

## Androgen Resistance Part 2

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*Editor's Note: This is the second part of a multi-part article Dr. Myers has written for Insights on the important subject of hormone resistance. Subsequent parts that will be published in future issues of Insights include such subjects as treatment options, the best combination of these options, how to sequence combinations for best effect, maintaining quality of life while on chemotherapy, the importance of rest intervals from chemotherapy and future prospects.*

### Treatment Options for Androgen Hypersensitization: Antiandrogens

In Part 1 of this paper, I reviewed how tumor cells can develop the capacity to grow well at low concentrations of androgen by increasing the androgen receptor level, increasing the sensitivity of the receptor through phosphorylation, or enhancing its action by altering the amount of co-activating proteins. In these studies, the anti-androgen Casodex (bicalutamide) was commonly added. This drug consistently blocks the ability of androgen to stimulate prostate cancer cell growth, despite these enhancements in androgen receptor function.

The usual dose of Casodex is 50 mg daily. This leads to sustained blood levels of 8-10 micrograms per milliliter of blood. Casodex can be safely administered at doses as high as 450 mg a day, but doses over 200 mg are not absorbed well. Thus, the maximal sustained blood level is 30-35 micrograms per milliliter. Most of the laboratory studies I have cited used the equivalent of less than 10 micrograms of Casodex per milliliter of blood. I found only one that used concentrations in excess of 35 micrograms per milliliter. Thus, Casodex blood levels in patients are typically well within the range where this antiandrogen should block the development of most of the known mechanisms for enhancing androgen receptor function.

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## Newly Diagnosed Prostate Cancer: Evaluating the Options

Part One of a Two-Part Article

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Prostate Oncology Specialists

Newly diagnosed prostate cancer is a disease in transition. Historically, because it was diagnosed in the advanced stages, the diagnosis of prostate cancer portended an early death just like many other common cancers. Over the last 10 years, however, the widespread use of PSA testing and ultrasound-directed biopsies has dramatically changed the nature of this disease for the better. These advances have, in a sense, created an entirely new entity, a cancer that is not very life threatening.

This is not to say that the risk of a prostate cancer death has been totally eliminated. A small percentage of newly diagnosed patients have high-grade variants that are more dangerous. We also still see men who have not availed themselves of the benefit of early PSA screening, men who already have advanced disease when they are diagnosed. Fortunately, these sad circumstances become less common every year as more and more men get PSA screening. However, realizing that some forms of prostate cancer are indeed dangerous does not take away from the fact that for most men the danger of dying from this disease is low when it is managed properly.

The transformation of prostate cancer into a treatable disease creates a whole new arena of challenges. Side effects of treatment take on added importance, and the quality of life becomes a priority when survival is no longer the central issue. Side effects from treatment tend to be immediate, whereas the slow-growing effects of untreated cancer may not be felt for 10 to 15 years. Potential side effects such as impotence or incontinence are not trivial.

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## Radical Prostatectomy – 2003

Commentary from an Experienced Urologist

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### HISTORY

As shown in Table 1 (see page 9), prostatectomies have been performed for more than a century. In 1891, in Tucson, Arizona, a frontier doctor named George Goodfellow performed the first known prostatectomy, using the perineal approach. Although he worked for many years in Los Angeles, he traveled the country, teaching this operation to many surgeons including the new chief of urology at Johns Hopkins, Hugh Young. Young modified the procedure to treat prostate cancer, and he published the first paper on the subject in 1904. It was not until 1947 that an English surgeon, Terrence Millin, reported on the retropubic

approach, which became the predominant technique used to surgically remove the prostate in an effort to eradicate this disease.

Prior to 1982, only 7% of men diagnosed with prostate cancer were considered to be candidates for surgery, and only a fraction of these men could be cured with surgery. The surgery was dangerous because of the large blood loss and the high risk of incontinence. Impotence almost always accompanied this procedure. Then, in 1982, Patrick Walsh, also from Johns Hopkins, described the anatomic, nerve-sparing technique for performing radical prostatectomy.

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Why is it common that large randomized controlled trials fail to show a survival advantage to adding an anti-androgen to medical or surgical castration? In the case of Eulexin (flutamide), the drug appears to induce mutations in the androgen receptor discussed in Part 1 of this paper. These mutant receptors then react to flutamide and its major metabolite **as though these were testosterone**. The result is that flutamide administration now fuels the growth of the cancer.

In one study of hormone-resistant bone marrow metastases in patients on complete androgen blockade with flutamide, five out of sixteen, or more than 30%, exhibited androgen receptor mutants stimulated by flutamide. In contrast, only one mutant receptor was found among seventeen patients who failed on surgical castration alone. The incidence of androgen receptor mutants in this study nicely match the common 20-30% response to flutamide-withdrawal in patients who progress on flutamide-containing programs of complete androgen blockade. The flutamide-withdrawal response is typically seen in patients who have been on flutamide for more than two years and is uncommon in those on therapy for less than one year. It seems very likely that the gradual appearance of androgen receptor mutations seriously limits the effectiveness of Eulexin in clinical trials where hormonal therapy is administered continuously.

Casodex appears to be much less likely to foster the emergence of androgen receptor mutants. Also, among the androgen receptor mutants that emerge after prolonged exposure to flutamide, most do not appear to have their growth stimulated by Casodex. As a result, Casodex is often effective in the treatment of men who have progressed on Eulexin. Withdrawal of Casodex appears to be less likely to induce a tumor response than withdrawal of Eulexin, presumably because of the lower likelihood of androgen receptor mutants.

Recently, investigators at Johns Hopkins University (Laufer, et al) were only able to gather a series of five patients who exhibited rapid cancer progression associated with Casodex administration. Four out of these five patients responded when Casodex was withdrawn.

If Casodex is unlikely to cause androgen receptor mutations, what happened in these men at Johns Hopkins that made their cancers grow when Casodex was used? In laboratory experiments, culture of human prostate cancer cells in the absence of androgen for prolonged time periods led to the development of cells whose growth is stimulated by the addition of Casodex. Where Eulexin or its active metabolites were tested, they also stimulated the growth of these cells. These cell lines did not show androgen receptor mutants or an increased amount of androgen receptors. Cells that contain increased amounts of androgen receptor coactivators, especially ARA70, increase their growth when exposed to Casodex and Eulexin. Paradoxically, addition of testosterone or dihydrotestosterone suppresses the growth of some of these cell lines that grow when Casodex is added.

This combination of laboratory and clinical observations suggest that **prolonged complete androgen blockade leads to the emergence of tumor cells that will grow faster in the presence of anti-androgens and might be suppressed by normal concentrations of testosterone**. These findings provide a rationale for intermittent hormonal therapy where androgen withdrawal and exposure to anti-androgens are limited to a year or less. Also, the fact that normal to high testosterone levels suppressed the growth of these prostate cancer cells provides a rationale for the use of testosterone in selected patients with hormone resistant disease and this concept is currently in clinical testing.

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## The Role of IGF-1

When the androgens are removed, both normal and cancerous prostate cells die. For normal prostate cells, death is fairly rapid and the gland can shrink to 90% of its original size within one month of surgical castration. Hormone-sensitive prostate cancer cells, however, die more slowly; their deaths are prolonged for over nine months.

In contrast, there are patients whose cancers stop growing when the androgen level is reduced by hormonal therapy, but whose tumor cells do not die. Consequently, tumor masses in the prostate gland, lymph nodes, and bone don't disappear or even shrink. These simple observations illustrate the apparent major changes that occur in the speed and completeness of cell death in normal prostate cells when compared to metastatic prostate cancer cells. Recently, major advances have broadened our understanding of how the suicide program is altered when prostate cancer cells develop the ability to survive hormonal therapy.

There is growing evidence that the cytokine, IGF-1, plays a major role in promoting the survival of prostate cancer cells. IGF-1 can stimulate growth in these prostate cells, but, more importantly, it sends a powerful signal to the prostate cells, informing them not to activate their suicide program. Current evidence supports the theory that IGF-1 triggers one of the most important survival signals for prostate cells — second only to androgen. How does IGF-1 stimulate the survival of prostate cancer cells? When IGF-1 binds to its receptor on the surface of the prostate cells, it triggers changes in protein phosphorylation that lead to the activation of a protein called Akt. (*Editor's note: the naming convention for signaling proteins allow nonsense three letter names. Thus, Akt and bcl-2 are not abbreviations, but full names for these proteins.*) In turn, Akt

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inhibits prostate cancer cell suicide by blocking many of the key components of the suicide “machinery.”

Perhaps the best evidence supporting the importance of IGF-1 comes from work on prostate cancer cells that survive well in the absence of IGF-1. These cells often show changes that ensure activation of Akt when IGF-1 is absent. The most important mutation involves a protein called PTEN. Under normal conditions, if IGF-1 levels are not optimal PTEN deactivates Akt and renders prostate cancer cells more susceptible to suicide. Genetic changes in prostate cancer cells can lead to a loss of PTEN. Without PTEN, it takes much less IGF-1 to trigger maximal activation of Akt and ensure cancer cell survival.

The human prostate cancer cell line, LNCaP, has proved very useful in deciphering the role of Akt. Since they lack any active PTEN, LNCaP cells have fully activated Akt. These cells will survive in the absence of androgen and will grow slowly under these conditions. In the laboratory, **when drugs inhibit Akt, these cells will live if androgen is present but die if it is removed.** While LNCaP cells survive if either Akt is activated or androgen is present, growth is faster in the presence of both circumstances. Additionally, activation of Akt makes prostate cancer cells less sensitive to chemotherapy. Clearly, these experiments illustrate the critical role that Akt activation plays in prostate cancer biology.

Evidence from patient samples suggests that IGF-1 and Akt activation play important roles at various points in the development of prostate cancer. Most of the well-designed studies show that the higher the IGF-1 blood level, the greater the risk of developing prostate cancer. Studies performed on prostate biopsies and radical prostatectomy specimens reveal that PTEN is absent in 10-20% of prostate cancers. Since this results in cancers where Akt is chronically active, these patients would not be expected to do well. In fact, **PTEN absence generally occurs in prostate cancers with Gleason Grade of 7 or greater, confirming the association between loss of PTEN and high-risk cancer.** PTEN was also more likely to be absent in locally advanced cancer

(involving both sides of the gland or invading into surrounding tissues) than in cancers that were smaller and limited to one area of the prostate gland.

The absence of PTEN can speed the growth of prostate cancer. It can also allow the cancer to survive hormonal therapy as well as chemotherapy, equipping the cells to survive further treatment and eventually kill patients. One recent study analyzed fifty metastatic prostate cancer lesions in nineteen fatal PC cases. In 80% of these patients, PTEN was absent from at least one metastatic lesion.

A number of approaches have been taken to solve the problem presented by the IGF-1 survival pathway. Most of the IGF-1 in the blood is produced in response to growth hormone. The drug Sandostatin blocks the release of growth hormones and causes a drop in IGF-1 levels. In laboratory models, Sandostatin (as well as other drugs that block growth hormone action) shows impressive activity against human PC cell lines. Human clinical trials of these drugs yield a mixed picture: some investigators report promising results and others see no activity at all. I think that these clinical differences may result from patient characteristics. For example, heavily pretreated patients may well have fully active Akt independent of IGF-1 levels, and they would not be expected to have a significant response to drugs designed to suppress growth hormone and IGF-1 production. **The few trials that have used the growth-hormone antagonists as part of initial hormonal therapy report anti-tumor activity that warrants further investigation in a patient population whose tumors are most likely to still be responsive to circulating IGF-1.**

A more promising approach is to identify drugs that work directly on Akt or on PI3 kinase, the protein that activates Akt. The drugs Wortmannin and LY294002 are widely used in the laboratory to block activation of Akt by inhibiting PI3 kinase. These drugs are very effective in triggering the suicide program in prostate cancer cells. I am aware of several major pharmaceutical firms who are developing Akt inhibitors with the hope of finding a useful anticancer agent. One drug already on

the market, Celebrex, has been reported to block Akt function and cause the death of human prostate cancer cell lines. Celebrex is widely used (and is FDA-approved) for treating arthritis; it is also much less toxic than most anticancer agents.

Rapamycin doesn't alter Akt activation but does block one of the survival pathways under Akt control. Charles Sawyers, from University of California, Los Angeles, has shown that rapamycin is able to kill cells lacking PTEN at concentrations that appear to be well tolerated. Rapamycin is currently available for clinical use and is used as an immunosuppressive drug in organ transplant patients.

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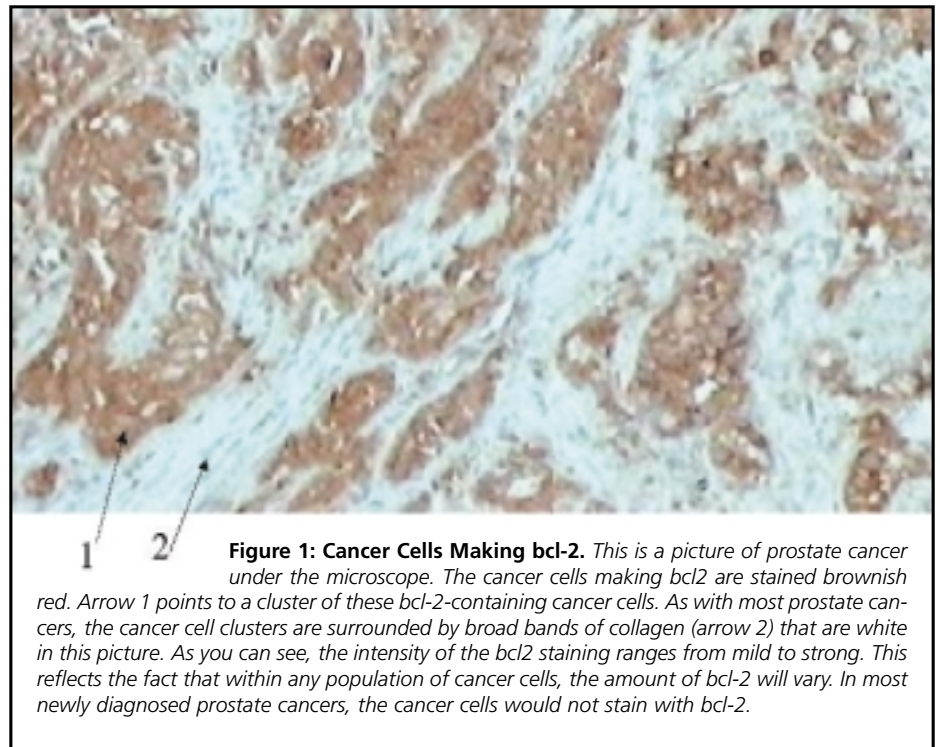
## Mitochondria and Cancer Cell Death

Mitochondria are the cell’s major energy generators; they are the powerhouses of the cell. They also play a major role in the function of cell suicide programs. When removal of androgen, lack of IGF-1, and other forces that push the cell toward suicide reach a critical point, the mitochondria release the compound cytochrome C, which initiates cell death. In this sense, the mitochondria act as a switch that determines the fate of the cancer cell.

A small protein, called Bcl-2 (see Figure 1), acts to prevent mitochondria from releasing cytochrome C. Laboratory techniques that can increase the amount of bcl-2 make prostate cancer cells resistant to a wide range of treatments, including radiation, removal of androgen, and various chemotherapy drugs. Prostate cancer cell lines with increased amounts of bcl-2 grow faster. In animal models, castration causes an increase in bcl-2 in prostate cancer cells and may limit the speed and magnitude with which cancer cells die. **In the same animal models, prostate cancer cell lines genetically engineered to have a higher bcl-2 content show increased resistance to hormonal therapy.** Bcl-2 is undetectable in about 70% of patients with hormone responsive cancers. In contrast, hormone resistant tumors showed high levels of the protein. Like the animal model, the amount of bcl-2 found in the remaining cancer increased during the course of hormonal therapy. A number of agents have been identified that decrease the amount or activity of bcl-2. Three of these drugs look particularly interesting:

1. Indol 3-carbinol
2. Phenylbutyrate
3. PC-SPES

**Indol 3-carbinol**, which normally abounds in cabbage, broccoli, cauliflower, kale, collard greens, and related plants, may play a major role in cancer prevention. For instance, diets high in these vegetables, and to



hence Indol 3-carbinol, are associated with a low risk of cancers of the breast, prostate, and other organs. It is also available in pill form from Life Extension Foundation ([www.lef.org](http://www.lef.org)). Although the compound appears to be relatively nontoxic, there are still no clinical trials testing Indol 3-carbinol in prostate cancer treatment.

**Phenylbutyrate** is approved by the FDA for the treatment of children with certain genetic abnormalities that cause mental retardation and early death. Phenylbutyrate is also relatively nontoxic, and, in the laboratory, it shows activity against prostate cancer. But, overall, the clinical trials testing the activity of this drug against advanced prostate cancer were not impressive.

Finally, the herbal combination **PC-SPES** suppressed the amount of bcl-2 present in prostate tumor cells in laboratory settings. However, the anticancer activity of PC-SPES is complex, and suppression of bcl-2 may play a role in the activity of this herbal preparation. Now that PC-SPES is gone, many patients are looking for herbal preparations with similar effectiveness. While most of the effort seems to have focused on preparations that contain extracts from the same plants, the alternative is to identify how PC-SPES functioned and to

duplicate those functions with the best agents possible. I think this is a more reasonable approach, and work on bcl-2 inhibitors may be a good place to start.

The bcl-2 protein can also undergo phosphorylation, but, unlike the androgen receptor, phosphorylation of bcl-2 renders it inactive. Two drugs that have been proposed to deactivate bcl-2 by phosphorylation are Paclitaxel (taxol) and Docetaxel (taxotere); their ability to alter bcl-2 phosphorylation may explain why they can enhance the anti-tumor activity of radiation therapy and interact synergistically with a range of other agents.

There is a third approach to the problem posed by bcl-2’s propensity to increase when responding to hormonal therapy, thereby decreasing the effectiveness of radiation and chemotherapy. Bcl-2 is one of the many cell survival proteins under the control of Akt. Increased active Akt means increased amounts of bcl-2, thus promoting cancer cell survival. PTEN blocks Akt activation, decreasing the amount of bcl-2 and promoting tumor cell death. Drugs able to block Akt (e.g., Wortmannin and LY294002) will also be likely to decrease bcl-2, simultaneously disposing of two mechanisms that reduce androgen withdrawal response.

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# What Others are Doing

Within the Prostate Cancer community are many organizations and Prostate Cancer centers other than PCRI that are doing innovative and valuable work in battling this disease. In each issue of *Insights*, we shall describe one of these sister organizations in an endeavor to familiarize our readers with as many of them as possible.



## Foundation for Cancer Research and Education



The Foundation for Cancer Research and Education (FCRE) was recently founded in Free Union, Virginia by Dr. Charles "Snuffy" Myers, Jr., President. According to Dr. Myers, the work of FCRE is based on the hypothesis that the best way to treat cancer patients is to integrate nutrition, stress reduction, and exercise with optimum use of surgery, drugs and radiation therapy. "This contrasts with standard management that typically focuses on the use of surgery, radiation, or drugs as single modalities," he explains. "The Foundation's two main purposes are to fund education and research which encompasses a truly integrated approach to patient care.

**"The Foundation's purpose in education of the public, patients, and physician groups is to acquaint them with recent advances in the diagnosis, treatment, and lifestyle changes that improve the outcome of prostate and other cancers. For example, current advances in our understanding of prostate cancer should allow a 50% reduction in death rates from this disease.**

"Clinical and laboratory research will focus on improving the survival and quality of life of men with prostate cancer. This will include improving the effectiveness of hormonal therapy by increasing the proportion of men who enter remission and the speed with which these remissions occur. It will also include testing of orally active nontoxic drugs designed to arrest the growth of cancer cells. Another goal will be to improve the duration of remissions obtained with chemotherapy. Finally, we will seek medical treatments that lessen the long-term side effects of surgery and radiation therapy."

The first major project of the foundation is working with PCRI to develop the **National Conference on Prostate Cancer 2003 to be held in Burbank, California, September 5-7, 2003.** Dr. Myers will be the moderator of the three-day conference.

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In Part 3 of this article, I will be dealing with the importance of genetic damage in prostate cancer progression. I will discuss the role that the protein p53 plays in detecting and repairing gene damage and the significance of an abnormal p53. I will also discuss the role that the protein Rb plays in the evolution of hormone-resistant prostate cancer. I will conclude with a summary of the American Institute for Disease of the Prostate's efforts to find the best way to combine androgen withdrawal with agents that block the known pathways to hormone resistance. ■

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The number of treatment options is increasing as technology continues advancing. The choices available can generally be thought of in terms of four categories.

■ **Local** treatment options (radical prostatectomy, brachytherapy, external radiation, cryotherapy) are directed at the eradication of the prostate gland and the cancer it contains. Modern technology in expert hands can accomplish the sterilization of the prostate gland from cancer with a high degree of consistency. However, there are two potential drawbacks to the local treatment options. One is the potentially irreversible side effects to the adjoining structures (e.g. the erectile nerves, bladder or rectum). The other is the disheartening possibility of undergoing the risks of local therapy only to later have a relapse because the cancer had already spread to elsewhere in the body.

■ **Systemic** treatment options (surveillance with dietary modification, antiandrogen monotherapy or combined hormone blockade for 12 or more months) treat the whole body but are suppressive, not curative in nature. The selection of one of these options is based on the philosophical belief that prostate cancer is a low-grade process. Therefore, effective suppressive treatment may be able to convert it into a chronic, non-progressive condition. The advantage of these options is that the side effects are usually reversible. The disadvantage is the absence of the possibility to get closure and move on; a systemic approach requires one to remain educated about the disease and watch the situation closely as it evolves.

■ **Combination** options (systemic plus local treatment) provide the best chance for outright eradication of the disease but using two treatments instead of one incurs a higher risk of side effects.

■ **Conditioning** options usually consist of some form of hormone blockade administered for three to six months as a lead-in to local therapy. Hormone blockade given in this fashion has not been shown to improve the cure rates of state-of-the-art local treatment. However, by reducing the size of the prostate gland prior to therapy, neoadjuvant hormone blockade reduces the potential side effects of the local therapy.<sup>2</sup>

The tension between the risk from the cancer and the risk from treating the cancer mandates a process of robust education that enables men to be fully aware of the short and long-term implications to the various options *before* they make irreversible choices. Fortunately, newly diagnosed early prostate cancer is a slow growing disease, permitting sufficient time for the problem to be studied.

The progressive educational process, which hopefully leads to selecting optimal treatment, can break down for a variety of reasons. This disease is unusual because patients themselves make the treatment decisions. Patients should be aware of some pitfalls inherent in a situation where they are selecting their own cancer strategy. Many patients are in a state of shock and grief for a few months after diagnosis. Strong emotions are also stirred up as patients reflect on the dramatic personal consequences attendant to a high-stakes situation that can affect sexual and urinary function permanently. The clear and objective reasoning that is needed can be difficult under these circumstances, but patients should be encouraged to persevere and weigh all the relevant factors.

This shift of responsibility from physicians to patients results from the fact that there are multiple different treatment choices with indistinguishable survival rates. Therefore, **examining the potential side effects of each treatment option and comparing it with the other choices is the only logical way to make distinctions among these many options.** Since it is the side effects that distinguish these alternatives, patients themselves must decide which type of side effects they are willing to personally risk.

### **Determining the Appropriate Intensity of the Treatment Plan**

Carefully comparing and contrasting treatment options prior to finalizing a plan is certainly important. But even more important, the initial step must be to determine the appropriate *intensity* of the treatment plan. In other words, how do we decide when the disease is serious enough to warrant the use of a combination of treatment options? When is the disease situation low-grade enough to be treated with a single modality therapy? Clearly a single modality approach, when it can be safely used, is always

preferable since there are fewer associated side effects. So before picking a local or systemic treatment option, patients must first determine their risk that their cancer has spread outside the gland, i.e. the risk of having micro metastatic disease. When the risk of micromets is low, single modality therapy is best. When the risk of micromets is high, combination therapy is best.

Understanding the concept of metastasis is essential to making correct decisions about what kind of treatment is appropriate. Cancer can enlarge and grow through the capsule of the prostate (increasing the risk of positive margins at surgery), but this is not what we are talking about when we use the term micromets. Prostate cancer cells also have the potential to separate from the primary tumor, enter the blood stream, and end up in other areas of the body – usually the bones or lymph nodes. The concept of metastasis is a little challenging because it is impossible to know with absolute certainty whether or not microscopic nests of metastatic cells exist in a given patient. There is no technology presently available that can scan your whole body and unfailingly detect the presence of a few prostate cells outside the gland; bone scans are positive only when the metastases are large enough to provoke an osteoblastic reaction resulting in new bone formation. Our lack of ability to definitely rule in or rule out the presence of metastasis is a severe disability when it comes to making treatment recommendations. Absolute information would, of course, be useful because we could then select the individuals who have no metastatic disease; these patients would certainly then be the best candidates for local therapy alone.

Since we cannot measure micromets directly our next best alternative is to estimate the likelihood that they are present. **When such an estimate is available, patients then can at least use this information to decide whether they personally feel that a combination approach is warranted.** One process for determining one's risk of micromets is via the Kattan nomograms.

The Kattan nomograms were developed by Dr. Michael Kattan, a biostatistician at Memorial Sloan Kettering in New York. These nomograms generally use a combination of three factors to determine the probability of PSA

(continued)

relapse after local therapy. These factors are PSA, Gleason score, and Clinical stage. Nomograms exist for surgery, conformal radiation, and for brachytherapy. Generally, the predicted relapse rates (the risk of micromets) is fairly consistent when the nomograms are compared with each other. The nomograms are derived from the results of treatment of thousands of patients who have been treated at reputable university centers. Hence, the relapse rates generally do not reflect the effects of poorly performed local therapy. Rather, the statistical likelihood of relapse is dependent upon the presence of micro-metastatic disease preexistent at the time the local therapy was performed. Therefore, the relapse rates determined by the Kattan nomograms can be taken as an indication of the likely presence of micromets at the time of local therapy.

Of course, the danger of micromets is that they eventually grow to larger dimensions and, when fully developed, impair function and ultimately lead to death. Patients are generally aware that for most common cancers (such as colon, lung, stomach etc.) micromets portend an almost certain early death within a couple of years. However, this is certainly not the case for prostate cancer. **Early relapse after local therapy (as detected by a rise in PSA) can, on the average, be controlled with the early administration of hormone blockade for up to 11 years!** And even when hormone blockade loses effectiveness, a variety of additional therapeutic alternatives are available.

Men need to keep in mind the relatively low-grade nature of prostate cancer relapses when weighing the pros and cons of using combination therapy to reduce the risk of relapse; clearly, elderly patients need not be unduly concerned about relapse (because of the efficacy of hormone blockade in controlling relapses), whereas for younger men the risk of a relapse translating into an eventual prostate cancer death (rather than from old age) should be taken quite seriously.

For decision-making and counseling purposes we have found it useful to initially categorize patients into four risk categories with the statistical information provided by the Kattan nomograms (see Table 1). As shown, we categorize patients who are less likely to have micro

metastatic disease (less than 50% chance) as Risk Category I patients. We categorize patients who are more likely to have micro metastatic disease (more than 50% chance) as Risk Category II patients. Risk Category III describes patients with a documented spread to the lymph nodes. Risk Category IV represents patients with a documented spread to the bones. Risk Category I patients are further subdivided to IA (a less than 10 % risk of micromets), to IB, (a 10–25% risk of micromets), and to IC, (a 25–50% risk of micromets).

### Modifying Predictive Factors

Besides PSA, Gleason score, and Clinical stage, other factors not included in the Kattan Nomogram provide additional predictive information about the risk of relapse. These include:

- A serum PAP elevated above normal range and confirmed with a repeat
- More than 50% of core biopsies positive for cancer
- An endorectal MRI showing seminal vesicle invasion
- A PSA > 0.5 after three months of conditioning hormone blockade.

In the interest of being systematic and consistent in providing patients with our best estimate of the likelihood of micromets, we modify the initial assigned Kattan stage accordingly.

For patients who have more than 50% of core biopsies positive, we automatically raised one sub stage from that initially assigned by the Kattan nomogram. For example, when the nomogram indicates a Risk Category IB, we would raise the Risk Category to IC. Risk Category IC patients would be raised to Risk Category II.

We assigned Risk Category II automatically (unless Risk Category III or IV is documented) regardless of the Kattan prediction when any one of the following exists:

- A consistently elevated serum PAP
- Documented seminal vesicle invasion
- A PSA > 0.5 after three months of hormone blockade

This analysis, which provides an estimate of relapse risk (and an estimate of risk of underlying metastasis), is a tool designed to aid in determin-

**Table 1. Patient PC Risk Categories**

|            |  |
|------------|--|
| <b>I</b>   | < 50% chance of micro metastatic disease |
| <b>IA</b>  | < 10% chance                             |
| <b>IB</b>  | 10-25% chance                            |
| <b>IC</b>  | 25-50% chance                            |
| <b>II</b>  | > 50% chance of micro metastatic disease |
| <b>III</b> | documented spread of PC to lymph nodes   |
| <b>IV</b>  | documented spread of PC to bones         |

ing the potential benefit of combining systemic hormone blockade with local therapy. Several randomized prospective trials adding hormone blockade to local therapy<sup>2,3,4,5,6</sup> conservatively indicate that relapse rates can be reduced by about 50% in patients treated with hormone blockade for an adequate period of time (the optimal time period is not known but appears to be between 12 to 24 months duration).

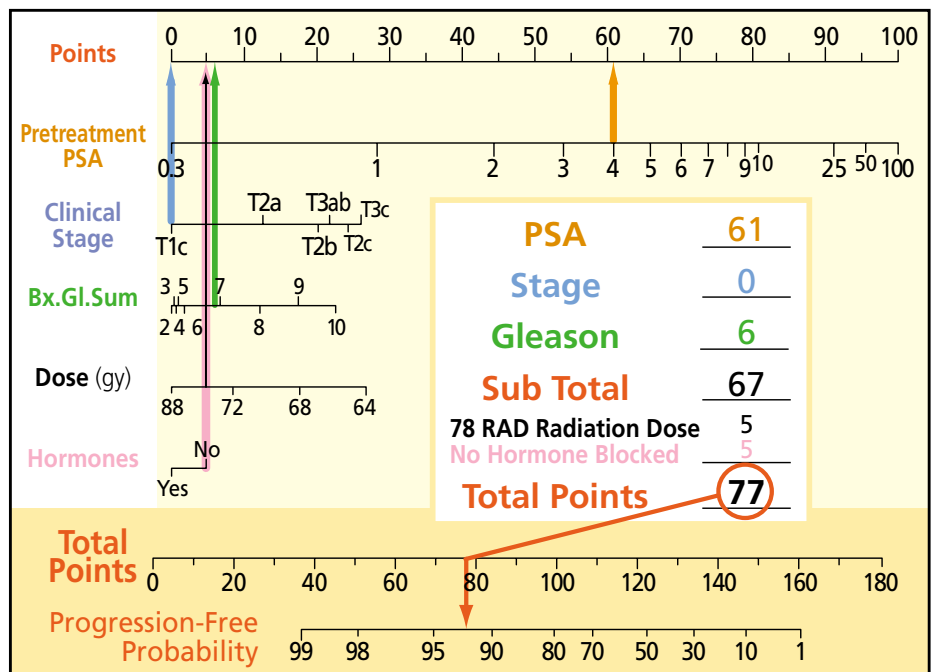
Therefore, this analysis using modified Kattan nomograms enables patients to measure the potential benefit of adding hormone blockade to local therapy and to weigh that benefit against the potential toxicity of therapy. This can be demonstrated with two examples. As shown in Figure 1 (on page 8), a patient with a PSA of 4, a stage of T1c and a Gleason of 7 has a total of 67 points on the Kattan nomogram (for conformal radiation). Five points are added for removing the effects of conditioning hormone blockade. An additional five points are added by selecting a typical standard dose of radiation e.g., 7800 rads. Sixty-seven plus ten equals 77 points. On the Kattan nomogram 77, points indicate a 94% probability that the disease will not progress in five years. Stated another way, the risk of relapse is 6% (100% minus 94%).

This patient has Risk Category IA disease if less than 50% of the core biopsies are positive, the PAP is not elevated, there is no evidence of seminal vesicle invasion, and the PSA is not greater than 0.5 after three months of conditioning hormone blockade (if it is being utilized). Since hormone blockade administered for 12 to 24 months cuts the risk of cancer relapse by 50%, the risk of relapse in this example is reduced from 6% down to 3%. In other words, in a patient with this particular profile, hormone blockade only improves the cure rate by 3%! In my experience, **most men eagerly forgo the potential side effects of hormone blockade when there is such a tiny chance it will have a beneficial impact.**

(continued on page 8)

Figure 1:

Kattan Nomogram Calculating a 5-year Progression-Free Probability With Radiation.



Another example may further illustrate these methods. In this example, the patient has a Gleason score of 8, a PSA of 15, and a clinical stage of T2b (a moderately sized nodule confined to one side of the prostate). This patient would have a total of 115 points on the nomogram. Again adding ten points for a dose of 7800 rads and no conditioning hormone blockade results in a total point score of 125. This translates into a 60% relapse rate! Hormone blockade for an adequate period of time is clearly indicated in such a patient and will reduce the risk of relapse by about half of 60% i.e. 30%.

The Sloan Kettering Cancer Center website at [www.mskcc.org/nomograms/prostate](http://www.mskcc.org/nomograms/prostate) presents a nomogram calculator that permits a similar analysis for surgery, conformal radiation, and brachytherapy based upon a patient's own staging parameters.

### Should Hormone Blockade Be Combined with Local Therapy?

These two examples, because they are at opposite ends of the spectrum, lead to fairly straightforward conclusions about the advisability of using or forgoing hormone blockade in combination with local therapy. Patients with less polarized relapse rates, say in the 15 to 30% range, are not as easy to counsel. Ultimately, these individuals themselves must make a deci-

sion that they feel is in their best interests. **To make this decision, a patient in this situation must carefully weigh the implications and relative risk of relapse in the context of their age, preexisting sexual function, and overall health priorities along with the known potential side effects of hormone blockade.**

Patients who are ambivalent about the options facing them will occasionally elect to initiate hormone blockade to see how well they themselves tolerate the treatment. If inordinate side effects are encountered, they can stop the treatment with the expectation that the side effects will reverse. The only exception to this rule is for patients considering nerve-sparing surgery. About a third of patients treated with hormone blockade develop capsular thickening; this thickening can render the nerve sparing surgery somewhat more difficult, thereby increasing the risk of impotence.

Forced by circumstances to act as "amateur doctors," patients may finalize a treatment plan before they become aware of all relevant treatment options. This mistake can occur not only as a result of incomplete knowledge due to a lack of information about some aspect of one of the long list of alternatives, but also because of a natural human propensity to seek rapid reso-

lution to a confusing situation. Despite reassurances, it is hard for patients to escape the lingering fear that "time's a wasting" while the cancer is growing and spreading.

Problems related to treatment selection do not merely originate from patient naiveté and lack of experience or a state of shock. Even doctors who contract this malady bemoan the frustrating lack of clear data and consensus among prostate cancer experts. They, like all patients, struggle with the marked variability in treatment skills among surgeons and radiation therapists and the absence of any objective method for measuring these skills.

This first part of this two-part article has focused on the process used to decide whether or not to initiate adjuvant systemic hormone blockade with a view toward eradicating micro metastasis. This decision logically is based on the projected risk of micro metastatic disease being present; hence, I have described an approach enabling a newly diagnosed patient to make this risk determination. Risk alone is not the only deciding factor, however. The individual patient's age and specific preferences are also important. In the second part of this article, I will try to provide some guidelines that incorporate these additional factors and enable the patient to make the best decision for his specific situation. ■

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Dr. Walsh was able to demonstrate that the nerves responsible for erection could be preserved and that potency could be retained. Dr. Walsh's other contributions to the surgical technique involved the ability to preserve continence and decrease blood loss. His anatomic surgical technique, which is now practiced worldwide, enables the sphincter to be saved so that incontinence has been greatly reduced and major blood loss is rare. The radical retropubic prostatectomy is a technically demanding procedure for the surgeon and a great deal of experience is necessary to perform the surgery safely, to maximize its effectiveness and limit the risk of complications.

However, prior to the 1990's, the ability to diagnose cancer that was confined to the prostate was extremely limited. More than 75% of men diagnosed with prostate cancer already had the disease growing beyond the prostate and many of these men already had metastatic cancer. The PSA blood test was introduced in 1986, but it was not widely used until the early 1990s. For the first time, it became possible to diagnose men whose cancer was confined to the prostate. The introduction of transrectal ultrasonography accompanied by transrectal needle biopsy in 1988 provided the opportunity for urologists to diagnose and identify men whose prostate cancer could be treated surgically. These diagnostic procedures revolutionized early detection of prostate cancer, and by 2001, 65-85% of men who presented with PC were found to have the cancer still confined to the prostate gland.

In 2002 there were approximately 195,000 men diagnosed with prostate cancer. Radical prostatectomy was performed on 55,000. Nearly 30% of all men found to have prostate cancer are selecting radical prostatectomy as the procedure of choice. In order to help men decide which form of therapy is most appropriate for them and to help them understand what is involved in the surgical procedure, this article will review this subject.

### Surgical Technique

Until recently there were just two techniques utilized in the surgical removal of the prostate:

1. The retropubic approach

2. The perineal approach.

The most common is the **retropubic approach** in which an incision is made in the lower abdomen. The incision is usually made up and down extending from the navel down toward the base of the penis. An alternative is an incision that extends transversely across the lower abdomen. There are no muscles cut with either of these incisions. Refer to Figures 1 and 2.

The top of the bladder is exposed and emptied by placing a catheter through the urethra. The lymph nodes on the side walls of the prostate and those closest to the prostate are examined for signs of cancer and often removed. The top and sides of the prostate are cleaned of fat that covers this area. There is a large group of veins known as the 'dorsal venous complex' that lies over the top of the prostate and extends down the sides. These veins must be separated and tied to obtain full exposure of the prostate.

In those patients who qualify, and most men do qualify, the nerves that control erections are carefully separated from each side of the prostate.

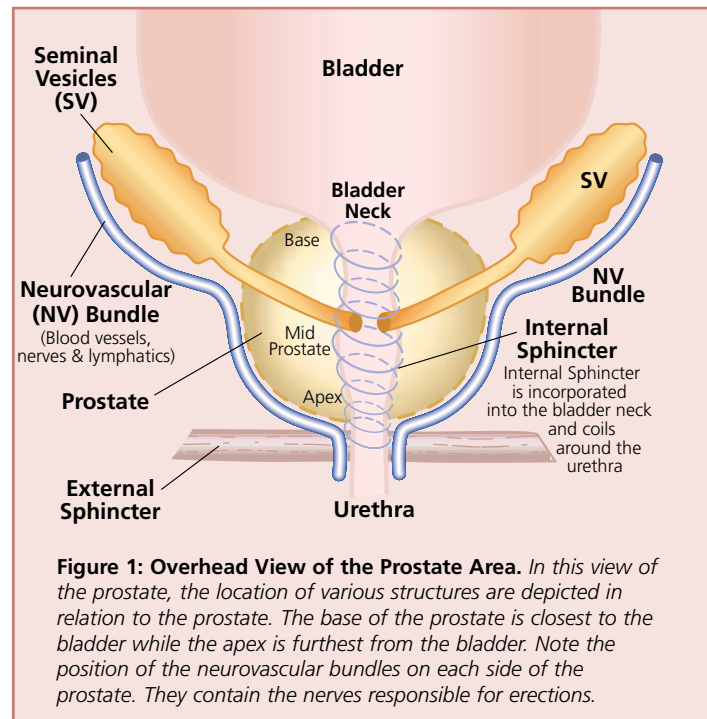
The apex of the prostate is detached from the urethra by opening the urethra, removing the catheter and cutting across the entire urethra. There is no real capsule at the apex of the prostate. In order to remove all prostate and cancer tissue in this area as well as preserve the nerve bundles that go alongside the prostate and urethra, a delicate dissection is necessary. Occasionally, the surgeon may want to make a biopsy and have the pathologist perform a frozen section to determine if there is any cancer involving the urethra or the neurovascular bundle. If so, additional urethra area and the affected bundle would be removed with the prostate. The external sphincter, which is necessary to preserve bladder control, is not disturbed.

When this portion of the operation is completed, the

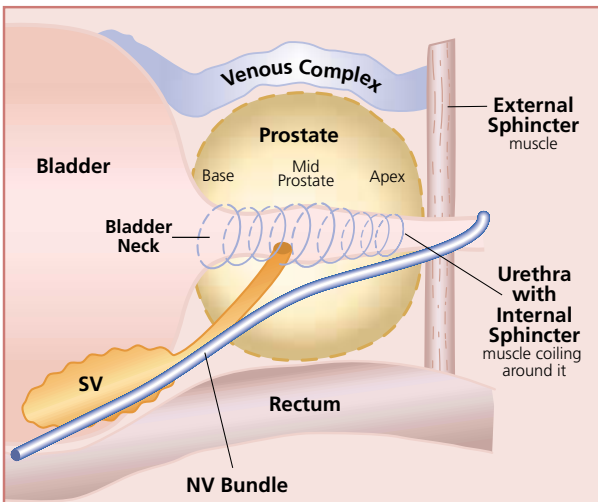
|      |   |
|------|---|
| 1891 | George Goodfellow, Perineal Prostatectomy                   |
| 1904 | Hugh Young, Perineal Prostatectomy (first paper published)  |
| 1947 | Terence Millin, Radical Retropubic Prostatectomy            |
| 1982 | 7% had surgery. Walsh introduces nerve-sparing RP           |
| 1986 | PSA introduced  |
| 1988 | Ultrasound-guided biopsies begun                            |
| 1995 | 35% diagnosed had RP  |
| 1998 | Laparoscopic Prostatectomy introduced                       |
| 2001 | 65%-85% present with localized cancer. 55,000 RPs performed |

prostate is lifted up and separated from the rectum. At the base of the prostate are two structures known as the seminal vesicles. They manufacture and store seminal fluid and are removed together with the prostate. Because this is one of the early locations of cancer spread, they are also removed. The bladder neck is opened, and the prostate is dissected away from the muscular wall of the bladder. The entire portion of the urethra extending from the apex of the prostate to the bladder neck is removed with the prostate and seminal vesicles. The bladder neck is reconfigured so

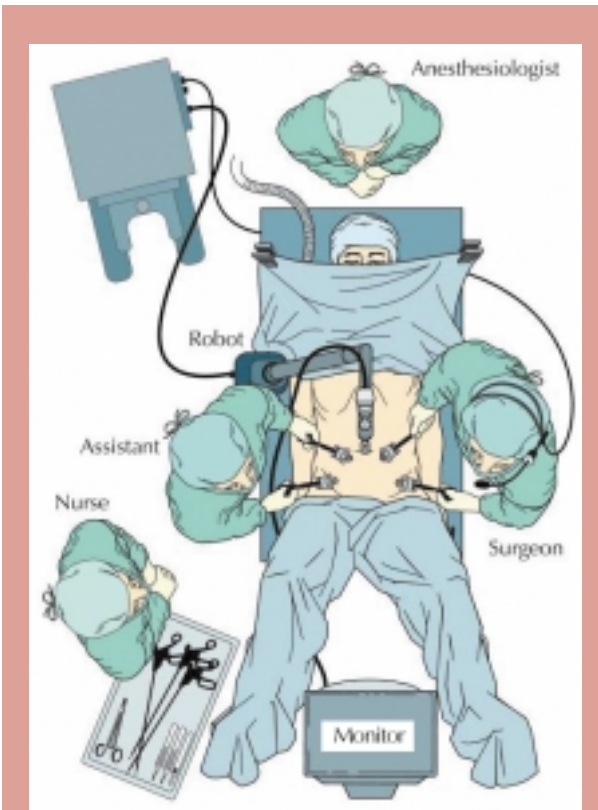
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**Figure 1: Overhead View of the Prostate Area.** In this view of the prostate, the location of various structures are depicted in relation to the prostate. The base of the prostate is closest to the bladder while the apex is furthest from the bladder. Note the position of the neurovascular bundles on each side of the prostate. They contain the nerves responsible for erections.



**Figure 2: Side View of the Prostate Area.** This view shows the closeness of the prostate to the rectum. The entire urethra contained within the prostate is removed together with the seminal vesicles.



**Figure 3: Laparoscopic Prostatectomy.** Five small incisions allow the introduction of the special working instruments and a video camera. The surgeons view the procedure on a monitor. A robot may be attached to the camera and can be controlled by voice commands from the surgeon. A different type of robot can be connected to all of the instruments and controlled by the surgeon at a computer keyboard and monitor. (Reprinted with permission of Krongrad Urology.)

that its size matches the open end of the urethra. A new catheter is inserted into the urethra and placed into the bladder. The urethra and bladder are sewn together. This catheter will remain in place 2-3 weeks.

With the **perineal approach**, an incision is made through the skin between the anus and scrotum. The bottom of the prostate sits on the top of the rectum. These two structures must be carefully separated. This is a delicate part of the operation and occasionally (about 5% of the time) the rectal wall tears and must be closed. If this occurs, the surgeon may decide to stop the operation. but this decision is based on many factors, such as the size and location of the rectal opening. Assuming that there is no rectal injury, the procedure is performed in a manner similar to the retropubic approach. The ‘nerves’ are preserved and the new bladder neck and urethra are sewn together after the prostate and the seminal vesicles are removed.

One of the differences between the perineal and retropubic approaches is that the lymph nodes in the pelvis cannot be examined or removed in the perineal approach. They are located too high in the pelvis to visualize. This is not necessarily a major drawback. Because there has been better selection of patients for surgery, the presence of lymph node metastases has become quite unusual. In my practice, we have found that less than three percent of men in the low to moderate risk categories had metastases in their pelvic lymph nodes. Many urologists are no longer removing these lymph nodes. In the past five

years, I have not had a single patient in these risk categories who has had a lymph node metastasis.

In 1998, a new technique using **laparoscopic surgery** to remove the prostate was introduced in Paris by surgeons Bertrand Guillonnet and Guy Vallancieu of the Institut Montrouis. As shown in Figure 3, the surgeon makes five small incisions in the lower abdomen to introduce a camera and instruments used to perform the surgery. The surgeon thereby has a magnified view of the surgery on a television monitor. The procedure is essentially the same as the retropubic surgical technique. Pelvic lymph nodes can be removed, the neurovascular bundles preserved (their size is greatly enhanced on the monitor), and the bladder neck sewn to the urethra usually with a watertight closure. This surgical technique is becoming more common in the United States and offers the promise of shorter hospital stays (one center is discharging most of their patients the same day as the surgery), a rapid recovery, and a shorter duration of time that the catheter needs to be worn. Moreover, because of the enhanced magnification, the procedure is associated with less blood loss and a better opportunity to preserve the neurovascular bundles.

By using special robotic devices which are connected to some or all of the instruments including the camera, the surgeon can manipulate the robot using voice commands. There is one type of robot with which the surgeon is stationed at a computer keyboard and delivers commands while watching on a monitor. The surgeon does not necessarily have to be in the operating room. I watched a demonstration in which the surgeon was in Florida doing a procedure on a patient who was in an operating room in Germany.

How does the surgeon decide which surgical method to use? This is largely based on the training and experience of the surgeon. Most surgeons are only trained to do the retropubic approach. As a result, more than 90% of all the surgeries have been done using this technique. Currently, more and more surgeons are learning the laparoscopic procedure, and in the next 5-10 years when the medical field has determined and published long-term results in the areas of PC recurrence, nerve-sparing capabilities, and side effects such as incontinence, this is

(continued)

likely to become the dominant form of surgery.

This evolution of radical prostatectomy procedures has produced such improved safety that the operative mortality is less than 0.1%. As shown in the results from 1,860 of my patients who had their surgery in the last 25 years (Table 2), intraoperative complications such as anesthetic problems and bleeding (when more than three units of blood are transfused) occurred in less than 10% of the patients; in the past eight years this has decreased to less than 3%. Postoperative complications such as infection, bleeding and malfunctioning catheters in the first 30 days after surgery occurred in less than 1% of these patients. The hospital stay averaged 2.8 days. Urethral strictures (scars that form at the site where the urethra and bladder neck are sewn together) occurred in 7.5% of these patients although none have occurred in the last five years. Strictures are corrected by stretching or incising the scar.

## What You Can Now Expect If You Have an RP

### Planning for Surgery

Once you have decided to proceed with surgery, there are preparations to be made. You need to get yourself in good condition both mentally and physically. Having a strong positive attitude that you have made the right decision and are supported by your family will help you to be in the best mental condition. It is never too late to start an exercise program or begin a good nutritional program. Usually there will be several weeks before surgery, so there is time to initiate these programs. It is helpful to stop smoking and reduce alcohol intake. You should plan for a recovery period of a month before returning to work although you will resume many of your other activities within a shorter period of time. The better condition you are in prior to surgery, the more rapid will be your recovery.

Some surgeons will ask you to donate several units of your own blood to be available should a transfusion be needed. Others recommend the use of blood from the American Red Cross. Family members may donate blood if they match your blood type.

Several days prior to surgery, your surgeon may request blood tests, an EKG and a chest X-ray. Your internist is likely to want to examine you as well. It is usually helpful to have your bowels

cleaned out before surgery. You don't want to have to worry about having to have a bowel movement during the first few days after surgery.

You will be asked to avoid having anything to eat or drink for 6-8 hours prior to the scheduled time of the surgery. If you are taking any medications, check with your physician as to whether or not they should be taken the day of surgery. Any medications, herbal supplements or anything else that might interfere with blood clotting should be stopped 10-14 days prior to surgery.

The day before surgery, the anesthesiologist will call and ask about your health, any allergies you might have, the medications you are taking, and any previous experience with anesthesia. You will have a general anesthetic, but some surgeons and anesthesiologists also prefer an epidural anesthetic, which is administered through the back and provides good pain control after the surgery.

### What to Expect During the Hospitalization

You should arrive at the hospital two hours before surgery. The nurse who checks you in will ask what type of procedure you are having and request that you sign a consent form giving the surgeon permission to perform the specific surgery. An intravenous solution of salt water will be started in your arm and an antibiotic may be given. If all of the previously requested blood tests have not been obtained, new tests may be ordered.

The anesthesiologist will talk to you again about the type of anesthesia. This is the time to ask any last minute questions. Intravenous sedation will probably be given and you will be moved to the operating room. The time you are scheduled for surgery is actually the time that the anesthesiologist begins to work. The actual surgery may not begin for a half hour after that.

You will recognize your surgeon who will be wearing a mask and meet the assistant surgeon. Shortly thereafter, you will be sound asleep. When you wake up about 2-3 hours later, you will be in the recovery room. You will have an intravenous line in your arm, a catheter in your bladder, a drain tube exiting from the side of the incision to carry away excess serum and fluids which collect from the area of the surgery, and special wrappings on your legs to prevent blood clots. You will

**Table 2. RP Results in 2002  
(n= 1860)**

- Surgical mortality: 0.1%
- Intraoperative complications: 9.7% (>3 units of blood)
- Post-op complications (first 30 days): 0.8%
- Hospital Stay: 2.8 days
- Stricture: 7.5%

remain in the recovery room for 1 to 2 hours before being transferred to your room. This is when you can visit with your family.

Later the same day or the next day you will probably be able to start drinking small amounts of fluids. You will also be helped out of bed and can start walking. Although it doesn't seem possible, you are not likely to experience much pain. In fact, many patients report that they experience a sense of exhilaration that the surgery is over and they feel so good. Pain control is provided by giving a long acting narcotic through the epidural catheter or by allowing the patient to administer his own pain medication intravenously using a system known as Patient Controlled Anesthesia. As soon as your stomach is comfortably accepting fluids, the intravenous fluids are discontinued. On the average, patients are ready to leave the hospital 2.8 days after the surgery. The drain tube is usually removed prior to discharge.

The catheter that was placed during surgery goes home with you. It is connected to a bag that can be strapped to your leg. Also, you will be provided with a large bag that can hold several quarts of urine and is particularly useful for use during the night. You will be given prescriptions for pain medicine and antibiotics prior to your discharge.

### At Home

You can expect to feel tired and to sleep a lot but each day your physical activity should be increased. There is no need to spend large amounts of time in bed. If they have not already been removed prior to discharge from the hospital, the skin staples/sutures will be removed 5-7 days following surgery. This will probably be done in the urologist's office. During this visit you can review the pathology report and look at the Kattan postoperative nomogram. The urologist will give you an idea as to what to expect in terms of future outcome and discuss the need for any additional therapy.

The catheter will remain anywhere from a week to three weeks. It is important that the connection between the urethra and the bladder be well healed before the catheter is removed so that

*(continued on page 13)*



**Meet Gail Betts.** She brings to the PCRI Helpline a professional background in urology from the University of Kansas Medical Center where she was employed as a Physician Assistant. Calm and unruffled, she supports the Helpline staff on a part-time basis, discussing individual patient situations with members of the PCRI Medical Review Board and other staff members. In addition, this working mother spends hours on the telephone with patients and their families. “We can make a real difference by giving families facing prostate cancer an additional perspective,” she says.

“For example, I remember a woman calling about her 65-year-old husband. His PSA had ranged from 2.2 to 2.6 for several years, but then his physician felt an abnormality in his prostate during a routine DRE. His physician then performed a biopsy and the pathology confirmed the presence of PC, which his local pathologist determined was a Gleason Score of 7 (3,4). The patient then underwent a bone scan and a CT scan, both of which were negative for metastatic disease. Therefore, they were considering local therapy, either a prostatectomy or radiation, but before proceeding, she wanted more information so she called the PCRI Helpline.

“I explained to her that I was not a physician and the information I shared with her should be discussed with her husband’s doctors. During our conversation, I referred her to pertinent medical literature, including several of our *Insights* newsletters, and shared with her experiences of other patients with prostate cancer. I reviewed dietary and vitamin supplement information, and that it is wise to have the Gleason Score validated by a pathologist who is an expert in the field of prostate cancer. We have found that about 50% of the time when an expert pathologist reviews the slides, the Gleason Score is changed. Because the Gleason Score (GS) is such a critical piece of data, it’s important to make sure the GS is accurate. I sug-

gested several prominent prostate cancer pathologists for a second opinion.

“She called back about two weeks later and informed me that they had had the GS validated by an expert, and it had been upgraded to a GS 4,3. She wanted to know whether that made a significant difference. I reviewed the 2001 Partin Tables, which PCRI has on its website ([www.pcri.org](http://www.pcri.org)). For a PSA of 2.6, the Partin Tables indicate that whereas a GS 3,4 indicated the chances that the disease is confined to the prostate are 41%, a 4,3 indicates that those chances are just 30%. I provided information about other tests, such as ploidy analysis, endorectal MRI with spectroscopy, ProstaScint, and blood biomarkers: PAP, NSE, CGA, and CEA, because the results of these tests could help them decide if they would still proceed with local therapy or systemic therapy.

“When she called again, she reported that they had obtained the results of most of the tests we had discussed. With great relief in her voice, she said that all the tests to date indicated that the prostate cancer was confined to the gland. However, they had not yet had the endorectal MRI with spectroscopy. They had decided to have it done ‘by an artist,’ she laughingly added. They had wisely scheduled the procedure

more than 8 weeks after the biopsy. It was likely that the biopsy site had healed, thus, there should not be any blood that might prevent a clean image on the screen.

“In her next call, she read to me from the report: ‘The eMRI and the MRSI are concordant for a moderate volume of the dominant tumor in the left apex. No extracapsular or extraprostatic disease is seen.’” She went on to say that her husband was now under the care of a leading oncologist and was embarking on a 6-8-month ADT3 program (Casodex and Proscar before adding Lupron). At the end of that period, he would have intensity-modulated radiation therapy (IMRT) or 3D conformal external beam radiation. Her husband would continue with the ADT3 during external beam radiation and for two months after radiation.

“I was very pleased. Here was a patient and his wife who hadn’t panicked, but had taken full advantage of all the staging tools and PCRI’s Helpline and had made an informed decision based on the data. People often thank me saying, ‘This is the kind of information we had hoped for, but hadn’t been able to find.’ Results of cases like this make us glad we spend the needed time with each Helpline caller we speak to.”

“We can make a real difference by giving families facing prostate cancer an additional perspective”



# Meet PCRI's Medical Advisory Board

To manage the expanding volume of knowledge about prostate cancer and translate it into useful, understandable recommendations for patients, PCRI formed a medical advisory board of 18 eminent physicians representing seven medical disciplines. These physicians are Drs. Duke Bahn, John Blasko, David Bostwick, Stan Brosman, Nicholas Bruchofsky, Douglas Chinn, Michael Dattoli, Peter Grimm, Patrick Kupelian, Richard Lam, Leonard Marks,

Charles (Snuffy) Myers, Gary Onik, Christopher Rose, Mark Scholz, Michael Steinberg, Nisar Syed, and Glenn Tisman.

We will continue to introduce these physicians to *Insights* readers in this and upcoming issues. This issue features two men, Dr. Mark Scholz and Dr. Stanley Brosman, each of whom has written an article exclusively for *Insights* readers that appears in this issue.



**Mark C. Scholz, M.D.** is a co-founder and past president of the Prostate Cancer Research Institute. A trained and board-certified oncologist, he is one of the few oncologists in this country to specialize exclusively in prostate cancer. He co-founded the Healing Touch

Oncology practice to specialize in prostate cancer in 1994 and has recently expanded the practice under a new and more descriptive name, Prostate Oncology Specialists. In addition to his practice responsibilities, he is a frequent lecturer to prostate cancer support groups and medical societies on the subject of prostate cancer staging and treatment. A prolific writer, he has published over 40 papers and articles on prostate cancer and its treatment in just the past five years.



**Stanley A. Brosman, M.D.** has been a leading urologist in the Southern California area for almost 40 years. He spent his urology residency at UCLA and was affiliated with UCLA for the next 15 years, rising to the positions of Chief of Urology, Professor in-Residence of Surgery/Urology, and Clinical Professor of Surgery/Urology. He then went into private practice, and today heads the Pacific Urology Institute. Throughout

his career, he has been active in research projects with special emphasis on prostate cancer in recent years. He is Medical Director of Pacific Clinical Research, a research site conducting laboratory and clinical studies. He has made over 200 presentations at medical meetings, delivered more than 200 invited lectures throughout the world, and has had more than 80 papers and articles published in medical journals plus over 100 abstracts, medical news articles, and reports published. In 1998, he organized and now directs a bimonthly Journal Club with 25 members who meet and discuss current articles involving prostate cancer.

## Radical Prostatectomy – 2003 continued from page 11

urine does not leak out and cause scarring.

You can resume your regular diet but should avoid foods that are likely to produce gas. One of the most common problems people experience is 'gas pains'. It takes a while before the intestines resume normal function and it is wise to progress slowly.

You can shower at any time. Soap and water does not hurt the wound. Any activity that would require straining, including bowel movements, should be avoided until the incision is solidly healed.

Following removal of the catheter, you can expect to leak urine. Usually an absorbent pad placed inside jockey underwear will be sufficient, and they are easy to change. Most men notice that they are drier at night when lying down. Bladder control improves in the morning when the muscles are fresh and tends to get worse as the day goes on and the muscles get weaker. It often takes several months before bladder control is good enough to give up the pads although many men still wear one when they go out – just in case. There are several effective aids to countering incontinence. Con-

sult your physician to learn the alternatives.

About a month after surgery, many urologists prescribe Viagra to help prime the system. Although it is unlikely that you will begin experiencing natural erections at this time, you may be able to speed up the process with this "priming" effort. There are several different methods of assisting erections. Consult your physician to learn the alternatives.

From this point on, it is just a matter of time before all of the systems have stabilized. You are likely to recognize differences in bladder and bowel function for months.

Everyone is eager to know their PSA level, but in the first month this is done more to satisfy curiosity rather than to make any decisions about therapy. Your physician will probably schedule your first post-operative PSA test about 2-4 weeks after your surgery.

### Conclusion

We are at a point in managing prostate cancer where we can give better advice to patients regarding the ability of surgery to eliminate the cancer and estimate the chances of incontinence and impotency. Our goal is to eradicate

the cancer with a minimum of adverse effects so that every man can maintain a high quality of life. Although surgery offers many benefits, it is not for every man. It is incumbent for each man and his doctor to work together in order to select the most appropriate therapy. ■

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## PC Climb Turns To Highest Mountain in Africa

**PROSTATE CANCER CLIMB**  
Hap Weyman Memorial Prostate Cancer Awareness Project

Preparations are underway for the Second Hap Weyman Memorial Prostate Cancer Climb in September 2003, when prostate cancer veterans and their supporters will be challenged by "The Snows of Kilimanjaro."

The Prostate Cancer Climb is a unique fundraising and awareness movement that began in 2001 when a team of fourteen climbers, including five with prostate cancer, climbed Argentina's 22,840-foot Mt. Aconcagua, the highest mountain in the Western Hemisphere. Mt. Kilimanjaro, the fabled 19,400-foot peak in Tanzania, will be the next high-altitude target for these dedicated men as they work closer toward their goal of raising \$1 million for prostate cancer research and education.

"Not only will these funds be invaluable in the fight against Prostate Cancer," said Glenn Weaver, the PCRI Executive Director who himself was part of the team that climbed Mt. Aconcagua, "the climbs represent a powerful symbol, too. We want to inspire all men with this disease that there is hope, and prove to them that a rich and rewarding life is possible after diagnosis."

The Prostate Cancer Climb program was established three years ago by Dr. Terry Weyman, a Los Angeles chiropractor whose father, Hollywood television director Hap Weyman, died of the disease in 1990. **Weyman's goal: To show that prostate cancer needn't be a death sentence and that**

**through proper awareness and education, prevention can be possible.** The cancer survivors on Weyman's first expedition learned they didn't have to set limits.

The tradition continues with the upcoming Mt. Kilimanjaro challenge. Donations are currently being sought from individuals and corporations across the country in the name of the Climb's Hap Weyman fund.

"The high altitude climb is a gritty task in itself, and for those who have the disease the challenge becomes harder," said Ken Malik, a prostate cancer survivor who took part in the Mt. Aconcagua expedition and who plans to tackle Kilimanjaro as well. "To get our message across, we need the support of one and all."

**"To get our message across, we need the support of one and all."**

**In order to make the journey to Mt. Kilimanjaro, each climber is required to raise at least \$2,000.** Donors will be recognized on the Climb Website and will have their names acknowledged in a flag salute at the Kilimanjaro summit. And most importantly, donors will rest easy in the knowledge that they've contributed to a most worthwhile cause.

To relive the exciting events surrounding the Mt. Aconcagua expedition and to learn more about the upcoming Kilimanjaro event, **please visit the Prostate Cancer Climb Website at:**

**[www.prostatecancerclimb.com](http://www.prostatecancerclimb.com)**

## PCRI Regional Conference Revisited



The raves keep coming in for PCRI's Regional conference that was held last October. The underlying sentiment? "It was a conference not to be missed." Well, if you did miss it, there's a way to see what went on. We videotaped the entire conference, and we'll send videocassettes to you for just \$15.00 each (\$99.95 for the set of seven videocassettes) plus shipping (\$8.00 for the complete set, \$6.50 for 4-6 videocassettes, \$5.00 for 1-3 videocassettes when shipped in the U.S.). Here's what you'll be getting:

### SC201V-Welcome & Introduction

Glenn Weaver, PCRI Executive Director; What is PIA? - Dr. Richard Reisman; Strategies for Success in the Treatment of Prostate Cancer - Stephen B. Strum, M.D.; A Patient's Perspective - Michael O'Hara.

### SC202V-Diagnosing & Staging Prostate Cancer

Duke Bahn, M.D., Leonard Marks, M.D., Samuel Kipper, M.D., Michael Dugan, M.D., Fred Lee, M.D.

### SC203V-Therapy for Systemic & Recurrent PC

Mark Scholz, M.D., Stephen B. Strum, M.D., Bob Leibowitz, M.D., Glenn Tisman, M.D., David Quinn, M.D., Richard Lam, M.D.

### SC204V-Primary Therapies

Stanley Brosman, M.D., Tim Wilson, M.D., Marc Botnick, M.D., Fred Lee, M.D.

### SC205V-Therapy for Advanced PC

Mark Scholz, M.D., Mitchell Gross, M.D., Steve Tucker, M.D., Stephen B. Strum, M.D., Glenn Tisman, M.D., David Quinn, M.D.

### SC206V-Live Demonstration of Color Doppler Ultrasound and Staging Biopsy

Duke Bahn, M.D., Fred Lee, M.D.

### SC207V-Panel Discussions (Q&A)

Stanley Brosman, Moderator; Closing Remarks - Duke Bahn, M.D., and Stanley Brosman, M.D.

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Also, if you would like to order **A Primer on Prostate Cancer**, Dr. Stephen B. Strum's comprehensive book on all aspects of PC and its treatment (\$28.95 at retail), it is available for just \$21.00 plus \$3.95 shipping, when ordered directly from **PCRI** at 5777 W. Century Blvd., Suite 885, Los Angeles, CA 90045 (Phone 310-743-2116 or Fax 310-743-2113).

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