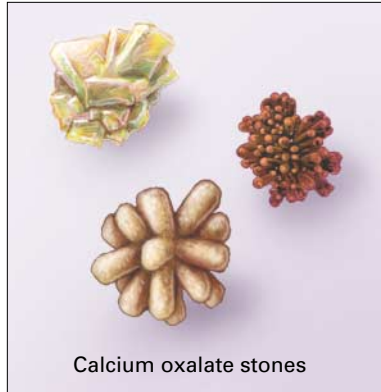




This Week in the Journal

January 10, 2002



Dietary Approaches to Prevention of Recurrent Kidney Stones

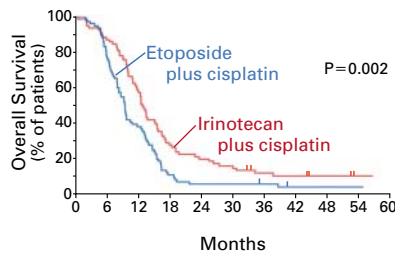
This randomized trial, involving men with recurrent calcium oxalate stones and hypercalciuria, compared the effectiveness of a low-calcium diet with one containing a normal amount of calcium but restricted amounts of animal protein and salt. After five years, only 12 of the 60 men on the diet with normal calcium, low animal protein, and low salt had recurrent stones, as compared with 23 of the 60 men on the low-calcium diet (relative risk of a recurrence among those on the normal-calcium, low-protein, low-salt diet, 0.49; 95 percent confidence interval, 0.24 to 0.98; $P=0.04$).

Restriction of both animal-protein and salt intake, coupled with normal calcium intake, is more effective than restriction of calcium intake in preventing recurrent nephrolithiasis.

see page 77 (perspective, page 74; editorial, page 124)

Irinotecan plus Cisplatin for Metastatic Small-Cell Lung Cancer

In this randomized trial, irinotecan plus cisplatin was compared with etoposide plus cisplatin for the treatment of metastatic small-cell lung cancer. The trial was stopped early because of a significant difference in survival, in favor of irinotecan plus cisplatin.



With the best current treatment, only 10 percent of patients with metastatic small-cell lung cancer survive for two years after receiving the diagnosis. In this study from Japan, the two-year survival among such patients who were treated with irinotecan plus cisplatin was approximately 20 percent. This small but important improvement could change the management of metastatic small-cell lung cancer.

see page 85 (editorial, page 126)

“None of four chemotherapy regimens offered a significant advantage over the others.”

Four Chemotherapy Regimens for Advanced Non–Small-Cell Lung Cancer

Four combinations of chemotherapy were compared in patients with advanced non–small-cell lung cancer. No one regimen appeared to be superior to the others. The overall survival rate at one year was 33 percent. The regimen of carboplatin plus paclitaxel was less toxic than the other regimens.

Non–small-cell lung cancer causes about one third of all deaths due to cancer. Patients with the advanced stage of the disease have a very poor prognosis; they often receive no chemotherapy and die in less than six months. Treatment that allows one third of patients to live for a year is therefore worth considering.

see page 92 (editorial, page 126)

PERSPECTIVE

Diet and Kidney Stones

Kidney and bladder stones cause excruciating pain, tend to recur, and are distressingly common. Roughly 10 percent of persons in the United States will have at least one stone in the course of their lives. The disorder has a long history. Stones have been found in Egyptian mummies and have been mentioned in histories of Babylonia and ancient China. Even the word “lithotomy” is from ancient Greek. Physicians at the medical school at Knidos, in Asia Minor, described renal colic with great clarity around the fifth century B.C. Indeed, the Hippocratic Oath specifically mentions stones. In recent years, much has been learned about renal and urinary tract stones, their causes, and their management. Despite our im-

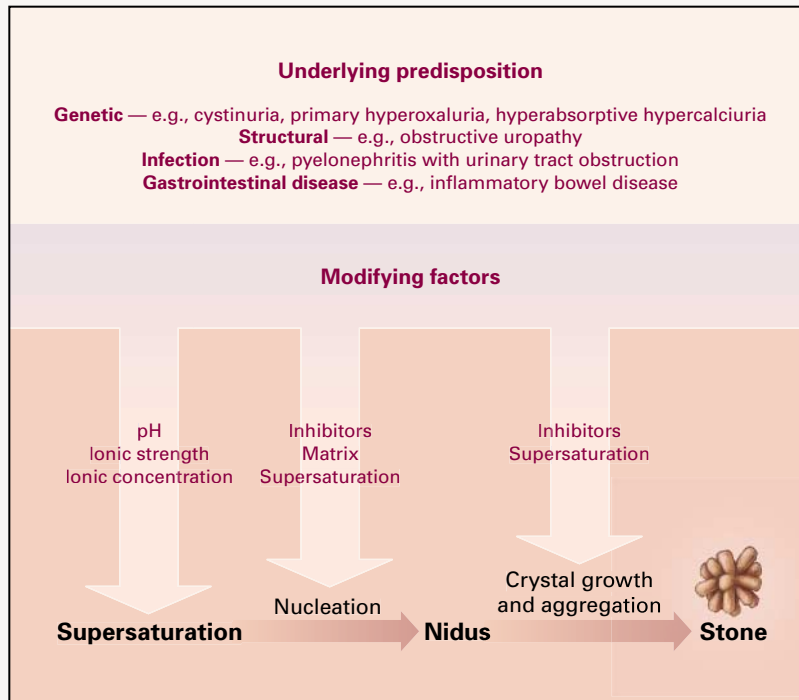


Figure 1. Formation of a Stone.

For a stone to form, there must be supersaturation, which, in the presence of a nidus, can lead to aggregation and growth of crystals. Both underlying predisposing factors and modifying factors can increase the likelihood of stone formation.



Inactivating *GNASI* Mutations in Progressive Osseous Heteroplasia

The rare disease progressive osseous heteroplasia (POH) is characterized by disabling skeletal-muscle and connective-tissue ossification that begins in childhood. It has been proposed that POH might have a common basis with another rare disease associated with extensive heterotopic ossification, Albright's hereditary osteodystrophy (AHO). Since heterozygous inactivating mutations in the *GNASI* gene are known to cause AHO, *GNASI* mutations were sought in subjects with POH. Heterozygous inactivating *GNASI* mutations were found in 13 of 18 probands with POH, all of whom inherited the defective allele exclusively from their fathers — a finding consistent with paternal imprinting.

The same mutation caused either POH or AHO within a single family, with the phenotype correlating with the parental origin of the mutant allele.

see page 99 (editorial, page 128)

proved knowledge, however, stone-related conditions account for billions of dollars annually in time lost from work and the costs of medical and surgical care.

Stones range from those that are microscopic to stones that are as large as light bulbs, and they come in a panoply of colors and shapes. Although over 200 components have been reported in kidney stones, most stones are composed of calcium oxalate — either monohydrate or dihydrate. Most persons with such stones have hyperabsorptive hypercalciuria, or higher-than-average intestinal absorption and urinary excretion of calcium.

Treatment for Stones

The best treatment both for calcium-containing stones and for other stones remains prevention. A stone requires supersaturation, a nidus, and time to form (Fig. 1). Thus, ample hydration, avoidance of infection, and good voiding habits minimize the chance of stone formation, whether initial or re-

current. Once a stone has formed, however, there is more than a 50 percent chance that a second stone will form at some point.

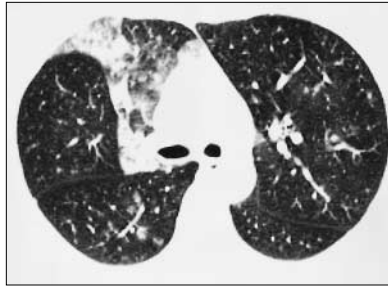
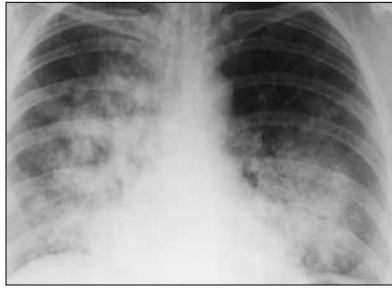
The options for the treatment of stones have increased. Surgery — that is, “cutting for stone” — is now rare. Most stones are expelled with ample hydration, plus analgesics to ease the pain. Medications such as calcium-channel blockers may help relax and dilate the ureter so that the stone can exit. Stones that are not passed can usually be handled with “minimally invasive” techniques. Stones can be snared, even in the ureter or renal pelvis, with fiberoptic instruments, dissolved with lasers, or fragmented with the use of lithotripsy. However, all these procedures may have side effects and may cause substantial renal or ureteral damage.

Given the complications of ablative procedures, to say nothing of the pain of renal colic, it is important to find better ways to prevent the formation of stones. Medications that reduce urinary calcium

excretion are attractive. However, thiazides — the most commonly used class of drugs — increase uric acid and cholesterol levels. Potassium citrate may add citrate to the urine and may also chelate calcium but is difficult to tolerate. The use of cellulose phosphate to bind calcium in the intestines may also prevent stone formation, but it causes bloating. Xanthine oxidase inhibitors such as allopurinol may be helpful but can occasionally lead to the formation of xanthine stones.

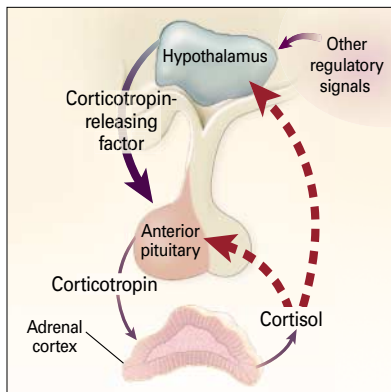
Dietary Approaches

Modifying dietary intake remains an attractive approach. A low-calcium diet by itself has been disappointing and, furthermore, may lead to or exacerbate a deficiency in bone density. In fact, more calcium rather than less may be better. A fair amount of data have suggested that a normal-calcium diet that is relatively low in animal protein, salt, or both may be effective in preventing stone formation. Until now, however, a head-to-head compar-



Images in Clinical Medicine: Bronchoalveolar-Cell Carcinoma

Chest radiography and high-resolution CT led to transbronchial biopsy and the diagnosis of cancer.
see page 107



Current Concepts: Post-Traumatic Stress Disorder

In the wake of the terrorist attacks on September 11, 2001, physicians have been confronted with patients who have suffered psychological trauma. This Review Article examines an extreme reaction, the post-traumatic stress disorder, which may follow a variety of traumatic events. The author defines the syndrome, its clinical features, and research findings on its biologic aspects. For patients who require therapy, she discusses both counseling and pharmacologic approaches.

see page 108 (editorial, page 130)

son of such a diet with a low-calcium diet has not been published. In this issue of the *Journal*, Borghi et al. report on their comparison of the effectiveness of these two approaches — a low-calcium diet and a diet relatively rich in calcium but low in animal protein and salt — for the prevention of recurrent stones in men with calcium nephrolithiasis (see pages 77–84). The amount of oxalate was similar in the two diets, since most calcium

stones are calcium oxalate stones and it was therefore important to equalize the oxalate intake. Over a follow-up period of five years, the men assigned to the normal-calcium diet had far fewer stones than those assigned to the low-calcium diet.

Whether the normal-calcium diet prescribed for the men in this study, who were all from the Parma region of Italy, will be effective in men and women with stones who live else-

where in the world remains to be seen. However, the diet is palatable, making it likely that patients will adhere to it. Furthermore, it will most likely not lead to osteoporosis or other deficiencies. For anyone who has had a stone or who has witnessed the suffering of a friend or family member with a stone, this dietary approach seems worth trying.

JULIE R. INGELFINGER, M.D.