The Recall of PC-SPES

The recall of PC-SPES last year left many prostate cancer patients with a mixture of emotions: confusion, anger, and despair. It also left them with a host of unanswered questions. How could prescription medications have gotten into a so-called "natural" supplement? Had the supplement's manufacturer intentionally defrauded desperate cancer patients? And what would patients who had experienced good results with the treatment do now that it was no longer available?

We may never know all the details of the PC-SPES recall. But there is still good news for men who found that PC-SPES worked for them when other treatments had failed.

A History of PC-SPES

PC-SPES was a nutritional supplement containing eight herbs that was purported to shrink prostate cancer tumors. It was developed by a pharmacist in the early 1990s and, starting in 1996, was manufactured in China for a California-based company called BotanicLab. The supplement was taken by as many as 10,000 American men, most of them with advanced prostate cancer that no longer responded to hormone therapy such as luteinizing hormone-releasing hormone (LH-RH) analogs or antiandrogens.

The supplement did seem to be effective at reducing prostate specific antigen (PSA) levels. A 2002 review of more than a dozen uncontrolled studies revealed that PSA levels dropped in 80% to 90% of hormone-sensitive patients (those not yet resistant to hormone treatment) and 65% of hormone-insensitive patients (those no longer responding to hormone therapy) taking PC-SPES. Some patients even experienced tumor shrinkage, along with improved pain control and better quality of life.

PC-SPES also produced some side effects: blood clots in the legs and lungs, breast enlargement, nipple tenderness, hot flashes, and loss of libido. The similarity of these side effects to those produced by estrogen therapy suggested that the supplement might have estrogen-like activity. Estrogen is an effective treatment for prostate cancer, but it was largely replaced by LH-RH analogs in the 1970s because it tended to cause blood clots and other cardiovascular side effects.

Then, in early 2001, a man taking PC-SPES started to bleed excessively. Doctors found the anticoagulant warfarin (Coumadin) in his blood, which led to the discovery that PC-SPES contained warfarin. Other supplements from BotanicLab were tested and found to contain ingredients such as alprazolam (Xanax), an anti-anxiety drug. The distributor recalled the supplements, and the National Center for Complementary and Alternative Medicine halted four studies of PC-SPES that it was funding.

Finally, at the annual meeting of the American Association for Cancer Research in April 2002, researchers from California and the Czech Republic revealed more startling news: Much of the PC-SPES produced between 1996 and 1999 contained diethylstilbestrol (DES), a type of estrogen, and indomethacin (Indocin), a powerful anti-inflammatory drug. Batches of the supplement produced after 1999 contained warfarin and smaller amounts of DES and indomethacin. These findings were later published in the *Journal of the National Cancer Institute*.

The researchers hypothesized that the manufacturers in China added

Neoadjuvant hormone therapy. In neoadjuvant hormone therapy, temporary androgen blockade is used prior to—or combined with—surgery or radiation therapy in an attempt to increase the chances of eradicating all cancer. Available evidence suggests that androgen blockade before surgery does not increase the probability of an undetectable PSA level after surgery for men with localized (T1 or T2) or locally advanced (T3) prostate cancer. In addition, the use of hormone therapy before surgery makes it more difficult to perform a nerve-sparing procedure and more difficult to assess the true pathological extent of disease.

Preliminary data suggest that hormone therapy combined with radiation may increase survival for men with high-grade, locally advanced (T3 or T4) disease. Further studies are needed to clarify

DES to the supplement because they knew it would have an effect on prostate cancer; they included warfarin and indomethacin to counteract the increased risk of blood clots associated with DES. It is unclear whether the company in California knew of the tampering.

Renewed Interest in DES

DES was used in the 1960s as a treatment for men with advanced prostate cancer. Interestingly, the results with PC-SPES have prompted renewed interest in DES. Studies show that DES seems to be just as effective against prostate cancer as LH-RH analogs and antiandrogens, without increasing the risk of osteoporosis (see the sidebar on page 53).

Few doctors prescribe DES because it increases the risk of blood clots. But some researchers have suggested that using DES at lower doses than those used in the 1960s might reduce the risk. Another option may be to combine DES with aspirin. Of course, men will still have to deal with the other side effects of estrogen, such as breast enlargement and loss of libido.

If you are one of the thousands of people who responded well to PC-SPES, the good news is that you may be able to get similar or even better results with DES. Taking DES requires a doctor's prescription, which ensures that you will receive a standard dose—usually 1, 3, or 5 mg a day. The study of PC-SPES published in the *Journal of the National Cancer Institute* found that a daily dose of PC-SPES could contain anywhere from 0 to 0.5 mg of DES, depending on the lot number. In addition, DES costs only $30 a month—a far cry from the $250 to $400 a month that men were spending on PC-SPES.

Eli Lilly stopped marketing DES several years ago, but a pharmacist can prepare the medication for you (a process called compounding) if you have a doctor's prescription. The International Academy of Compounding Pharmacists (www.IACPrx.org or 800-927-4227) can direct you to a compounding pharmacist near you.

What You Need To Know About Herbal Supplements

The discovery that a supposedly natural remedy contained several undisclosed prescription drugs is frightening, especially because about 30% to 40% of men with prostate cancer use some type of complementary or alternative medicine. Unfortunately, dietary supplements do not have proven safety and efficacy because the U.S. Food and Drug Administration (FDA) does not regulate them. This means that dangerous supplements such as ephedra are readily available over the counter and that other products may be contaminated with or contain prescription drugs.

The only real protection you have against taking a harmful or ineffective supplement is to avoid all products that have not been approved by the FDA. You can reduce your risk of taking an inaccurately labeled supplement by buying supplements that meet U.S. Pharmacopeia standards (look for the "USP" symbol on the label), but this does not imply that the supplement is safe or effective.

Be sure to tell your doctor if you decide to take any complementary or alternative remedies and if you experience any side effects from them. This is for your own safety, as well as for the safety of others who might take the product.

which patients are most likely to benefit from this approach and the optimal length of time to use androgen blockade.

Intermittent androgen suppression. In this approach, androgen blockade is achieved chemically (using an LH-RH analog alone or in combination with an antiandrogen) until PSA levels fall. Treatment is then discontinued until PSA begins to climb again. The rationale for this approach, though not tested scientifically, is the belief that hormone therapy encourages the growth of androgen-insensitive cancer cells (the cells that ultimately cause the tumor to continue to grow despite hormone therapy). Some doctors believe that cycling therapy on and off may delay the emergence of these deadly cells. In addition, intermittent androgen suppression is associated with fewer side effects since men discontinue therapy for pe-