IMMUNOLOGICAL BASIS,IMMUNOPATHOGENESIS AND MARKERS FOR DIAGNOSIS OF OSTEOARTHRITIS

ESSAY

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By

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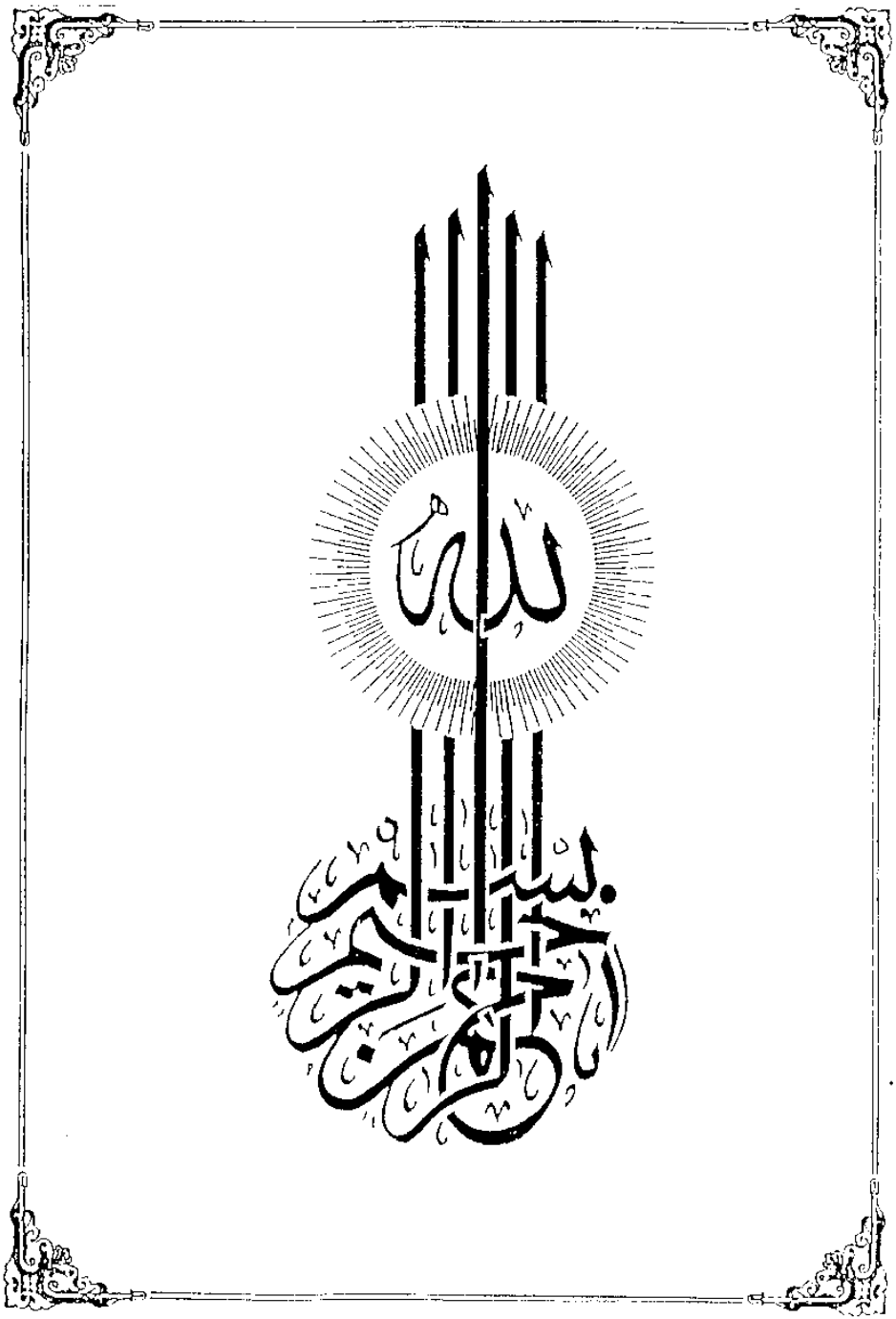

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INTRODUCTION

Osteoarthritis is by far, the most prevelant of the clinical entities that fall within the domain of the Rheumatologist or Orthopedist.With a disorder such as osteoarthritis for which the cause remains unknown , the disease is best described by an analysis of its clinical , pathologic , and biologic characteristics (Mankin , 1988).

Osteoarthritis is a slowly progressive monoarticular (or less commonly , polyarticular) disorder.It is evident that osteoarthritis can be caused by or at least associated with a multiplicity of primary disorders (in which the osteoarthritis is "secondary") or can be considered as "primary" or at least without known cause and of obscure pathogenesis.The condition occurs late in life, principally affecting the hands and large weight- bearing joints and it is characterized clinically by pain , deformity , crepitation and abnormal gate (Mankin ,1988).

Perhaps one of the more provocative theories related to the cause of alterations in the articular cartilage in idiopathic osteoarthritis is the suggestion that because of the aneural and avascular state of the cartilage the remainder of the body is unaware of their existence.Of perhaps greater importance is the possibility that some of the proteins of the matrix are unrecognized by the immune system as autogenous and when they -or fragments of them escape -from the cartilage into the synovial fluid, the theory provides a hypothetical explanation for the method by which even a minor injury to the cartilage may serve as the initiating event in a local (synovial) autoimmune causation or perpetuation mechanism that, over time becomes severe enough to destroy parts of the cartilage by humoral or cellular cytotoxic antibody responses (Cooke , 1986).

For the most, plain radiograph of joints affected by osteoarthritis are so characteristic that sophisticated technology rarely is required to establish the diagnosis (Martin et al, 1993).

The problem that faces the clinical investigation is that , despite obvious familiarity with the disease, there remain a number of un-answered questions regarding the nature of the disorder and its epidemiology , clinical presentation , causation ,and pathogenesis. The recently developed specific "markers" for cartilage injury and OA can be used to establish the disease early in the course. One of the first potential markers was advocated by thonar and associates (1991), who suggested that a keratan sulfate epitope circulating in the blood stream may be in fact a significant and accurate marker (Heinegard et al, 1991).

The interleukins known to play a role in cartilage degradation have been considered to be a likely marker ,and both IL-1 and IL-6 have been implicated. Superoxide free radicals and phospholipase have also been suggested as markers .Higher molecular weight fragments that could serve as markers include the matrix proteins, and recent studies have suggested that this latter material shows a greater specificity than many of the others. Finally some of the more recent efforts in molecular biology suggest that dna probes may ultimately be of value in studying the disease (Yosake et al , 1995).

PATHOGENESIS, IMMUNOLOGICAL BASES, IMMUNOPATHOGENESIS IN OSTEOARTHRITIS

Definition :

Human osteoarthritis is a heterogeneous and multifactorial disease characterized by the progressive deterioration of the cartilage of diarthrodial joints .Multiple aetiological and pathogenic mechanisms have been implicated in its development and progression . In many instances OA is an acquired process secondary to various metabolic , mechanical , or inflammatory - immunological events (Sergio et al , 1994) .

Structural & Biochemical Features of Normal Articular Cartilage

The normal cartilage matrix is hyperhydrated , with water content ranging from 65 to almost 80 % , the water appears to be principally in the form of either a proteoglycan or a collagen gel. It is hence freely exchangeable with the synovial fluid although a small portion of the water is tightly bound to matrix (Maroudas et al, 1986).

A small inorganic component is almost always found in the form of a calcium salt , but this usually accounts for less than 5 % of the dry weight of the tissue . The bulk of the remaining material is accounted for by the complex and interactive macromolecules , proteoglycans (both subunit and aggregate) , and type II collagen . The most typical proteoglycan subunit molecule has a molecular weight of approximately 2 million daltons. (Rosenberg and Buckwalter 1986) .Individual proteoglycan subunits rarely , exist as such in normal cartilage instead , they aggregate on long filaments of hyaluronic acid in an interaction stabilized by low molecular weight link glycoproteins to form enormous structures with molecular weights of 100 million daltons or greater .(Hardingham and muir 1974).