This study measured cadmium and protein HC (±1-microglobulin) in the urine of 1021 people living in two Swedish communities with nickel-cadmium battery factories. (One plant had closed in 1974; the other was still operating.) Protein HC, a low molecular weight protein, indicates the development of cadmium-induced renal lesions in the renal tubules. Over time, tubular dysfunction can lead to glomerular damage and a decreased glomerular filtration rate. After making an adjustment for age-related protein in the urine, the Swedish researchers found "a positive, highly significant, linear relation...between dose (cadmium in urine) and effect (urinary protein HC)." They discovered that people with urine-cadmium levels of 1 nmol/mmol creatinine (the upper part of normal range) showed a "threefold increase in risk of having increased urinary protein HC." (Creatinine, formed from the metabolism of creatine, is an indicator of kidney function used in blood and urine tests.) An expert group at the World Health Organization set a 'health-based limit' of about 5 nmol Cd/mmol creatinine.

The researchers also found that bone density decreased as urinary cadmium and urinary protein HC increased. They state that other studies have found an increased incidence of kidney stones, osteoporosis, and urinary excretion of calcium among cadmium-exposed workers. Because of the health consequences of cadmium intake, the researchers believe that "measures should be taken to reduce exposure to cadmium in the general population, including lowering of current standards for intake of cadmium in food."


Calcium Intake & Kidney Stones

Recent studies offer conflicting advice about dietary calcium intake and its contribution to kidney stone formation. About 80% of all kidney stones are composed of calcium phosphate or calcium oxalate. The headline for a widely-publicized, 2005 press release from the University of Texas Southwestern Medical Center of Aging recommends restricting calcium intake. A 2004 study, however, that used data from the Nurses' Health Study II found that women with a higher dietary calcium intake had less risk of developing kidney stones. "UT Southwestern Researchers Find Calcium Intake Contributing Factor In Formation Of Kidney Stones" reads the headline for the university press release and corresponding article at www.sciencedaily.com. The article refers to two studies. The first looks at formation of calcium oxalate stones and appears in *Kidney International* (November 2004). The other focuses on calcium phosphate stones and appears in the *Journal of Urology* (December 2005). Both conclude that "urinary calcium - the amount of calcium in a person's urine - is an important contributing factor in the formation of both types of kidney stones." Both studies use data from UT Southwestern's kidney stone registry: 667 patients with predominantly calcium oxalate stones for the first and 133 patients with predominantly calcium phosphate stones for the second. Using "a newer, lower stability constant [mathematical formula]," the researchers found that urinary calcium is as important as oxalate or phosphate in kidney stone formation. However, neither study looked specifically at how much calcium the patients actually consumed. Several conditions lead to increased blood levels of calcium (affecting urinary calcium levels), including primary parathyroid dysfunction, sarcoidosis, hyperthyroidism, and renal tubular acidosis. Yet, two of the authors quoted in the press release take the leap that people with stones "may need to carefully monitor their calcium dietary intake."

In the 2004 study, Gary C. Curhan, MD, ScD, and colleagues examined dietary factors and risk of kidney stone among 96,245 female nurses (age 27 to 44 years) in the Nurses' Health Study II (*Arch Intern Med.* 2004; 165:885-891). None of these women had a history of kidney stones. The researchers documented the development of 1,223 kidney stones over an eight-year period. "Women who consumed the most calcium (top 20% of calcium intake) had a 27% lower risk of developing kidney stones compared to women who reported consuming the least amount of calcium (lowest 20% of calcium intake)."

In the Background section of the Nurses' Health Study II article, Curhan and colleagues said that previous studies involving older women and men showed that "greater intakes of dietary calcium, potassium, and total fluid reduce the risk of kidney stone formation, while supplemental calcium, sodium, animal protein, and sucrose may increase the risk." This study, involving younger women, showed no association between calcium supplementation and kidney stone risk. The researchers also found that "women who consumed the most phytate (top 20% of phytate intake) in the study group had a 37% lower risk of developing kidney stones compared to women who consumed the least amount of phytate (lowest 20% of phytate intake)." Phytate inhibits mineral absorption and is found in whole grains, pulses (peas, beans, lentils), and soy beans.

Dietary Calcium Associated with Reduced Risk of Kidney Stones in Younger Women. www.sciencedaily.com 27 April 2004
UT Southwestern Researchers Find Calcium Intake Contributing Factor in Formation of Kidney Stones. www.sciencedaily.com 19 January 2005

Kidney Disease & Diabetes

Kumar Sharma, MD, at Thomas Jefferson University (Philadelphia, Pennsylvania) and Erwin Böttinger, MD, of Mount Sinai School of Medicine (New York) have identified a protein that may explain why kidney disease is so common among people with diabetes. One in three people with type 1
diabetes and one in ten people with type 2 diabetes develop kidney disease. Diabetic nephropathy accounts for over 40% of all patients who develop end-stage chronic kidney disease.

Sharma and Böttinger observed the effects of high glucose levels on kidney cells from humans and mice – with and without diabetes. They found that high glucose levels change the surface of proximal tubular epithelial cells in the human kidney. The cells then increase production of the protein CD36. CD36 combines with proteins and free fatty acids often found in the urine of people with diabetes, triggering apoptosis (cell death). Accelerated cell death gradually leads to kidney failure. By blocking CD36 activity in cell cultures, Sharma and Böttinger were able to prevent apoptosis. Their article appears in *PloS Medicine* (February 2005).

### Dietary Supplement Safety & Efficacy

"Benefits and Safety of Dietary Supplements," a 2004 white paper distributed by Metagenics, Inc., reviews the science and regulation of supplement use in the US. The paper was written by Miriam G. Zacharias, MS; Jeffrey Bland, PhD; Jeffrey Katke; Alexander G. Schauss, PhD; Richard Conant, MS., LAc, and Loren D. Israelson, JD. By providing accurate information, the paper’s authors hope to “promote good public policy and regulations for dietary supplements that are based upon fact rather than misinformation and exaggeration.” Media reports and some legislators and government officials propagate the idea that ‘unregulated’ dietary supplements threaten public health. "Benefits and Safety of Dietary Supplements" explains the safeguards provided by the Dietary Supplement Health and Education Act of 1994 (DSHEA). The paper also reviews documented safety records, refuting the contention that dietary supplements should meet the same guidelines as pharmaceutical drugs.

DSHEA gives FDA’s Center for Food Safety and Applied Nutrition the job of identifying harmful and/or misleading products on the market. Like food manufacturers, those who make supplements have primary responsibility for ensuring that the products that they produce are safe and accurately labeled. DSHEA also lets FDA set up Good Manufacturing Practice (GMP) regulations to direct the safe preparation, packing, and warehousing of dietary supplements. Contamination and low product quality are the most common problems regarding dietary supplement safety. Establishing GMP regulations for dietary supplements promotes quality assurance and consumer confidence. FDA, however, has never finalized GMP regulations for dietary supplements. Despite this lapse, authorities have several ways to remove an unsafe product from the market. FDA can restrict any product that it has shown is unsafe. Individual states can also prohibit harmful supplements within their jurisdiction. Finally, the US Secretary of Health and Human Services may declare a product or supplement ingredient a health or safety hazard.

Is more stringent regulation of dietary supplements necessary? Should they undergo the same testing required of pharmaceutical drugs? The authors turned to the Poison Control Center TESS database, one of the few sources for gauging dietary supplement safety. In 2002, Poison Control Center data received reports of 73,600 exposures to vitamins and minerals, resulting in 6,130 adverse events (8%) and 7 deaths (0.009%). (Four deaths were reportedly due to mineral iron; one death due to a multi-vitamin with iron overdose; one due to potassium; and one from vitamin E. One drawback of this database is that it does not provide objective explanations behind the incidents.) Botanical exposures (including Ephedra products) reported to Poison Control in 2002, number 15,187 and 3 deaths. Excluding Ephedra products (which the authors note may have been adulterated with the synthetic drug ephedrine), the number of exposures drops to 4,861 and 0 deaths. During that same year, Poison Control Center had information on 1,132,631 exposures to pharmaceutical drugs (including over-the-counter), resulting in 301,524 adverse events (nearly 27%) and 1877 deaths (0.16%). A 1998 study published in the *Journal of the American Medical Association* estimates that 106,000 people die and over 2 million are hospitalized because of adverse drug reactions each year. Adverse drug reactions rank between the fourth to sixth leading cause of death in the US. Dietary supplements do not come close to causing that kind of hazard.