SERUM COMPLEMENT VERSUS SEROPOSITIVITY IN RHEUMATOID ARTHRITIS

THESIS

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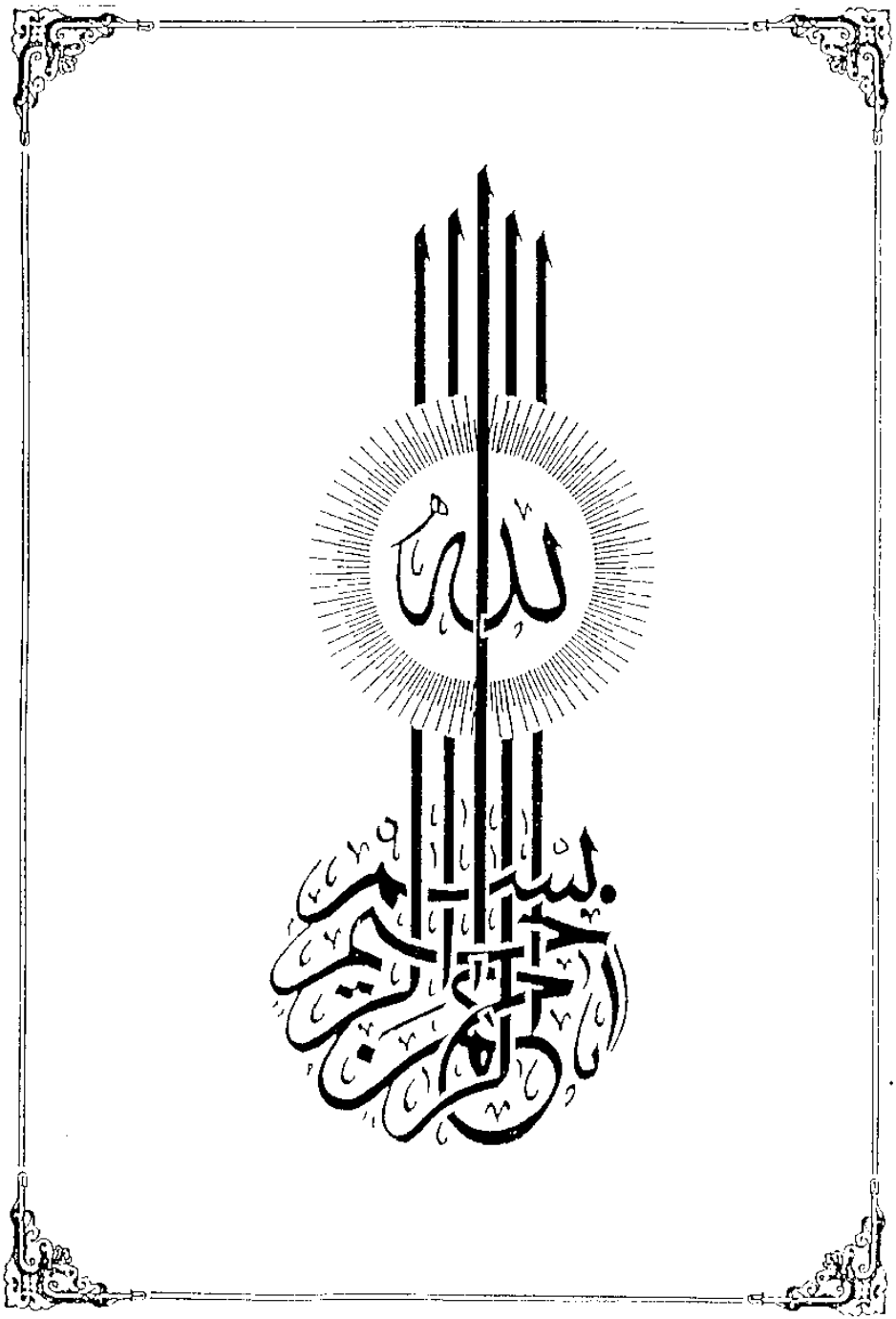

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INTRODUCTION AND AIM OF WORK

INTRODUCTION

Rheumatoid arthritis is one of the systemic immune complex diseases. It is accompanied by change in the level of serum complement.

It is well known now that rheumatoid arthritis consume the complement (Winchester et al., 1970). In the affected joint, the level of the complement in the synovial fluid is known to be low (Hedberg et al., 1970).

Changes in serum complement were also described. Some studies showed that serum complement was elevated in rheumatoid arthritis (Cohen, 1975), while others stated that serum complement decreased as the antigen-antibody reaction will fix the complement with subsequent decrease (Ecker, 1946). Some studies had observed the decrease in C_4, C_1 and C_3 (Peltier, 1978), while others (Vaughan et al. 1951) stated that serum complement was lowered on correlation with disease activity which marked by great antigen-antibody activity.

From this short introduction around serum complement and rheumatoid arthritis , we notice that the results were variable. Also most of these studies did not classify the patients into seropositive and seronegative groups which marked by the presence of rheumatoid factor. The level of serum complement C_3 in rheumatoid patients was

not discussed clearly, and the changes that occur to its level during the disease in Egyptian patients.

By this work we will try to shed light on the level of serum complement C_3 in seropositive and seronegative patients and to correlate this with various clinical and laboratory findings.

AIM OF THE WORK

The aim of this work is to study the level of the complement (C_3) in patients with rheumatoid arthritis and to correlate this with various clinical and laboratory findings.

REVIEW OF LITERATURE

RHEUMATOID ARTHRITIS (R.A.)

Definition:

Many different definitions were put for rheumatoid arthritis. It can be defined as a chronic polyarthritis affecting mainly the periphral Joints, and runsin a prolonged course with remissions and exacerbations. accompained by general systemic diturbances. It is characterized by swelling of synovial membrane and periarticular tissue with subchondral osteoporosis, erosion of cartilage and bone, associated with wasting of related muscles. But it can be defined better as "a systemic disease characterized by chronic proliferative and inflammatory reaction in synovial membrane which eventually is erosion and destruction of Joint cartilage and supportive structures, giving rise to typical Joint deformities and characteristic radiological abnormalities. Synovial inflammation occurs with proliferation of the living cells many of which become laden with hydrolytic enzymes. Masses of inflammed and hypertrophied tissues (pannus) extend into, and erod the articular cartilage especially at their margin and weaken or destroy the soft tissues as ligaments and tendons. Another character but less common and constant feature is the rheumatoid granuloma or nodule which most frequently situated in

subcutaneous tissues adjacent to joint but may also occur in synovial membrane, viscera. These granulomas are responsible for extraarticular manifestations of disease "(stevens , 1976).

The Etiology Of Rheumatoid Arthritis

Introduction

An enormous amount of evidence supports the concept that the pathology of rheumatoid arthritis has its basis in an inflammatory response involving the immune system. Even though there are indications that rheumatoid arthritis is an autoimmune disorder, in the sense that it involves antibodies against autologous immunoglobulin G, there is no mandatory reason to infer that this has occurred de novo. On the contrary, there are many data which indicate that some initiating event, such a specific external etiologic agent, is responsible for setting the disease process into motion.

In considering disease phenomena associated with autoimmunity it is important to distinguish between states which are directly mediated by this process, and those in which autoantibodies can be demonstrated but whose pathological effects are unproved.

Thromocytopenic purpura and hemolytic anemia are situations in which there seems to be a true autoimmunity, with antibodies directed at the target cells(Miescher, 1976) leading to their destruction in the peripheral blood . In co ntrast, occurrence of rheumatoid factors in rheumatoic arthritis, antinuclear antibodies in a variety of connective tissue diseases, and antithyroid antibodies in many patients with diverse conditions are all associated with no obvious specific target pathology.

In most of these situations it remains uncertain as to wh e ther the apparent autoimmunity results from the acquisition of some new antigen from an external stimulus or from some primary abnormality in the regulation of cells which mediate these reactions (Fundenberg, et al., 1978). Although the concept of "forbidden clones", as originally expounded by Burnet in 1959, has dominated the thinking relative to autoimmunity, it seems in the light of new evidence that some kind of alteration of the immunoregulatory system must be at fault in certain of these autoimmune processes. This might involve, for example, alteration of the control mechanism in such a way that the appropriate balance between immunologic "help" and "suppression" is disrupted (Gershon, 1974). Other levels of immunoregulation apparently are influenced by such things as anti-idiotypic antibodies, as was proposed by Jerne

in 1974, in his "network hypothesis". In this latter concept, antibody itself acts in a manner of continuing regulation so that anti-antibodies from one clone act on the preceding clone to regulate its response. Such intricate regulatory mechanisms are of primary importance for keeping the immune system in smooth operating order. Absence of such regulation could allow an imbalance that permits the initiation of an autoimmune process with clinical consequences.

On the other hand, examples can be found in which specific external agents seem to initiate an inflammatory arthritis that in many respects parallels truerheumatoid disease. It, therfore, seems logical to assume that an initiating agent activates an immune response in a host of appropriate genetic makeup, so that the resultant inflammation leads to continual disease activity. Although investigations in the general areas of bacteriology, virology, and immunology have contributed enormously to our understanding of inflammatory disease and host responses, the specific documentation of the eitologic agent in rheumatoid arthritis has proved disappointing. Pyogenic bacteria, mycobacteria, certain fungi, and certain viruses, such as smallpox, are classic examples in which there is multiplication of the agent directly within the joint space. The second situation is one in which the infectious agent localizes in the joint space and initiates