Chapter 2

Urinary Stones

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INTRODUCTION

Urinary stones are by no means a modern affliction. One stone was detected in a 7,000-year-old Egyptian skeleton (136), and infection-induced stones were familiar to Hippocrates (67). The long history of urinary stones, however, has not been accompanied by a thorough understanding of their underlying causes. Today, technologies to treat the most common kinds of urinary stones are far ahead of techniques to identify those individuals at risk and to prevent initial stone formation. One of the best predictors of urinary stone formation is still a history of urinary stone disease in the past.

The crystalline concretions known as stones (or "calculi") can occur in many parts of the body besides the urinary tract. It has been estimated, for instance, that 1.5 million Americans harbor gallstones, although most of these stones are asymptomatic *(66).* Calculi also appear in joints and in such diverse organs as the prostate and mammary glands. Urinary stones, however, are the only ones widely amenable to extracorporeal shock wave lithotripsy (ESWL) at present, and they are thus the focus of this chapter.

Although urinary stones have been present for thousands of years, industrialization seems to have affected the locations in the body where stones tend to form and the distribution of urinary stones in the population. Bladder stones are common in developing countries and rare in industrialized nations; the converse is true for kidney and ureteral stones. Affluence and male sex have been associated with an increased risk of stone formation, but the reasons are not clear. Dietary changes (increased protein) and decreased fluid intake are attractive, but unproven, hypotheses that may partly explain the observed associations with stone disease (33). Hereditary factors may also be an important predictor of the risk of developing urinary stones (44), but again the precise mechanisms that lead to stone formation are, for the most part, poorly understood.

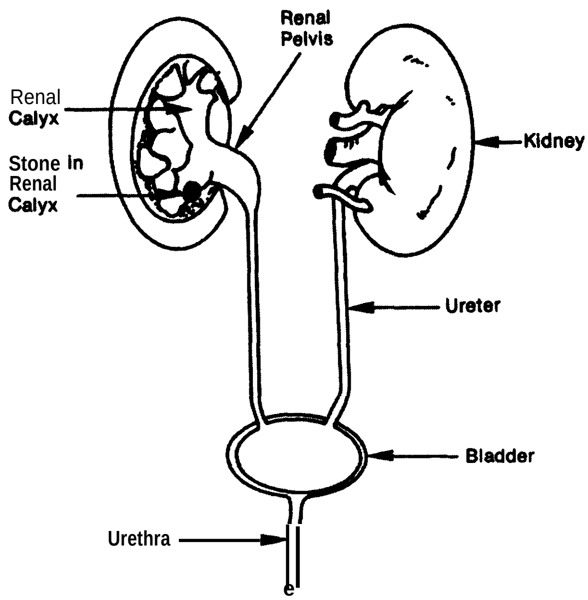
This chapter briefly reviews the structure and function of the urinary tract and the types of stones that occur. It then presents estimates of upper urinary stone incidence in the U.S. population and summarizes current thinking regarding the distribution, causes, and predictors of upper urinary stones, those most amenable to ESWL treatment. It concludes with a brief discussion of the applications and limitations of these estimates of stones and stone recurrence as they apply to discussions of ESWL.

STRUCTURE AND FUNCTION OF THE URINARY TRACT

The urinary system can be thought of as a series of connected structures that filter, collect, channel, and store urine (155). In each of the body's two kidneys, blood is filtered through a multitude of microscopic filtering units. The resulting urine, containing soluble body wastes and electrolytes that must be discarded to keep the body's fluids in balance, drains into the hollow core of each kidney by way of the renal calices. These calices, finger-like protrusions that extend up into the solid substance of the kidney, collect the urine and channel it into the core, the renal pelvis. From each renal pelvis, urine then passes through one of the two respective tube-like ureters to the urinary bladder. There it is collected and stored until urination occurs and the urine passes through the urethra out of the body. Figure 1 diagrams the structure of the urinary tract.

Stones tend to be located at specific sites in the urinary tract. A renal calix, where the urine first filters into the kidney's core, is a natural alcove where stones may lodge and grow. Because there are numerous calices, a single calix stone may not

Figure 1.—Diagram of the Urinary Tract



NOTE Figure is not drawn to scale

SOURCE: Adapted from Blue Cross and Blue Shield Association, "Extracorporeal Shock Wave Lithotripsy: Clinical Assessment, Utilization, and Cost Projections," Chicago, IL, May 1985

obstruct urine flow or lead to any other symptoms of stones. Larger stones may form in the renal pelvis itself. If these grow to mold themselves to the inner contours of the pelvis and calices, they are called "staghom" because of their obvious and dramatic appearance on an X-ray. Large staghom stones are potentially life threatening, and they can also be quite difficult to remove.

Stones are frequently found at the junction of the renal pelvis and the ureter or at a position approximately one-third down the ureter, where the ureter's diameter tapers slightly as it crosses blood vessels. Migrating stones may lodge at these points, blocking urine flow and necessitating removal. Finally, stones can be found at the junction of the ureter and the bladder or in the bladder itself. Lower urinary stones—those occurring in the urethra, bladder, or lower portions of the ureters—are relatively uncommon in the United States,

The causes of urinary stones have been vigorously discussed for some time and are still the subject of intensive research. Among the credible theories are that stones are the result of supersaturation and crystallization of mineral substances in the urine; that there exists a natural stone inhibitor in urine that is absent in some people; and that abnormal macromolecules or crystalline structures may induce stone formation. A combination of these theories probably is the best explanation for the cause of upper urinary tract stones (20,33,44,138,198), And, although in some cases urinary stones can be attributed to a specific disease or a metabolic abnormality,[1] in most cases the factors leading to the onset of stone disease are obscure (198).

I Primary hyperparathyroidism, renal tubular acidosis, cystinuria, primary hyperoxaluria, recurrent infections, and sarcoidosis all play a role in stone formation (33).

EPIDEMIOLOGY OF UPPER URINARY STONES

There are four main types of upper urinary stones, which are summarized in table 1 according to their relative frequencies in the stone-forming population and their densities as they appear radiographically (on X-rays). Calcium-based stones are by far the most common in the United States and are generally subcategorized according to their secondary components. They are also the least well understood in their etiology. Struvite stones, composed of magnesium ammonium phosphate crystals, are also fairly common and are associated with urinary tract infections. The least common stones are those composed of cystine (a sulphur-containing amino acid) or uric acid. Cystine stones are associated with an inherited disease that results in elevated excretion of this and other amino acids. Uric acid stones occur in persons with elevated levels of uric acid in the blood (such as persons with gout) or urine and in persons with low urinary pH (52,198).

Table 1 .— Relative Frequencies and Radiodensities of Major Types of Urinary Stones

Stone type	Relative frequency among stones	Radiodensity[a]
Calcium stones	70-80%	most dense
Calclum phosphate	5-10	
Calcium oxalate/phosphate	30-45	
Calcium oxalate	20-30	
Struvite	15-20	
Cystine	3- 3	least dense
Uric acid	5-10	radiolucent

aThe radiodenslty of a stone indicates the ease with which It can be visualized on X ray

SOURCE K N Van Arsdalen, "Pathogenesls of Renal Calculi, ' *Urologic Radio/-ogy* 665-73 spring/fall 1984

Incidence of Urinary Stones

Data on the incidence of urinary tract stone disease in the United States come from three sources: targeted surveys of hospitals, hospital discharge abstract data collected by the National Center for Health Statistics (NCHS) and the Commission on Professional and Hospital Activities (CPHA), and studies of urinary stones in specific populations. The estimates of stone incidence discussed in this section are summarized in table 2.

[2]Incidence" is defined as the number of newly diagnosed cases in the general population over a specified time period. It is distinct from ' prevalence" which refers to the total number of cases exist - ing in the population during a specified time.

As this table shows, the estimates vary considerably and do not lend themselves to simple interpretations.

The first estimate of urinary tract stone incidence was obtained from a survey of U.S. hospitals in 1952 (16). A discharge diagnosis of urinary tract stones was used to define a case, and incidence was estimated at 0.95 per 1,000 persons for that year. Another questionnaire survey, conducted in 1975, yielded an estimated incidence of 1.64 per 1,000 persons for 1974 (157). Although these figures suggest a 73-percent increase in perceived incidence over the 22-year period, they are of questionable accuracy because the two studies were greatly hampered by low response rates, which may introduce biases. (The response rates for the 1952 and 1975 surveys were 11 and 27.2 percent, respectively.) More recent data from NCHS, collected through the annual National Hospital Discharge Survey, indicate that the incidence of a primary hospital discharge diagnosis of upper urinary tract stones in the United States was 1.29 per 1,000 persons in 1982 and 1.42 per 1,000 persons for 1983 (195,196). Data from CPHA have produced similar estimates of incidence with considerable geographic variation (37).

A limitation of all of these estimates of the incidence of urinary stone disease in the United

Table 2.—Summary of Estimates of the Incidence of Urinary Stones in the United States

Source	Year	Urinary stones per 1,000 population	Population studied
Johnson, et al., 1979	1950	0.57[a]	Rochester, MN, residents
Boyce, et al., 1956	1952	0.95	U.S. inpatients
Hiatt, et al., 1982	1970-72	1.22	San Francisco area inpatients
Sierakowski, et al., 1978	1974	1.64	U.S. inpatients
Johnson, et al., 1979	1974	0.80[a]	Rochester, MN, residents
Hiatt, et al., 1982	1971 -75	0.36	Northern California ambulatory patients
National Center for Health Statistics	1982	1.29	U.S. inpatients
National Center for Health Statistics	1983	1.42	U.S. inpatients
Commission on Professional and Hospital Activities	1983	1.42	U.S. inpatients

aFigures given here are implied Reported figures are O 79 (males) and O 36 (females) for 1950 and 1.24 (males) and 0 36 (females) for 1974

SOURCES W H Boyce, F K Garvey, and H E Strawcutter, "Incidence of Urinary Calculi Among Patients in General Hospitals, 1948 to 1952, ' *J. Am Med Assoc 161 1437.1442,* 1956; R A Hiatt, L G Dales, G D Friedman, et al , "Frequency of Urolithiasis in a Prepaid Medical Care Program, " Arn *./ Epidemiology 115(2)* 255-265, 1982, C M Johnson, D M Wilson, W M. O'Fallen, et al , "Renal Stone Epidemiology A 25-Year Study in Rochester, Minnesota, " *Kidney International* 16624-831, 1979, R Sierakowski, B Finlayson, R R Landes, et al , "The Frequency of Urolithiasis in Hospital Discharge Diagnoses in the United States, " *Investigative Urology* 15 438-441, 1978, U S Department of Health and Human Services, Public Health Service, National Center for Health Statistics, "Number of Inpatients Discharged from Short..Stay Hospitals, by Category of First Listed Diagnoses, United Slates, 1982 (table 4), in National Center for Health Statistics—1982 Summary' National Hospital Discharge Survey, No. 95, Dec 27, 1983, U S. Department cf Health and Human Services, Public Health Service, National Center for Health Statistics, "Detailed Diagnoses and Surgical Procedures for Patients Discharged from Short-Stay Hospitals, United States, 1983, " *Vital* and *Health Statistics* 13, No 82, DHHS Pub No (PHS)85-1 743, Hyattsville, MD, March 1985, Commission on Professional and Hospital Activities data as cited in H Alder, *Lithotripters Noninvasive Devices for the Treatment of Kidney Stones* (Chicago, IL American Hospital Association, 1983)

States is their reliance on hospital discharge data. Counting discharges overestimates the incidence of “hospitalizable” stone disease because of possible multiple admissions for the same stone. Furthermore, in the case of the NCHS estimates, the data include only discharges for which urinary stones were the primary diagnosis. Including discharges with a secondary diagnosis of stones increases the estimates by about one-third (3). On the other hand, as demonstrated by one of the following studies, a large proportion of stones—perhaps a majority—do not require hospitalization. Thus, on balance, these hospital studies probably underestimate the true incidence of stone disease. Still, they do indicate a trend towards an increase in incidence of urinary stones in the United States over time.

One of the best available estimates of the incidence of urinary tract stones comes from a 25-year study of Rochester, Minnesota residents, which showed an increase in the annual age-adjusted incidence of urinary tract stones from 0.79 per 1,000 men in 1950 to 1.24 per 1,000 men in 1974 (83). The incidence in women remained stable for this period at 0.36 per 1,000. These data represent as close to a complete sample as feasible and include diagnoses made in ambulatory as well as in hospitalized patients. The 57-percent increase in incidence rates of urinary tract stones in men supports the observed trend from the hospital surveys.

The most recent study on the epidemiology of urinary tract stones was reported from the Kaiser Foundation Health Plan in northern California. First, ambulatory clinic diagnostic information from the San Francisco Medical Center was examined for “new or recurrent” stones covering the period 1970 to 1972. The results showed an age-adjusted annual incidence rate of 1.22 per 1,000 members—l .81 per 1,000 men and 0.59 per 1,000 women (75), A second calculated incidence rate was based on hospital discharge diagnoses for the entire Northern California Kaiser Foundation Health Plan from 1971 to 1975. Based on the hospital data, the age-adjusted annual rate for urinary tract stones was calculated at 0.36 per 1,000 members—().52 per 1,000 men and 0.19 per 1,000 women (75). Although the geographic populations compared in this study are by no means identical, the results suggest that estimates of incidence based solely on hospital discharge data may underestimate the total incidence of diagnosed urinary stones by a considerable amount.

Distribution of Stones

It has long been noted that urinary stones are more common in some populations than in others. Some of the predisposing factors to stone formation, such as certain diseases that lead to metabolic disorders, clearly have genetic components (33). Racial, ethnic, and familial tendencies toward stone formation have also been postulated more generally; for example, in the United States, Caucasians have a higher recognized incidence of urinary stones than Native Americans or persons of African or Asian ancestry *(44,75,165).* However, it is often difficult to separate hereditary factors from dietary and other lifestyle differences.

Distribution of urinary stones in the population varies considerably according to age and sex. The Rochester and Kaiser studies found consistently higher stone incidence in men than in women (75,83). NCHS data confirm this tendency for the United States as **a** whole (195), but as a generalization it requires two important qualifications. First, it may not be true for some subpopulations; black men and women appear to have approximately equal probabilities of developing stones (165). Second, the incidence of stones at autopsy is also approximately equal for men and women in the United States. This fact implies that much of the higher incidence in men is due to earlier onset and recurrence of stones (44).

The lifetime incidence of urinary tract stone disease also varies by sex, ethnicity, and socioeconomic factors, but researchers have estimated it at approximately 10 percent for American men (16,83,157). Stones peak in incidence in men between 40 and 60 years of age, and a stable rate persists through the seventh decade (83). A decline in incidence in men and women older than 70 years of age was observed in both the Rochester and Kaiser studies (75,83). The incidence of urinary tract stones in persons older than 65 years of age is therefore similar to the average incidence in the general population.

The Southern United States is frequently referred to as the “stone belt, ” and with good cause. The incidence of upper urinary stones there in 1983, as measured by hospital primary discharge diagnosis, was 1.84 per 1,000 population, compared to 1.39 in the Midwest, 1.16 in the Northeast, and 1.00 in the Western United States (37). Differences in diet and climate have been cited as possible reasons for these disparities (44), but it is possible that physician and hospital practice patterns also play a role in the apparent regional differences in stone incidence (3).

Because a high incidence of upper urinary stones seems to be influenced by diet and by the industrial development of an area, it has been associated with affluence. However, the Kaiser study found an inverse correlation between a history of urinary tract stones and the educational background of the person (75).

Stone Recurrence

A majority of patients who have had one upper urinary stone develop another one (83). More precise estimates of stone recurrence are available, but they tend to be difficult to compare because they use different followup periods and other measurements. Comparability is also hampered by possible confounding factors, such as distributional factors (e.g., geography) and diet and treatment regimens.

One retrospective evaluation of 538 patients with upper urinary tract stone disease for a minimum of 10 years reported that 75 percent had recurrences over a mean period of 18.5 years (206), In another study, researchers followed 416 patients at a London stone clinic for a mean period of 7.6 years and reported that 36.1 percent of the sample developed a second stone (99). The Rochester study sample had a symptomatic recurrence rate of 30 percent for women and 45 percent for men over 14 years of followup, with the highest recurrence in the first year (83). Other investigators have reported an overall average interval between first and second stones of 4.5 years, and they believe that natural recurrences approach 100 percent if patients are followed for a long enough time (33).

Second stones can often be prevented with medical treatment, even when the exact cause of the metabolic disorder leading to the stone is obscure. For example, the factors stimulating the body to create an environment leading to calcium stones are largely unknown. However, metabolic evaluations of people with calcium stones show that up to 60 percent have high concentrations of calcium and/or uric acid in the urine (33). The presence of high uric acid concentrations alone appears to predict a more severe course of stone formation, with comparatively shorter inter-event intervals, than when high concentrations of both are present (34). Medical treatment of the metabolic abnormalities in calcium stone formers decreases the recurrence rate in patients with frequent episodes (32,50,118,130).

UPPER URINARY STONES AND TREATMENT TECHNOLOGIES

The above discussion suggests that upper urinary tract stones in the United States are commen, have increased in incidence over the past 30 years, vary in distribution across regions and populations, and primarily affect men during the economically productive period of their lives. Although persons at risk of stone formation can be identified in a few cases before they develop their first stone and stone recurrence can often be controlled or prevented, a large number of people develop upper urinary stones for reasons still unclear to modern medicine.

Of all the factors discussed, one of the most important considerations for treatment technologies remains difficult to quantify: the precise number of stones to be treated. Most current estimates of the number of stones requiring treatment are based on 1983 hospital survey data from NCHS. Used alone, this incidence of 1.42 kidney and ureteral stones per 1,000 population (196) implies the xistence of over 336,000 stones per year that lead to hospitalization.[3] This number includes readmis-

[3]This figure assumes a U.S. population of 237 million (184).

sions for the same stone but does not include patients in Federal hospitals, such as Veterans Administration and military hospitals, that are not included in the NCHS survey. Increasing this figure by 30 percent to include all patients with a secondary hospital diagnosis of kidney or ureteral stones (3) yields an estimated 437,000 patients hospitalized with stones. If, furthermore, 50 percent of all patients with stones are treated solely in ambulatory settings, as many as 874,000 persons each year may be diagnosed with stones.

Not all of the patients hospitalized with stones undergo aggressive treatment; in 1983, approximately 65,000 patients in non-Federal hospitals underwent surgery of the kidney or ureter (155) and approximately 120,000 underwent either surgical or transurethral procedures on the urinary tract (3), A substantial but unknown number of these procedures were for stone removal. Thus, the annual number of patients treated for newly diagnosed kidney or ureteral stones may be as high as 874,000; the annual number having open surgery or its equivalent as treatment for stones may be as low as some proportion of 65,000. The number for whom ESWL is appropriate has been independently estimated by at least four different groups (3,11,14,155) and lies somewhere in this range. That unknown number affects both the *use* and the costs of ESWL and is itself affected by alternative technologies, patient preferences, physician decisions, and the availability of the technology. These subjects are the topics of the subsequent chapters in this case study.