



شبكة المعلومات الجامعية

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ





شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأفلام قد أعدت دون أية تغييرات



يجب أن

تحفظ هذه الأفلام بعيدا عن الغبار

في درجة حرارة من 15-25 مئوية ورطوبة نسبية من 20-40%

To be Kept away from Dust in Dry Cool place of
15-25- c and relative humidity 20-40%



شبكة المعلومات الجامعية التوثيق الالكتروني والميكرو فيلم

**PLASMA INTERLEUKIN-8 AND ENDOTHELIN-1
CONCENTRATIONS IN SYMPTOMATIC AND
ASYMPTOMATIC ASTHMATIC CHILDREN**

Thesis

Submitted for the degree of Ph. D. Childhood studies
Institute of postgraduate for Childhood studies
Ain Shams University

By

Amr Ibrahim Ali
M.B.B.CH, M.SC.

National Centre for Radiation Researchs and Technology

Under supervision of

Prof. Dr. Zinab Radwan

Professor of Pediatrics
Faculty of Medicine – Cairo University

zinab

Dr. Gamal Samy Ali

Assi. prof. In medical department
Institute of postgraduate for Childhood studies
Ain Shams University

Gam

Dr. Nessrin El-Abiad

Assistant prof. of Pediatrics
Faculty of Medicine – Cairo University

Nessrin

Dr. Mohamed Samy Soliman

Assistant prof. of Clinical Pathology
National Center for Radiation Researchs and Technology

Samy

2000

ACKNOWLEDGEMENT

I wish to express my deepest appreciation and sincerest gratitude to **Prof. Dr. Zinab Radwan**, professor of pediatrics, Cairo University, whose ideas brought forward this subject. Her extreme patience, meticulous supervision, precious advise gave me the valuable opportunity to benefit from her faithful guidance and constant support. I will always remember her unforgettable encouragement and kindness.

My deepest thanks goes to **Dr. Gamal Samy Ali**, assisstant prof. of pediatrics, Childhood Institute – Ain Shams University, for his great help and for offering me much of his time and effort.

I do feel greatly indebted to **Dr. Nessrin El-Abiad**, Assisstant prof. of pediatrics, Cairo University, who was very generous in offering me a lot of her valuable knowledge and effort.

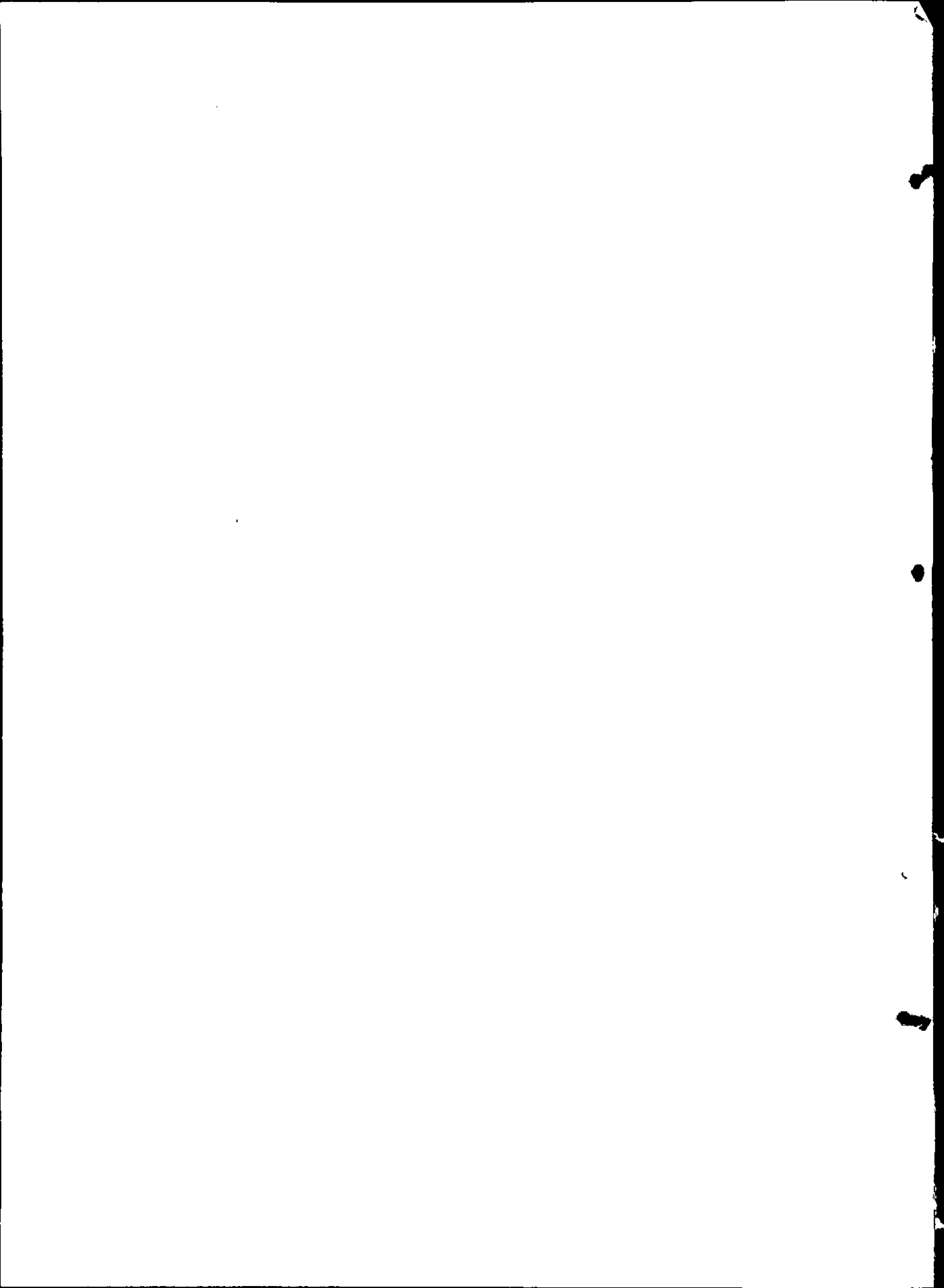
My sincere gratitude should be expressed to **Dr. Mohamed Samy Soliman**, Assisstant prof. of clinical pathology, National Centre for Radiation Researchs and Technology, for his kind guidance and supervision and for the unlimited time and effort he generously offered me.

Thank you all,
Amr Ibrahim Ali

ABSTRACT

Two asthmatic groups each included 20 patients, the asymptomatic group where patients were free of symptoms, the symptomatic group where patients were suffering from acute exacerbation of their asthma and both of asthmatic groups were subclassified into mild and moderate subgroups each of 10 patients according asthma severity. All subjects were subjected to clinical study, chest X-ray for subclassification of patients, peak expiratory flow rate (PEFR) recording for subclassification of patients, skin prick testing using common allergens (patients only) and laboratory investigations which included complete blood count (CBC) including absolute eosinophil count (AEC), urine and stool examination, total serum IgE level, plasma IL-8 level and plasma endothelin-1 level. There was no significant difference between the study groups as regards AEC. There was a highly significant elevation in serum IgE of the asthmatic groups in comparison to control group. There was a highly significant elevation in plasma endothelin-1 and plasma IL-8 levels of the symptomatic asthmatic subgroups in comparison to control group and asymptomatic asthmatic subgroups. In conclusion: despite this profile, a causal link between IL-8, ET-1 and asthma has not been definitively established, but surely, it is now clear that those mediators, their receptors, synthesis and degradation pathways offer potentially important therapeutic targets.

Keywords: Bronchial asthma, Interleukin-8, Endothelin-1, Immunoglobulin-E and Absolute eosinophilic count.



CONTENTS

| | |
|---|-----|
| I-INTRODUCTION AND AIM OF THE WORK..... | 1 |
| II-REVIEW OF LITERATURE..... | 3 |
| 1-ASTHMA..... | 3 |
| 2-INTERLEUKIN-8..... | 24 |
| 3-ENDOTHELIN-1..... | 45 |
| III-SUBJECTS AND METHODS..... | 67 |
| 1-SUBJECTS..... | 67 |
| 2-METHODS..... | 72 |
| IV-RESULTS..... | 82 |
| V-DISCUSSION..... | 104 |
| VI-CONCLUSION..... | 115 |
| VII-SUMMARY..... | 116 |
| VIII-REFERENCES..... | 120 |
| IX-APPENDIX. | |
| X-ARABIC SUMMARY. | |

LIST OF ABBREVIATIONS

| | |
|------------------|---|
| AEC | Absolute eosinophilic count. |
| Ala | Alanine. |
| Asp | Aspartate. |
| BAL | Bronchial fluid lavage. |
| β -TG | β -thromboglobulin. |
| Ca^{++} | Calcium ion. |
| cDNA | Recombinant DNA |
| C.H | Cat hair. |
| Con A | Concanavalin A. |
| CTAP-III | Connective tissue activating peptide III. |
| DMSO | Dimethyl sulphoxide. |
| dsRNA | Double-stranded RNA. |
| EASIA | Enzyme Amplified Sensitivity Immunoassay. |
| EDRF | Endothelium derived relaxing factor. |
| ET | Endothelin |
| FMLP | Formylmethionyl-leucyl-phenylalanine. |
| FMLP | Formylmethionyl peptides. |
| Frs | Feathers. |
| Glu | Glutamine. |
| GM-CSF | Granulocyte-Monocyte Colony Stimulating Factor. |
| Gss | Grass |
| GTP | Glutamine triphosphate. |
| H.D | House dust. |
| H.D.M | House dust mite. |
| HRP | Horseradish peroxidase. |

| | |
|----------|---|
| ICAM-1 | Interacellular adhesion molecule-1. |
| IFN | Interferon. |
| IgE | Immunoglobulin E. |
| IgG | Immunoglobulin G. |
| IL | Interleukin |
| Kd | Kilo dalton |
| LAI | Leukocyte adhesion inhibitor. |
| LAMMA | NG-monomethyl-L-arginine. |
| LA-PF4 | Low-affinity platelet factor-4. |
| LAR | Late asthmatic response. |
| LPS | Lipopolysaccharid. |
| LTC4 | Leukotrein-4 |
| MCAF | Macrophage chemoattractant and activating factor. |
| MEIA | Microparticle enzyme immunoassay. |
| MGSA | Melanoma growth-stimulatory activity. |
| MIP | Macrophage inflammatory protein. |
| MK | Milk. |
| M.M | Mixed moulds. |
| M.P | Mixed pollen. |
| mRNA | Messenger RNA |
| NAN | Nocturnal airway narrowing. |
| NAP-1 | Neutrophil-activating protein. |
| NK cells | Natural killer cells. |
| PAF | Platelet activating factor. |
| PBP | Platelet basic protein. |
| PDGF | Platelet derived growth factor. |
| PEFR | Peak expiratory flow rate. |
| PGD | Prostaglandin |
| PF4 | Platelet factor 4. |

| | |
|--------------|---------------------------------------|
| PHA | Phytohaemagglutinin. |
| PMA | Phorbol 12-myristate 13-acetate |
| ppET | Prepro-endothelin. |
| SEA | Staphylococcus enterotoxin A. |
| TGF- β | Transforming growth factor- β . |
| TNF | Tumour necrosis factor. |
| TPA | Tetradecanoylphorbol 13-acetate |
| VCAM-1 | Vascular adhesion molecule-1 |
| VIC | Vasoactive intestinal constrictor |
| WL | Wool. |

LIST OF TABLES

Page No.

| | |
|---|----|
| Table (1): Cellular sources of human IL-8..... | 26 |
| Table (2): Purification procedure for IL-8..... | 29 |
| Table (3) : Classification of asthma severity according National Asthma Education and Preven- tion Program, 1991..... | 69 |
| Table(4) : Estimation of severity of acute exacerbation of asthma according National Heart, Lung and Blood Institute, 1991..... | 70 |
| Table(5) : Predicted normal values for PEFR (L/min.). Ethnic difference negligible. (Hargreove et al., 1990)..... | 75 |
| Table(6): Comparison of age (years) between control and asymptomatic asthmatic groups..... | 83 |
| Table(7): Comparison of age (years) between control and symptomatic asthmatic groups..... | 84 |
| Table(8): Comparison of age (years) between asymptomatic and symptomatic asth- matic groups..... | 85 |

| | |
|---|----|
| Table(9): Comparison of AEC (cell/mm ³) between control and asymptomatic asthmatic groups..... | 87 |
| Table (10) : Comparison of AEC (cell/mm ³) between control and symptomatic asthmatic groups..... | 88 |
| Table (11) : Comparison of AEC (cell/mm ³) between asymptomatic and symptomatic asthmatic groups..... | 89 |
| Table (12) : Comparison of serum total IgE (IU/dl) between control and asymptomatic asthmatic groups..... | 91 |
| Table (13) : Comparison of serum total IgE (IU/dl) between control and symptomatic asthmatic groups..... | 92 |
| Table (14) : Comparison of age (years) between asymptomatic and symptomatic asthmatic groups..... | 93 |
| Table (15) : Comparison of serum endothelin-1 (pg/ml) between control and asymptomatic asthmatic groups..... | 95 |
| Table (16) : Comparison of serum endothelin-1 (pg/ml) between control and symptomatic asthmatic groups..... | 96 |