

**Transplacental Passage Of Foetal Red Cells
In Normal And Complicated Pregnancies**

Thesis
Submitted for Partial Fulfilment
of Master Degree in Clinical Pathology

BY

OMAYMA ABD EL MONEM EL GANDEL

Supervised by

Prof. Dr. TARIF HAMZA SALLAM

Professor of Clinical Pathology
Ain Shams University

Dr. SALWA MOHAMED ABU EL HANA

Lecturer of Clinical Pathology
Ain Shams University

Faculty of Medicine
Ain Shams University
1991

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ
قَالُوا سُبْحَانَكَ لَعَلَّنا نَكْفُرُ لَكَ إِلَّا مَا مَلَكْتَنَا نَفْسُكَ أَنْتَ الْعَظِيمُ
الْحَكِيمُ
صَدَقَ اللَّهُ الْعَظِيمُ

سورة البقرة - الآية ٣٥



ACKNOWLEDGEMENT

I would like to express my deepest thanks and gratitude to professor Dr. TARIF HAMZA SALLAM, Professor Of Clinical Pathology, Faculty Of Medicine, Ain Shams University, for his unlimited help and continuous guidance which enabled me to accomplish this work. I am definitely indebted to him more than I can express.

I would like also to express my heartfelt gratitude and deepest thanks to Dr. SALWA MOHAMED ABU EL HANA, Lecturer Of Clinical Pathology, Faculty Of Medicine, Ain Shams University. I have been most fortunate in having her indispensable advice and continuous encouragement.

To My Parents

CONTENTS

- INTRODUCTION AND AIM OF THE WORK	1
- REVIEW OF LITERATURE	
- Rhesus Blood Group System	
Antigens of Rh system	4
Chemical nature of Rh antigen	6
Rh antibodies	7
Incidence of Rh isoenimmunization	8
Other blood groups systems	10
- Pathogenesis Of Transplacental Haemorrhage And Rh Isoimmunization	
Placental barrier	13
Etiology of transplacental haemorrhage	14
Massive transplacental haemorrhage	19
Clearance of fetal red cells from the maternal circulation	22
- Detection And Quantitation Of Transplacental Haemorrhage	
Acid elution method	25
Immunofluorescence techniques	27
Erythrocyte rosette and indirect antiglobulin test	29
Estimation of Alpha-fetoprotein in maternal serum	30
- Rh Haemolytic Disease Of The Fetus And Newborn	
Mechanism of haemolysis	33
Clinical manifestations of haemolytic disease	34
Diagnosis	37
Treatment	43
- Prevention Of Rh Haemolytic Disease	
Rh (D) immune globulin	47
Current Rh prophylaxis recommendations	50
- SUBJECTS AND METHODS	53
- STATISTICAL METHODS	61
- RESULTS	64
- DISCUSSION	90
- SUMMARY AND CONCLUSIONS	96
- RECOMMENDATIONS	99
- REFERENCES	100
- ARABIC SUMMARY	

ABBREVIATIONS

ADCC	:	Antibody dependent cell mediated cytotoxicity
AFP	:	Alpha fetoprotein
C.S.	:	Caesarean section
F:M	:	Fetal : Maternal
HDN	:	Haemolytic disease of the newborn
min	:	Minute
mcg	:	Microgram
ng	:	Nanogram
N.S.	:	Non significant
NVD	:	Normal vaginal delivery
O.D.	:	Optical density
RhIG	:	Rh immune globulin
S	:	Significant
TPH	:	Transplacental haemorrhage

**INTRODUCTION
AND
AIM OF THE WORK**

INTRODUCTION

Transplacental haemorrhage (TPH) was first postulated by *Dienst* in 1905 who concluded that eclampsia is nothing but a transfusion of the incompatible blood of the fetus into the mother's circulation. However, almost 50 years passed before direct proof of the presence of fetal red cells in the maternal circulation was obtained. *Chown* (1954) serologically demonstrated a minor population of Rh-positive red cells in a blood specimen from a newly delivered Rh-negative woman and concluded that the anemia of her Rh-positive infant was due to TPH. The acid elution test described in 1957 by *Kleihauer et al.* has been a key in the study of the transplacental passage of fetal red cells and the cause and prevention of Rh haemolytic disease of the newborn.

The larger the dose of Rh positive fetal red cells passing to the maternal circulation, the more likely is Rh immunization to occur. Haemorrhage of more than 30 ml of whole blood from the fetus into the maternal circulation not only can result in the death of the fetus, but the standard dose of 300 µg of Rh immune globulin (RhIG) is not enough also to protect against Rh sensitization and a dose of 10 µg for every 1 ml of TPH should be added (*Sebring and Polesky, 1990*).

AIM OF THE WORK

This work aimed to detect the incidence of transplacental haemorrhage following pregnancy and delivery among Egyptians and to compare this incidence in both normal and complicated pregnancy and delivery.

**REVIEW
OF
LITERATURE**

CHAPTER 1: RHESUS BLOOD GROUP SYSTEM

- Antigens of the Rh system
- Chemical nature of Rh antigens
- The Rh antibodies
- Rh isozimmunization
- Other blood groups system

RHESUS BLOOD GROUP SYSTEM

The rhesus (Rh) blood group system is of considerable clinical importance because the majority of Rh negative individuals make antibody when Rh positive red cells enter the circulation either by transfusion or by transplacental haemorrhage (*Bowman, 1990*).

The rhesus blood group system was so named because an antibody against red cells of the monkey *Macacus rhesus* was found to agglutinate the red cells of certain humans. Such persons are said to be rhesus positive and they comprise 83% of population. The red cells of the other 17% are not so agglutinated and are said to be Rhesus negative (*Mollison, 1987a*).

The highest incidence of Rh negativity occurs in the Basques (34%) and the lowest incidence occurs in the Chinese and American Indians (1%). Among black Americans there is less incidence of Rh negative individuals (7-8%) than among white Americans (13%) (*Pritchard et al., 1985*). The incidence of Rh negative individuals in Egypt is 1.2% (*El Shiemy et al., 1978*).

ANTIGENS OF THE Rh SYSTEM

The Rh factor is not a simple one but composed of numerous antigens. The loci of Rh system are present on the short arm of chromosome 1 (*Mc Kusick, 1989*). *Fisher (1944)* proposed that Rh antigens are controlled by three closely linked allelic gene pairs, which produce the antigenic determinants C or c, D or d and E or e respectively. *Wiener, (1951)* suggested that the inheritance of Rh antigens is determined by a number of allelic genes at one locus. For example, the inheritance of CDe is determined by the gene R¹ rather than by a gene complex CDe. The discovery that D and c are separate proteins suggests that Wiener's view is incorrect (*Mollison, 1987a*).

Du phenotype:

With anti-D, Du red cells react more weakly than normal D positive cells.

The frequency of the Du phenotype is about 0.2% overall, 0.6% among Caucasians and about 1.5% of all Rh-negative gravid women. At least three different mechanisms may be responsible for the expression of Du:

- 1) hereditary absence of a portion of the D mosaic.
- 2) gene interaction with suppression of D by C in the transposition.

3] a D gene producing a weak antigen.

Rh-negative women who complete pregnancy with a Du baby are rightful candidates for Rh immune globulin (Rh IG). The production of alloanti-D in Du positive blood has led to transfusion reactions and also to haemolytic disease of the newborn. (White et al., 1983).

Use of RhIG in Du positive women:

Although some authorities advise routine Rh IG administration of Du positive women after delivery of a D positive baby (Issitt, 1979.) most authorities prefer not to give RhIG routinely because of low incidence of Du phenotype and the improbability of cost/benefit effectiveness (Giblett, 1990).

Antigens of the Rh system other than C, c, D, E and e:

Ag G: In 1958 Allen and Tippert described the antigen G that is found on nearly all C or D positive erythrocytes and absent in almost all C or D negative ones. This co-distribution of the G antigen with either the C or D antigens gives anti G antibody with apparent anti-C plus anti-D specificity.