EBF.

1956 Bevis[4] reported the significance of increased blood pigments in the amniotic fluid of a fetus with EBF. He demonstrated that spectrophotometric analysis of the amniotic fluid provided a means of predicting the severity of EBF and established the value of amniocentesis in treating the disease.

1958 Levine[14] demonstrated that, when fetal blood is incompatible in the ABO blood groups with that of the mother, a protective mechanism is invoked against Rh immunization.

1960 Gorman[11], Freda, and pollack in New York and Finn[8] and Clarke in Liverpool independently embarked on programs to prevent Rh immunization with passively administered Rh antibody.

1963 Liley[16] reported the first successful intrauterine transfusion for prevention of stillbirths due to EBF.

1965 Freda[10], Gorman, and Pollack and Woodrow[24] and associated reported the successful prevention of maternal immunization to the Rh factor by administration of an anti-Rh_o (anti-D) preparation following delivery.

1968 Rh_o (D) immune globulin (Rh immune globulin) received food and Drug Administration (FDA) approval for postpartum administration.

For simplicity, Rh_o (D) immune globulin will be referred to as Rh immune globulin.

1970 Freda[9] and associates and Queenan and co-workers[20] demonstrated the role of spontaneous abortion in Rh mmunization.

They found the risk of immunization with spontaneous abortion followed by dilatation and curettage to be 3-4%.

1971 Queenan[21] and co-workers demonstrated the role of induced abortion in Rh immunization.

They found that 7% of patients undergoing suction curettage and 20% undergoing intramniotic saline abortions had transplacental hemorrhage.

They determined a 5.5% risk of immunization for induced abortion and recommended the use of Rh immune globulin prophylaxis.

New blood factors that can cause EBF are continually being discovered, so that what appeared to be a clear-cut matter in 1940 (when the Rh factor was isolated) is now quite complex.

However, throughout the world there has been a marked increase in research activity to study the diagnosis and treatment of the disease.

Moreover, the increasing ability to diagnose and treat EBF has led to the study of means of prevention.

Rh prophylaxis by administration of Rh immune globulin has proven effective.

Fewer patients are becoming immunized today than a decade ago.

Although this system of prophylaxis works, it has signiflcant pitfalls: it is passive immunization and therefor must be administered with each exposure to the Rh antigen; occasionally patients become immunized during pregnancy; and there are still patients who are not receiving Rh immune globulin protection.

Even allowing for these deflciencies the prevention program should decimate the incidence of Rh immunization. The decreasing incidence and the trend toward smaller families mean that this disease will become infrequent. Nonetheless, Rh immunization is still capable of causing perinatal mortality and, therefore, it must be approached with great vigilance and concern.

SEROLOGY OF ERYTHROBLASTOSIS FETALIS