FREQUENTLY ASKED QUESTIONS ABOUT PROSTATE CANCER

1. How common is prostate cancer?

Prostate cancer is the most common cancer that men get in the United States behind skin cancer. In the United States, approximately 234,460 cases will be diagnosed in 2006, and 27,350 deaths will occur. In men, this malignancy is second only to lung cancer as the leading cause of cancer death.

2. What are the risk factors for prostate cancer?

Some of the most important risk factors for prostate cancer include:

- **Age**: every man over the age of 45 is at risk for prostate cancer. Although prostate cancer can

occasionally strike younger men, the risk of developing prostate cancer increases with age. The incidence of prostate cancer rises quickly after the age of 60, and the majority of men will have some form of prostate cancer after the age of 80. More than 70 percent of men diagnosed with prostate cancer are over the age of 65.

- **Ethnicity**: prostate cancer is more common in African-American and Latino men than Caucasian men. African-American men are 1.6 time more likely to develop and die from prostate cancer than Caucasian men. The median survival of black patients was 1.8 years lower than that of whites. The reason for this is not completely understood. Asian and Native American men have the lowest chances of getting prostate cancer. There is some evidence that differences in diets may be the cause. This is supported by the fact that when Asian men move to Western countries like the United States, their chance of getting prostate cancer rises. Men who live in the United States and Northern Europe have the highest rates of prostate cancer, while men who live in South America, Central America, Africa, and Asia all have much lower chances of developing prostate cancer.

- **Family history**: Having a first degree relative with prostate cancer doubles the risk of developing prostate cancer. The risk is even higher if relatives develop prostate cancer at a young age. A variety of different genetic factors are currently being researched. The presence of BRCA1/2 mutations may increase the risk of developing prostate cancer by 2-5 times.

3. What are the symptoms of prostate cancer?

One of the difficulties in diagnosing prostate cancer early is that early stage prostate cancer often does not cause any symptoms. We therefore have to rely on PSA tests and digital rectal exams, rather than symptoms.

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More advanced prostate cancers can cause a variety of symptoms including:

- trouble starting urination
- urinating much more frequently than usual
- urinating small volumes
- pain on urination or ejaculation
- blood in your urine or semen
- impotence
- bone pain

All of these symptoms can be caused by a variety of things besides prostate cancer, so experiencing them doesn't necessarily mean you have prostate cancer. When older men have problems urinating, it is usually caused by process called benign prostatic hyperplasia (BPH) which is not prostate cancer. These symptoms can also be seen in prostatitis (inflammation of the prostate).

4. Is it possible to prevent prostate cancer by adhering to a certain diet?

There is some evidence that a man's diet – such as a high fat diet, particularly high in animal fats – may increase the risk of developing prostate cancer. Also, a few studies have suggested that a diet low in vegetables increases the risk of prostate cancer. There are a few foods that have been implicated in decreasing prostate cancer risk; diets high in tomatoes (lycopene), omega-3-fatty acids (oils found in fish like salmon and mackerel), selenium, vitamin D, and soy have all been suggested to decrease prostate cancer risk but we still need more data before any particular food or supplement can be endorsed for preventing prostate cancer. Currently, there are studies looking at selenium, lycopene, vitamin A and other retinoids, vitamin D, vitamin E, and soy for prostate cancer prevention.

5. Are there any medications that could prevent prostate cancer?

There is also interest in preventing prostate cancer by using drugs. We know that hormones like testosterone can cause prostate cancers to grow and develop, so there are experiments looking at drugs that can decrease the levels of testosterone in the prostate to attempt to stop prostate cancer from forming and growing. Drugs like Flutamide and Finasteride work in this manner, and they are currently under investigation for prostate cancer prevention.

6. Are there any screening tests available that help in early detection?

Currently, there are two methods that physicians use to screen for prostate cancer. One of them is called a digital rectal exam (DRE). A digital rectal exam is done in your primary care physician's office. A PSA (prostate specific antigen) test is a blood test that looks for a protein that the prostate makes. The PSA test isn't perfect either, because some tumors won't elevate the PSA and some other processes (like benign prostatic hyperplasia and prostatitis) can cause it to be falsely elevated. However, the higher your PSA is, the more likely there is prostate cancer. The cut-off that your doctor usually uses is 4.0 ng/ml, meaning that anything below 4.0 ng/ml is normal and anything above it is abnormal. If your PSA is elevated or you have an

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abnormal digital rectal exam, then you need to get further evaluation; however, this doesn't necessarily mean that you have prostate cancer.

If either of those two tests are abnormal, then most likely the next step involves a biopsy. This is usually combined with a transrectal ultrasound. The ultrasound probe is inserted into the rectum and allows the doctor to view the prostate and choose where to remove tissue from. Any suspicious areas are biopsied, plus some tissue will be removed from all of the different parts of the prostate (to make sure they don't miss any cancers that may be small and growing in one particular area). The procedure does not require anesthesia. Once the tissue is removed, a doctor known as a pathologist will review the specimen. The pathologist can tell if it is cancer or not.

7. What is the "official" recommendation with regard to prostate cancer screening?

The American Cancer Society and the American Urological Society recommend regular prostate cancer screening. The American Cancer Society recommends that men start getting annual PSAs and digital rectal exams starting at age 50, unless they are high risk (meaning they have a family history of prostate cancer or are African-American), in which case they should begin screening at age 45. However, they mention that screening should only be carried out if your life expectancy is greater than 10 years, so men in their 80s and 90s (especially if they have other serious medical problems) should probably not be screened.

8. How many lives have these screening procedures saved?

The value of screening for prostate cancer is an intensely debated issue and somewhat controversial. In general, if screening for cancer is expected to be successful, at least three conditions need to be
met:

a) Screening should primarily able to identify patients with an aggressive form of prostate cancer that often leads to death. The majority of prostate cancer patients discovered by screening have less aggressive, slow growing tumors that tend well even without early detection. The more aggressive tumors tend to spread quickly, and the period when they are truly localized and amenable to detection by screening is short.

b) Screening can only benefit prostate cancer patients if the detection of the disease is followed by effective treatment. Unfortunately, aggressive types of prostate cancer are not always curable with the current treatments available. Right now, there is no good data showing that screening for prostate cancer reduces deaths from prostate cancer. There are currently very large trials ongoing to see which populations of men will benefit most.

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9. What determines the survival chances (prognosis) once prostate cancer is diagnosed?

Aside from the condition the patient is in as far as his general health is concerned, the most important factors that determine a patient's prognosis are:

- **The grade or aggressiveness of the prostate cancer**

The pathologist will characterize the cancer in terms of how aggressive the tissue appears when looked at under a microscope. This is known as the tumor grade. Aggressive tumors move rather quickly and are likely to have already infiltrated areas outside the prostate (lymph nodes or other organs) even at the time of biopsy.

The most commonly used grading system is called to the "Gleason score." The Gleason score runs from 2 to 10. Higher numbers indicate a more aggressive tumor. We characterize grades on a scale because, together with staging, it gives us a way to offer a prognosis and it often guides our choice of therapy.

- **The stage**

Prostate cancer is divided into four different stages to help guide our treatments and offer information about the chances for a cure. This staging is done in a limited fashion before surgery, taking into account whether or not the tumor can be felt on digital rectal exam and the results of any imaging modalities:

Stage I -tumor cannot be felt during a digital rectal exam; it was detected by an elevated PSA blood test or incidentally found during another prostate procedure for a benign condition.
Stage II -tumor can be felt during a digital rectal exam, but it has not spread beyond the prostate to lymph nodes or other organs
Stage III -tumor extends outside the prostate and can be in the seminal vesicles, but not in any other organs or lymph nodes
Stage IV -tumor has spread to other organs or lymph nodes

After a surgical procedure that removes lymph nodes and allows a pathologist to examine them for signs of cancer, this staging is more definitive. This staging information is called pathologic staging.

10. What this can be used to make sure that cancer has not spread outside the prostate or to distant organs?

Tests like CT or MRI can examine the prostate and localized lymph nodes. Some patients are referred for a bone scan, which is a test using a radioactive tracer to look for metastasis to any of your bones. Another test that you may be referred for is called a ProstaScint scan, which uses a

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radioactive tracer that can localize prostate cancer to either bones or lymph nodes. Unfortunately none of these tests is very reliable in determining the stage of the disease. Finally, if your doctors are very worried about spread to lymph nodes, they may choose to perform a surgical lymph node sampling before proceeding with any definitive treatment.

11. What are the different forms of treatments for prostate cancer?

There are many different ways to treat prostate cancer, and several specialists should be consulted before a final recommendation is formulated. Most commonly these consultations involve an urologist, radiation therapist and medical oncologist. They will inform the patient about the pros and cons of the different treatment approaches. Physicians are not always in agreement as to the way to proceed because there haven't been enough large trials that compare the different treatment modalities. In general the different forms of treatment are: surgery, radiation therapy, hormonal therapy and chemotherapy. The following treatment approaches may be considered:

Careful observation without further immediate treatment, depending on the patient's age and other conditions.

Radiation therapy. Radiation therapy uses high energy rays (similar to x-rays) to kill cancer cells. Radiation therapy is another option besides surgery for early stage prostate cancer; and when advanced stage prostate cancer needs to be treated, it is usually done with radiation therapy. Radiation helps avoid surgery in patients who are too ill to risk having anaesthesia. Radiation is usually offered to older patients in the case of early stage prostate cancer because of its side effect profile is less than surgery in the elderly. Radiation can have impotence rates similar to surgery, but the risk of urinary incontinence is very low. Impotence develops months to years after the radiation treatment, unlike with surgery, which tends to have the side effects occur immediately. Other side effects from radiation include bladder irritation, which can cause urinary frequency and urgency as well as bladder pain, and diarrhea or rectal bleeding. Your radiation oncologist tries to limit the amount of radiation to other organs, but often the bladder and rectum can get some dosage because they are in such close proximity to the prostate.

Radiation therapy for prostate cancer either comes from an external source (external beam radiation) or an internal source where small radioactive seeds are implanted into the patient's prostate (brachytherapy).

External-beam radiation therapy requires patients to come in 5 days a week for up 6-8 weeks to a radiation therapy treatment center. The treatment takes just a few minutes, and it is painless.
Brachytherapy is done as a one-time insertion, in the operating room.
Brachytherapy cannot be done in all patients and is usually reserved for early stage prostate cancers. Short term results in these patients are similar to those for radical prostatectomy or external-beam radiation therapy. The rate of maintenance of sexual potency with brachytherapyhas been reported to be 86 to 92 percent, which compares with rates of 10 to 40 percent with radical prostatectomy and 40 to 60 percent with external-beam radiation therapy. Other consequences, such as urinary tract frequency, urgency, and (less commonly) urinary

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retention, are seen in most patients but subside with time. Rectal ulceration may also be seen. Long-term follow-up with these patients is necessary to assess treatment efficacy and side effects.

Surgery is a common form of treatment for men with prostate cancer. Surgery attempts to cure prostate cancer by removing the entire prostate. An attempt at a surgical cure for prostate cancer is usually done with early stage prostate cancers, but sometimes surgery will be used to relieve symptoms in advanced stage prostate cancers. Surgery for prostate cancer is generally felt to be equivalent to radiation for prostate cancer in terms of survival, especially in early-stage, low-to intermediate-grade cancers. The decision to have surgery versus radiation is often determined by the patient's age and health status.

The most common surgical procedure for prostate cancer is known as a radical prostatectomy. Radical prostatectomy means that the entire prostate gland is removed from around the tube that connects the bladder to the penis (the urethra). Radical prostatectomies are very safe surgeries with few life-threatening complications; however, there is a significant risk for other side effects. Both urinary incontinence (not being able to hold your urine) and impotence (inability to achieve an erection) are commonly associated with this procedure. However, long-term incontinence occurs as a significant quality-of-life issue in only about 5 percent of men who undergo prostatectomy, and between 10 and 40 percent of patients maintain their sexual potency. The risk for having either of these side effects increases with age. The skill of a particular surgeon influences your chances of having these side effects during a radical prostatectomy. Sometimes a nerve sparing prostatectomy can be performed. This type of prostatectomy can decrease the chances that you will be impotent after the procedure. However, not every patient is a candidate for a nerve sparing prostatectomy.

Hormonal Therapy exploits the fact that prostate cancers depend on male sex hormones, called androgens, to grow and replicate. One way to treat prostate cancer is to lower male hormone levels in the body. There are a few different ways to remove androgens: you can remove a man's testicles (called an orchiectomy), you can give a man drugs that block the production of androgens (called LHRH agonists), you can give a man drugs that prevent prostate cancer cells from responding to androgens. Giving female hormones is another approach more commonly used in the past. When patients with metastatic disease are treated with hormonal therapy, there prostate cancer will eventually become resistant to hormonal therapy. However, this often takes many years and hormonal therapy can buy a lot of time in patients with extensive disease or patients who choose not to undergo surgery or radiation. There are a number of side effects associated with hormonal therapy. Hormonal therapy will almost universally cause impotence and the loss of your sex drive. It can also cause hot flashes, and muscle and bone loss (osteoporosis).

Chemotherapy is prescribed by medical oncologists, who are experts at choosing appropriate regimens for particular patients. Chemotherapy for prostate cancer is generally only reserved for very advanced cancers that are no longer responsive to hormonal therapy. There are a number of chemotherapy drugs that can be used for prostate cancer, and they are often used in combinations. A common chemotherapy regimen is Mitoxantrone with Coritcosteroids. Other

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regimens that are becoming increasingly popular use a drug called Estramustane with drugs called Taxanes.

12. What do the terms “local treatment” and "systemic treatment" mean?

Surgery and radiation therapy are considered "local treatments" since they focus on the prostate and surrounding area only. Hormonal therapy and chemotherapy attack any prostate cancer cell anywhere in the body and are called "systemic treatment."

13. Does every patient with newly diagnosed prostate cancer need treatment?

Some patients choose to receive no therapy for their prostate cancer in the hopes that it will grow very slowly. By avoiding any therapy, they avoid the side effects that come along with surgery, radiation, or hormones. Watchful waiting is appropriate for older men with small, low-grade tumors, and slowly rising PSAs, and multiple other medical problems. Watchful waiting can be considered in patients who have a life expectancy less than 10 years, as long as the cancer isn't large or of a high grade.

14. What are the signs of prostate cancer coming back (metastasizing) after radiation therapy or surgery?

If prostate cancer is not controlled by local measures or if the disease is already advanced at the time of diagnoses, it is likely to spread to other places in the body traveling through the blood stream or lymphatic system. Prostate cancer typically spreads to the bones (spine, ribcage, skull, leg and arm bones) and pelvic lymph nodes. Though less frequent, it can also travel to the lungs, liver or other organs. Bone pain, leg swelling or symptoms such as fatigue, loss of appetite and weight loss may occur. Occasionally the patient is without symptoms, so a relapsing prostate cancer is detected through laboratory studies, such as a steadily rising PSA level, increase in the calcium level (hypercalcemia) and kidney problems.

15. What are the treatment options for patients with metastatic prostate cancer?

Radiation therapy to areas causing pain frequently results in a significant improvement in the quality of life of prostate cancer patients.

In addition, hormonal agents, including the ones mentioned above, in combination with a medication called Ketokonazol/hydrocortisone can be used. Eventually, these medications will fail. The term "hormone refractory prostate cancer" is applied to the situation.

Only recently has chemotherapy been shown to afford benefits both in terms of improved quality of life and also in improving the survival. The combination of mitoxantrone, plus corticosteroid, was the first chemotherapy regimen; it was shown to accomplish a significantly better pain control without changing the overall survival. A subsequent study demonstrated that regimens containing taxanes (such as Taxotere and Taxol) were even more superior. These regimens

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showed higher response rates and a significantly longer median survival duration. A regimen of every Taxotere every three weeks plus daily prednisone became the new standard of care.

Taxotere has been combined with other agents such as Estramustine. This combination may be slightly more effective but has fallen out of favor because of significant side effects, mainly a 10 percent rate of blood clots in the veins and arteries. In other studies Taxotere has been combined with Calcitrol, a substance related to vitamin D, with some promising results. Another medication with activity and prostate cancer is a drug called Navelbine. The combination of Estramustine with Taxotere and Carboplatin every three weeks was studied in 40 men. ThePSA decline in 68 percent. Four patients had thromboembolic events despite the prophylactic use of low-dose Coumadin.

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