# The New Epidemiology of Nephrolithiasis



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Historically nephrolithiasis was considered a disease of dehydration and abnormal urine composition. However, over the past several decades, much has been learned about the epidemiology of this disease and its relation to patient demographic characteristics and common systemic diseases. Here we review the latest epidemiologic studies in the field. © 2015 by the National Kidney Foundation, Inc. All rights reserved.

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## HISTORICAL PERSPECTIVE

Descriptions of the treatment of urolithiasis can be found in ancient Indian, Chinese, Babylonian, and Greek texts.<sup>1</sup> Although estimates of prevalence are not available, it was common enough that to not "cut for stone" was a central tenet of the Hippocratic oath. In the year 2015, nephrolithiasis is a common cause of morbidity, with nearly 11% of men and 7% of women in the United States reporting a lifetime stone event.<sup>2</sup> Here we review epidemiologic characteristics of nephrolithiasis in the modern era—much of the focus of this review is on calcium stones that account for the majority of stones in developing countries.

## INCIDENCE, COST, AND GENDER

Multiple studies over the past decade have documented an increased incidence of nephrolithiasis. The National Health and Nutrition Examination Survey (NHANES) is a cross-sectional survey of noninstitutionalized adults in the United States that has been used to estimate the prevalence of kidney stones. Comparing NHANES II (1976-1980) and NHANES III (1988-1994), it was estimated that stone prevalence had increased from 3.8% to 5.2% for a period of 20 years covered by the surveys.<sup>2,3</sup> A recent updated analysis of NHANES data from 2007 to 2010 reported that the prevalence had increased to 8.8% (10.6% among men compared with 7.1% among women) compared with 5.5% in NHANES III.<sup>2</sup> Stone disease also appears to be more common in whites than blacks, with Hispanics and Asians falling in between.<sup>2,4</sup> Studies using claims data from the Healthcare Cost and Utilization Project found that the costs associated with kidney stones have also increased from 1994 to 2000. Although inpatient stays for urolithiasis decreased from 1994 to 2000 by 15%, there were substantially more outpatient physician visits for the evaluation of stone disease between those 2 years. This resulted in a total cost of \$2.07 billion in 2000 from \$1.37 billion in 1994. This 50% increase occurred despite the shift from an inpatient to an outpatient setting for stone treatment, with the total proportion of total expenditure on outpatient treatment increasing from 43% to 53%.<sup>5</sup> Retrospective claims-based data have also been used to evaluate the incidence of nephrolithiasis in the United States: in 2000, it was estimated that more than 1% of working-age adults were treated for an episode of nephrolithiasis. On average, per person work loss was 19 h/y, and the incremental costs of nephrolithiasis (conditional on receiving treatment) were nearly \$3500 per person per year.<sup>6</sup>

The population of Rochester Minnesota has provided some of the best long-term data on stone prevalence and incidence. In a cohort followed from 1950 to 1974, the age-adjusted incidence of first episode of kidney stones remained stable among women (36 per 100,000) but increased significantly among men (124 per 100,000 from 79 per 100,000).<sup>7</sup> Interestingly, observations of this cohort from 1970 to 2000 found that the increase in incidence did not continue in men but actually decreased by 1.7% per year. This decrease was offset by an increase in prevalence among women of 1.9% per year, such that the overall incidence being relatively unchanged.<sup>8</sup>

Studies in other countries have also identified an increasing prevalence of nephrolithiasis. A report from Germany using a nationally representative survey found that urolithiasis prevalence had increased from 4.0% to 4.7% from 1979 to 2001. In this survey, the prevalence among those older than 65 years increased from 6.8% to 9.5%. The authors were also able to estimate the incidence of urolithiasis in the year 2000 and found that it had increased to 1.47% from 0.54% in 1979.<sup>9</sup> Similarly, a report from a village near Milan, Italy, in 1986 and 1998, found that stone prevalence had increased from 6.8% to 10.1% over that period.<sup>10</sup> The prevalence of stones increased in Japan as well. By examining patient visits with a diagnosis of upper tract stones, it was estimated that the annual incidence of first upper tract stones had increased steadily from 54.2 per 100,000 in the population in 1965 to 114.3 per 100,000 in 2005.<sup>11,1</sup>

When considering the relation between gender and nephrolithiasis, recent data from NHANES corroborated earlier findings that nephrolithiasis is more commonly found in men than women, with respective lifetime prevalence in the United States of 10.3% vs 6.7%. However, other data have demonstrated that stone disease may be increasing in women at a greater rate than in men. Using

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**CLINICAL SUMMARY** 

• Large epidemiologic cohort studies have contributed

The epidemiology of adult and pediatric nephrolithiasis is

It is now understood that nephrolithiasis is related not only

to diet and hydration, but to common systemic conditions

including metabolic syndrome, cardiovascular disease,

significantly to our understanding of nephroloithiasis.

evolving in terms if incidence and risk factors.

and chronic kidney disease.

the Nationwide Inpatient Sample, Scales and colleagues<sup>13</sup> evaluated discharges for stone disease from the US hospitals from 1997 to 2002 and reported a reduction in the male:female ratio among treated stone patients from 1.7:1 to 1.3:1. Another study, using statewide ambulatory surgery and inpatient databases, noted that for a period of 6 years (1998-2004), 38% of discharges for stone disease occurred in women. However, the growth rate for women was greater than for men: although both groups increased in utilization of outpatient and ambulatory surgery, only women had increased inpatient utilization.<sup>14</sup> The Rochester Epidemiology Project also described greater increases in women compared with men from 1970 to 2000.<sup>8</sup>

# STONE RECURRENCE RATES

Early studies reported that the recurrence of stone disease after an initial episode occurred in nearly 30% to 50% within 5 to 10 years of the initial stone event.<sup>15,16</sup> Of note, a majority of the imaging in these earlier studies was plain radiography and ultrasound, with few, if any, computerized tomographic (CT) scans. Using data from the Rochester Epidemiology Project, followed from 1984 to 2003, which included CT scans, the recurrence of

stone (ROKS) kidney nomogram for predicting stone recurrence was developed.<sup>17</sup> The data used to develop the ROKS nomogram noted symptomatic recurrence after the initial stone event at the following rates and time points: 11% in 2 years, 20% in 5 years, 31% in 10 years, and 39% in 15 years. Some of the factors that increased the risk and rate of recurrence in this included model the following: family history of

stones, any nonobstructing stone on imaging, and uric acid stone composition.

#### URINE AND STONE COMPOSITION

Calcium stones (pure calcium oxalate, pure calcium phosphate, or mixed calcium) predominate in developed nations.<sup>18,19</sup> Calcium-containing stones comprise 70% to 85% of all stones, uric acid 5% to 10%, struvite 1% to 5% (more common in women than men), and rare stones (eg, cystine) 1% or less.<sup>19</sup> A recent analysis of more than 200,000 stone analyses for a period of 30 years from Germany reported stable rates of uric acid stones, decreasing rates of struvite stones, and increasing calcium stones in patients aged 40 to 49 years.<sup>19</sup> Another report, comparing stone analyses from a single laboratory in the years 1990 and 2010 noted a decrease in the proportion of uric acid stones in men (from 9.7% to 7.6%) although the proportion of uric acid stones in women remained constant. Among those with calcium stones, the proportion of hydroxyapatite per stone increased significantly in men (8.7% to 11.4%), whereas it decreased in women (19.7% to 11.7%).<sup>20</sup>

## **GEOGRAPHY AND TEMPERATURE**

It has been recognized for some time that there appears to be a "stone belt" in the Southern United States. One of the earlier studies characterizing this geographical distribution used the second Cancer Prevention Study that surveyed 1,185,124 men and women regarding kidney stone history. Using the state-level data available from this survey, it was found that residents in the Southeast were nearly twice as likely to have a stone history than those in the Northwest (odds ratio were 1.79 for men and 1.84 for women). The prevalence of stones in men ranged from 5.6% in North Dakota to 14.9% in North Carolina.<sup>2</sup> Higher temperatures have also been associated with clinical kidney stone presentation, with daily mean temperature of 30°C associated with significantly increased episodes compared with daily mean temperature of 10°C in 4 major metropolitan areas studied (Atlanta, Chicago, Dallas, and Philadelphia).<sup>22</sup> Mathematical modeling has been used to examine the association between geography and stone incidence. Brikowski and others<sup>23</sup> used predictions based on climate modeling to show a concentration of greatest increase in nephrolithiasis over the next century to be in California, Texas, Florida, the eastern United

States, and a geographic band stretching from Kansas to Kentucky—states that on the whole are affected by much warmer temperatures than the rest of the country.

### DIET

Although many dietary factors have been suggested to contribute to stone disease, the best characterized contributors are dietary calcium and fluid intake. Longitudinal cohort studies have been particularly valuable. The

Health Professionals Follow-up Study (HPFS) in men and the Nurses' Health Studies I and II in women involve nearly 46,000 men and 195,000 women followed prospectively for more than 4 decades. Studies evaluating these cohorts have shown the following dietary factors to be "protective" against stone recurrence in men: greater fluid intake, calcium from dairy and nondairy sources, magnesium, and potassium.<sup>24,25</sup> In women, foods that reduced kidney stone risk were greater fluid intake, dietary calcium, and phytate.<sup>25</sup> Dietary intake of fruits, fiber, and vegetables has also been shown to decrease risk of incident kidney stones in another large cohort of more than 83,000 women, the Women's Health Initiative.<sup>26</sup> Coffee (caffeinated or decaffeinated), tea, wine, beer, and orange juice all decrease risk of stone formation.<sup>27</sup>

Animal protein intake did increase risk of nephrolithiasis only in men with body mass index less than 25 kg/m<sup>2</sup>, as did high intake of vitamin C (in men who consumed >1000 mg/d compared with men who consumed <90 mg/d) but not in women.<sup>25,28</sup> Sugar-sweetened noncola beverages, in addition to sugar-sweetened juices Download English Version:

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