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July 2005 "Prostate Cancer & BPH" 707-000-05-007-H01

THIS MONTH
"Prostate Cancer & BPH"

IT'S ALWAYS A GOOD IDEA TO GET QUIZZES IN TO US AS EARLY IN THE YEAR AS POSSIBLE.

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HAVE YOU RECENTLY MOVED? PLEASE NOTIFY US.

Prostate cancer and benign prostatic hyperplasia (BPH) are common diseases that mostly affect men over the age of 45. Our goal is to provide information regarding recognition and treatment of these conditions. This lesson provides 1.25 hours (0.125 CEUs) of credit, and is intended for pharmacists in all practice settings.

The program ID # for this lesson is 707-000-05-007-H01.

Pharmacists completing this lesson by July 31, 2008 may receive full credit.

To obtain continuing education credit for this lesson, you must answer the questions on the quiz (70% correct required), and return the quiz. Should you score less than 70%, you will be asked to repeat the quiz. Computerized records are maintained for each participant.

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The objectives of this lesson are such that upon completion the participant will be able to:

1. State the signs & symptoms as well as the diagnosis of prostate cancer.
2. List the risk factors associated with prostate cancer.
3. Describe the treatments for both localized & metastatic prostate cancers.
4. Differentiate between prostate cancer & BPH.
5. State the signs, symptoms and treatment associated with BPH.

BACKGROUND

Prostate cancer and benign prostate hyperplasia (BPH) are common diseases that mostly affect men over the age of 45. The main disorders of the prostate are due to infection and growth. In the scope of this lesson, focus will be placed on prostate cancer which is the main and most serious growth disorder. Benign prostatic hyperplasia will be briefly discussed.

PROSTATE CANCER

Prostate cancer (prostate carcinoma) continues to be a leading cause of morbidity and mortality in men. In 1997, approximately 210,000 cases were identified, and 41,000 deaths were reported in the U.S. It is the third leading cause of cancer in men (after cancers of the lungs and colon). Prostate cancer is different because it may stay dormant for many years, and it does not cause health problems or significant symptoms. However, some types can be aggressive. If the disease is not diagnosed in a timely fashion, or is misdiagnosed, it may metastasize to other parts of the body. Prostate cancer is rare in young men, but its incidence increases with each decade after the age of 45. Approximately 14 deaths per 100,000 men occur annually in the U.S. as a result of this disorder, compared to 22 in Sweden and 2 in Japan. It is important to observe that American Japanese experience the same death rate as Caucasian Americans, indicating that diet and environmental causes play a role in these differences. Additionally, the disease is more common among African Americans.

SIGNS AND SYMPTOMS

More than 95% of prostate cancers are adenocarcinomas. In the vast majority of cases, the carcinoma arises in either the outer portion of the prostate gland (periphery), or in both the periphery and the center. The origin of the carcinoma in over 85% of the patients is multifocal rather than a single site. In general, prostate cancer is a slowly progressing disease and may be asymptomatic at the time of diagnosis. In symptomatic cases, that may occur late in the course of the disease, the patient may complain of urethral obstruction such as dysuria, difficulty in voiding, increased urinary frequency, urinary retention, pyuria, and hematuria. The disease metastasizes either by local extension or through the lymph system or blood. If it remains untreated, it may extend to the urethra, bladder neck, and seminal vesicles. Involvement of the bones may occur as a result of hematogenous dissemination. Bone metastases usually occur in the pelvis, lumbar spine, femur and ribs. Less common sites of metastases involve the lungs and liver. Back or hip pain may develop.

DIAGNOSIS

Digital rectal examination (DRE) may indicate a healthy prostate gland, or it may raise suspicion that the tissue is malignant. A diseased prostate is usually hard, nodular and irregular. However, these signs must be differentiated from the fibrous tissue that may occur in benign prostatic hyperplasia, granulomatous prostatitis, and prostatic calculi. Induration of the cancerous gland may extend laterally into the seminal vesicles that often can be detected by DRE. Measurement of the PSA, which is a protein found in semen and blood, often rises in men with prostate cancer. A PSA level of less than 4 nanograms per milliliter (ng/ml) is considered normal. However, the PSA results can become somewhat complicated. A range of PSA values of 4 to 10 ng/ml are somewhat ambiguous. About 65% of cases show elevation in the PSA, and 35% indicate false-negative results. While PSA measurement is helpful for early detection, it should not be considered as the perfect tumor marker. Elevation of PSA may occur in patients who suffer from BPH, prostatitis, and prostate infection. The levels of PSA are

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higher in African American men who are more likely to develop earlier and more aggressive types of the disease. Furthermore, it has been reported that some patients with PSA levels less than 4 did have prostate cancer. It appears that rapidity at which the PSA is rising is a better predictor of aggressive cancer. For these reasons, the use of PSA for prostate cancer screening is a controversial issue in disease prevention and detection. PSA screening should be performed on an individual basis after the age of 50. A combination of DRE and PSA serum level allows detection of cancer. If DRE indicates an abnormality and/or PSA level is about 10 ng/ml, a transrectal or transperineal needle biopsy should be performed. If the DRE is negative and PSA value is less than 4 ng/ml, an annual examination is warranted. The issue becomes unclear if the DRE is negative and PSA level is between 4 and 10 ng/ml. Some physicians may seek ultrasound tests or may perform a biopsy. Biopsy is fundamental in confirming the diagnosis. It is employed when abnormality is suspected by DRE or PSA level measurement. Ultrasonagraphy and magnetic resonance imaging (MRI) as well as computed tomography (CT) of the prostate are helpful in diagnosis.

RISK FACTORS AND PROGNOSIS

The risk factors include age, family history, race, and smoking. Although the intake of a well-balanced diet is useful for the general health and well being of an individual, diet habits do not appear to increase the incidence of prostate cancer. BPH appears to be an insignificant risk factor.

Prognosis is good when disease is detected early. When the carcinoma is well differentiated, a five-year survival rate occurs in approximately 95% of patients, and 15-year survival rate occurs in approximately 83% of the patients. Poorly differentiated cases have approximately 58% five-year survival rate and a 25% 15-year survival rate. Confirmation of metastases at the time of diagnosis of the disease leads to a poor prognosis.

TREATMENT

Depending on its progression, prostate cancer can be localized or metastatic in nature. The method of treatment depends on the extent of tumor involvement.

Localized Prostate Cancer: Treatment of patients with localized prostate cancer in the early stages (A, B, and C) varies from observation with regular checkups to specialized therapy. Stage A is occult and non-palpable; Stage B constitutes the stage in which the tumor is confined to the prostate gland; and, in Stage C, the tumor is localized to the periprostatic area. The standard therapy for localized prostate cancer includes observation, irradiation, or radical prostatectomy. Not all physicians agree on the best course of treatment. Maintaining a good quality of life and increasing the rate of survival are goals that clinicians attempt to realize. There is no perfect method of treatment because each mode is associated with undesirable adverse effects. Nonetheless, treatment should be individualized and the selection of which course to follow depends on these factors: patient's age, disease stage, comorbid disorders, lifestyle, life expectancy and general health of the patient. In cases where the cancer is in the early stage and is confined to the prostate gland and is asymptomatic, some physicians may decide that **observation** is the best course of treatment. The patient, however, will be advised to have regular checkups to ensure that the malignancy remains confined to the prostate gland. An alternate treatment is **radical prostatectomy** that involves removal of the gland. The surgery is not required if the carcinoma is in the early stages where simple prostatectomy may be performed. In the past, such procedures resulted in impotence in most patients and increased the risk of urinary incontinence. However, progress in surgical techniques has enabled surgeons to preserve the neurovascular supply to the corpora cavernosa of the penis, thereby maintaining potency in most patients, in particular those under the age of 60. **Radiation** may be utilized in treating localized prostatic malignancy and to relieve pain associated with metastases of the bone. This method of treatment was instituted to avert impotency and incontinence caused by prostatectomy. Mega voltage radiation to the prostate over a period of several weeks may be used. Side effects of external radiation include impotency in 30% to 60% of patients, chronic proctitits, and rectal bleeding. In interstitial radiation, radioactive seeds are implanted retropubicaly or perianaly to provide radiation to the diseased tissue. In this method, potency is maintained by 90% of the patients and side effects are fewer and milder than those encountered in external beam radiation. Reports indicate that radiotherapy may be less effective than prostatectomy.

Metastatic Prostate Cancer: Hormonal therapy is among the first treatments that are usually attempted upon the initial detection of metastatic prostate cancer. Androgens are responsible for the growth of the normal cells of the gland at puberty and during the fourth decade of life. Thus, both normal and neoplastic cells of the prostate are testosterone dependent. Because of such relationships, it became apparent that depriving the body of its androgen might lead to suppression of growth of the diseased cells and provide relief in the metastatic prostate cancer. Androgen deprivation can be achieved by several methods: 1) surgical excision of testicles (orchiectomy, castration) or medical castration; 2) combined androgen blockade; 3) antiandrogen withdrawal; 4) intermittent therapy; and, 5) antiandrogen monotherapy. It should be remembered that hormonal deprivation and hormonal therapy are not curative. With time, the cancer cells that initially respond positively to hormone deprivation ultimately progress to hormone-refractory (resistant) cancer, and any hormonal therapy becomes ineffective in cancer suppression. Currently **chemotherapy** may be utilized in such cases for its palliative effect. **Surgical excision of testicles or medical castration** leads to reduction in endogenous androgen. Orchiectomy is an uncomplicated surgical procedure that results in androgen (most importantly testosterone) deprivation. In spite of its effectiveness, patients prefer medical castration because of the emotional distress caused by removal of the testicles. Medical castration can be accomplished by using drugs such as estrogens, luteinizing hormone-releasing hormone (LHRH, also known as gonadotropine-releasing hormone GnRH), antiandrogens, and progestational agents.

1. **Estrogens such as diethylstilbestrol (DES)** alone or in combination with orchiectomy were a standard therapy for many years. The testes secrete about 95% of blood testosterone, and the adrenal is responsible for secreting the remainder. Since it inhibits the release of luteinizing hormone (LH), the gonatropine that regulates the production of testosterone, DES intake can result in a decline in testosterone blood level similar to that caused by orchiectomy. The main drawback of administering high doses of DES is increased incidence of thromboembolic events. Currently, LHRH analogues have for the most part, replaced DES therapy.

2. **LHRH analogues** such as leuprolide and goserelin act by inhibiting LH secretion and lowering plasma testosterone levels. **Leuprolide** is used mainly for palliative effect because it is ineffective in changing progression of the disease. It is used as an alternative to surgical castration and estrogen therapy. Its advantages include avoidance of the psychological factors associated with surgical castration and the cardiovascular adverse effects caused by estrogens. The drug is administered subcutaneously once daily, or intramuscularly once a month by employing long-acting injections. In the early stages of therapy, leuprolide mimics the action of LHRH. This activity results in stimulation of the pituitary gland to release LH, which in turn acts to stimulate the testes to produce testosterone. However, as the treatment continues, the pituitary LHRH receptors become desensitized, resulting in a decrease in the release of LH, and ultimately a decline in testosterone plasma levels that may reach those observed after castration. Side effects of leuprolide include hot flashes, impotence, loss of libido, and urinary obstruction.

Goserelin has similar mechanisms of action and side effects like leuprolide. It is administered as a pellet that is implanted by subcutaneous injection in the upper abdominal wall.

3. **Antiandrogens**, also known as androgen receptor antagonists, include flutamide, bicalutamide, nilutamide, ketoconazole, and aminoglutethimide. As the name indicates, these medications act by blocking androgen receptors in the prostate and seminal vesicles where arrest of the growth of the tumor cells occur.

Flutamide: Flutamide is a nonsteroidal selective antiandrogen with no hormonal activity. The drug is used in combination with a gonadotropine-releasing hormone agonist such as leuprolide or goserelin. The survival rate of the use of flutamide along with leuprolide is 3 years compared to 2.3 years when leuprolide is used alone. Inhibition of androgen receptors in the prostate cell may result in suppression of growth of the hormone-sensitive cancerous cells. Flutamide possesses no antiestrogenic, antiprogestational, or antigonadotropic activities. During therapy, PSA levels should be monitored periodically in order to determine the efficacy of the treatment. Because of its potential for causing hepatic toxicity, serum transaminase levels should be determined on a monthly basis for the initial 4 months of therapy and periodically thereafter. If the patient becomes jaundiced, or if liver function tests become elevated, the use of the drug should be discontinued. Other adverse effects include gynecomastia, nausea, vomiting, diarrhea, and facial flushing, which can be aggravated if alcohol is consumed during therapy. The drug is administered orally after which it is absorbed rapidly. Most of the dose is converted to at least 6 metabolites on the

first pass through the liver. Flutamide and its metabolites are excreted in the liver. The drug is not recommended for patients with severe liver dysfunction. The usual dose is 250 mg, 3 times daily.

Nilutamide: Nilutamide is related to flutamide in structure and mechanism of action. If used alone, it may cause an initial increase in testosterone level due to blockade of the negative feedback mechanism that causes testosterone release.As a result, the drug should be used in combination with either orchiectomy or the administration of LHRH analogues. Nilutamide may cause hepatitis and an increase in transaminase levels, dyspnea, cough, chest pain, photophobia and lack of adaptation to changes in light to dark. Patients should be cautioned about driving at night. Nilutamide is administered orally in doses of 300 mg once daily for 30 days followed by 150 mg once daily.

Bicalutamide: Bicalutamide has a structure and pharmacologic activity similar to flutamide and nilutamide. It is usually used in combination with LHRH analogues such as leuprolide and goserelin. Precautions suggested during flutamide and nilutamide therapy should be followed when using bicalutamide. The drug is administered orally. The usual dosage is 50 mg, once daily.

Ketoconazole: Ketoconazole belongs to the azole antifungal agents. In addition to its antifungal activity, studies have shown that it is capable of inhibiting testicular and adrenal steroid synthesis, and, thus, reduces the androgen production. In addition, ketoconazole acts as a cytochrome P-450 system inhibitor. The drug is administered orally in a dose of 400 mg, three times daily compared to the antifungal activity dose of 200 mg, once daily. Adverse effects of ketoconazole include hepatotoxicity, rash, itching, nausea, constipation, diarrhea, photophobia and headache. The drug should be discontinued at the first signs of liver dysfunctions.

Aminoglutethimide: Aminoglutethimide is considered a corticosteroid synthesis inhibitor. It accomplishes this by blocking the first step in the synthesis of adrenal steroids. However, its mechanism of action in prostate cancer therapy is unknown. It may be used as an alternative to bilateral adrenalectomy. It is used mainly to provide palliation.

Chemotherapy: Orchiectomy and the use of antiandrogenic agents and estrogens as well as other agents such as ketoconazole and aminoglutethimide do not provide a cure for either localized or metastatic prostate cancer. The hormone-sensitive cancerous cells of the prostate may initially respond to hormonal therapy. However, after a lengthy treatment, these cells become hormone-refractory and hormone therapy becomes ineffective. Once this refractory phase is reached, the disease is classified as androgen-independent prostate cancer (AIPC). In such patients, therapies are mainly palliative and do not improve survival rate. Chemotherapy provides palliation, improvement in quality of life, especially pain reduction, and a decline in PSA levels in patients with AIPC. Two chemotherapeutic agents have been approved by the FDA for managing metastatic prostate cancer: mitoxantrone and estramustine.

Mitoxantrone: Structurally, it is similar to the antineoplastic antibiotics doxorubicin and daunorubicin. Its mechanism of action is not fully understood. It has been postulated that it may exert its antineoplastic action by blocking the activity of the enzyme topoisomerase II. Mitoxantrone is used mainly in combination with prednisone in palliative treatment of hormone-resistant metastatic prostate cancer. The use of these drugs did not improve the survival rate, but may cause pain relief and better quality of life. The drug is administered by IV infusion. The mitoxantrone concentrate must be diluted prior to injection. The recommended dosage is 12 –14 mg/m^2, administered as an IV infusion once every 21 days, along with oral prednisone, 5 mg, twice daily.

Estramustine: As the name indicates, estramustine is a combination of estradiol and nitrogen mustard. This drug, which is considered an antimicrotubule antineoplastic agent, has shown some effect on AIPC when used alone. Some synergistic activity occurred when the drug was used in combination with other microtubule inhibitors. Occurrence of adverse effects such as granulocytopenia, nausea and edema formation prompted patient non-compliance.

Paclitaxel and docetaxel: Paclitaxel, a natural or semisynthetic drug obtained from the bark of the western yew, or produced from the needles and twigs of more prevalent yew, is an antimicrotubule antineoplastic agent. Docetaxel is obtained from the needles of European yew. Both drugs have similar actions and may be used in the management of metastatic prostate cancer. No significant effect on AIPC is indicated when paclitaxel is used alone; however, when used in combination with estramustine, positive responses were observed in PSA levels. Monotherapy with docetaxel caused improvement in AIPC and median survival rate was 27 months. Better results were obtained when docetaxel is used concurrently with estramustine.

BENIGN PROSTATIC HYPERPLASIA (BPH)

Hyperplasia is defined as excessive proliferation of normal cells in the normal tissue. BPH is a non-malignant enlargement of the prostate gland that occurs as a result of excessive growth of prostate nodules causing variable degrees of urinary bladder outlet obstruction. It is usually encountered in men 50 years of age and over. Microscopic examination of the prostate revealed that 70% of men by age 60, and 90% of men by age 70, have BPH. Routine clinical examinations indicate that nearly every man over the age of 45 exhibits some degree of enlargement of the prostate gland. Over a half million surgical procedures are performed annually in the U.S. to rectify this disorder. There is no clear evidence that BPH is a predisposing factor for the occurrence of prostate cancer.

ETIOLOGY

The growth of the prostate gland is stimulated by androgens. Dihydrotestosterone stimulates the epithelial and stromel cells of the prostate gland. While estrogen has no direct stimulatory effect on the prostate tissue, it increases the number of hormone receptors on the prostate, thereby intensifying the stimulation caused by testosterone and dihydrotestosterone. A result of this growth is an increase in the size of nodules within the prostate. The enlarged prostate located around the urethra may place pressure on the urinary bladder outlet, restricting the flow of urine from the bladder. The enlarged prostate may compress posteriorly to obstruct the rectum, causing constipation.

SIGNS AND SYMPTOMS

Obstruction of the bladder outlet is the main symptom. It is characterized by frequent urination, difficulty in starting or stopping urinary stream, which is usually weak, nocturia, resulting from incomplete voiding, frequent urination, feeling of incomplete emptying, terminal dribbling, incontinence, and obstruction of all urinary flow (urinary retention). Urinary tract infection, bladder hypertrophy and kidney damage may develop. Hematuria may occur as a result of rupture of the congested superficial veins of the prostate while the patient is straining to void. Even though BPH is not a life-threatening disorder, there are risks. Stagnant urine remaining in the bladder may initiate an infection. Likewise, kidney infection may occur as a result of the pressure generated within the bladder as a result of blocked or hampered urinary outflow. Additionally, chronic BPH may result in dysfunction of the muscles of the bladder, causing lack of expelling of urine (urine retention) which can be acute.

DIAGNOSIS

Men over the age of 50 who complain of symptoms of urinary bladder outlet obstruction should be suspected as a candidate of BPH. DRE usually reveals an enlarged rubbery prostate. Cystoscopy allows estimation of the extent of enlargement.

TREATMENT

Treatment is required in about 50% of men who develop BPH. Individuals with mild symptoms often require no treatment, but patients who experience moderate to severe symptoms may need intervention. Treatment includes drug therapy, transurethral resection of the prostate, transurethral incision of the prostate, prostatectomy or balloon dilation. Drug therapy is usually the first treatment of choice, with surgery attempted in patients whose symptoms persist after the use of medications. The main drugs used for treating BPH are $alpha_1$–adrenergic blocking agents and 5-alpha reductase inhibitors. The $alpha_1$–adrenergic blocking agents include doxazosin, tramsulosin, and terazosin. By blocking the alpha-adrenergic receptors, these agents act as a smooth muscle relaxant in the prostate, as well as the neck of the bladder, with subsequent increase in urinary flow. Side effects of these medications include orthostatic hypotension, reflex tachycardia, nasal congestion and inhibition of ejaculation. To minimize the postural hypotension caused in the initial doses, the medications should be started in lower doses and gradually increased. Patients should be cautioned about the first-dose effect that may cause fainting. The 5-alpha reductase inhibitors, such as finasteride, act by inhibiting the conversion of testosterone to dihydrotestosterone in the prostate gland. This inhibitory action results in reduction in the size of the prostate by causing atrophy of the prostate glandular epithelium. Side effects include impotence, decreased libido and decreased ejaculatory

volume. Saw palmetto is an herbal agent that has been used for BPH. Its mechanisms are unknown, and the FDA has not approved it for such treatment.

The intent of surgical treatment is the removal of the hypertrophied prostate tissue with a loop-shaped resection device. Laser electrothermal intervention or open prostatectomy may be utilized. Most surgical procedures result in relief of urinary problems associated with BPH, and such problems seldom recur. Patients seldom become impotent after surgery, but some may have normal erection but may become sterile due to the backward flow of semen into the bladder without causing any detrimental effects. However, sterility is not a critical issue for most men over 55 years of age.

SUMMARY

Prostate cancer is a leading cause of morbidity and mortality worldwide among men over 45 years of age. The disease is somewhat silent in that it may stay dormant for many years without causing serious health problems or significant symptoms. Certain types of prostate cancer can be aggressive. In symptomatic cases, that may occur late in the progression of the disease, the patient may complain of urethral obstruction, difficulty in voiding, increased urinary frequency, pyuria, hematuria and even urinary retention. Untreated, prostate cancer may metastasize to the bones. Diagnosis of the disease consists of a combination of tests such as DRE, PSA and cone-needle biopsy. Other helpful tests include MRI, ultrasonagraphy and CT of the prostate gland. The main risk factors of prostate cancer are advanced age, family history, race, and smoking. Diet as well as BPH appear to be insignificant risk factors.

Prostate cancer can be either localized or metastatic in nature. The treatment is based on the extent of the tumor involvement. In confined, localized prostate cancer, observation, irradiation, or radical prostatectomy may be attempted. The treatment is usually individualized depending on the age of the patient, disease stage, comorbid disorders, lifestyle, and life expectancy. Treatment of metastatic prostate cancer includes androgen deprivation (orchiectomy or medical castration), combined androgen blockade, antiandrogen withdrawal, intermittent therapy and antiandrogen monotherapy, and chemotherapy.

Benign prostate hyperplasia is a nonmalignant enlargement of the prostate gland. Nearly all men over 45 years of age have some degree of enlargement of the prostate. Symptoms of BPH include frequent urination, hesitancy, weak stream, nocturia, feeling of incomplete emptying, terminal dribbling, incontinence, and, in severe cases, urinary retention. Treatment of BPH may be required in 50% of the patients. Individuals with mild symptoms often require no treatment. However, those with moderate to severe symptoms may need medical attention. Treatment may be achieved by pharmacologic therapy or surgery. The drugs used are alpha$_1$–adrenergic blocking agents and 5-alpha reductase inhibitors. Many use the herbal agent, saw palmetto; however, this agent has not been approved by the FDA for treating BPH.

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LESSON EVALUATION

Please fill-out this section as a means of evaluating this lesson. The information will aid us in improving future efforts. Either circle the appropriate evaluation answer, or rate the item from 1 to 7 (1 is the lowest rating; 7 is the highest).

1. Does the program meet the learning objectives?

State signs, symptoms & diagnosis of prostate cancer	Yes	No
List risk factors of prostate cancer	Yes	No
Differentiate between prostate cancer & BPH	Yes	No
State the signs, symptoms & treatment of BPH	Yes	No

2. Was the program independent & non-commercial? Yes No

	Poor			Average			Excellent
3. Relevance of topic to your practice	1	2	3	4	5	6	7
4. Author's ability to communicate	1	2	3	4	5	6	7

5. What did you like most about this lesson?_____

6. What did you like least about this lesson?_____

7. How would you improve this lesson?_____

8. Further comments or suggestions for future programs_____

(WATCH OUR WEBSITE FOR RESULTS OF PARTICIPANT EVALUATIONS)

Quiz—Please Select the Most Correct Answer

1. Finasteride acts as:
   A. Inhibits conversion of testosterone to dihydrotestosterone in the prostate
   B. Acts as an anti-inflammatory agent
   C. Relaxing the bladder smooth muscle
   D. Blocks the $alpha_1$ –adrenergic receptors
2. Prostate cancer:
   A. Is aggressive
   B. Metastasizes only in the bones
   C. Causes the prostate gland to become hard, nodular & irregular
   D. Results in a PSA level of less than 4
3. Which of these is not a risk factor?
   A. Diet
   B. Family history
   C. Age
   D. Race
4. Which of these is NOT standard therapy for localized, asymptomatic prostate cancer?
   A. Observation
   B. Radiation
   C. Prostatectomy
   D. Orchiectomy
5. Which of these methods will NOT achieve androgen deprivation?
   A. Use of luteinizing hormone-releasing hormone
   B. Use of corticosteroids
   C. Androgen blockade
   D. Antiandrogen withdrawal
6. Which of these drugs is considered an LHRH analogue?
   A. Diethylstilbestrol
   B. Flutamide
   C. Ketoconazole
   D. Leuprolide
7. Which of these is NOT a common side effect of flutamide?
   A. Hepatotoxicity
   B. Peptic ulcer
   C. Gynecomastia
   D. Facial flushing
8. Orchiectomy & the use of antiandrogenic agents provide a cure for localized or metastatic prostate cancer.
   A. True B. False
9. Which is correct regarding BPH?
   A. A predisposing factor for the occurrence of prostate cancer
   B. Observed in men 20 years & older
   C. Rarely causes urinary bladder outlet obstruction
   D. It is a non-malignant enlargement of the prostate gland
10. The main disorders of the prostate gland are due to:
    A. Infection
    B. Growth
    C. Injury
    D. Drug abuse
    E. A & B

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