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News
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***New drug for kidney stone prevention announced at UTHSCD.

IMPORTANT: Not to be released until noon CST, Dec. 1, 1982.

*********A PRESS CONFERENCE is scheduled for 10:30 a.m. CST, Wed., Dec. 1, at The University of Texas Health Science Center at Dallas (Room E1.403) to allow time for questioning Dr. Charles Pak on selective therapy for kidney stone prevention, including a drug for use in preventing formation of one of the most common types of kidney stones.

DALLAS--A drug shown effective in preventing kidney stones was announced here today by Charles Y.C. Pak, M.D., director of the National Institutes of Health-supported General Clinical Research Center and professor of Internal Medicine at The University of Texas Southwestern Medical School, a component of UTHSCD. The drug was developed under the sponsorship of the health science center and by research grant support from the NIH. FDA approval of the drug is expected shortly, Dr. Pak said.

After 15 years of clinical trials, the drug, sodium cellulose phosphate (SCP), has shown clinical effectiveness in inhibiting painful stone formation in patients with "absorptive hypercalciuria," Pak says. This common kidney stone-forming disorder is frequently associated with increased absorption of calcium from food.

Pak says the drug is useful in treating the more severe forms of absorptive hypercalciuria. Diet modification can often prevent stone formation in the disorder's milder forms.

Non-absorbable in the body, SCP given by mouth works by binding calcium from food, thereby lowering the amount of calcium absorbed from the intestines. In so doing, SCP lowers calcium in the urine and makes the urine less likely to undergo precipitation of stone-forming calcium salts. Such salts include calcium oxalate and calcium phosphate.

Pak's findings on sodium cellulose phosphate are being reported in the December issue of The Journal of Urology (The Williams and Wilkins Company, Baltimore).

While the drug was deemed un-patentable and impractical to market by six major drug companies, the Mission Pharmacol Co. (San Antonio) has agreed to prepare and market the former "orphan" drug.

Pak first studied the effects of SCP in 16 patients when he was head of the Section on Mineral Metabolism, Endocrinology, at the National Heart and Lung Institute, before coming to the health science center in 1972. During three years immediately prior to treatment, these patients (all with absorptive hypercalciuria) had passed 372 renal (kidney) stones over 48 cumulative years. The group averaged 7.75 stones per patient per year. During the study, lasting up to five years for some patients, only 11 stones were passed. This averaged 0.27 stones per patient per year over 41 cumulative years of treatment. Eighty-one percent of patients were in remission and did not form any new stones.

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In a subsequent study conducted in the General Clinical Research Center in Dallas, 18 patients with absorptive hypercalciuria formed 123 stones during the three years before treatment. For this group the stone formation rate was 2.28 stones per patient per year prior to SCP therapy. During treatment, averaging 2.37 years per patient, only 10 stones were passed. This showed a stone formation rate of 0.23 stones per patient per year. The remission rate was 77.8 percent. All 18 patients showed reduced stone formation rates individually.

"Drug studies of this nature would have been impossible to carry out without the controlled environment available in the GCRC," says Pak. The General Clinical Research Center in Dallas is one of 74 such centers located around the country, sponsored by the Division of Research Resources, NIH. Pak's research is also being supported by grants from the National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases.

Pak also reported in The Journal of Urology that by using new techniques he and his research team can determine the causes of stone formation in about 95 percent of his patients. Until recently doctors were unable to determine the cause of kidney stones much of the time.

In persons who form kidney stones, the recurrence rate is usually high -- about 70 percent. Yet people often go untreated, or a "shotgun" approach to drug therapy is used in which drugs are prescribed on a hit-or-miss basis.

"The main thing to remember is that there are many different causes for kidney stones -- it is not a single disease," Pak says. "It therefore demands many different modes of treatment." Pak has identified a dozen of these different causes. For seven of the more common causes, all of which are associated with calcium stones, he has formulated medical treatment for each. Treatment is tailor-made to correct the underlying cause.

While kidney stones are rarely fatal, many people live in dread of passing their next kidney stone. Kidney stones are rough and spiny, often causing excruciating pain as they move through the urinary tract to be expelled, or in some cases, to become trapped and obstruct urine flow. Emergency surgery is sometimes required. Symptoms include colicky pain in the flank and groin associated with bloody urine. Unremitting pain may last several days as the stone makes its way through the ureter from the kidney to the bladder.

Kidney stone disease, affecting about five per 1,000 persons in the U.S., is an important health problem resulting in many lost work days and costing hundreds of millions of dollars annually in hospitalization and treatment.

In more than 500 patients treated by Pak and his team over the years, stone formation has been prevented in 72 to 91 percent of the patients and stone formation has been reduced in 90 to 100 percent of patients, depending on the type of disorder.

With careful diagnosis and selective therapy, Pak treats his patients individually. While the majority of his patients form calcium stones, the causes can vary greatly. Calcium stones, made of calcium oxalate and calcium phosphate, can form when there are excessive amounts of calcium, oxalate or uric acid in the urine, or when the urine contains low levels of citrate.

In the high urinary calcium group three classifications are made -- absorptive hypercalciuria, mentioned above; resorptive hypercalciuria, where calcium is "leached" from bone in excessive amounts, usually from an excess of parathyroid hormone from a tumor in the parathyroid gland (here surgery is required), and renal hypercalciuria, the result of a kidney defect where calcium is leaked into the urine. In renal hypercalciuria a form of diuretic, thiazide, may prevent the calcium leak.

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Patients who form calcium stones because they excrete excessive amounts of oxalate, comprise a second major grouping. Here the most common cause is a bowel disease or abnormality. Persons who have had intestinal bypass surgery for morbid obesity are candidates for these stones.

Another broad grouping involves high uric acid in the urine, called "hyperuricosuria." Often this results from too much animal protein in the diet, producing an excess of purines which are converted to uric acid.

Some patients' urine contains low levels of citrate, an inhibitor of stone formation. Pak's group is using an investigational drug, potassium citrate, to correct this defect.

In about five percent of kidney stone cases there is no metabolic abnormality, says Pak. Instead, these people often don't like to drink water and have concentrated urine from inadequate fluid intake.

Pak says that reliable methods for detecting the causes of stone disease are available, involving three outpatient visits.

On the first visit, patients are asked to collect a 24-hour urine sample while on their customary diet and fluid intake. They then are asked to follow a diet restricted in calcium and sodium for one week. At the end of the week another 24-hour sample is collected.

Urine samples are analyzed for calcium, oxalate, uric acid, citrate and other common constituents.

At the third collection, a test called "fast and load" is done. A urine sample is taken after the patient has fasted 10-12 hours. Then a "milk shake" containing one gram of calcium is taken, followed by another urine sample.

"The fasting test can tell us if the patient has renal hypercalciuria. If the calcium in the urine is high when they are fasting and blood calcium is normal, this indicates they are leaking calcium into the urine. If the urine calcium level is abnormally high after the patient has taken large amounts of calcium by mouth, this provides indirect evidence of excessive calcium absorption." Blood tests for parathyroid hormone, calcium and uric acid readings are also part of the workup.

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