# LITHOGENESIS AND HYPOVITAMINOSIS

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In earlier times, prior to one hundred years ago, lithiasis, particularly of renal origin, was much more prevalent than today. It was in fact the major cause of surgical intervention at that time. As evidence of the former medical prominence of this subject there are some eighty words with the prefix "lith" in medical dictionaries. During the last century, however, there has been in most countries a general decline in the incidence of urinary calculi, which has been noted clinically by some of our older urologists even in the span of their own experience. In America, where calculous disease has always been less prevalent than in Europe, the decline in incidence has been particularly noticeable.

The incidence of lithiasis is still known to be unusually high in certain countries, notably India and Egypt, which would seem to suggest a nutritional etiology. Additional "stone areas" have been reported in southern China (Kwangsi Province), Indo-China, Siam, Palestine, Dalmatia, Mesopotamia, and the valley of the Volga in Russia. Clinicians in these areas have attributed the high "stone" incidence to impoverished diets. Kwangsi Province is the poorest part of China. The diet there consists mostly of boiled rice (polished); whereas fruit, vegetables, milk and meat are only occasionally included. It is significant that most of these areas are districts where a form of civilization has existed since remotest historical time, and where antiquated sanitation, faulty personal hygiene and poor nutrition are still the rule. Recently, in a nutritional survey of Newfoundland (1), the prevalence of renal stone is referred to as possibly related to faulty diet. During the previous century urinary lithiasis was a disease of infants and young children mostly; whereas now the generally lessened incidence involves mostly the older age groups. A possible explanation for these features of incidence will be offered later.

Joly (2) states "I believe the hypothesis that stone is a deficiency disease is the most plausible and probable that has yet been advanced. It explains not only all the principal features of the condition today, but also the changes in incidence during the past years. I believe that vitamin starvation acts primarily on the renal epithelium and through it on the colloidal mechanism of the urine; also that once this mechanism is deranged, stone formation must follow as a direct result of the laws of physical chemistry."

Aside from clinical observations, experimental work on laboratory animals suggests a relationship between urinary calculi and dietary deficiency. Osborne and Mendel (3), in 1917, found that urinary calculi, both vesical and renal, could be produced in rats on a diet deficient in vitamin A. (It should be recognized, however, that vitamin A was the principal vitamin known at that time.) In 1926, Fujimaki (4) found that rats on a vitamin A deficient diet developed phosphate stones in the urin-

*Reprinted from* MEDICAL RECORD *Vol. 159, No. 7, Whole No. 2762, July 1946.*

ary tract and cholesterol stones in the bile ducts. In 1931, McCarrison (5) demonstrated the keratinizing effect of vitamin A deficiency on the epithelium of the urinary tract. He believed that desquamation of this keratinized epithelium might provide the nuclei for calculi. He also found that if vitamin C were also removed from the diet renal calculi were more likely to be produced. Hughes (6), however, in 1928, did not find calculi in hogs reared on a mixed diet lacking in vitamin A, although other symptoms of vitamin A deficiency were present. Furthermore, Abderhalden (7), in 1931, reports an unusually large number of urinary calculi in rats fed on milk and rice, a diet apparently not lacking in vitamin A. It has also been noted that calculi are found frequently in the urinary tracts of cattle and sheep feeding on alfalfa, grass and other green pasturage, which obviously would contain an ample supply of vitamin A.

Accordingly it would appear that the literature regarding experimental production of urinary calculi is still in a state of flux, and lacking conclusive evidence regarding the dietary factors responsible for the disease in man.

The immediate predisposing cause of urinary calculi is undoubtedly the presence of crystalline material in the urine. This usually consists of uric acid, calcium oxylate, carbonate and phosphate, the latter generally predominating. The crystalline concretions are laid down in an albuminous matrix around a nucleus of organic material such as blood clots or epithelial shreds. Once the nucleus is formed it is surrounded by mucopurulent albuminous material, which is stirred up by its presence; and thus conditions favorable to the deposition of new layers of stone are initiated.

Since the time of Pliny even to the present day, search has been made for something, which, taken orally, might be capable of dissolving urinary calculi or preventing their formation. Pliny's remedy was ashes of snail shells. The most serious efforts of modern times in this direction were those of Roberts (8) and Garrod (9) of England, the former using long courses of potassium citrate or bicarbonate, and the latter employing the same salts of lithium in smaller doses. Keyes (10) reports favorable litholytic effects from the habitual use of apple cider.

In my own clinical experience I believe I have discovered the secret of the beneficient effect of apple cider in the dissolution and prevention of renal calculi—its content of vitamin C (ascorbic acid). In many of my cases I have observed that a cloudy urine, heavy with phosphates and epithelium, is generally associated with a low vitamin C status, as determined by titration with dichlorphenal-indophenol (Hoffmann-La Roche); and that as soon as corrective administration of the vitamin effects a normal ascorbic acid level the crystalline and organic sediment disappears like magic from the urine. I have found that this change can usually be brought about in a matter of hours by large doses of the vitamin—500 to 2000 mg.—oral or parenteral. Subsequently maintenance doses of 100 to 300 mg., daily, are usually sufficient to keep the urine free from these deposits. It would thus appear that deficiency of vitamin C, which is the predominating dietary defect in the various "stone areas", may provide the determining factor in urinary lithogenesis.

The exact nature of the biochemical mechanism involved in this rapid physiochemical transformation of the renal excretion is not yet determined. It is most likely to be caused by metabolic changes effected catalytically by the vitamin, since it is inconceivable that such small amounts of ascorbic acid eliminated in the urine, usually about one mg. per ounce, could effect dissolution of the crystalline sediment by any resultant change in the pH status of the urine. To check this possibility vitamin C was added *in vitro* to phosphatic urine in quantity much larger than the amount found normally present under optimal intake, but with no apparent dissolution of the calcareous precipitate.

As further evidence that this associated biochemical change is metabolic or systemic and not merely local in the urinary tract I have made the further observation that calcareous incrustation at the inner canthus of the eye and on the cornea, and salivary or dental calculi (deposit of tartar on the teeth or dentures) are also associated with C hypovitaminosis. The ocular calcareous deposits I find may be cleared away in a few days by correction of vitamin C status, and I find also that dental calculus, which lays the foundation for so much dental havoc, can be quickly suppressed and prevented by an adequate intake of vitamin C.

My attention was first called to the possibility of this correlation by frequent spontaneous reports from my patients to the effect that since adopting the regimen which I frequently prescribe to correct basic nutritional deficiency they have noticed that their teeth or dentures feel much smoother to their tongue and that their dentists had noted a marked reduction in dental tartar. Other patients had reported an unusual clarity of the urine following adoption of the regimen. In another instance a nurse in charge of a rest home where one of my patients was in residence noted an unusual freedom from calcareous deposits on the urinary utensils used by this patient, in contrast with the heavy deposits on the urinary vessels used by the other inmates. The dietary regimen referred to above included all the vitamin B complex factors as well as a liberal intake of vitamin C. By trial and error and process of elimination I finally found that the vitamin C component of the regimen was the major factor in bringing about not only freedom from dental deposits of salivary calculus, but complete and prompt elimination of precipitates of calcium phosphates from the urine. I found also that continued use of a liberal vitamin C intake resulted in rapid clearing of epithelium and other organic detritus from the urine, and in the mouth a marked reduction in gingival erosions and epithelial desquamation. I have now observed these effects in so

many cases that the correlation between C hypovitaminosis and lithogenesis in general seems indubitable. Desquamated epithelium and amorphous or crystalline phosphates are so frequently observed in the urine of apparently healthy subjects, and dental deposits of salivary calculi are so widespread that we have been inclined to regard these conditions as normal. And this opens up the wider concept that calculi found in many other parts of the body, as in the biliary tract (gallstones), the pancreas, the tonsillar crypts, the appendix vermiformis, the conjunctiva (in the ducts of the Meibomian glands), the nasal tract (rhinoliths), the mammary glands, the uterus, the ovaries, the testicles, the prostate gland, the blood (hemoliths), the gastrointestinal tract (gastroliths and enteroliths), and even the calcareous deposits in arteriosclerosis and in arthritic and gouty tophi, may all have a similar nutritional deficiency background. In other words, we may now have the basic etiological solution of the so-called "diathetic lithiasis", which was formerly thought to be constitutionally hereditary.

There are two ways in which C hypovitaminosis may predispose to lithogenesis aside from the metabolic disturbance as manifested in the increased deposition of calcium phosphate in the various body fluids. In the first place a lack of vitamin C definitely tends to fragility of the perivascular, submucous and subcutaneous connective tissues as a result of the liquefaction of the collagenous intellecular cement substance. This condition is manifested clinically by easy bruising of the tissues generally, due to rupture of the small blood vessels. In the mouth the gums become tender and subject to hemorrhagic abrasions in brushing the teeth or by friction of dentures. Desquamation of the buccal mucosa becomes accentuated. This material, augmented by food remnants, forms a necrotic detritus, which, when deposited in the interdental spaces provides an excellent nidus for ubiquitous microorganisms, pyogenic and mycelial. This conglomerate supplies the matrix or nucleus for the deposition of calcareous material (tartar), which, in turn, sets up inflammatory changes in the gingival tissues, these having lost their natural resistance to infectious invasion by reason of the C hypovitaminotic breakdown in the connective supporting tissue. Thus a vicious circle is established, accentuating calculus formation and gingivitis, and leading to pyorrhea and serious destructive periodontal lesions.

In the genitourinary tract the same fragility of tissues, consequent to C hypovitaminosis, is manifested by increased desquamation of epithelium and vulnerability of the mucosa. The resulting detritus provides the nuclei for lithogenesis, renal and vesical. The superimposed mechanical irritation by the calculi predisposes to infectious invasion by otherwise innocuous organisms such as the ubiquitous staphylococcus, streptococcus and colon bacilli. The resultant inflammatory exudate and the swing of the urinary pH to the alkaline side favor further lithogenesis, and thus again the vicious circle is brought into action.

In further confirmation of the hypothesis of C hypovitaminosis as the basic etiological factor in lithogenesis the following clinical data seem pertinent: Agnew (11), reporting on the dental condition of the Tibetans and people of the west China border, states that heavy deposits of salivary calculi, sometimes sufficient to mask the dental formation, are very common. He further states that the diet of these people is very deficient in vitamin C, consisting mostly of butter, tea and barley flour or rice. Very scant supplies of fresh fruits are available, and then only seasonally. Arkle (12, 13), reporting on dental conditions of the Indians of James Bay and Labrador, in northeastern Canada, states that few mouths were without calculus formation. Even the very young children were affected. The diet of these tribes consisted mostly of white flour biscuits, oatmeal, lard, fish, wild game, tea and sugar. Their supply of fresh fruits and vegetables was limited to seasonal berries, sprouting buds and moss, the latter being obtained from the stomachs of caribou and other wild animals. Such a diet would be obviously deficient in vitamin C. MacGregor and Simpson (14) have observed that children with celiac disease, on special diet of high protein and low fat content with little or no fresh fruit or vegetables, showed rapid dental calculus formation. The diet in these cases was predominently deficient in vitamin C. Adamson et al. (1), in a recent survey of nutritional conditions in Newfoundland, report the concurrent widespread prevalence of urinary calculi and periodontal disease; while Goodwin (15) reports heavy deposits of dental calculi as a prominent feature of periodontal disease in Newfoundland. According to this survey, deficiency of vitamin C is the major nutritional defect in Newfoundland.

H. E. James (16) reports an incidence of almost one hundred percent of cholecystitis and a correspondingly high incidence of cholelithiasis among the Tibetans and Szechwanese. The diet of these peoples consists mostly of butter, tea, barley flour and rice with little or no fresh fruits or vegetables, —obviously very deficient in vitamin C. The high fat content of this diet, the butter being used in large quantity, probably contributes to the predominence of biliary calculi; while the increased acidity of the urine, due to increased absorption of fatty acids, may prevent an otherwise high incidence of urinary calculi. As stated by Agnew, these people are subject to heavy formation of dental calculus. In South China, where rice is the staple diet and butter less in use, the incidence of both urinary and dental calculus is very high. Shaw et al (17), in a recent report on "acute and chronic ascorbic acid deficiency in the Rhesus monkey", note the early appearance of a "white sticky residue" on the teeth, which progressed to heavy deposits of dental tartar.

On the basis of the hypothesis of vitamin C deficiency as the major etiological factor in lithogenesis, the marked reduction in the incidence of urinary calculi in the last century, and the shift in age incidence from infancy and childhood to the older age

groups, could be explained by the more widespread distribution and increased supply of citrus and other fruits, and by the advances in modern pediatric nutrition whereby citrus and other fruit juices rich in vitamin C are included in the diet of early infancy. This dietary revolution has not been adopted so freely by the older age groups.

## Summary

Clinical observations and laboratory experimentation by the author on the effect of administration of vitamin C in altering the physiochemical properties of the urine and other body fluids, principally in eliminating deposition of phosphates, has led to the hypothesis of C hypovitaminosis as the basic etiological factor in lithogenesis in general—urinary, salivary, biliary, etc. A correlated study of the literature regarding the history of calculous disease and the changed trends in nutrition, particularly in the matter of vitamin C intake, lends support to this hypothesis.

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16 GOTHIC AVENUE.