CONSIDERATIONS ON THE AETIOLOGY OF URINARY CALCULI*

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In 1934 Mr. Swift Joly,[1] Senior Surgeon to St. Peter's Hospital for Stone, London, whose book on Stone is a classic, remarked in his Ramon Guitteras lecture to the American Urological Association that the incidence of urinary stones had greatly diminished in the previous century. This had occurred principally in countries where living standards had improved, and mainly amongst children and young adults. In marshalling factors he considered to be of importance in the aetiology of urinary calculi he brought out the following points.

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(A) *Geographical distribution.* Well demarcated areas exist where stones are more commonly found. These areas differ from one another geologically, climatically, and phylogenetically, and no common denominator to account for the higher incidence of urinary calculi in the populations of these localities has been found.

(B) *Diet.* Urinary stones are commoner where cereals are the staple food, and this ties in to a certain extent with the geographical distribution of stones, but by no means explains it completely. For instance, Southern China, which is a stone area, has rice as its staple diet, yet this is generally considered to have a lower

stone-forming potential than cereals such as whole-meal flour or oatmeal. At the time of this lecture, vitamin A was in vogue as an aetiological factor in urinary lithiasis; it was believed that the desquamated epithelial cells resulting from a deficiency of vitamin A formed nuclei on which urinary salts were precipitated, but this theory, attractive from a therapeutic point of view, is now largely discredited.

(C) *Disease.* 1. Immobilization leads to decalcification of the skeleton and this may give rise to the formation of renal calculi. This occurred frequently in cases of tuberculosis when immobilization was first instituted as part of the treatment of this disease, and it still occurs in patients who are paralysed by poliomyelitis and other conditions.[2]

2. Urinary stasis is a potent factor in calculus formation; the most frequent examples of this occur in hydronephrosis and in bladder-neck obstructions.

3. Urinary infection is often associated with urinary lithiasis but it is difficult to determine in most instances whether infection is the cause or the effect of the stone.

4. Hyperparathyroidism appears to be a more frequent factor in the incidence of bilateral or recurrent urinary calculi than was at one time recognized,[3-5] but reports on the association of the two conditions vary enormously.

(D) *Metabolic defects.* Certain individuals have increased urinary excretion of uric acid, cystine or xanthine amongst other products of body metabolism. These substances may precipitate to form calculi but their presence in urine does not mean that calculi will necessarily be formed.

In concluding his lecture, Swift Joly stated the theory of the mechanism of stone formation as understood at that time: 'Normal urine is a supersaturated solution of stone-forming salts held in solution by the adsorption action of the urinary colloids. Any condition which reduces the surface area of the colloids reduces the solubility of the stone-forming salts'.

In the past quarter of a century much work has been done to elucidate the causation of urinary calculi and many concepts have been refuted or have had to be modified. Most work has been to discover why stones form, but little has been done to explain how they form. The first major advance in this field was made by Randall,[6] who in 1937, reported the results of his observations on kidneys which he had laboriously and painstakingly dissected at autopsy. He discovered minute calcium plaques in the interstitial tissues of the renal papillae. Small calculi were seen arising from these plaques where they had eroded through the papillary membrane and he believed they form the nuclei on which the urinary salts precipitate. This process was thought to be a degenerative one, and no further advance was made until 1953, when Carr[7] put forward his theory on the formation of renal calculi. He examined kidneys by micro-radiographic techniques both at operation and at autopsy. The kidneys were cut in fine slices and any calculi, no matter how small, were analysed. By this technique nearly all kidneys from patients over 9 years of age were shown to have concretions large enough to be visible to the naked eye. It was demonstrated that in reality the plaque described by Randall is composed of multiple concretions aggregated together. Smaller concretions gravitate to join the larger ones at the tips of the papillae. Behind the base of a large stone smaller ones are found and, behind these, concretions of diminishing size. This explains why some patients continue to pass one stone after another from the same calyx. The kidney contains extensive lymphatic plexuses from which efferent vessels pass through the hilum along the renal vessels to the para-aortic glands. There is a ready communication between the calyces and these lymphatics as evidenced by the pyelolymphatic backflow that occasionally occurs during retrograde pyelography. It would appear that these concretions are normal structures due to the precipitation of salts, and their mechanism of excretion is through the lymphatics in a manner analagous to the removal of foreign particles from the alveoli of the lungs to the mediastinal lymph nodes. Renal calculi may arise when the drainage mechanism breaks down as a result of one of the following factors:

(*a*) Overloading of the excretory mechanism by an excessive number of microliths, as occurs in disorders of calcium metabolism.

(*b*) Impairment of lymphatic drainage caused by fibrosis consequent on inflammatory processes. Concretions become arrested, pressure causes necrosis, and seepage of urine takes place. Once this communication with the collecting system has been established a true renal calculus is born. By diffraction X-ray analysis these concretions have been found to be identical in composition with renal stones.

Urinary calculi are composed of salts and colloids and until fairly recently most attention has been focused on their salt content. With advances in colloid chemistry the urinary colloids are attracting more serious study but much remains to be done in this field. In 1946 Prien[8-10] published the first of his classical papers on the composition of urinary calculi and refuted much that had until then been accepted as fact. Crystalline substances may be analysed by chemical, optical or X-ray methods. Before Prien's work, chemical analysis had been relied on to determine the composition of urinary calculi, and this had given rise to many false presumptions. Prien employed methods which are not only more accurate in analysing crystalline materials, but which may also be employed in the analysis of minute quantities of ground material taken from different portions of the stone. Over 6,000 urinary calculi were eventually analysed by these methods and were divided into the following groups:

(*a*) 67% were pure calcium oxalate or mixtures of calcium oxalate and apatite. These are the 'hemp seed' stones which usually arise in acid sterile urine.

(*b*) 21% were phosphatic calculi, which include pure stones of triple phosphate and mixed stones composed of triple phosphate and apatite. These 'staghorn' calculi occur most often in alkaline infected urine.

(*c*) 6% were uric-acid calculi.

(*d*) 4% were cystine calculi.

(*e*) 2% were xanthine and indigo calculi.

Apatite is a complex calcium phosphate, sometimes containing carbonate. Calcium carbonate as such is not found in urinary calculi. By these studies, the theory that calculi developed on a nucleus of pus, desquamated cells or bacteria was shown to be highly improbable and it has lost ground ever since.

The hypothesis has been advanced that urine is a supersaturated solution of salts which precipitate at varying pH, thereby forming centres of crystallization which act as nuclei for the further deposition of urinary salts. The composition of urinary stones would then depend on the degree of supersaturation of the various salts and the pH of the urine at any time. With increasing alkalinity the solubility of apatite and triple phosphate diminishes markedly, while the solubility of calcium oxalate remains fairly constant. Infection influences stone formation largely through its effect on urinary pH. As was demonstrated by Prien, only about 21% of calculi are associated originally with infection. These are staghorn calculi of triple phosphates, either pure or mixed with apatite. It should be noted, however, that not all staghorn calculi are associated with infection. Pure apatite stones are not common, but when they occur, they are frequently staghorn and the urine is acid and uninfected. Analysis of a series of triple phosphate stones has shown them to be associated most frequently with the following organisms:[11] Micrococcus 38%, *B. proteus* 24%, *E. coli* 12%, Pseudomonas 12%, Aerobacter 5%, Staphylococcus 5%, Streptococcus 4%. These are the so-called 'urea-splitting' organisms, which produce ammonia and thereby render the urine alkaline. The influence of the urinary pH on stone formation has formed the basis of the treatment of urinary lithiasis in which the pH of urine is altered by various drugs. The dilution of the urinary salts by a high urinary output consequent on high fluid intake has also been advocated for many years. Unfortunately, as a result of improved methods of chemical study, serious doubt has been cast whether, in fact, the stone-forming salts in urine are in a supersaturated state.[12]

As already noted, the importance of urinary colloids has been assumed for a long time, but not until recently have suitable methods for their study been devised. Colloids, or materials in a state of colloidal suspension, are in a position between the microscopic and molecular systems. They appear to be clear to the naked eye or when viewed under the ordinary microscope. When examined under the ultra-microscope they exhibit Brownian movement. It has been estimated that 1 g. of colloidal material in urine has a surface area of approximately 5,000 square metres. One of the most important consequences of this is the unsaturation of the ions located on the surfaces of the colloidal particles, causing adsorption of ions dispersed in the surrounding medium. This is accompanied by the formation of electrical charges around

the particles, preventing their coalescence into larger aggregates. Furthermore, sedimentation of finely divided particles may be almost completely counteracted by the Brownian motion of the colloid. Certain electrolytes are effective in the precipitation of some colloids and, as concentration of urine relatively increases the proportion of electrolytes and decreases the proportion of colloids, the possibility of their precipitation is thereby greater. This may explain dehydration as a factor in stone formation.

In 1951 Butt[13] published his paper on the role of the protective urinary colloids. It is a well-known fact that urinary calculi are extremely uncommon in the Negro races irrespective of their social, economic or domiciliary status. Butt found that the colloidal activity in the urine of Negroes was much higher than in Whites. In fact the only urine from a Negro which showed low colloidal activity was from one who was found to be harbouring a renal calculus. Urine from White patients with urinary calculi displayed significantly lower colloidal activity than in the control group without stones.

As more and more work is done on this important problem, so the issues become more complex. What 25 years ago could apparently be explained by a relative simple theory has been replaced by a number of complicated physical and chemical phenomena which are difficult to correllate; and still we seem no nearer a solution to the problem. This is reflected by the fact that in a quarter of a century no real advance has been made in the prophylactic treatment of urinary calculi.

SUMMARY

The literature of the past quarter of a century on the aetiology of urinary calculi is reviewed. Although the concepts regarding the formation of urinary stones have had to be modified as a result of the advances in chemical and radiological methods of investigation, no real advance in the prophylaxis of urinary lithiasis has resulted.

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