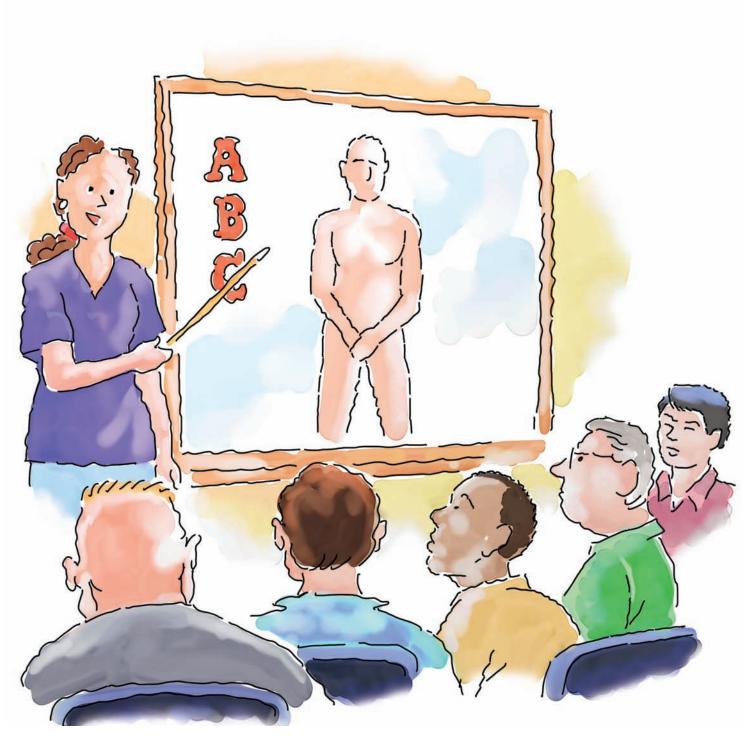
The ABCs of male



28 Nursing made Incredibly Easy! July/August 2011

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reproductive cancer

Reproductive cancer represents a significant risk to the male population. Prostate cancer is the most common nonskin cancer in the United States, testicular cancer is the most common solid malignancy affecting men ages 15 to 35, and penile cancer comprises 20% of cancers in men in Africa, Asia, and South America. We'll take a look at all three.

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The author has disclosed that she has no significant relationships with or financial interest in any commercial companies that pertain to this educational activity.

Mr. B is a 67-year-old retired attorney in New York, Mr. T is a 21-year-old college student in Southern California, and Mr. K is a 63-year-old farmer in Kenya. What could all three of these men have in common? They represent groups of men most at risk for developing reproductive cancer, more specifically, prostate, testicular, and penile cancer.

The male population is at significant risk for reproductive cancer. Prostate cancer is the most common nonskin cancer in America, affecting one in six men (see *Picturing prostate cancer*). Testicular cancer is the most common solid malignancy affecting men ages 15 to 35. The National Cancer Institute (NCI) estimates that one in 271 men will be diagnosed with cancer of the testis in their lifetime (see *Picturing testicular cancer*). Penile cancer is rare in developed countries, but comprises 20% of cancers in men in Africa, Asia, and South America. In this article, I'll give you an overview of all three types of male reproductive cancer.

Prostate cancer

At his annual checkup, Mr. B mentions to his physician that he has been having trouble urinating and is experiencing some pain in his pelvic area. His physician performs a digital rectal exam and feels some areas that are tender and hardened in the prostate. Because of this finding, in addition to Mr. B's age and symptoms, the physician orders a prostate-specific

antigen (PSA) test, which comes back elevated with a level of 23 ng/mL. Mr. B is scheduled for a transrectal biopsy.

Testing for prostate cancer

- PSA. This blood test measures PSA (a protein produced by prostate cells) levels in the bloodstream. It's normal for men to have a level under 4 ng/mL. According to the American Cancer Society, there's a 25% chance of prostate cancer with PSA levels of 4 to 10 ng/mL, and a 50% chance of prostate cancer with levels greater than 10 ng/mL. This test is meant to be a screening; there are some issues that can elevate the PSA that are noncancerous, such as ejaculation (no ejaculation for at least 2 days before the test), advancing age, inflammation of the prostate gland, and benign prostatic hyperplasia (an enlarged prostate).
- *Digital rectal exam*. During this test, the healthcare provider inserts a lubricated, gloved finger into the rectum to feel the back wall of the prostate gland to determine if it's enlarged, tender, or has any lumps or hard areas.
- *Transrectal ultrasound*. During this test, a small probe, which uses sound waves to create a picture of the prostate gland, is inserted into the rectum.
- *Transrectal biopsy*. A biopsy gun is inserted into the rectum to obtain biopsies of the prostate gland. The gun retrieves small sections of tissue through a thin needle, and



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the samples are analyzed in the lab to determine if cancer is present.

Staging

The Gleason grading system is a scoring system based on microscopic tumor patterns that are measured by the pathologist. The system is subjective by nature and requires considerable skill by the pathologist. Scores range from 2 to 10, and the prognosis becomes poorer as the score increases.

Staging describes the severity of a person's cancer and whether it has spread to other parts of the body. It's useful in determining the most effective plan of care (see *NCI prostate cancer staging*).

The results are in...

Mr. B's biopsy comes back positive for cancer. The prostate samples are evaluated and graded at Stage II, with a Gleason score of 2. These results indicate that the cancer

	Prostate	Testicular	Penile	
Statistics	 Most common nonskin cancer in America Affects 1 in 6 men More than 65% of all prostate cancers are diagnosed In men over age 65 	Most common solid malignancy Affects men ages 15 to 35 Responsible for 1% of all cancer in men	Rare in developed countries Responsible for 20% of cancers in men in parts of Africa, Asia, and South America	
Signs and symptoms	Changes in urinary or sexual function Frequent pain or stiffness in the lower back, hips, or upper thighs	Nodule or painless swelling of the testicle Dull ache or heavy sensation in the lower abdomen, perianal area, or scrotum 10% of patients experience acute pain; some show gynecomastia (male breast enlargement)	 Redness Irritation A sore or lesion A lump on the penis 	
Risk factors	 Tall height Lack of exercise and a sedentary lifestyle High calcium intake African descent Family history 	Cryptorchidism (undescended testicle) Orchiopexy (surgery for an undescended testicle)	Phimosis Chronic inflammatory conditions Smoking Human papillomavirus	
Diagnostics	PSA test Digital rectal exam Transrectal ultrasound Transrectal biopsy	Scrotal ultrasound Lab tests for tumor markers (alpha-fetoprotein, beta-human chorionic gonadotropin, and lactate dehydrogenase); up to 50% of early state non-seminomas won't show these markers Biopsy	BiopsyUrethroscopyMRI	

hasn't yet spread outside his prostate. His physician explains the results of the biopsy and together they discuss treatment options, including "watchful waiting," radiation therapy, hormone therapy, chemotherapy, and surgical removal of the prostate.

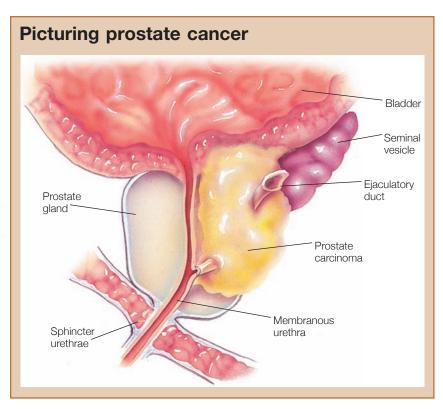
Treatment options

If prostate cancer is in the very early stage, hasn't spread, and is slow growing, *watchful waiting* may be an appropriate treatment option in consultation with a physician. This is also sometimes called active surveillance. The patient has regular follow-up screenings and testing to monitor the progression of the cancer.

According to the National Comprehensive Cancer Network's Clinical Practice Guidelines in Oncology for prostate cancer, additional treatment may be indicated based on the following PSA test results:

- for men who've been in the watchful waiting phase and whose PSA level has doubled in fewer than 3 years, or they have a PSA velocity (change in PSA level over time) of greater than 0.75 ng/mL per year, or they have a prostate biopsy showing evidence of worsening cancer
- for men who've had a radical prostatectomy (removal of the prostate gland) whose PSA level doesn't fall below the limits of detection after surgery, or they have a detectable PSA level (greater than 0.3 ng/mL) that increases on two or more subsequent measurements after having no detectable PSA
- for men who've had other initial therapy, such as radiation therapy with or without hormonal therapy, whose PSA level has risen by 2 ng/mL or more after having no detectable PSA or a very low PSA level.

The goal of *radiation therapy* is to kill the cancer cells. Adverse reactions include painful urination and frequency, erectile dysfunction, and rectal symptoms such as loose



stools or pain. There are two types of radiation (grouped by method of delivery) that can be considered:

- external beam radiation therapy. Computed tomography (CT) scans and magnetic resonance imaging (MRI) are used to identify where the cancer cells are located. For therapy, the patient lies on a table and a machine delivers the radiation treatment to the area of the body where the cancer has been located. Treatment is usually 5 days a week for several weeks as an outpatient.
- brachytherapy. Radioactive iodine or palladium in metal pellets, about the size of a grain of rice, is placed in the prostate tissue using an ultrasound-guided needle. Over several months, these pellets deliver a low-dose, constant delivery of radiation. After a year or so, the pellets will stop giving off radiation and can remain in the prostate. This therapy allows the patient the freedom to not have to return to the hospital as frequently as external beam radiation therapy.

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Proton therapy allows for extreme precision in targeting prostate cancer cells. The machines to deliver this therapy cost between \$25 and \$150 million, and are consequently not widely available. As technology advances, this may become a more accessible option.

Hormone therapy is another treatment option. Most prostate cancer cells need the male hormone testosterone to grow. Adverse reactions include erectile dysfunction, decreased libido, loss of muscle and bone mass, and weight gain. There's also some concern regarding the long-term use of hormone therapy and increased risk of cardiovascular problems. Some prostate cancer cells aren't dependent on testosterone and don't respond to hormone therapy. However, for those cells that do respond to testosterone, the goal of hormone therapy is to significantly decrease the amount of hormone available in the body. This can be accomplished in one of three ways:

- *medication to decrease testosterone production.* Gonadotropin-releasing hormone agonists inhibit the pituitary gland from stimulating the testicles to make testosterone. Examples of these medications include leuprolide and histrelin.
- *medications to block testosterone*. Antiandrogen medications are antagonists that block testosterone from reaching the cancer cells. Examples of these types of drugs are bicalutamide and flutamide.

NCI prostate cancer staging				
Stage	Definition			
Stage 0	Carcinoma in situ			
Stage I, II, and III	Higher numbers indicate more extensive disease: larger tumor size or spread of the cancer beyond the organ in which it first developed to nearby lymph nodes or organs adjacent to the location of the primary tumor			
Stage IV	The cancer has spread to another organ(s)			
Source: National Canc Detection/staging.	er Institute. http://www.cancer.gov/cancertopics/factsheet/			

• removal of the testicles (orchiectomy). Although it seems odd to remove the testicles to treat prostate cancer, the testicles are responsible for producing 90% of the body's testosterone. Removing the testicles will significantly lower the testosterone level. This procedure is done on an outpatient basis, and is permanent and irreversible.

Chemotherapy drugs are aimed at rapidly growing cancer cells. Adverse reactions include hair loss, gastrointestinal upset, fatigue, leucopenia, thrombocytopenia, and some neuropathy. Chemotherapy may be considered in conjunction with other therapies, especially for treating cancers that aren't responsive to testosterone-limiting therapies. Docetaxel has been shown to prolong the survival of men with advanced prostate cancer that no longer responds to hormonal therapy. Cabazitaxel was approved in 2010 for patients who no longer respond to docetaxel.

Surgical options include:

- radical prostatectomy. This procedure is the removal of the entire prostate gland and some of the surrounding tissue through an open incision in the abdomen or scrotum. The abdominal approach has a lower risk of nerve damage that can cause erectile dysfunction and bladder control problems. The perianal approach has a quicker recovery time, but has an increased risk of nerve damage and lymph nodes aren't as easily accessible.
- *laparoscopic radical prostatectomy*. This procedure is similar to the radical prostatectomy, but there's no open incision. The prostate is removed via a laparoscope. A surgical robot may also be used to assist the surgeon. Incisions are made that are only large enough to insert the tools and scope. Recovery time is usually quicker than an open incision surgery.

Keeping up with our patient

Mr. B opts for undergoing a prostatectomy. As his post-op nurse, you're aware that pain control, wound management, preventing

immobility complications, and facilitating urination are the most important priorities following his surgery. You'll need to work closely with the physician and Mr. B to manage his pain at an appropriate level. Mr. B may have abdominal drains in place for 3 to 5 days, depending on the amount of output. His dressings should be changed according to the surgeon's orders. Encourage Mr. B to sit up and ambulate as soon as possible following surgery to decrease the chance of deep vein thrombosis and pulmonary complications.

The prostate gland is very close to the rectum; following surgery, the rectum is vulnerable for injury. Stool softeners and laxatives will be given to reduce the amount of straining. Enemas and rectal thermometers should be avoided.

If the surgeon determines that the nerve bundles on the sides of the prostate that are responsible for erections are cancer-free, these may not have to be removed during the procedure. This is called a nerve-sparing radical prostatectomy (NSRP). NSRP has significantly decreased the incidence of erectile dysfunction. After a radical prostatectomy, male patients will no longer experience fluid ejaculation, but can still experience sexual desire and arousal and achieve orgasm.

Because the urethra runs through the middle of the prostate, the urethra has to be cut above and below the prostate and then reattached to the bladder. In an effort to decrease incontinence and prevent urethral strictures from scar tissue, the patient will require a urinary catheter until the reconnection has had time to heal, sometimes up to 2 to 3 weeks. After prostatectomy, 25% of patients report leakage or lack of control requiring pads for 6 months. Routine in-hospital urinary catheter protocols should be followed, and you should teach Mr. B in-home care, as he'll be discharged with the urinary catheter in place.

Mr. B is discharged home with his drains removed and a urinary catheter in place. He has decided after consulting with his physician to begin an active surveillance plan of treatment. He'll be returning for post-op follow-up in addition to regular screenings to monitor any potential advance of the disease.

Testicular cancer

Mr. T notices a swelling and a lump in his left testicle over the past several weeks, and a dull ache in his lower abdomen has recently developed. Because Mr. T is a college student, he makes an appointment with the university's nurse practitioner, who refers him to his primary care physician. After ruling out other possible causes, such as inguinal hernia, orchitis (inflammation of the testicles), epididymitis (inflammation of the epididymis), and torsion, and based on his symptoms and physical exam, the physician orders a

Your
prostatectomy
patient will
be discharged
home with
a urinary
catheter.

Testing for testicular cancer

testicular ultrasound.

- Scrotal ultrasound. During this test, the patient lies on his back with his legs spread and a handheld ultrasound probe is placed on the scrotum to obtain the ultrasound images. The ultrasound helps the physician evaluate the lump in the testicle to determine if it's solid or filled with fluid and if it's inside the testicle.
- Lab tests. These tests include a complete blood cell count and tumor markers used for testicular cancer (alpha-fetoprotein, beta-human chorionic gonadotropin, and lactate dehydrogenase). These tests may detect a tumor that isn't large enough to be felt on exam or X-ray, but negative markers don't guarantee that there isn't a tumor. Tumor markers are also used in the follow-up of the disease after treatment.
- *Radiographic imaging*. A high-resolution CT scan of the abdomen and pelvis and a chest X-ray are used to look for evidence of regional lymph node metastasis.

Staging

The overall prognosis for each patient is significantly impacted by the stage of the disease and the type of tumor. The testicles produce both testosterone and sperm. The germ cells in the testicles produce immature sperm cells that travel through the tubules and are stored in the epididymis as they mature. Most (95%) testicular cancers are germ cell tumors and are divided into two main types: seminomas and nonseminomas. Seminoma tumors are more sensitive to radiation. Nonseminoma tumors are more aggressive and likely to spread to other parts of the body. The earlier the disease is identified, the more

positive the prognosis (see *The International Germ Cell Consensus Classification*).

The results are in...

The ultrasound shows that the lump in Mr. T's left testicle is a solid mass. Fortunately for Mr. T, his cancer is identified as Stage I seminoma, which has a cure rate of greater than 95%. The initial tumor markers are elevated, and after discussion with his physician, Mr. T decides to pursue surgery with a radical inguinal orchiectomy.

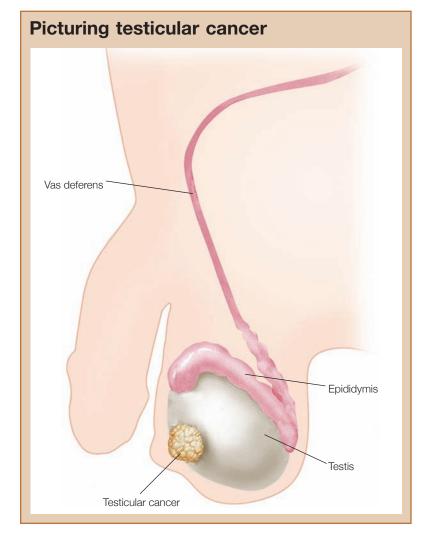
Although removal of a testicle seems like an extreme approach, biopsy of the testicle through the scrotum is generally not performed due to the risk of the biopsy puncture spreading cancer to other tissues. In some cases, when the tumor markers are normal but the ultrasound identifies a nonpalpable mass, a biopsy may be done to determine the need for the orchiectomy. The testicle is surgically removed and the tissue samples are analyzed by the lab to determine if the cells are cancerous.

Before the surgery, Mr. T elects to cryopreserve semen as a precautionary measure. Many testicular cancer patients have sperm abnormalities before treatment and will be oligospermic during chemotherapy. However, a study has shown that 70% of patients were able to father children following treatment.

Post-op care is relatively routine following orchiectomy. You'll facilitate pain control and wound management. Provide ice packs to the groin for 15 to 20 minutes every hour to help with the swelling. An athletic supporter may also help with comfort.

Treatment options

In addition to orchiectomy, a plan consisting of frequent monitoring, chemotherapy, or radiation therapies will be considered. The physician and patient will discuss the best options based on the stage of the cancer cells, whether the tumor is seminoma or nonseminoma, and the tumor marker levels. Treatment options for Stage I testicular cancers include:



34 Nursing made Incredibly Easy! July/August 2011

	Percentage	Assessment/involvement	Survival rate
Good prognosis			
Nonseminoma	• 56% to 61% of nonseminomas	Testis/retroperitoneal primary, and No nonpulmonary visceral metastases, and Good markers: —Alpha-fetoprotein (AFP) less than 1,000 ng/mL —Human chorionic gonadotropin (hCG) less than 1,000 ng/mL —Lactate dehydrogenase (LDH) less than 1.5 times the upper limit of normal	 5-year progression-free survival (PFS) is 89% 5-year survival is 92% to 94%
Seminoma Intermediate prog	• 90% of seminomas	 Any primary site, and no nonpulmonary visceral metastases, and normal AFP, any hCG, any LDH 	5-year PFS is 82%5-year survival is 86%
Nonseminoma	• 13% to 28% of	Testis/retroperitoneal primary, and	• 5-year PFS is 75%
Nonsemmonia	nonseminomas	No nonpulmonary visceral metastases, and Intermediate markers: —AFP 1,000 ng/dL or more —hCG 1,000 ng/dL or more —LDH 1.5 times the upper limit of normal or more	• 5-year survival is 80% to 83%
Seminoma	• 10% of seminomas	Any primary site, andNonpulmonary visceral metastases, andNormal AFP, any hCG, any LDH	5-year PFS is 67%5-year survival is 72%
Poor prognosis			
Nonseminoma	• 16% to 26% of nonseminomas	 Mediastinal primary, or Nonpulmonary visceral metastases, or Poor markers: —AFP more than 10,000 ng/mL —hCG more than 10,000 ng/mL —LDH more than 10 times the upper limit of normal 	5-year PFS is 41%5-year survival is 71%
Seminoma	No patients are classified as poor prognosis		

• Stage I seminoma

—radical inguinal orchiectomy, no radiation, and frequent monitoring

- —radical inguinal orchiectomy, followed by single-dose carboplatin adjuvant therapy
 —radical inguinal orchiectomy followed by radiation therapy
- Stage 1 nonseminoma
- —radical inguinal orchiectomy with retroperitoneal lymph node dissection (RPLND)

—radical inguinal orchiectomy with no RPLND, followed by exams every 1 to 2 months, serum marker tests, and periodic CT scan evaluations.

Keeping up with our patient

After considering the treatment options, Mr. T and his physician decide to follow a treatment plan that involves only frequent monitoring versus additional chemotherapy or radiation. Mr. T agrees to follow the

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After
testicular
cancer
treatment,
your patient
requires lifelong
monitoring.



recommended plan and is discharged home with instructions.

Recommended follow-up after testicular cancer treatment includes:

- year one—monthly serum marker tests, chest X-rays, and physical exam
- year two—bimonthly serum marker tests, chest X-rays, and physical exam
- lifelong—serum markers, chest X-rays, and monthly physical exams. Periodic CT scans are also recommended.

Penile cancer

Mr. K notes a sore that hasn't healed near the tip of his penis. Finally, after many months and the development of a lump, he agrees to see a physician. Mr. K's history reveals that he has chronic phimosis (the foreskin can't be pulled back over the glans), has had several sexual partners, has smoked since he was age 14, and appears to have poor personal hygiene. All of these are risk factors for developing penile cancer. Because this type of cancer has a wide variety of ways it can present, the physician who examines Mr. K is concerned about the possibility of the lesion being cancerous.

Testing for penile cancer

Mr. K agrees to a biopsy of the area. After receiving a local anesthetic, a small tissue sample from the area and some of the fluid and cells from the growth are taken. These will be sent to a pathologist for evaluation. In addition, a urethroscopy and MRI are performed to evaluate the lesion and possible metastasis.

Staging

The Tumor Node Metastasis, or TNM, staging system is used to stage penile cancer (see *Staging penile cancer*).

The results are in...

Most penile malignancies are squamous cell carcinomas, and Mr. K's is no exception. Unfortunately, Mr. K's cancer has progressed

beyond carcinoma in situ (premetastatic stage), but hasn't invaded the lymph nodes and isn't poorly differentiated (T1a, N0, M0).

Treatment options

One of the challenges of determining the best treatment option for penile cancer is identifying the best option to remove the risk of cancer reoccurring and preserving as much normal function of the organ as possible. Similar to other cancers, the treatment options that are considered for penile cancer include surgery, radiation therapy, and chemotherapy.

Surgical options include:

- Mohs micrographic surgery. In Mohs microsurgery, very thin layers of skin are removed. After each layer is removed, it's viewed under a microscope to check for cancerous cells. This procedure allows the surgeon to take just enough tissue to remove the cancerous cells while leaving as much healthy tissue as possible to retain normal function.
- partial or total penectomy. Depending on the involvement of the surrounding tissues, surgical treatment may involve a partial penectomy (removal of any part of the penis) or a total penectomy (removal of the entire penis). The goal is to preserve as much urinary and sexual function as possible; however, if the surgery compromises the patient's ability to urinate, the surgeon will create a perineal urethrostomy. The urethra is diverted to the perineal area between the scrotum and the anus. The patient would then need to sit when urinating.

Radiation therapy can be used to treat early-stage penile cancer instead of surgery, in addition to surgery to reduce the risk of reoccurrence, or in advanced cancer to try to slow cancer growth or relieve symptoms. Men who'll be receiving radiation who aren't already circumcised are circumcised to prevent swelling and constriction of the foreskin during treatment. The types of radiation therapy that are considered for penile cancer include:

- *external beam radiation*. This type is given 5 days a week over a period of approximately 6 weeks.
- brachytherapy. This type of interstitial radiation allows for the radioactive material to be placed right next to the tumor. The radiation only impacts a relatively small area so the other tissues are relatively safe. Hollow needles are placed in the penis and tiny radioactive pellets are then inserted through the needles. These pellets remain in place for several days and then the needles are removed.
- *plesiobrachytherapy*. This type of brachytherapy utilizes plastic cylinders around the penis or a mold of the penis to hold the radioactive material in place for several days.

More research is needed regarding cytotoxic drugs to treat penile cancer. The available studies have been limited and the results have been somewhat inconclusive. However, cisplatin, bleomycin, and methotrexate are three examples of drugs that have been used with some success.

Keeping up with our patient

The surgeon is able to perform a partial penectomy with the hope of preserving Mr. K's sexual and urinary functions. If his residual penile length hadn't been able to be preserved, a perineal urethrostomy would've been performed. Due to difficulty with healthcare access for Mr. K, the decision is made for brachytherapy following the penectomy. If there had been evidence that the disease had progressed farther, chemotherapy agents, such as cisplatin, bleomycin, methotrexate, or vincristine, would've been considered.

Following surgery and 5 days of interstitial radiation and hospitalization, Mr. K is discharged home with instructions for wound care, pain, and a follow-up visit within a week. The effects of the brachytherapy may be worse in 1 to 2 weeks, so Mr. K is taught to be aware of changes in the penis and the surrounding tissues and to notify the physician of any problems. A prescription to

Staging penile cancer

Stage 0 (carcinoma in situ)

In stage 0, abnormal cells are found on the surface of the skin of the penis. These abnormal cells may become cancer and spread into nearby normal tissue. Stage 0 is also called carcinoma in situ.

Stage I

In stage I, cancer has formed and spread to connective tissue just under the skin of the penis.

Stage II

In stage II, cancer has spread to:

- connective tissue just under the skin of the penis and to one lymph node in the groin or
- erectile tissue (spongy tissue that fills with blood to make an erection), and may have spread to one lymph node in the groin.

Stage III

In stage III, cancer has spread to:

- connective tissue or erectile tissue of the penis and to more than one lymph node on one or both sides of the groin or
- the urethra or prostate, and may have spread to one or more lymph nodes on one or both sides of the groin.

Stage IV

In stage IV, cancer has spread to:

- tissues near the penis and may have spread to lymph nodes in the groin or pelvis or
- anywhere in or near the penis and to one or more lymph nodes deep in the pelvis or groin or
- distant parts of the body.

Source: Cleveland Clinic. Stages of penile cancer. http://my.clevelandclinic.org/disorders/Penile_Cancer/hic_Penile_Cancer.aspx.

address potential nausea and GI upset is also given to Mr. K.

At the post-op visit, it's assessed that his urinary functions have continued to remain intact. Sexual function won't be assessed for several more weeks.

Get equipped!

No matter in which geographical location you work, reproductive cancer has the chance of impacting your patients. Being aware of the risk factors, signs and symptoms, assessment findings, and treatment options can help you become more comfortable with this sometimes uncomfortable men's health topic and better equipped to be a strong patient advocate.

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38 Nursing made Incredibly Easy! July/August 2011

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