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The Etiology Of Urinary Calculi

Present day theories

K. T. Maddy, '45

Much remains unknown as to the complete etiology of urinary calculi. Calculi are not a disease but a symptom. Sound therapeutics must be based upon an accurate diagnosis of the etiological agent.

Information in this report will not be restricted to the veterinary field. Material relative to human medicine and the fields of experimental animals will be included so as to give possible clues to etiological factors as yet thought unimportant in the veterinary field.

Altering Factors

It has been suggested that some time in the future a single fundamental cause will be determined that allows for the stone formation. The composition of the stone will thus be seen to be altered by secondary factors.

Heredity, race, sex and age have a bearing upon the occurrence of calculi in humans. Whole families have been known to develop calculi. Urinary calculi were found by Schenken, Burns and McCord in 4 per cent of the males and 5 per cent of the females of a control strain of inbred mice indicating hereditary predisposition. (Incidentally, following treatment with α-estradiol benzoate, calculi were found in 43 per cent of the males and 3 per cent of the females of other mice of the same inbred strain. Both metabolic and inflammatory factors were responsible for the calculi formation. The metabolic factor was related to a derangement in the calcium metabolism. The inflammatory factor seemed to be related to hyperplasia and desquamation of the genito-urinary tract epithelium and infection and inflammation of the urinary tract epithelium.) Incidence of kidney stones in Dalmatian dogs has been found to be much greater than in any other breed. There is an inherited predisposition to this.

As a distinct racial characteristic, Negroes of all parts of the world are free of urinary calculi. Urinary calculi in the human are more commonly found in the male. This also holds true for the lower animals. As to age, one investigator in the field of human medicine determined the causes in early life to be due to continued dietetic error. In midlife, the causes were determined to be largely of an inflammatory nature; and in late life, the calculi usually developed due to an obstruction to outflow from the bladder. In old animals there is a lessening of the use of mineral for bone formation, and an increasing amount is eliminated thus predisposing the animal to lithiasis.

Other Factors

Geographical and climatic influences are of some importance. Cattle raised in areas in which green food is not readily available get dry and bulky feeds. As a result an excess of lime and a lack of phosphates tend to produce calculi. In the United States the greatest incidence of calculi in man has been found to be in Southern California and Southern Florida. In certain “stone areas” of various parts of the world the incidence of this condition is quite high.

The formation of a calculus is dependent upon processes which alter the state of the urine. The mineral salts may exist in a
supersaturated state. This state is maintained by the protective action of colloids. Disturbances in the chemical and physical nature of the colloid may reduce or completely remove the protective action allowing the salts to precipitate. In some cases the mere alteration of the colloidal state may act as the nucleus for subsequent deposition of minerals. Randall\(^2\) states that renal calculus formation is dependent upon a preexisting renal lesion. There is a slow crystallization of urinary salts upon a lesion of the renal papilla. The calculus then forms around this original deposit. At other times the nucleus may be desquamated epithelial cells, fibrin, blood, clumps of bacteria, or mucus.

**Formation**

Once the process is begun, the conditions for its maintenance is continued for the precipitated mass furnishes a surface for the continued absorption of salts.

The calculus itself serves as a foreign body and further irritates the urinary passage producing more pathologic changes which predispose the urinary system to multiple urinary lithiasis.

Water with a high mineral content has been incriminated as a factor. The drinking of small quantities of water due to a lack of water due to a drought or freeze or due to a lack of desire if the water is too cold has been pointed out by many as causative factors in cattle and sheep. In sheep an excess of calcium or an excess of magnesium in the water has been shown to have caused calculus formation. The alkalizing effect of the carbonates is also a factor\(^5\).

Sheep and cattle fed on roots and fodder grown on land heavily dressed with artificial manure or grazed on fields top-dressed with lime or basic slag frequently suffer from urinary lithiasis.

An excess of calcium and an excess of phosphorus have been found in clinical cases\(^7\). These may gain access to the diet through the feeding of a ration too high in minerals due to the high mineral content of the soil on which the food is being grown or due to the presence of too great a percentage of the ration being made up of a mineral supplement.

Beeson and Beveredge\(^1,7\) state that it is an unbalance of the calcium-phosphorus ratio that predisposes animals to the condition. Bran, wheat and cottonseed cake have calcium-phosphorus ratios of 1:10, 1:14, and 1:6, respectively. Potatoes and mangels have calcium-phosphorus ratios of 1:5 and 1:3, respectively; these feeds also produce calculi.

Cunningham\(^9\) reports that a deficiency of magnesium causes urinary calculi in rats. Steers fed silo grain, cottonseed meal and sargo silage in a Texas experiment were said to have developed calculi due to the high content of magnesium in the ration\(^26\). With regard to nutrition of the sheep, Eveleth and Milken\(^11\) report that diets high in magnesium and low in calcium are a factor in the production of urinary lithiasis.

A too large proportion of nitrogenous material in the ration, especially if accompanied by a lack of exercise, is said by some to favor the condition. Because of this feeder sheep and cattle being fed cake, grains and bran are often said to be affected. The feeding of sugar beets has been followed by a considerable incidence of this condition; the exact cause is as yet undetermined.

The deposition of urinary salts depends to a considerable degree upon reaction. Calculi consisting of uric acid, oxalate and systin are most commonly found in acid urine. Phosphate and carbonate calculi form in alkaline urins. Concretions of the latter type are most commonly found in the urine of cattle and sheep. Ketogenic and acid-ash diets are believed by Higgins\(^17\) to have actually dissolved calculi in rats and in man. Some feeders believe the calculi may be dissolved in steers by withholding feed for some time. There may be something to this theory since an animal living on its own tissues has an acid urine.

**Exercise**

In humans, lack of exercise due to recumbency stasis and bone decalcification produces calculi. There is only one report of value of this occurring in sheep. Renal rickets of children produce a chronic nephritis\(^8\). A large amount of calcium...
passes through the kidney, resulting in concretion formation. Renal calculi frequently follow fractures of the spine and pelvis.

In man a deficiency of renal function stimulates hyperfunction and hyperplasia of the parathyroid glands, the actual stimulating factor being some upset in the calcium-phosphorus balance due to the renal deficiency. As a result there is an excess of calcium and a deficiency of magnesium in the circulation. In severe cases, osteitis fibrosa cystica, in adults, or renal rickets in children is produced. Hyperparathyroidism itself produces renal lesions of a distinctive type which results in renal failure. Disturbance in calcium metabolism is the main cause of damage in the kidney, though other factors also play a part in the development of renal disease. Calcium deposits causing tubular obstruction in the kidney are a characteristic feature.

Little work has been done on hyperparathyroidism in the lower animals. Such a study should also consider the effect of other factors such as a vitamin deficiency, mineral unbalance and diet on the parathyroids themselves.

**Experimental Tests**

In order to determine whether or not disfunctions of liver and thyroid play a role in urolithiasis, Erickson and Morrison performed liver and thyroid function tests upon 59 individuals who had or had had renal calculi. Thirty-four per cent of these patients showed evidence of liver disfunction. Of these 61 per cent showed an abnormal basal metabolic rate and 54 per cent hypercholesteremia. Of 17 patients with active urinary symptoms, 59 per cent showed liver disfunction, whereas of 42 patients without urinary symptoms, only 24 per cent showed liver disfunction. Liver and thyroid disfunctions are evidently concerned with the development of certain types of calculi. It is quite likely that this may also be a factor in domestic animals although as yet it has not been reported.

There have been a number of reports that avitaminosis A is a factor. In rats and guinea pigs calculus formation has been attributed to epithelial changes in the renal pelvis and ureters. It consists of a metaplasia of the normal uroepithelium to stratified squamous epithelium. Large plaques of cells break loose and act as niduses for calcium carbonate deposition. There have been a number of reports in the human literature of similar effects.

**Vitamin A**

The fact that calculi in cattle and sheep are most frequently seen in the winter may be an argument for a vitamin A deficiency as being an etiological agent, but one must also consider the possibility of a lack of water. The experience of the sheep feeder that experienced severe losses after removing alfalfa hay from the ration may be considered, but one should also consider the increase in phosphates in this case. Calculi are quite prevalent in the drylands of eastern Colorado where avitaminosis A is quite prevalent in the rations. However, when alfalfa hay is fed in abundance, the calculi still develop in the cattle and sheep.

Vitamin D also plays a part. When it is deficient, it upsets the calcium-phosphorus ratio and thus predisposes the urinary system to eliminatory troubles. A vitamin D excess has been accredited with producing concretions in the urinary tract of rats and guinea pigs.

In man, according to Bidyabhed, bladder stones induced by an excess of vitamin D when vitamin A is deficient, occur in the Thailand “stone areas” where practically no source of vitamin D exists in the diet. The excess vitamin D is elaborated by the sunlight upon the scantily clad bodies, especially of children.

In recent years there have been a few reports of concretions following the administration of various sulfonamides (sulfanilamide, sulfathiazole and sulfa-pyradine), usually in excessive amounts. They have been experimentally produced in rats, rabbits and monkeys. They have occurred in man. When analyzed, they have been found to be made up of a derivative of the sulfonamide used or merely of calcium carbonate. In the latter case, the elimination of the sulfonamide caused...
a nephritis which predisposed the urinary tract to nephrolithiasis.

Infection is the most serious complication of upper urinary tract lithiasis. The possibility of infection reaching the urinary tract is great considering the fact that the urinary organs are bathed by great quantities of urine, a fluid which serves the important purpose of eliminating waste products and bacteria from the body. Infection causes a rapid destruction of kidney tissue which soon hinders its functional ability.

Bacillary and cocci infections are most commonly found in connection with calculi. Eschericia coli and Staphylococci are the types most frequently found. Chronic kidney infections often occur as complications of upper respiratory tract infections, septic wounds and various cutaneous infections. Although urine may show little evidence of kidney infection, most investigators agree as to its presence. True bacterial calculi develop entirely of bacteria or they may merely act as nuclei for depositions of minerals.

The relation of infection to calculi in dogs was shown by Rosenow23. The teeth of a group of normal dogs were artificially infected with cultures from teeth, tonsils and urine of human patients suffering from nephrolithiasis. Calculi or lesions of the medulla of the kidney were produced in 87 per cent of the dogs. These calculi or lesions were similar in physical properties and chemical characteristics to those present in the men from whom the infecting organisms were obtained.

Colloids

The crystalline matter which is normally held in solution by true colloids normally existing in the urine is an additional etiological factor. These colloids have a direct effect on the highly insoluble urinary substances which are of a protective nature. When these colloids are altered, agglutination and precipitation of the urinary substances takes place. A change in the amounts of the colloids or crystalline substances upsets this balance and precipitation results, with the materials being thrown down are ready for other factors to utilize in the formation of a stone. Colon bacilli and other organisms cause precipitation of the normal colloids of the urine.

Staphylococci in the urine split urea, causing an increase of ammonia, resulting in an alkaline urine which bears directly upon the formation of calculi.

In experiments with rabbits, Davalos11 came to the conclusion that bacterial infection alone could not be an etiological factor without some other irritation being present. Hager and McGath15 also came to this conclusion.

It has been suggested that in a very few cases a purely local disturbance of the kidney may be a factor. The action of uric acid upon renal tissue may lead to necrosis, thus providing niduses for calculus formation.

Grossman14 as attempted to prove the theory that the increase of lithiasis of certain parts of central Europe in man is due to traumatization and increased inhalation of motor car exhaust gases. In a controlled experiment, 6 of 28 rats that had been shaken 5 to 7 minutes for 2 to 3 times per week for 120 days developed calculi. Five of the 28 rats exposed to motor gases for 15 to 30 minutes per days, 2 to 3 times per week for 120 days showed calculus formation.

Cystinuria, oxaluria and xanthinuria sometimes produce calculi in man, and there are a few reports of occurrences in animals.

After surgical removal of calculi from 200 cases, Higgins16 as stated that the

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etiological factor causing recurrence has been infection in 80 per cent of the cases. Vitamin A deficiency was found of next importance, with hyperparathyroidism being of next importance. In cattle and sheep, a continued unbalance of minerals in the diet seems to be the most important factor related to recurrence of the condition.

In considering the etiological factors presented, it can be seen that the problem is quite complicated as a whole and that the individual case may also be relatively complicated. It appears that an unbalance of minerals is the most important factor whether it is due to excess of calcium, excess phosphorus, excess magnesium, the alkalizing effect of the carbonates, or due to an upset ratio of this minerals to each other. The causes of this are very numerous and have already been pointed out.

Deficiencies

Vitamin A deficiency may play a part but sufficient evidence does not seem to be available to definitely incriminate it. Infection is of some importance. Heredity is of some importance especially in the case of the Dalmatian dog. Bone diseases, upset in liver function, upset in thyroid function, hyperparathyroidism, avitaminosis D, and vitamin D excess are probably of quite minor importance as are cystinura, oxaluria, xanthinuria, the traumatic, toxic and the locally disturbing factors.

BIBLIOGRAPHY


Research work at Wisconsin Experiment Station has shown that vitamin deficiency is the principal cause of calf scours. Paul H. Phillips, biochemist at that station, suggests as a preventive a vitamin capsule containing 5,000 International units of vitamin A, 50 milligrams of Niacin, 250 milligrams of ascorbic acid and 200 units of vitamin D.

Veterinary supply houses are now stocking a capsule with all of the above that will preserve potency of the materials for a year or more at room temperature.

Phillips recommends 2 capsules a day as a treatment in acute cases and one as a preventive in suspected cases where trouble has been encountered before. This must be combined with cleanliness in order to gain any benefit.