News
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****Dr. Charles Pak to receive award
for orphan products development

DALLAS -- Kidney stone expert Dr. Charles Y.C. Pak is the recipient of the prestigious United States Public Health Service Award for Exceptional Achievement in Orphan Products Development. Pak has been responsible for developing a number of drugs for preventing the recurrence of kidney stones.

Pak, chief of Mineral Metabolism at The University of Texas Southwestern Medical Center at Dallas, received the high honor for "aiding significantly in the development of orphan products for rare diseases or conditions." The awards ceremony took place at the March 11 meeting of the Department of Health and Human Services' Orphan Products Board in Washington, D.C.

Said Neil Abel, executive secretary of the Orphan Products Board, "Dr. Pak's dedication to the orphan drug cause and tireless commitment to the research in the prevention of cystine nephrolithiasis in patients with homozygous cystinuria is laudatory." Pak was further commended for his activities in bringing other products through the drug approval process.

Abel says that the development of orphan products for rare diseases and conditions remains one of the Public Health Service's major initiatives. Significant gains have been recognized during the past five years since the enactment of the Orphan Drug Act.

In general, kidney stone sufferers can expect a 70 percent chance of recurrence without treatment. Rather than treating all kidney stones alike with a traditional "shot-gun" approach, Pak has successfully identified 16 separate stone-forming disorders and has developed selective treatment for each.

Pak began his kidney stone studies at the National Institutes of Health in 1968 and has continued at UT Southwestern since 1972, supported by the NIH and aided by the FDA. His drug development studies are noteworthy because in most cases Pak's group conceived the ideas, found how the drugs work and tested them for safety and effectiveness -- tasks normally undertaken by large pharmaceutical companies.

One ingredient in Pak's success has been his unique relationship with the Mission Pharmacal Company of San Antonio. Pak and Neill Walsdorf, president of Mission, began to collaborate in the early 1980s when Pak was trying to find a company to begin making and marketing sodium cellulose phosphate, an "orphan drug" that he had developed. Despite a limited market, Walsdorf willingly consented, commenting, "Being a stone former myself, I know how important such orphan drugs are."

While the NIH has provided much of the support for his ideas and research, and the university has acted as the sponsor for his drugs, Mission has been invaluable in supplying uniquely formulated drugs in a timely manner, Pak says.

Among his many accomplishments in treating kidney stones, Pak has developed the following orphan drugs:

*Sodium cellulose phosphate was approved by the FDA in 1983 for use in kidney stone patients with "absorptive hypercalciuria." This common kidney stone forming disorder is frequently associated with increased absorption of calcium from food. While diet modification can often prevent stone formation in the disorder's milder forms, the drug is useful in treating severe forms of the disorder.

During the three years prior to the study, a group of kidney stone patients had passed 372 stones, averaging 7.75 stones per patient per year. During the study, lasting up to five years for some patients, only 11 stones were passed. Remission occurred in 81 percent of the patients and they did not form new stones while taking the drug.

(More)

*Potassium citrate, approved by the FDA in 1984, was found effective by Pak's group in reducing the rate of stone formation or stopping stone production in patients with hypocitraturia. This condition is characterized by having a low urinary citrate level, and patients in this group form stones composed of calcium oxalate or calcium phosphate.

In a test group of more than 100 patients with hypocitraturia, 82 percent stopped forming stones while on drug therapy and 98 percent had a reduced rate of stone formation. When treatment ended, the rate of stone formation jumped to its former elevated level.

Potassium citrate, moreover, virtually eliminated the need for surgery due to new stones in these patients. During the three years prior to initiation of treatment, 78 patients had undergone 56 surgeries. Following treatment with potassium citrate for periods of 18 months to two years, only nine surgeries were required, all for pre-existing stones and none for new stones.

Citrate, a substance normally found in urine, is an inhibitor of stone formation since it is capable of preventing the crystallization of stone-forming calcium salts, says Pak. Patients with hypocitraturia are therefore more prone to form calcium stones. In such persons, potassium citrate increases urinary citrate and significantly reduces stone formation. Hypocitraturia affects about 50 percent of all people requiring medical treatment for kidney stone disease.

Another group who can benefit from potassium citrate treatment are those with gouty diathesis. By increasing urinary pH and citrate, this treatment can avert formation of both uric acid and calcium stones.

*Thiola, a Japanese-made kidney stone drug, was found effective by Pak's group in controlling the formation of cystine kidney stones. A new drug application for this drug is currently under review by the FDA.

Symptoms of cystine stones are typically severe. Multiple large stones, often "staghorn" in shape, form in the kidney. And the underlying stone-forming disorder, if unchecked, may sometimes progress to kidney failure and the need for lifelong dialysis. Pak explains that cystine stones are caused by an inherited metabolic disorder affecting about 10,000 Americans. The disorder is thought to involve a defective reabsorption of cystine into the kidneys.

Pak and his research team found that the serious side effects that are common among patients taking the standard drug for cystine stones, d-penicillamine, are significantly less common during Thiola therapy. Also, the reduction in urinary cystine produced by Thiola is equal to or better than that obtained with d-penicillamine.

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Distribution: AA,AB,AC,AC1,AF,AF1,AG,AG1,AH,AI,AK,AK1,ADM,ADM1,SL

Note: The University of Texas Southwestern Medical Center at Dallas comprises Southwestern Medical School, Southwestern Graduate School of Biomedical Sciences and Southwestern Allied Health Sciences School.