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PROSTATE CANCER OVERVIEW

Cancer of the prostate is the most common type of cancer among American men and the second leading cause of cancer deaths among them. It's estimated that one out of every 10 American men will develop prostate cancer before age 85. An estimated 165,000 new cases will be diagnosed and approximately 35,000 men died from the disease during 1993.

The risk of developing prostate cancer greatly increases with age. It rarely occurs in men younger than 50. The average age is 72. Black American men are at a greater risk than white American men, but the reason for this is not known. The cause of prostate cancer is also unknown.

THE FUNCTION OF THE PROSTATE

The prostate is a male gland normally about the size of a chestnut. It secretes a milky fluid that is part of the semen needed for ejaculation.

The prostate gland lies at the base of the penis, just below the urinary bladder and the front of the rectum. It surrounds the first inch of the urethra, the tube that carries urine from the bladder. Its location allows a physician to feel through the rectum that part of the gland where most tumors occur.

WHAT IS CANCER?

Cancer is really a number of diseases caused by abnormal growth of cells. Normally, the cells that make up the body divide and reproduce in an orderly manner, so that we can grow, replace worn-out tissue, and repair any injuries. Sometimes, however, cells get out of control. They divide too much and form masses known as tumors. Some tumors may interfere with body functions and require surgical removal, but they do not spread to other parts of the body. These are known as benign tumors. Malignant--or cancerous--tumors not only invade or destroy normal tissue, but, by a process known as metastasis, cells break away from the original tumor and migrate to other parts of the body.

The rates of growth and spread of prostate cancer vary. Some tumors grow rapidly while most grow slowly with a doubling time of approximately 18 to 24 months.

RISK FACTORS

The cause of prostate cancer remains unknown. Several factors associated with a higher rate of prostate cancer, however, have been identified. The risk of developing prostate cancer increases as a man ages. Almost all patients with prostate cancer are more than 50 years old and 80% are over age 65. For reasons not known currently, black Americans have the highest incidence rate in the world. A family history of prostate cancer in a brother or father also doubles one's chances of getting prostate cancer.

There is some evidence that diet, environment, and/or nutrition may play a role in developing clinically significant prostate cancer. Recent animal studies suggest that a diet high in protein and low in fat may decrease the growth rate of prostate cancer.

SIGNS AND SYMPTOMS

In the early stages of prostate cancer, there usually are no symptoms. When symptoms do develop, they vary according to the size and location of the tumor, and are often the same as those for benign prostate conditions. In fact, it is more likely that any of these symptoms would indicate prostate enlargement, known as benign prostatic hypertrophy, infection, or other conditions rather than cancer. Still, any symptom should be checked by a physician. Only a physician conducting the proper tests can determine for sure whether the condition is cancerous or benign. Symptoms of prostate problems include:

- Weak or interrupted urine flow
- Inability to urinate
- Difficulty in starting or stopping urination
- Need to urinate frequently, especially at night
- Painful or burning urination
- Continuing pain in lower back, pelvis, or upper thighs

EARLY DETECTION

Every man over the age of 40 should have a digital rectal examination as part of his regular annual physical checkup. The physician inserts a gloved, lubricated finger into the rectum to palpate (feel) any irregular or abnormally firm area that may indicate a tumor is present. Almost all prostate cancers begin in that part of the prostate gland that can be palpated by rectal examination. This exam also helps detect early rectal cancers.

In addition, the American Cancer Society recommends that men 50 and over have an annual prostate-specific antigen (PSA) blood test. If there is a family history (father or brother), screening should begin at age 40. If either the digital rectal examination or the prostate-specific blood test is abnormal, further evaluation should be considered.

DIAGNOSIS OF PROSTATE CANCER

Removal of a small tissue sample and its examination under a microscope, a procedure known as a biopsy, is the ONLY way to determine conclusively if a growth is cancerous. For prostate cancer, tissue samples are usually obtained by inserting an ultrasound probe into the rectum to visualize the prostate on a TV monitor. A thin needle is placed through the probe into the prostate. This procedure is known as needle biopsy. No anesthesia is needed for a needle biopsy of the prostate. It is an outpatient procedure, usually done in the doctor's office.

THE STAGES OF DISEASE

If prostate cancer is found, your doctors will need more information about the extent of the cancer. That is, has the cancer spread farther than the prostate? The treatment of prostate cancer and the expected outcome depend greatly on the stage, or extent, of the disease. Although there are several staging systems, newly diagnosed cases can generally be considered in one of the following stages.

STAGING AND GRADING OF PROSTATE CANCER

INTRODUCTION:

When a patient is found to have prostate cancer, his physician must learn two pieces of information about that cancer before a decision about treatment can be made -- the STAGE and GRADE of the tumor.

STAGING PROSTATE CANCER:

The STAGE is defined as the extent of the tumor at the current time. More specifically, how extensive is the cancer within the prostate and if it has spread to tissues around the prostate, or to other parts of the body. The studies vary from patient to patient depending on various factors. The usual initial staging studies include the ultrasound report from the initial biopsy, the pathology report, rectal examination, and bone scan. On occasion, a CAT scan (computerized axial tomography) or MRI (magnetic resonance imaging) will be done of the pelvic and abdominal areas, and a chest X-ray. The stage of the cancer is the most important deciding factor in which treatment will be used.

The following stages are most commonly used for cancer of the prostate:

---- Stage A ---

Prostate cancer at this stage cannot be felt and causes no symptoms. The cancer is only in the prostate and was unsuspected. This stage of cancer is found when surgery is done for other reasons, such as for BPH (benign prostatic hyperplasia).

Stage A1: Cancer cells are found in only one area of the prostate. Usually the cancer cells found are low-grade (discussed below).

Stage A2: Cancer cells are found in many areas of the prostate or are high-grade or aggressive cancer.

---Stage B---

The tumor can be felt in the prostate during a rectal exam, but the cancer cells are found only in the prostate gland.

Stage B1: The cancer involves only one side of the prostate and is less than 1.5 cm (3/5 of one inch) in size.

Stage B2: The cancer involves both sides of the prostate OR is greater than 1.5 cm (3/5 of one inch) in size.

---Stage C---

Cancer cells have spread outside the covering (capsule) of the prostate to tissue around the prostate. The other glands that produce semen (seminal vesicles) may have cancer in them.

---Stage D---

Cancer cells have spread (metastasized) to lymph nodes or to organs and tissues far away from the prostate.

Stage D1: Cancer cells have spread to lymph nodes near the prostate. (Lymph nodes are small, bean-shaped structures that are found throughout the body. They produce and store infection-fighting cells.)

Stage D2: Cancer cells have spread to lymph nodes far from the prostate or to other parts of the body, such as the bone, liver, or lungs.

---Recurrent---

Recurrent disease means that the cancer has come back (recurred) after it has been treated. It may come back in the prostate or in another part of the body.

GRADING PROSTATE CANCER:

The pathologist who performed the prostate biopsy defines the GRADE. The grade gives us an idea of how fast the cancer might be growing or how aggressive it might be. High-grade cancers grow faster and spread earlier than low-grade cancers. Today, cancer specialists usually use the Gleason grading system, named after pathologist Dr. Gleason, from the University of Minnesota. Dr. Gleason's system involves looking for two different patterns of aggressiveness within the prostate and then giving two scores of 1 - 5. These two scores are added up to give the total Gleason score which will range from 2 - 10. The higher the score, the more aggressive the tumor will be.

The older system of grading used only three different grades: well differentiated, moderately differentiated, and poorly differentiated.

Well-differentiated meant the cancer had more resemblance to normal prostate tissue and therefore usually did not grow or spread quickly. Poorly differentiated tumors did not resemble normal prostate and

usually grew quickly and spread to other tissues earlier. Moderately differentiated were in the middle. To compare systems we say that Gleason 2, 3, and 4 are well differentiated, Gleason 5, 6, and 7 are moderately differentiated and Gleason 8, 9, and 10 are poorly differentiated. Grade, while important, has less bearing on the treatment decisions than the Stage. After the grade and stage are known, other factors also come into play before making any decision about future treatment. Most important are each individual's health, life expectancy, and current medical conditions.

PSA EXPLANATION

WHAT IS PSA AND HOW DO WE MEASURE IT?

PSA stands for Prostatic Specific Antigen and is a blood test that is used to screen for the presence of prostate cancer. More accurately, the PSA is found in the blood's serum, which is the fluid that the red blood cells and white blood cells travel.

Antigen is a medical or biological term for a substance that stimulates the body to make antibodies.

Prostate is the gland sitting between the urinary bladder and the urethra (the urinary channel that runs through the penis). The prostate's function is to make seminal fluid or semen that is ejaculated during intercourse. Note that sperm is made in the testicles, which is only a small fraction of the seminal fluid.

Prostate Specific Antigen is, therefore, a protein found in the serum that is unique or specific for the prostate. No other tissue in or out of the body can make Prostate Specific Antigen. The PSA levels can be measured in an individual's serum and with the help of this information we are able to detect prostate cancer.

WHAT CAUSES THE PSA TO RISE?

PSA is only present in men. PSA is present in all normal prostate tissue. The normal prostate cell holds onto most of the PSA and lets very little leak into the blood stream. The small amount that leaks out is the PSA that is measured by the blood test. Prostate cancer cells actually have less PSA in each cell, but the cancer cell tends to leak more PSA into the blood stream, hence the reason for measuring PSA levels. Knowing this fact, we have come up with a range of expected values in patients with normal prostate glands. We believe that the PSA value should be less than 4.0. This number is somewhat arbitrary but reflects our feelings that most men (95% or so) with normal prostate glands have a PSA value of 4.0 or less. The catch is the word 'normal'. Any condition that affects the prostate can make the PSA rise. Any type of inflammation of the prostate (prostatitis) can cause the PSA to rise. Most men with prostatitis have no symptoms, but the PSA leaks out of the cells and causes the blood PSA level to be higher than normal. Even a simple rectal exam can cause the PSA to rise somewhat. What this means is that PSA is NOT a cancer measurement, and that an elevated PSA does NOT mean you have cancer. The only test that will determine the presence of cancer is a biopsy of the prostate.

FIRST TIME MEASUREMENT OF PSA

(Note: This assumes that the rectal examination found no suspicious nodules or hardness within the gland. Even if one's PSA level is unmeasurable, a suspicious nodule must be evaluated.)

PSA of 4 or less - If your PSA level has been measured for the first time and is less than 4, we recommend repeating the test on a yearly basis.

PSA between 4 and 10 - If your PSA is greater than 4 but less than 10, we recommend a diagnostic ultrasound and biopsy of your prostate. If the ultrasound shows no suspicious areas, then nothing further is done. A repeat PSA should be drawn in 4-6 months or no later than one year. If the ultrasound shows a suspicious area, then biopsy of the area needs to be done (usually at the time of ultrasound, if you have been prepared with antibiotics).

PSA greater than 10 - If your PSA is greater than 10, we recommend a diagnostic ultrasound of your prostate with biopsies of the prostate. If the ultrasound shows no suspicious areas, then random biopsies

of the prostate are taken. If the ultrasound shows suspicious areas, then biopsy of the areas along with random biopsies need to be done.

IF YOU HAVE PREVIOUS MEASUREMENTS OF PSA

(Note: This assumes that the rectal examination found no suspicious nodules or hardness within the gland. Even if one's PSA level is unmeasurable, a suspicious nodule must be evaluated.)

When we have the luxury of previous PSA values, we look at numbers a little bit differently. The PSA level will almost always rise in the face of cancer that is growing. Any PSA level that is rising is suspicious. As mentioned earlier, the high PSA level may NOT mean that cancer is present. In those cases, we hope to see stable PSA levels. For example, a stable PSA of 15 over a three-year period (15, 15, 15) is probably at less risk than a PSA of 2, 3, 4 over the same time frame. The second patient's rising levels suggest growth and have to be considered suspicious for cancer. If the first patient with repeating 15 values had a negative biopsy when first discovered, then there is no need to repeat the biopsies. If his levels jumped to 20 or 25 for no apparent reason, then repeat ultrasound and biopsies would be indicated. Recent studies suggest that a 20% rise in PSA in one year should prompt a closer look and possibly an ultrasound and biopsy. Additional investigation into the percentage of FREE PSA versus the TOTAL PSA may further help to identify those patients at risk for having prostate cancer.

FOLLOW-UP

At this time, no formal recommendation of PSA follow-up has been declared by the major American medical institutions. However, most urologists believe that a yearly PSA along with a rectal examination of the prostate should be done. Given a normal, and unrising PSA value, a routine ultrasound of the prostate is not indicated.

In addition, the Prostate Specific Antigen or 'PSA' blood test can be used as a marker for the effectiveness of treatment. If the prostate gland is removed (radical prostatectomy) we expect the PSA level to be unmeasurable (less than 0.3). If any PSA is measured after radical prostatectomy, then the presence of prostate cancer cells somewhere in the body has to be suspected. Prostate cancer cells that have spread to other areas also leak PSA. Even if we cannot find the areas of spread with scans or other tests, the presence of PSA means that the cancer is present. If the treatment of the cancer was with any form of radiation, chemotherapy or hormone therapy, the PSA level will not necessarily become unmeasurable. The normal prostate cells may not be destroyed and may still leak normal amounts of PSA. However, the PSA level should be stable if the treatment is working. That means a rising PSA level suggests growth of the cancer.

In summary, all treatments discussed above are appropriate and acceptable, perhaps some more than others in certain situations. This handout is an outline of the important points of each treatment. More than likely you will have other questions to be answered. You may have heard of other treatments for cancer that might be applicable. If you have any questions concerning the above, please ask.

TREATMENT OF LOCALIZED PROSTATE CANCER – CURRENT THOUGHTS

If the diagnosis of prostate cancer has been made, and the additional studies and scans suggest that there is NO spread of the cancer from the prostate. Assuming these studies are accurate, any treatment that can control the cancer in the prostate will therefore control all the cancer. The following are the choices that are available to us in the treatment of localized prostate cancer.

WATCHFUL WAITING (NO TREATMENT)

This option consists merely of close observation of the cancer, looking for any signs of progression with blood tests, scans, and physical examinations. Specific cancer treatment will be undertaken only when problems arise from the cancer growth. While this approach may seem out of the question in most circumstances, withholding treatment is appropriate and justifiable in certain circumstances. The treatments might be more risky than the disease. For instance, an elderly male (in his late 80's) with localized cancer, and with no symptoms, may never have problems from his prostate cancer. In the

absence of symptoms, and in the presence of other medical situations which are more threatening, watchful waiting is a viable option.

In some medical environments, Sweden, for example, watchful waiting or observation has become a fairly standard approach to early prostate cancer. They believe that in some patients, the disease will grow so slowly that radical treatment is unneeded because patients will die of other diseases. In patients whose prostate cancers grow quickly, they feel comfortable in treating the spread with medical treatment, non-curative. For the most part, this approach goes against the attitudes of most American cancer specialists. Still, observation has many supporters and should be considered in certain situations.

CHEMOTHERAPY

Chemotherapy is the use of medicines or drugs to stop the growth of cancers. Chemotherapy is used for the most part in patients whose disease has spread to other parts of the body (metastases) and is resistant to other forms of treatment.

The drugs are very powerful and work by killing cells that tend to grow quickly. Cancers tend to grow quickly, but unfortunately, so do cells in bone marrow, gut, and other areas. Anemia, weakness, nausea, vomiting, diarrhea, and other side effects can occur. Unfortunately, chemotherapy rarely cures prostate cancer, but merely palliates or temporizes the cancer growth. Because of the poor track record with prostate cancer, chemotherapy tends to be used only when all other avenues of treatment have been exhausted.

HORMONE THERAPY

The prostate gland is uniquely male. Its very existence is due to the presence of male hormones, which the prostate and most prostate cancers require to grow. This observation led urologists to the use of hormone reduction to treat prostate cancer in the 1940s and except for newer drugs, the principles of hormone reduction still stand today. The usual ways of effecting hormone reduction are either a monthly shot (Lupron or Zolodex) or surgical removal of the testicles (orchiectomy). Pills may be added to either of these treatments to potentiate hormone reduction.

Unfortunately, hormone therapy is effective only temporarily in most patients. Seven out of 10 men will have an initial reduction in the tumor, but within 2 - 3 years most men that do respond will no longer and the cancer will again grow. Because hormone therapy is not curative, we usually do not recommend this for localized cancer with reasonable life expectancies.

SURGERY

Surgical removal of the prostate is felt to be the *standard therapy for localized prostate cancer*. Simply, the entire prostate is removed and the bladder is reconnected to the urethra (channel through the penis). Removal of part of the prostate or just the cancer is not recommended. Too many prostate cancers have multiple areas of involvement within the gland that are undetected, making partial removal a poor choice. Also, partial prostatectomy is not technically feasible.

The major advantage of total prostate removal is the simple fact that ***IF*** the cancer is localized to the prostate, as we believe, then removal of the prostate will cure the cancer -- it is out!

The major disadvantages are:

Incontinence -- 2 - 4% of men will have permanent problems with urinary control -- they will require some form of protection (diapers). In those rare cases, a surgical appliance can be implanted to control incontinence if it does remain a problem after surgery.

Impotence -- The nerves that stimulate erections run adjacent to the prostate on their way to the penis. If all of these nerves are removed during total prostatectomy, impotence (inability to achieve an adequate erection) will result. In certain circumstances, some of the nerves that create erections can be spared with a success rate between 40 - 60%. Not every male is a good candidate for nerve sparing because of the extent of disease. Patients who develop impotence, and even those whose erections were not

adequate before the surgery, can be treated with a variety of modalities. Treatment of impotence in post-prostate surgery includes vacuum pumps, self-injections of medications, and placement of prostheses -- all of which work in appropriate patients.

Blood loss -- Radical prostatectomy carries with it an average blood loss of greater than one unit of blood. On occasion, the blood loss can be more than three or even four units. To prevent the use of bank blood, patients may donate their own blood prior to surgery for subsequent use, if needed.

Surgical complications -- pain, infection, anesthetic problems, pneumonia, blood clots, and heart problems can occur with any major operation. Unique to prostatectomy are injury to the rectum (adjacent to the prostate), and scarring of the new connection between the bladder and urethra, which might require stretching, in the office or outpatient surgery.

Recovery time: The operation lasts two to three hours and the hospitalization lasts 2 to 4 days. All patients go home with a catheter in place, continually draining the urine into a special leg bag. You will be seen two to three weeks after discharge from the hospital to have the catheter removed. Most men have poor urinary control at the beginning and will require some form of protection, such as a diaper. Within three weeks, most men have achieved reasonably good control and require minimum protection and have resumed their normal activities. Sometimes, the recovery is slower but rarely more than three to six months.

RADIATION THERAPY – EXTERNAL BEAM

External beam radiation therapy is by far the simplest of therapies. Over a six to seven week period, the patient will receive a radiation treatment lasting about 15 minutes, 5 days a week. The radiation is aimed at the prostate from many different angles in an attempt to reduce the dosage to the surrounding tissues while maximizing the dosage to the prostate and the cancer.

The advantage of external radiation therapy is its ease of administration. No surgery, no anesthesia, no blood loss. The biggest disadvantage is that the cancer is left in place and one must hope that the amount of radiation delivered is enough to cure the cancer. Unfortunately, with the surrounding structures, namely, bladder and rectum, being sensitive to overdoses of radiation, the prostate cancer is often stunned but not cured. Recurrence rates of the cancer at later times are in the range of 60% as measured by rising of the tumor marker, PSA. During the last two to three weeks of treatment, diarrhea and urinary urgency and frequency are quite common and on occasion so severe that the treatments need to be temporarily halted. These symptoms usually resolve two to three weeks after the radiation treatments have ceased. Permanent radiation injury to the bladder or rectum occurs in a small percent of patients creating chronic pain and/or bleeding. Difficulty with erections (impotence) occurs in 35% of patients who were having no problems pretreatment.

IMPLANT THERAPY

Implants are forms of radiation therapy with many of the same risks and benefits. Implants are often combined with external therapy, depending on the type of implanted radiation and the extent of the cancer. Implants are ultrasound-guided radiation treatments done under anesthesia. The operation lasts from 1 to 2 hours and hospitalization lasts from 1 to 2 days. Some implants are permanently left in place (Iodine, Palladium, Gold) and some are temporary (Iridium). Implants allow for higher doses to the prostate while sparing the surrounding tissues. A theoretically higher cure rate should be observed. Implants have been around since 1970 and were done initially with free-hand techniques. The results with free-hand implantation were not very encouraging. Ultrasound-guided implants became available in the mid-1980s and long-term data is still not available to determine how effective these treatments might be. Bladder and rectal irritability does occur. Implants must be considered experimental at this time until more is known about long-term survival and cure rates.

CRYOTHERAPY

Cryotherapy or 'freezing' the prostate has been around for 40 years. The original technique involved open surgery and placement of liquid nitrogen directly into the prostate cancer. The overall success rate was marginal and the technique was abandoned in the early 60's. More recently, cryotherapy using ultrasound as a guide to place needles has returned. To date, insufficient data exists to know how effective cryotherapy might be. The frozen tissue dies and is then either urinated out or re-absorbed into the body. Whether all of the cancer will be removed is the major drawback of cryotherapy.

FOLLOW-UP TO TREATMENT

After your treatment is rendered, regardless of which treatment is undertaken, we will be following your progress very closely. If surgery or observation is chosen, the follow-up will be through our office. If radiation or implants are used, the follow-up will be shared by our office and the radiation therapists.

The keys to follow-up in most circumstances will be the rectal exam of the prostate, or in the case of surgery, the area where the prostate was. We will be looking for evidence of recurrence or regrowth of the tumor. If suspicious areas occur, ultrasound and biopsies may be indicated.