VARIATION IN CELL-MEDIATED IMMUNITY AFTER OPEN HEART SURGERY

THESIS

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The Degree of M. D. in
CLINICAL & CHEMICAL PATHOLOGY

BY

Dr. MOSHIRA HALIM SABRI MOSTAFA

SUPERVISED BY

Prof. Dr. SAWSAN HOSNEY HAMZA

Prof. & Head of Clinical Pathology Dept.
Faculty of Medicine, Ain Shams University

Assist. Prof. MONA MOHAMED RAFIEK

Assist. Prof. of Clinical Patholgoy
Faculty of Medicine, Ain Shams University

Assist. Prof. EZZ EL-DIN ABD EL-RAHMAN MOSTAFA

Assist. Prof. of Cardiosurgical Dept.
Faculty of Medicine, Ain Shams University

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جامعة عين شمس
كلية الطب

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لجنة الاشراف

أ٠د٠ سوسن حسنى حمزة
أستاذ الباثولوجيا الاكلينيكية
كلية الطب – جامعة عين شمس

أ٠د٠ منى محمد رفيق
أستاذ مساعد الباثولوجيا الاكلينيكية
كلية الطب – جامعة عين شمس

عز الدين عبد الرحمن مصطفى
أستاذ مساعد جراحة القلب والصدر
كلية الطب – جامعة عين شمس

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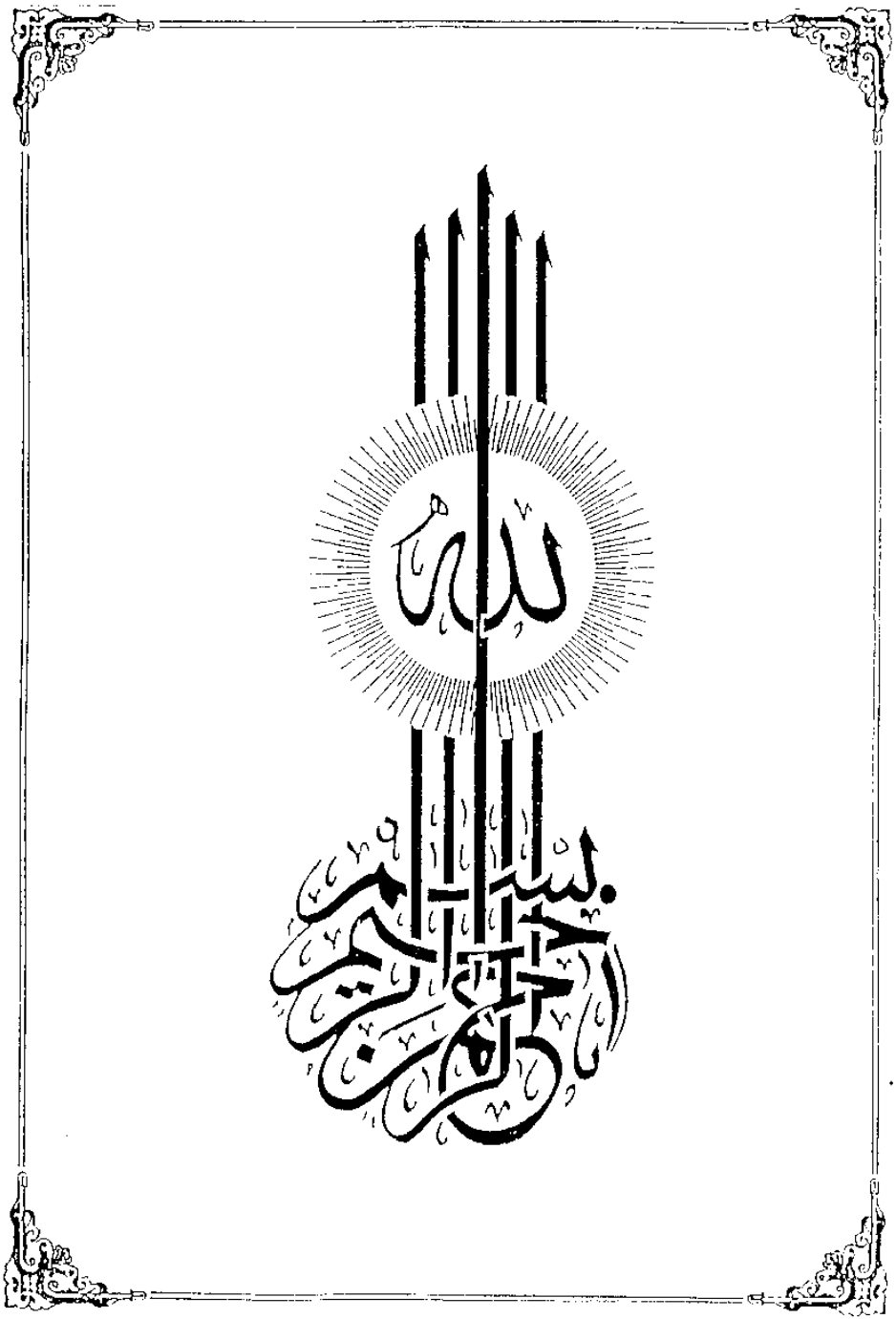

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CONTENTS

LIST OF ABBREVIATIONS

ACTH	Adrenocorticotropic hormone.
ADCC	Antibody-dependent cell-mediated cytotoxicity.
Ag	Antigen.
APC	Antigen presenting cells.
BAF	B cell-activating factor.
BCDF	B cell differentiation factors
BCGF	B cell growth factors.
BSA	Bovine serum albumin.
cAMP	Cyclic adenosine monophosphate
CBG	Cortisol binding globulin.
CD	Cluster of differentiation.
CD3	Antigenic marker on T cell associated with T cell receptor.
CD4	An antigenic marker of helper/inducer T cells (also designated OKT4, T4, Leu 3).
CD8	An antigenic marker of suppressor / cytotoxic T cells (also designated OKT8, T8, Leu 2).
CFU	Colony forming unit.
CFU-C	Colony forming unit of cell grown in culture.
CFU-GEMM	Colony forming unit of granulocytes/erythrocytes, monocytes and megakaryocytes.

CSF. GM	Colony stimulating factor of granulocyte and macrophage.
CFU-S	Colony-forming unit of cells grown in the spleen.
CMI	Cell-mediated immunity.
CML	Cell-mediated lympholysis.
CPB	Cardiopulmonary bypass.
CRH(F)	Corticotropin-releasing hormone or (factor)
CRP	C-reactive protein.
CTL	Cytotoxic lymphocytes.
E	Erythrocyte
EA	Erythrocyte amboceptor (sensitized erythrocytes)
EAC	Erythrocyte amboceptor complement.
EBV	Epstein-Barr virus.
ECF	Esinophil chemotactic factor.
EIA	Enzyme immunoassay.
ELISA	Enzyme linked immunosorbant assay.
Fc	Crystallization fragment.
FITC	Fluorochrome conjugated reagents for T cell typing.
GC	Germinal centers.
GVHD	Graft-versus-host disease
HPA axis	Hypothalamic-pituitary adrenal axis
HSF	Hepatocyte stimulating factor.

Ig	Immunoglobulins
IL-1-IL-10	Interleukins 1—8 and 10
IL-1 R	IL-1 receptor
INF	Interferon.
LDCF	Lymphocyte-derived chemotactic factors.
LMIF	Leukocyte migration inhibitory factor.
LPS	Lipopolysaccharide (adjuvent)
MAF	Monocyte macrophage-activating (-arming) factor.
MCAF	Monocyte chemotactic and activating factor.
MCF	Macrophage chemotactic factor.
M-CSF	Monocyte-macrophage colony-stimulating factor.
MDNCF	Monocyte-derived neutrophil chemotactic factor.
MDP	Muramyl dipeptide (adjuvent)
MFF	Macrophage fusion factor
MHC	Major histocompatibility complex.
MIF	Migration inhibitory factor
	Macrophage inhibitory factor.
MLC	Mixed lymphocyte culture.
MMI	Macrophage migration inhibition.
MSH	Melanocyte-stimulating hormone.
NAD	Nicotinamide adenine dinucleotide.
NCF	Neutrophil chemotactic factor.
NK	Natural killer (cells)
PAF	Platelet activating factor.

PBMC	Peripheral blood mononuclear cells
PBS	Phosphate buffer saline.
PDGF	Platelet derived growth factor.
PG	Prostaglandin
PGE	Prostaglandin E (PGE, PGE 2, PGE 2α)
PHA	Phytohemagglutinin
PWM	Pokeweed mitogen.
sIg	Surface immunoglobulin
SIRS	Soluble immune response suppressor.
Tac	T cell activating receptor.
TAF	T-cell activating factor.
Tc	Cytotoxic T-cells
TCGF	T cell growth factor
TCR	T cell receptor
TGF	Transforming growth factor.
TGFB	Transforming growth factor B
Th	Helper T cells.
Thy	Thymus-derived
TMIF	Tumor migration inhibitor factor
TNF	Tumour necrosis factor.
Ts	Suppressor T-cells.

INTRODUCTION
&
AIM OF THE WORK

INTRODUCTION

The modern cardiac surgery became possible with the development of cardiopulmonary bypass (CPB). CPB is a technique in which blood is diverted away from the heart and lungs into a machine that substitutes for pumping and ventilatory function of these organs. The major component of CPB system are venous catheter, blood reservoir, pump, oxygenator, heat exchanger, filter and arterial catheter. This system also involves two cardiotomy sucker systems and a venting system for the left ventricle *(Edmunds and Stephenson1978).*

CPB has been found to be associated with a wide variety of early postoperative physiological and immunological derangements, including an observed increase in capillary permeability and interstitial fluid, mild fever, leukocytosis, bleeding diathesis and hepatic, cardiac, pulmonary and renal dysfunction with a wide spectrum of severity *(Kirklin et al., 1987).*

The pathogenesis of these changes is complex and is thought to depend in part on leukocyte margination and tissue sequestration with complement, neutrophil and cytotoxic T cell

activation with release of inflammatory mediators causing wide spread endothelial injury *(Westaby, 1987).*

Both humoral and cell-mediated immunity have been shown to be adversely affected for a short period after CBP. For instance, neutrophil functions that are relevant to antibacterial host defenses, such as chemotaxis and bactericidal activity, were shown to be depressed *(Barrows et al. 1987).* Furthermore, the in vivo proliferative response of lymphocytes was noted to be markedly impaired for variable period after CPB *(Tonnesen et al., 1987). Eskola et al. (1986)* found an increase in the percent of B lymphocytes on the first day postoperative accompanied by a decrease in total lymphocytes and T lymphocytes.

Maisel et al. (1988) noted that lymphocytes from patients undergoing heart valve replacement had significant decrease in erythrocyte (E), erythrocyte amboceptor (EA), and erythrocyte amboceptor complement (EAC) rosettes and reduced phytohemagglutinin (PHA), pokeweed mitogen and MLC responses on the second day postoperative. These returned to normal one week after the operation.

The mechanism responsible for the decrease in circulating T lymphocytes following operation is still not completely defined.

Elevation of serum corticosteroids may cause decrease in circulating T-cells level, although this is usually mild or transient *(Frey et al., 1989)*.

On the other hand *(Marty et al., 1990)* found that serum cortisol levels were elevated following open heart surgery but there was lack of correlation between changes in serum cortisol and changes in lymphocyte number and function which suggested that serum cortisol is not an etiological factor in postoperative immunosuppression. Moreover, they noted the highest level of serum cortisol one week after operation at a time when all factors involved in lymphocyte function had returned to preoperative levels.

AIM OF THE WORK

This work is a trial to study the effect of cardiac operations on cell-mediated immunity and serum cortisol levels and the relationship between both of them after open heart surgery.

The aim of this study are:

1) To determine the changes of T-lymphocyte subpopulations following open heart surgery as parameters of cell-mediated immunity.
2) To detect changes of serum cortisol following open heart surgery.
3) To define the relationship between serum cortisol level and T-lymphocyte subpopulations as parameters of cell-mediated immunity.