



شبكة المعلومات الجامعية

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ



شبكة المعلومات الجامعية
@ ASUNET



شبكة المعلومات الجامعية التوثيق الالكتروني والميكروفيلم



شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكرو فيلم

قسم

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



يجب أن

تحفظ هذه الأفلام بعيدا عن الغبار

في درجة حرارة من ١٥-٢٥ مئوية ورطوبة نسبية من ٢٠-٤٠%

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

بعض الوثائق الأصلية تالفة

بالرسالة صفحات لم ترد بالاصل

INTERLEUKIN 10 IN CHILDHOOD ASTHMA

THESIS

*Submitted In partial fulfilment of Master Degree in
PEDIATRICS*

By

Sherif Louis Rezk Allah Abd El-Nour
(M.B.B.CH)

SUPERVISORS



Prof.

Samia S. El-Hennawy
Prof. of Pediatrics ,
Benha Faculty of Medicine ,
Zagazig University

Prof.

Iman Abd El-Rehim M.
Prof . of Pediatrics ,
Benha Faculty of Medicine ,
Zagazig University

Dr.

***Usama Abou El-Fotouh El-
Feky***
Lecturer. of Pediatrics
Benha Faculty of Medicine ,
Zagazig University

Prof.

Ahmed M. El-Gazzar
Prof . of Microbiology
Benha Faculty of Medicine ,
Zagazig University



***FACULTY OF MEDICINE
ZAGAZIG UNIVERSITY***

2000

Acknowledgment

I fell always indebted to GOD the most kind and the most merciful .

*I wish to express my deepest gratitude to **Prof. Samia El-Hennawy Prof. of Pediatrics** , Benha Faculty of Medicine , Zagazig University, for giving me the privilege to work under her supervision, and for her generous advice and guidance through the accomplishment of this study.*

*I am also grateful to **Prof. Iman Abd El-Rehim Prof. of Pediatrics** , Benha Faculty of Medicine , Zagazig University for her helpful supervision, instructive guidance and valuable efforts to making work achievable .*

*I also wish to express my thanks to **Dr. Usama Abou El-Fotouh Lecturer of Pediatrics** Benha Faculty of Medicine , Zagazig University for his constant, support without which this work couldn't be fulfilled.*

*Thanks to **Dr. Ahmed El-Gazar Assistant Prof . of Microbiology** Benha Faculty of Medicine , Zagazig University for his cooperation and valuable advices .*

Thanks to patients and their parents for cooperation and your hope good health to all of them.

Contents

*- Introduction and aim of the work	1
* - Review of Lecture	
<u>I- Bronchial Ashma</u>	
Definitions of Asthma	3
Epidemiology	3
Types of Asthma	4
The risk factors of childhood asthma	5
Pathogenesis of asthma	13
Pathology of asthma	19
diagnosis of asthma	21
differential diagnosis of asthma	25
Complication of asthma	26
Cause of death from asthma	28
Managment of asthmatic child	29
New frontiers in asthma therapy	33
<u>II- Cytokines - IL-10</u>	
a) Cytokines :	36
Functions	37
Synthesis	39
Types	39
b) Interleukin - 10	
Introduction	43
IL - 10 Structure	44
Interleukin-10 Production Function-Regulation..	45
Interleukin - 10 in Bronchial Asthma	52
IL-10 and steroid therapy	56
Role of IL-10 in specific immuno therapy	57
*- Subject and Methods	60
*- Results	68
*- Discussion	87
* - Summary and Conclusion	99
*- Recommendations	101
*- References	102
*- Arabic Summary	121

List of Abbreviations

APC	: Antigen presenting cells
BALF	: Bronchoalveolar lavage fluid
CD	: Cluster differentiation antigen
CDNA	: Complementary deoxyribonucleic acid
CSIF	: Cytokine syntehsis inhibitory factor.
EBV	: Epstein-Barr virus
FEF	: Forced expiratory flow
FEF 25-75%	: Forced expiratory flow between 25% and 75% of vital capacity .
FEV	: Forced expiratory volume in the first second
FVC	: Forced vital capacity
G.CSF	: Gronulocyte-colony stimulating factor .
GM-CSF	: Granulocyte-monocyte colony stimulating factor
HLA	: Human leucocyte antigen
ICAM	: Intercellular adhesion molecule
IgE	: Immunioglobulin-E
IL	: Interleukin
INF γ	: Interferon gamma
Kd	: Kilodalton
LPS	: Lipopolysaccharide
LT	: Leukotreine
M.CSF	: Monocyte-colony stimulating factor .
MCP-1	: Monocyte chemoattractant protein-1
MCS	: Mast cells
MHC	: Major histocopatibility complex
MIP-1 α	: Macrophage inflammatory protein-1 α
mRNA	: Messenger ribonucleic acid
MW	: Molecular weight
NK	: Natural killer cells
PEFR	: Peak expiratory flow rate recording.
PFA	: Potentially fatal asthma

Pg/ML	Pico grame / milliliter
PMN	: Polymorphonuclear leukocytes
RANTES	: Regulated upon activation, normal T-expressed and persumbly secreted .
RSV	: Respiratory syncytial virus
SCF	: Stem cell factor
TCR	: T cell receptors
TGF	: Transforming growth factor
TH	: Helper T cell
TNF	: Tumour necrosis factor
VRI	: Viral respiratory infections

List of Tables

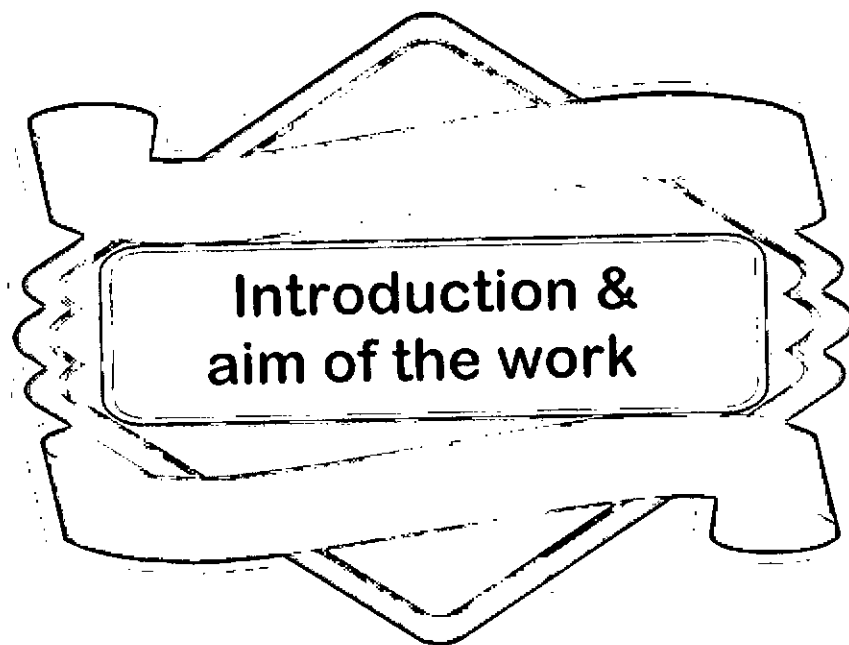
✿ Tables of review of literature are written in roman letters:-

Table (I)	Epithelial - derived cytokines	18
Table (II)	Laboratory tests in asthma	23
Table (III)	Cause of death from asthma	28
Table (IV)	Asthma medications by category	31
Table (V)	Stepwise approach for managing asthma : severity classification and management	32
Table (VI)	Characteristic properities of Interleukines	40
Table (1a)	Individual Clinical Data of Patients	71
Table (1b)	Individual Clinical and Laboratory Test Results of patients	73
Table (2)	Individual Clinical and Laboratory Data of the Controls	75
Table (3)	Some clinical data of asthmatic patients in comparison to control group	76
Table (4)	Distribution of the studied cases according to the age of onset of disease	76
Table (5)	Distribution of the studied cases according to diurnal variation of asthma symptoms	77
Table (6)	Distribution of the studied cases according to seasonal variation	77
Table (7)	Distribution of the studied cases according to complaint	77
Table (8)	Distribution of the studied cases according to frequency (number of attacks / year)	78
Table (9)	Distribution of the studied cases according to number of hospital admissions / year	78
Table (10)	Distribution of the studied cases according to results of skin prick testing	79

Table (11)	Comparison between PEFR results among cases during attack of asthma and after treatment (Litre/Minute)	79
Table (12)	PEFR in asthmatic patients (after ttt) compared to control group (Litre/Minute)	80
Table (13)	Comparison between cases and controls as regards serum level of IL10 (Pg/mL)	80
Table (14)	Correlation coefficients between IL-10 and other variables in studied cases	81

List of Figures

Fig. (I)	The epithelium produces cytokines that can recruit and activate inflammatory cells.	19
Fig. (II)	Normal and inflammatory airways	20
Fig. (III)	IL-10 Protein in BAL fluid	52
Fig. (IV)	IL-10 Production by PBMCs	53
Fig. (V)	Effect of anti IL-10 on spontaneous production IFN- γ by PBMCs	53
Fig. (1)	Sex Distribution among Cases and Controls	82
Fig. (2)	Age Distribution among Cases and Controls	83
Fig. (3)	Results of Skin Prick Testing in asthmatic patients	84
Fig. (4)	Range and mean levels of serum IL-10 in asthmatic and control group (Pg/mL)	85
Fig. (5)	Mean Serum IL-10 Level in the Studied Children (pg/mL)	86



INTRODUCTION :

Bronchial asthma is one of the most common pediatric chronic diseases that is responsible for significant morbidity, school absenteeism and mortality. (Mori et al, 1995). A recent comprehensive definition of asthma is that; A chronic inflammatory disorder of the airways in which many cells play a role. In susceptible individuals, this inflammation causes symptoms which are usually associated with widespread, variable airway obstruction that is often reversible either spontaneously or with treatment, and causes an increase of airway responsiveness to a variety of stimuli. (NHLBI, 1995). Interleukin-10 is an intrinsic antiinflammatory peptide, originally identified and cloned as cytokine synthesis inhibitory factor, which has major downregulatory influences on inflammation. (Borish et al, 1996). Human IL-10 is produced by both T_{H1} and T_{H2} lymphocytes however, blood monocytes and tissue macrophages may be its most important source. (Del Prete G, et al, 1993). It has effects on inhibition of interferon (IFN)- γ and IL-2 Production by T_{H1} lymphocytes, IL-10 acts to inhibit cytokine production by mononuclear phagocytes, natural killer cells, T_{H2} lymphocytes. (Hsu D-H, et al, 1992). Expression of IL-10 by antipresenting cells may have a role in lessening allergic inflammation through its ability to inhibit the synthesis of nonspecific proinflammatory cytokines such as IL-1, IL-6, tumor necrosis factor (TNF)- α and IFN- γ , as well as cytokines associated with allergic inflammation including IL-4 and IL-5. (Del Prete G, et al, 1993). It was speculated by Borish et al, 1996 that diminished IL-10 Production may contribute to development of asthma.