

Holistic Primary Care

VOL. 4, No. 3

• NEWS FOR HEALTH & HEALING® •

JULY 2003

MEN'S HEALTH

Columbia's Center for Holistic Urology Tests New Botanicals for Prostate Disease

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Editor in Chief

It was through listening to his patients that urologist Aaron Katz, MD, found a new career direction, one that put him at the leading edge of research on botanical medicines for prevention and treatment of prostate cancer.

As director of the Center for Holistic Urology at New York's Columbia-Presbyterian Medical Center, Dr. Katz has been exploring ways in which herbal medicine and other holistic interventions can improve outcomes in prostate cancer, sexual dysfunction and genitourinary disorders. His current research endeavor is on a novel botanical combination that inhibits cyclooxygenase-2 (COX-2), thus reducing prostate cancer cell growth and angiogenesis.

"I'm a board certified urologist, and I had gone through conventional training. I was doing a fellowship at Columbia, studying urinary tract cancers," he told *Holistic Primary Care* in an interview. "I started really listening to the patients, some of whom had been referred to Columbia by Dr. Robert Atkins (recently deceased) here in New York. Many were already taking herbals that seemed to be controlling their prostate cancer. Others were using herbs to man-

age urinary complaints like urine stream interference or incomplete bladder emptying. The herbs seemed to be helping, and that was news to me. So we started looking at some of these compounds in the lab."

Fast-forward a decade and a half, and you'll find Dr. Katz heading a center that sees more than 1,000 patients each year, offering them nutritional counseling, acupuncture, botanical



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medicine, exercise classes and training in mind-body techniques. "A lot of patients who come to see us are already on botanicals or nutritional supplements and antioxidants. Some are using these in conjunction with conventional therapies. Others come for advice on whether or not to use or stay on herbals, or whether they should opt for conventional therapies."

Preventing Progression of PIN

Many of his patients have prostatic hypertrophy (BPH), prostatic intraepithelial neoplasia (PIN), or frank prostate cancer, giving Dr. Katz a unique vantage point from which to study prostate disease progression. The center's main research focus is on the mechanisms, clinical efficacy, and potential therapeutic impact of herbs to prevent and treat prostate disease. He is particularly interested in the possibility of preventing or delaying the transition of PIN into prostatic carcinoma.

"Depending on whose study you read, 40%–60% of men with PIN will have prostate cancer within a year. It is almost inevitable that these guys will develop prostate cancer." Obviously preventing progression or, ideally, reversing PIN, is a holy grail for prostate cancer researchers, Dr. Katz included.



TURMERIC: ROOTS OF THE TURMERIC PLANT CONTAIN COMPOUNDS THAT INHIBIT COX-2, AND MAY PREVENT CANCER. (PHOTOS COURTESY NEW CHAPTER WWW.NEW-CHAPTER.COM)

The just-published 7-year trial suggesting finasteride (Proscar) could reduce prostate cancer by 25% compared to placebo is being hailed as a major treatment advance in some circles. But Dr. Katz stressed that the data also showed a major downside: patients on finasteride in whom the disease did progress had far more aggressive tumors than those on placebo (Thompson IM, et al. *N Engl J Med* 2003; 169(9)).

Conventional pharmacotherapy still has very little to offer PIN patients by way of preventing progression to cancer,

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and Dr. Katz believes it is essential to take an open-minded look at herbs.

He and his research team have been studying a new product called Zyflamend, manufactured by the US-based nutraceutical company, New Chapter (www.new-chapter.com or 800-543-7279). The product contains extracts of 10 plants, including: Turmeric (*Curcuma longa*), Ginger (*Zingiber officinale*), Holy Basil (*Ocimum sanctum*), Green Tea polyphenols, Rosemary (*Rosmarinus officinalis*), Skullcap (*Scutellaria baicalensis*), and Oregano (*Origanum vulgare*). Many of these plants individually have inhibitory effects on the COX-2 enzyme, and Dr. Katz' team has confirmed that the Zyflamend combination, taken as a whole, is a COX-2 inhibitor in prostate cancer cell lines.

In data presented at last year's meeting of the Society for Urologic Oncology, they demonstrated that the 10-herb formula could decrease prostate cancer cell growth, induce apoptosis, and inhibit angiogenesis. "COX inhibition is being looked at throughout oncology as a potential mechanism for chemoprevention," he said.

Is COX-2 Inhibition the Key?

Debra Bemis, PhD, a biochemist working in Dr. Katz' lab, explained that COX-2 levels are elevated in a wide range of cancers, including lung, colon, pancreatic, head & neck, and prostate tumors. This enzyme is essential for conversion of arachidonic acid into prostaglandins, which are key inflammatory signalling molecules. Further, synthesis of vascular endothelial growth factor (VEGF), a molecular signal for angiogenesis, is also regulated by COX-2. Increased COX-2 activity is found in many disorders, notably arthritis, and it is clearly associated with many forms of cancer, including prostate cancer.

Dr. Bemis pointed out that while localized prostate cancer recurrence rates are fairly constant throughout the world, metastatic recurrences are far more common in Western industrialized nations compared

with other parts of the world. This suggests environmental or lifestyle factors, and she believes that the typical American high-fat diet, rich in arachidonic acid, is fueling COX-2 mediated inflammatory cascades that promote development of neoplasms like prostate cancer, and also make them more likely to metastasize.

"We know that Zyflamend can inhibit COX-2 in prostate cell cultures. We are not sure yet if it exclusively inhibits COX-2 or if it will also inhibit COX-1 as well," she told *Holistic Primary Care*.

Whether Zyflamend will prevent prostate cancer growth in men with the disease or its precursor (PIN) is still to be determined. Dr. Katz and his colleagues hope to have an answer in the near future. They have just



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designed a 3-year clinical trial to answer that question. The Columbia trial will follow 100 men treated with the herbal combination, assessing disease status via biopsies every 6 months.

This is one of a number of trials at the Center for Holistic Urology. The center is participating in the massive NCI-funded multicenter SELECT trial, a 7-year study that will evaluate the efficacy of selenium and vitamin E in preventing prostate cancer among more than 32,000 men.

His group is also studying Genistein Combined Polysaccharide (GCP), a combination of substances derived from fermented soy and the Basidiomycetes mushroom, which is used as an

anti-tumor therapy in Japan. Preliminary animal studies by Japanese investigators suggest GCP can inhibit angiogenesis, promote apoptosis, and stimulate immune system anti-tumor activity. Cell culture work from Dr. Katz' lab indicate GCP can interrupt prostate cancer cell cycling, and induce apoptosis.

Life After PC-SPES: Redoubling Research Efforts

It is not always easy to pioneer a new direction in medicine, or to try and bridge worlds as highly divided as those of conventional and "alternative" medicine. Dr. Katz and his group have had their share of disappointments, the biggest being last year's PC-SPES debacle.

was used as a treatment for prostate cancer several decades ago. Many patients still view PC-SPES as a lifeline that they desperately want back. Dr. Katz said that unfortunately, we will probably never know if the botanicals in the product had any anti-tumor effects or whether the observed PSA reductions and prolonged survival were solely attributable to the pharmaceutical contaminants.

The PC-SPES affair underscores the dire need for careful clinical investigation of natural products, especially those used for serious diseases like prostate cancer. Rather than shying away from further botanical studies, Dr. Katz and his team have intensified their efforts in the wake of PC-SPES' demise. Like it or not, many patients with life-threatening illnesses are going to seek treatment options outside of conventional practice, and it is essential to listen to their experiences and study modalities that seem to be working for them.

It is equally important to look closely at the quality of the products patients are using. Dr. Katz said he was particularly interested in New Chapter's Zyflamend, because the company grows most of its own constituent herbs organically, and obtains its extracts using a supercritical CO₂ process, meaning there are no toxic solvent residues such as acetone or hexane, as is the case with other extraction techniques.

In working holistically with urologic patients, Dr. Katz has learned that there are no one-size fits-all protocols for any particular disease. Treatment must always be individualized, making optimal use of all appropriate therapies. Asked what he recommends for a common problem like BPH, he answered simply, "It depends."

"For mild to moderate symptoms, we recommend a combination of β -sitosterol, Saw Palmetto, Pygeum, and Stinging Nettles. For more severe symptoms, I might use those but add in an α -blocker." Flexibility and open-mindedness are the keys to providing effective integrative health care. ☺