GOUT

IN THE UPPER LIMB

THESIS

SUBMITTED FOR PARTIAL FULFILMENT

OF THE MASTER DEGREE

IN ORTHOPAEDIC SURGERY

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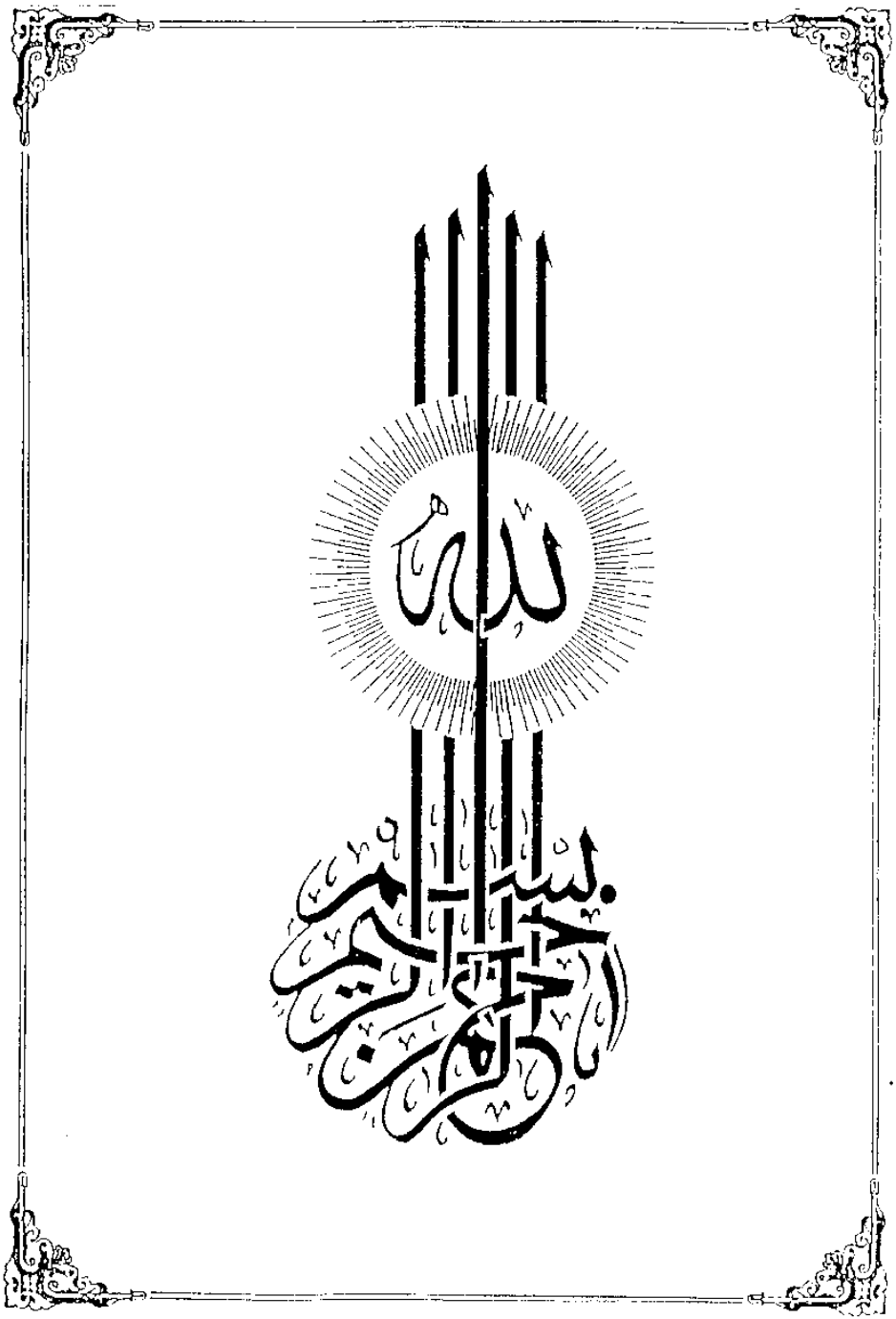

C O N T E N T S

CLASSIFICATION

Gout is a term representing a heterogenous group of diseases found exclusively in man, which in their full development are manifest by :

a) An increase in the serum urate concentration.

b) Recurrent attacks of a characteristic type of acute arthritis in which crystals of monosodium urate monohydrate are demonstrable in leucocytes of synovial fluid .

c) Aggregated deposits of monosodium urate monohydrate (tophi) occuring chiefly in and around joints of the extremities and sometimes leading to a severe crippling and deformity .

d) Renal disease involving glomerular, tubular and interstitial tissues and blood vessels .

e) Uric acid urolithiasis .

These manifestations can occur in different combinations . (Kelly , 1981) However, essential hyperuricemia alone , even when complicated by uric acid lithiasis should not be called gout , as the term gout signifies inflammatory arthritis or tophaceous diseases . (Wyngaarden, 1982) .

Classification :

Gout may be primary or secondary. In primary gout of which there are several biochemically distinct forms. The hyperuricemia is a consequence of an inborn error of metabolism. Secondary gout is an acquired disease in which acute and possibly chronic tophaceous gouty arthritis develop as a complication of hyperuriemia caused by another disorder .

A. Primary gout : is commonly divided into the following stages .

1. Asymptomatic Hyperuricemia :

There is normally a rise in serum urate concentration at puberty greater in the male than in female .

This rise may be exaggerated beyond the range of normal only about one third of hyperuricemic subjects develop articular gout. The average age of onset is about forty five years.Renal calculi composed wholly or partially of uric acid may occur in the prearticular stage or in hyperuricemic subjects who never develop gout .

Rarely, tophi may antedate the development of articular gout . Very rarely, renal injury may occur in asymptomatic hyperuricemic persons .

2. Acute gouty arthritis :

The first attack of acute arthritis usually occur suddenly about one half of initial attacks involves the great toe other common sites are ankle, heel, knee,wrist joints and olecranon and subdeltoid bursae .

The untreated attack may last few days to few weeks recovery is generally complete .

3. Interval phase of gout :

Initially the asymptomatic intervals may be of months or even years duration. Characteristically the attacks recur with increasing frequency and severity . Later attacks are often polyarticular, longer and perhabs febrile. Roentegenographic changes may develop and the attacks abate more gradually than before but the joints recover complete symptomless function .

4. Chronic gouty arthritis :

Less than one half of gouty subjects who experince recurrent accute attacks develop chronic gouty arthritis .

The duration of time from initial attack to the begining of chronic symptoms or visible tophaceous involvement is highly variable ranging in one large series

from three to forty years . With an average of 11.7 years. Chronic gouty arthritis may develop as a residue of an acute attack or develop insidiously in a previously uninvolved joint . Acute attacks may be superimposed on the chronically affected Joint.

Late in the chronic ph se they may disappear altogether . Chronic gouty arthritis is generally poly-articular. The arthritis may be totally disabling although tophi are relatively painless .

Tophi may ulcarate and drain chalky material. Severe tophaceous gout is almost always associated with marked hyperuricemia and limited renal excretion of uric acid .

B. Secondary Gout :

It may evolve through these same stages. The acute attacks are indistinguishable from those of primary gout .

In secondary gout associated with hematopoietic disease , the interval phases tend to be shorter than in primary gout and tophaceous disease and chronic gouty arthritis occur earlier and are often more severe (Wyngaarden,1976) .

Furtherly gout is classified into :

I. Primary :

A) Idiopathic .

B) Associated with specific enzyme defects .

1- Glucose 6-phosphatase deficiency or absence .

2- Hypoxanthine-guanine phosphoribosyl transferase deficiency, partial or "virtually complete " .

3- Glutamine PP-ribose-P-amidotransferase : feed back resistance .

4- Glutathione reductase variant : increased activity .

II. Secondary :

A) Associated with increased nucleic acid turn over .

B) Associated with decreased nucleic acid turn over .

(Wyngaarden, 1976)

AETIOLOGY AND PATHOGENESIS

Aetiology and Pathogenesis

Aetiology of Primary Idiopathic Gout :

The biochemical hallmark of gout is hyperuricemia . The concentration of uric acid in body fluids is determined by the balance between ratio of production and elimination. Uric acid is formed by oxidation of purine bases which may be exogenous or endogenous in origin.

About two-thirds of uric acid is excreted in urine 300-600 mg per day and approximately one third is excreted into the gastro intestinal tract, where it is ultimately destroyed by bacteria. Hyperunicemia may be due to an excessive production, a decrease in the renal excretion or both events.

Definition of Hyperuricemia :

The serum urate vlalue is elevated in an absolute sense when it exceeds the limit of solubility of mono-sodium urate in serum. At 37°C the saturation value of urate in plasma is about 7.0 mg per 100 ml a value above this represents supersaturation in a physico chemical sense. The serum urate concentration is relatively elevated when it exceeds the upper limit of an arbitrary normal range, usually defined as the mean serum urate value plus two standard deviation in a healthy population matched for age and sex .

In most epidemiologic studies the upper limit is about 7 mg per 100 ml in men and 6 mg per 100 in women A serum urate value in excess of 7.0 mg per 100 ml carries an increased risk of gouty arthritis or renal stones . Gout is primarily a disease of adult men and only about 5 % of cases in women. The usual form of gout is uncommon before the third decade and the peak incidence is in the fifth decade . (Kelly, 1980) .

The mean serum uric acid values are higher in men than in women. Age has no effect on uric acid levels in men, either in the population as a whole or in those with gouty arthritis. In women, the levels are progressively higher in older women .

The rise occurs gradually with the greatest increment in the decade between forty and fifty, an effect presumbly related to the menopouse . (Hal, et al, 1967) .

The sex difference in serum urate level is in part attributed to greater renal clearance of uric acid in Premenopausel women . In prepubertal children, mean values 3.6 mg/ 100 ml. In postmenopausal women,mean values approach or equal those in men. (Wyngaarden, 1976) .

In general, with increasing levels of uric acid there is an increased risk of developing gouty arthritis

In clinical terms, there is about one chance in five that a patient with an elevated uric acid concentration will develop an acute gouty attack . (Liang and Fries, 1978) .

The familial nature of gout has been recognized long time ago. The genetic concept imply that there may be multiple metabolic aberrations responsible for hyperuricemia, but that a single type of defect is apt to characterize a given hyperuricemic family .

(Wyngaarden , 1976)

Role of the Kidney in Hyperuricemia

Man by nature is hyperuricemic. In most mammals the urate filtered at the glomerulus is promptly reabsorbed in the proximal convolution and recycled to the liver where it is converted by uricase enzyme to allantoin a substance soluble enough to be eliminated by the kidneys in quantity without difficulty, this is not the case in man due to absence of uricase enzyme. In addition, the normal renal clearance of urate in man is low for a metabolic waste, roughly 10% of the inulin clearance . The kidney is of course so constituted as to eliminate, not retain, most of the metabolic wastes brought to it, but, in the case of uric acid, the reverse is true (Gutman, 1972) .

In normal man, about two-thirds of uric acid is excreted in the urine. Recent evidence has suggested .

a- 4. Component mechanism for urate transport in man :

1) Complete filtration of plasma urate at the glomerular membrane ;
2) Virtually complete reabsorption of filtered urate .
3) Subsequent secretion of urate at a rate of at least 50% of the original load;