THE SIGNIFICANCE OF SPECIFIC FOOD ANTIBODIES AND FOOD ELIMINATION-CHALLENGES IN RHEUMATOID ARTHRITIS

THESIS

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The M.D. Degree of Internal Medicine

By

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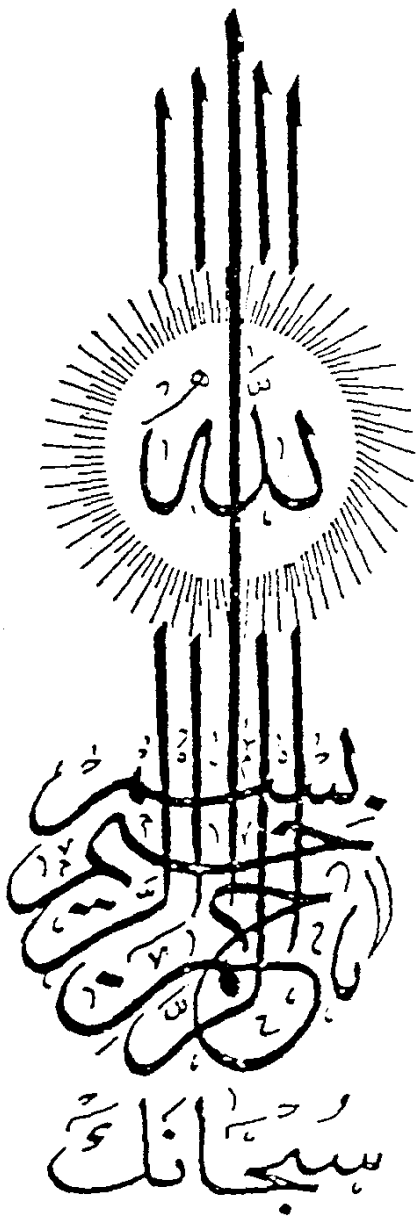

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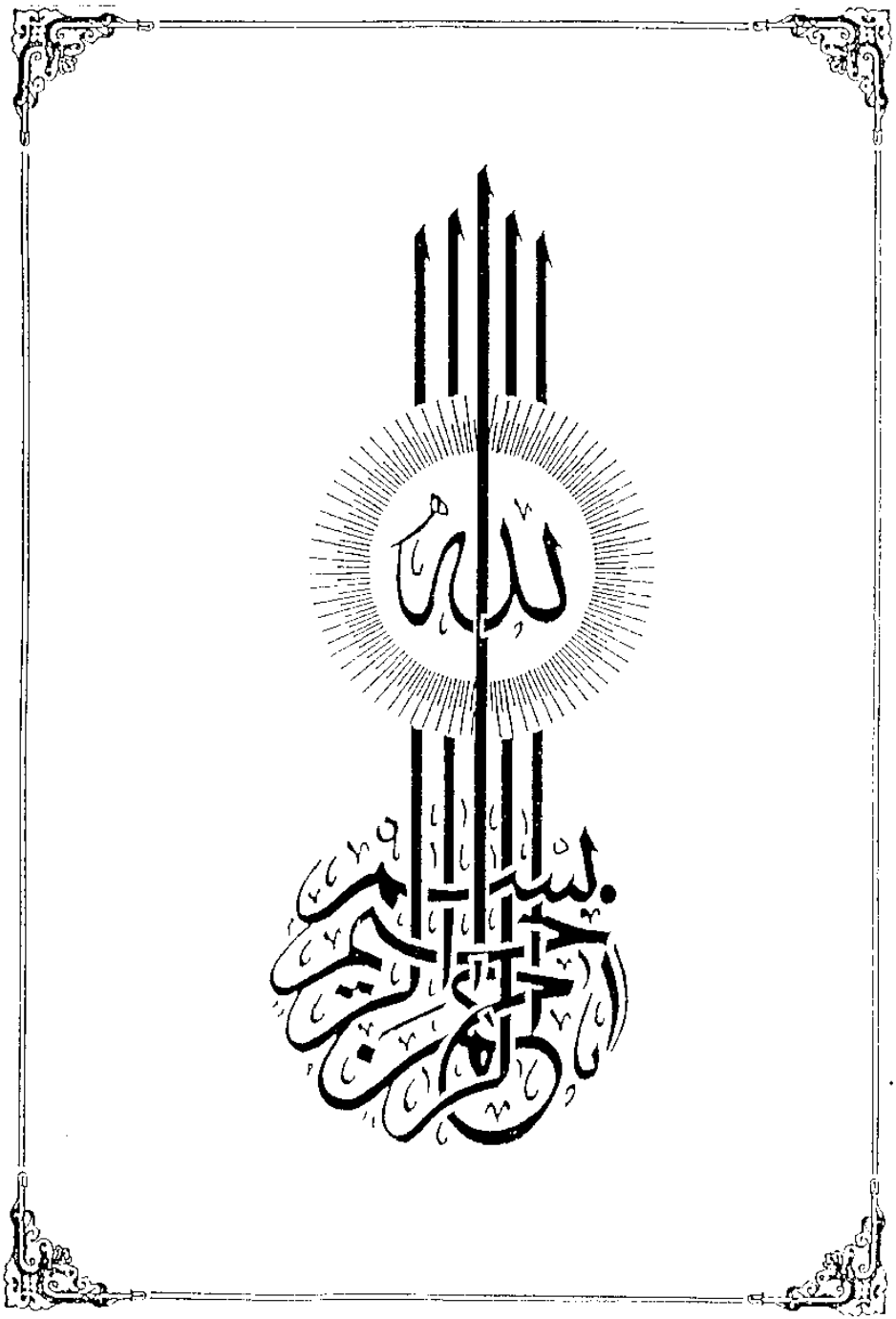

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DEDICATED TO MY SON

" Mahmoud "

ABBREVIATIONS

- A.Ch. = After Challenge.
- A.E. = After elimination.
- A.I. = Articular index.
- ANA = Antinuclear antibody.
- ARA = American Rheumatism Association.
- B.L. = Base line.
- CICs = Circulating immune complexes.
- C-RP = C-reactive Protein.
- CT = Connective tissue.
- ELISA = Enzyme linked immune sorbent assay.
- ESR = Erythrocyte Sedimentation Rate.
- 5-HT = 5-hydroxy tryptamine (serotonine).
- GIT = Gastrointestinal tract.
- Gr. = Group.
- GS = Grip Strength.
- Hb% = Haemoglobin percent.
- IDA = Index of disease activity.
- Ig = Immunoglobulin.
- J. = Joint.
- J-RA = Juvenile Rheumatoid Arthritis.
- MAO = Monoamine oxidase.
- MCP = Metacarpophalangeal Joints.
- MDGA = Mean Disease Grading Activity.
- MHC = Major histo-compatibility complex.
- Mid.Tar. = Mid-tarsal Joint.
- MS = Morning Stiffness.
- MTP = Metatarsophalangeal Joints.
- NSAID = Nonsteroidal Anti-inflammatory Drugs.
- PCM = Protein calorie malnutrition.
- PIP = Proximal Interphalangeal.
- PS = Pain scale.
- RA = Rheumatoid Arthritis.
- RAST = Radio allergo Sorbent test.
- RF = Rheumatoid Factors.
- Tal.Cal. = Talo-calcaneal Joint.
- TIP = Terminal Interphalangeal.

CONTENTS

INTRODUCTION

Suggestive but largely unproven observations have associated rheumatoid arthritis (RA) with environmental antigens including foods. Orthodox medical opinion however tends to ignore the subject, but interesting results from recent studies suggest that further investigations would now be appropriate.

It is possible that foods which consist of many antigens can alter immunological functions. It would seem logical particularly in view of uncertainty about efficacy and safety of the various drugs used in the management of RA - let away the largely unknown etiology of the disease - to determine scientifically whether dietary manipulation has any value in the management of the disease.

The data that accumulated recently about the association of food with RA is already very interesting. Intestinal mucosal biopsy revealed subtotal villous atrophy of the small intestine; ***(Siurala et al., 1965 and Soliman et al., 1991).*** One possible sequence of events is excessive intestinal absorption of antigens such as food; ***(Paganelli et al., 1981)***, or bacteria; ***(Bjarnason et al., 1984)*** with joint inflammation and damage due to immune complex mechanism in synovium. Support for this theory comes from

study of patients whose joint symptoms improved on diet elimination; *(Hicklin et al., 1980 and Wraith, 1982)*, and worsened on diet reconsumption *(Parke and Hughes, 1981 and Little et al., 1983)*.

Even in experimental models, *Coombs and Oldham, (1981)* found that animals fed on cow's milk developed arthritis.

Increase in circulating immune complexes (CICs) and the presence of complexes containing IgE with positive RAST (Radio Allergo Sorbent Test) to foods is reported and correlated with waxing and waning of symptoms of RA. Also, IgE and IgM anti-IgG antibodies are present in the sera of some patients with RA *(Williams, 1981 and Corman and Panush, 1985)*. Mean-while, juvenile RA. (J-RA) due to milk allergy has been documented by *Hill, (1984) and Ranter et al. (1985)*.

AIM OF THE WORK

The possibility is therefore real that at least a subgroup of RA patients have an external dietetic exacerbating cause. The present thesis has been devoted to explore and document this possibility.

RHEUMATOID ARTHRITIS

(Etiopathogeneses)

RHEUMATOID ARTHRITIS (RA)
(ETIOPATHOGENESIS)

Definition:

RA is a chronic systemic and articular inflammatory disorder of unknown etiology, it has a world-wide distribution, affecting about 2-3% of the population and involves all racial and ethnic groups. Women are affected two to three times more often than men. The disease occurs at any age and generally increases in incidence with advancing years. The peak incidence in women is between the fourth and sixth decades *(Panush, 1979 and Kay and Punchak, 1988).*

RA can also be defined as a chronic polyarthritis affecting mainly the peripheral joints, and runs a prolonged course with remissions and exacerbations accompanied in some cases by general systemic disturbances. It is characterized by chronic proliferative and inflammatory reactions in synovial membrane and periarticular tissues, with subchondrial osteoporosis, erosion and destruction of the joint cartilage, associated with wasting of the related muscles, giving rise to typical joint deformities and radiological abnormalities *(Zvaifler, 1988).*

Synovial inflammation occurs with proliferation of the living cells, many of which become laden with hydrolytic enzymes. Masses of inflamed and hypertrophied tissues (pannus) extend into and erode the articular cartilages especially at their margin and weaken or destroy the soft tissues as ligaments and tendons. Another less common feature is the rheumatoid granuloma or nodule which is most frequently situated in the subcutaneous tissues adjacent to the joint, but may also occur in the synovial membrane, or in the viscera. These granulomas are responsible for the extra-articular manifestations of RA ***(Stevens, 1976).***

* Extra-articular manifestations of RA:-

Organ lesion	Manifestations
. Skin	-Hyperhidrosis of extremities -Palmer erythema -Subcutaneous nodules
.Muscle	-Wasting -Myopathy
.Nerve	-Rheumatoid neuropathy
.Tendon	-Thickening, degeneration & fibrosis
.Vascular	-Vasculitis, thrombosis of digital pulp. -Raynaud's phenomenon
.Reticuloendothelial	-Lymphadenopathy -Splenomegaly
.Eye	-Episcleritis -Keratoconjunctivitis sicca -Iritis
.Cardiac	-Pericarditis
.Respiratory	-Pleural effusion -Isolated rheumatoid nodules in lungs -Rheumatoid pneumoconiosis (Caplan's syndrome) -Fibrosing alveolitis -Pulmonary vasculitis
.Blood	-Anemia of chronic infection -Hyperviscosity -Raised ESR in active stages -Leucopenia
.General	-Fever -Weight loss -Fatigue -Oedema of legs

(Hurd, 1979)

DIAGNOSTIC CRITERIA AND EXCLUSIONS

American Rheumatism Association (ARA) Criteria for the diagnosis of RA:

- Eleven criteria are available for three different degrees of certainty of diagnosis:
    * Classic RA:- seven criteria or more are needed.
    * Definite RA:- five or six criteria are needed.
    * Probable RA:- three or four criteria are needed.
- To meet criteria 1 to 5, symptoms or signs must be present for at least 6 weeks.
- Criteria from 2 to 6 must be observed by the physician.

Criteria:

1- Morning stiffness:
   This symptom is very useful as an indicator of inflammation; while its absence in a chronically painful joint is a good evidence that synovial inflammation is minimal or absent.
2- Pain on motion or tenderness in at least one joint.
3- Swelling of one joint, representing soft tissue or fluid.
4- Swelling of at least another joint (soft tissue or fluid) with an interval free of symptoms no longer than 3 months.
5- Symmetrical joint swelling (simultaneous involvement of the same joint, right and left). Terminal interphalangeal

joints (TIP) are rarely involved in RA and therefore are not acceptable for this or other criteria.

6- Subcutaneous nodules over boney prominences, extensor surfaces or near joints.

7- Typical radiographic changes which must include demineralization in periarticular bone as an index of inflammation; degenerative changes do not exclude diagnosis of RA.

8- Positive test for rheumatoid factors (RFs) in serum.

9- Synovial fluid; a poor mucin clot formation on adding synovial fluid to dilute acetic fluid.

10- Synovial histopathology consistent with RA:

a- Marked villous hypertrophy.

b- Proliferation of superficial synovial cells.

c- Lymphocyte/plasma cell infiltration in subsynovium.

d- Fibrin deposition within or upon microvilli.

e- Foci of cell necrosis.

11- Characteristic histopathology of rheumatoid nodules.

(Ropes et al., 1958)

Exclusions (differential diagnosis):

ARA "exclusions" (any one of which excludes diagnosis of RA) is a convenient list of conditions which may be confused with the disease:

8- Tuberculous arthritis. Often confused with monoarticular RA. Synovial fluid culture only occasionally positive and diagnosis usually rests on synovial biopsy.

9- Reiter's syndrome. Presence or history of urethritis and conjunctivitis.

10- Hypertrophic osteoarthropathy. Wrists and ankles are involved, radiography shows periosteal reaction.

11- Shoulder-hand syndrome (form of algodystrophy). Swollen, painful hand resembles RA but frozen shoulder occurs at the same time with a lack of constitutional symptoms and normal ESR.

12- Neurogenic arthropathy. Characteristic radiological changes and associated neurological signs.

13- Ochronotic arthropathy. Homogentisic acid in urine detected on alkalinization.

14- Sarcoid arthritis. Sarcoid involvement of joints (rare) may resemble RA but other features of sarcoidosis will be present. Positive Kveim test and synovial biopsy. Erythema nodosum and arthritis, associated with pulmonary sarcoid (hilar lymphadenopathy), usually involves lower-limb large joints.

15- Myeloma. Increased plasma cells in the bone marrow, paraprotein or abnormal immunoglobulin present.

16- Arthritis with erythema nodosum. Usually transient, affecting joints of lower limb.