BACTERIOLOGICAL STUDIES IN PATIENTS WITH RENAL CALCULI

A THESIS

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PRESENTED BY
NAGY WILLIAM GOUBRAN
M.B., B. Ch.

SUPERVISED BY

Prof. Dr. HATEM EL-BEIALY
Professor of Urology,
Faculty of Medicine,
Ain Shams University

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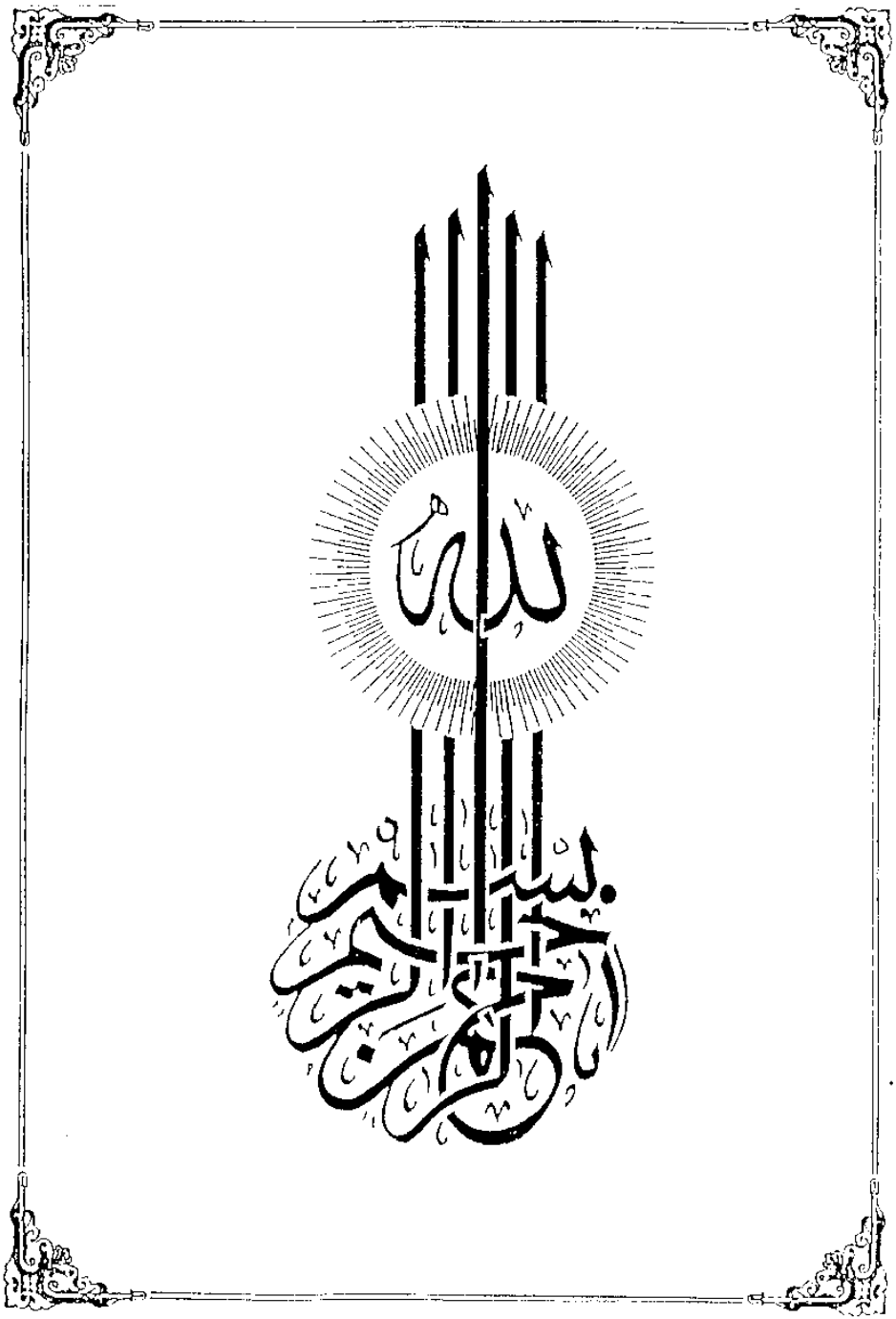
TO THE SOUL OF MY FATHER

CONSULTANT WILLIAM GOUBRAN

WHO GAVE ME EVERYTHING

AND GAINED NOTHING



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Introduction

I. INTRODUCTION

Hippocrates was the first to recognize the cause and effect relationship between putrefying urine and urinary stones. In 1817 Marcet suggested the cause and effect association of ammonia formation, alkaline urine and the precipitation of phosphatic salts. In 1910 Brown reported the co-existence of urease- splitting bacteria and triple phosphatic stones. In 1923 Hagar and Magrath suggested that the bacterial enzyme urease was responsible for the formation of infection-induced urinary stones. Since then; extensive experimental and clinical investigations have contributed data to support the premise that infection- induced urinary stones form primarily, and perhaps solely as a consequence of urea hydrolysis by the bacterial enzyme urease. "Triple phosphate" (Magnesium-ammonium-calcium phosphate) stones, which are induced by infection and urea hydrolysis are composed of struvite ($Mg(NH_4)PO_4.6H_2O$) and carbonate-apatite ($Ca_{10}(PO_4)_6(CO_3)$).

Our aim in this work is to identify the bacteriological organisms associated with renal calculi and to evaluate the various types of treatment of the patients with renal calculi whether surgical, medical or instrumental and their effects on the bacteriological studies before and after the treatment.

STONES OF URINARY INFECTION

II. Stones of Urinary Infection

Infection stones account for approximately 15 to 20% of all urinary calculi. When located in the kidney, usually assume a staghorn configuration.

Although all infection stones are associated with infection of the urinary tract with urea - splitting organisms, it is more than 50% of those satients with infection stones have specific, identifiable, metabolic disorders that are responsible for the initial stone formation (Resnick 1980).

Only 60 to 90% of all staghorn stones are purely infectious in nature and the percentage is greater in women (80%) than in men (50%).

The hydrolysis of urea by the bacterial enzyme urease pathologically increase urinary ammonia; bicarbonate, carbonate and alkalinity. These are favourable conditions in which urine is supersaturated with respect to magnesium ammonium phosphate and calcium phosphate and rapid crystallization occur (Griffith 1978, Nordin 1979). These conditions also may be an important biochemical determinant of virulence in proteus species organisms (Griffith 1976).

Magnesium ammonium phosphate is relatively soluble in urine within the normal pH range of 5-7, but becomes increasingly insoluble under more alkaline conditions owing to the formation of the insoluble po_4^{3-} ion.

Normal urine is well undersaturated with MAP. Only in patients with urinary infections with urea - splitting organisms does urine become sufficiently alkaline to cause MAP to precipitate. (Griffith et al 1976, Nordin et al 1979).

The two main urinary risk factors for MAP precipitation and infected stone formation are namely, pH and ammonium ion concentration.

Although phosphatic stones arise in many patients from persistant oversaturation of urine with MAP very few stones stones is calcium phosphate (caP) (Hodgkinson et al 1969).

Indeed Ca P crystalluria is likely to be more common than MAP crystalluria in these patients, sincethe saturation level with CaP more often exceed the level of spontaneous precipitation than do those of MAP (Nordin et al 1979). clearly infected stone formers are at considerable risk of persistant Ca P crystalluria.

The three main urinary risk factors for Ca P precipitation, namely, calcium and phosphate (combined into concentration product) and pH.

Infection stones occur in patients with urinary tract infection secondary to urea - splitting bacteria; particularly Proteus mirabilis, providencia (P. valgaris, P. rettgeri), Klebsiella and occasional strains of pseudomonas, and occasional strains of Staphylococcus.

Escherichia coli do not produce urease and when associated with struvite stone, likely represent a superimposed infection on an already existing stone.

Pseudomonas organisms are often most difficult to treat (occasionally) associated with the highest incidence of interactable infection and stone recurrence (Resnick 1980).

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A. Incidence

Reference laboratories analyzing large numbers of urinary calculi report the incidence of struvite - containing stones at between 15% and 20%. However the exact incidence is unknown. At baylor affiliated urolithiasis laboratory 60% of struvite stones occured in female and 40% in male patients. However there are other series that report female patients comprise 50% of their population with infection - induced stones. The higher risk in female patients is probably due to their susceptibility to urinary tract infection (Sleight & Wickham 1977).

There are other groups of patients who are particularly prone to infection induced stones. Patients who are susceptible to recurrent infection are likely to be on chronic antimicrobial treatment where common org anisms of low pathogenicity are controlled but virulent resistant organisms emerge. Urea splitting organisms such as proteus and pseudomonas species commonly emerge during chronic antimicrobial treatment. Patients with neurogenic bladders requiring indewelling catheters or intermittent catheterization "Burr 1978"and "Kracht and Buscher 1974" and patients with supravesical urinary diversion such as ileal conduits or nephrostomy tubes are examples of high risk patients groups (Dretler 1973)

B. Pathogenesis

Calculi may be a protected nidus for bacterial infection within the urinary tract. When theyare, these so-called infection stones are the cause of persistent or recurrent bacterial urinary infection. Although theterm infection stone is often used to refer to the magnesium ammonium phosphate (struvite) and calcium phosphate (apatite) stones that form in intimate association with bacterial infection, other stones can become infected secondarily.

Differences in composition between stones that are infected and those that are not have been noted for years. In the 1940s Chute and Suby described the association of urea-splitting bacteria, alkaline urine, and recurring stones (primarily calcium phosphate) in patients seen in a stone clinic at the Massachusetts General Hospital. Although the exact mechanism of stone formation is unknown, urinary infection with urea-splitting bacteria is fundamental. The enzyme urease produced by these urea-splitting bacteria causes urinary urea to split into ammonia and carbon dioxide. Hydrolysis of these products makes the urine alkaline (Fig. 1). The alkaline urine allows supersaturation of magnesium ammonium phosphate, calcium phosphate, and carbonate apatite crystals, a favorable situation for stone formation. If stone formation occurs, the urea-

splitting organisms are embedded within the interstices of the stone, thereby becoming impervious to treatment. In fact, soaking infected urinary calculi in 3 per cent iodine in absolute alcohol or antimicrobial solutions has failed to sterilize these stones in vitro.

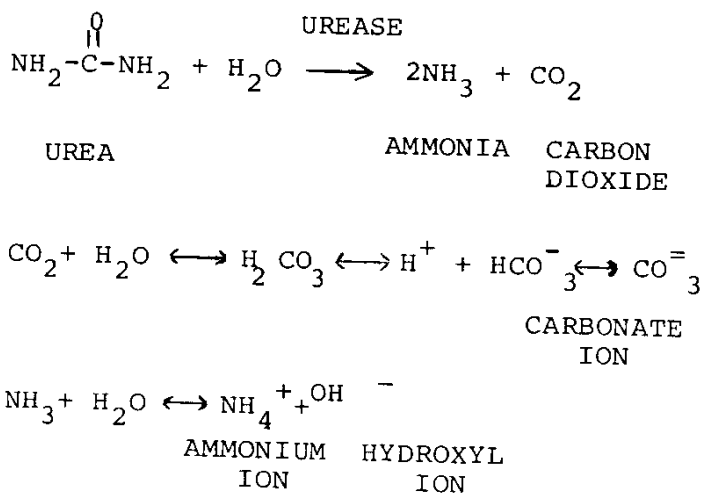

Figure 1. In the presence of the enzyme urease produced by the urea-splitting bacteria, urea forms ammonia and carbon dioxide. Hydrolysis of the cabon dioxide and ammonia causes alkalinization of the urine by producing carbonate and hydroxyl ions.

Urea-splitting bacteria found commonly in the urinary tract are Proteus, Klebsiella, Staphylococcus epidermidis, and Pseudomonas; others include Providencia, Ureaplasma urealyticum, and Enterococcus. Although staphylococcus was

reported in the 1930s and 1940s to be a ureasplitting organism commonly associated with stone formation, more recent literature has noted Proteus to be more common.
The reasons for this change in organism prevalence are unclear, but antimicrobial selection created by changing antimicrobial treatment practices may be related. In dogs, however, staphylococcus remains the most common organism associated with struvite stones. Recently, there is also evidence that Ureaplasma urealyticum may be associated with struvite stone formation. This is important in instances in which struvite formation cannot be associated with other urea-splitting organisms, because Ureaplasma urealyticum will not grow in conventional culture media. Special cultures must be taken if this organism is suspected.

Whether patients who form struvite and apatite infection stones have a metabolic abnormality in addition to their urea-splitting urinary infection is controversial. Although some investigators claim that metabolic abnormalities are related to the formation of infection stones in many patients, most of these studies have failed to distinguish carefully, among the various stone types. At least one study examining urinary excretion of calcium, magnesium, phosphours, and oxalate in patients who formed calcium phosphate and magnesium ammonium phosphate stones