

THE MEDICAL MANAGEMENT OF URINARY LITHIASIS

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In certain countries, the incidence of urinary calculi varies considerably. In Great Britain "stone areas" are well recognized; urinary calculi occur more frequently along the east coast, and in parts of Derbyshire and in North Wales. Joly¹ stated that in the east and southeast of France, kidney and bladder stones are prevalent but are found infrequently in Normandy. In Africa, urinary calculi frequently occur in the region of the lower but not of the upper part of Egypt. The relationship of bilharziasis to the frequency of calculi and the variation in the two regions was investigated by Pfister² who stated that the ova formed the nucleus for stones in approximately 10 per cent of the cases. Holmes and Coplan³ made an intensive study as to the prevalence of urinary calculi in the various sections of this country. From personal communications with urologists throughout the United States, they concluded that calculi occurred more frequently in southern Florida and in southern California than in other parts of the country.

In 1931 McCarrison⁴ stated that in some regions in India, stones were so prevalent among the populace that these places were designated as "stone areas," while in other localities, they were encountered but rarely. McCarrison observed the frequent occurrence of stones in regions in which there was not proper balance of food constituents in the diet.

Fujimaki⁵, under the supervision of Dr. Saiki, while investigating the vitamin content of food materials, observed the frequency of the occurrence of bladder and renal calculi in rats maintained for a long period of time on a diet either lacking or deficient in vitamin A.

Fujimaki⁵ in 1926 reported the results of his experiments upon rats fed for varying intervals of time upon a vitamin A deficient diet. He demonstrated conclusively that calculi could be formed by this means. In 1917 Osborne and Mendel⁶ found 81 cases of urinary calculi in the course of necropsy investigation of 857 rats. Of this group, 35 rats or 43 per cent had never received butter fat or any other food containing vitamin A. Upon further investigation, they noted that in every instance in which urinary calculi were found, the rats had been without an adequate amount of vitamin A at some time during the experiments.

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In addition to these experimental data, there are many clinical observations that lead us to presume a definite relationship between faulty diet and the development of urinary calculi.

According to the literature, the presence of vesical calculi in children was quite common in England and France fifty years ago. In England, Thompson⁷ collected 2583 cases of urinary calculi of which 1281 cases occurred in children under sixteen years of age. Later, Joly¹ reviewed 536 cases of urinary calculi taken from the records of St. Peter's Hospital from 1915 to 1924, and he emphasized the marked decrease in the incidence of urinary calculi in English children during recent years. The same observations have been made by Desnos and Minet⁸ in France.

In 1900, however, Assendelft⁹ reviewed 630 cases of vesical calculi seen in various Russian hospitals and reported that 77 per cent occurred in children under ten years of age, and that 86.5 per cent occurred in young persons under twenty years of age.

Such statistics show that there can be little doubt but that the occurrence of vesical calculi in children has diminished markedly in countries in which training in nutrition and hygiene has received attention. In countries where better standards of living and dietary regulations have not been emphasized, urinary calculi are still frequently observed in children.

In view of the apparent relationship existing between the improper balance of the daily diet and the development of urinary calculi, certain experiments were performed in an effort to elucidate the problem, and these investigations have been reported in previous communications.^{10,11}

Urinary calculi developed in a high proportion of albino rats which were maintained on a diet deficient in vitamin A. When this deficiency in the diet was continued for a period of 250 days, vesical calculi developed in 85 per cent of the experimental animals, and renal calculi developed in 42 per cent. The calculi thus produced were light brown, spherical, and varied in size from 0.5 to 8 mm. in diameter. They were composed chiefly of calcium phosphate, and a small amount of mucoid substance and traces of carbonates were present. Neither oxalates nor uric acid were detected.

Three constant findings which might be associated with the formation of calculi were present in these experimental animals. They were (1) keratinization of the epithelium of the genito-urinary tract; (2) the presence of infection in the genito-urinary tract; and (3) the presence of alkaninuria.

The *keratinization of the epithelium of the genito-urinary tract* was noticed after the diet had been deficient in vitamin A for a period of from eight to ten weeks. This finding was not confined to the genito-urinary tract, but involved other mucous membranes also.

This experimental finding is in accordance with the clinical observations of Wilson and Du Bois¹², who, in 1923, noticed the presence of keratinization of the epithelium of the trachea, bronchi and other mucous membranes in infants who died as the result of infection associated with vitamin A deficiency. Similar observations were made by Mori¹³, Blackfan and Wolbach¹⁴, and others.

Infection in the genito-urinary tract developed in a large proportion of rats maintained on a diet which was deficient in vitamin A for a long period of time. Infection of the bladder occurred usually after thirty days, and renal infection occurred after a period of from sixty to ninety days. When the experiment had progressed from 200 to 250 days, infection of the bladder was present in 72 per cent of the rats, and in 42 per cent of these a co-existing renal infection was present.

Streptococci, staphylococci, and mixed cultures were the organisms found most frequently.

Alkalinuria was a constant finding when the rats were maintained on the diet deficient in vitamin A. By the addition to the diet of vitamin A alone, the urine reaction became acid.

SOLUTION OF URINARY CALCULI

It has likewise been demonstrated that, by the addition to the diet of vitamin A alone, the formation of calculi can be prevented. In order to determine whether stones which already were present might be dissolved by the administration of vitamin A, observations were made on thirty rats in which bladder or renal calculi were present. Except for the addition of cod liver oil, the diet remained the same as that by which the calculi had been produced. In every instance the stones disappeared during periods which varied from 50 to 107 days.

In those rats in which a pronounced infection was present, a longer period of time was required for the solution of the calculi than was required in those animals in which an infection was not present. Thus, by experimental investigations, we proved that if white rats were maintained on a diet deficient in vitamin A for a sufficient period of time, urinary calculi could be produced; and that, by the restoration of vitamin A to the diet, these calculi could be dissolved and made to disappear.

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APPLICATION OF ABOVE FINDINGS TO CLINICAL CASES

During the past year, a selected group of patients, in whom urinary calculi were present, has been treated by means of a dietary regimen in order to ascertain whether observations made in the experimental laboratory might be applied to clinical cases.

It is obvious that all patients suffering from urinary calculi can not be treated by conservative measures. If the calculus is producing a definite obstruction and thereby causing further damage of the renal parenchyma and impairing the renal function, it may not be advisable to temporize with medical treatment when by surgical intervention the obstruction may be relieved immediately and thus prevent the further injury of the kidney tissues.

During the past year, dietary treatment has been used in the following groups of cases:

1. Those in which the patients refused to have the calculus removed by surgery;

2. Those in which calculi were present in one of the calices of the kidney, but were not producing obstruction;

3. Those in which small calculi were present in the renal pelvis but were not producing obstruction;

4. Those in which bilateral renal calculi were present but in which surgical intervention was not deemed advisable;

5. Those in which we desired to prevent the recurrence of calculi following removal of stones by operation;

6. Those in which calculi were of sufficient size to require treatment by nephrectomy;

7. Those in which calculi were passed at frequent intervals but could not be demonstrated roentgenographically;

8. Those in which elderly patients who had fractures or osteomyelitis were required to remain in a recumbent position for a long period of time.

Before a diet may be prescribed, certain urologic observations are essential. Our procedures are as follows:

A roentgenogram of the kidneys, ureters, and bladder is first made to determine whether or not a calculus is present. This is followed by an intravenous urogram to determine the location of the calculus in the kidney, and to determine whether the calculus is obstructing the passage of urine from the kidney itself. The urogram may also reveal the presence of a non-opaque stone and is of additional value in indicating an estimation of the function of each kidney.

A cystoscopic examination is then made to ascertain the function of each kidney by means of the phenosulphonephthalein

test. Samples of the urine from each kidney and from the bladder are taken for the determination of the hydrogen concentration, bacteriologic culture and routine study.

Blood chemistry studies are also of utmost importance. Determinations of blood urea, creatinin, sugar, uric acid, calcium, phosphorus and phosphatase are made in each case. These studies are of extreme importance in cases in which calculi of the uric acid type are present and also in those in which changes in the blood calcium and blood phosphorus may indicate the presence of parathyroid disturbances.

If calculi have been passed previously and the specimen is available, it is examined in our chemistry laboratory.

The patient is hospitalized for a period of from three to seven days in order that he may grasp the full significance of the diet, that he may have a thorough understanding of the principles involved, and that he may be instructed regarding the routine to be followed after he has left the hospital. Our dietitian visits the patient daily to explain the details of the diet and to furnish and discuss sample menus. With this instruction, the patient, within a short period of time, can prepare his meals with a remarkable degree of accuracy.

As a general rule, in the absence of infection, the high vitamin A acid-ash diet is sufficient to render the reaction of the urine strongly acid; but in patients in whom an infection such as the proteus organism is present, an acidifying agent must be added to the prescribed diet. This is usually given in the form of sodium acid phosphate in capsules or ammonium chloride in enteric coated tablets. It is important that the pH of the urine be kept between 5 and 5.4, and the medication necessary to maintain this level can be determined while the patient is in the hospital. The pH determinations are made daily under similar conditions. The first morning specimen of urine is discarded and the specimen voided just before breakfast is sent to the laboratory for examination. By this routine the effect of awakening respiratory changes on the pH of the urine are eliminated and the effect of the alkaline tide is avoided.

Just as the blood sugar determination is of value in the management of a patient with diabetes, the determination of the pH of the urine is of value in the management of a patient with urinary lithiasis. In each case, also, the patient must rigidly follow his prescribed diet. The patient is instructed concerning the method for making his own pH determination and a very simple, inexpensive apparatus* may be procured for this purpose. The

*We recommend the apparatus manufactured by the La Motte Chemical Products Company.

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patient makes the determination daily and presents a chart to his physician at regular intervals. In this way the physician can determine whether the dosage of sodium acid phosphate or of ammonium chloride must be increased or decreased. Consultation and advice from the family physician is required frequently and the patient should report for observation at regular intervals. The diet and medication must be followed exactly without any alteration, unless the physician advises some change.

CLINICAL OBSERVATIONS

Since these clinical investigations have been undertaken, it has been a routine procedure at the Cleveland Clinic during the past two years to prescribe an acid-ash diet high in vitamin A in all cases in which urinary calculi have been removed. Other therapeutic measures such as eradication of renal infection, or elimination of stasis in the urinary tract have not been neglected.

During this time, only one patient has had a recurrent calculus following the removal of a stone from the lower portion of the right ureter. An associated infection and hydronephrosis of the right kidney were also present in this case. Following the operation, the patient neither followed instructions nor reported for post-operative therapy, and one year later a large calculus was present in the pelvis of the right kidney.

From our observations thus far, we are most optimistic regarding the efficacy of this regimen as a prophylactic measure against the recurrence of urinary calculi.

END RESULTS

At the present time, we have a series of twenty-one cases in which renal calculi have undergone complete solution. In this series of cases, stones have been present which varied in size from a small calculus in a calyx of the kidney to large stones in the kidney pelvis.

In a larger group of patients who have been placed on this dietary regimen, there has been a definite diminution in the size of the calculi, but insufficient time has elapsed for complete disintegration to take place.

In a group of 11 patients, all of whom happen to be physicians, the histories state that calculi had been passed at frequent intervals. After the institution of medical treatment, all of these patients have been free from symptoms for a period of 18 months. Although this series of cases is too small, and insufficient time has elapsed to permit definite conclusions to be drawn regarding the clinical application of this method, the outlook for the med-

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ical treatment of urinary calculi seems exceedingly hopeful in selected cases in which urinary calculi are present.

REFERENCES

1. Joly, J. Swift: Stone and calculous disease of the urinary organs, St. Louis, C. V. Mosby Co., pp. 79, 1931.
2. Pfister: cited by Joly, op. cit. 1.
3. Holmes, R. J. and Coplan, M. M.: A study of the geographic incidence of urolithiasis with consideration of etiological factors, *J. Urol.*, 23:477-489, (April) 1930.
4. McCarrison, R.: The experimental prevention of stone in the bladder in rats, *Brit. M. J.*, 2:159-160, (July 30) 1927.
5. Fujimaki, Y.: Formation of urinary and bile duct calculi in animals fed on experimental rations, note on treatment, *Japan M. World*, 6:29-35, (February) 1926.
6. Osborne, T. B. and Mendel, L. B.: The incidence of phosphatic urinary calculi in rats fed on experimental rations, *J.A.M.A.*, 69:32-33, (July 17) 1917.
7. Thompson: cited by Joly, op. cit. 1, pp. 89.
8. Desnos, E. and Minet, H.: Calculs de la Vessie, *Encyclopedie francais d'Urologie*, 4:294-295, 1914.
9. Assendelft, E.: Bericht ueber 630 stationar behandelte Steinkranke, *Arch. f. klin. Chir.*, 60:669-686, 1900.
10. Higgins, C. C.: The experimental production of urinary calculi, *J. Urol.*, 29:157-185, (February) 1933.
11. Higgins, C. C.: The experimental production of urinary calculi in rats, *Urol. and Cutan. Rev.*, 38:33-39, (January) 1934.
12. Wilson, J. R. and Du Bois, R. O.: Keratomalacia in infant, with post-mortem examination, *Am. J. Dis. Child.*, 26:431-446, (November) 1923.
13. Mori, D.: Changes in para-ocular glands which follow the administration of diets low in fat-soluble A; effect of same diets on salivary glands and mucosa of larynx and trachea, *Bull. Johns Hopkins Hosp.*, 33:357-359, (October) 1922.
14. Blackfan, K. D. and Wolbach, S. B.: Vitamin A deficiency in infants; clinical and pathological study, *J. Pediatrics*, 3:679-706, (November) 1933.