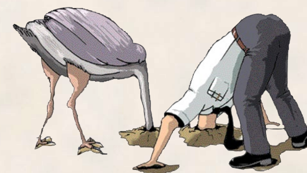
"It is senseless to die of embarrassment! 15 seconds of discomfort can save your life"

— Charlie Wilson



Charlie Wilson has grammy nominations for Best R&B Album ***"Uncle Charlie"*** and Best Male R&B Vocal Performance for ***"There Goes My Baby"***

The quote is from Charlie Wilson, the Grammy nominated R&B singer. Like many men, Charlie avoided getting screened for prostate cancer, partly because he was embarrassed to get a Digital Rectal Exam. During the Digital Rectal Exam, the doctor inserts a gloved finger into the rectum to feel the prostate gland for any signs of irregularity that might be prostate cancer.

"Fifteen seconds of discomfort can save your life" says Charlie, referring to the DRE. "It is nothing. I urge all men, especially black men who are at higher risk of prostate cancer to get regular screening. You do not want to wait and be diagnosed with advanced cancer all through your body before it is detected. Get a regular PSA test and Digital Rectal Exam. That way you can catch prostate cancer while it is still easily treated." Charlie credits his wife for pushing him until he finally got screened, which led to a biopsy and diagnosis of prostate cancer.

Charlie's cancer was caught early and he decided to be treated with radioactive seed implant, a one-day procedure called brachytherapy. Read about seeds on the PCRI web site www.pcri.org. Aside from the short term discomfort from the procedure, Charlie reports he is feeling very well, with no significant side-effects from the treatment. His PSA numbers are great, meaning there is no sign of the cancer.

PART 1: ELEVEN CONSIDERATIONS BEFORE PROSTATE BIOPSY
By: Nathan Roundy

PART 2: THE BIOPSY – WHAT TO EXPTECT
By Stanley Brosman, MD

PART 3: YOUR PATHOLOGIST, THE IMPORTANT DOCTOR YOU NEVER GET TO MEET
By Daniel J. Luthringer, MD

Part 1: Do You Need A Prostate Biopsy?

If screening indicates elevated risk of prostate cancer, there are at least eleven tests and judgments that guide the decision to do a biopsy. The decision whether or not to get a biopsy is both an art and a science. However, none of these tests, whether considered alone or combined, can guarantee a man has or does not have prostate cancer. Each test contributes to an evaluation of risk of a prostate biopsy being positive for prostate cancer.

For further discussion about when to get a biopsy, please see this paper by Dr. Strum What We Should Have Learned About Prostate Cancer (PC) in the Past 10 Years: Part Three http://www.prostate-cancer.org/pcricms/node/132 and the PCRI Views On PSA Testing http://www.prostate-cancer.org/pcricms/node/118

The American Urological Association has a well referenced free download about PSA Best Practice here http://tinyurl.com/AUA-PSA-BEST-PRACTICE *(Continued on page 4)*

1. **ABNORMAL DRE** – If the doctor can feel something unusual on the prostate during a Digital Rectal Exam (DRE), a biopsy is often recommended. Some high-risk variants of prostate cancer produce little PSA . Those dangerous cancers can be caught early if the DRE is abnormal and a biopsy is performed, even though PSA is low.

2. **PSA TOO HIGH** – Some men without cancer produce relatively high blood levels of PSA while other men who actually have prostate cancer, can have relatively low levels of PSA. However, on average, the higher the PSA, the more likely there is cancer present.

   Men with close relatives with prostate cancer, African American men, or younger men with slightly elevated PSA might use a lower PSA cutoff for a deciding to biopsy. Consideration of the factors below may raise or lower the threshold for an individual man. See Table 2 from Dr. Catalona[2].

3. **PSA DENSITY TOO HIGH** – Many doctors use a simple rule-of-thumb that a PSA over 4.0 signals the need for a biopsy. Unfortunately that simple rule can result in over-biopsy in men with large prostates, and risks missing aggressive cancer in men with small prostates. Large prostates, even when cancer is not present, produce more PSA than small prostates. PSA Density takes into account the size of the prostate. Divide the PSA by the size of the prostate in cubic centimeters (cc). The resulting PSA Density should be about 0.10. PSA Density of 0.15 implies a high PSA relative to the size of the prostate and might trigger a biopsy.

   Another simple way to take into account prostate size is to divide the prostate size in cc by ten. For example a 50 cc prostate might be expected to produce a PSA of 50/10 = 5.0. In that case PSA Density would be 5/50 = 0.10, considered normal. Even though the PSA of 5 is considered elevated (above 4.0), it may be explained by the large prostate. Perhaps biopsy could be deferred or avoided. On the other hand, A man with a small 25 cc prostate and a PSA of 3.75 would have cause for concern. His PSA should be about 25/10= 2.5. His PSA Density is 3.75/25 = 0.15, also too high.

   While the doctor can estimate the size of a prostate with the Digital Rectal Exam, a more accurate measurement is with a special ultrasound machine at the office of a urologist. The Trans Rectal Ultra Sound (TRUS) examination report will state the size of the prostate in Cubic Centimeters (cc) or Grams. The two terms are roughly equivalent.

4. **PROSTATITIS** – Prostate infection or inflammation can raise PSA, sometimes suddenly and dramatically. The doctor may test for bacteria in the urine, or may try a course of antibiotic and then retest PSA. Prostatitis is not always detected by a urine culture. It is important to note that prostatitis has been shown to cause a low free % PSA, but not BPH.(5) See our Insights article from March 2010, Prostate Disorders Other ThanCancer – Part 2 BPH PDF •Stanley Brosman, MD 2010

5. **PERCENTAGE OF FREE PSA TOO LOW** – In addition to the standard PSA test, your doctor can order a % Free PSA test. Research has shown that men with low % free PSA have a higher risk of having cancer. In Table 6, we see a man with PSA between 4-10 has an overall risk of 25%. But if we break it down by %Free PSA, we see that if his free PSA is >25%, his risk is only 8%. See Catalona (2)

TABLE 2. Current **Clinical Practice and Proportion of Men With Cancer Based on PSA and DRE Results***

	PSA, ng/mL							
	0-2		2-4		4-10		>10	
DRE Results	Biopsy	% With Cancer	Biopsy	% With Cancer	Biopsy	% With Cancer	Biopsy	% With Cancer
Normal	No	= 1	No	15	Yes	25+	Yes	>50
Indicative of cancer	Yes	5	Yes	20	Yes	45	Yes	>75

Table 6. — Probability of Cancer Based on PSA and Percentage of Free PSA Results*

PSA, ng/mL	Probability of Cancer, %	Free PSA, %	Probability of Cancer, %
0-2	= 1	. . . +	. . .
2-4	15	. . .	. . .
4-10	25	0-10	56
		10-15	28
		15-20	20
		20-25	16
		> 25	8
> 10	> 50	. . .	. . .

* Data are for men with normal digital rectal examination results, regardless of patient age. Data for prostate-specific antigen (PSA) results are from Catalona et al[1] and Keetch et al.[21] Percentage of free PSA can further stratify risk for men with PSA values between 4 and 10 ng/mL.

6. **PSA VELOCITY TOO FAST** – Men without prostate cancer can have widely different levels of PSA, but whatever the level, it should not go up very fast. PSA Velocity is computed in nanograms per milliliter per year. A rise in PSA of more than 2 ng/ml within one year (confirmed by repeat testing) suggests the possibility of high-grade prostate cancer(4). On the other hand, a PSA rise of less than 0.2 ng/ml/year may simply be the slow expansion of the prostate from progressive benign prostatic hypertrophy. It is also important to note that prostatitis can cause a PSA velocity similar to prostate cancer. (6)

7. **PSA DOUBLING TIME TOO FAST** – Each time the cancer cells multiply by two, the PSA produced by the cancer will approximately double. As the cancer grows, the PSA goes up at a non-linear rate. Fast growing cancers, indicated by the PSA doubling time, are more dangerous. One of the best ways to calculate PSA Velocity and PSA Doubling time is to use the PSA Calculator at the Memorial Sloan Kettering Cancer Center web site. http://www.mskcc.org/applications/nomograms/prostate/PsaDoublingTime.aspx

8. A PSA doubling time of less than three years may be cause for concern.

9. **PCA3 TEST TOO HIGH** – The PCA3 test is more specific for estimating prostate cancer risk than is PSA alone. The doctor will do an "attentive prostate exam", meaning to massage the prostate and cause it to slough material into the urethra. Then urine is collected and sent to the lab for DNA analysis. For a complete discussion visit http://www.prostate-cancer.org/pcricms/node/12. Studies show that men with PCA3 below 35 are less likely to have a positive biopsy. PCA3 in excess of 100 raises concern of a high-risk cancer. See Figure 1.

10. **FAMILY HISTORY OF PROSTATE CANCER** – A grandfather, father or brother with prostate cancer increases risk of developing prostate cancer. That may lower the threshold where a man decides to get a biopsy.

11. **ADDITIONAL IMAGING** – For most men, the above steps will lead to when a biopsy is

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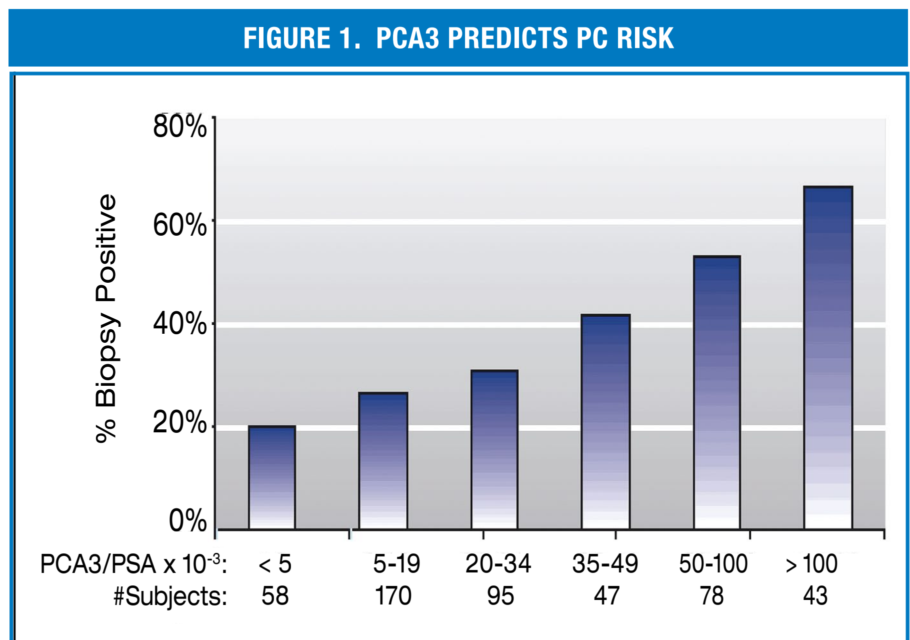
FIGURE 1. PCA3 PREDICTS PC RISK



suggested. For those still concerned, a Color Doppler Ultrasound scan and / or MRI Scan with contrast and diffusion may provide additional evidence of possible cancer that should be biopsied. This may be especially useful for men who had previous negative biopsy. See the PCRI Papers at www.pcri.org.

- Targeted Biopsies and Active Surveillance PDF • David. Agus, MD 2010
- MRI for Prostate Cancer PDF • Daniel J A Margolis, MD 2010
- Color Doppler and Tissue Harmonic Ultrasound • Duke Bahn, MD 200
- Magnetic Resonance Anatomic and SpectroscopicImaging of Prostate Cancer – CurrentStatus • John Kurhanewicz, Christopher K. Sotto and Fergus Coakley 2006

12. DO NOTHING FOR NOW – If, due to poor health or other circumstance, a man would choose not to treat prostate cancer even if it were detected, he may prefer to stop screening for prostate cancer and to not get a biopsy because he would not treat the disease if it were found.

If, after reviewing the eleven considerations above, the doctor suggests a biopsy, how is that performed? Urologist Dr. Stanley Brosman describes the process.

Part 2: PROSTATE BIOPSY – IT DOESN'T HAVE TO BE A MEMORABLE EXPERIENCE By: Stanley Brosman M.D.

Once the decision has been made that a prostate biopsy is necessary, it's helpful to know what to expect. Each urologist has her/his own protocol for doing biopsies so these are some of the basics followed by the majority of urologists. The biopsies are usually done in the urologist's office although a light general anesthetic can be used if you're willing to pay the anesthesia charges and facility fee for the procedure which is done in an outpatient surgical unit. This type of anesthesia is much like you have when a colonoscopy is done. The charges can range from $1000-$1500. Insurers don't cover these services anymore and you may have to pay in advance.

All blood thinning medications should be stopped 5-7 days prior to the biopsy and not resumed for several days afterwards. Antibiotics are started on the previous day or sometimes on the same day and are continued for 1-2 days afterwards to help prevent an infection that might occur as a result of the procedure. About 3% of men will develop an infection which is one of the potential complications of a prostate biopsy. A laxative or an enema is usually recommended on the day preceding the biopsy. Some of our very nervous patients are given a Valium or similar relaxant just before coming to the office.

After taking off your pants and underwear (no holes please) you will be asked to lie down on an examining table on your left side with your knees bent up toward your chest. Your urologist will do another DRE and apply an anesthetic gel around the anus and into the rectum. An ultrasound probe is placed into the rectum. This is an ouch. The prostate is visualized and measured. This is a good time to ask the size of the prostate. The type of ultrasound machine varies from office to office since there are many manufacturers who claim that theirs is the best. It turns out they're all about the same and naturally price wins out.

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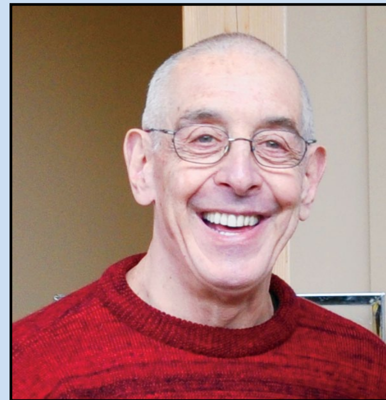

Stanley Brosman MD is a Clinical Professor of Urology at UCLA and practices in Santa Monica, California. He specializes in urologic oncology. He has authored numerous papers and textbook chapters and has delivered lectures throughout the world. He is actively involved in clinical and laboratory research involving cancers of the urinary tract. He is on the Board of Directors of the PCRI.

The main purpose of the ultrasound is to identify the prostate so that the biopsies can be obtained in the appropriate areas. A color Doppler can be helpful in directing a biopsy to a specific area and may be very helpful in situations where prior biopsies have been negative but there is still a suspicion that a cancer may be present. Are the biopsy results dependent upon the type of ultrasound machine? No. Like most things they are dependent upon the skill and experience of the person doing the biopsy.

The next step is to inject a local anesthetic around the prostate. It's the same type of anesthetic that dentists use prior to their procedures. The idea is to "numb" the prostate as much as possible. This requires injecting the anesthetic through the rectum and this is another ouch.

The last step is obtaining the biopsies. The number of biopsies usually depends on the size of the prostate. The prostate is arbitrarily divided into 12 segments and each core of tissue is placed in a separate container. You can expect to have at least 12 biopsies if your prostate is less than 50cc in volume. Additional cores are obtained from larger prostates and from areas in the prostate that felt suspicious on DRE. This means that the biopsy needle will be placed 12 or more times through the rectum and into the prostate to extract a piece of tissue that is about a half inch in length and tenth of an inch in width. The biopsy feels like getting a jolt in the rectum but the prostate is numbed so you don't feel much pain. The biopsy procedure takes only a couple of minutes but the preceding events take about 15 minutes. Afterwards everyone is glad that it's over but people commonly say that "it wasn't as bad as I expected". Thank you for local anesthesia.

During the next 4-5 days there is likely to be blood in the urine and with bowel movements. The seminal fluid turns a brownish color and this can last four to six weeks. Sexual activity can resume after 3-4 days. There are no dietary restrictions and regular activities can resume the next day. Vigorous exercise should be delayed for about a week.

The results of the biopsy are usually available in the next 2-4 days depending upon which pathology lab is doing the examination. Complications of the procedure include infections and bleeding. Continued active bleeding should be reported to the doctor immediately. There may be difficulty urinating particularly if there was difficulty prior to the biopsy. Medications can be started to prevent or manage this problem.

The time waiting for the results of the biopsy is generally filled with anxiety, even more than that experienced before the biopsy. Getting the results to the patient as soon as they are available is the biggest help but everyone tends to expect the worse. To minimize this situation, the biopsy procedure and its possible outcomes should be discussed in advance. Knowing that 60%-65% of the biopsies will reveal no cancer and of those that do show cancer, a third are likely to be of the variety that require no therapy can decrease the anxiety level.

Another issue for patients is how they would like to be notified of the results. Is an office visit necessary? Is a phone call too impersonal? This is something that should be discussed with your physician. Certainly if there is a diagnosis of cancer, the doctor will want a meeting in the office with the patient, spouse and any other family members and friends. Patients don't usually remember the meeting very well. The others in attendance are there for that purpose.

PART 3: YOUR PATHOLOGIST, THE IMPORTANT DOCTOR YOU NEVER GET TO MEET

By: Daniel J. Luthringer, MD

Immediately after the biopsy procedure, the tiny cylindrically-shaped prostate tissue fragments, called "cores", are placed in small containers of formalin, which serves as a "fixative", to stabilize the tissue during transportation and handling. These containers are labeled with the patient's name and other identifying information so they can be tracked properly for final reporting. The specimens are then transported to the laboratory, usually by a courier, or sometimes via an overnight mailing service such as Fed Ex. Urologists generally try to utilize laboratories which have some degree of specialization and expertise in urologic pathology, as the handling of these small core biopsies is a bit different than other types of tissue samples and sometimes there is a need for special testing which may not be available in some laboratories. In some situations, the biopsies must be sent to a particular lab as dictated by the health insurance provider.

(Continued on page 8)

Once the specimen has arrived at the laboratory (generally the same day that the biopsy was performed), it is logged into a computer system with the patient's demographic information and given a case number for identification, tracking and reporting purposes. The tissue is then removed from the container and the numbers and sizes of cores are recorded. The tissue cores are inserted into special plastic holders by a laboratory technologist and then placed in computerized machines called tissue processors. These processing machines will then run overnight, basically impregnating the tissue with different solvents which ultimately allow the cores to be removed and embedded in paraffin wax the next morning. These so-called "tissue blocks" are then cut on a microtome by a specially trained technologist, who generates extremely thin slices from each tissue core in the wax, and places them onto glass slides. The slides are then stained with dyes (hematoxylin and eosin) and subsequently covered with a second extremely thin glass or plastic cover. The final product commonly referred to as the "glass slides" are what the pathologist examines under the microscope to look for prostate cancer.

The pathologist is a physician like your urologist, internist or anesthesiologist, who is specially trained in the field of laboratory medicine and pathology (the study of diseases). Some pathologists have additional expertise in urologic pathology either by training, experience or academic interest. Although most pathologists can appropriately examine prostate biopsy samples, there are some situations where an expert (uropathologist) with greater experience might be needed. This is another reason why many urologists choose to use a laboratory which specialize in uropathology, as the pathologist reviewing your slides can be more experienced with such cases.

In the event that the patient or urologists wants a second review or opinion on a biopsy case, the glass slides (or even the tissue blocks) can be shipped via mail to another laboratory or pathologist. It is not uncommon for patients to go directly to the laboratory to retrieve their slides and take them as they go to institutions or physicians in search of education on treatment options. We at Cedars-Sinai Medical center are commonly asked to perform secondary reviews on both routine and diagnostically challenging cases such as those with extremely limited amounts of abnormal cancer cells or those in need of specialized testing to confirm the diagnosis.

Once the glass slides are made, the pathologist examines them under the microscope to look for evidence of cancer or other disease conditions such as inflammation, atrophy or processes which might mimic cancer such as high grade prostatic intraepithelial neoplasia (PIN). Cancer is characterized by the presence of abnormal cells growing in the prostatic core biopsies, and in most instances, the cancerous cells are readily identifiable. However, in some cases, there are either too few abnormal cells or the features of malignancy are not sufficiently well developed to make a definitive diagnosis of cancer. In these situations, it is some-

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PREVENT OVER TREATMENT

The Prostate Cancer Research Institute believes men should be screened annually to know if they have prostate cancer. Read our paper The PCRI Views Regarding Testing for Prostate Cancer Using PSA as a Principal Marker http://www.prostate-cancer.org/pcricms/node/118

But, not every newly diagnosed man needs treatment, at least not right away. For men with low risk prostate cancer, studies have shown men can safely delay treatment, sometimes for life, by a system of careful monitoring called Active Surveillance. That avoids treatment side effects such as impotence and incontinence and bowel damage. See the many PCRI Papers at http://www.prostate-cancer.org/pcricms/node/16

- Active Surveillance For Favorable Risk Prostate Cancer:What Are The Results, and How Safe Is It? - Laurence Klotz, MD et al. 2006
- Active Surveillance with High Resolution Color-Doppler Transrectal Ultrasound Monitoring Duke Bahn, MD, Mark Scholz, MD, and Richard Lam, MD 2007

times useful to employ special testing, where unique antibodies are applied to the tissue sections to highlight features specific to cancer and hopefully make an accurate diagnosis. Once the pathologist has carefully reviewed all of the slides, a report will be generated which should include the critical details of the cancer, including a quantitative assessment of involvement (length of cancer, % of core involved), indication of specific sites where the cancer is found, and important prognostic information such as Gleason grade and the presence of cancer spread around nerves (perineural invasion), into lymphatics or outside the capsule of the gland. It is fairly common that prostate cancer biopsy reports include a map of where cancer is found. In most straightforward cases (i.e. negative or with obvious abnormal cancer cells), the final report can be generated and completed the day after the biopsy, and a copy of the report can be either e-mailed, FAXed or delivered to the urologist. Special testing will add a day or two to complete the case.

A copy of the report is maintained by most laboratories for an indefinite period of time (most are kept as electronic records). The glass slides and tissue blocks are maintained by the lab for at least many years, and in some instances forever as part of the permanent medical record. In some circumstances, it is necessary to retrieve these slides for review (such as in the event of late metastatic disease or development of a new type of cancer). Additional slides can generally be made from the tissue blocks as well if sufficient tissue is present. The tissue blocks can also be useful for any additional testing that might be warranted (such as the Prostate Px+ from http://www.aureon.com.

OK, YOU HAVE PROSTATE CANCER! NOW WHAT?

First, do not panic! There are lots of options and the great majority of men diagnosed with prostate cancer do very well. Research has shown that taking time to research your options and possibly getting additional imaging and testing, does not reduce the chances of a good outcome. You have time to get second opinions from expert prostate cancer doctors in surgery, radiation therapy, cryotherapy, or other treatments. Your clinical diagnosis has the clues to how dangerous and aggressive is your particular type of prostate cancer. For more information about learning your risk factors and treatment options, go to the Newly Diagnosed section of the PCRI web site www.pcri.org. http://www.prostate-cancer.org/pcricms/node/126

If you need assistance understanding this article, contact the free PCRI Helpline 1 800 641 7274 or email help@pcri.org.

Material provided by PCRI is intended for educational purposes for discussion with your physician and should not be considered as medical advice.

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