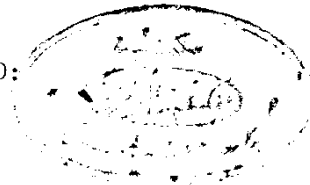
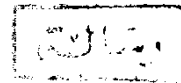


AN ESSAY
ON
RECENT ADVANCES IN AUTOIMMUNE
DISEASES IN INFANCY AND CHILDHOOD:
DIAGNOSIS AND MANAGEMENT



SUBMITTED FOR PARTIAL FULFILMENT
OF THE DEGREE OF M.S. IN
PEDIATRICS



PRESENTED BY:
HISHAM A.S. AWAD

20934

618-720079
H.A

UNDER SUPERVISION OF

Prof. DR. ABDEL KHALEK KHATTAB - Prof. DR. MAHMOUD ESSAWY
Prof. OF PEDIATRICS Prof. OF PEDIATRICS

FACULTY OF MEDICINE
AIN SHAMS UNIVERSITY

CAIRO

1985

Handwritten notes and signatures at the bottom right, including a large signature and the date 1987/4/20.

A C K K N O W L E D G M E N T

I would like to express my deep gratitude and appreciation to my eminent Professor Dr. Abdel Khalek Khattab, Professor of Pediatrics, Faculty of Medicine, Ain Shams University; for giving me the privilege to work under his supervision for his advice~~s~~, his patience and his guidance throughout the whole work.

I am also greatly indebted to my Professor Dr. Mahmoud Essawy Professor of Pediatrics, Faculty of Medicine, Ain Shams University for his great encouragement and support.

Again I am sincerely grateful to Dr. Mohamed Salah El Kholy for his helps and advices.

Lastly I owe my thanks and gratitude to all those who have participated in one way or another to let this work come to such a final form.



TABLE OF CONTENTS

=====

	<u>PAGE</u>
* INTRODUCTION.....	1
* AIM OF THE ESSAY.....	2
* REVIEW OF LITERATURE.....	2
- <u>Definition of autoimmune diseases</u>	2
- <u>Mechanism of self tolerance</u>	3
A/ Central tolerance.....	3
B/ Peripheral Tolerance.....	5
- <u>Theories and pathogenesis of autoimmune diseases</u>	8
A/ Immunological factors.....	9
B/ Genetic factors.....	21
C/ Accelerating factors.....	24
- <u>Classification of autoimmune diseases</u>	26
- <u>Mechanism of tissue injury in autoimmune diseases</u> ..	28
- <u>Diagnosis of autoimmune diseases</u>	32
I. Antibody detection in different diseases.....	34
Miscellaneous autoantibodies & their detection.	65
II. Classical tests of appraisal of disease activity	70
III. Clinical detection of immune complexes.....	76
Laboratory techniques of immunopathologic	81
assessment.....	81
- <u>Approach to the management of autoimmune disease</u>	87
- <u>Conventional drugs used in therapy of rheumatic</u>	
<u>diseases</u>	97
I. Salicylates.....	97
II. Non steroidal anti-inflammatory drugs.....	100
III. Slow acting remittive agents.....	103

./...

TABLE OF CONTENTS (CONT'D)

	<u>PAGE</u>
- <u>New methods of using old drugs</u>	104
I. Corticosteroids	104
A/ Alternate day therapy.....	105
B/ Short term high dose or pulse therapy.....	110
II. Cytotoxic drug therapy.....	113
- <u>Non conventional methods of treating autoimmune diseases</u>	117
I. Thymopoietin pentapeptide.....	118
II. Cyclosporin A	121
III. Plasma exchange & plasmapheresis.....	133
IV. Levamisole.....	166
V. Intravenous immunoglobulins.....	177

6/10/10 A.

INTRODUCTION

Normally, the human immune system is so regulated internally that vigorous immune responses are mounted against foreign antigens, but immune reactions directed to self antigens are kept under strict control by what is called "self-tolerance". When these controls are rendered ineffective by disease, the response may be directed against the body's own proteins or tissues.

These autoimmune reactions result in inflammation, causing tissue damage. The variety of symptoms seen in patients with autoimmune diseases reflects the variety of forms of the immune response, with the site of organ damage depending on the location of the immune reaction. The term autoimmune disease is generally applied to any pathologic condition that is associated with demonstrable auto-antibodies or cytotoxic cells directed to self-antigens whether or not this "autoimmune" response is specifically determined to be the cause of the disease (Ashman, 1981).

Most autoantibodies develop without apparent cause, fluctuate inexplicably, and either disappear enigmatically or persist indefinitely. A single mechanism could hardly explain these phenomena, nor could a single aberration account for the many varieties of autoimmunization (Shoenfeld, 1984).



AIM OF THE ESSAY

The field of autoimmunity is a steadily expanding one. An autoimmune aetiology is being implicated in an increasing list of diseases.

This essay aims at throwing light on some aspects in autoimmunity, chiefly new methods to diagnose these diseases as well as new approaches to their management.

Also, some future hopeful issues in the management are mentioned.

DEFINITION

Autoimmune diseases are usually defined as states in which circulating antibodies are formed, not against a foreign antigen such as part of bacterium or virus, but against some normal component; this is often part of the surface of a particular cell type, such as the TSH receptor on thyroid cells in autoimmune thyroiditis or the acetylcholine receptor on cholinergic neurons in myasthenia gravis.

REVIEW OF LITERATURE

MECHANISMS OF SELF-TOLERANCE

If cells recognizing self-antigens are present in everyone, why does the normal immune system seem outwardly tolerant of self? A state of apparent unresponsiveness might be achieved either by 'silencing' all self-reactive lymphocytes (Central tolerance) or by inhibiting the effects of these cells (Peripheral tolerance). (Bowry 1980).

A. CENTRAL TOLERANCE

In central tolerance, no antibody is produced after antigenic challenge because the relevant B lymphocytes have been inactivated, a phenomenon termed 'clonal anergy'.

1- Clonal anergy or clonal abortion

A clone is a family of lymphocytes with identical receptors for antigen. Virgin clones of lymphocytes circulate until they meet their specific antigens; then they transform and divide into many daughter cells of the same specificity. The specificity of an antibody is identical to its antigen-combining site and determined solely by structural genes beyond the influence of antigen.

It is believed that during differentiation from stem cells into antibody forming cells, immature B lymphocytes go through a phase when contact with either self or foreign antigens induces tolerance rather than immunity (Teatle and Mackay, 1979). In some way, the cell receives a tolerizing signal which produce functional inactivation without cell death. Since B cells have a rapid turnover and are produced throughout life, this form of tolerance induction must be a continuous and active process (Holborow, 1981).

2- Antigen blockade

Central tolerance can result also from antigen binding in circumstances which favour cell inactivation rather than cell triggering. For example, certain multivalent antigens with repeating regularly spaced determinants can immobilize surface receptors and 'freeze' the cell membrane, while monovalent antigens may saturate the cell's antigen receptors without affecting the cross-linkage needed to activate the cell. (Theofilopoulos & Dixon, 1982).

B. PERIPHERAL TOLERANCE

The immune system has evolved complex ways of preventing an excessive response to antigen stimulation. In peripheral tolerance, antigen-reactive lymphocytes are continually and actively inhibited by suppressor T lymphocytes, anti-idiotypic antibodies or immune complexes.