COMPLEMENT SYSTEM AND PHAGOCYTIC CELLS DISTURBANCES IN ATOPIC DISEASES OF CHILDHOOD

Essay

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BY

HESHAM MOHAMED YOUNES
M.B., B.Ch.

Supervised by

Prof.Dr.MOHAMED FOUAD BADRAWY
Professor of Pediatrics
Faculty of Medicine
Ain Shams University

Dr. MOHAMED FARID
Assistant Professor of
Pediatrics
Faculty of Medicine
Ain Shams University

Faculty of Medicine
Ain Shams University

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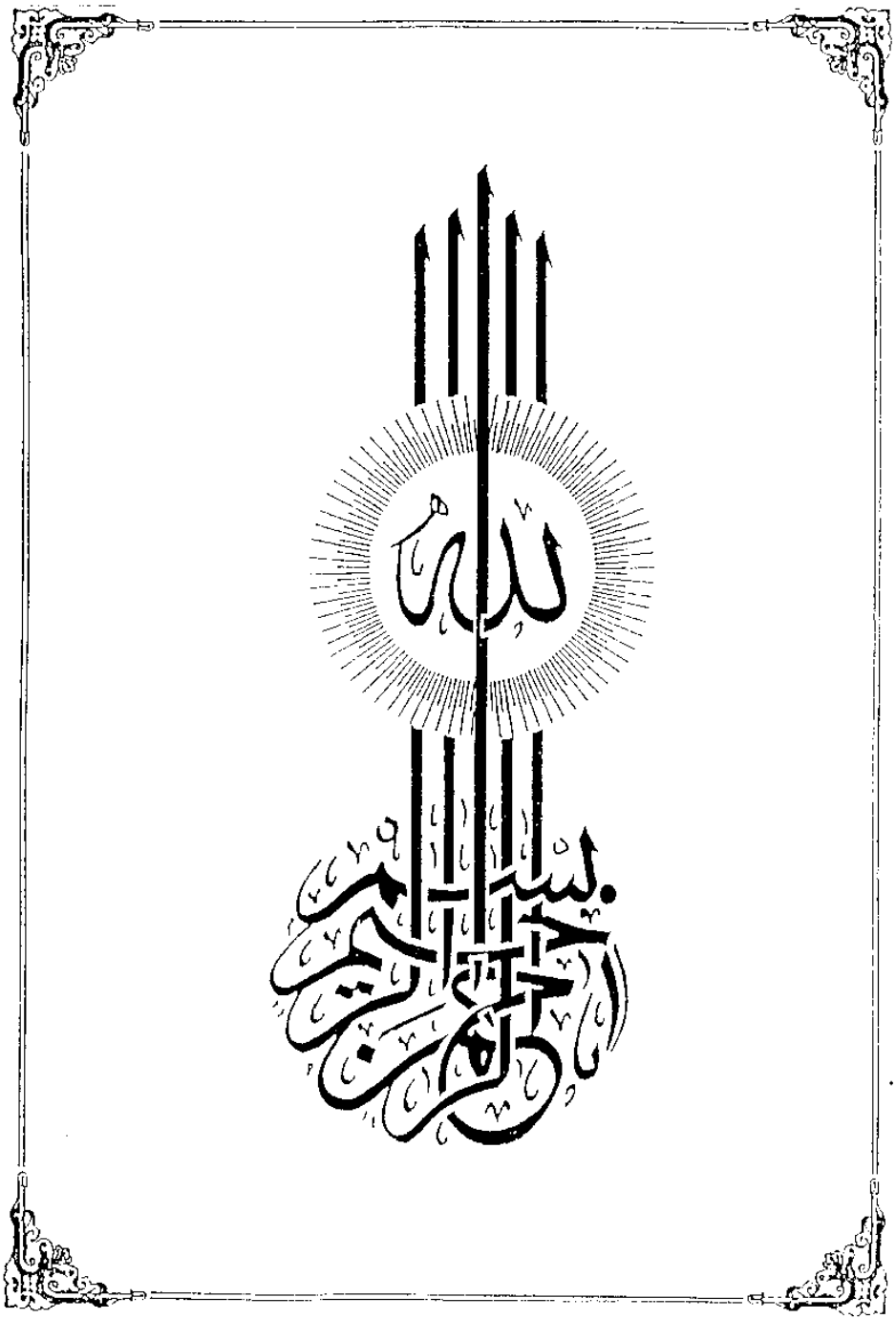

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LIST OF ABBREVIATIONS

ADMMC	:	Antibody-dependant monocyte-mediated cytotoxicity.
APC	:	Antigen processing cell.
BM	:	Bone marrow.
C	:	Complement system.
cAMP	:	Cyclic adenosine monophosphate.
CR3	:	Receptor or regulatory protein (foriC3b).
C1:INH	:	C1 - inhibitor.
DAF	:	Decay accerelating factor (cell surface protein)
E	:	Eosinophils
EAF	:	Eosinophil activating factor.
ECF-A	:	Eosinophil chemotactic factor of anaphylaxis.
ECP	:	Eosinophilic cationic protein.
EDF	:	Eosinophil differentiating factor.
Fab	:	Antigen binding fragment of immunoglobulins.
Fc	:	Crystallizable fragment of immunoglobulins.
HLA system	:	Histocompatibility complex.
H_2O_2	:	Hydrogen peroxide.
Ig	:	Immunoglobulin.
LFA-I	:	Cell surface protein related to CR3 and P150,95.
LIF	:	Leucocyte inhibitory factor.
LT	:	Leukotriens.
MBP	:	Major basic protein.
MOs	:	Monocytes.
MØ	:	Macrophages.

N	:	Neutrophils.
NCA-HMW	:	High molecular weight-neutrophil chemotactic activity.
"O_2^-"	:	Superoxide anion.
P	:	Properdin
PAF	:	Platelets activating factor.
P150,95	:	Receptor for iC3b
PG	:	Prostaglandines.
PMN	:	Polymorphonuclear leucocytes.
RAST	:	Radioallergosorbent test.
T_H	:	T helper cells.
T_S	:	T suppressor cells.
TNF	:	Tumour necrosis factor.

I -INTRODUCTION

INTRODUCTION

The use of the term atopy or atopic in designating allergic reaction implies a hereditary factor expressed as susceptibility to bronchial asthma, hay fever and eczematoid dermatitis in the families of affected individuals .

The complement system is one of several activation systems which have been identified in the blood of all higher vertebrates. The anomaly of the complement system most often in atopic children was an increase of C4. An increase of C3 was also observed in some cases together with the increase of C4. Only in some cases of atopic asthmas, a decrease of the serum concentration values of C3 was observed.

There are two types of professional phagocytes, the polymorphonuclear leucocytes and mononuclear phagocytes. Surface receptors of polymorphonuclear leucocytes and monocytes for the crystallizable fragment "Fc" of immunoglobulins and complement were found to decrease significantly in asthmatic children than normal .

Neutrophil chemotaxis was found to be depressed in some children with cow's milk protein intolerance and in others with hay fever.

The aim of this essay is to outline the changes in the complement system and phagocytic cells in childhood atopy like bronchial asthma, hay fever, atopic dermatitis and gastrointestinal allergy to be able to understand the consequences of their disturbances on the course of illness.

II.-CHILDHOOD ATOPY

CHILDHOOD ATOPY

When an adaptive immune response occurs in an exaggerated or inappropriate form, causing tissue damage, the term hypersensitivity is applied . Hypersensisitivity is a characteristic of the individual and is manifested on second contact with a particular antigen. Coombs and Gell (1963) have described four types of hypersensitivity reaction (Type I,II,III and IV) but in practice, these types do not necessarily occure in isolation from each other . The first three types are antibody mediated, and the fourth is mediated primarily by T cells and macrophages (Roitt et al. 1985).

Type I.or immediate hypersensitivity occurs when an IgE response is directed against innocuous antigens,such as pollen, and the resulting release of pharmacological mediators, such as histamine, by IgE sensitized mast cells. produce an acute inflammatory reaction with symptoms such as asthma or rhinitis.

Type II. or antibody dependant cytotoxic hypersensitivity occurs when antibody binds to antigen on host cells leading to phagocytosis or complement mediated lysis.

Type III. or immune complex mediated hypersensitivity develops when complexes are formed in large quantities or

can not be cleared adequetaly by the reticuloendothelial system, leading to serum sickness type reaction.

Type IV. or delayed type hypersensitivity is most seriously manifested when antigen, for example tubercle bacilli trapped in macrophages, can't be cleared. T lymphocytes are then stimulated to elaborate lymphokines which mediate a range of inflammatory responses (Roitt et al., 1985).

The term atopy was originally described by Coca and Cooke (1923). It describes the clinical features of type I hypersensitivity, which includes bronchial asthma, eczema hay fever, urticaria and rarely gastrointestinal allergy, in subjects with a family history of similar complaints and showing immediate wheel and flare skin reactions to common inhalent allergens (Roitt et al., 1985).

The first description of the mechanism of the allergic reactions was by Prausnitz and Kustner (1921) who showed that a serum factor (termed reagin) could mediate the reaction on passive transfer to the skin of a normal subject. Some years later Ishizaka and his colleagues showed that this "atopic reagin" was a new class of Immunoglobulins-Immunoglobulin E (IgE). So these reactions are dependent on the specific triggering of IgE - sensitized mast cell by antigen, resulting in the release of pharmacological mediators of inflammations. (Roitt et al., 1985).

When cell-bound IgE antibody is complexed with allergen, a series of intracellular reactions (resulting in lowering of cyclic AMP) culminates in a release of mediators of anaphylaxis, such as histamine, slow reactive substance of anaphylaxis, eosinophilic chemotactic factor of anaphylaxis and platelet activating factor. However one molecule of IgE bound to a cell is not sufficient to produce mediator release. At least two adjacent IgE molecules of identical specificity must be bridged or cross linked by di-or polyvalent antigen to one Fab region of each IgE molecule (Fig. 1) (Geha et al., 1987). This specific union of allergen with homocytotrophic IgE antibody induces conformational changes in the Fc receptor molecules of the mediator cells which alter their relationships and bring the receptor molecules into close proximity. These changes, in turn, initiate a complex series of enzymatic reactions at the cells membrane and lead to a decrease in intracellular c.AMP and enhanced mediator release.

Receptor bridging by IgE antibodies activates methyltransferases and induces the stimulation of phospholipid methylation in the plasma membrane. Phospholipid methylation is followed by calcium influx and mediator release . Intracellular calcium influx into mast cell or basophil is essential in the initial cell activation prior to mediator release (Fadal , 1985).