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THE ASSESSMENT OF EFFICACY OF PIRPROFEN IN RHEUMATOID ARTHRITIS

Thesis

Submitted for Partial Fulfillment of
Master Degree of *General Medicine*

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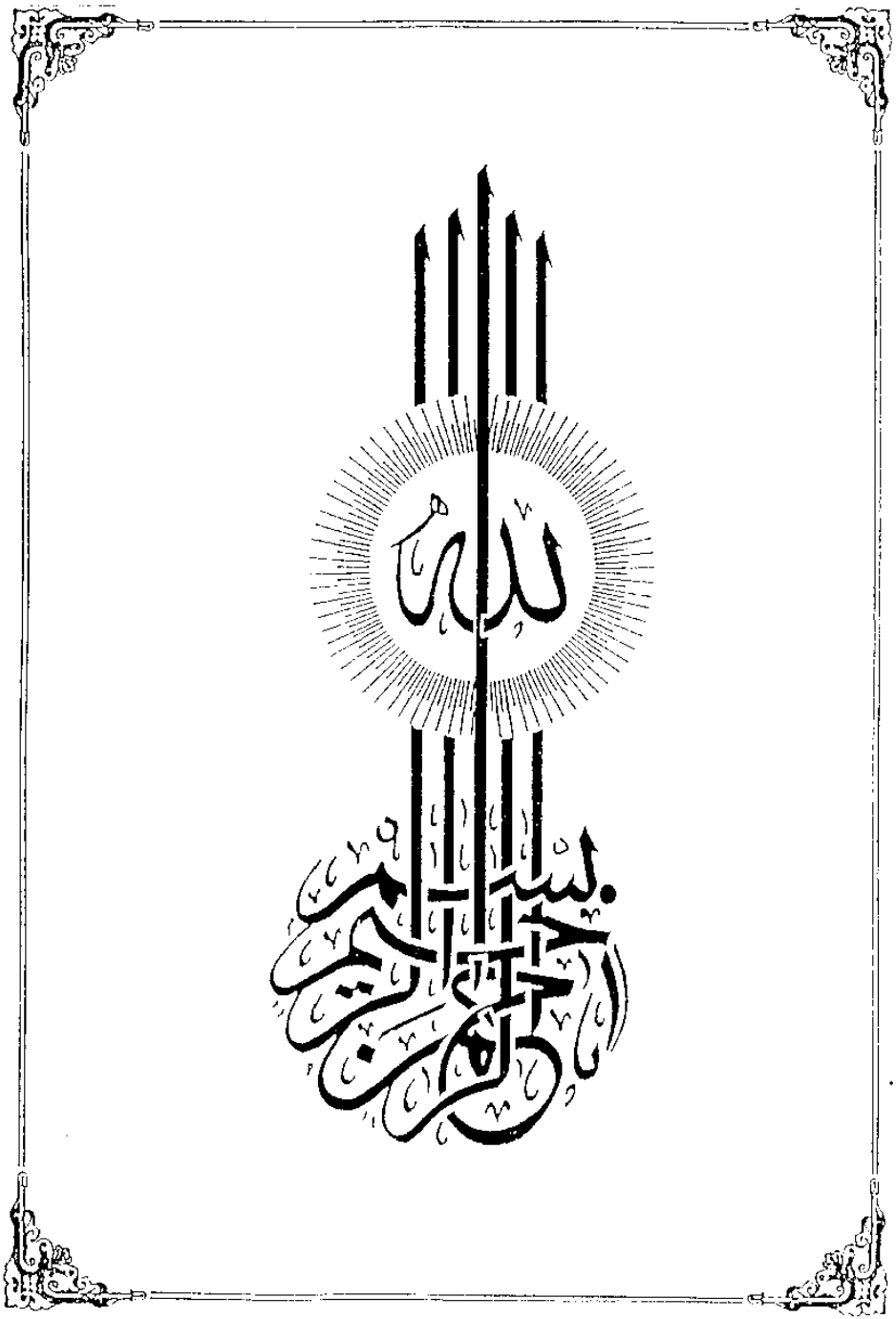

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To My Wife

and To My Daughter

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ABBREVIATIONS

A.R.A.	*American Rheumatism Association.*
CRP	*C-Reactive Protein.*
EBV	*Epstein-Barr Virus.*
ESR	*Erythrocyte Sedimentation Rate.*
NSAID	*Non-Steroidal Anit-Inflammatory Drug.*
PIP	*Proximal Interphalangeal.*
RA	*Rheumatoid Arthritis.*
RF	*Rheumatoid Factor.*

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INTRODUCTION

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INTRODUCTION

Rheumatoid arthritis (RA) is a symmetrical peripheral subacute or chronic non-suppurative inflammatory polyarthritis of unknown cause, characterised by inflammation of the synovium, which leads to destructive joint changes. Although arthritis is the most prominant manifestation, many other systems may be involved, so that it can be more correctely called rheumatoid disease *(Mason, 1979)*. It is a very common disease which occurs in 3% of the adult population *(Golding, 1982) (A)*.

Articular manifestation is sometimes remitting but if continued, usually results in progressive joint destruction and deformity, leading to variable degrees of incapacitation *(Ehrlich, 1981)*.

The aetiology of RA is still unknown many theories have been proposed. Immunological reactions appear to play a major role in the prepetuation of rheumatoid inflammation. Extra-articular manifestation are once, thought to be complication of RA, they are now recognized as integral parts of the disease and serve to emphasize its' systemic nature *(Rodman, and Schumacher, 1983)*.

The clinical manifestation, patterns of involvement as well as the prevalence of RA varies from place to place. However, there is no relationship between climatic conditions and sedimentations rate or level of C-reactive

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protein *(Latman, 1980)*. In Egypt, the manifestations of RA are milder than seen in western parts of the world with less systemic involvement *(El-Badawy, 1979)*.

Many drugs are used in the treatment of RA. Recently, pirprofen is introduced as one of propionic acid derivaties, non-steroidal anti-inflammatory drug (NSAID). The aim of this work is to study the of efficacy of pirprofen in the treatment of RA in thirty patients. The drug is given to the patients for four weeks.

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REVIEW OF LITERATURE

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AETIOLOGY AND PATHOGENESIS OF RHEUMATOID ARTHRITIS

The basis of pathogenesis of RA is an inflammatory response involving the immune system. RA is considered as an auto-immune disease. The demonstration of antibodies against autologus immunoglobulin G, nucleoprotein and collagen in serum and synovial fluids of patients with RA suggests an impairment of discrimination between self and non-self in this disease *(Zavaifler, 1979)*.

Immunogenetic Factors:

Individuals with HLA-DW4 and DR4 antigens are at increased risk of developing RA, whereas HLA-DR2 subjects have a decreased relative risk *(Young et al, 1984)*.

There is a possibility that HLA itself is a recepter for some external agent, such as a virus or toxin. HLA may mimic to a new antigen by virtue of an autologus cell surface component *(Stastny, 1978)*. The presence of HLADR-W4 was almost exclusively associated with more severe disease *(Roitt et al, 1978)*.

Familial aggregation of the disease have been observed. The prevalence in the first degree relatives of such patients being three times greater than in normal controls *(Mason, 1979)*.

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Infective Theory of RA:

There is no conclusive evidence linking diphteroids or mycoplasma to the disease *(Mackay et al, 1983)*. A possible evidence of Epstein-Barr Virus (EBV) role for viral aetiology of RA was postulated *(Parson et al, 1973)*. Several factors argue against the role of EBV in RA; patients do not all secreat virus and many people are infected with the virus without developing arthritis *(Decker et al, 1984)*.

Immunopathology of RA:

The hypothesis most widely accepted propose that RA results from abnormal immunological response to an unidentified triggering agent (possibly a virus) in a genetically susceptiable individual. Humoral and cell mediated mechanisms are both involved *(Edmonds, 1985)*.

Rheumatoid Factors (RA):

Rheumatoid factors (RF) are immunoglobulin with antibody specificity directed against sites on the Fc portion of the heavy chain of IgG, for this reason, they are also termed antiglobulins. Immunoglobulins with RF may belong to IgM, IgG and IgA classes.

IgM RF is capable of fixing complement and facilitates the phagocytosis of immune complexes by neutrophils in the synovial fluid. IgG RF may have a more significant role in immune complex activity within the joint *(Edmonds, 1985)*.

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High serum IgE RF levels were found in patients with RA, having significant extra-articular symptoms *(Mizushima et al, 1984)*.

Immune Complex:

Cirulating immune complexes are present in both blood and synovial fluid of patients with RA *(Reeback et al, 1985)*. Evidence of complement activation and consumption in the synovial fluid and the by products attract neutrophils which release damaging lysosomal enzymes following the ingestion of immune complexes *(Edmonds, 1985)*.

Abnormal Cell Mediated Immunity:

In the absence of effecient suppressor-T-cells, stimulation of T-lymphocytes of the inducer type may lead to activation of B-lymphocytes and immunoglobulin synthesis *(Janassy et al, 1980)*.

Epidemology:

Rheumatoid arthritis occurs more commonly in females. Three out of four cases of RA occur in women. The sex-related host factors may play an important role in determining the onset and severity of RA. Males may acquire a relative protective factor at adolescence which may be lost in older ages *(Alfonse et al, 1979)*. *Linos et al (1980)* noticed a significant fall in the rate of RA affecting females using oral contraceptives.

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The commonest incidence of RA occurs in age group of 35-45 years *(Melvin, 1983) (A)*. However, the disorder may begin at any time of life *(Williams, 1979)*.

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