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PROSTATE CANCER TESTING CAN HELP GUIDE DIAGNOSIS AND TREATMENT

Whether to undergo prostate cancer screening with a prostate-specific antigen (PSA) test isn't always an easy decision for men. The test can be useful in finding prostate cancer, but sometimes it finds cancer that isn't growing quickly and may not need treatment. New biomarker tests are helping physicians determine which men have fast-growing prostate cancer, and which ones can be managed with watchful waiting, or "active surveillance," according to CAPT Sean P. Stroup, MD, Chairman of the Department of Urology and Director of Urologic Oncology at the Naval Medical Center in San Diego.



"Guidelines from the American Urological Association recommend PSA screening for men ages 55 to 69 who are at average risk of prostate cancer, after the doctor and patient have had a full discussion of the risks and benefits of testing," Dr. Stroup said. Men who are at increased risk of prostate cancer should consider PSA screening earlier. These include African-American men, those with a family history of metastatic prostate cancer, a family history of ovarian or breast cancer or veterans exposed to Agent Orange. PSA testing should be done one to every two years, Dr. Stroup noted.

While he says there is less evidence to support screening in men over age 70, some older men with a long life expectancy do decide to continue screening.

Almost 175,000 men in the United States are expected to be diagnosed with prostate cancer this year. One in four of those men will have slow-growing, non-aggressive cancer. "If a man with slow-growing, or indolent, prostate cancer is diagnosed, he may end up undergoing unnecessary treatment," Dr. Stroup said.

Biomarker Tests for Diagnosis

The PSA test is a type of biomarker test. It simply shows whether a man has elevated levels of prostate-specific antigen, a protein made by the fluid-making cells that line the small glands inside the prostate. These cells are where most prostate cancers start growing.

Some types of biomarker testing can help doctors determine which men should undergo a biopsy for prostate cancer because they are at risk of having more fast growing or aggressive prostate cancer. These tests include urine-based tests such as SelectMDx, ExoDx and PCA3, and blood-based tests such as 4Kscore and Prostate Health Index (PHI).



Capt. Sean P. Stroup, MD, Chairman of the Department of Urology and Director of Urologic Oncology at Naval Medical Center San Diego (NMCSD) speaks with a patient about prostate cancer testing, diagnosis and treatment.

"Biomarker tests help doctors find those men most likely to have clinically significant prostate cancer," Dr. Stroup said. "They're looking for genetic abnormalities that are more likely to be found in men with clinically significant prostate cancer, and can help differentiate between prostate cancer and benign or non-cancerous prostate enlargement."

Many primary care doctors may still be uncertain about incorporating PSA testing into their annual evaluation of patients, Dr. Stroup said. "I recommend men talk to their doctor about whether they should be tested. If their PSA comes back over 1.5 ng/mL, ask to be referred to a urologist, who may consider doing further biomarker testing to see whether the man is at increased risk of aggressive prostate cancer."

The doctor may also use an MRI to help identify which men are most likely to have clinically significant prostate cancer. A 3T, multi-parametric MRI (called mpMRI) can help determine where the cancer is in the prostate, and assess features of the cancer.

Three Types of Biopsy

If testing suggests a man may have prostate cancer, the next step is a biopsy. There are three basic types: transrectal, MRI/ultrasound fusion and transperineal biopsy.

- **Transrectal ultrasound (TRUS) biopsy**, the most common type, uses an ultrasound device and is done through the rectum. The doctor inserts needles through the wall of the rectum and into the prostate to take 12 or more samples from different parts of the prostate. This is also known as a systematic biopsy.
- **MRI/ultrasound fusion guided biopsy** combines a specialized MRI scan with an ultrasound image to help precisely target the area of the prostate that needs to be biopsied. This is often accomplished through the transrectal route, and includes samples of the MRI target lesion as well as 12 systematic samples.
- In **transperineal biopsy**, the doctor inserts needles through the perineum to take tissue from the prostate. This approach may reduce the risk of infections.

A pathologist will evaluate the tissue to determine if there is a presence of prostate cancer, and if present, will assign a Gleason Score—the grading system used to determine the aggressiveness of the cancer.

CONTINUED ON PAGE 4 ►



Military Supports Prostate Cancer Research

The Department of Defense Prostate Cancer Research Program has been appropriated \$100 million this year to support high-impact prostate cancer research. The goal is to fund research that will lead to the elimination of death from prostate cancer.

THE FUNDS WILL BE USED TO SUPPORT RESEARCH AIMED AT:

- Improving the quality of life for survivors of prostate cancer.
- Developing treatments to improve outcomes for men with lethal prostate cancer.
- Reducing lethal prostate cancer in African Americans, Veterans and other high-risk populations.
- Defining the biology of lethal prostate cancer to reduce death.

Another military initiative is the Center for Prostate Disease Research (CPDR), which has been following military members, beneficiaries and retirees diagnosed and treated for prostate cancer for almost three decades.

CPDR INCLUDES:

- A prostate cancer clinical trials center at Walter Reed National Military Medical Center.
- The only free-standing military prostate cancer research center in the U.S.
- The largest, most comprehensive prostate cancer database in the United States, involving the Army, Air Force and Navy at multiple medical centers.

The views expressed are those of those interviewed or the author(s) and do not reflect the official policy of the Department of the Army, the Department of the Navy, the Department of Defense, or the U.S. Government.

“I believe if my primary care doctor hadn’t recommended a PSA test, I wouldn’t be here today.”

◀ CONTINUED FROM PAGE 3

Using Biomarkers to Guide Treatment

When prostate cancer is found in biopsied tissue, the doctor can do further biomarker testing to help guide treatment decisions. These tests include Oncotype DX, Decipher and Prolaris. They can be used to help determine which risk grouping the prostate cancer falls into (see chart, page 5).

For example, the Oncotype DX test can help determine if a man should remain on active surveillance or should be treated with surgery or radiotherapy. The Decipher test can help determine if a man should receive adjuvant radiation therapy. Confirm MDx can be used in cases where a man has a negative biopsy, but there is still concern there may be prostate cancer cells in the area.

Testing Can be a Lifesaver

Anthony McClure discovered he had prostate cancer when he had a routine PSA test. “My PSA level spiked. I went for a biopsy, and two days later I was scheduled to consult with a surgeon to have my prostate removed,” he said. In 2016, McClure, a patient of Dr. Stroup’s, started a combined regimen of external beam radiotherapy with a brachytherapy boost. After several years, there was evidence of a rise in his PSA. A bone scan showed the cancer had spread into his right hip. He underwent stereotactic radiotherapy to the hip, and he now takes a combination of medications, plus shots of a hormone every three months. McClure, retired from active duty in the Navy, still works for the Department of the Navy. “My wife says I’m too young to retire,” he said with a laugh.

“Since I’ve been on this treatment, I haven’t felt any pain,” McClure said. “Life is very good right now. I believe if my primary care doctor hadn’t recommended a PSA test, I wouldn’t be here today. Early detection can help you live a longer life. I recommend every man should get the test.”

For more information and resources, please visit:

UrologyHealth.org/PCInfoCenter

UrologyHealth.org/ProstateCancer

NCCN RISK GROUPING AND TREATMENT OPTIONS FOR PROSTATE CANCER

	Risk Grouping	Est. Life Expectancy	Initial Treatment Options	Treatment Benefits	Treatment Risks
VERY LOW RISK	T1c, Gleason score ≤6, PSA <10 ng/mL, Fewer than 3 prostate biopsy cores positive, ≤50% cancer in each core, PSA density <0.15ng/mL/g	10 to <20 years	Active Surveillance	Avoid side effects of any unnecessary definitive therapy; retain quality of life and normal activities; reduce risk of treating small, indolent cancers; and lower costs	Cancer could grow and spread between tests
		>20 years	Radiation Therapy (RT) or Brachytherapy	Less invasive than surgery to treat early stage prostate cancer	Leaves the prostate in the body; can include a treatment course of up to 9 weeks; surgery is difficult if cancer comes back; side effects may include: blood in urine, bladder or bowel problems and erectile dysfunction
		>20 years	Radical Prostatectomy (RP)	Removes cancer with the prostate	Surgical side effects include: bleeding, erectile dysfunction and loss of bladder control
			Active Surveillance		
LOW RISK	T1-T2a, Gleason score ≤6, PSA <10 ng/mL	<10 years	Active Surveillance	Same as Above	Same as Above
			RT or Brachytherapy		
			RP		
		>10 years	Observation		
FAVORABLE INTERMEDIATE RISK**	T2b-T2c OR Gleason score 3+4=7/grade group 2 OR PSA 10-20 nI/mL AND percentage of positive biopsy cores less than 50%	<10 years	EBRT/brachytherapy		
			Observation		
		>10 years	Active Surveillance		
			EBRT/brachytherapy		
UNFAVORABLE INTERMEDIATE RISK**	T2b-T2c OR Gleason score 3+4=7/grade group 2 or Gleason score 4+3=7/grade group 3 OR PSA 10-20 ng/mL	<10 years	EBRT + ADT for 4-6 months; or EBRT+ brachytherapy and/or ADT for 4-6 months		Nausea, vomiting, hot flashes, loss of libido, loss of muscle mass and strength, anemia, feeling tired, osteoporosis, swollen/tender breasts, ED and greater risk for diabetes and heart disease (in older men)
			Observation		
		>10 years	Radical prostatectomy with or without PLND		Same as Above
			EBRT + ADT for 4-6 months; or EBRT+ brachytherapy and/or ADT for 4-6 months		
HIGH RISK OR VERY HIGH RISK**	High risk: t3a OR Gleason score 8/grade group 4 or Gleason score 4+5=9/ grade group 5 OR PSA more than 20 nI/mL Very high risk: t3b-T4 OR Primary Gleason pattern 5 OR more than 4 cores with Gleason score 8-10/grade group 4 or 5		RT + ADT (2-3 y) RT + Brachytherapy +/- ADT (2-3 y)		
			RT + Brachytherapy +/- ADT (2-3 y)		
			RP + Pelvic Lymph Node Dissection (PLND)		

* Risk grouping and treatment options based on National Comprehensive Cancer Network® Guideline for prostate cancer

** Patients with multiple adverse factors may be shifted into the next highest risk group.

VOICE OF THE EXPERTS



WHAT IS NOCTURIA? SUSAN LAHEY, MD

Nocturia is waking from sleep two or more times each night to use the bathroom. About 1 in 3 adults over the age of 30 experience nocturia. Although anyone can have the condition, it's more common in older adults. Common causes include drinking too much fluid or caffeinated beverages close to bedtime. Other causes include bladder or urinary tract infections, overactive bladder and pregnancy. Some medications like diuretics, also known as "water pills", also cause nocturia.

To diagnose nocturia, your doctor will ask several questions about your health, family history of bladder problems or diabetes, and the types of medications you're taking. You may also be asked to keep a journal to record how much fluid you drink, times a day you urinate, and how much fluid is eliminated when you go to the bathroom.

Treatment may include mediations and behavior changes like limiting fluid intake at night. If your nocturia is due to taking diuretics, it may be helpful to take your medication earlier in the day. Talk to your doctor if nocturia is keeping you up at night and affecting your quality of life.

Susan Lahey, MD, practices urology at the Veterans Affairs San Diego Healthcare System in San Diego, Calif.



WHAT IS NEUROGENIC BLADDER? TIMOTHY C. BRAND, MD, FACS

Neurogenic bladder is when a person lacks bladder control because of a brain, spinal cord or nerve condition. This problem can be the result of a spinal cord injury or a health condition like Parkinson's disease, multiple sclerosis (MS), diabetes or stroke.

Normally, muscles and nerves work together to help your bladder hold urine until you're ready to go to the bathroom. But sometimes this process gets disrupted or cut off. As a result, your muscles may not be able to tighten and relax at the right time.

The good news is lifestyle changes and medications can help people manage neurogenic bladder. Scheduling regular trips to the bathroom and limiting your intake of bladder-irritating foods and beverages can help. There are also several medications to help with overactive and underactive bladders. In certain situations, a urinary catheter may be used temporarily or continuously help to ensure the bladder empties completely when you go to the bathroom.

Timothy C. Brand, MD, FACS, is a urologist and the director of the urology residency program at Madigan Army Medical Center in Fort Lewis, Wash. He is also the Urology Consultant to the US Army Surgeon General.



WHY IS FERTILITY PRESERVATION IMPORTANT? HOSSEIN SADEGHI-NEJAD, MD, FACS

Not being able to have children (infertility) can be a short- or long-lasting result of some cancer treatments.

These include such treatments as radiation, surgery, chemotherapy or hormone therapy for testicular, prostate or bladder cancer.

Two types of fertility preservation for men that can be done before cancer treatment are sperm banking and sperm extraction.

Sperm banking is one of the most successful and least costly. This is when you freeze your sperm until you need them, even if it's many years later. With freezing, sperm often do not get damaged.

With sperm removal, a health care provider removes pieces of the testicle tissue. If the tissue has sperm, then the sperm can be used to fertilize a woman's egg. It can also be frozen and used at a later time.

Hossein Sadeghi-Nejad, MD, FACS, is a urologist specializing in male infertility and erectile dysfunction. He is Professor of Urology at Rutgers New Jersey Medical School in Newark, N.J. He is also Chief of Urology at the New Jersey Veterans Affairs Hospitals.



WHAT IS THE DIFFERENCE BETWEEN GENETIC AND GENOMIC TESTING? KYLE RICHARDS, MD

The terms "genetics" and "genomics" sound similar, but they are not the same. Genetics is the study of genes and the way certain traits or conditions are passed down from one generation to the next. Genomics is the study of all of a person's genes (the genome). It includes interactions of those genes with each other and with a person's environment.

Genetics explain the color of a person's eyes, hair and skin. Genomics includes the scientific study of complex diseases that are typically caused more by a combination of genetic and environmental factors than by individual genes.

Genetic testing looks for certain genetic mutations a person may have inherited that may increase the chance of developing cancer. For instance, a woman with a family history of breast cancer may want to have a test for the BRCA1 gene. Women with the gene have a higher chance of developing breast cancer.

Genomic testing looks at your genes, but also looks at their behavior. Genomic testing can be used to help doctors decide the best treatment for your cancer. Understanding how the cancer behaves can help the doctor decide on the best treatment.

Kyle Richards, MD, FACS, is a urologic oncologist with the University of Wisconsin School of Medicine and Public Health. He is also Chief of Urology at the William S. Middleton Memorial Veterans Hospital in Madison, Wisc.





Healthy CHOICES



Diet and Exercise Tips for Urological Health

A healthy diet and regular exercise can reduce your risk of developing heart disease, some cancers and diabetes. Did you know diet and exercise are also good for your urological health? For example, drinking enough water reduces your risk of urinary tract infections. And losing weight helps some people manage urinary incontinence (leaking urine).

HERE ARE A FEW DIET AND EXERCISE TIPS TO KEEP YOU HEALTHY.

1. Have "walking meetings" to catch up with friends, family members and co-workers.
2. Aim for a rainbow of fruits and vegetables on your plate. Examples include blueberries, carrots, yellow peppers, asparagus, strawberries, eggplant, collard greens and cauliflower.
3. Be active. You can walk outside or on a treadmill at the gym. You can also swim, ride a bike, go dancing or try yoga. The main thing is to find an activity you enjoy and will stick with.
4. Learn to read nutrition labels. This will help you be mindful of the sugar, sodium, fat and calorie content of your favorite foods.
5. Take the stairs instead of the elevator.
6. Organize your pantry so healthier foods like nuts, seeds and whole grains are within reach.

Urological Conditions Caused by Smoking and Vaping

When people think about the harmful effects of smoking, lung cancer often comes to mind. But smoking and vaping can also impact urologic conditions.

HERE ARE A FEW FACTS TO KNOW.

1. Smoking and prolonged exposure to second-hand smoke are among the leading causes of bladder and kidney cancers. In 2019, an estimated 80,470 new cases of bladder cancer and 73,820 new cases of kidney cancer were reported in the U.S., according to the American Cancer Society. Did you know? Veteran's who have smoked have a 40% greater risk for developing kidney cancer vs. veterans who have never smoked.
2. Recent studies have shown harmful associations between e-cigarettes, or "vaping", and a person's risk of bladder cancer. Most of the liquid in e-cigarettes that a user inhales has nicotine, which has been proven to be addictive. About 90 percent of inhaled nicotine is excreted into the urine. Researchers at New York University recently found e-cigarette smoke led to DNA harm in the lining of the bladder.
3. Smoking increases your risk of kidney stones.
4. In men, smoking contributes to erectile dysfunction (ED). That's because smoking harms blood vessels, which in turn, impacts blood flow to the penis.
5. Interstitial cystitis (IC), or painful bladder syndrome, impacts more women than men. Smoking irritates the bladder and can worsen IC symptoms.



It's About Time... *and it's about you*

KEEPING INFORMED

Overactive Bladder

Overactive bladder (OAB) is the name for a group of urinary symptoms. The most common symptom of OAB is a sudden, uncontrollable urge to urinate, one in which you are not sure if you are going to make it to the bathroom in time. Another common symptom of OAB is the need to urinate 8 or more times a day and more than once at night.

Up to 30 percent of men and 40 percent of women in the United States are believed to be living with OAB symptoms. Unfortunately, many people with OAB do not ask for help, perhaps due to embarrassment. It's important to get the facts.

If you have OAB symptoms, your doctor will take a detailed medical history and perform a physical exam. Your doctor may also ask you to keep a bladder diary. A bladder diary helps you keep track of how often you go to the bathroom and when, if at all, you leak urine (urinary incontinence).

Dealing with OAB can be frustrating, but there are many ways to manage it. Lifestyle changes are often the first step. For example, you may want to avoid bladder-irritating foods such as citrus fruits, tomato-based or

spicy foods. It's also a good idea to limit your intake of bladder-irritating fluids like coffee, tea, alcohol and carbonated drinks. Smoking also irritates the bladder and can make symptoms worse.

Other lifestyle strategies include "timed urination". That's when you go to the bathroom on a set schedule instead of every time you feel the urge to go. For example, some people try to go to bathroom every 2 to 4 hours, even if they don't feel the need. Kegel exercises to strengthen your pelvic muscles may also help.

Your doctor may prescribe medications to calm your bladder muscles and nerves. Other treatments for OAB include nerve stimulation and bladder Botox injections. In rare cases, surgery is used.

Get more information on OAB by
visiting: ItsTimeToTalkAboutOAB.org

Inside Look

HEMATURIA

Hematuria is the presence of blood in urine. There are two types of hematuria: Gross Hematuria and Microscopic Hematuria. Gross hematuria is when a person can see blood in the urine. The urine appears pink, red or brown. Microscopic hematuria is when a person can't see blood in the urine, but a health care professional can see it under a microscope.

Hematuria is an early sign of both bladder and kidney cancer. 3,500 veterans are estimated to be diagnosed or treated for bladder cancer each year. Did you know 1,300 veterans will be diagnosed with kidney and renal pelvis cancer annually?

There are a number of reasons a person may have blood in the urine. These include:

- Anti-swelling drugs (joint swelling and pain pills)
- Bladder cancer (mostly in smokers)
- Blood thinning drugs (aspirin, coumadin/warfarin)
- Enlarged prostate in older men
- Kidney cancer
- Kidney disease
- Kidney or bladder stones
- Kidney trauma
- Prostate cancer
- Prostate infection
- Rigorous exercise
- Urinary infection
- Vaginal bleeding

If you see blood in your urine, it's important to tell your doctor. While in many cases hematuria is not caused by a serious health problem, in some cases it can be a serious issue that needs medical care.

A doctor treats hematuria by identifying its underlying cause. Hematuria caused by a urinary infection is treated with antibiotics. If hematuria is caused by cancer, then more serious treatment will be needed.

If there is no serious condition causing a person's hematuria, then treatment may not be needed.

Listen to our special Urology Care Podcast episode called "Hematuria: What Does Blood in the Urine Mean?" by visiting UrologyHealth.org/Hematuria



Spotlight on Clinical Trials

What You Need to Know About Clinical Trials in the Veterans Health Administration

Clinical trials help researchers find new ways to prevent, screen, diagnose and treat various health conditions. Researchers also use clinical trials to explore other aspects of patient care such as improving the quality of life for people living with chronic pain or mental health conditions.

Did you know many clinical trials are conducted in the VA? Or that in 2018, the National Cancer Institute (NCI) and the VA began a collaboration to boost veterans' access to cancer clinical trials? The NCI and VA Interagency Group to Accelerate Trials Enrollment, or NAVIGATE, launched this collaboration at 12 VA facilities across the country.

The VA has a robust clinical research program that includes clinical trials in cancer and other diseases at about 100 sites nationwide. However, VA facilities often face challenges initiating and completing externally funded trials because of the need for partners to navigate the system. The NAVIGATE program aims to overcome these challenges with dedicated staffing and a sustainable infrastructure.

How do clinical trials work?

In a clinical trial, participants receive specific interventions according to the research plan or "protocol." These interventions may be drugs, devices, surgical procedures or behaviors such as diet or physical activity.

Informed consent

Informed consent is the process of providing potential participants with the key facts about a clinical trial. This includes the anticipated risks, benefits, time commitment and tasks involved.

Where can I find clinical trials in the VA?

ClinicalTrials.gov is a good place to start. Just list "VA" as a search term.

You can also visit UrologyHealth.org/ClinicalTrials to learn more!

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