



# OSTEOPOROSIS AND PROSTATE CANCER

PAUL R. SIEBER, M.D., F.A.C.S.  
Chief, Division of Urology, Lancaster General Hospital  
Urological Associates of Lancaster, Ltd.



## ABSTRACT

Men who are diagnosed with prostate cancer often have pre-existing osteoporosis. Androgen deprivation therapy (ADT) is effective in slowing advanced cancer, but contributes to bone loss. ADT-resistant cases often metastasize to bones that have been weakened by osteoporosis and ADT, resulting in significant morbidity and increased mortality. Several agents have been developed to reduce testosterone levels while building bone. If they prove effective in current clinical trials, they may save thousands of men from a life sentence of severe pain and disability.

## INTRODUCTION

Osteoporosis and prostate cancer have too much in common: they affect people at about the same age; they share several risk factors; and while they're rarely fatal, they both have a profound effect on the patient's quality of life. If you think we've overlooked an obvious "difference"—that osteoporosis is a "women's disease" and prostate cancer is a "man's disease"—then you need to be reminded of an interesting statistic: 1 out of every 5 Americans with osteoporosis is male.<sup>1</sup> That means that every man who gets prostate cancer has a good chance of having or developing osteoporosis as well. The literature provides a wealth of material on prostate cancer, but osteoporosis in men is just beginning to pique the interest of clinical investigators. Because of the high risk for comorbidity with prostate cancer, key aspects of the disease that are relevant specifically to men need to be explored.

In this article, we will examine the pathophysiology of osteoporosis in men, then take a look at prostate cancer to determine how these two disorders affect each other, and, finally, explore treatment issues in prostate cancer that must be addressed to preserve bone health.

## OSTEOPOROSIS: NOT FOR WOMEN ONLY

The most common image of the patient with osteoporosis is the older, postmenopausal woman who's lost a few inches in height and has had a fracture or two—usually in the hip, spine or wrist—from a fall that wouldn't

have caused more than a bump or a bruise a few years ago. Her clinician would automatically assume that she's lost some estrogen, which normally helps bone remodel itself fast enough to keep up with compression and load and repair lesions caused by injury or disease.<sup>2</sup> No matter what her primary complaint may be, it would be unusual for her clinician to not include a work-up for osteoporosis. For most women, the diagnosis is *primary osteoporosis*, which is associated with aging and hypogonadism.<sup>1</sup> Her clinician might prescribe an antiresorptive agent to reduce the risk for future fractures and advise her to correct as many of the risk factors for the disease (Table 1) as possible.<sup>3</sup>

## How Do Men Get Osteoporosis?

Surprisingly, men get osteoporosis the same way women do: by losing estrogen.

More specifically, they lose *estradiol*, a metabolite of testosterone that is released through aromatization and carries out the same bone-related activities seen in women. A second major testosterone metabolite—*dihydrotestosterone (DHT)*—also plays a role in bone health. This role is not yet entirely clear, although preliminary studies suggest that it promotes periosteal apposition and modulates the activity of several bone growth factors, including insulin-like growth factor I.<sup>4</sup>

With the continued production of testosterone and aromatase being virtually ubiquitous, the average 50-year-old man can produce about twice as much estradiol as a menopausal woman of the same age.<sup>4</sup> Consequently, the effects of aging leading to osteoporosis are usually not seen in men until about 15 years after they appear in women. Unlike women, however, men are more likely to develop osteoporosis secondary to an underlying condition or as an adverse effect of pharmacotherapy, i.e., his diagnosis is more likely to be *secondary osteoporosis* (Table 2).<sup>5</sup> A key contributor to osteoporosis in men is androgen deprivation therapy (ADT), a common approach to advanced cases of prostate cancer.

TABLE 1. RISK FACTORS FOR OSTEOPOROSIS IN MEN.

Type of Risk Factor	Risk Factor	Osteoporosis in Men	Prostate Cancer
Demographic	Age >50	Yes*	Yes*
	Race	White, Asian	Black > white > Asian
	Residence	beyond latitude 37° north and 37° south	N/A?†
	Environment	Heavily polluted	Carcinogens, radiation
Clinical	Serum IGF- I	Low	High
	Serum testosterone	Low	High
Genetic	Family history (1 <sup>st</sup> -degree relative)	Yes	Yes
	Inherited genetic mutations	<i>COLIA1</i> Sp1 polymorphism?‡	<i>BRCA1</i> , <i>BRCA2</i> , and <i>HPCG1</i>
Lifestyle	Sedentary	Yes	Yes
	Cigarette smoking	Yes	Yes
	Alcohol intake	Excessive	Excessive
	Sun exposure	Inadequate	Inadequate?†
Diet	Vitamin D	Low	Low
	Calcium intake	Low	High
	Red meat	N/A	High
	Fruits, vegetables	N/A§	Low

\* Risk increases dramatically at approx. age 65 years.

† Risk may apply, because it reduces sun exposure, thereby reducing an important source of vitamin D.

‡ Ralston SH, Uitterlinden AG, Brandi ML, et al, for the GENOMOS Investigators. *PLoS Medicine*. 2006;3:0515-0523. Available at: [www.plosmedicine.org](http://www.plosmedicine.org). Accessed August 2006.

§ Fruits and vegetables are important components of the diet for men with osteoporosis; however, few fruits and vegetables are rich sources of vitamin D or calcium, which are critical for bone health.

Sources: National Osteoporosis Foundation. Men and Osteoporosis. Available at: [www.nof.org/men/index.htm](http://www.nof.org/men/index.htm). Accessed on September 3, 2006.

Office of Dietary Supplements. What is Vitamin D? Available at: <http://dietary-supplements.info.nih.gov/factsheets/vitaminD.asp>. Accessed on July 23, 2006.

Are the Consequences of Osteoporosis Different in Men and Women?

Although men start adulthood with a greater bone mass than women, they face greater morbidity and mortality from osteoporosis.<sup>5</sup> That threat is most likely to result from clinical neglect. The detection of osteoporosis in men is often delayed because many clinicians simply don't look for it in men. An Australian study of more than 13,000 medical records of men older than 59 years revealed that fewer than 4% had been diagnosed with osteoporosis by a general practitioner (GP)—this in a country where prevalence rates run as high as 29% in men older than 60 years.<sup>6</sup> Furthermore, the GPs who did make a diagnosis failed to prescribe an antiresorptive agent—which reduces the risk for fracture—for almost half (46.6%) of their patients.<sup>6</sup> It shouldn't be surprising to learn, then, that half

of all age-related osteoporotic vertebral fractures occurs in men—even though men comprise only one fifth of the population with osteoporosis—and that men are at much greater risk for permanent disability due to a fracture and much more likely to die within 5 years of having one.<sup>4</sup>

The reasons for this oversight may sound familiar: the Australian GPs had only limited information about risk factors (Tables 1 and 2), accurate methods of diagnosis (Table 3), and appropriate methods of treatment (Table 4).<sup>6</sup> These are not mere excuses. Clinical guidelines for managing osteoporosis in men are lacking, principally because most of the research about this disease has been conducted in women. Although many of the findings in these studies are applicable to men, gender-specific issues have not yet been adequately addressed.<sup>4</sup>

TABLE 2. CAUSES OF SECONDARY OSTEOPOROSIS.<sup>11</sup>

Clinical		Pharmaceutical
AIDS/HIV	Liver disease, chronic	Adrenocorticotropin
Alzheimer's disease	Low IGF-I	Aluminum-containing antacids
Amyloidosis	low testosterone	Anticonvulsants
Ankylosing spondylitis	Lymphoma and leukemia	Aromatase inhibitors
Bed rest, prolonged	Malabsorption syndromes	Chemotherapy
Celiac disease	Movement disorders (e.g., Parkinson's disease)	Corticosteroid therapy
Cerebrovascular accident	Multiple myeloma	Glucocorticoids, excessive
COPD	Multiple sclerosis	Glucosteroids
Congenital porphyria	Pernicious anemia	Gn-RH agonists
Cushing syndrome	Renal insufficiency	Heparin (long-term use)
Gastrectomy	Rheumatoid arthritis	Immunosuppressants
Gaucher's disease	Severe liver disease	Lithium
Hemochromatosis	Spinal cord transection	Methotrexate
Hemophilia	Sprue	L-Thyroxine, overreplacement
Hyperparathyroidism, primary	Stroke	TPN
Hyperthyroidism	Systemic lupus erythematosus	
Hypogonadism	Thalassemia	
Idiopathic scoliosis	Thyrotoxicosis	
Inflammatory bowel disease	Type I diabetes mellitus	

IGF-I, insulin-like growth factor-I; COPD, chronic obstructive pulmonary disease; Gn-RH, gonadotrophin-releasing hormone; TPN, total parenteral nutrition.

**Is Osteoporosis Management Different for Men and Women?**  
Not really.

The *clinical assessment* is similar in men and women (Table 3). The diagnosis is based on *bone mineral density (BMD)*, preferably measured in the hip and spine with dual energy x-ray absorptiometry.<sup>7</sup> This method is useful in both sexes after age 65 years, when bone loss rates are similar,<sup>5</sup> but it is limited in at least two ways. First, BMD is only one aspect of bone strength. Most work-ups don't address bone mass, which helps bone to withstand mechanical stress. Second, total reliance on BMD for the diagnosis means that early signs of osteoporosis could be missed in younger men, whose bone mass is greater to begin with. In such cases, non-BMD values should also be scrutinized carefully to find early signs of this disease. You should also *look for a cause of secondary osteoporosis* (Table 2). As discussed in the article by Reese in this Journal,<sup>8</sup> you'll need the patient's T-score—the number of standard deviations (SDs) between the patient's BMD and the mean BMD for a healthy 30-year-old—and Z-score—the number of SDs between the patient's BMD and the mean BMD for individuals of the same age, sex, and race. Patients with a Z-score at least 2 SDs lower than average (i.e., -2.0) and evidence of an osteoporosis-

inducing condition, and patients with a T-score lower than -2.0 coupled with a history of minimal-trauma fracture or physical signs of vertebral fracture should be evaluated for an underlying condition using relevant blood and urine studies before osteoporosis therapy is initiated (Table 3).

Because many of the risk factors (Table 1) for osteoporosis are under the patient's control, you should *encourage the patient to provide input for the treatment plan*. The choice of pharmacotherapy may be up to the clinician (Table 5), but other aspects of treatment are strongly related to lifestyle (Table 1) and require your patient's input to ensure optimal compliance.

*Follow-up* is an extremely important component of patient care. Encourage patients to keep regularly scheduled appointments so you can follow their progress and adjust treatment plans to meet their ongoing needs.

**THE SEARCH FOR OSTEOPOROSIS IN PATIENTS WITH PROSTATE CANCER**

Prostate cancer is the most common type of cancer (other than skin cancer) in the United States. It is diagnosed in more than 230,000 men each year<sup>9</sup>—which means that,

TABLE 3. DIAGNOSIS OF OSTEOPOROSIS.

Measurement	Rationale	Procedures	Normal Values*
BMD	To determine bone density	DEXA of hip, posteroanterior lumbar spine, femoral neck, or distal radius (nondominant arm)	<i>T-score:</i> ■ Normal: 2.1 – (–1.0) ■ Low bone mass: –1.0 –2.5 ■ Osteoporosis: ≤ –2.5 <i>Z-score:</i> + value: BMD exceeds average for age, race, sex – value: Bones are thinner than average for age, race, sex
Height	To find evidence of vertebral fractures	■ Change in linear height ■ Distance between lowest rib and pelvis ■ wall-to-occiput distance	■ Same, or decreased by ≤3 cm ■ ≥2 finger breadths ■ 0 cm
Chemistry profile	To rule out secondary osteoporosis	<i>Common tests (serum values):</i> ■ albumin ■ alkaline phosphatase ■ calcium ■ creatinine ■ phosphate ■ Testosterone, total ■ TSH ■ 25(OH)D  <i>Additional tests†:</i> ■ Celiac antibody profile ■ Cortisol, plasma (fasting--8:00 AM) ■ Protein electrophoresis (serum, total)	<i>Common tests:</i> ■ 3.3-5.2 g/dL ■ 35-150 U/L ■ 8.4-10.6 mg/dL ■ 0.2-0.5 mg/dL ■ 3.0-4.5 mg/dL ■ 300-1200 ng/dL ■ 0.4-4.8 μIU/mL ■ 32 ng/mL  ■ 6-23 μg/dL ■ 6-8 g/dL

\* Source: Andreoli TE, et al, eds. *Dorland's Illustrated Medical Dictionary*. 30<sup>th</sup> ed. Philadelphia, Pa: Saunders; 2003.

† Ordered when indicated by patient's clinical history.

potentially, 230,000 cases of osteoporosis go undetected every year.

**Why?**

Because nobody's looking for it—not in the primary care office, even though up to 25% of male patients are hypogonadal by their 70<sup>th</sup> year of life; not in the urology suite, even though the risk for osteoporosis increases in as many as 15% of patients in whom prostate cancer isn't cured by surgery (and in almost twice as many who aren't cured with radiation plus surgery) when they are given ADT (Table 5) to stop the cancer or slow its progression; and not the Rheumatologists, because they aren't asked to see these patients unless a complication develops and the diagnosis has been made.

**Osteoporosis in Prostate Cancer: How Do We Find It?**

Because of the age range in which prostate cancer develops, many men have a detectable degree of bone loss before they walk through our office door. For this reason, a work-up for osteoporosis should be part of the routine urological examination.

When the patient is also found to have prostate cancer, his risk for osteoporosis rises dramatically if he has substantial androgen activity. As long as his testosterone levels are high, he can produce enough estradiol to prevent osteoporosis, but when he responds to treatment, his testosterone level will fall, causing him to lose some of the protection estradiol provides. If the cancer starts to spread beyond the prostate, he may be switched to ADT,<sup>9</sup> which, if successful, will lower his testosterone

TABLE 4. TREATMENT OPTIONS BY STAGE OF CANCER.<sup>12</sup>

Stage	Patient Description	Treatment Options
I	<ul style="list-style-type: none"> <li>■ small, slow-growing tumor</li> <li>■ low Gleason score</li> </ul>	<p><i>For men who are asymptomatic, elderly, or who have serious comorbid disorders:</i></p> <ul style="list-style-type: none"> <li>■ watchful waiting</li> <li>■ radiation therapy: external beam or brachytherapy</li> </ul> <p><i>For younger, healthy men</i></p> <ul style="list-style-type: none"> <li>■ watchful waiting</li> <li>■ radical prostatectomy</li> <li>■ radiation therapy: external beam or brachytherapy</li> </ul>
II	tumors likely to spread without treatment	<p><i>For men who are asymptomatic, elderly, or have serious comorbidity:</i></p> <ul style="list-style-type: none"> <li>■ watchful waiting</li> <li>■ radical prostatectomy</li> <li>■ radiation therapy<sup>^</sup></li> </ul> <p><i>For men you are younger; otherwise healthy:</i></p> <ul style="list-style-type: none"> <li>■ radical prostatectomy with lymph node removal; may follow hormone therapy</li> <li>■ external beam radiation only</li> <li>■ brachytherapy only</li> <li>■ combination radiotherapy (external beam and brachytherapy)</li> </ul> <p><i>For men with stage T3 or high Gleason score:</i></p> <ul style="list-style-type: none"> <li>■ radical prostatectomy followed by external beam radiation radiation may be combined with hormone therapy x 3-6 mo</li> </ul>
III	<ul style="list-style-type: none"> <li>■ cancer has spread beyond prostate, but not to bladder, rectum, lymph nodes, or distant organs</li> <li>■ less of a chance of a cure</li> </ul>	<ul style="list-style-type: none"> <li>■ external beam radiation + hormone therapy</li> <li>■ hormone therapy only</li> <li>■ radical prostatectomy:                             <ul style="list-style-type: none"> <li>○ not nerve-sparing</li> <li>○ lymph nodes may be removed</li> <li>○ may following hormone therapy</li> <li>○ may be followed by radiation therapy</li> </ul> </li> </ul>
IV	<ul style="list-style-type: none"> <li>■ cancer has spread to bladder, rectum, lymph nodes, or distant organs (e.g., bone)</li> <li>■ not considered curable</li> </ul>	<p><i>In most cases:</i></p> <ul style="list-style-type: none"> <li>■ hormone therapy</li> <li>■ external beam radiation + hormone therapy</li> <li>■ TURP to relieve symptoms</li> </ul> <p><i>For older men without symptoms or with serious comorbidity:</i></p> <ul style="list-style-type: none"> <li>■ watchful waiting</li> </ul>

levels dramatically, removing estradiol protection virtually altogether and, thus, sentencing him to a lifetime of significant bone-related morbidity, especially when the cancer metastasizes to bone.

**Current Osteoporosis-fighting Options for Patients With Prostate Cancer**

The best defense against osteoporosis in prostate cancer is to identify patients with a high risk for fracture during the first clinical visit, select an effective anti-osteoporosis agent, and advise the patient to change his lifestyle and diet to prevent further bone loss. The only reliable pharmacotherapeutic option currently available

is the bisphosphonate alendronate (Fosamax); another bisphosphonate—risedronate (Actenol)—is also indicated for men, but has not been studied in men receiving ADT. Two intravenous bisphosphonates have been suggested as alternatives for patients who cannot tolerate the oral formulation: pamidronate (Aredia) and zoledronate (Zometa). Pamidronate appears to slow the rate of bone loss in patients with prostate cancer, but does not seem to increase bone mass. Moreover, its tolerability is poor because of a prolonged perfusion period. It has virtually been replaced by zoledronate, which has a considerably shorter infusion time (4 h vs ≥15 min) and builds bone in men with prostate cancer.



Bisphosphonates are adequate during the earliest stages of the disease, when the options are watchful waiting and a radical prostatectomy, radiation therapy, or both. If the cancer does not respond and starts to spread beyond the prostate gland, we usually switch to ADT, often with radiation therapy.<sup>9</sup> All efforts must be made to preserve bone strength because of the risk for metastasis to bone. Unfortunately, bone-building drug choices are slim to none at this point. *Alendronate* is still the best choice in advanced cancer. If that doesn't work, we could try *low-dose estrogen*—but we'd have to monitor the patient for thromboembolic events. And there's always *zoledronate*—which has been tested on all of 100 men. If none of these options is suitable, the patient may face a future of severe pain and disability.

#### WHAT DOES THE FUTURE HOLD FOR TREATMENT OF PROSTATE CANCER?

Several new therapeutic approaches to hormone-refractory prostate cancer are currently under investigation.

##### New drugs

New agents include *denosumab*, a human monoclonal antibody that inhibits the RANK ligand (RANKL). RANKL promotes the formation, activity, and survival of osteoclasts and, thus, supports the breakdown of bone. Denosumab blocks its effects by inhibiting osteoclast activity and enhancing osteoblast activity to build bone mass. Interim data from two phase 2 studies suggest that denosumab rapidly suppresses bone turnover after the cancer has metastasized to bone, whether the patient is receiving IV bisphosphonate therapy or not.<sup>10</sup> This drug has been investigated in patients with breast cancer (N = 255) or multiple myeloma (N = 49) receiving chemotherapy or hormone therapy. A phase 3 trial in prostate cancer is currently under way, with preliminary results expected shortly.

*Selective estrogen receptor modulators (SERMs; e.g., raloxifene)* modulate estrogen receptors to stimulate their beneficial effects in bone while blocking harmful effects in the prostate. Additional benefits include the suppression of hot flashes in men<sup>11</sup> and the promotion of a positive lipid profile, coupled with an ability to increase bone density and reduce the risk for fracture at rates similar to those achieved with bisphosphonates.

The *selective androgen receptor modulators (SARMS)* have demonstrated their ability to reduce peripheral levels of

testosterone while maintaining its anabolic effects in bone and muscle.<sup>12,13</sup> *Toremifene (Fareston)* is a nonsteroidal agent that binds with estrogen receptors in breast, bone, and prostate tissue, where it acts as an agonist or antagonist, depending on the tissue, duration of treatment, gender of the patient, or target organ.<sup>14</sup> In a recent study in men with high-grade prostatic intraepithelial neoplasia (N = 447), toremifene 20 mg was associated with a significant reduction in the risk of prostate cancer and in its prevention, compared with a placebo, with the same overall incidence of drug-related and serious adverse events as seen with placebo.<sup>15</sup>

Because exogenous parathyroid hormone (PTH) can thwart the bone-resorbing activity of the endogenous hormone, PTH analogs have been investigated for their ability to prevent osteoporosis in patients with advanced prostate cancer, but the results have been disappointing. The PTH analog *teriparatide (Forteo)* cannot be recommended for this purpose because it carries a black box warning of an increased risk for osteosarcoma.<sup>16</sup> Also it is associated with increased bone turnover rates during ADT and cannot be used in patients who require radiation.

##### Treatment design

Some investigators suggest *watchful waiting* to avoid the adverse effects of ADT. While the tumor is still well localized and slow-growing, and the patient has no symptoms, they recommend monitoring its progress with an annual biopsy, twice-yearly prostate serum antigen (PSA) and digital rectal exams, and frequent monitoring of the BMD and chemistry panel (calcium, PTH, liver function tests, etc.).<sup>9</sup> If the PSA doubles in less than 3 years, they recommend starting treatment and continuing BMD and biochemical monitoring throughout ADT.<sup>17</sup>

Others have suggested *intermittent hormone therapy*—an on-again/off-again ADT dosing strategy—to minimize the risk of its long-term effects. Some prescribe an LHRH agonist until the PSA falls to its lowest level (<4 ng/mL), then reinstate ADT when the PSA rises to its maximum level (10-20 ng/mL).<sup>18</sup> This approach is problematic, however, because the side effects don't stop when the therapy does, especially during the first 6 to 12 months of administration. This strategy slows the rate of bone loss, but it doesn't build bone effectively, and is unlikely to be the most efficient way to restore bone strength.

## CONCLUSION

We have a tendency to overlook osteoporosis in men. Whether this is because of a lack of male-specific guidelines or a bias toward thinking of osteoporosis as a “woman’s disease,” the result has been an unacceptable number of men experiencing permanent disability—even death—following an osteoporotic fracture. With prostate cancer and osteoporosis sharing many risk factors, there is a considerable risk for comorbidity. Certain anti-cancer drugs—particularly androgen deprivation therapy (ADT)—exacerbate osteoporosis

by removing testosterone and its anabolic effects on bone, thereby sharply increasing the risk for fracture. These effects can be reduced by improving BMD before initiating cancer therapy, selecting antineoplastic agents carefully (especially true for ADT), and monitoring patients closely for early signs of recurrence. The future holds promise for drugs that can modulate hormone receptors to reduce testosterone levels while building bone. Perhaps we’ll soon have the tools to fight prostate cancer effectively without threatening the integrity of bone.

## REFERENCES

1. National Osteoporosis Foundation. Fast Facts. Available at: [www.nof.org/osteoporosis/diseasefacts.htm](http://www.nof.org/osteoporosis/diseasefacts.htm). Accessed August 21, 2006.
2. Kaji H, Sugimoto T, Kanatani M, Nasu M, Chihara K. Estrogen blocks parathyroid hormone (PTH)-stimulated osteoclast-like cell formation by selectively affecting PTH-responsive cyclic adenosine monophosphate pathway. *Endocrinology*. 1996;137:2217-2224.
3. Rizzoli R, Bonjour J-P, Ferrari SL. Osteoporosis, genetics, and hormones. *J Mol Endocrinol*. 2001;26:79-94.
4. Rochira V, Balestrieri A, Madeo B, Zirilli L, Granata ARM, Carani C. Osteoporosis and male age-related hypogonadism: roles of sex steroids on bone (patho)physiology. *Eur J Endocrinol*. 2006;154:175-185.
5. US Department of Health and Humans Services. *Osteoporosis in Men*. Bethesda, Md: National Institutes of Health Osteoporosis and Related Bone Diseases—National Resource Center; 2005.
6. Chiang A, Jones J, Humphreys J, Farnell B, Martin C. Osteoporosis: diagnosis and treatment in a general practice population. *Aust Fam Physician*. 2006;35:166-168.
7. National Osteoporosis Foundation. *Physician’s Guide to Prevention and Treatment of Osteoporosis*. Washington, DC: National Osteoporosis Foundation; 2003. Available at: [www.nof.org/physguide](http://www.nof.org/physguide). Accessed on August 24, 2006.
8. Reese, RW: Vitamin D and Bone Health. *Jl Lancaster Gen Hosp*. 2006; Vol 1, No. 3:78-87.
9. American Cancer Society. Cancer Reference Information. Detailed Guide: Prostate Cancer. Available at: [www.cancer.org/docroot/CRI](http://www.cancer.org/docroot/CRI). Accessed on September 3, 2006.
10. Amgen. Press Release Detail: Phase 2 Interim Data Show Denosumab Decreased Bone Turnover in Advanced Cancer Patients With Bone Metastases. Available at: [www.amgen.com/media\\_pr\\_detail.jsp?releaseID=868226](http://www.amgen.com/media_pr_detail.jsp?releaseID=868226). Accessed September 12, 2006.
11. GTx Discovery Innovation. SERM. Available at: [www.gtxinc.com/tech/serm.htm](http://www.gtxinc.com/tech/serm.htm). Accessed September 12, 2006.
12. Chen J, Hwang DJ, Bohl CE, Miller DD, Dalton JT. A selective androgen receptor modulator for hormonal male contraception. *J Pharmacol Exp Ther*. 2005;312:546-553.
13. GTx Discovery Innovation. SARM. Available at: [www.gtxinc.com/tech/sarm.htm](http://www.gtxinc.com/tech/sarm.htm). Accessed September 12, 2006.
14. FARESTON® Prescribing Information. Memphis, Tenn: GTx, Inc.; 2004.
15. Price D, Stein B, Sieber P, et al. Toremifene for the prevention of prostate cancer in men with high grade prostatic intraepithelial neoplasia: results of a double-blind, placebo controlled, phase IIB clinical trial. *J Urol*. 2006;176:965-970.
16. Forteo® teriparatide (rDNA origin) injection Prescribing Information. Indianapolis, Ind: Eli Lilly and Company; 2004.
17. Holmes-Walker DJ, Woo H, Gurney H, Do VT, Chipps DR. Maintaining bone health in patients with prostate cancer. *MJA*. 2006;183:176-179.
18. McLeod N, Huynh CC, Rashid P. Osteoporosis from androgen deprivation therapy in prostate cancer treatment. *Aust Fam Physician*. 2006;35:243-245.

Paul R. Sieber, M.D., F.A.C.S.  
 Chief, Division of Urology, Lancaster General Hospital  
 Urological Associates of Lancaster, Ltd.  
 2106 Harrisburg Pike, Suite 200  
 Lancaster, PA 17604  
 717-393-1771  
 psieber610@aol.com