

Questions
& Answers
about
Prostate Cancer
Metastatic
to Bone

A publication of

The Paget Foundation
for Paget's Disease of Bone
and Related Disorders

and the

National Institutes of Health
Osteoporosis and Related
Bone Diseases~National
Resource Center

Introduction

In 1978, The Paget Foundation was founded as an organization devoted to helping patients with Paget's disease of bone, a disease in which increased bone resorption is an important factor. Since 1992 the foundation has expanded its programs to include other disorders of increased bone resorption. The foundation currently addresses the following disorders: Paget's disease of bone, primary hyperparathyroidism, fibrous dysplasia, osteopetrosis, breast cancer metastatic to bone, and prostate cancer metastatic to bone. Foundation programs and services include patient education and assistance, professional education, public education, research, and advocacy.

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General Information about Prostate Cancer

1. Q. How common is prostate cancer in the United States today?

A. In 1999 it was estimated that 179,000 men would be diagnosed with *prostate* cancer, making it the second most common cancer diagnosed in men, following skin cancer.

2. Q. How is prostate cancer diagnosed?

A. Prostate cancer is usually diagnosed by one of three means:

- ◆ Measurement of *prostate-specific antigen (PSA)*—a protein produced by the prostate gland. Its level goes up in the blood of some men who have prostate cancer and other conditions.
- ◆ *Digital rectal examination (DRE)*—a procedure in which a doctor inserts a gloved finger in the rectum to examine the rectum and prostate gland.

(Since neither the DRE or PSA test can confirm diagnosis of prostate cancer, a needle *biopsy* of the prostate gland is also required)

- ◆ Surgery for an enlarged prostate (*benign prostatic hypertrophy/BPH*). This surgery can reveal prostate cancer.

Occasionally men may be diagnosed with advanced prostate cancer that has already spread to bones or elsewhere.

3. Q. How is prostate cancer initially treated?

A. The treatment of early prostate cancer continues to be controversial because its behavior may be difficult to predict. Patients may undergo *watchful*

waiting if they are asymptomatic (having no symptoms) and have a *low-grade tumor* that is quite small. Treatments for other patients include:

- ◆ Removal of the prostate gland—a common treatment that can be accomplished through an incision in the abdomen or between the *scrotum* and *anus*.
- ◆ *Radiation therapy*—may be delivered by a machine (*external radiation*) or by implants placed in the prostate gland (*brachytherapy* or seed implant therapy).
- ◆ *Hormone therapy*—not curative and may be used if the *tumor* has a significant risk of being outside the prostate gland. The goal of hormone therapy is to reduce the main male hormone *testosterone* to very low levels. In the past this was done by removal of the *testes* or by administration of *estrogen*, which blocks production of testosterone by the testes. More recently, drugs have been developed that reduce testosterone levels by diminishing the production of a *pituitary gland* hormone that controls testosterone release by the testes. These drugs, such as Zoladex® (goserelin acetate) and Lupron® (leuprolide acetate) are administered in the doctor's office by injection every 1 to 3 months. In addition to reducing testosterone production, some patients are given an antiandrogen, such as Casodex® (bicalutamide), Eulexin® (flutamide), or Nilandron® (nilutamide), that blocks the effect of remaining amounts of testosterone and other male hormones on prostate cells. When both types of drugs are given, this is *total androgen blockade*. (Please see chart on page 7.)
- ◆ In some patients, a combination of surgery, radiation therapy, and combined hormone therapy is utilized.

The Spread of Prostate Cancer

4. Q. How often does the initially treated prostate cancer return?

A. If the tumor is localized to the prostate gland at the initial time of treatment by surgery or radiation therapy, there is an excellent chance that the patient will be cured. However, if the tumor is large or aggressive (growing quickly and ready to spread), tumor recurrence is common and the overall survival rate is about 50 percent lower than what would be expected 15 years after initial treatment. If the tumor has spread outside the prostate gland since the time of original diagnosis, survival rates are lower.

5. Q. Where in the body does prostate cancer spread?

A. When cancer spreads from the organ of origin, the distant tumor is termed a *metastasis*. Prostate cancer frequently spreads into nearby organs, the *lymph nodes* and distant organs. The lymph nodes in the pelvis are the first to be affected, but lymph nodes in the abdomen, chest, and those above the clavicles may be affected. The most common site of distant spread is to the bone (80 percent of late-stage patients). Prostate cancer may also spread to the liver, lung, and pleura (lining of the lung).

6. Q. What happens when prostate cancer spreads to bone?

A. When prostate cancer grows in bone, it may stimulate an increase in the number of osteoblasts (cells that produce bone) and osteoclasts (cells that break down bone). Usually this results in an excess of abnormally dense bone, although some areas of bone loss may also be seen.

The presence of prostate cancer in bone causes a variety of symptoms. Although some patients are pain-free, the majority have moderate to severe pain. The spine is the most common site of pain, followed by the pelvis, skull, and ribs. As the disease progresses, fractures are common complications.

Tumors growing from vertebrae may produce spinal cord compression and nerve damage if untreated.

In patients with widespread disease, *anemia* may occur from testosterone deficiency and possibly the overall toxic effect of the cancer.

Blood *calcium* levels can be affected by prostate cancer in bone. In some patients there may be hypocalcemia (a slight lowering of blood calcium levels) due to the stimulation of new bone by the tumor, which requires a large amount of calcium. Rarely patients with widespread disease may develop hypercalcemia (a high blood calcium concentration) due to a high level of bone breakdown. Nausea, vomiting, impaired mental function, and weakness are some symptoms of high calcium levels.

7. Q. How is the spread of prostate cancer to bone detected?

- ♦ A. Bone scan—the most sensitive means of detecting bone metastases and other abnormal processes in bone. A safe amount of a radioactive substance is injected and circulates through the bloodstream. This substance then localizes in areas where there is new bone formation associated with prostate cancer metastases. A bone scan may reveal bone metastases before they are visible in an x-ray.
- ♦ X-ray—since a bone scan does not specifically diagnose bone metastases, x-rays are often used

to help confirm the diagnosis of a bone metastasis. *CT scans* or *MRI* examinations are also sometimes helpful.

- ◆ Bone biopsy—in a small percentage of patients it may be necessary to remove a small piece of bone for microscopic evaluation if the bone scan and x-ray results are inconclusive.

Treatment of Prostate Cancer That Has Spread to Bone

8. Q. What types of physicians and other health professionals treat patients with prostate cancer affecting the bone?

A. It is likely that more than one health care professional will care for the patient with bone metastases. *Urologists, radiation oncologists, and medical oncologists* may provide care depending on the individual condition of the patient.

If there is risk of a fracture, or if a fracture has occurred, an orthopedic surgeon will provide appropriate surgical care, possibly with the assistance of a neurosurgeon if a tumor in the spine is causing pressure on the spinal cord or nerves. Physical medicine physicians may assist in prescribing physical therapy.

Oncology nurses, orthopedic nurses, and physical therapists will often be called upon to assist with the use of medications and rehabilitation needed to return patients to their usual daily activities.

Because of the emotional and social impact of prostate cancer in bone, patients may want to consult mental health professionals (e.g., psychologists, social workers, or psychiatrists). Psychotherapy, antidepressant medication, and/or support groups may be helpful for some individuals.

9. Q. Once the prostate cancer has spread to bone, what treatments are given?

A. The treatment of patients with prostate cancer metastases in bone depends in part on prior treatment of the cancer. Prostate cancer cells are initially dependent on male hormones (testosterone mainly) for growth. If surgery or radiation was the initial treatment, measures can be taken to reduce testosterone production. This could be accomplished with medication or surgical removal of the testes. Some patients also receive antiandrogen medications.

If bone metastases develop despite these types of therapies, or if these therapies fail to relieve bone pain, there are several other choices of treatment. Second-line hormone therapy such as Cytadren® (aminoglutethimide), Stilphostrol® or Stilbestrol® (diethylstilbesterol), Nizoral® (ketocozanole), and Megace® (megastrol), utilizes drugs that can further suppress production of *androgens*, or block their actions at the cancer cell itself. The benefits of second-line hormone therapy are modest at best.

If hormone therapy fails, chemotherapy (treatment with anticancer drugs such as Emcyt® [Estramustine]) may be offered. Though still an active area of research, chemotherapy may benefit one third to one half of patients with progressive prostate cancer, including reduction of bone pain or shrinkage of tumors.

Radiation therapy, which can be delivered externally, may relieve pain in 70-90 percent of patients. However, if there are multiple painful bone metastases, it is more feasible to treat with *intravenous* radioactive drugs such as Metastron® (strontium-89) or Quadramet® (samarium-153). These agents may relieve pain in 65-80 percent of patients, though the duration of the effect is limited. (Please see chart on page 7.)

A class of drugs called *bisphosphonates* helps to prevent breakdown of bone. One of these, Aredia® (pamidronate), has been approved for treatment of bone metastases from breast cancer and for bone disease in patients with *multiple myeloma*. The bisphosphonates are being studied in *clinical trials* to determine their effectiveness in treating patients with prostate cancer.

In patients whose pain is not helped by the above types of treatment, nonspecific pain medications are an important means of relieving pain. The most severe pain may require narcotic therapy and referral to pain management specialists. Often pain medications are combined with the above therapies to achieve adequate pain relief.

Drugs Approved by U.S. Food and Drug Administration (FDA) for the Treatment of Prostate Cancer

Chemotherapy See Question #9

Emcyt® (estramustine)

Novantrone® (mitoxantrone)

Hormone Therapy See Question #3

Zoladex® (goserelin acetate)

Lupron® (leuprolide acetate)

Radioactive Drugs See Question #9

Metastron® (strontium-89)

Quadramet® (samarium-153)

Second-Line Hormone Therapy See Question #9

Cytadren® (aminoglutethimide)

Stilphostrol®, Stilbestrol® (diethylstilbesterol)

Nizoral® (ketoconazole)

Megace® (megestrol)

Antiandrogens See Question #3

Casodex® (bicalutamide)

Eulexin® (flutamide)

Nilandron® (nilutamide)

10. Q. What can be done if the tumor has weakened the bone so that a fracture is likely or has already occurred?

A. In patients with prostate cancer metastases in bone there is an increased risk of fractures in the long bones, spine, and pelvis. Fractures are usually preceded by an increase in pain aggravated by standing or walking. An x-ray may suggest a risk of fracture or indicate that a fracture has occurred. If there is a risk of fracture, external radiation may decrease pain and possibly reduce fracture risk.

Improved surgical techniques for impending or established fractures have produced excellent results in the great majority of patients. Pain relief and restoration of the ability to walk can be achieved in a high percentage of individuals.

11. Q. Can anything be done to prevent the spread of prostate cancer to bone?

A. The most effective means of preventing bone metastases is surgery or radiation therapy prior to the spread of the tumor from the prostate. This gives the best chance of cure.

General Bone Health in Men with Prostate Cancer

12. Q. What can be done to preserve bone health in men with prostate cancer?

A. Good nutrition including adequate vitamin intake, and maintenance of normal weight are helpful in preserving bone. Cigarette use and a high level of alcohol intake should be avoided, as both can cause bone loss.

Recent studies of men whose testosterone production is reduced by removal of the testes or by

drug therapy suggest that reduction of testosterone production may lead to bone loss and greater risk of fractures. Early studies indicate that if such patients are treated with a bisphosphonate, bone loss can be prevented or even partially restored.

13. Q. Is exercise useful and safe in men with prostate cancer?

A. Exercise is beneficial for all men, but men with prostate cancer should consult with their physicians to create an appropriate exercise plan. Exercise may be particularly important for prostate cancer patients who have reduced testosterone, which can lead to loss of muscle mass. Muscle weakness may cause falls and fractures. It has been shown that increased exercise can partially overcome muscle loss caused by testosterone deficiency and thereby contribute to fracture prevention. However if patients already have bone metastases, exercise may cause fracture.

Glossary

Anemia Having too few red blood cells. Symptoms include tiredness, weakness, and shortness of breath.

Anus Opening at the lower end of the rectum through which solid waste leaves the body.

Benign prostatic hypertrophy (BPH) Enlargement of the prostate, blocking urine flow. BPH is not cancer, but can cause some of the symptoms. Also called benign prostatic hyperplasia.

Biopsy Removal of a sample of tissue, examined under a microscope to check for cancer cells.

Bisphosphonate Drug used to prevent breakdown of bone.

Brachytherapy Internal radiation achieved by implanting radioactive material into the tumor or close to it. Also called internal radiation therapy, interstitial radiation therapy, or seed implant therapy.

Calcium Major mineral component of bone, important for normal function of nerves and other organs.

Clinical trial Research study involving volunteers, designed to answer medical questions and find better ways to prevent or treat disease.

CT scan (computerized tomography or CAT scan) Series of detailed pictures of areas inside the body, created by a computer linked to an x-ray machine.

Digital rectal examination (DRE) Procedure in which the doctor inserts a gloved finger into the rectum to examine the rectum and prostate.

External radiation Use of a machine to aim high-energy rays at cancer.

Hormones Body chemicals secreted by glands. Male hormones include androgen and testosterone (produced primarily by the testes, plays important role in a man's sexuality and fuels the growth of prostate cancer). Estrogen is a female sex hormone. These hormones circulate in the bloodstream, and control the actions of certain cells or organs.

Hormone therapy Use of medications or surgical removal of the testes to prevent male hormones from stimulating further growth of prostate cancer.

Intravenous Into a vein.

Low-grade Of little degree.

Lymph nodes Small, bean-shaped organs that are part of the body's immune system. They are located throughout the body along the channels of the lymphatic system. Also called lymph glands.

Medical oncologist Doctor trained in the diagnosis and treatment of cancer.

Metastasis (pl., metastases; v. metastasize) Spread of cancer cells throughout the body. Cells that have metastasized are the same as those in the original tumor.

MRI (magnetic resonance imaging) Imaging technique that produces detailed pictures of areas inside the body by linking a computer with a powerful magnet.

Multiple myeloma Disease of the bone marrow in which certain cells grow out of control and break down bone.

Oncology Branch of medicine dealing with cancer.

Pituitary gland Master gland in the brain that makes hormones that control hormone production in other glands such as the testes.

Prostate Male sex gland that produces fluid that forms part of semen.

Prostate-specific antigen (PSA) Protein produced by the prostate gland. PSA circulates in the blood and can be measured with a blood test. PSA levels go up in some men who have prostate enlargement, inflammation, infection, or prostate cancer.

Radiation oncologist Doctor who specializes in using radiation to treat cancer.

Radiation therapy Treatment with high-energy rays to kill cancer cells.

Scrotum External skin pouch containing the testes.

Testes Pair of egg-shaped glands contained in the scrotum that produce sperm and male hormones. Also called testicles.

Total androgen blockade Complete blockage of androgen production. Also called combination hormone therapy.

Tumor Abnormal growth of tissue. A tumor can be malignant (cancerous) or benign (noncancerous).

Urologist Doctor who specializes in disorders of the urinary system and male reproductive system.

Watchful waiting Following the patient closely, postponing aggressive therapy unless signs of disease progress.

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Selected Resources for Patients and Family Members

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Man to Man
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