Value of Tissue Typing in Pulmonary Affection in Rheumatoid Arthritis

THESIS

Submitted In Partial Fulfilment of the Requirements for M.D. in Physical Medicine

BY

Yasser Mahrous Abdel Halim El-Miedany
M.B., B.Ch., M.Sc., Physical Medicine
Faculty of Medicine, Ain Shams University

UNDER SUPERVISION OF

Prof.
Nadia Abdel Salam El-Kadery
Prof. of Physical Medicine
Ain Shams University

Prof.
Rasha Khalil
Prof. of Microbiology and Immunity
Ain Shams University

Prof.
Mohammed Gamal El-Din Zaki
Prof. of Physical Medicine
Ain Shams University

Dr.
Mohammed Sadek El-Beblawy
Senior Consultant of Chest Diseases
Air Forces Hospital

Dr. Nora Salwa Saad Allah Haroun
Lecturer of Physical Medicine
Ain Shams University

1993

ACKNOWLEDGEMENT

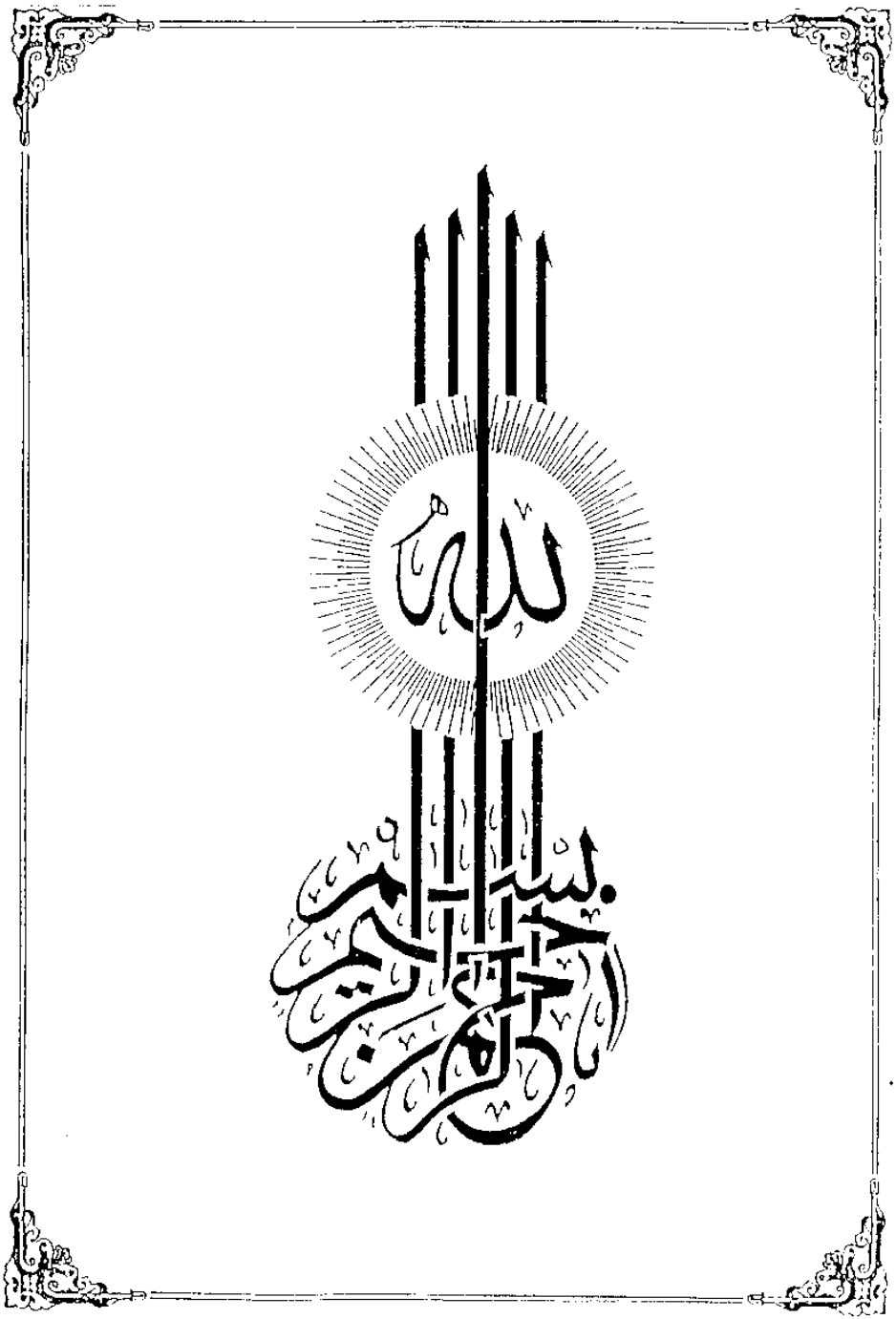
Thanks to God who granted me the ability to perform this thesis and for the helpful opportunities He has granted me through my sincere supervisors.

I would like to express my deepest gratitude and respect to **Dr. Nadia Abdel Salam**, *Head of Physical Medicine Department, Ain Shams University, for her invaluable supervision and expert guidance during this research. Her honest assistance was of great help to me. Actually I am indebted to her more than I can express.*

I am grateful to **Dr. Mohamed Gamal Zaki**, *Physical Medicine Department, Ain Shams University, for his expert supervision, generous support and kind advice. He has given me careful assistance to perform my work.*

I appreciate very much, the kind help, unfailing advice and encouragement offered to me all through the work by **Dr. Rasha Khalil**, *Microbiology and Immunity Department, Ain Shams University. Her precious guidance was very essential for my work to be finally achieved.*

It is a pleasure to acknowledge my debt to **Dr. Nora Salwa Haraoun**, *Physical Medicine Department, Ain Shams University, for her skilful assistance and kind co-operation.*



I am also grateful to **Dr. Mohamed Sadek El Beblawy,** *Senior Consultant of Chest Diseases, Air Forces Hospital, for his helpful guidance and kind advice. He has provided considerable time and effort which made this work possible.*

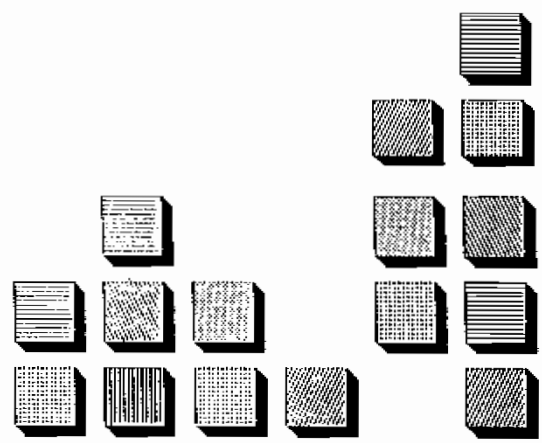
I wish to express my profound gratitude and cordial appreciation to **Dr. Nadia El Arousy,** *Physical Medicine Department, Ain Shams University;* **Dr. Ayman Farghaly,** *and* **Dr. Ahmed Hanafy** *from Chest Diseases Department and Rheumatology and Rehabilitation Department, Air Forces Hospital, for their precious help and kind co-operation which were very essential for my work to be achieved.*

My Sincere gratitude should be expressed to **Dr. Manal Housney,** *Chest Diseases Department and* **Dr. Maha El Gaafary,** *Community Medicine Department, Ain Shams University for their precious guidance and faithful co-operation throughout this work.*

I am also grateful to **Mr. Mohey El Din Taher,** *and* **Miss Manal Afify,** *Chemists in the Immunity Lab., Ain Shams Univeristy Specialized Hospital for their skillful assistance which was so important for my work to be finally achieved.*

Lastly, but certainly not the least, I would like to extend my sincere thanks to every one who has helped me and all the staff of Physical Medicine Department, Ain Shams University, for their co-operation and encouragement.

INTRODUCTION



INTRODUCTION

Rheumatoid disease is a systemic inflammatory disorder of unknown etiology characterized by the manner in which it involves the joints. Rheumatoid disease is not confined to the locomotor system. Extra-articular features have been found in cutaneous, cardiovascular, digestive and nervous systems. Haematological and ocular alterations have also been described **(Cervantes-Perez et al., 1980)**.

In 1948, **Ellman and Ball**, coined the term rheumatoid disease when they postulated a systemic relationship between pulmonary abnormalities and rheumatoid arthritis. Since then it has become well established that rheumatoid disease is a multisystem disorder in which the respiratory system may be affected variably.

Respiratory disorders associated with rheumatoid disease include:

I- Pleural disorders:

Pleurisy and effusion: preceding or occurring with polyarthritis.

II- Disorders of lung parenchyma:

1- Pulmonary nodules: solitary or multiple.

2- Pneumoconiosis: occurring with the development of rheumatoid arthritis.

3- Diffuse pulmonary fibrosis: idiopathic or drug related.

4- Pulmonary vasculitis: with or without pulmonary hypertension.

5- Apical fibrocavitary lesions of the lung.

6- Rheumatoid pneumonia.

7- Amyloidosis.

8- Bronchocentric Granulomatosus.

9- Bronchogenic carcinoma.

III- Airway obstruction

1- Upper laryngeal involvement.

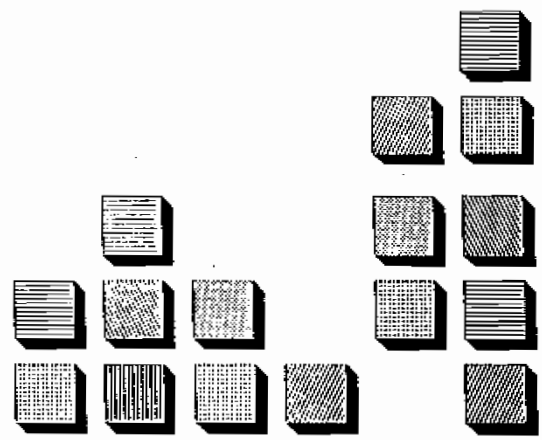
2- Lower airway obstruction:

- Acute obliterative bronchiolitis.
- Chronic obstructive airway disease.

There are various risk factors which may aggravate or predispose rheumatoid patients to these conditions. They include:

- Age and sex: complications are worse in males.
- Duration, severity and course of the disease.
- Genetic factors: The major histocompatibility complex and alpha-1-antitrypsin.
- Occupation: exposure to mineral and organic dust.
- Cigarette smoking: past or current.
- Antirheumatic medication.

AIM OF THE WORK



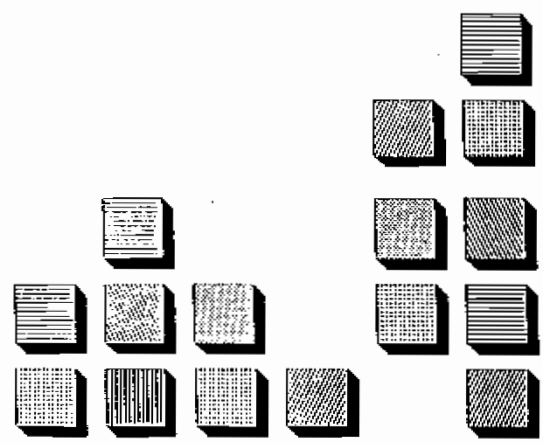
AIM OF THE WORK

The aim of this work is to find out:

1) Prevalence of lung affection in Egyptian patients with rheumatoid disease.

2) Use of HLA tissue typing in prediction of lung affection in rheumatoid disease.

REVIEW OF LITERATURE



REVIEW OF LITERATURE

Pleural Disorders

Pleurisy and Effusion

This is the most frequent manifestation of rheumatoid disease. At autopsy, approximately one half of patients with rheumatoid disease were found to have old adhesive pleurisy, effusion or both **(Walker and Wright, 1968)**.

A higher incidence of extra-articular features of rheumatoid disease, including pulmonary disorders, were recorded in men. This is in marked contrast to the over all predominance of females to males with rheumatoid disease **(Gordon et al., 1973)**. Pleurisy and effusion may be the first manifestation of the disease or may develop after the disease has become clinically obvious. However, clinical manifestations of these lesions are less frequent. Pleurisy may be associated with febrile illness. Pleural friction rub may be detected as well **(Mac Farlane et al., 1978)**.

As many as one third of the pleural effusions are asymptomatic and are detected only by routine chest roentgenograms. Similarly, in

such patients, clinically unsuspected pericardial effusions may be detected by echocardiography **(Hunninghake and Fauci, 1979)**.

Pleural effusion is usually unilateral. The patient usually comes with dull aching chest pain. On examination there are:

a) Restriction of respiratory movements on the affected side.

b) Marked (stony) dullness on percussion.

c) Diminution or absence of breath sounds and vocal resonance and fremitus. At the upper level of dullness, bronchial breathing (conducted through the relaxed lung) may be heard.

With small effusions the signs are best elicited at the base posteriorly, large effusions will displace the trachea and the apex beat to the opposite side **(Crofton and Douglas, 1981)**.

The effusion is presumably due to rheumatoid disease of the pleura. As many as one third of the patients may have associated intrapulmonary manifestations of rheumatoid disease **(Hunninghake and Fauci, 1979)**.

Although in some instances the effusion may resolve rapidly, there is a tendency for these effusions to persist for months and in some cases several years. It may recur after aspiration but to a gradually diminishing extent. A rare complication of rheumatoid pleuritis is pleural thickening with fibrotic lung entrapment. By chest roentgenograms, pleural effusion usually appears as dense,

homogeneous opacities. The effusions are of all degrees of size. A very small effusion may only be represented by obliteration of the costophrenic angle. In most cases the fluid occupy between one third and one half of the hemithorax **(Crofton and Douglas, 1981)**.

Examination of the pleural fluid is the best mean of establishing a diagnosis of pulmonary disease in a patient with rheumatoid disease **(Lillington et al., 1971)**.

The pleural fluid is characteristically an exudate, turbid, greenish yellow in color, with high concentration of protein (usually in excess of 3 gm/100 ml) and a white cell count below 5000/mm^3 **(Turner and Courtney, 1977)**. Fluid from long standing pleural effusions may appear milky because of cholesterol crystals. True chylous effusion, however, develop only with lymphatic obstruction **(Baim et al., 1979)**.

The pleural effusion in patients with rheumatoid disease may present certain characteristic features. The differential cell counts in the pleural fluid bear a striking resemblance to rheumatoid arthritis synovial fluid in that there are usually large numbers of both polymorphonuclear and mononuclear leucocytes **(Halla et al., 1980)**. However the lower white cell count seen in the patient's pleural fluid may explain why the pleuritis of rheumatoid disease is milder than synovitis, and frequently asymptomatic **(Gordon et al., 1985)**.

The polymorphonuclear leucocytes may contain dense black granules approximately 0.5 to 1.5 um in diameter ("RA cells"). These

cells contain cytoplasmic inclusions and ingested immune complexes and release rheumatoid factor when they disintegrate. They were initially described by **Hollander and associates (1965)**.

Other characteristics of rheumatoid pleural fluid include increased lactate dehydrogenase (LDH) activity relative to serum, acidic PH, increased cholesterol content and low concentration of glucose. Interestingly, very low concentrations of glucose (less than 30 mg per 100 ml) are found in pleural fluid despite normal blood sugar concentrations **(Petty and Wilkins, 1966)**. In this regard, **Dodson and co-workers (1966)** have suggested that a certain unidentified factor associated with rheumatoid pleural inflammation interferes with the transport of glucose across the pleural surface. However, **Bywaters (1981)**, suggested that it may result from increased metabolism in an inflammatory cavity . Regardless of the mechanism, this finding is of considerable value in the differential diagnosis. Glucose concentrations in pleural and synovial fluid may be low in sepsis and malignancy as well but are rarely below 30 mg/100 ml in these disorders **(Gordon et al., 1985)**.

Increased cholesterol level is one of the characteristic findings in examination of rheumatoid pleural fluid as well. Microscopy may show typical polyhedric crystals of cholesterol. **Ferguson (1966)** reported that the main aetiologic factor is chronicity of effusions from whatever cause. He considered that aging or chronic effusions

produced gross pleural thickening which reduced the resorptive power of the pleura and allowed cholesterol to accumulate. Other authors have considered the cholesterol to be a breakdown product, whether of tubercle bacilli, red cells or lymphocytes. It seems unlikely that tubercle bacilli would be present in sufficiently large numbers in the pleural fluid. Moreover, although the cholesterol/cholesterol ester ratio in the effusion resemble that of red cells, the haemorrhage in such cases would have to be gross. Thus a lymphocytic origin seems to be the most likely. All authors agreed that these effusions are not associated with any alteration in the serum cholesterol level or clinical evidence of disturbed cholesterol metabolism such as xanthomata **(Hunninghake and Fauci, 1979)**.

Ocana et al., 1983, found an increase in adenosine deaminase enzyme activity in rheumatoid pleural effusion. Increased enzyme activity is also found in tuberculous pleural effusion. Rheumatoid disease seems to be the unique entity that can not be differentiated from pleural tuberculosis on the basis of this test. The abundance of polymorphonuclear cells in rheumatoid pleural effusion may account in part for the adenosine deaminase increase. Later in 1988 the same authors reported that the predominance and degree of stimulation of T helper/inducer lymphocytes as a response of cell mediated immunity in rheumatoid and tuberculous pleural effusion may explain the selective increase in adenosine deaminase activity in both conditions.