

**VIEWS FROM THE “OTHER SIDE”:  
PERSONAL REFLECTIONS ABOUT  
PROSTATE CANCER FROM TWO  
UROLOGICAL ONCOLOGISTS\***

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Dr. Lange has served on many editorial boards including the New England Journal of Medicine. He is a member of numerous professional and honorary societies, served as President of the Society of Urologic Oncology and is a Trustee of the American Board of Urology. He is internationally recognized for his clinical and experimental work in a variety of genitourinary cancers especially prostate and testis and has received national recognition for this work. Currently in addition to being Chairman of the Department, he conducts a large clinical practice in urologic oncology, and is Director of the Institute for Prostate Cancer Research, a multi-disciplinary research initiative of the University of Washington and Fred Hutchinson Cancer Research Center.



Paul F. Schellhammer, MD (PFS)

Dr. Paul Schellhammer received his undergraduate education at the University of Notre Dame and his medical school training and Cornell Medical College in New York City. His surgical and urologic training were taken at the University Hospital of Cleveland in Cleveland, Ohio and the Medical College of Virginia, Richmond, Virginia. This was followed by a fellowship in urologic oncology at Memorial Sloan Kettering Cancer Center in New York. Subsequently he joined the practice of Devine Poutasse Fiveash Urology and became a faculty member of Eastern Virginia Medical School where he eventually achieved the rank of Professor and then also served as Chairman of the Department of Urology and Program Director of the Resident Training Program.

Dr. Schellhammer has made many contributions to the field of urologic oncology and published widely in that discipline, especially in prostate cancer. He serves on several editorial boards, and has served as a trustee of the American Board of Urology as its President. He has also served as President of the Society of Urologic Oncology, as President of his Mid-Atlantic Section of the American Urologic Association, as a member of the Board of Directors of the American Urologic Association, and has been elected President of the American Urologic Association in the year 2007.

We wrote this article to transmit to urologists and patients with prostate cancer certain subjective events surrounding the diagnosis and treatment of this cancer. These efforts could be useful for several reasons. First we both had radical prostatectomies several years ago and were emotionally and in one case practically involved in each other's surgical process (i.e. PHL performed the radical prostatectomy on PFS). Second we are urologists whose research and practice efforts have principally centered on prostate cancer. Finally, as will be elaborated subsequently, we have been close friends for many years and thus have had frequent occasions to reflect and discuss many facets of prostate cancer both before and after our own experiences. We will individually describe the experiences surrounding our diagnoses, surgeries, and subsequent events, using them as discussion points for well accepted and recently revealed information about the disease. Finally we will present our mutual insights about these experiences.

### **Reflections of Paul H. Lange, M.D. (PHL)**

Background: Though we had known of each other early in our careers as urologists, our friendship deepened over events involving prostate cancer in my family. Briefly, my father-in-law who lived in the Norfolk area had an operation to relieve urinary symptoms for benign prostate disease by PFS's practice partner. PFS subsequently took over his routine care, and we then began to communicate regularly about that care. Several years later, in 1990, I got a letter from PFS apologizing because my father-in-law, now 82 years old, had a PSA (Prostate Specific Antigen) blood test obtained by mistake, and it was 20 ng/ml. Because I had by then started speaking and publishing on the use of this new PSA test<sup>(1)</sup>, he asked for my advice. In 1990, we did not appreciate the seriousness of a PSA of 20, and while healthy, my father-in-law was 82! I remember asking some of my urological oncology friends for their opinion regarding management, and I particularly remember one very famous friend who looked at me as if I were crazy to even contemplate following up on the PSA in a man of that age. So I advised (and PFS agreed) that nothing be done or even followed, and thwarted off the confusions of my wife and my extended family about why was I not concerned if PSA was so important and prostate cancer so serious. PFS confirmed that his DRE (Digital Rectal Exam) was normal.

Over the next 2 years my father-in-law watched his brother-in-law and two of his close golfing partners die from prostate cancer. During this time I tried to convince him that prostate cancer was much less likely to threaten his life than a host of other illnesses, as for example blood vessel diseases or diabetes. He was a very intelligent person, but a business man "bottom line" personality at heart, and he kept questioning if prostate cancer was possibly present in him, didn't I want to diagnose and possibly treat it especially since his mother was still alive at the age of 102 yrs. Finally Paul and I acquiesced, and obtained another PSA, which was now 30ng/ml. This led to a biopsy and prostate cancer was found. Under the microscope it was an aggressive variety (technically a Gleason 4 + 3). A bone scan to search for cancer spread was normal. My father-in-law had recently lost his wife, was uninterested in sexual activity, and was adamant about beginning some form of therapy. At age 85, hormone therapy (i.e. lowering the testosterone level by periodic shots of a medicine called an LHRH agonist) was considered by both of us to be the most effective and appropriate treatment with the least side effects. This therapy lasted for 14 yrs, his PSA remained undetectable, and he had no obvious complications from the therapy. He died at age 97 of cardiac failure. My wife's family, and my father-in-law

when he was alive, were incredulous that anyone would say that this aggressive approach to diagnosis in an octogenarian and his subsequent therapy didn't extend his life. Despite our reservations about initially pursuing this path, we are hard pressed to deny their position.

During this time Paul and I used this management dilemma, and my yearly trips to the Norfolk area to visit family, to deepen our relationship and converse about prostate cancer in general. Little did we suspect that later in our acquaintance this subject would become more personally important.

PFS Comments: As the urologist who Paul Lange's family looked to for counseling and care, I shared the misgivings of treating prostate cancer in an asymptomatic octogenarian. When treatment was begun and the PSA level plummeted to and remained undetectable, the patient's anxiety and apprehension vanished, and his energy seemed primed as each visit continued to reveal a normal rectal exam and a zero PSA. I was providing medicine that was certainly good for his soul and well being regardless of how important or essential it was in extending survival. I also achieved somewhat of a heroic status as a healer and was so recognized at the large family reunions I was fortunate to attend. As physicians we are often privileged to enjoy this respect and gratitude, but we must be cautious not to become enamored and entitled by it.

PHL's Radical Prostatectomy: I was involved in the early elucidation of PSA's clinical value<sup>(1)</sup> and as such I first measured my serum PSA in 1984 when I was in my early 40's as part of our research efforts. The level was 0.7ng/ml. I was reassured; that value was considered normal. Of course today we have a different perspective for a variety of reasons. One reason is the Prostate Cancer Prevention Trial (PCPT) which was a double blind randomized study testing finasteride vs. placebo for prostate cancer prevention. In that study, 15% of men in the placebo group, with PSAs <4 ng/ml after a 7 year waiting period, were found to have prostate cancer, and 5% of the cancers were present when the PSA was <0.5 ng/ml. Also some of these cancers in these PCPT "controls" were of intermediate or high grade<sup>(2)</sup>.

We now know the median PSA level for a 40 year old is <0.7<sup>(3)</sup>. Indeed as we write this article, there is a hotly debated National Cancer Center Network's clinical care pathway for prostate cancer diagnosis, which recommends measuring PSA's at age 40 in all men. If the PSA is >0.6 ng/ml, the patient should have yearly PSA's and DRE's, and if the PSA level rises too quickly or the DRE become "suspicious", the man should have a prostate biopsy.<sup>(4)</sup> Conversely, Dr. Thomas Stamey, who was one of the first to bring the value of PSA in prostate cancer to the attention of medicine over 20 years ago<sup>(5)</sup>, now claims that levels between 2 and 10 ng/ml are attributed primarily to benign prostate enlargement or hyperplasia rather than to cancer, and that biopsying men with these low levels of PSA may be ill advised.<sup>(6)</sup> And so the debate will ebb and flow. While a very helpful marker of prostate cancer, PSA is imperfect and its interpretation must take a number of factors into consideration such as age, health, race, testosterone level, and maybe most importantly, the rate at which the PSA levels rise over time (so-called PSA slope or velocity). The good news is that cancers are discovered early in their course. The bad news is that some cancers are detected that may never be of any health concern and will only cause worry and side effects from treatment applied unnecessarily. The smart news now and in the future will be the separation of cancers into favorable and unfavorable ones or into what I previously had characterized as the turtles and the birds<sup>(7)</sup>. Very briefly, prostate cancer can be conceptualized as either turtles or birds in an enclosure. The turtles grow slowly and escape only if they become large and even then only rarely. The birds on the other hand grow much faster

and always escape (i.e. metastasize and kill the patient) when they get to a certain size. Obviously the best goal is to detect the birds early and eliminate them, while ignoring the young turtles or at least most of them, thus avoiding unnecessary diagnoses and/or therapies.

Over the years I regularly checked my PSA value and noted that very gradually, and in a somewhat “saw tooth” fashion, the values rose. When it “hit” 3.0 ng/ml, I remember reassuring myself that the yearly increment (i.e. slope) was  $<0.75$  ng/ml/yr, which according to studies by Carter et al<sup>(8)</sup> was a good sign. Then about 2 yrs later it was 3.7ng/ml - still a reassuring slope. However there was talk from my good friend Dr. William Catalona about lowering the normal cut-off to 2.5 ng/ml.<sup>(9)</sup> Accordingly I somewhat whimsically decided to have a biopsy. I confidently expected it to be negative because the rate of rise of my PSA was slow and because there was absolutely no prostate cancer in what was a very large family of male relatives. I had the sextant biopsy performed by my colleague Dr. Bill Ellis somewhat secretly (only he, my nurse, and our main prostate pathologist Larry True knew). I remember remarking that the biopsy was not as uncomfortable as a sigmoidoscopy but that local anesthesia (then not given or studied) might be very useful, especially if more than 6 biopsies were taken. That prediction was based on my observations years before when we conducted our trial of prostate resections under local anesthesia<sup>(10)</sup>. Of course now almost all prostate biopsies are done under such local anesthesia. I was shocked when pathological analysis of my biopsies revealed one mm of Gleason 3+3 on the left side in one of six cores.

What to do? I pondered, reread the literature, reflected especially on “watchful waiting”, and flirted with denial. The idea of doing nothing and just watching it (so-called active surveillance) did not seem attractive with my somewhat proactive personality. Yet I reasoned, maybe I could compromise between aggressive treatment (e.g. radiation therapy or radical prostatectomy surgery) and nothing, by placing myself temporarily on hormone therapy and then watching it. Accordingly I called my friend Dr. Martin Gleave who was leading the neoadjuvant androgen ablation clinical trial in Canada<sup>(11)</sup>; that is, giving temporary hormone treatment for 3 or 8 months prior to surgery. I didn’t wish to reveal that I was conducting an information search for treatment of my prostate cancer, so I obfuscated my problem by stating that “I had a patient who wanted to know about....,” and asked what the pathological no tumor ( $P_0$ ) rate was after 8 months of hormone therapy. When he told me that the number of men who had no tumor in their prostate specimen after this temporary treatment was less than 10%, I abandoned my escapist solution to my illness. That solution was to go on hormone therapy for 8 months; keep up a tan and follow a strict diet in order to avoid the pale appearance and weight gain side effects of hormone therapy (and thus avert suspicion of my illness); and then get periodic PSA’s and biopsies to delay or infinitely postpone aggressive treatment.

Finally I decided to have a 2<sup>nd</sup> biopsy and again 1 mm of Gleason 6 was found in about the same place. That was it! I wanted to be treated despite all my scholastic ruminations about surveillance, the turtles and birds, and length and lead-time biases (these biases are terms used by population scientists to explain why screening for a disease especially prostate cancer may not be useful).

What treatment should I have was not a problem. The dilemma did highlight my intellectual realization that despite my surgical orientation and practice, the relative value of surgery vs. radiation therapy regarding quality of life and survival is unknown, and I remember feeling ashamed that this information was not available, and I gained more sympathy for the layman

who has to make a treatment decision amidst this confusion. I could only imagine the frustration and anger that must prevail among laymen who have no fore knowledge about prostate cancer or even about the prostate gland in general.

Surgery was my only option for several reasons. First if I had had radiation therapy, the opprobrium from my urologic colleagues would have been too much. Parenthetically, I discussed this issue sometime later with my former colleague, John Blasko, who is a world famous radiotherapist in Seattle. In jest he remarked that if I had gotten radiation therapy, I would have received many speaking invitations to and honorariums from radiation oncology meetings. John also said that in the same circumstance he, for similar reasons of loyalty to his procedure and profession, could hardly have considered surgery and would have selected the radioactive “seed” option. So it is clear that we are products of our educational training and mentoring environment. When giving advice, we have to recognize this bias in fairness to the patient and ourselves. In fact, a survey was done where radiation oncologists and urologic surgeons were asked what treatment they would pick if they had prostate cancer and, as expected, the vast majority picked the treatment of their specialty.<sup>(12)</sup>

The second reason I chose surgery was because with my experience, I had little fear of the surgery, and with my personality I wanted to know what was in there and to get the problem behind me if possible. This, I have come to realize, is the main legitimate reason for a surgical choice and is what I now seek to hear from those of my patients who chose surgery.

I was surprised at the amount of trepidation I experienced. I thought that with all I had seen and done over the years regarding prostate cancer, that I would embrace this necessity with aplomb. I was wrong. With my good cancer parameters, I feared impotence and incontinence, not diminished survival. This was despite the realization that most of my patients seemed to do very well on those scores. “When it’s you, it’s different” now had more poignant meaning.

Who was going to do my surgery was not a very difficult problem once analyzed. I realized that going somewhere else to “keep it quiet” from my colleagues would be impossible. Also I knew that my associate Bill Ellis did the operation pretty much as I did (so it seemed almost like fulfilling a cocky surgeon’s dream of using a mirror), and I trusted him. He agreed and did a wonderful job under what must have been some significant pressure. Before the operation, I announced my diagnosis and pending surgery to my department and other friends. “Going public” was a relief! I also discovered that a comfortable and very personal sense of trust, and the reassurance of “home ground”, in addition to expertise, were more important elements than I had heretofore acknowledged.

Why did I initially try to keep my diagnosis secret? Why do many of my patients do the same thing? I suppose its related to the predominantly male impulses to show no weaknesses, to fear loss of power, and so many other emotions that psychologists write about. This secretive impulse is a mistake. It creates undue tension and deprives the man (and possibly the significant other) of needed emotional support. Nationally it has impeded efforts to increase awareness of and support for prostate cancer. Thanks to the efforts of organizations like the Prostate Cancer Foundation and patient support groups, this tendency is disappearing . I am even more vigorous now in urging my patients to “go public”.

While awaiting my surgery, I was running an errand and passed an alternative medicine store that I had passed many times before. I must admit I had been very vocal in my criticism of alternative medicine approaches, believing that medicine needed to defend its hard-won evidence-based position. Yet this time I entered the store and was so enthralled with all the optimistic advertisements and comforting labels with pictures of fruit and such on the bottles of pills. Before I knew it, I walked out with 2 bottles. One was selenium; the other I have forgotten. Later that day when I reflected upon what I had done, I appreciated more the power of self-treatment and the control it offers. I never took those pills, but later, on the weekend before my surgery, I thought I was getting a cold. The prospects of having to reschedule was overwhelming. Thus I literally snuck into a drug store and bought a bottle of Echinacea. I didn't get a cold and I had my surgery. I began to wonder about Echinacea's validity but was brought to the truth by the results of a randomized study on Echinacea's effectiveness for preventing colds which was announced 6 months later and showed the drug to be "ineffective"<sup>(13)</sup>. But I came to realize that empowering the patient to do something for himself, even if through the use of yet unproven remedies, has merit. More importantly, I realized that established medicine must figure out better ways to retain the placebo effect without lying, and to teach it to future practitioners in a more systematic way. I remember thinking: if only the results of more trials were available to guide us regarding our decision-making. Like many investigators in prostate cancer, I am looking forward to the results of the now ongoing large trial testing the effectiveness of selenium and/or Vitamin E in preventing prostate cancer.<sup>(14)</sup>

I recovered easily. The pain was very manageable, though the catheter was more bothersome than I imagined. The only real surprise was the degree of fatigue that I experienced over a three to four week period. This was not from blood loss (I lost very little), but something else hard to define. Yet I was playing tennis at 4 weeks though with less effectiveness than usual. I look forward to a truly scientific analysis of laparoscopic and robotic assisted radical prostatectomy in that regard. From the experience in our department, I suspect the fatigue factor will be less with the laparoscopic/robotic approach.

The catheter was removed at 2 weeks and its discomfort has pushed me to shorten that period for wearing the catheter in most patients. For three weeks I was not continent and I was very unhappy. Leaking urine despite all my best efforts was nerve-racking. I did finally learn that once accepted, pads are not that odious. Like any good Northern European Lutheran, I feared the worst – permanent incontinence! After 3 weeks I gained continence very quickly and I am now firmly ensconced in the continence group.

Yet I am not as continent as I was before surgery. Though I use no pads or such, there are times when I do leak a little though never to the point of social embarrassment; these times include such events as the need to pass flatus, an overly full bladder precipitated by coffee, sexual anticipation, more than my usual alcoholic intake, or when extremely fatigued. Yet leakage with these events is unpredictable and rare. I have now begun to question my heretofore continent patients in ways I never did before and found similar though never quite the same stories even among those who scored very well on the continent questionnaires. Of course when I queried them why they hadn't told me this before, it was because I never properly asked. I have come to believe that almost no post radical prostatectomy patient is totally continent and that the current Quality of Life questionnaires need further refinement. Furthermore there are more physiological factors relating to incontinence in this context than we realize, and these factors have little to do with how the radical prostatectomy is performed and/or how the patient heals.

For years now I have told my patients that they can generally expect social continence, but I cannot promise that they will be “trampoline dry”. More about this in our comments section.

For obvious reasons I will not say a lot about my sexual recovery except to indicate that I never lost my potency and have no need for “Viagra-like” medication. With regard to the dry ejaculation that results from the surgery and the quality of the orgasm, the best description is one I hear from many of my patients: “its different but not that different”. In my case I certainly feared loss of potency more than reduction in survival since my cancer seemed almost certainly curable. However personally I wasn’t really afraid that impotence would adversely affect my marriage or even my quality of life. Rather the fear of impotence was more a catalyst to greater fears: loss of control and identity, and an unwelcome premature symbol of the aging process. I also came to better appreciate why many of my patients seemed to be more concerned with potency before the operation than after. Finally I’ve come to appreciate the tensions that can develop after surgery between the patient and his partner especially if their relationship is characterized by a lack of communication about sexual matters. It seems to me that if attempts at intercourse fail for too long, the sexual relationship becomes fatigued on both sides (but more with the female partner), and continued pursuit of satisfactory erections wanes. Thus I now try much harder to get the patient’s erections functional quicker by whatever means necessary, and I am more alert to the feelings of the female partner.

My PSA has remained undetectable for 7 years, and I must admit that emotionally I have dismissed prostate cancer as a worry, and neglect getting my PSA in a timely fashion. Yet initially and even now, waiting for the PSA’s to come back gives me some anxiety. More about PSA anxiety however from PFS and in our final comments.

In closing I am often glad I had this experience with prostate cancer. In ways that are hard to articulate, I think it has made me a better person and urologist when it comes to dealing with patients with the disease. I listen more; I am more empathetic; I have better insight into the morbidities of the surgery, and more confidence that surgery offers a very good therapeutic solution. As an academic surgeon scientist, I have a greater sense of purpose in conducting and administrating research on prostate cancer. I have often been asked “would I do it again; would I have surgery if I wasn’t a urologist; would I have more seriously considered watch and wait with a Gleason 6, one mm cancer”? One academic urologist who has made many contributions to prostate cancer, even expounded that I should not have had a biopsy. And if I had been so unwise as to have a biopsy he explained, I should not have had the surgery even if I had known what my surgical pathology revealed; namely, 1cc of low-grade cancer with negative margins. He furthered stated that: 1) theoretically by rate of tumor growth considerations, it would have taken almost thirty to forty years to reach “lethal” volumes, and 2) I could have at least waited another 10 years. No way! Taking a chance on the surgery was infinitely less fearsome than taking a chance on cancer theory. Besides, I feel that I have made the correct decision: no real morbidities, I’m almost certainly cured, and it made me a better servant in the care of patients and in the struggle to find better ways to manage the disease and even to cure it.

## Reflections of Paul F. Schellhammer, M.D. (PFS)

Background: When Paul Lange and I discussed a personal reflection piece, we came to a uniformly enthusiastic “let’s start”. We have known each other for thirty years. The cementing of our friendship and prostate cancer relationship was originally based on the fact that Paul’s father-in-law, who resided in my local area, had prostate cancer, and was my patient. As Paul has stated, on his visits East from Seattle, our mutual interest, prostate cancer, was often a subject of discussion and became even more so after Paul’s diagnosis and surgery in 1999, and my diagnosis and surgery by him in 2000. We often concluded our discussions with the promise that we needed to write a booklet or at least a chapter on our experiences. PHL did write a general information book for laymen – *Prostate Cancer for Dummies*.<sup>(15)</sup> However a more personal discussion in print was a project we both believed would be useful to others in many ways and would help dispel the tendency of men to “keep it quiet”. As is always the case, we found that our views were sharpened and more clearly defined when we had to put our thoughts, feelings, and opinions “to paper”.

In writing my personal experience, I realized two important principles. First, one cannot place oneself in another’s shoes when walking a decision pathway, since each individual processes and acts on information based on certain genetic predispositions and environmental conditioning. Even the closest of biologic and environmental human experiments, identical twins, will not process and react identically on each and every issue. I am married to an identical twin and can testify to this. Second, in situations like the diagnosis and treatment of prostate cancer, a person can be very positive in his pronouncements when faced with hypothetical scenarios only to be a lot less certain when confronted with the reality of a diagnosis. To use a military analogy, there is a huge difference between boot camp and the battlefield, or a sporting analogy – between the practice and playing field.

My annual PSA readings (from 1990 to 1997), beginning at age 50, had been very stable at 2.0-2.5 ng/ml. Due to a faltering urinary stream, the need to get up several times each night to urinate, and the sensation of incomplete bladder emptying, I began treatment with Finasteride in 1997 at age 57. My PSA level 6 months later was 1.1 ng/ml. A myocardial infarct (see below) interfered with my 1999 annual PSA determination. My PSA in the year 2000 was 2.5 ng/ml. Because I was on Finasteride this required a correction factor of 2.0-2.5x because a 5-alpha reductase inhibitor typically lowers the PSA levels by this amount. Thus my level of 2.5 ng/ml represented a significant rise from my previous levels; indeed, my true PSA was likely between 5.0 and 7.0 ng/ml. It was intuitively clear to me that I had prostate cancer. For example my PSA levels of 2.0-2.5 ng/ml beginning at age 50, and with which I was then very content, have since been shown to be associated with a 5-fold increase in prostate cancer risk<sup>(16)</sup>. Moreover at age 50-60, an absolute PSA velocity of >0.75 ng/ml/yr when compared to a PSA velocity of <0.7 ng/ml/yr is associated with a 3.5 fold increase in risk for prostate cancer by age 70.<sup>(17)</sup> Finally the PCPT (Prostate Cancer Prevention Trial) has demonstrated a 23% incidence of prostate cancer at PSA levels between 2 and 3 ng/ml<sup>(2)</sup>. A PSA of 5.0 to 7.0 ng/ml was quite abnormal by any standard for a 60 year old on Finasteride.

Several strategies materialized in my mind. I decided I would have numerous (20-25) initial biopsies, not the then routine 6 biopsies, to avoid the possibility of repeat biopsy sessions to clarify the etiology of the PSA elevation. I did not want to come back to the biopsy scenario again and again, as I knew would be the case if the initial biopsies were negative, because I was

convinced prostate cancer was present. I presumed a Gleason 3+3 cancer since it was the grade most commonly found amongst patients with a prostate cancer diagnosis in this PSA range, and which I diagnose on almost a daily basis in my practice.

PFS's Radical Prostatectomy: What treatment approach? I was debating this question pre-biopsy. As a surgeon, I was viscerally inclined to surgery, although intellectually I could not consider radiation by either interstitial implant or external beam as any less effective. I was also attracted to a definitive pathology report. I put erectile dysfunction and incontinence in perspective and had the advantage of first-hand knowledge of interventions that could soften their impact. Having been to France to observe the new laparoscopic approach and being quite impressed with the facility with which it was done, I considered this option for the anticipated 3+3 low risk cancer. The biopsy session was uneventful and I was correct in my first hunch. Prostate cancer was found. Only 3 (all on one side) of 25 cores were positive, and I was certainly pleased that I had chosen the multiple biopsy (i.e. "saturation biopsy") approach. Fewer cores might have missed the cancer. However my second hunch, that the cancer would be scored Gleason 3+3, was incorrect. All biopsies had predominant pattern 4. A bone scan and CT scan to detect possible spread of disease were normal. I put aside the adventure of a laparoscopic procedure for the tried and true open prostatectomy with an extended lymph node dissection.

Should I have the operation in my home hospital by my partner or take the "monkey off my partner's back" and go elsewhere? I consulted with my good friend, Paul Lange, who had had a prostatectomy, and we had operated together. He kindly agreed to do the surgery. I traveled to the University of Washington. The Gleason pattern influenced my attitude of weighing surgical side effects with benefits. My focus was on prolongation of life; the risk of urinary and sexual dysfunction became very secondary. This is contrasted to my co-author's primary concern about side effects when dealing with focal 3+3 cancer. Gleason 4 pattern cancer carries a higher risk for more rapid local progression and distant spread.<sup>(18)</sup> I was less focused on nerve sparing but on removal of a wide tissue margin. I considered unilateral nerve-sparing on the biopsy negative side, only if, at surgery, all circumstances (prostate size, the adherence and feel of the tissue, ease of dissection) were favorable. A radical retropubic prostatectomy with pelvic node dissection was performed by my co-author (PHL); nerve sparing could be performed on the opposite side of the cancer.

The pathology report brought the good news of absence of lymph node involvement and a unilateral pT2 (no spread outside of the prostate) lesion of 2 cc's with negative margins. This means that all the cancer appeared to be contained in the removed prostate. After any therapy, there is always a risk for future problems from disease that may have escaped the prostate but is, as yet, undetected. I was at increased risk due to the Gleason 3+4 grade with some pattern 5.<sup>(18)</sup> The decision that I needed to address was should I have additional (adjuvant) treatment by radiation or hormone therapy to "mop up" any remnants of cancer that might remain. My PSA after surgery was undetectable (<0.01 ng/ml). Despite the high Gleason score, no margins, seminal vesicles or nodes were involved with cancer. I decided to watch my PSA levels and hope for the best, which would be continued zero readings. Any rise in PSA would be my prompt for additional therapy.

A year after surgery, the dreaded PSA "creep" began. Fearing a PSA failure, I was obtaining frequent PSA tests and I watched the values rise through 0.1 and 0.2 ng/ml. When my PSA

exceeded 0.2 ng/ml on two occasions (0.27 and 0.34), I chose to initiate external beam radiation therapy to the prostate bed. This application of radiation is often called salvage radiation therapy and is the usual treatment when a PSA rise is noted after surgery, although some urologists might choose against local therapy for a PSA that rises within one year especially if there are no positive margins and the tumor is a Gleason > 7 cancer. Temporary androgen deprivation (i.e. hormone therapy) was a choice I also decided upon based on information from clinical trials that suggested a synergistic or at least additive benefit of androgen deprivation when radiation is the choice for treating the primary cancer. Extrapolation of this information to my situation, namely radiation after surgery, is not considered evidence-based medicine. It would require a trial to address this specific question. But the combination made sense to me.

The duration of androgen deprivation therapy in many of the randomized radiation therapy trials stretched over 2 years or 3 years. I wished to avoid side effects of 2-3 years androgen deprivation and so I arbitrarily decided to limit the duration of my hormone therapy to 6 months. There is some support for this decision from two uncontrolled salvage radiation therapy case series, which demonstrated a benefit for 6 months of hormone therapy.<sup>(19, 20)</sup> We also now know that 5-year biochemical control is best when radiation is initiated “early” (when the PSA level is <1.0 ng/ml or even 0.6 ng/ml).<sup>(21)</sup> The opportunity for a “2<sup>nd</sup> chance” at a cure or at least long term control was very attractive to me as it is to most patients who have a rising PSA after surgery – even if the “odds” of success are small. I had made a surgical effort at cure. My PSA was still low at < 0.6 ng/ml. I decided for another try.

In the months after completion of radiation and androgen deprivation, I anticipated each periodic PSA check with apprehension. I found myself delaying the blood draw until after important events like weddings, holidays, and family visits so as not to risk blunting the “joie de vivre” associated with these events. I modified the pace of my life, and began appreciating more the interesting future that prostate cancer patients are faced with – a cancer that is chronic, that mimics life with its slow and steady attrition but, thankfully, permits rather extended life with good quality. However the blessing and curse of PSA, especially the latter, cannot be underestimated. Even in the elderly male, for whom life expectancy is limited, the knowledge that a particular process is measurable and that increases, however small, indicate disease activity focuses attention almost exclusively on that disease to the extent that other more debilitating and life threatening issues are relegated to secondary importance or ignored completely. A ticking clock, regardless of how slow the tick, still is an audible and repetitive reminder of the limitations of life. Yes, we all are subject to the ticking clock, but there is something quite powerful in seeing its face as cancer and envisioning a disabling period before the end of life.

I experienced some side effects of hormone and radiation therapy. Hot flashes, some fatigue and general loss of vim, vigor, and vitality occurred. It was tolerable, but I was glad to stop hormones and await the return of normal testosterone levels. The side effects of radiation therapy were somewhat more than I anticipated because most of my patients who get this therapy seem to have virtually no or minimal side effects. I experienced significant proctitis (pain in the rectum) towards the end of my treatment course, which persisted for four to six months. Subsequent colonoscopy revealed no visible evidence of damage, and all symptoms have resolved.

Prostate cancer can sometimes be described as mirroring the slow but inevitable attrition of the human life cycle. PSA recurrence with its initial and then subsequent interval elevations might be considered examples of general health deterioration much like joint pain, cardiac events, visual difficulties or general fatigue. These problems are addressed by a number of minor or major medical or surgical interventions, which correct, usually temporarily, or at a minimum alleviate the problem. And so too with a rising PSA: measures are undertaken to lower and stabilize the level.

After a radical prostatectomy, a course of salvage radiotherapy, six months of androgen deprivation and then almost three years of undetectable PSA readings, my PSA has begun to rise. I, like many other patients in that circumstance, must deliberate as to the next best course of action. The menu of choices is diverse and data for evidence of benefit is lacking. It is surprising that for a circumstance, which is so common and so problematic, there is this relative dearth of firm evidence to guide decision-making. I will allow the PSA to rise unhampered for a while to establish a profile; that is, a determination of PSA velocity and doubling time. Then I will consider agents, which have been shown to affect PSA by either causing reduction or modulating the rate of rise. I will consider a course of “industrial strength” vitamin D following the limited data that show that PSA can be stabilized and perhaps lowered with such therapy.<sup>(22)</sup> I will investigate the very interesting immunotherapy options for men before hormone therapy; for example, a trial is planned to investigate the vaccinia fowl-pox TRICOM vaccine in patients with rising PSA after local therapy.<sup>(23)</sup> Parenthetically several other immunotherapy based trials are currently in process for patients with metastatic hormone independent prostate cancer. GVAX (Cell Genesys)<sup>(24)</sup> is being tested in Phase III trials as a single agent against Taxotere and also in combination with Taxotere vs. Taxotere alone. Provenge (Dendreon) has been successfully tested in a Phase III trial; that is, a survival benefit was demonstrated. A review by the FDA is planned.<sup>(25)</sup> However, when all options are considered, androgen deprivation in one of its many forms (i.e. monotherapy, combined androgen blockade, intermittent or continuous therapy, with or without 5-alpha reductase inhibitors such as Proscar or Avodart) continues to be the standard and probably the most effective strategy. While my access to these trials and my knowledge base about the therapies for a rising PSA is enhanced by the fact that they are subjects of my daily scientific study and clinical practice; nevertheless, I share the same degree of uncertainty in the decision making process. There is no clearly defined “next best step”. It is predicted that in the future we will replace the current trial and error paradigm for selecting therapies with sophisticated genes and protein analyses of tissue and serum to better “clarify” the tumor and the host. Then such “molecular profiling” will allow the selection of individualized specific therapies with more predictable outcomes. For the present, it is a matter of choosing a therapy, monitoring its success or failure, and continuing it while successful, and then changing to another because of a rise in PSA and/or new symptoms. And so, together with literally hundreds of thousands of fellow prostate cancer patients in the United States, I will try one and then another of these options while keeping my attention tuned for advances in basic and clinical science that may provide better solutions to the problem.

I will make a comment about Paul Lange’s statement that after a number of undetectable PSA levels he felt as if he had “won”. As someone who had failed primary treatment with a rising PSA and experienced that rise again after salvage therapy, I did not want to feel that I had lost. Our American heritage, unfortunately, has been marked by conflict and war, and this predisposition translates into a war mindset in business, in sports, and in disease. So we see the term “war on cancer” frequently. One of our presidents declared a war on cancer in 1971 with a

very unrealistic 1975 target for victory or cure. Using cure as the only measure of success sends the signal to patients that disease recurrence represents failure and that they may no longer be as valuable or important if cure is not achieved. War brings a battlefield with combatants to mind and logically implies a winner and loser. However, cancer and certainly prostate cancer is a process, often a long process, and as a patient I have become a participant in this process. The mindset of a warrior in constant battle is too energy depleting. Furthermore, to use a common sports saying, it is not whether you win or lose but how you play in the game. I am more comfortable and at peace thinking of myself as a participant rather than a warrior, and in viewing prostate cancer as a chronic disease to be kept at bay for as long as possible.

A brief comment regarding urinary function is applicable here. The return of continence was prolonged in part due to a psoas abscess and the vesicle irritation that it produced. Briefly I began experiencing some mild intermittent right leg pain and toe numbness about 12 days after surgery, which was not very bothersome until I experienced fever and chills 6 weeks after surgery. A CT diagnosed a psoas abscess, which was percutaneously drained, and all problems quickly resolved. However, I am reminded that all surgery is not complication and risk free.

Eventually satisfactory urinary control returned. I use only one small safety pad a day, and often it's still dry at the end of the day. I'm sometimes tempted to go without a pad, but the thought of a sudden cough or sneeze and the small leakage it might cause makes me reach for a pad each morning if just for reassurance. I agree that return to the state described as "trampoline dry" is probably quite rare post-prostatectomy. And relying on a patient interview to assess and report perfect continence is a trap for the unwary urologist. When my surgeon asks me if I'm continent, I respond with a strong "yes". Only if specifically asked, as in a Quality of Life questionnaire which many patients now complete, or I am coached to a detailed description, will I state the exact situation, and I do this to provide academic information and not to describe bother or displeasure. However I am not perfectly continent and I would have been disappointed if I had been promised so as a patient.

Sexual interactions are extraordinarily complex. Men treated for prostate cancer and their significant other must now deal with the additive burdens of the natural decline of sexual function associated with aging and the sexual side effects associated with prostate cancer treatment. Personally I can still achieve satisfactory erections with the aid of Viagra-like drugs.

As part of an ongoing Quality of Life study at our institution, it is evident that all therapies have an adverse effect on sexual function.<sup>(26)</sup> The degree to which recovery occurs after treatment is very dependant on the pretreatment baseline function. Pretreatment function is affected by the age, the general health, and the sexual interest of the patient and his partner. There are various solutions and approaches to this delicate interaction and they can be quite helpful. However, I believe that "success" in the sexual sphere, regardless of these solutions and approaches, is significantly handicapped by reduction in ,or failure of, erectile capacity. While a spontaneous and "adequate" erection is only a part of the sexual act, it plays a major role in sexual initiation. By that I mean that an otherwise neutral disposition can quickly change into a sexually charged attitude by the physical change that occurs in the penis. This may be initiated by a momentary thought, casual glance, or an encouraging word. When spontaneous and reliable erections do not easily occur, the sexual act requires more effort, and is therefore more likely derailed and abandoned if this effort is not expended. I believe post-treatment dissatisfaction and failure would be more successfully addressed if couples were counseled better about the "work" that

may be required. And as stated initially, all treatments for prostate cancer contribute to the risk of accelerating nature's steady decline. And so, while the mature and long lasting relationship will strive to find other outlets besides sexual intercourse to express love and affection, and many couples will testify to their success in this regard, it would be misleading to be insensitive to these issues in pre- and post-treatment counseling.

PHL Comments: I was of course flattered when PFS asked me to do his surgery. Being a professional, the surgery was not particularly stressful for my team or me, and it went very well in all respects. I was very aggressive on the side of his cancer with the lymphadenectomy; no wider surgical margin was technically possible. On the other side, I reflected on PFS's wishes but saved the nerves nonetheless. I was very happy with the procedure as we closed and his recuperation at my house. I was pleased that the margins were negative and that there was no cancer on the nerve sparing side.

However, after surgery I took every event in Paul's recovery and clinical course very personally. I have never had a patient with a psoas abscess after a radical prostatectomy, and cannot think of a surgical cause for this one. Yet this result and the rising PSA continue to elicit that irrational response: I could have done better. I would want it no other way, for him and in fact for all my patients.

Further Background and Reflections by PFS: Approximately two years prior to the diagnosis of prostate cancer, I experienced an event which, even more than prostate cancer, comprises a rite of passage for the aging male. Sudden crushing chest pain brought me to my knees and a 911 call. Fortunately this occurred at home rather than in a hotel room, car, or airplane. A prompt angioplasty and stent corrected obstruction of the left anterior descending coronary artery. There are several reasons for mentioning this event. Prior to transfer from the Emergency Room to the angio suite, the cardiologist outlined for me a four-arm clinical trial and inquired about my participation. The trial randomized to angioplasty +/- stent with anti-coagulation A or B. I am sure every individual addresses instant information and decisions differently. I am also certain that most individuals, myself included, would ask the consenting physician, in this circumstance, "do you think this is a good idea and should I participate?" In this urgent situation, an affirmative from the physician almost invariably results in consent to the proposed trial. And so I consented. I can only contrast this process with the laborious explanations, interactions, and reviews with patients and significant others that were required to inform and encourage patients to consider the so-called SPIRIT trial. This trial was initiated by the American College of Surgeons Oncology Group in the USA and Canada and was a randomized trial between brachytherapy and radical prostatectomy for low risk disease. Both PHL and I spent many months trying to get this trial underway in the USA, but were ultimately unsuccessful. The deck is certainly stacked, at least in this situation, in favor of a cardiology intervention trial vs. a prostate cancer intervention trial. This was so, despite the fact that both arms of the prostate trial had a proven track record of success, whereas the cardiology trial was constructed to measure the unknown of adding a new stent procedure to angioplasty. The trial playing field is overwhelmingly tipped in favor of a cardiology intervention due to the urgent status of a cardiac event.

Another reason for mentioning this cardiac event is to compare the visceral responses and emotions associated with the diagnosis of cardiac disease and prostate cancer. After my coronary occlusion, my mindset was one of establishing a program of understanding and

cooperation with my heart. Through diet modifications, exercise, and other strategies, I committed to a partnership for mutual recovery. Implementing this life style change was both satisfying and comforting. My reactions generated by a prostate cancer diagnosis were totally different. A sense of betrayal and hostility toward the betraying organ was overpowering and was followed by a committed investment to destroy it by whatever means. Initially, my mindset was much more in the combat and war mode toward my cancer than my heart. Parenthetically my cardiac rehabilitation experienced in the company of fellow patients was beneficial, and I believe that group interaction is good for both body and soul. My cardiac experiences probably were a factor in my decision to be very public about my prostate cancer from the beginning. Now I urge my patients even more to be open about their cancer and to participate in post-prostate cancer treatment support groups.

The fields of psycho-neuroimmunology and other mind-body interaction disciplines are now receiving much more attention and study. The work of these disciplines has strengthened support for a robust relationship between mental attitude and physical recovery. For example prayer and meditation tend to relax the mind and body, offset stress, and exert many positive influences.<sup>(27,28)</sup> As we learn more about these approaches, it becomes more evident that responses to therapy are dependent not only on the application of traditional allopathic medicine modalities, but also on the patient's state of mind. The astute diagnostician William Osler recognized this interaction years ago when he stated: "It is more important to know about the patient who has the disease than about the disease the patient has". I therefore concur with PHL's comments about paying attention to the placebo effect – which may really be better translated into an "attitude" effect.

Finally prostate cancer patients should not forget that their risk as aging males for cardiac death is often greater than their risk of a prostate cancer death. This is an appropriate opportunity to mention supplements and diet. A purported prostate healthy diet and lifestyle is also a well accepted heart healthy diet and lifestyle. So a double benefit is obtained from a reduced caloric low-fat diet, which avoids meat and encourages fish, and from a responsible exercise schedule. A useful website that provides information on supplements and herbal products is [www.MSKCC.org](http://www.MSKCC.org).

### **Final Reflections and Conclusions by PHL and PFS**

Although much has already been written about personal reactions to the events surrounding radical prostatectomy, we hope our accounts have been interesting and informative, perhaps because two men who have had long careers treating prostate cancer experienced them. In reflecting on our individual and somewhat different situations and reactions, we find several common themes that deserve reemphasis.

Fear: We were both surprised at the degree of fear we felt despite our familiarity with the disease and its management. The objects of these fears are of course survival, suffering, loss of control, and the concerns about incontinence and impotence. After the initial diagnosis the question arises: "Will I (we) ever be able to be happy and laugh again." "Can life as we know it ever be the same?" "Will people now treat us differently?" We experienced fear and these questions in different proportions, but we were both humbled by their disruptive power.

Significant Others: An extremely important issue that was not discussed as part of our decision making process requires an explanation. Where are our wives in this story and what role did they play? Unlike most men diagnosed with prostate cancer, both our lives have been immersed in the disease process for decades, and the shared information gathering process, discussion of options, and mutual decision-making, was short-circuited because of this. The conversation between wife and husband that might have begun “listen to what I learned about prostate cancer” did not occur. On the one hand, the shared decision-making that may bring a man and wife together in a unity of approach and effort was lost, but on the other hand, much of the anxiety that comes from wondering if a patient is getting all of the information and the appropriate information from a knowledgeable and unbiased source was eliminated. Obviously our situations were not applicable to the general community of prostate cancer patients. In this circumstance a partnership of exploration and understanding between the patient and significant other is very important.<sup>(29)</sup>

Yet we can make certain observations about the “significant others” of prostate cancer patients during the decision process, especially if they are female. It seems very common that the wife takes charge in accumulating information, looking at the dilemma dispassionately, and often doing a great deal of the talking at the first encounter with the physician. If possible initial discussions with the patient should include the significant other. However it becomes very tempting in this first encounter for the physician to begin talking directly to the wife. This is a mistake; every effort to increase the engagement of the patient with his disease should be made. It is also common, when discussing sexual issues, for the wife to indicate that she is more interested in the husband “being around” than in sexual performance. While this may seem (and is) reassuring, it can also convey a disappointing message to the patient. Finally there seems a natural inclination, when discussing therapeutic options, for the wife to indicate her preference for the surgery. It seems important to remember that usually this preference is due to a conscious or unconscious impression that knowing the true local pathology will give better knowledge about what the future will hold. This assumption on the part of the wife should be taken into account when counseling the patient about therapeutic choices.

Uncertainty: Of course one cause of fear is the uncertainty surrounding the relative effectiveness of the various local treatments. Clinical trials provide the best avenue to accurate decision-making. PFS has already commented on why such trials are particularly difficult. However we both feel strongly that urologists and their patients should do a better job of participating in clinical trials; otherwise today's questions remain unsolved and only come to live another life as tomorrow's questions.

Quality of Life (QOL): Urinary, sexual and bowel function can be impacted substantially by local therapies. Much has already been written about this subject. How an individual patient will react to this alteration probably depends on a number of factors including the degree of alteration, realistic pre-operative counseling, and his attitude toward the changes. We believe that there is a general underestimation and reporting of the impact of side effects.

We have several particular observations about incontinence. First wearing pads, especially if it is temporary, are not as bad as we anticipated once we got used to it. It could be that familiarizing men to wearing them before the surgery may have merit despite its negative connotations. Also continence after a radical prostatectomy is relative and rarely absolutely achieved. Thus the current QOL surveys may need modification especially regarding mild

incontinence. We believe the use of so-called safety pads such as “panty liners” should be included in the assessments. This is because most pads can absorb as much as 60cc with the wearer never really feeling wet while liners can tolerate little more than a few drops. In our view acceptable continence after a radical prostatectomy is no pads or just one liner a day. The difference in those groups regarding continence is small (or even non-existent), while “one pad” can cover many different degrees of incontinence some of which are “limiting”. Also it appears that the precipitating events surrounding what causes mild incontinent episodes vary greatly between men and may not be related to the usual events associated with stress incontinence such as lifting, straining, etc. Some men leak upon wiping after defecation, others do not; some with significant alcohol intake, but not everyone; some with sexual foreplay or just mental anticipation; many but not all when passing flatus. We need to better understand these differences and the neurological aspects of continence they represent if we are to continue to strive to understand and improve continence after radical prostatectomy.

Sexual dysfunction can become an insider force that slowly weakens a relationship. When prostate cancer is diagnosed, the female places significant emphasis on treatment to enhance survival and to prevent death. Under these circumstances sexuality is placed very much to the side against the background of concerns about their spouse's health, comfort and life expectancy. They often will clearly voice that mindset during treatment related discussions. A common refrain is "we have been together and enjoyed many years of sexual activity, but now this must be put aside to face the life and death issue before us." The man hears this statement, appreciates the background from which it arises, and intellectually accepts its meaning, but he may subconsciously reflect upon it later with a different attitude and from a different perspective.

After the disruption of surgery and recovery has passed and life resumes, either in occupation or retirement, a “cycle” may develop which is precipitated by diminished sexual ability and activity. The female significant other, recalling her words describing the very secondary importance of sexual function, might not wish to initiate or encourage sexual activity for fear of her partner's failure and the depression it might cause him. The patient, her partner, remembering the comments made concerning the secondary importance of sexual activity, may further interpret the lack of initiating as a reflection of her diminished interest. Certainly if this cycle continues, sexual intimacy will suffer. Open discussion is critical and may, for some, provide satisfactory outcome. However, in many situations some degree of professional help and guidance is beneficial.

The uncommunicated disparity between the male and female perceptions of sexual activity was recently studied and the findings are best summarized by a direct quote from the article: "Partners reported that patients had lower levels of sexual performance and poorer quality erections than study patients themselves reported."<sup>(28)</sup> The sexual horizon was quite different depending on whether the male or female was questioned, and the likelihood was that the female perceived a less active and satisfactory situation. For the last decade the discipline of QOL assessment has made significant contributions toward the understanding of treatment option selections among men with localized prostate cancer. Because several treatment options provide very similar cancer related outcomes, decision for one or another treatment has become more centered toward QOL preservation after therapy. The issues of sexual and urinary function or dysfunction must be realistically addressed and their impact measured. Validated questionnaires have replaced physician impression as a more accurate reflection of the post-treatment status. And where couple interaction is as critical as in the arena of sexual function,

patient and partner status provides important information. Satisfaction with quality of life is a complex issue. Physicians need to be wary that they do not become overconfident in their ability to return the patient to his preoperative state. Such embellished reassurances can lead to unrealistic expectations in some patients with devastating effects postoperatively.

Alternative/complementary/integrative medicine and patient control: We both experienced the power of the complementary/integrative medicine movement. We must work harder to legitimately interface with that world and develop better ways to empower patients to participate substantially in their disease management. If nothing else, the placebo effect must not be labeled as a nefarious phenomenon but exploited honestly to the patients benefit.

PSA anxiety: Of course this varies among patients and the severity of disease, but it exists in almost all. This burden is mostly unavoidable and an acceptable price for the value of PSA monitoring, but perhaps it can be lessened by giving the patient more control over when he has the test and more importantly how he gets the result. Waiting for a doctor or nurse to call or return a call produces stress. Perhaps some web-based system allowing more patient control could be developed. Undoubtedly there are other areas besides PSA anxiety and alternative/complementary medicine whereby the patient can have more control over their experiences surrounding surgery or other local therapies.

PSA recurrence: The options for treating PSA failure carry as much or even more uncertainty than that involved with the discussion of primary therapy. The patient recognizes that, with failure of primary therapy, there is diminishing likelihood of cure, and his apprehension is heightened. Practitioners should make every effort to couch their explanations and directions with a sense of assurance and hope. To do otherwise would risk the patient's emotional state and compound the negative impact of recurrent disease. When cure may no longer be the operative word, long periods of disease control with satisfying quality of life are possible.

A final comment: As previously implied, in retrospect both of us are thankful that we had this experience because it has made us more empathetic in many ways, some of which are hard to convey. We are certainly more effective (and we think more even-handed) at initial orientation during discussions regarding prostate cancer diagnosis and treatment. We are better listeners. Also we both have developed more effective ways of relating to patients during their management of the disease. We appreciate more the need to provide hope, to develop trust, and to encourage a sense of control. Finally we have become more passionate about facilitating progress in prostate cancer diagnosis and cure. And when therapy fails to cure, we are better at directing our efforts toward helping the patient live well for as long as possible with his cancer.

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