

1 111110

FETOMATERNAL TRANSFUSION
IN VARIOUS TYPES
OF ABORTIONS

THESIS
SUBMITTED FOR PARTIAL FULFILLMENT
OF
M.D. DEGREE IN
OBSTETRICS & GYNAECOLOGY

13 33

BY

24279

SAMEH MAHMOUD AMIN ABDEL-HAFEZ

UNDER SUPERVISION OF

PROFESSOR
AMIN EL-ZENEINY
PROFESSOR OF GYNAECOLOGY
AND OBSTETRICS
AIN SHAMS UNIVERSITY

PROFESSOR
HAMDY EL-KABARITY
PROFESSOR OF GYNAECOLOGY
AND OBSTETRICS
AIN SHAMS UNIVERSITY

Dr. SALWA YOUSSEF
ASS. PROFESSOR OF CLINICAL
PATHOLOGY
AIN SHAMS UNIVERSITY

1986

Central Library - Ain Shams University

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ



(i)

ACHNOWLEDGEMENT

I wish to express by deepest thanks and profound gratitude to **PROFESSOR AMIN EL-ZENEINI** for giving me the privilege to work under his supervision, for his continuing encouragement and for his eminent fatherly guidance.

I express my utmost appreciation and gratitude to **PROFESSOR HAMDY EL-KABARITY** for his kind supervision and energetic help spending long hours in careful review of this work and in following its details with constructive advice and criticism.

I also convey my appreciation to **Dr. SALWA YOUSSEF** for her encouragement, her continuous help and her perfectionist meticulous work.

My warm thanks to **Dr. SAID EL-TOHAMI** to whom I will always be indebted for his invaluable help.

4

(ii)

I extend my thanks to Dr. MOHSEN ABDEL HAMID, to my colleagues Dr. SALWA ABUL-HANA, ZAHRA SHAABAN and to all who provided me with assistance and support.

5
(iii)

DEDICATION

TO MY DEAR FATHER, MOTHER, MY
BROTHER MAGDI AND MY WIFE MONA
FOR THEIR EVERLASTING SELFLESS
LOVE AND ENCOURAGEMENT

	<u>Page</u>
ACKNOWLEDGEMENT	i
DEDICATION	iii
TABLE OF CONTENTS	iv
LITERATURE REVIEW	1
1. HISTORICAL REVIEW OF RHESUS ISOIMMUNIZATION	1
2. FETAL HAEMOGLOBIN AND ERYTHROCYTES	8
2.1 Fetal Haematopoiesis	8
2.2 Fetal Haemoglobin	9
2.3 Fetal Circulation	10
2.4 Rhesus Antigen Expression in the Fetus	10
3. THE RHESUS FACTOR	12
4. INCIDENCE OF RHESUS ISOIMMUNIZATION	17
5. IMMUNOLOGY OF RH SUS ISOIMMUNIZATION ...	19
5.1 Definition	19
5.2 The Anti Rh Antibody	21
5.3 Mechanism Of Haemolysis	23
5.4 Primary Antibody Formation	23
5.5 Antibody Detection in the Infant ..	26
5.6 Factors Influencing Sensitization .	27
6. NON ANTI D ANTIBODIES	31
6.1 Importance of Antibodies Other Than Anti RhOD	31
6.2 Non Rh Antibodies	34

7

(v)

	<u>Page</u>
7. PATHOLOGY	38
7.1 The Pathophysiology of Haemolysis .	38
7.2 Congenital Haemolytic Anaemia	39
7.3 Icterus Gravis Neonatorum	40
7.4 Hydrops Fetalis	42
7.5 Non Immunologic Hydrops Fetalis ...	46
8. PATHOGENESIS OF FETOMATERNAL HAEMORRHAGE AND ISOIMMUNIZATION	48
8.1 Pathogenesis of Fetomaternal Haemorrhage	48
8.2 Aetiology of Fetomaternal Haemorrhage	50
8.3 Maternofetal Haemorrhage	59
9. DETECTION AND QUANTITATION OF FETOMATERNAL HAEMORRHAGE	61
9.1 The Principle of the Acid Elution Technique	61
9.2 The Technique of the Acid Elution Procedure	63
9.3 Enzyme Linked Antiglobulin Test ...	67
9.4 Specific Mixed Agglutination	68
10. DETECTION OF FMH BY ALPHAFETOPROTEIN ASSAY	69
10.1 Historical Perspective	69
10.2 Chemical Structure	72
10.3 AFP Heterogeneity	74
10.4 Physiology of AFP in Pregnancy	76
10.5 Causes of Elevation of Maternal Serum AFP	90
10.6 Clinical Significance of Low MSAFP.	96
10.7 Clinical Use of MSAFP in Screening Neural Tube Defects	98
10.8 Detection of FMH by Measurement of MSAFP	105
10.9 MSAFP in Abortion	108
10.10 Measurement of AFP	115

	<u>Page</u>
11. PREVENTION OF Rh ISOIMMUNIZATION	119
11.1 Preparation of the RhOD immune Globulin	119
11.2 Presentation	119
11.3 Hazards of Preparation	120
11.4 Route of Administration	120
11.5 Side Effects	120
11.6 Mechanism of Action	121
11.7 Indications	122
11.8 Failures	131
11.9 Future Directions	133
SUBJECTS AND METHODS	134
RESULTS	140
DISCUSSION	175
APPENDIX	191
SUMMARY	200
REFERENCES	206
ARABIC SUMMARY	

1

REVIEW OF LITERATURE

...

1 A

1. HISTORICAL REVIEW OF RHESUS ISOIMMUNIZATION

Man's knowledge of erythroblastosis fetalis (E.B.F) dates back to around 400 BC when Hippocrates described a syndrome which has been accepted as the first report of hydrops fetalis (Queenan, 1977). Felix Plater, a famous Renaissance physician described in 1641 the first clear cut appearance of hydrops fetalis and in 1875 Orth described kernicterus.

In 1892 Balantyne described oedema, anaemia, hepatosplenomegaly and placental enlargement with bilirubin staining of the amniotic fluid as the pathological criteria for the diagnosis of hydrops fetalis. The term erythroblastosis was first used by Rautmann in 1912. Then in 1932 Diamond et al. reported that hydrops fetalis, icterus gravis neonatorum and acholuric anaemia of the newborn were manifestations of the same disease process.

Darrow (1938) suggested that the pathogenesis of EBF was due to formation of maternal antibodies against a component of fetal blood. In the same year Hellman and Hertig noted the rarity of EBF among first born infants (Queenan, 1977).

Levine and Stetson (1939) were the first to suggest that a fetus in utero might by means of a property inherited from its father produce antibodies in the mothers serum which when reacting on the blood of a donar might cause haemolysis and thus a transfusion accident (Queenan, 1977).

Landsteiner and Wiener (1940) showed by means of rabbit sera prepared by injection of Rhesus blood that a large proportion, about 85% of white people, contain a factor in their red blood cells (but not in the tissue fluids) similar to that found in Rhesus monkeys and hence called Rh.

Wiener and Peters in 1940 showed the practical importance of this discovery and described four cases in which reported blood transfusions of the proper groups gave rise to severe (and in two of the cases fatal) haemolytic reactions. They found that in three of the cases the patients blood contained an antibody which was identified as anti-Rh and suggested that the donor's blood had been Rh positive with the result that the reported transfusions had led to the production of Rh antibodies in the recipient and acute haemolytic reactions at subsequent transfusions with Rh positive blood (Browne and Dixon, 1970).

Finally, Levine et al. in 1941 presented data showing that fetal erythroblastosis resulted from isoimmunization of the mother by dominant hereditary blood factors in the fetus and the subsequent passage of these maternal antibodies back across the placenta into the fetal circulation where they acted on the susceptible fetal blood causing haemolysis of the red blood cells. They showed that in the majority of cases the blood factor involved was identical with the Rh

factor described by Landsteiner and Wiener.

In 1944 Fisher found that there was more than one Rh antigen and he established the CDE classification (Browne and Dixon, 1978).

Wallerstein in 1946 performed the first exchange transfusion for treating an infant having EBF.

Allen et al. (1950) demonstrated that severe hyperbilirubinaemia lead to kernicterus and showed that exchange transfusion minimized the hyperbilirubinaemia and reduced the frequency of kernicterus.

Claireaux et al. (1953) showed that kernicterus was due to unconjugated bilirubin and one year later Allen et al. (1954) proved the value of preterm delivery in decreasing the number of stillbirths due to isoimmunization (Queenan, 1977). In the same year Chown documented the phenomenon of fetal red cells crossing the placental

barrier to enter the maternal circulation. This phenomenon was confirmed by Gunson in 1957. These authors described examples of massive fetomaternal haemorrhage in which the Rh_D positive fetal red cells were detected in the maternal Rh_D negative blood by using differential agglutination to agglutinate the minor population of fetal cells with anti Rh_D.

Bevis (1956) 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 managing the disease (Queenan, 1977).

Levine (1958) demonstrated that protection against Rh immunization occurs when fetal blood is ABO incompatible with the maternal blood.