

HTLV-III ANTIBODIES IN POLYTRANSFUSED CHILDREN

THESIS

SUBMITTED IN PARTIAL FULFILMENT
FOR THE (M.D.) DEGREE IN
(PAEDIATRICS)

BY

Shahira Abdel-Latif El-Nazer

M.B., B.Ch.

M. Sc., Paediatrics

SUPERVISORS

Prof. Dr.

Ahmed Samy Khalifa

Prof. of Paediatrics

Faculty of Medicine

Ain Shams University

Prof. Dr.

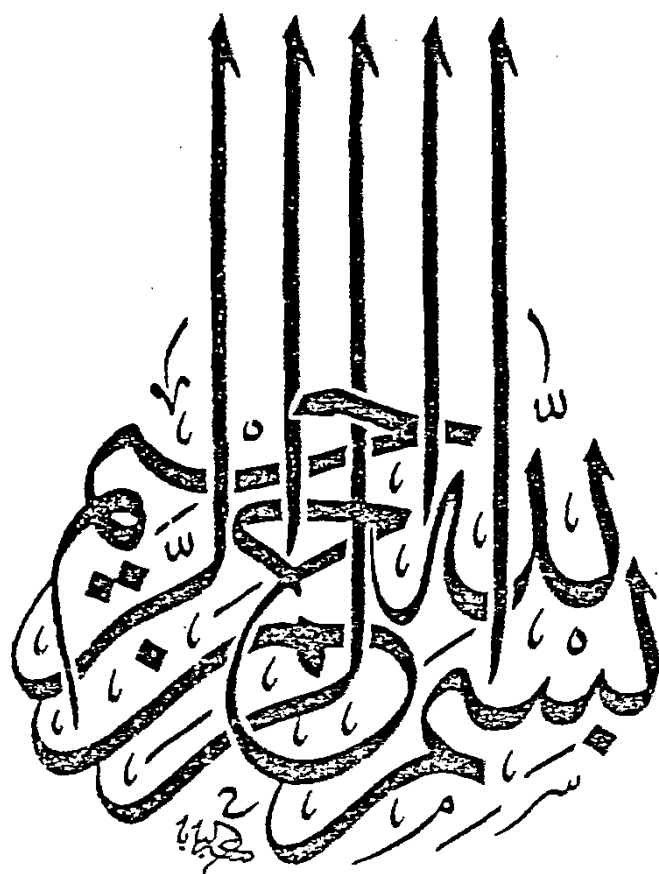
Sawsan Hanem Mohamed El-Tayeb

Prof. of Clinical Pathology

Faculty of Medicine

Al-Azhar University

1990





ACKNOWLEDGEMENT

I would like to express my profound gratitude to Professor Dr. Ahmed Samy Khalifa, Professor of Paediatrics, Faculty of Medicine, Ain-Shams University who honoured me with supervising this thesis. His constant support and encouragement throughout the entire period of my work makes me feel deeply indebted to him.

I owe my cordial appreciation, and deepest gratitude to Professor Dr. Sawsan Hanem Mohamed El-Tayeb, Professor of Clinical Pathology, Faculty of Medicine, Al-Azhar University for her continuous guidance, and help in the laboratory work in this thesis.

To Dr. Galila Mokhtar, Assistant Professor, Faculty of Medicine, Ain-Shams University, I owe my thanks and gratefulness for checking and revising with me most of the pages of this thesis.

I wish to thank Dr. Mohamed Abdel-Monem Hosni, Lecturer of Clinical Pathology, Faculty of Medicine, Al-Azhar University for making the technical difficulties in the laboratory work a lot easier.

To Dr. Mahasen Ghanem and Dr. Salwa Khashaba, Central Labs., Ministry of Health, I express my gratefulness for their cooperation and help.

I also wish to thank Dr. Niel Constantine, Department of Virology, NAMRU 3 for his consultation, and help in the confirmation of our results and in providing me with latest papers on the subject.

Lastly I thank my colleague doctors and nurses in the haematology clinic, Faculty of Medicine, Ain-Shams University for their extreme help.

C O N T E N T S

	<u>Page</u>
. List of Abbreviations-----	i
. List of Tables-----	ii
. List of Figures-----	v
I- Introduction and Aim of Work-----	1
II- Review of Literature-----	
A. Hazards of blood transfusion-----	2
. Types of blood products-----	7
B. Retroviruses-----	9
. General characteristics-----	9
. Taxonomy and families-----	11
. Virion structure and proteins-----	12
. Pathological conditions caused by retro- viruses-----	15
. Cell killing-----	17
. Human Immunodeficiency virus-----	18
* Geographical distribution of HIV infection-----	20
* Morphology of the virus-----	24
* Tissue sources of human immunodeficiency virus-----	26
* Target cells-----	27
* Modes of transmission-----	28
* Cytopathic effect and immune- suppression-----	28

	<u>Page</u>
C. Immunological background-----	
- Normal immune response-----	33
* Humoral immune response-----	34
* Cell-mediated immune response-----	35
- Immunological abnormalities with human immunodeficiency virus infection-----	37
- Antigenemia and antibody titers to cor and envelope antigens-----	45
- Immunization program for HIV infected children-----	47
D. Clinical picture-----	48
- Case definition-----	50
- Incubation period-----	
- Common clinical findings in infants and children-----	50
- Neurological manifestations in children---	54
- Pneumocystis carinii-----	55
- Cryptosporidum-----	59
- Kaposi's sarcoma-----	60
- Recent definitions of paediatric AIDS-----	65
- Recent classification of paediatric AIDS--	66
E. Methods of Diagnosis-----	
- ELISA-----	69
- Western-blot-----	72
- IFA-----	75

	<u>Page</u>
- RIPA-----	77
- Future HIV antibody tests-----	77
- clinical significance and use of HIV antibody testing-----	79
- HIV antigen detection-----	80
- HIV culture-----	83
- Hybridization technique-----	85
F. Prevention and Treatment-----	
- Stability and inactivation of the virus in lab.-----	86
- Trials of treatment-----	88
III- Subjects and Methods-----	97
IV- Results-----	109
V- Discussion-----	152
VI- Summary, Conclusion and Recommendations-----	171
VII- References-----	178
VIII- Arabic Summary-----	

LIST OF ABBREVIATIONS

AIDS	Acquired immunodeficiency syndrome
HTLVIII	Human-T-lymphotropic virus III.
HIV	Human immunodeficiency virus
Env.	Envelope
Cor.	Core
CDC	Centra l for Disease Control
KS	Kaposi's sarcoma
PCP	Pneumocystis carinii pneumonia
CMV	Cytomegalovirus
EBV	Epstein-Barr virus
ELISA	Enzyme-linked immunosorbent assay
EIA	Enzyme immunosorbent assay

List Of Tables

	<u>Page</u>
Table 1: Blood products for replacement therapy in Haemorrhagic diseases-----	7
Table 2: Taxonomy of retroviruses-----	12
Table 3: Retroviruses virion proteins-----	13
Table 4: Mammalian and avian retroviral diseases-----	16
Table 5: Patterns of HIV infection in the world-----	20
Table 6: Global statistics of HIV infection-----	23
Table 7: Tissue sources of HIV isolation-----	26
Table 8: Recommendations for immunization of those with HIV infection or exposure-----	47
Table 9: Diseases accepted by CDC as indicative of underlying cellular immunodeficiency-----	49
Table 10: Stability/Inactivation of HIV-----	87
Table 11: In vitro activity of antiviral agents against HIV-----	94
Table 12: Select properties of compounds active against HIV in clinical studies-----	95
Table 13: Evaluating potential source of error with ELISA-----	104
Table 14: Results of clinical examination of Thalassemia major group-----	111

	<u>Page</u>
Table 15: Results of testing of sera of Thalassemia major using Abbott-EIA technique-----	114
Table 16: Results of western-blot of ELISA positive cases of Thalassemia major-----	117
Table 17: Results of clinical examination of cases of Leukaemia-----	122
Table 18: Results of testing of sera of Leukaemia using Abbott-EIA technique-----	124
Table 19: Results of clinical examination of cases of Haemophilia A and Von Willebrand-----	128
Table 20: Results of testing of sera of Haemophilia A and Von Willebrand using Abbott-EIA-----	130
Table 21: Results of western-blot of ELISA positive cases of Haemophilia and Von Willebrand---	133
Table 22: Results of clinical examination of cases of idiopathic thrombocytopenic purpura----	138
Table 23: Results of testing of sera of idiopathic thrombocytopenia purpura among Abbott-EIA-----	139
Table 24: Results of western-blot of ELISA positive cases of idiopathic thrombocytopenic purpura-----	140

	<u>Page</u>
Table 25: Results of EIA technique for 3 mothers of seropositive children-----	142
Table 26: Results of testing of adults using Abbott- EIA technique-----	143
Table 27: Results of testing of sera of children of general population using Abbott-EIA-----	144
Table 28: The percentage of cases positive for HIV antibodies-----	151

LIST OF FIGURES

	<u>Page</u>
Fig. (I): Replication cycle of HIV-----	19
Fig. (II): The structure of HTLV-III virion-----	25
Fig. (III): Stunted memory clone from HTLV-III infection-----	32
Fig. (IV): The role of T ₄ lymphocyte in immune- response-----	36

INTRODUCTION AND AIM OF WORK

INTRODUCTION AND AIM OF WORK

In 1981, the acquired immunodeficiency syndrome was identified in the United States.

The first cases were homosexual men (Jaffe et al., 1985). In 1982, this pattern of illness was recognized in I.V. drug abusers, persons with haemophilia, blood transfusion recipients (CDC, 1981, CDC, 1982) and infants borne to mothers with AIDS.

The war on AIDS requires a global effort on the part of governments, scientists, doctors and public health workers in order to identify cases and pattern of transmission in each country so as to minimize the spread of infection.

This necessitated this study in Egypt on the high risk group children, recipients of multiple blood transfusions, bearing in mind that transfusion of whole blood or blood components has been implicated in transmission of the syndrome (Amman et al., 1983, Shannon et al., 1983; Church, 1984; Curran et al., 1984).

Our aim of work in this study is to identify the presence of acquired immunodeficiency syndrome in children who receive multiple blood transfusions through testing the sera of those children for the presence of HIV antibodies and to trace the source of contaminated blood or blood component received, to identify the main pattern of transmission of this disease in Egypt.