PROSTATE CANCER HOT SHEET

US TOO! INTERNATIONAL MARCH 2003

DEVELOPING A HEALTH STRATEGY FOR *YOUR* PROSTATE CANCER

By "Bill" Blair
Chairman, Us Too! International
Scientific Advisory Council

This article is for people who have advanced cancer or those who want to make changes in their life right now. It's for warriors and fighters and can be used as a starting point for discussions with your medical oncologist or other physician caregiver. ***It is not intended as a substitute for competent medical advice. Remember, only you – in conjunction with your physicians and care givers - can select the course of treatment that is best for you.*** This is only a suggested starting point for discussion based on my experience and study as a breast- and lung-cancer researcher for 45 years, and as an advanced-prostate-cancer patient for seven years. These items do not guarantee results. But they may well help you and your physician(s) determine a course of treatment for you – best of all they probably won't hurt if used judiciously.

This compilation is subject to change as new data and knowledge accumulates and I'll provide updates as possible.

It's the search process that keeps hope alive. Hope is an expectation for a good outcome.

A Health Strategy

· Develop a health plan, even though you might not always follow it to the letter. If a cancer cannot be disabled by removing it or killing it, it may be disabled by containing it and keeping it under control. That is, it may be changed from an acute condition into a chronic condition.

· Include the spiritual. Keep hope alive. Have the intention to go forward with life no matter what happens. If you search, you can find. Hope and determination makes you healthier.

· Find others who have dealt with your type of cancer. There are many long-term survivors. Get into a positive, activist support group—with others who are taking responsibility for their own health. There are a lot around. You can find them through groups like ***Us Too!***, Y-Me (Breast Cancer) or the American Cancer Society – you may also find other local resources by asking a librarian; or local health center or by checking the Internet.

· ***Get educated.*** Do more and more to learn about and to improve your health. Realize that you are the one who has the ultimate responsibility for your health; that's very important. In prostate cancer, there is sometimes a disconnect between what scientists know (or suspect) and what doctors do. This is true in other medical fields as well.

· Get a detailed pathology report from your surgery. That report is the foundation of your treatment plan.
- Was there tumor left behind?
- How much?
- Where located?
- Is it growing slow or fast? This is extremely important to know.
- What else is in the report?

· Consider biochemical marker testing. These tests are inexpensive. The results can act as "canaries in the coal mine," indicating possible need for other, more expensive tests.

- Immune system indicators: White blood count, T-cell count, etc.
- Serum markers appropriate for your specific disease (for instance, PSA for prostate cancer). Result can be used as a gauge of the effectiveness of a treatment, alerting you earlier to a need to switch to a different treatment.
- Pyrilinks-D urine test, as a measure of bone loss. (Costs about $50, vs.

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PSA TESTING APPEARS TO IMPROVE SURVIVAL:

CPDR Publishes Promising Results on Impact of Prostate-Specific Antigen Testing

By Justine A. Cowan
Technical Writer – CPDR

In a recent study, researchers in the United States sought "to determine how the implementation of prostate-specific antigen (PSA) testing has affected disease-specific survival and other characteristics of prostate cancer.

Physicians at the DoD Center for Prostate Disease Research (CPDR) in Rockville, Maryland announced the publication of a novel and groundbreaking manuscript in the Rapid Communication section of the medical journal, *Urology*. The manuscript, entitled "Improved Prostate Cancer-Specific Survival and Other Disease Parameters: Impact of Prostate-Specific Antigen Testing" by Paquette et al. (*Urology*, 60(5), 756-759, 2002) explains the premise that Prostate-Specific Antigen (PSA) testing, which is the current method used by physicians to detect a protein in a patient's blood which might indicate the presence of prostate cancer, has improved survival for prostate cancer patients. The second conclusion is that PSA testing has decreased the percentage of patients that present with metastatic disease or disease that has spread from the prostate to other parts of the body or vital organs.

Data for this study were collected from 2,042 patients at the Walter Reed Army Medical Center (WRAMC) in Washington, D.C. between 1988 and 1998. Statistical analyses were used to summarize trends over time in survival, mortality, and clinical stage," wrote E.L. Paquette and colleagues,

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PROSTATE CANCER NEWS YOU CAN USE

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AstraZeneca

REPETITION MAKES BEST SURGEONS FOR COMPLEX PROCEDURES, STUDIES FIND

The Boston Globe - Feb 05, 2003

A growing body of research is pinpointing the surgeons most likely to cause harm or death during operations, creating powerful benchmarks for obtaining safer medical care. A simple question posed to surgeons, the research shows, can often separate the talented from the average: How often do you do this? The work builds on earlier research that established that busy hospitals generally deliver better care. But it adds a new level of precision, citing the specific risks patients face in the hands of low-volume surgeons, who don't frequently and regularly perform certain procedures. These surgeons become most dangerous, the studies found, during AIDS treatments, carotid artery blockage surgery, pediatric heart surgery, as well as surgeries for cancers of the lung, pancreas, esophagus, rectum, and prostate. These are complex procedures, often requiring precise cuts and scrapes near the nerves and arteries of gravely ill patients. One study estimated that up to 13 out of every 100 surgical deaths in these procedures could have been prevented in the hands of high-volume surgeons. Other studies have shown slightly smaller risks from low-volume surgeons during coronary artery bypasses, coronary angioplasties, and some orthopedic procedures. Health specialists said the new data, collected mostly in the last three years, should encourage patients with these afflictions to exercise extra vigilance when selecting surgeons. In a study released last week, researchers found the volume pattern held for radical prostatectomies, the most common US treatment for localized prostate cancer, which afflicts 333,000 American men annually. Low-volume surgeons had twice the rate of complications, which include impotence and incontinence, and their patients were hospital-bound for an extra day, compared with high-volume surgeons' patients. "It's the type of an operation that requires a certain skill. If you really practice, you can get better," said the study's author, Dr. Mark S. Litwin, a University of California at Los Angeles urology professor. High volume in Litwin's study meant 40 or more procedures annually. The urology chief at Brigham and Women's Hospital, Dr. Jerome P. Richie, performs the surgery up to 200 times a year, four times a week on average. Richie notes that radical prostatectomy methods have changed drastically in the last 15 years. Frequent practice, he said, was necessary to master the precarious procedure, which involves cutting deep into the pelvis where thick veins weave around the prostate. "How can I put this delicately?" he said. "I don't want to sound high-handed, but volume matters . . . I would recommend that patients seek surgeons that do at least 50 to 100 cases a year." After all, said Richie, "they are placing their trust in the hands of someone else."

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KETOCONAZOLE: CHEAP AND EFFECTIVE IN THE FIGHT AGAINST HRPC

DataMonitor CommentWire
February 03, 2003

Hormone refractory prostate cancer (HRPC) is an advanced stage of the disease. At this stage, drugs that reduce the level of androgens in the body no longer control the growth of the tumor, and the average metastatic patient survives for around six to nine months. Survival rates are low due to the advanced state of the disease and the lack of effective drugs to treat it. There are currently just two approved agents for the treatment of HRPC, mitoxantrone and estramustine, but these are usually only effective for a short period. In early studies, however, the anti-fungal agent ketoconazole, which causes complete androgen deprivation, appeared to be effective against HRPC. But the drug also caused severe liver damage, and the resulting publicity reduced its usage. More recently, a phase II trial investigating the use of ketoconazole in second line HRPC has shown the drug to be less toxic than first thought. Dr Garcia Velasco from the Universidad Doce de Octubre, Madrid gave a group of HRPC patients that had failed a median of three previous treatments either 600 or 1200 mg/day of ketoconazole. Far more patients responded to therapy in the high dose group, and these patients also had a longer duration of response. Interestingly, no hepatic toxicity was reported, but 8% of patients did withdraw because of gastrointestinal toxicity. At present, HRPC is an indication for which a number of high profile chemotherapy agents are under investigation, most notably, the taxane drugs paclitaxel and docetaxel, and the vinka alkaloid vinorelbine. By comparison to these drugs, ketoconazole scores highly. It is both

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PATIENT GROUPS AIM TO REVIVE A BANNED PROSTATE TREATMENT

By ANDREA PETERSEN
THE WALL STREET JOURNAL

It was April 9, 2002, when Bob Greenberg swallowed his last PC-Spes capsule, the herbal concoction he credits with keeping his prostate cancer in check for a year.

Two months earlier, government regulators found that PC-Spes was contaminated with prescription drugs, including blood-thinner warfarin, and yanked it from store shelves.

Left in the lurch were 10,000 men who relied on the remedy, a product routinely recommended by mainstream oncologists and its efficacy supported by clinical trials. Since he ran out of PC-Spes, Mr. Greenberg has slowly seen his level of prostate-specific antigen — a marker of how aggressive the cancer is — triple. "PC-Spes worked," says the 67-year-old Mr. Greenberg. "I'd like to see them bring it back."

Indeed, at least two patient groups are trying to bring the original PC-Spes (the name refers to "prostate cancer" plus the Latin word for "hope") formula back to market. One hopes to have a product on the market within six months. Also, the National Institutes of Health, which halted four studies it had been funding of PC-Spes, has resumed three of them, aiming to determine which compounds in the product are beneficial.

Clearly there are hurdles to bringing back PC-Spes. BotanicLab, the Brea, Calif., maker of PC-Spes, went out of business in June. And the patient groups concede that it may be difficult to avoid the kind of contamination that got BotanicLab in trouble. In China, drugs and herbs are often made in the same facility, which can lead to cross-contamination. Also, some research suggests that it was the prescription drugs — the contaminants themselves — that may account for PC-Spes's beneficial effects.

There is also the fear of litigation. Former PC-Spes patients have sued BotanicLab, alleging the company, its founders and numerous distributors of PC-Spes engaged in "unlawful, unfair and/or deceptive business practices," among other things.

A lawyer for Botanic-Lab said there is "no reason to believe there is any merit to the validity of their claims," which were filed in California state superior court in Los Angeles County. The groups that are trying to bring back PC-Spes are concerned that they too may be vulnerable to litigation.

Still, the efforts are gaining momentum. The Cancer Cure Coalition, a nonprofit patient-advocacy group, says it has uncovered the complex recipe of PC-Spes (the original formula is patented) and is close to securing a manufacturer. The group says it could have a product on the market in the next six months. Another patient group, Natural Approaches to Prostate Cancer Inc., says it is about one month away from securing a manufacturer to produce a clean PC-Spes equivalent. The group says it will conduct clinical trials before making it available to consumers.

In the meantime, cancer patients are doing what they can. Besides conventional radiation treatment and chemotherapy, some are trying a host of new herbal products. A slew of PC-Spes knockoffs, with names like PC Hope and PC Calm, have recently appeared on the market.

Some are even being prescribed by oncologists. Often, they include some or all of the same eight herbs in the original formula. One treatment, PC Plus, claims to be an "improvement" on PC-Spes. But there are no clinical trials supporting the use of the copycats. The Food and Drug Administration won't say if it has scrutinized any of them.

Along with popping the copycat pills, some who had the foresight to stockpile PC-Spes are rationing it to make their dwindling supply last longer. "I'm getting towards the end of my reserve," says Fulton L. Saier, a retired obstetrician-gynecologist and founder of the Natural Approaches to Prostate Cancer group. "I used to take six pills a day and now I'm taking three." There is also a small black market in the contraband capsules. Last month, a visitor to NAPC's chat room held a silent auction to sell to the highest bidder what he claimed were two unopened bottles of PC-Spes.

PC-Spes became part of mainstream cancer care a few years ago after studies showed that it reduced PSA levels. There was also evidence that it shrank tumors. Oncologists were particularly encouraged by the results in men who weren't responding to traditional prostate cancer treatments. "It worked," says Aaron Katz, associate professor of clinical urology at Columbia University College of Physicians and Surgeons. "Some of these patients had a few weeks to live and they are still living because of PC-Spes." PC-Spes does have severe side effects, including breast tenderness and an increased risk of blood clots.

The history of PC-Spes highlights the quirkiness of the $17 billion dietary-supplement industry. Unlike pharmaceuticals, herbs and other dietary supplements are only loosely regulated by the government. Manufacturers don't have to prove that their products are safe or effective before marketing them, and often the list of ingredients on the label doesn't match what is actually in the bottle.

Indeed, loose oversight may have contributed to the rise and fall of the original PC-Spes. The manufacturing faced little scrutiny, and it was only after it had been on the market for more than five years that government regulators spotted a problem. In February 2002, California health regulators found that PC-Spes was contaminated with warfarin, a prescription blood thinner. Researchers later found that PC-Spes also contained indomethacin, an anti-inflammatory drug, and diethylstilbe strol, or DES, an estrogen that had been commonly used to treat prostate cancer in the 1960s and 1970s but had serious side effects such as blood clots. Regulators ordered a recall.

That could have been the death knell of PC-Spes, but some science seems to be vindicating the compound. One recent study comparing men on PC-Spes with those on DES showed better results in the men who were taking PC-Spes, casting doubt on the idea that DES was responsible for all of the herbal compound's positive effects.

There is also new evidence showing that at least one of the components in PC-Spes, a flavonoid called baicalin contained in the herb skullcap, kills prostate-cancer cells. Other researchers are investigating saw palmetto, a herb that is already taken by many prostate-cancer patients. There is also evidence that taking vitamin E and selenium may be beneficial.

This article appeared in the Wall Street Journal on Feb 18, 2003

DEVELOPING A HEALTH STRATEGY

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$800 for a bone-density test.) This is a useful test for patients who are elderly or have cancers that can spread to the bone: prostate cancer, breast cancer, lung cancer, etc. A higher-than-normal reading suggests that bone loss is occurring. In that case-

- Get a bone-density test.
- Possibly test for vitamin-D deficit.
- Take remedial action.
- Take vitamin-D.
- Take Calcium and Magnesium. (See "Supplements," below)
- Investigate your need for boron, silica, and maybe copper.
- Ask about bisphosphenates. * Fosamax (oral). * Zometa (intravenous).
- Allow for effects of therapy on markers.

For instance: If you're on chemotherapy, and your hemoglobin, white-blood cells, or platelets are low, it could be due to the chemotherapy, and in that case would be correctable.

Treating advanced cancer

Chemotherapy

- Look into minimizing the side effects. These are specific to the particular chemo agents. For instance, if taking taxanes: Cool your scalp to minimize hair loss. Cool hands and feet to minimize fungal infections on your nails. You can use ice packs for this purpose. They constrict the blood vessels to the cooled areas, thus lowering distribution of the chemo agent to those areas.

- If you have any skeletal problems, consider using bisphosphonates. For instance, Zometa (zoledronic acid), a 15-minute infusion once a month. (Taking once a year may be a preventative for osteoporosis.) Stay well-hydrated both before and after administration. If you have cardiovascular problems, inform your physician before taking Zometa. It is a great down-regulator of skeletal metastases. In my opinion, as penicillin is for bacterial disease, Zometa is for skeletal metastases. It may help pre-empt metastases in prostate cancer.

Exercise

- The number two thing you can do to fight cancer is to exercise every day. It fights depression, produces endorphins (makes you feel good, enhances immune- system function), and has other benefits. Walking, light weights, yoga, Tai Chi, etc. Studies show that physically active patients do much better than sedentary patients.

Diet

General

- The number one thing you can do to fight cancer is to eliminate excess caloric intake.

- Lose excess weight: Stored body fat produces hormones, which stimulate tumor growth.

- Avoid red meat. Contains arachidonic acid, which can stimulate cancer growth.

- Most people consume 40% or more of their calories from fat. There may be benefit in reducing this to 10% - 20%.

- Elmininate saturated fat and partially hydrogenated oils from your diet.

- Increase intake of omega-3 fatty acids (DHA and EPA). Found in cold water fish and walnuts.

- Use only monosaturated oils and/ or the "good" polyunsaturated oils.

- Avoid sugar. Tumors gorge themselves on it.

- Take lycopene, found in red fruits and vegetables: Tomato products (eat cooked, with olive oil), watermelon, ruby red grapefruit, etc.

Breakfast:

- Eat a cereal that's high fiber, low fat, and low sugar. For example, Fiber 1.

- Eat some protein. (Take some protein at every meal). Good choices: Two teaspoons of:
  - Whey protein. (Stimulates bone-marrow production, helps maintain muscle mass. Also good for treating weakness.)

  or

  - Soy protein. (Low in methionine, a possible cancer stimulator.)

- Lots of fresh fruit. (Wash skins to remove pesticides.) Good for smoothies. Some good choices:
  - Strawberries
  - Apples.
  - Pears.
  - Banana.
  - Frozen raspberries.
  - Frozen cranberries.
  - A lot of sprinkles of raw green tea. (For even smaller particles, run the tea through a coffee grinder.)

For liquid in the smoothies, you can use low-fat soy milk, apple juice, or water.

Supplements

* Take throughout the day, in two or three batches.

Unless advised otherwise, avoid taking supplements within one hour of eating. Food can interfere with absorption of some supplements.

- If you have metastases, and your type of cancer makes a lot of COX-2, explore the use of a COX-2 inhibitor. COX-2 is produced by colon, breast, lung, and prostate cancers, as well as others. Celebrex is a COX-2 inhibitor, used for relieving inflammation from arthritis. In some animal studies, Celebrex coverted about 40% of pre-cancerous polyps in the colon into benign polyps. It appears that Celebrex shrinks blood vessels that feed tumors and polyps. I'm taking 400 mg of Celebrex twice a day. I take it only with food. If I couldn't get Celebrex, I'd use ibuprofen, 200 mg, no more than 4 times a day, with food.
- Vitamin E, preferably in the form of "mixed tocopherols," otherwise as "d-alpha tocopherol". 400 IU twice a day. Take with food. Absorption of vitamin E is enhanced by eating with dietary oil.
- Beta-carotene, 15 mg/day
- Vitamin B supplement (B-50 or B-100), one a day. Can also help alleviate neuropathy.

- Vitamin C, 500 mg twice a day.
- Calcium citrate, 500 mg twice a day.
- Magnesium, 250 mg twice a day. Take at evening meal, and at bedtime. Absorption is aided by a little non-processed sugar: honey, jam, or dried fruit.
- Selenium, 200 mcg (micrograms) once or twice a day.
- Zinc gluconate, 20 mg once a day.
- Omega-3 (EPA and DHA) supplements. Helps nervous system and immune system. 1000 mg twice a day.
- Cod liver oil. (Contains vitamin D, vitamin A and essential fatty acids.) 250 mg or one teaspoon, once a day in morning.
- CLA (conjugated linoleic acid). 400 mg, three times each morning. Comes in a 1000 mg tablet, but only 600mg of that is CLA. Comes from sunflowers, and from cattle that eat them. Moderately expensive. Maintains muscle mass. May inhibit some cancers (breast, prostate). Counteracts linoleic acid, a promoter of some tumors.

Finally, stay well hydrated - Drink lots of water. About one gallon throughout day is only about one 8oz glass every waking hour.

PSA IMPROVES SURVIVAL

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Uniformed Service University Health Science, Department of Surgery.

The researchers found that "between 1988 and 1998, a total of 2042 patients with prostate cancer were registered at Walter Reed Army Medical Center. The 5-year disease-specific survival rate was 86.9% and 93.7% for patients diagnosed in the respective year groups of 1988 to 1991 and 1992 to 1994, with follow-up through December 1, 2000 ($p<0.001$). Prostate cancer was the cause of death for 37.5% of the patients in 1988 to 1989 versus 15.4% in 1999 to 2000. Marked stage migration has occurred; from 1988 to 1998, the percentage of patients presenting with metastatic disease decreased from 14.1% to 3.3% ($p<0.001$)."

The researchers concluded: "A statistically significant improved 5-year disease-specific survival and a decreased chance of dying from prostate cancer has occurred after the widespread implementation of PSA. We suspect that PSA testing has resulted in fewer patients presenting with metastatic disease and more patients presenting with localized disease amenable to curative treatment. This portends well for the use of PSA screening to improve outcomes for prostate cancer. However, randomized trials are needed to confirm the improvements in survival and mortality."

Dr. Judd Moul, CPDR Director and Colonel in the Medical Corps, US Army, is encouraged by these results. "The whole issue of population-based screening for prostate cancer has been controversial. Our data is tantalizing early evidence that early detection efforts using PSA are making a favorable difference for men and their loved ones. We're now working to confirm these results in the larger military population that we're studying." Moul continued to discuss the benefits to researchers and clinicians utilizing the CPDR Database for their work. "With over 17,000 men with prostate disease enrolled from nine major centers, the CPDR Tri-service Multicenter Patient Database is becoming a national treasure." The military services routinely start PSA testing of soldiers, airmen, and sailors at the over age 40 health evaluation. Moul concluded, "The CPDR studies in this equal-access population should shed much future light on this important issue."

CPDR is a program of the Uniformed Services University of the Health Sciences and administered by the Henry M. Jackson Foundation for the Advancement of Military Medicine. For more information on CPDR, visit www.cpdr.org.

Paquette and colleagues published their study in Urology (Improved prostate cancer-specific survival and other disease parameters: Impact of prostate-specific antigen testing. Urology, 2002;60(5):756-759).

The contact person for this report is J.W. Moul, Uniformed Service University Health Science, Dept. of Surgery, Center for Prostate Diseases Research, 1530 E Jefferson St., Bethesda, MD 20892 USA.

NEWS YOU CAN USE

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cheaper and has fewer side effects, and is especially suitable for use by elderly patients, many of whom are reluctant to undergo chemotherapy. Although vinorelbine will soon be available in tablet form, making it far more convenient to administer, ketoconazole's advantages in terms of cost and convenience look set to drive increasing usage in HRPC patients.

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PROSTATE CANCER SURVIVORS MAY BENEFIT FROM SOY; SOYFOODS AND SUPPLEMENTS SEEN AS 'REASONABLE'

Soy can be recommended for survivors of prostate cancer who "want to know whether soy might prevent recurrence," Tufts University's Health & Nutrition Letter reports in its coming February issue. A new review of medical evidence by health experts has found that plant estrogens in soy "might possibly have benefit in delaying prostate cancer progression," the Tufts publication said. Experts at Harvard Medical School, the National Institutes of Health, and two Canadian institutions have concluded that there's little or no risk for prostate cancer survivors to include soy in their diets, the health letter added. Lead author of the review of evidence was Dr. Wendy Weiger, who said: "It generally appears reasonable to accept the consumption of soy supplements or soyfoods by patients with prostate cancer." Many cancer survivors today are looking to nutrition to help prevent future illness, the Health & Nutrition letter said in its lead article — "eating specific foods, taking supplements, or following certain diet regimens." Fortunately, the publication said, "scientists have made inroads on the nutrition front for survivors." Soy has been touted for prevention of hormone-sensitive cancers, including prostate cancer, for a number of years, the Tufts letter said.

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FOR POTENTIAL CURE BY IRRADIATION, A PSA NADIR MUST BE ACHIEVED WITHIN 5 YEARS

"A prostate specific antigen (PSA) cutoff point of 0.2 ng/ml has been suggested as the standard definition of disease freedom for curative treatment of localized prostate cancer. The time to achieve this goal after irradiation was

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10 QUESTIONS WITH AARON KATZ, MD ON THE CENTER FOR HOLISTIC UROLOGY AND RESEARCH INTO A POTENTIALLY PROMISING NEW COMPOUND TO TREAT PROSTATE CANCER.

In January 1999 The Department of Urology at Columbia-Presbyterian Medical Center opened The Center for Holistic Urology. This Center is dedicated to the complementary treatment of men and women with disorders of the urinary tract. These include cancers of the prostate, bladder, and kidney, chronic urinary tract infections, benign prostatic enlargement, prostatitis, and kidney stones. The Center focuses on the use of natural therapies which will improve the overall health and well being of the individual patient. Currently, the Center has several areas of treatment. These include:

- Nutritional therapy
- Herbal therapy
- Immunologic therapy
- Mind-Body therapies
- Exercise therapy
- Acupuncture

The Director of the Center, Dr. Aaron E. Katz, is an Assistant Professor of Urology at Columbia. By using a complementary approach and natural therapies, Dr. Katz hopes to improve the current cure rates of traditional therapies such as radiation, chemotherapy, and surgery. "Evidence is mounting that we can prevent many illness such as cancer by modifying our lifestyle. The type of diet that we eat, amount of exercise, and the way we deal with stress are all related to the development of cancer and other diseases", said Dr. Katz.

Q1: Why did you set up the Center for Holistic Urology at Columbia University?

A: We wanted to look at natural therapies, such as herbs and nutritional modification, to determine their role in treating prostate cancer. We take a conservative treatment approach, carefully monitor our patients' cancer, and if necessary resort to definitive treatments such as radiation or surgery.We're investigating natural therapies in the lab as well as the clinical arena. Our mission is to perform clinical trials that allow us to responsibly offer innovative natural therapies to our patients and to educate other physicians about the potential role of botanicals and nutrition in urological cancer management – specifically bladder, prostate and kidney cancer.

Q2: What is unique about the Center's approach to treatment?

A: We of course still do a lot of mainstay treatments such as radiation and surgery. But we're also looking into alternative therapies to integrate them into the management of patients with cancer. We have assembled a very capable team of clinicians and researchers dedicated to these alternative approaches. We've tried to take a lead in the study and use alternative and complementary therapies for urological cancers.

Q3: Why weren't you satisfied to continue with the established modes of treatment?

A:For one thing, many of the established treatments have side effects. When you're talking about prostate cancer surgery, the side effects are well known including impotence, incontinence, surgical incision infection, and so on. And with radiation you also have side effects such as rectal injury, bladder injury, and sexual side effects as well. And so there are many cancer patients whose cancer may not be very aggressive and can be "observed," so to speak, rather than treated with these aggressive approaches.

The other consideration is that not all of the patients that are treated with radiation or surgery are cured. And although the cure rates are fairly high when the cancer is treated early, there are a number of situations where the cancer can return or where the patients are at high risk for recurrent cancer, and then those complementary therapies would be appropriate to try and see if we can reduce the risk of recurrence.

Q4: How much choice does the patient have, if he's been diagnosed with prostate cancer, in terms of using these alternative therapies?

A: A patient always has a choice. With any therapy, there's always a risk and a benefit. The benefits of the complementary therapies are that they're not going to have any significant side effects. And I let patients know that in a thorough discussion. When any patient is diagnosed with cancer I try to engage the patient and let them know there are choices nowadays and thankfully, there are different approaches. We somewhat tailor the approach, based on the individual patient and his age, his medical status, and the type of cancer. Some cancers are more aggressive than others.

When we involve a patient in a consultation, we go through the various treatment options explaining the various risks and benefits we were talking about. Obviously, in the case of complementary therapy, the benefits are that you're taking natural therapies so there are no significant side effects. But there are risks. And the risks are that the cancer that you have, if not treated in a standard fashion, could potentially spread. I always try and engage the patient and then let them make the decision. They always have the choice—it's never a one-sided thing, where the physician decides that this is what he has to do.

Q5: In general, do you find that patients are open to alternative therapies?

A: I think a lot more so. Patients do hear about the risks of surgery and radiation, and there's also lots of data coming out to show the benefits of nutrition and herbal medicine. And we also know that in many cases the cancer can be very slow growing, such that it may be 10 or 15 years before the cancer has any impact on the patient's life. So during that time the patient may want to maintain sexual activity and urinary control and so forth, and treat it with a holistic approach.

Q6: Can you discuss your preliminary research with Zyflamend®?

A: What we found works best here at Columbia is that when we have an interesting compound like Zyflamend we first do some testing in the laboratory against human prostate cancer cells. And the way the study was devised was to take different extracts of Zyflamend and expose them to these prostate cancer cells and see whether or not there is an effect, whether or not these cells die in the presence of Zyflamend. And we did find in fact a dose response where at higher doses Zyflamend seems to stop cells from growing and dividing. And it causes these cells to undergo a process of cell death called apoptosis. This Zyflamend is a very exciting compound. It's in a class known as COX-2 inhibitors, and the COX-2 enzyme seems to be necessary for cancer cells to grow. And so when you inhibit the enzyme you cause cells to regress and to die.

It's an exciting area in the oncology field, these COX-2 inhibitors. There are a couple of pharmaceutical companies that have come out with COX-2 inhibitors and they're mainly used in the anti-inflammatory areas such as arthritis and several areas of inflammation. They do have some side effects. With Zyflamend, we're finding that really there are no side effects to date. And the true activity in this compound against cancer is yet unknown. But we hope to initiate a clinical trial within the next few weeks to determine its true value in the human patient.

Q7: Can you talk about that study?

A: We're probably going to need over 100 patients. And the population we've decided to use are patients that have been diagnosed with what's called PIN, which is a pre-cancerous form of prostate cancer – cells that are about to turn into cancer but haven't yet. We're going to treat patients with Zyflamend for about six months to see if we can reduce the incidence of cancer in these patients. Many of these patients that have this PIN will go on to develop prostate cancer, and so if we can prevent prostate cancer in these patients this would be a tremendous outcome.

Q8: How did you hear about Zyflamend?

A: I heard that New Chapter had a novel compound, Zyflamend, a COX-2 inhibitor with lots of preliminary data from different sources, and it sounded like an exciting compound.

Q9: Do you have a concluding statement for ***Us Too!*** members regarding cancer therapies?

A: What I say to patients of prostate cancer is that even if you decide to use a traditional therapy like surgery or radiation, that nutrition, diet, and herbal supplements can be helpful in the long run in potentially reducing a recurrent cancer. And they may also have some other health-related benefits. And at this time we are investigating this new compound Zyflamend, which at least in the laboratory appears to be quite promising. And we will pursue it further with a clinical investigation.

Q10: If your research on people is as promising as your in vitro studies, do you see a different picture emerging in the next decade regarding treatment?

A: I think that many of the patients with localized, low-grade cancer may opt for this complementary type of approach and modulating their PSA value, rather than embarking on surgery and radiation right away.

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determined in this study," researchers in the United States report. "From August 1992 to December 1996, 539 consecutive men with clinical stage T1T2NX prostate cancer who had a minimum 5 year PSA follow-up and achieved a PSA nadir of 0.2 ng/ml without hormones were evaluated. All patients were treated with simultaneous irradiation with a transperitoneal prostate I-125 implant, followed by external beam irradiation. Time to achieve a PSA of 0.2 ng/ml was retrospectively calculated from the date of implantation in all men, according to various factors. Recurrence was defined as a subsequent increase above a PSA of 0.2 ng/ml. Minimum follow-up was 5 years (median 6.5, range 5-9)," wrote F.A. Critz and colleagues from the Radiotherapy Clinic of Georgia, Decatur, USA. The researchers found that "in all 539 men the median time to a PSA nadir of 0.2 ng/ml was 27 months, while 534 (99%) achieved this level by 60 months of follow-up. Median time to achieve this PSA goal was 20 and 39 months in patients without, and with, a PSA bounce, respectively. Pretreatment PSA, disease status and ultimately PSA bounce, Gleason score, and stage had little or no effect on time to a PSA of 0.2 ng/ml." The researchers concluded: "With rare exceptions, to be potentially cured of prostate cancer by simultaneous irradiation, men must achieve a PSA nadir of 0.2 ng/ml within 5 years of implantation. Failure to reach this goal by 60 months of follow-up almost always indicates persistent disease." Critz and colleagues published their study in Journal of Urology (Time to achieve a prostate specific antigen nadir of 0.2 ng/ml after simultaneous irradiation for prostate cancer. J Urol, 2002;168(6):2434-2438).

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EXTERNAL IRRADIATION EFFECTIVE IN ACHIEVING CURE RATES

Researchers in the United States studied "the biochemical cure rates (biochemically no evidence of disease) after external irradiation (RT) in patients with high-risk prostate cancer after radical prostatectomy. "Seventy-six patients who underwent radical prostatectomy and subsequent RT were included in this analysis. No patient received hormonal therapy. Adjuvant RT was administered in 35 patients

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(46%), and 41 patients (54%) underwent salvage RT. After prostatectomy, the Gleason score was<7 in 87%, and 24% had seminal vesicle invasion. "The median RT dose in the adjuvant RT and salvage RT groups was 60 Gy and 65 Gy, respectively. The biochemical cure rate was defined as a serum prostate-specific antigen of less than or equal to0.2 ng/mL," stated J.A. Kalapurakal and colleagues, Northwestern Memorial Hospital, Department of Preventive Medicine. The researchers reported that "the overall 5-year Kaplan-Meier biochemical control rate from the end of RT was 70%. The 5-year biochemical cure rate for adjuvant RT was significantly superior to that after salvage RT (86% vs. 57%). The significant predictors of biochemical failure were seminal vesicle invasion in the adjuvant RT group and the presence of Gleason grade 4 or 5 in the salvage RT group. The clinical local control rate in the prostate bed was 100%." Kalapurakal and colleagues concluded: "This report demonstrates the efficacy of RT in achieving high biochemical cure rates after radical prostatectomy. Additional clinical studies are required to determine the optimal treatment of patients at high risk of biochemical failure after postprostatectomy RT." Kalapurakal and colleagues published the results of their study in the International Journal of Radiation Oncology Biology Physics (Biochemical disease-free survival following adjuvant and salvage irradiation after radical prostatectomy. Int J Radiat Oncol Biol Phys, 2002;54(4):1047-1054).

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FLAXSEED SUPPLEMENTATION INHIBITS TUMOR GROWTH IN TRANSGENIC MICE

In a recent study, researchers in the United States investigated "the effects of flaxseed supplementation on prostatic neoplasia in the transgenic adenocarcinoma mouse prostate (TRAMP) model. "A total of 135 male TRAMP mice 5 to 6 weeks old were randomized to a control group (AIN-76A diet) or an experimental group (AIN-76A diet plus 5% flaxseed by weight). One-half of the mice in each group were treated for 20 weeks and the remainder for 30 weeks. At autopsy, urogenital tissues (four prostatic lobes, seminal vesicles, and emptied bladder), lungs, lymph nodes, and grossly abnormal tissues were collected for histologic evaluation," wrote X. Lin and colleagues, Duke University Medical Center. The researchers found that "of the control mice, 100% developed prostate cancer versus 97% of the mice in the flaxseed group. The tumor/urogenital weight was 3.6 ± 0.4 g in the controls vs. 1.9 ± 0.2 g in the flaxseed-treated mice (p=0.0005). At 20 weeks, no significant difference in tumor grade was seen between the two groups; however, at 30 weeks, the flaxseed-treated mice had significantly less aggressive tumors than did the controls (p=0.01). "The prevalence of lung and lymph node metastases was 13% and 16%, respectively, in the control mice vs. 5% and 12%, respectively, in the experimental group (difference not significant). After 20 weeks of treatment, cellular proliferation (Ki-67) differed significantly between the control and experimental groups (38.1 ± 2.03 vs. 26.2 ± 2.03; p<0.0001), and the apoptotic index (deoxynucleotidel transferase-mediated dUTP-digoxigenin nick end labeling) was 1.45 ± 0.14 vs. 3.3 ± 0.31 (p<0.0001). Similar differences were seen after 30 weeks of treatment." The researchers concluded: "A diet supplemented with 5% flaxseed inhibits the growth and development of prostate cancer in the TRAMP model." Lin and colleagues published their study in Urology (Effect of flaxseed supplementation on prostatic carcinoma in transgenic mice. Urology, 2002;60(5):919-924).

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PHYTOESTROGENS MAY PLAY ROLE IN PROGRESSION OF MALIGNANCY

According to recent research from Austria, "soybean products are highly represented in the traditional Asian diet. Major components of soy proteins are phytoestrogens, such as isoflavones. They may be responsible for the extremely low incidence of prostate and mammary tumors and possibly also of colon cancer in countries such as China and Japan." "Serum 1,25-dihydroxyvitamin D-3 level is inversely related to incidence of some cancers. Levels are determined by skin exposure to ultraviolet light or, to a minor extent, nutritional uptake and by subsequent conversion of the precursor vitamin D to the active hormone by the cytochrome P450 hydroxylases CYP27A1, CYP27B1 (responsible for synthesis), and CYP24 (responsible for catabolism) in liver and kidney. However, vitamin D synthesis is also found in colonocytes and is enhanced during incipient malignancy. This may indicate an autocrine/paracrine role for this differentiation-inducing hormone in defense against progression," wrote E. Kallay and colleagues, University Vienna, School of Medicine. The researchers concluded: "We were able to demonstrate that either a single large oral dose of genistein or feeding soy protein for 4 months elevated CYP27B1 and decreased CYP24 expression in the mouse colon. Our data therefore suggest that an inverse correlation of soy product consumption with colon tumor incidence may be consequent to enhanced colonic synthesis of the antimitotic hormone 1,25-dihydroxyvitamin D-3." Kallay and colleagues published their study in Journal of Nutrition (Phytoestrogens regulate vitamin D metabolism in the mouse colon: Relevance for colon tumor prevention and therapy. J Nutr, 2002;132(11 Suppl.):3490S-3493S).

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TETRACYCLINE OFFERS PROMISE FOR HALTING CANCER

A cancer treatment is being developed that's safe, cheap, and almost completely effective. It's been around for decades but no one ever thought about using it to fight the disease. The treatment is tetracycline, a family of inexpensive acne antibiotics. The drug is being researched for its ability to prevent metastases, the migration of cancerous tumour cells that migrate throughout the body, creating secondary tumours. Dr. Gurmit Singh of the Hamilton Regional Cancer Centre in Hamilton, Ontario, Canada is leading research on the drug. Singh learned over the past four years that tetracycline is not only effective at preventing metastases from forming in bones, it also has the ability to kill tumour cells in the bone. In tests on mice, his team found the drug cut the spread of certain cancers to the bone by 70 per cent. "This was very exciting to us so we continued on with our experiments and what we found was that it actually improved the bone itself. In some ways, it healed the bone," says Dr. Singh. Tetracycline has been used to treat acne and periodontal disease. The drug is absorbed by teeth and bones, and blocks a group of enzymes called matrix metalloproteinases, a cause of gum degradation. The drug has caught the eye of the Canadian Breast Cancer Research Initiative, which is funding a small human study of 60 patients. Dr. Singh is the lead investigator of the project