METABOLIC EVALUATION OF PATIENTS WITH UROLITHIASIS IN EGYPT

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BY

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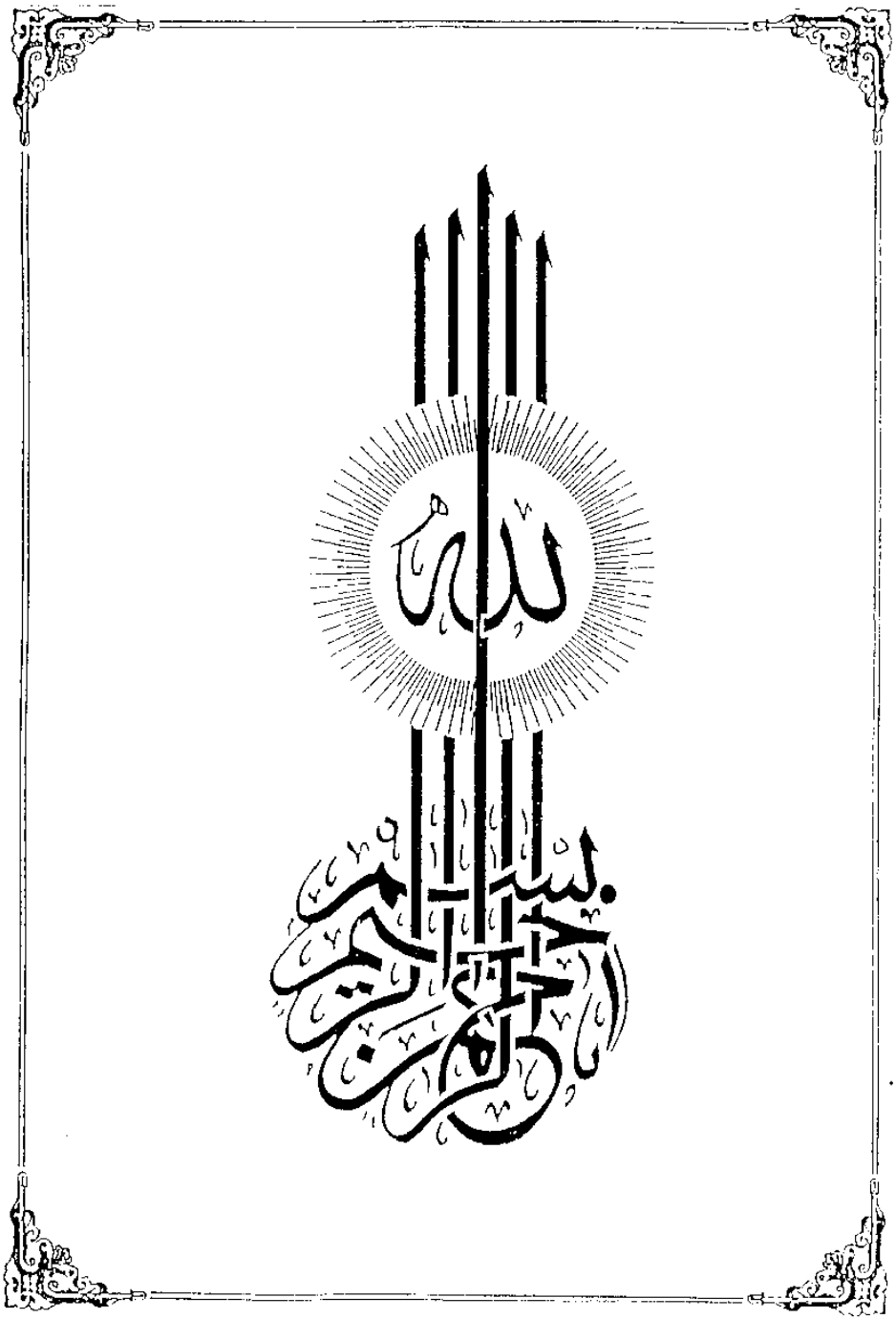

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TO THE SOUL OF MY LATE PROFESSOR

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REVIEW OF LITERATURE

MODERN THEORETIC BASIS OF ETIOLOGY OF URINARY LITHIASIS

Modern theories of aetiology of calculous formation can be conveniently separated into the following main categories:-

SATURATION:-

If increasing amounts of substances capable of crystallization are added to pure water at a given pH and temperature, eventually a high enough concentration is reached for crystals to form. When crystals begin to form, we say that the solution has become saturated with the substance. There is a specific limit to the amount of solids or solute that can be held in solution. When this amount is exceeded, crystals must form. When two or more substances are combined to form the crystal as in calcium oxalate, the level of saturation is governed by the product of concentrations of the two or more substances. The point at which saturation is reached and crystallization begins is referred to as the solubility product (SP). Temperature and pH must be specific for any crystallization process. But in case of urolithiasis, it must occur at body temperature at or near 37C. Since urine varies widely in pH, this factor

must be considered in any explanation of urolithiasis (Drach, 1978).

Urine has the ability to hold more solute in solution than pure water. Although all elements and molecules in urine are suspended in water, the mixture of many electrically active ions in urine causes interactions that change the solubility of their elements. In addition, many organic chemical molecules such as urea, uric acid, citrate, and the complex mucoproteins of urine, all mutually affect the solubility of other substances (Darch, 1978).

* SUPERSATURATION:-

The most significant and beneficial effect of these ionic and protein elemental interactions is to increase the solubility of various substances that otherwise might crystallize in the concentrations present in urine. Hence, if a given amount of calcium and oxalate that would crystallize when placed in a solution of water at a given pH and temperature is placed in urine, it will be held in solution. If the amount of calcium and oxalate is increased progressively in the same volume of urine at constant pH and temperature, the calcium and oxalate will stay in solution even though the solubility product has been exceeded, thus creating a state of supersaturation. The area of supersaturation between the solubility product and the point at which spontaneous crystallization occurs is called the

metastable region for a given substance . The point at which spontaneous nucleation of crystals occurs is called the formation product (FP) of urine (Finlayson 1974, Williams 1974).

* Crystal Nucleation:

Crystal nucleation occurs when active ions and molecules in a solution no longer flow randomly in a completely dissociated fashion but cluster together closely enough to form the earliest crystal structure that will not dissolve .

* Crystal Growth:

Once nucleation has occurred, certain nuclei may continue to grow if the urine remains supersaturated. Not only will such nuclei continue to grow in the zone above the formation product, they will continue to grow even if the saturation of urine falls into the metastable zone between solubility product and formation product (Finlayson, 1974).

The concept of increasing the urine concentration to the level where the formation product is exceeded is critical to certain theories of urinary stone formation in which homogeneous nucleation is a critical event. In other theories, however, saturation is required only to the range of metastable saturation; it is postulated that adequate heterogeneous nuclei are already created by biological

processes in the kidney . stones then grow on these preformed nuclei (Malek & Boyce, 1973).

These two concepts of nucleation may be further separated into the free particle theory and the fixed particle theory (Finlayson, 1974). In free particle nucleation, multiple crystals are formed simultaneously in the upper urinary system when the formation product of a substance is exceeded. In the theory of fixed particle nucleation, it is suggested that because of excessive concentration of a certain ion in the kidney, precipitation of crystals or spherules may occur in the renal papillae either within the tubular lumina or beneath the surface of the papillae (Darch & Boyce, 1972). These particles remain fixed and serve as nuclei for further growth .

* Crystal Aggregation

If multiple nuclei and crystals are formed spontaneously and float freely, these nuclei become active kinetically and bounce about in urine. If they remain small, free, and independent within the solution, they will then pass through the urinary tract within a given amount of time and will be voided. Under certain conditions, however, these nuclei can grow and may come close enough to each other to be bound together by various chemical forces. Therefore, nuclei of large growing crystals may aggregate to form larger crystal masses. Should they become large enough to

become lodged in a given position in the urinary tract, they may then continue to grow by one of two processes. They may add additional crystals to their surfaces by the process of aggregation , or they may grow by adding new crystal mass to their surfaces. It is likely that both processes are important in the creation of urinary calculi (Darch, 1987).

* Epitaxy

If a crystal has a pattern or organization of ions that is regular and predictable, this structure is called lattice. This surface lattice may resemble closely that of a second but different type of crystal. Depending upon the closeness of resemblance, the second type of crystal may grow upon the surface of the first. Calcium Oxalate may grow easily upon the previously formed uric acid crystals as they do have crystal lattices that are similar enough to permit this process of epitaxy (Finlayson, 1974)

* RELATIONSHIP BETWEEN TIME ALLOWED FOR CRYSTAL GROWTH AND SIZE OF PASSAGES.

Crystals form best at the points of greatest supersaturation of urine, usually the renal papillae . As soon as these crystals form, they can flow within 3-5 minutes into renal pelvis, down the ureter into the bladder, where they remain for a period approximately 3-6 hours (Vermeulen & Lyon, 1968).

The lumen of the nephron is smallest at the level of the collecting duct, where its diameter is 50-200 micrometers. Anatomically, this portion occurs in the renal papilla . If the crystal does not have time to grow large enough to obstruct any renal tubule, it then passes into the ureter, where the minimum diameter that can cause obstruction within 10 minutes is 2 millimeters (Lentonen , 1973; Sutor & Wooley 1975). After the crystal has reached the bladder, it may still grow and may reach a size that exceeds 6 millimeters, such a crystal could still be voided through the urethra without difficulty (Finlayson, 1974).

For a urolith to achieve adequate size to create symptoms , we must suppose that within the brief period of time in transit from the kidney to the bladder, the supersaturation of urine is so great that the crystal will grow very rapidly into a structure that can pass no longer through the urinary system. To try to avoid this problem, the urinary tract is anatomically constructed like an inverted cone. The diameters are smallest in the renal tubules and become progressively larger in the ureter, the bladder and the urethra. If somehow the crystal mass becomes lodged in a renal papilla or in a tubule, it is no longer able to move through the system . It resides at that point and continues to grow in supersaturated urine. If the crystal breaks off or breaks away from the renal papilla, when it is smaller than necessary to obstruct the ureter, it

will pass through the system without causing symptoms. But if it attains a diameter of greater than approximately 2 millimeters, it may pass into the ureter and create urinary obstruction (Lonsdale, 1968). If the stone could pass into the bladder and there is bladder outlet obstruction, it will remain in the bladder and continue to grow and may attain a large size.

* INHIBITORS OF CRYSTALLIZATION:

Some individuals with supersaturated urine seem to be capable of holding some crystallizable urinary substances in solutions. This is due to the presence of a certain substance called inhibitor of crystallization. A relative lack of crystallization inhibitors in the urine of stone formers was proved by many investigators (Elliot, 1973).

Inhibitors may be classified as predominantly organic or inorganic. Of the inhibitors within the organic group perhaps the most famous is the peptide inhibitor (Smith et al., 1969). This low molecular weight peptide enables the urine to hold in solution considerably greater amounts of calcium than is possible when it is absent (Barker et al., 1974).

Most of inhibition that was found in urine could be accounted for by the polyelectrolyte interactivity of the multiple ions of urine (Finlayson, 1974).

Other organic inhibitors may be present. Matrix may have the ability to inhibit the formation of urinary calculi (King, 1971). Boyce and his co-workers indicated that matrix may be important in enhancing the formation of calculi (Boyce et al., 1969).

Amino acids, especially alanine, may be important in improving the solubility of calcium substance in some types of urinary lithiasis (Chow et al., 1973).

Urinary citrate appears to have some part in the solubilization of calcium, oxalate and phosphate in urine (Finlayson, 1974).

Inorganic inhibitors of crystallization: When magnesium is excreted in urine in significant amounts, it increases the solubility of calcium phosphate, and perhaps calcium oxalate (Moore and Gowland, 1975). A high calcium to magnesium ratio has been implicated as one of the causes of calcigerous renal calculi (King, 1967).

Some authors have implicated trace metals in inhibition of urinary stone formation, especially stones of the calcigerous type. Zinc seems to be the most frequently mentioned of these substances (Elliot et al., 1973).

It is likely that calcium stone formers have deficiencies in not only one but several of the inhibitors that should be present in urine. This may be why patients