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UROLOGY

Contributors

5 Urology: New Treatments and Technology Alter Treatment Options for Common Diagnosis
By Nikhil L. Shah DO, MPH

6 Robotic-Assisted Surgery in Urology
By Rajesh Laungani, MD & Nikhil L. Shah DO, MPH

10 Kidney Stone Management and Prevention in 2014
By Raymond W. Pak, MD, PharmD, MBA

16 The Great Debate: The Efficacy of PSA Testing
By Rajesh Laungani, MD FACS

19 Male Sexual Health
By Chad Hansen, MBA & Nikhil L. Shah DO, MPH

24 Low Testosterone in Men: Diagnosis, Treatment and Monitoring
By Cara Cimmino, MD

30 Benign Prostatic Hypertrophy (BPH): Current Management & Treatment
By Nikhil L. Shah DO, MPH

SPOTLIGHT

Gynecology & Obstetrics
By Helen K. Kelley

BOOK REVIEW

The Ultimate Guide to Ovarian Cancer: Everything You Need to Know About Diagnosis, Treatment and Research
By Barry Silverman MD

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currently serves as the Men’s Health Program Manager for Piedmont Healthcare in Atlanta. As a certified health coach and patient advocate, Chad supports men and their partners by improving overall satisfaction rates with a specific focus on therapeutic compliance, outcomes data analysis and reporting. His mission is to guide men to improved sexual health and wellness through comprehensive integrated specialty programs. He holds degrees in Computer Information Systems Management and Accounting as well as a Certified Professional Cancer Coach (CPCC) and Certified Personal Trainer (ACT). His unique background connects the business of men’s health with the performance-driven results men demand.

CONTRIBUTING WRITERS
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We believe in life well-lived.
This month, Atlanta Medicine magazine is dedicating the issue to urology.

Historically, the medical condition that established the specialty of urology as being distinct from general surgery was the treatment of obstructive urinary symptoms. Over time, we have advanced our understanding of the diverse disorders of the genitourinary tract as well as novel treatment interventions. This month, we explore such conditions as an up-to-date review of urologic afflictions seen in common medical practice.

Calculus disease of the urinary tract has always provided a substantial portion of general urologic practice. The introduction of endourology and lithotripsy greatly improved the capacity of the urologist to deal with renal, ureteral and bladder calculi. Dr. Ray Pak explores the current management of kidney stone disease. Collectively these techniques have largely rendered open surgical procedures obsolete. In addition, advances in the diagnosis and metabolic management of nephrolithiasis allow urologists to treat the medical basis of stone formation in patients at risk.

The treatment of malignant disease is a very large portion of urologic practice. Some of the most encouraging results in the surgical management of genitourinary cancers have been with minimally invasive techniques such as laparoscopic and robotic surgery. Drs. Rajesh Laungani and Nikhil Shah explore the history of minimally invasive surgery, especially in the treatment of prostate and kidney cancers. In addition, Dr. Laungani discusses the controversy surrounding PSA testing and its role in prostate cancer screening for the medical practitioner.

Hyperplasia of the prostate affects aging males, especially over the age of 50. Dr. Shah reviews the symptoms and treatment of BPH and obstructive uropathy. Similarly, Dr. Alenore Gilchrist has written a comprehensive overview on incontinence. She discusses the diagnosis and treatment of common conditions such as urgency and stress urinary incontinence. The diagnosis and therapy of urinary incontinence constitute a significant portion of most urology practices. New therapies, both surgical and non-surgical, are being constantly developed.

Male sexual dysfunction and hypogonadism have become subspecialties. Chad Hansen, a men’s health expert, discusses the management of impotence, which has been revolutionized first and foremost by the introduction of oral Phosphodiesterase 5-inhibitors. The area of sexual dysfunction in urology is also expanding to encompass not only the various forms of erectile dysfunction, but also the relationship to circulation and cardiovascular disease. The management of low testosterone in the aging male, sometimes called “Male Menopause” is gaining increased attention by both urologists and internists. Dr Cara Cimmino provides an insightful overview of hypogonadism. Continued improvements in the medical management require a high level of expertise in the area of hormone axis physiology and endocrinology.

The specialty of urology is constantly changing. Much of this change has been the result of improved technology. Refinements in the area of endoscopic surgery have revolutionized the therapy of urinary tract stones. Urology has always been a leader in minimally invasive surgical (MIS) interventions. The field has evolved in the area MIS where many urologic operations, which have been performed by open surgery in the past, are now performed through the use of a surgical robot or a laparoscope.

The development of new diagnostic tools, innovative surgical treatments and novel medical therapies have significantly altered therapeutic options for many commonly diagnosed urologic conditions. Urology is a rapidly changing and exciting specialty of medicine that mandates a close working relationship between primary care physicians and their community urologists.
Historically, urology has embraced and even pioneered the use of innovative technology, especially with respect to integrating minimally invasive means for both diagnosis and treatment of disease.

This trend began with endoscopy – the use of a patient’s natural openings, in our case the urethra, to access the bladder, ureters and kidney with the intent to be both diagnostic and therapeutic. Then came the advent of laparoscopic and minimally invasive techniques for treatment of urologic cancer, namely kidney cancer and prostate cancer. Advocates of laparoscopy cite improvements in convalescence, such as decreased time to recovery, reduced hospital stay and decreased postoperative pain. In the prostate cancer patient, minimally invasive approaches also offer patients significant decreases in blood loss compared to open surgery.

The origins of robotic-assisted surgery date back more than a decade ago to around 2000 or 2001. Initially created for cardiac surgery, robotic-assisted surgery found its home in the male pelvis, as it has gained the most ground in the hands of urologists. It is currently used for the treatment of localized prostate cancer, kidney cancer and bladder cancer as well as a multitude of urological reconstructive procedures, including Ureteropelvic Junction (UPJ) obstruction as well as Sacrocolpopexy for treatment of vaginal prolapse.

More than ever, technology continues to influence our lives on a day-to-day and even minute-to-minute basis. Medical technology may not be changing as quickly as the newest smartphone, but its influence, particularly in the surgical...
arena, is evident. The goal of any surgeon continues to be to provide the best possible care for his/her own patient while minimizing morbidity and mortality and maximizing outcomes. Yet, the definition of outcomes has changed dramatically in the new healthcare environment, as patient safety and providing quality care must also encompass equal parts efficiency and cost savings.

What minimally invasive and robotic surgery has allowed the urologist to do is to perform an equivalent, if not superior, operation on the patient for his/her particular disease with a recovery period and morbidity far decreased compared to more traditional techniques (Figure 1).

For example, for a patient with localized prostate cancer, standard of care five or 10 years ago would have the patient undergo an open radical prostatectomy. This would typically involve a large incision extending from just below the navel to just above the pubic bone. There was usually 500-800 cc of blood loss, catheterization for two weeks and five to seven days in the hospital.

Robotic surgery allows the same patient, with the same disease spectrum, four to five keyhole-sized incisions, 50-75 cc’s blood loss, catheterization for five days and an overnight stay in the hospital.

Smaller incisions lead to less pain, quicker recovery, a shorter hospital stay and less risk of infection. Decreased blood loss results in a transfusion rate of <1 percent. A shorter catheter duration and hospital stay result in a quicker return to work, friends and family. The same trends and benefits extend to patients for treatment of kidney cancer; robotic-assisted radical/partial nephrectomy; and robotic-assisted radical cystectomy for bladder cancer.

What drives the technology continues to be human hands, and what leads to superior outcomes continues to be greater experience in regards to case volume. Surgeons with high case volume and greater experience have been shown to have a significantly decreased complication rate along with superior overall outcomes as compared to those surgeons with a lesser volume.
It’s important to understand, both from a primary care perspective as well as a patient perspective, that just because a hospital has a robotic surgical system does not mean they have the urologists skilled enough to perform robotic surgery at a level that will significantly decrease complications as well as provide your patients with excellent outcomes.

The authors have a combined robotic surgical case experience of more than 5,000 cases dating back to 2002. They were both part of the pioneering robotics team at the Vattikuti Urology Institute - Henry Ford Health System in Detroit. It was there that robotic surgical techniques were established for robotic prostatectomy (2000), robotic-assisted nephrectomy (2003) and partial nephrectomy (2003) as well as robotic-assisted radical cystectomy (2004). They were both mentored by Dr. Mani Menon, who many consider the “godfather of robotic-assisted urologic surgery.”

The inherent advantages of the robotic surgical system lies in what the technology can provide.

1. 10x magnification with 3-D visualization, which allows for more precise dissection and tissue manipulation with identification of nervous tissue and blood vessels that are imperative to preserve for maintenance of urinary control and sexual function after radical prostatectomy.

2. 180-degree range of motion with stereotactic stabilization, which allows the human wrist to manipulate instruments in a way that would not be possible with traditional surgery with complete steadiness.

3. Instruments that are approximately the width and length of the human pinky nail, allowing for small incisions, less pain and decreased infection risk post operatively.

The technological advantages inherent to the robotic surgical system along with a skilled, fellowship-trained urologist have resulted in better patient outcomes. It has become evident that robotic surgery continues to gain ground, although slowly, but it will surely establish itself as the standard of care for many urologic surgical procedures.
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Kidney stones affect 1 in 11 Americans. The estimated cost of managing kidney stones in the U.S. has exceeded $10 billion annually. Worldwide, the incidence of nephrolithiasis has been on the rise with an estimated lifetime prevalence of 12 percent in men and 6 percent in women in the Western hemisphere.

Geographically warmer climates tend to have a higher incidence of kidney stones with global warming a possible cause of the rise in other regions. One of the factors for the rising incidence of kidney stones is the identification of asymptomatic stones by the increased quality and number of imaging studies performed today (computerized tomography scans, ultrasonography).

Clinical Presentation

Kidney stones are readily diagnosed with well-defined clinical symptoms of renal colic that include flank pain, radiating groin pain, nausea with or without vomiting, fever, chills, urinary frequency and hematuria. Presentation can change based on the location of the stone and degree of obstruction. Patients with staghorn renal stones often don’t present with renal colic and are largely asymptomatic. Acute emergency presentations can include urosepsis and renal failure requiring prompt attention.

Pathogenesis

Prevention of kidney stone formation starts with understanding mechanisms that lead to the development of stones. Kidney stones form secondary to a relative state of dehydration. Stones form in the urinary system when crystallization of salts occurs after reaching a state of super saturation. Kidney stones can be composed of (Table 1): calcium oxalate (monohydrate and dehydrate), uric acid, struvite (magnesium ammonium phosphate), calcium phosphate and cysteine.

Calcium (Ca) based kidney stones can precipitate as a result of hypercalciuria secondary to increased renal excretion (renal leak), resorptive hypercalciuria (hyperparathyroidism)
or gastrointestinal absorption of dietary calcium (absorptive). High urinary oxalate levels (hyperoxaluria) can be caused by dietary factors, idiopathic, enteric and primary hyperoxaluria (types I, II). Distal renal tubular acidosis (type I) can cause calcium kidney stones from multiple ways: metabolic acidosis leading to bone buffering and calcium release, alkalinization of urine leading to phosphate precipitation and finally reduction in urinary citrate excretion.

Uric acid stones can develop secondary to high dietary protein and purine metabolites leading to hyperuricosuria. The acidic urinary pH thus leads to uric acid stone formation. Struvite or infection stones form due to excessive ammonia in the urine secondary to urease-producing bacteria such as Proteus and Klebsiella. Cystine stones form secondary to a defect in amino acid transport in the kidney affecting cystine, ornithine, lysine and arginine reabsorption from urine. This leads to precipitation of cystine, which is relatively insoluble.

High intake of dietary sodium (Na) can affect the renal tubular transport exchange of sodium and calcium, leading to hypercalciuria. Patients who have undergone gastric bypass have altered fat saponification, which leads to reduced enteric calcium levels and increased oxalate absorption.

Risk Factors

Several patient demographic, disease states, genetic disorders, dietary and medication factors have been identified that increase the risk of stone formation in the urinary tract. Men are twice as likely to develop stones when compared with women, although recent trends show a narrowing of the gender gap. Disabled or elderly dependent patients living in facilities are often dehydrated and at risk for kidney stones. Obesity nearly doubles the risk of developing kidney stones, and the degree of obesity doesn’t change that risk.

Metabolic disorders such as diabetes and hypertension have been strongly associated with uric acid and calcium oxalate kidney stone formation. Gastrointestinal tract conditions such as inflammatory bowel disease and previous gastric bypass surgery alters enteric calcium-oxalate binding, thereby increasing the risk of calcium oxalate stone formation. Cystinuria is an autosomal recessive disorder of protein metabolism that results in excessive urinary excretion of cystine. These patients are at the greatest risk for a lifetime of recurrent problems from cystine kidney stones. Excessive intake of dietary animal proteins, calcium, salt and oxalate can all lead to stone precipitation in the urinary system.

Prescription medications such as Crixivan (indinavir) and Topamax (topiramate) have been linked with stone formation and urolithiasis. In addition, dietary supplements such as calcium, vitamin D and ascorbic acid (Vitamin C) can cause stones. Silicon dioxide found in tablet formulations has been reported to cause silica stones. Over-the-counter (OTC) calcium containing antacids have also been abused by patients leading to kidney stone formation. Rare reports have also linked OTC ephedrine and guaifenesin with nephrolithiasis.
Prevention and Medical Treatment

The best way to address kidney stones is to prevent the formation in the first place. By increasing fluid intake and watching dietary intake, the vast majority of stones can be prevented. Twenty-four hour urine studies are commonly performed to identify and monitor factors such as urine volume, urine pH, calcium levels, super saturation levels, oxalate and citrate levels that may predict recurrence.

If a stone former does not change risk factors, the estimated recurrence rate is 50 percent within five years. Studies have shown that stone formers need to ideally maintain adequate water consumption of between 64 and 128 ounces in 24 hours to achieve a minimum of 2 liters of urine production in 24 hours.

Dietary measures include the need to maintain normal calcium intake in the diet to absorb oxalate in the GI tract, reduction of protein load and metabolism, reduction of salt intake to prevent excess urinary calcium excretion, reduction of consumed dietary oxalate and increase the intake of citrate and magnesium products. Common sources of citrate include oranges and lemons. Medical treatment of stones aims to modify super saturation by addressing hypercalciuria (hydrochlorothiazide), the pH of urine (potassium citrate or sodium bicarbonate) and excretion of uric acid (allopurinol). D-penicillamine and Alpha-mercaptopropionylglycine are used to alter cystine stone formation in cysteinurics. Presented in Table 2 are the available medical treatments to dissolve or prevent kidney stones based on composition and pathogenesis.

Surgical Treatment Options

The management of kidney stones can vary by the acuity of the presentation, location of the stone, size and number of stones, stone composition and patient factors. The success of any approach is commonly measured by the stone-free rates (calculated based on follow-up imaging), the need for repeated intervention and safe uncomplicated outcomes.

Up until the 1980s, open surgery and retroperitoneal exploration was common practice for the treatment of obstructive kidney stones. Fortunately, the trend has become less invasive with increased proliferation of shockwave lithotripsy (SWL) and advanced endoscopic technology.

Today, the surgical management can include endoscopic (ureteroscopy), percutaneous (PCNL) or laparoscopic/robotic techniques. SWL however, is still the most common procedure performed for renal or ureteral calculi.

Shockwave Lithotripsy (SWL)

Shockwave Lithotripsy (SWL) was first introduced to clinical practice in 1984 with the Dornier HM3 bath system (Dornier medtech, Kennesaw, GA) and is still the most effective device to date. Despite advances in technology, no currently offered products have been able to match the stone-free rates of the original HM3 machine. Few centers still have this machine running, however, as it is no longer manufactured.

The lower success of current machines has been attributed to reduction in the physical size, smaller focal zone and different coupling mechanisms. Intervention with SWL, although non-invasive, still requires limited anesthesia and recovery. Due to the nature of the treatment and effect on surrounding structures, any organ in the path of the soundwave has been injured and reported including the spleen, lung, liver and colon. Some studies suggested a link with development of hypertension and diabetes, but recent well-designed reviews did not confirm these long-term concerns. Moreover, there have been no reports of diminished renal function or growth long term after SWL in adults or children.

### Table 2: Medications used to treat or prevent kidney stones

<table>
<thead>
<tr>
<th>Stone Composition</th>
<th>Mechanism of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrochlorothiazide</td>
<td>Calcium</td>
</tr>
<tr>
<td>Allopurinol</td>
<td>Uric acid</td>
</tr>
<tr>
<td>Sodium Bicarbonate</td>
<td>Uric acid</td>
</tr>
<tr>
<td>Potassium Citrate</td>
<td>Calcium and uric acid</td>
</tr>
<tr>
<td>D-penicillamine</td>
<td>Cystine</td>
</tr>
<tr>
<td>Alpha-mercaptopropionylglycine</td>
<td>Cystine</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>Struvite (MAP)</td>
</tr>
</tbody>
</table>
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The reported stone-free rates of SWL treatment ranges from <50 percent to over 90 percent. The success of SWL can only be affected by a few controllable factors such as patient selection (obesity, stone size, stone composition, stone location, number of stones), number of shocks delivered, shockwave rates and power settings. Factors predicting reduced success include patient obesity, large stones (>1 cm), multiple stones and hard stones (cystine or calcium oxalate monohydrate). Contraindications to SWL include pregnancy, anticoagulation, sepsis and aneurysms. The most common reported side effects include shock-site pain and bruising, hematuria and renal hematomas that can occur up to 12 percent of the time. Patients can also subsequently develop “steinstrasse” (German for string of stones) when trying to pass multiple stone fragments in the ureter leading to pain and obstruction.

**Ureteroscopy (URS)**

Ureteroscopy (URS) is the process of passing a small endoscope retrograde from the urethra through the bladder and into the ureter and/or kidney. URS was first described as a diagnostic procedure as early as the 1960s, but it wasn’t until the 1980s that urologists were able to perform interventions.

URS has become an increasingly popular option with advances in endoscope technology, stone breaking energies (laser, EHL) and stone retrieval instruments. Although most ureteroscopy is performed to address ureteral stones, over time the use in treating renal stones is on the rise.

Ureteroscopic surgery requires general anesthesia and is performed in an outpatient setting. URS can be performed with a rigid or flexible scope (Figure 1). Due to the use of natural urinary orifices and channels, no incision is required and therefore recovery is fairly quick (return to work in 24-72 hours). Temporary ureteral stents are usually placed after the procedure to ensure adequate renal drainage, minimize complications related to edema formation or blockage from stone fragments and to reduce the development of ureteral strictures. They are routinely removed anywhere from 24 hours to a week after surgery.

The reported success of URS has been reliably higher within a smaller range than SWL (>80 percent) with lower retreatment and/or re-intervention rates. The success rates again can also be adversely affected by stone size, number and composition. The advantage of this approach is that an acutely obstructed kidney can be drained promptly to relieve sepsis, renal failure and colic.

Some of the practical limitations of URS include the reliance on technology and the increased costs of treating stones because of the need for delicate flexible ureteroscopes, lasers for stone breaking, baskets for stone retrieval and ureteral stents for recovery. In the western world, access to these technologies is not a problem. Other parts of the world adopt techniques to minimize costs at the expense of stone-free rates and safety of ureteroscopy. In addition, the training and skill-set required of ureteroscopic procedures can sometimes be limited based on practice setting, hospital equipment and generation.
of the surgeon. Reported complications of URS include hematuria, infection, pain, stricture, ureteral perforation and ureteral avulsion.

**Percutaneous Nephrolithotomy (PCNL)**

Percutaneous stone surgery requires general anesthesia and involves a 1-cm incision in the flank to gain access into the kidney. This approach has traditionally been recommended for stones > 2-cm or staghorn renal stones and is very successful when compared to URS or SWL. It is, however, considered more invasive with a higher potential for serious complications and longer hospitalizations.

The access into the kidney is usually performed by an interventional radiologist through the flank with placement of a nephrostomy catheter. Urologists then access the pre-placed tubes, following and dilating a tract along the nephrostomy access to accommodate passage of a large scope and sheath. Large stones are then broken up with a combination of various methods including mechanical, ultrasonic or laser energies. Stone fragments are then removed directly from the kidney using graspers. PCNL usually requires a one- or two-night stay in the hospital with a recovery period of about five to seven days.

The reported success rates for PCNL generally range above 95 percent stone-free rates with one procedure. Common and rare complications include bleeding, hematuria, pain, infection, renal hematoma, renal injury, urine leak, intrarenal obstruction, pneumothorax, hydrothorax, bowel injury, spleen injury, and pseudoaneurysms. The incidence of complications range from <1 percent to 7 percent.

**Laparoscopic/Robotic Stone Surgery**

Laparoscopic and robotic techniques to treat kidney stones are an attractive option that has been reserved for very limited indications of severe stone disease. The initial experience started with the management of ureteropelvic junction obstruction (UPJ), which often co-presents with kidney stones in the same kidney. Robot-assisted laparoscopic pyelolithotomy (incising the renal pelvis to remove stones) and anatrophic nephrolithotomy (bivalving the kidney to remove stones) have been performed. These were traditionally major open stone operations that have experienced a resurgence due to advanced robotic surgery techniques that can achieve high levels of success in a minimally invasive fashion with few complications.

**References**


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**Table 3: Summary of Treatment Options for Nephrolithiasis**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Ideal stone</th>
<th>Setting</th>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expectant management</td>
<td>Asymptomatic kidney stones</td>
<td>Home</td>
<td>Avoid intervention</td>
<td>Stones may pass emergently, stones may become larger</td>
</tr>
<tr>
<td>Trial of passage</td>
<td>Small (&lt; 5 mm)</td>
<td>Home</td>
<td>Avoid intervention</td>
<td>Pain, inconvenience, time-off, need</td>
</tr>
<tr>
<td>Shockwave Lithotripsy (SWL)</td>
<td>&lt; 1 cm stones visible on X-ray</td>
<td>Outpatient</td>
<td>Avoid invasive procedure, very successful if ideal</td>
<td>Failure and need for other intervention, hematoma or tissue damage</td>
</tr>
<tr>
<td>Ureteroscopy</td>
<td>Ureteral or renal</td>
<td>Outpatient</td>
<td>Very successful if ideal situation</td>
<td>Invasive, ureteral injury, ureteral stent</td>
</tr>
<tr>
<td>Percutaneous Nephrolithotomy (PCNL)</td>
<td>Single or multiple large renal stones (&gt;2-3 cm)</td>
<td>Inpatient</td>
<td>Highest stone-free rates for larger stones with one procedure</td>
<td>Invasive, hospitalization required, nephrostomy tube, bleeding, kidney damage</td>
</tr>
<tr>
<td>Robotic-assisted Laparoscopic Surgery</td>
<td>Staghorn or &gt; 5</td>
<td>Inpatient</td>
<td>Potential high success rate, may combine with pyeloplasty</td>
<td>Invasive, requires additional training, risk of bowel injury or catastrophic vascular injury</td>
</tr>
</tbody>
</table>
To screen or not to screen, to treat or not to treat. The gold standard for prostate cancer screening is for men to undergo both a digital rectal exam (DRE) and a Prostate Specific Antigen (PSA) blood test (Figure 1).

The debate on prostate cancer continues to revolve around the efficacy and usefulness of PSA as a valid screening tool as well as the decision-making ability of clinicians to appropriately decide which patients should undergo treatment and which should not. In all honesty, it is a reasonable debate given the information and the current tools that we have at our disposal.

There is no doubt that the future of medicine and cancer lies within the “double helix.” The ability to unlock the DNA code will one day give us some insight in regards to predicting who will die of cancer and who may succumb to more natural causes. This insight is lacking in our PSA/prostate cancer decision tree and has led many patients to be overtreated, but it has also led many patients to be poorly screened, leading to delayed and late presentation of disease.

Let’s try and break down the debate with a few examples of patients you see everyday in your practice.

**Patient 1**

A 75-year-old healthy male walks into your office for a routine physical exam. You will obtain a lipid profile, check his blood sugar, check his urine and stool for blood, check his LFT’s and do a thorough physical exam. But, should you check his PSA this year?

Every year prior, his PSAs have been within normal limits. What are the chances at age 75, having not been diagnosed with prostate cancer thus far, that he will die from this
If we think his overall chance of death from prostate cancer is very low, why screen for it? In other words, why search for something that may likely be present (given the fact that as you get older your risk of prostate cancer rises) but may likely be clinically insignificant and may not require treatment. This would be a prime example of a patient that, if screened and diagnosed, could be overtreated (treated for a disease he will likely not die from).

**Patient 2**

A 55-year-old male presents to your clinic for his yearly physical. He recently completed a colonoscopy, exercises 3 times per week, does not smoke or drink and takes only a medication to help lower his cholesterol. Do you obtain a PSA as part of his routine laboratory evaluation? Based on new government guidelines, PSA is a poor screening test and does not impact the overall death rate from prostate cancer. But he is healthy, has at least a 25- to 30-year life expectancy and detecting prostate cancer (if in fact he is harboring it) at an early stage can potentially be curable. If you choose to adopt the government guidelines, you risk ignoring and missing the most common cancer seen in men and the leading cause of cancer-related death in men. This is a prime example of a man who could be underscreened and potentially die from a disease given his long life expectancy.

**Recommendations**

It has been established that those patients with risk factors for development and diagnosis of prostate cancer need to be aggressively screened and potentially treated. These men include those with a family history of prostate cancer (first-degree relative such as a father or brother) as well as those men who are African American. The American Urological Association (AUA) Guidelines (Figure 2) recommend that for men with risk factors, there should be an establishment of a baseline PSA value in their 40s, with annual screening beginning in their 50s. It advocates screening for all men to start in their 50s, regardless of risk factors.

The AUA has not accepted the recent statement put out by the United States Preventative Services Task Force (USPSTF) in regards to prostate cancer screening but has commented on the fact that interpretation of the PSA test and evaluation by the correct individuals may contribute to identifying those patients who would benefit most from annual PSA testing and screening.

The debate comes down to a simple fact: the error with PSA does not lie within the test itself, but instead in how we choose to use the test and how the test is interpreted. There is no doubt that PSA as a screening tool is far from perfect. We know that PSA may be elevated naturally with...
BPH, infection, inflammation, recent catheterization or urinary retention. At very high levels, PSA may correlate with aggressive prostate cancer, but on its own it is not diagnostic.

PSA can be interpreted based on absolute value as well as trend and change. PSA velocity as well as PSA doubling time have been shown to play a role in predicting diagnosis of prostate cancer as well as even death from prostate cancer. Other PSA tests, including Free PSA, PSA Density and Pro PSA, may help to differentiate benign elevations in PSA as well as differentiate slow-growing from more aggressive, rapidly growing tumors. Molecular marker testing provided by certain companies, recently highlighted in The New York Times, has brought some insight into predicting who may be harboring more aggressive disease, therefore allowing physicians to avoid overtreatment.

**HIGH RISK PATIENT**

BASELINE PSA AT AGE 40 AND 45

PSA ANNUALLY AFTER AGE 50

**LOW RISK PATIENT**

NO BASELINE PSA NECESSARY

PSA ANNUALLY STARTING AGE 50

*Risk of prostate cancer in regards to age, absolute value of PSA as well as rate of change of PSA should be made by your urologist. Determination of need for a prostate biopsy for diagnosis of prostate cancer should be made by your urologist.

**HIGH RISK PATIENTS:** FAMILY HISTORY (1ST DEGREE RELATIVE DIAGNOSED WITH PROSTATE CANCER) or AFRICAN AMERICAN

**LOW RISK PATIENTS:** NO FAMILY HISTORY or CAUCASIAN, ASIAN, MIDDLE EASTERN

*Figure 2:
PSA Screening Recommendations*

It has been established that those patients with risk factors for development and diagnosis of prostate cancer need to be aggressively screened and potentially treated.

**Summary**

We as physicians have all come to realize that medicine in all of its perfection continues, in many regards, to still be an imperfect science. Decisions that we make on how to manage and treat our patients are based on the current tools that we have at our disposal, in this case PSA, but appropriate use of those tools is what defines us as physicians. A better screening and diagnostic test for management of prostate cancer is inevitable, as are the case for so many things in medicine, as technology advances us to see things on a molecular level. However, abandoning a test altogether continues to put a population of men at risk of dying from disease that is potentially very curable. Once again, it is not the test that is flawed as much as it is the interpretation and use of it.
Introduction
– Men’s Health & Sexual Health
When it comes to managing personal health, men continue to miss the mark as compared to their female counterparts. Consistently, men avoid opportunities to address even the most basic medical problems; issues which are treatable, and far less threatening to their overall health when early detection is applied. No other health problem has affected so many across such a vast spectrum of epidemiological, financial and sociologic sectors as have suffered from the neglect, awareness and inaction with regards to men’s health. So what can be done? How can we change this generational problem and an inherent fear of going to the doctor? The answer: We must get creative in our approach and work on optimizing his body’s ‘Performance’. No other word better describes the male than how he measures up. Performance is measured in multiple ways; at work, on the field of play and most importantly, (to him) performance in the bedroom. Men have always been result-driven creatures and focused on outperforming others. So, instituting a partnership with the male patient to provide quality care with definable outcome measures thereby producing quantifiable results can be a winning formula.

Erectile Dysfunction in the United States
An estimated 30 million American men are affected by ED. Fewer than 5% of those affected will seek a physician for treatment.1 Many men may feel uncomfortable discussing this topic with a physician, family or friends. The majority of men suffering from ED have significant underlying medical problems, especially cardiovascular disease. In fact up to 2/3rd’s of men with significant ED at the time of presentation to health care provider will suffer from a heart attack or stroke within the following 3 - 5 years.2
The importance of men’s sexual health takes into account a variety of factors involved in a man’s level of sexual fulfillment, including erectile function, libido, intimacy, sexual satisfaction along with overall health and wellbeing. Despite what many people think, being sexually active is a natural part of a man’s life that doesn’t have to end simply because he’s getting older. Satisfying sexual health is an essential component of overall health and happiness. In our Urology practice, we tell our men and couples that sex is not only natural but that the health benefits extend far beyond the bedroom.
ED is caused by organic, physiologic, endocrine, and psychogenic factors.3 In general, ED can be categorized into organic and psychogenic. Given the multiplicity of possible etiological factors, it may be difficult to determine how much any given factor is contributing to the problem. A thorough evaluation is necessary to correctly identify the specific etiology in any given individual.

More Than Just An Erection
Just as good sexual health signals good overall health, poor sexual health can often be a signal for future problems. A change in a man’s sexual health can be an early warning sign for more serious problems, such as heart disease, diabetes, high blood pressure, high cholesterol and risk for stroke.2 Additionally, a change in sexual health maybe linked to chronic infection, neurological problems, or medications.

Table 1: Causes of Erectile Dysfunction in Men (adapted from MMAS, 1994)

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>DISORDERS</th>
<th>PROBLEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychogenic</td>
<td>Performance Depression</td>
<td>Loss of libido overinhibition, Impaired nitric oxide release</td>
</tr>
<tr>
<td>Neurogenic</td>
<td>Stroke, Spinal cord injury</td>
<td>Lack of nerve impulse, or Interrupted transmission</td>
</tr>
<tr>
<td></td>
<td>Diabetic retinopathy</td>
<td></td>
</tr>
<tr>
<td>Hormononal</td>
<td>Hypogonadism, Hyperprolactinoma</td>
<td>Inadequate nitric oxide release</td>
</tr>
<tr>
<td>Vasculogenic (arterial or venous)</td>
<td>Atherosclerosis, hypertension</td>
<td>Impaired arterial or venous flow</td>
</tr>
<tr>
<td>Medication-induced</td>
<td>Antihypertensives, Antidepressants, Alcohol cigarette use</td>
<td>Central suppression, Vascular insufficiency</td>
</tr>
</tbody>
</table>
hormone deficiency, medication complications, nerve damage and/or physiological issues. Even being less interested in sex or no longer enjoying sex can be a signal that something is wrong, such as low testosterone (see Dr. Cimmino’s article in this issue).

A sexual problem, or sexual dysfunction, typically refers to a physical or satisfaction problem related to a man’s sexual activity. While research suggests that 31% of men (regardless of age) report some degree of difficulty or dissatisfaction in their sex life, it’s a topic that many people are hesitant to discuss. Fortunately, most cases of sexual dysfunction are treatable. That’s why it is important for patients to share their concerns with their doctor. In turn, it is important for the health care provider to ask ALL men about their sexual health during a routine office visit.

**The Use of Formal Questionnaires**

Questionnaires have been developed to gather objective data regarding erectile dysfunction (ED) and to assist clinicians in

| Table 2: Amended IIEF – The Sexual Health Inventory Scale (SHIM) Form Over the past 6 months |
|-------------------------------------------------|-----------------|----------------|-----------------|-----------------|----------------|
| How do you rate your confidence that you could get and keep an erection? | Very Low | Low | Moderate | High | Very High |
| | 1 | 2 | 3 | 4 | 5 |
| When you had erections with sexual stimulation, how often were your erections hard enough for penetration (entering your partner)? | No Sexual Activity | Almost Never or Never | A Few Times (much less than half the time) | Sometimes (about half the time) | Most Times (Much more than, half the time) | Almost Always or Always |
| | 0 | 1 | 2 | 3 | 4 | 5 |
| During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner? | Did Not Attempt Intercourse | Almost Never or Never | A Few Times (much less than half the time) | Sometimes (about half the time) | Most Times (Much more than, half the time) | Almost Always or Always |
| | 0 | 1 | 2 | 3 | 4 | 5 |
| During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse? | Did Not Attempt Intercourse | Extremely Difficult | Very Difficult | Difficult | Slighty Difficult | Not Difficult |
| | 0 | 1 | 2 | 3 | 4 | 5 |
| When you attempted sexual intercourse, how often was it satisfactory for you? | Did Not Attempt Intercourse | Almost Never or Never | A Few Times (much less than half the time) | Sometimes (about half the time) | Most Times (Much more than, half the time) | Almost Always or Always |
| | 0 | 1 | 2 | 3 | 4 | 5 |

Add the numbers corresponding to questions 1-5. The Sexual Health Inventory for Men further classifies ED severity with the following breakpoints: 1-7 Severe 8-11 Moderate ED 12-16 Mild to Moderate ED 17-21 Mild ED

the evaluation of their patients. The International Index of Erectile Function (IIEF) is a 15-item instrument that evaluates 5 domains: erectile function, orgasmic function, sexual desire, intercourse satisfaction, and global satisfaction. A shorter version of the IIEF for office use has been developed called the ‘Sexual Health Inventory for Men’ (SHIM), as shown in Table 2. A score of greater than 21 is typical for a healthy man, while scores of 17 or less indicate moderate-to-severe ED. Completion of the SHIM coupled with a thorough evaluation of the patient’s history and a detailed physical exam, the provider should have a good understanding of the nature and scope of the patient’s problem.

**Current Treatment Options For Erectile Dysfunction First Line Therapy**

- **PDE5 inhibitors**
  - **Oral Medications**

  The FDA approved sildenafil (Viagra) sixteen years ago. Soon after, vardenafil (Levitra) and tadalafil (Cialis) came onto
the market and men’s sexual health has never been the same. These drugs are all phosphodiesterase (PDE) inhibitors and should be taken an hour before sexual activity. They work by enhancing the effects of nitric oxide, which relaxes smooth muscles in the penis during sexual stimulation and allows increased blood flow. While these drugs improve the response to sexual stimulation, they do not trigger an automatic erection. The majority of men with ED will respond to these drugs and for this reason, they are considered first line therapy for ED.

Second Line Therapy – Local

Penile Injections

Many men achieve stronger erections by injecting drugs into the penis, causing it to become engorged with blood. Drugs such as papaverine hydrochloride, phenylephrine, and alprostadil (Prostaglandin E1) vasodilate blood vessels thereby inducing and maintaining erections. These drugs may create unwanted side effects, however, including persistent erection (priapism) and scarring.

Intraurethral Suppository

A system for inserting a pellet of alprostadil into the urethra is marketed as MUSE. The system uses a pre-filled applicator to deliver the pellet about an inch deep into the urethra. An erection will begin within 8 to 10 minutes and may last 30 to 60 minutes. The most common side effects penile pain, warmth or burning sensation in the urethra; redness from increased blood flow to the penis; and minor urethral bleeding or spotting.

Vacuum Erection Devices

Mechanical vacuum devices induce erections by creating a partial vacuum, which draws blood into the penis, engorging and expanding it. The devices have three components: a plastic cylinder, into which the penis is placed; a pump, which draws air out of the cylinder; and an elastic band, which is placed around the base of the penis to maintain the erection after the cylinder is removed and during intercourse by preventing blood from flowing back into the body.

Surgery

Surgical procedures to improve erections are performed primarily to implant a device that can cause the penis to become erect. Implanted devices, known as penile prostheses, are excellent at restoring erections in men with ED. Implants are devices, however and have complications that include mechanical breakdown, erosion and infection. Malleable implants consist of paired solid rods, which are inserted surgically into the corpora cavernosa. The user manually adjusts the position of the penis. Adjustment does not affect the width or length of the penis. Inflatable implants consist of paired cylinders that are surgically inserted inside the penis and then expanded using pressurized fluid from a co-implanted fluid reservoir and a pump (Figure 1). The cylinders are inflated by pressing on the scrotal pump and reproduce a more natural erection with expansion of both the width and length of the penis.
Psychosexual Therapy

Exploring stress factors such as tension at work or at home can assess whether a man’s psychological state has been altered possibly causing diminished sexual function. Indications of psychosexual issues affecting erections include depression, loss of libido, intimacy issues with his partner, sleep disorders, lethargy, and mood swings.7,8 A therapist will often elicit information by asking the following types of questions:

1) Did the onset of ED coincide with a specific event such as a major surgery or a divorce?
2) Have you experienced the death of a spouse or family member?
3) Do you have diminished sexual desire? If so, how long have you had this?
4) Is your lack of sexual desire a primary symptom or a reaction to past poor sexual performances?
5) Do you have any feelings of performance anxiety?

Pure psychogenic erectile dysfunction is diagnosed objectively with the presence of good nocturnal and morning erections in addition to negative findings on all other evaluations. However, a psychogenic component often is present with organic erectile dysfunction simply due to the fact that sex is such a high performance activity for the male. Another indication would be a history of highly variable erections that can be totally absent one day but virtually normal the next which suggests a psychogenic cause. Virtually 100% of men with severe depression have ED. Men derive much of their masculinity

<table>
<thead>
<tr>
<th>Table 3: Summary of Commonly used PDE5-Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>On-demand phosphodiesterase type 5 (PDE-5) inhibitors — Summary</strong></td>
</tr>
<tr>
<td><strong>Onset</strong></td>
</tr>
<tr>
<td>• Sexual arousal is essential for a response</td>
</tr>
<tr>
<td>• May Occur as early as 20 minutes after administration</td>
</tr>
<tr>
<td>• High-fat foods limit speed and extent of absorption of sildenafil but not tadalafil or avanafil</td>
</tr>
<tr>
<td>• Detumescence occurs immediately following ejaculations or cessation of sexual arousal</td>
</tr>
<tr>
<td><strong>Duration of response</strong></td>
</tr>
<tr>
<td>• Sildenafil: 4 — 6 hours</td>
</tr>
<tr>
<td>• Vardenafil: 6 — 8 hours</td>
</tr>
<tr>
<td>• Tadalafil: up to 36 hours</td>
</tr>
<tr>
<td>• Staxyn: 4 — 5 hours</td>
</tr>
<tr>
<td>• Avanafil: up to 2 hours</td>
</tr>
<tr>
<td><strong>Dose</strong></td>
</tr>
<tr>
<td>• Assess patient fitness for renewed sexual activity before initiating treatment</td>
</tr>
<tr>
<td><strong>Drug</strong></td>
</tr>
<tr>
<td>Sildenafil</td>
</tr>
<tr>
<td>Vardenafil</td>
</tr>
<tr>
<td>Tadalafil</td>
</tr>
<tr>
<td>Staxyn (vardenafil)</td>
</tr>
<tr>
<td>Avanafil</td>
</tr>
</tbody>
</table>

**Drug selection**

• Choice of drug should be individual to patient’s needs
• No comparative studies are available
• The extended period of responsivity of tadalatil may suit some patients

**Metabolism**

• Rapidly absorbed after oral administration
• Maximum plasma concentrations are reached with 15 — 120 minutes in the fasted state
• Pharmacokinetics are dose-proportional over the recommended dose range
• Extensively metabolism by CYP3A4 (major route) and CYP2C9 (minor route) hepatic microsomal isoenzymes

**Adverse effects**

• Adverse effects are released to dose and are usually of mild to moderate severity
• Most common are headache, facial and upper truck flushing, dyspepsia, muscle or backache and nasal congestion
• Temporary alteration in vision may occur with sildenafil and vardenafl
• Cases of priapism very rare

**Drug interactions**

• Concomitant use of potent CYP3A4 inhibitors (e.g. erythromycin, ketoconazole, itraconazole, protease inhibitor) as well as the non-specific CYP inhibitor, cimetidine, is associated with increased plasma levels
• Concomitant administration of CYP3A4 inducers, such as rifampicin, will decrease plasma levels
• PDE5 inhibitors potentiate the hypotensive effects of nitrates — their use in patients on nitric oxide donors or nitrates in any for is contraindicated
from the ability to attain and maintain an erection suitable for sexual activity. In our practice, we refer men for Counseling as a part of an overall strategy to identify sexual stressors and assist in the overall improvement of sexual function.

Summary

Erectile Dysfunction is a sensitive subject between partners and involves psychosocial as well as organic causes. Issues such as cardiovascular problems, neurological conditions, substance use or abuse, psychological and emotional issues, relationship problems, and unhealthy lifestyles all play a role. Prescription medications focus on a singular problem and ignore other etiologies. More importantly, ED can often be an “early warning sign” of a deeper problem, such as cardiovascular disease. It is therefore imperative for the treating clinician to engage the patient and his partner to address all the potential causes in order to successfully treat ED.

References


The two primary functions of the male gonad are facilitation of sperm production and production of sex steroids, primarily testosterone. While low testosterone (hypogonadism) in the male is literally defined as a failure of the testis to perform either of these basic functions, clinically this term is more commonly used in reference to inadequate production of testosterone. Testosterone production is regulated by a series of hormonal and enzymatic interactions, as well as feedback mechanisms, through the hypothalamic-pituitary-gonadal (HPG) axis. Normal levels of testosterone act to stimulate normal growth and development of sex organs and regulate maintenance of secondary sex characteristics. Deficits in testosterone production have been referred to clinically as Androgen Decline in the Aging Male (ADAM), Late-Onset Hypogonadism (LOH) and Testosterone Deficiency Syndrome (TDS). All of these monikers refer to the clinical and biochemical syndrome associated with advancing age and are characterized by symptoms and a deficiency in serum testosterone levels.

Age-Related Declines in Serum Testosterone

Studies have repeatedly demonstrated that there is an age-related decline in total serum testosterone and free testosterone levels in a significant number of men over the age of 60. Additionally, the standard circadian rhythm of serum testosterone tends to become increasingly irregular as men age. The European Male Aging Study demonstrated an unadjusted annual age trend for total T decline of 0.04 nmol/L/year (1.2 ng/dL/year) after a population-based study of more than 3,000 men from eight European centers [Lee 2011]. Conversely, dihydrotestosterone (DHT) and estradiol levels tend to remain constant. Sex hormone-binding globulin (SHBG) has also been demonstrated to increase with increasing age, leading to an increased amount of bound testosterone and a decrease in bioavailable testosterone.

Diagnosis

The diagnosis of hypogonadism requires a combination of subjective and objective parameters. In order to merit treatment, a patient must present with symptoms of low testosterone, as well as evidence of low testosterone on serum studies. Without both, the indications for treatment are less clear.

Objectively, there are a variety of laboratory tests for testosterone, including total testosterone (TT), free-testosterone (free-T) and bioavailable testosterone (bioavailable T). TT includes both bound and unbound testosterone and therefore does not necessarily reflect the amount of active testosterone in the serum. Free testosterone refers to testosterone that is not bound by albumin or SHBG. Testosterone is known to bind tightly to SHBG, which makes this bound testosterone inactive. On the other hand, testosterone bound to albumin is able to dissociate relatively freely and therefore still contributes to the amount of active testosterone in the circulation. Therefore, bioavailable T
refers to both free and albumin bound testosterone, as these two forms are biologically active.

While these various testosterone levels can be evaluated relatively easily through serum collection, there is a wide variability in measurements between various laboratories. Additionally, variability exists in definition of normal serum levels of testosterone, making interpretation imperfect. The Endocrine Society Clinical Practice Guidelines recognize a total testosterone level less than 300 ng/dl as diagnostic of hypogonadism (Bhasin et al, 2010). However a practically accepted alternative interpretation of total testosterone >350 ng/dl are typically considered normal, values <200 ng/dl are considered hypogonadal, and levels in the range of 200-350 ng/dl are borderline and should be assessed and treated on a case-by-case basis dependent upon clinical presentation (Figure 1). It is important to also look at the reference range of normal for each individual laboratory, as there are a variety of assays utilized, and normal reference ranges vary accordingly.

Subjectively, the clinical presentation of hypogonadism is described by numerous nonspecific symptoms. Arguably the most frequently described symptom leading to this diagnosis is decreased libido and subsequent erectile dysfunction. Additional sexual symptoms of low testosterone include ejaculatory dysfunction and reduced intensity of orgasm. Non-sexual symptoms of hypogonadism include depressed mood, easy fatigue and decreased energy, decreased muscle mass and poor concentration, and decreased motivation. These symptoms are unfortunately nonspecific, and a high index of suspicion must be maintained for the diagnosis of hypogonadism to be made, as well as vigilance to rule out other treatable causes.

There are a number of questionnaires that have been developed to assess the existence of symptoms of low testosterone in men. The most commonly used questionnaire clinically is the St. Louis University Androgen Deficiency in Aging Males (ADAM) questionnaire (Table 1). One study evaluating the former three questionnaires demonstrated a sensitivity of 97 percent for the ADAM questionnaire, but a low specificity of 30 percent (Morley 2006). Overall, these questionnaires alone cannot make the diagnosis of hypogonadism, but they can assist in this endeavor and provide a tool for monitoring and reporting.

### Options for Treatment of Low Testosterone

As previously stated, the constellation of symptoms described in patients with hypogonadism is somewhat nonspecific. As a result, it is important to rule out and address other causes of fatigue, decreased libido and decreased motivation such as personal habits, depression and obesity that may contribute to the patient’s symptom spectrum. Lifestyle modifications such as healthy diet, increased exercise, tight blood sugar control in diabetics, smoking cessation, good sleep habits and avoidance of excessive alcohol intake can all act to improve overall health, energy and well-being. These non-pharmacologic interventions should be encouraged in addition to testosterone replacement therapy. Additionally, concomitant depression and/or systemic illness should be diagnosed and treated appropriately in conjunction with low testosterone.

While addressing these lifestyle modifications, testosterone replacement therapy (TRT) should also be initiated with a goal of reaching a therapeutic serum level of testosterone, improving symptoms and avoiding negative side effects. Numerous preparations of testosterone are available, and appropriate selection of which form to utilize should be a decision made after counseling between the physician and patient.

Oral formulations of testosterone do exist but are not used frequently in the U.S. secondary to unacceptable hepatic side effects and lack of availability. An alternative to oral testosterone replacement is the sustained-release buccal form, which is administered as a mucosal-adhesive strip placed against the buccal mucosa. Absorption is directly into the circulation and bypasses intestinal or hepatic absorption and metabolism. This formulation is administered in a 30mg dose twice per day, as the half-life is 12 hours. The mucosal strip is placed on the inside of the gums and remains in place for 12 hours, providing a sustained release of testosterone and maintaining a stable daily serum level of testosterone. Unfortunately the strip does not dissolve completely and needs to be removed after 12 hours. Some patients find this aspect of the buccal tabs inconvenient as there is a constant presence of the tab within the mouth. Overall, this formulation is not readily available or utilized frequently in the U.S.

Several transdermal formulations of testosterone replacement are currently available for use, including patch and gel options. These formulations allow for daily dosing of testosterone. Transdermal testosterone patches have a half-life of 10 hours and a daily dosage of 5-15 mg/day. One benefit of this replacement option is a mimicking
of the normal circadian rhythm of testosterone secretion achieved through the consistent delivery of testosterone into the circulation. One common complaint with this method is the visibility of the patch, as well as reports of skin sensitivity and local rash at the application site. For this reason it is recommended to alternate the location of these patches daily.

Topical gels are another transdermal option for testosterone replacement therapy. Half-life of this formulation is approximately six hours. Recommended application sites are variable and include the chest, axilla and thigh. These formulations tend to have good tolerability, and dosing can easily be adjusted for each individual. One precaution with this formulation is the possibility of partner transference from skin to skin, causing an unintentional elevation of serum testosterone in the patient’s partner. Additionally, patients need to wait two to four hours before showering or swimming after application of the medication, and this can be restricting for some.

Intramuscular injection of testosterone is another method of delivery, with the major difference being half-life and frequency of administration. When testosterone is injected into the muscle, it is absorbed directly into the bloodstream. Testosterone cypionate and testosterone enanthate have half-lives of eight days and four days respectively. Both are given at a dose of 100-400 mg SC every one to three weeks. Peak serum testosterone level is typically seen after 24 to 48 hours, and trough is typically after two weeks. Because of this non-physiologic variation in testosterone level, patients tend to report peak relief of symptoms just after administration but can complain of return of symptoms towards the end of a two-week cycle.

Testosterone propionate has a shorter half-life of only 20 hours. Given this rapid metabolism, it is given on a more frequent schedule of 100mg SC each week. Because of this more frequent administration, this formulation tends to be less popular. Alternatively, a preparation of IM testosterone formulated in castor oil, testosterone undecanoate, has a significantly longer half-life of 34 days, allowing for less frequent dosing of 700-1000 mg SC every 10 to 12 weeks. This formulation has just become FDA approved and is now available in the U.S. Side effects can include pulmonary oil microembolism reactions, and patients need to be made aware of this.

Another long-acting preparation of testosterone comes in pellet form, deposited subcutaneously. Typically two 1275 mg pellets composed of pure crystals of testosterone are implanted subcutaneously every three to six months. Insertion of this medication does require a small incision and in-office procedure. Physiologic levels have been proven to be achieved and maintained throughout the treatment course. The stable levels and further decreased frequency of treatment is appealing to some patients. However the need for an incision and the risk of infection or extrusion (5 percent to 10 percent) of the pellets is a negative.

### Monitoring of Testosterone Replacement

While prescribing TRT for a patient, it is important to monitor several parameters prior to initiation of treatment at regular intervals every three to six months during the first year of replacement therapy and at least annually thereafter. Follow-up visits should include assessment of serum testosterone to monitor therapeutic dosing. Serum prostate-specific antigen (PSA) should be obtained and a digital rectal exam performed to rule out interval development of prostate pathology. Prostate biopsy should be reserved for patients with interval development of palpable prostate abnormalities or significant elevation in PSA. As polycythemia is a possible complication of TRT, assessment of HCT and estradiol levels is an essential surveillance parameter to prevent increased cardiac events. If polycythemia is identified, the dose of testosterone should be immediately reduced or discontinued completely. If estradiol is elevated, aromatase inhibitors can be utilized to try to manage this response. Metabolic parameters such as lipid profile and hepatic enzymes should be monitored as well.

### Benefits of Testosterone Therapy

Numerous benefits of testosterone replacement have been reported in those men with symptoms of hypogonadism. Sexual symptoms associated with hypogonadism such as erectile dysfunction, decreased libido and decreased volumes
of ejaculate have been reported to improve with treatment of low testosterone levels. Additionally, patients with erectile dysfunction being treated with phosphodiesterase-5 inhibitors show improved response to these pharmacologic therapies when their testosterone is corrected to a normal physiologic level.

Osteoporosis has been shown to improve in hypogonadal men after testosterone therapy. In fact, a significant increase in cortical and trabecular bone mineral density is documented over the course of testosterone replacement therapy. A slight but significant increase in paraspinal muscle area is also noted. In long-term regularly treated hypogonadal men, the Z-score, or bone mineral density for age-matched controls, is within the normal range (Zacharin 2003).

An association between hypogonadism and Type II diabetes, dyslipidemia, metabolic syndrome and visceral adipose tissue has been identified. Testosterone replacement therapy in men with hypogonadism and diabetes has been shown to reduce insulin resistance and improve glycemic control (Kapoor 2006).

**Risks of Testosterone Therapy**

As with most pharmaceutical interventions, there are side effects and risks associated with testosterone replacement therapy that need to be discussed with patients prior to initiation of therapy. Some common side effects include decrease in testicular size, gynecomastia, polycythemia and negative impact on spermatogenesis.

There is much recent controversy in the media regarding increased risk of cardiac events associated with the use of TRT. A recent study in JAMA released in November 2013 reported an increase in negative cardiovascular events in men over 65 years old and those with cardiac history under 65 years old within nine months of initiation of TRT when compared to age-matched men without use of TRT (JAMA 2013).

The issue with this particular retrospective paper is that values such as HCT and estradiol were not included in the study, and abnormalities in these values can greatly affect the decision to initiate treatment with TRT and also guide adjustments to the doses. Additionally it was not reported whether these patients were being treated appropriately for their low testosterone according to guidelines of positive symptomatology and low serum testosterone. It is this author’s opinion that no definitive evidence exists at this time to indicate whether testosterone has a negative or positive impact on cardiovascular health, if any impact at all.

At this time, a conversation must be carried out between physician and patient discussing the possibility of increased cardiac events in these populations prior to initiating therapy. Additionally, as with all patients treated with testosterone, close monitoring should be performed during therapy as outlined above. If there is any question of a patient’s cardiac health, a referral to cardiology should also be made.

Another area for concern regarding selection of appropriate patients for TRT are those patients with prostate cancer. Active prostate cancer is an absolute contraindication for testosterone replacement therapy at the present time, secondary to concerns that it may lead to progression of disease. It is not, however, thought that testosterone causes prostate cancer in patients who otherwise would not have developed this malignancy. There are conflicting opinions regarding testosterone replacement therapy in patients with a history of prostate cancer, but no current evidence of disease. Most physicians will proceed to replace testosterone in men with hypogonadism, demonstrating symptoms, who have an undetectable PSA for more than six months. Again, an informative conversation should take place between patient and physician discussing the risks and benefits in this context before initiating therapy. Counseling is also advised in those patients with risk factors for development.
of prostate cancer in their lifetime, such as a strong family history and African American ethnicity.

Overall, patients with low-serum testosterone exhibiting symptoms of this condition may benefit from testosterone replacement therapy. Monitoring of symptom response, physical exam and serum evaluation should be done periodically to ensure response to therapy, therapeutic levels of testosterone and to prevent unwanted side effects. The route of administration should be determined by patient desires and insurance coverage. Risks, benefits and alternatives should be thoroughly discussed with patients as well prior to initiation of treatment. Additional counseling should be provided in those patients with cardiovascular disease, history of prostate cancer or a desire to preserve fertility.

### Table 2: Treatment options for low Testosterone

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Route</th>
<th>Dosage</th>
<th>Half-life</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testosterone buccal system</td>
<td>30 mg buccal system</td>
<td>30 mg buccal system</td>
<td>12 hours</td>
<td>-Noninvasive</td>
<td>Gum related adverse events</td>
</tr>
<tr>
<td>-Testosterone enanthate</td>
<td>IM injection</td>
<td>100-400 mg Q1-3 weeks</td>
<td>-8 days</td>
<td>-Less frequent dosing</td>
<td>-Injection required</td>
</tr>
<tr>
<td>-Testosterone cypionate</td>
<td>IM injection</td>
<td>700-1000 mg IM Q 10-12 weeks</td>
<td>34 days</td>
<td>-Less frequent dosing than other IM forms</td>
<td>-Risk of oil pulmonary embolism</td>
</tr>
<tr>
<td>Testosterone undecanoate</td>
<td>IM injection</td>
<td>75 mg/pellet, 8-15 pellets Q3-6 months</td>
<td>10-100 minutes, delayed release</td>
<td>-Less frequent dosing, delayed release</td>
<td>-Requires office procedure for implantation</td>
</tr>
<tr>
<td>Testosterone patch</td>
<td>Transdermal administration</td>
<td>2,4, or 6 mg patch transdermal Q 24 hours (titrate to 2-15 mg/day)</td>
<td>10 hours</td>
<td>-Once-daily application</td>
<td>-Adverse skin reactions</td>
</tr>
<tr>
<td>Testosterone gels</td>
<td>Transdermal application</td>
<td>Starting dose 40-60 mg transdermal daily, then titrate</td>
<td>6 hours</td>
<td>-Once daily application</td>
<td>-Possible partner or child transference</td>
</tr>
</tbody>
</table>

References


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Benign prostatic hyperplasia (BPH) is one of the most prevalent health problems affecting men older than 50, and the incidence increases with age. Longstanding BPH that is not treated can lead to urinary tract infection, hematuria, bladder stones, urinary retention and renal insufficiency. As baby boomers age, primary care providers including nurse practitioners will be seeing more men older than 50. It is imperative that we are able to make a proper assessment of their urinary symptoms. This article outlines a clinical approach for the evaluation and diagnosis of men with BPH and provides an overview of treatment options.

Defining Urinary Symptoms

BPH and benign prostatic enlargement (BPE) are often used to describe urinary symptoms in older men. Unfortunately, the terminology implies that the symptoms have a prostate origin. Since voiding symptoms are neither gender-specific nor always related to the prostate, a more accurate term is lower urinary tract symptoms (LUTS).

Symptoms of LUTS can be categorized as irritative (filling) or obstructive (voiding) (see Table 1). Categorizing the symptoms often assists in making the correct diagnosis and thus treatment interventions. Irritative or filling symptoms suggest a bladder origin. These symptoms include urinary frequency, urgency, nocturia, incontinence and bladder pain. The symptoms of hesitancy, dysuria, straining and urinary flow problems suggest a urethral origin.

The key to unlocking the diagnosis for LUTS is obtaining a thorough history. To assist in the assessment of urinary symptoms, the American
<table>
<thead>
<tr>
<th>Symptom</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INCOMPLETE EMPTYING:</strong> Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td><strong>FREQUENCY:</strong> Over the past month, how often have you had to urinate again less than 2 hours after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td><strong>INTERMITTENCY:</strong> Over the past month, how often have you found you stopped and started again several times when you urinated?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td><strong>URGE TO URINATE:</strong> Over the past month, how often have you found it difficult to postpone urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td><strong>Weak stream:</strong> Over the past month, how often have you had a weak urinary stream?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td><strong>STRAINING:</strong> Over the past month, how often have you had to push or strain to begin urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td><strong>URINATION AT NIGHT:</strong> Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

**Symptom Score:**
1-7 Mild, 8-19 Moderate, 20-35 Severe

**Bothersome Score Due to Urinary Symptoms**

<table>
<thead>
<tr>
<th>Delighted</th>
<th>Pleased</th>
<th>Mostly</th>
<th>Mixed</th>
<th>Mostly</th>
<th>Unhappy</th>
<th>Terrible</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

**Quality of Life Due to Urinary Symptoms:** How would you feel if you had to live with your urinary condition the way it is now — no better, no worse — for the rest of your life?
Urological Association’s (AUA) measurement committee developed a validated symptom tool in 1991 that contains seven key questions analyzing symptoms and a separate question about the symptoms’ effects on quality of life (Table 2). Since 1991, international consultants on BPH have adopted the questionnaire and termed it the International Prostate Symptom Score (IPSS).

Originally designed to be a tool for research, the IPSS is now widely used in the United States and abroad for evaluation of men with LUTS. The IPSS scores can be put into categories ranging from mild symptoms to moderate symptoms (8-19) to severe symptoms (more than 20).

In addition to the patient’s symptoms, the impact on quality of life seems to drive treatment. Your patient’s answers to the symptom questions, as well as any alleviating or aggravating factors, will provide comprehensive assessment for the current urologic complaint. We also use this tool to assess the efficacy of our treatment interventions. Men will often show improvement of their score after being placed on treatment. We have found that quantifying such information in the patient record has been also helpful with respect to reimbursement.

History & Familial Considerations

After evaluating the patient’s urinary symptoms, the next step is a thorough medical history. This must be complete and accurate, since many urologic and non-urologic conditions can mimic BPH. Differentiation between the patient’s symptoms and medical history has the most bearing on diagnosis.

Urinary symptoms that have a storage or outlet origin can be greatly influenced by multiple factors. Anticholinergics, antihypertensives, allergy or cold medications (both over-the-counter and prescription), diuretics and herbs or vitamin supplements may potentiate urinary symptoms. Obtain a complete list of medications taken and any correlation with the onset of urinary symptoms.

Family history plays an important role in symptom assessment. Ask the patient if he has or had male relatives with prostate cancer or BPH. Data have established a familial component for prostate cancer, and more recent data suggests hereditability of BPH. Social habits can contribute to urinary symptoms; for example, caffeine ingestion can cause increased urinary frequency. Inquire about alcohol, recreational drug and tobacco use.

All past medical history is pertinent, but pay particular attention to previous genitourinary problems such as urinary tract infections, sexually transmitted diseases or previous urologic procedures. A review of symptoms would not be complete without inquiring about sexual and neurological function.

Conducting the Physical Exam

Some of the physical exam is driven by history. Observe the patient for signs of anemia, edema or uremia, since these can occasionally be associated with BPH or other urologic conditions. An abdominal exam including observation, auscultation and palpation is considered routine, although seldom diagnostic. Bladder distention may be palpable in some patients.

A genitalia exam is useful to assess for any abnormalities that may hinder urine flow, such as meatal stenosis, phimosis or balanitis. Perform a digital rectal exam (DRE) with a focused neurological examination on any man with urinary symptoms. During the DRE, you can examine the anal sphincter tone and bulbo-cavernous reflex. This exam may help rule out colorectal cancer or a neurological

<table>
<thead>
<tr>
<th>Table 2: Differential Diagnosis List for BPH</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bladder Tumor</strong></td>
</tr>
<tr>
<td>May present with irritative (storage) symptoms</td>
</tr>
<tr>
<td>Hematuria on urinalysis</td>
</tr>
<tr>
<td>Higher incidence with smoking history or chemical exposure</td>
</tr>
<tr>
<td><strong>Infection (UTI)</strong></td>
</tr>
<tr>
<td>Associated with frequency, urgency and dysuria</td>
</tr>
<tr>
<td>Urinalysis with positive nitrates and bacteria</td>
</tr>
<tr>
<td><strong>Neurogenic Bladder</strong></td>
</tr>
<tr>
<td>Usually present with obstructive (voiding) symptoms</td>
</tr>
<tr>
<td>Patients with diabetes or neurological conditions</td>
</tr>
<tr>
<td><strong>Overactive Bladder</strong></td>
</tr>
<tr>
<td>Urinary frequency, urgency and urge incontinence</td>
</tr>
<tr>
<td>Urinalysis negative</td>
</tr>
<tr>
<td><strong>Prostate Cancer</strong></td>
</tr>
<tr>
<td>Often asymptomatic (symptoms are often from associated Prostate Hypertrophy)</td>
</tr>
<tr>
<td>Urinalysis often negative (advanced stages can present with hematuria)</td>
</tr>
<tr>
<td>PSA is usually elevated, above established baseline</td>
</tr>
<tr>
<td>May have abnormal prostate exam (nodularity)</td>
</tr>
<tr>
<td><strong>Polyuria</strong></td>
</tr>
<tr>
<td>Symptoms of frequency and nocturia</td>
</tr>
<tr>
<td>Noted in uncontrolled diabetes mellitus or diabetes insipidus</td>
</tr>
<tr>
<td>Per history in patients who take diuretics or drink water excessively</td>
</tr>
<tr>
<td>Coronary artery disease (nocturia due to increased excretion at night)</td>
</tr>
<tr>
<td><strong>Prostatitis</strong></td>
</tr>
<tr>
<td>Dysuria, frequency and possible pelvic pain</td>
</tr>
<tr>
<td>DRE provides evidence of tender, boggy prostate</td>
</tr>
<tr>
<td>Urinalysis may have bacteria</td>
</tr>
<tr>
<td><strong>Urethral stricture</strong></td>
</tr>
<tr>
<td>Any age</td>
</tr>
<tr>
<td>Higher incidence in patients with history of STD, trauma or previous urethral instrumentation</td>
</tr>
</tbody>
</table>
origin for urinary symptoms. Palpate the prostate for size, texture and symmetry. Asymmetry or a palpable nodule suggests prostate cancer, prompting further evaluation. Prostate size by DRE does not necessarily correlate with the degree of obstruction or symptom severity.

**Diagnostic Tests**

For diagnostic evaluation of a man with lower urinary tract symptoms, minimum recommended tests are a urinalysis and serum creatinine. The urinalysis may be by dipstick or microscopic exam. Either method can help rule out urinary tract infection and hematuria. A serum creatinine is useful to assess renal function.

A prostate-specific antigen (PSA) test is considered optional in the initial evaluation to evaluate for BPH. PSA is not specific for prostate cancer, and a high percentage of men with BPH have an elevated PSA. Therefore, a PSA test does not differentiate well between BPH symptoms and prostate cancer. Furthermore, PSA testing may prompt further evaluation with a prostate biopsy. Further diagnostic tests may be needed based on differential diagnosis.

**Differential Diagnosis**

Differentiating between a BPH diagnosis and other conditions can be challenging. Table 2 provides a list of potential conditions that present with LUTS. The history, exam and diagnostic tests may help differentiate between these conditions and eliminate some with high confidence. The differential diagnosis of BPH can be made if other diagnoses can be eliminated. Red flags that require further evaluation are urinary retention, infection, hematuria, elevated creatinine and elevated PSA.

**Treatment Choices**

Once you make a diagnosis of BPH, the most important factor driving treatment is the degree to which the patient is bothered by symptoms. This is another reason why we rely on the IPSS survey in the office setting (see Figure 1). Treatment options range from conservative (expectant management) to more invasive approaches (surgery).

For a majority of patients, expectant management is an appropriate choice as long as none of the red flags mentioned earlier are present (see Figure 2). The progression of BPH and development of complications is hard to predict, therefore it is reasonable to follow these patients every six months initially.

**Medical Therapy**

Until the advent of medical therapy, prostate surgery was considered the gold standard for symptomatic BPH. Medical therapy has been considered first-line treatment since the advent of alpha-adrenergic receptor antagonists, or alpha-blockers. The sympathetic nervous system influences contraction of the prostatic smooth muscle. This is activated by the alpha receptor activity (predominately alpha-1a adrenoceptors) within the prostate. Alpha blockers, therefore, bind these receptors, found on the bladder neck and prostate tissue, causing relaxation of smooth muscle. Alpha blockers typically used in our institution for BPH are outlined in Table 3. Numerous clinical studies have demonstrated that these medications are effective at reducing urinary symptoms and improving urinary flow. Alpha blockers vary in dosing schedule, duration of activity, cost and receptor activity.

Hormone manipulation has been used for years in the treatment of BPH, mainly with finasteride (Proscar), which was approved in 1992. Finasteride is an anti-androgen that inhibits 5 alpha-reductase, thus blocking the conversion of testosterone to dihydrotestosterone (DHT). Clinical data has shown that finasteride decreases prostatic volume and improves urinary flow. A baseline PSA is suggested prior to initiation of treatment, since finasteride can lower PSA by 50 percent.

In our practice, men with moderate to severe BPH are often placed on combination therapy with an alpha-blocker and a 5-alpha reductase inhibitor. Numerous studies in Europe and the U.S. have shown greater clinical efficacy using both medications together. Currently, Jalyn (from GlaxoSmithKline) is a formulation available that contains both dutasteride and tamsulosin in a single pill.

### Table 3: Pharmacologic Therapy for BPH

<table>
<thead>
<tr>
<th>Medication</th>
<th>Receptor Selectivity</th>
<th>Dosing Range</th>
<th>Generically Available</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alpha Antagonists</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alfuzosin</td>
<td>-</td>
<td>10 mg daily</td>
<td>No</td>
</tr>
<tr>
<td>Doxazosin</td>
<td>-</td>
<td>1-8 mg daily</td>
<td>Yes</td>
</tr>
<tr>
<td>Silodosin</td>
<td>+</td>
<td>8 mg daily</td>
<td>No</td>
</tr>
<tr>
<td>Tamsulosin</td>
<td>+</td>
<td>0.4-0.8 mg daily</td>
<td>Yes</td>
</tr>
<tr>
<td>Terazosin</td>
<td>-</td>
<td>1-10 mg daily</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>5-Alpha-Reductase Inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dutasteride</td>
<td>+</td>
<td>0.5 mg Daily</td>
<td>No</td>
</tr>
<tr>
<td>Finasteride</td>
<td>+</td>
<td>5 mg daily</td>
<td>Yes</td>
</tr>
</tbody>
</table>

+ : selective; -: not selective; BPH: benign prostatic hyperplasia

* Adapted from Johns Hopkins University, Brady Urological Institute
Surgical Therapy

Invasive or surgical treatment options are usually considered for patients who do not respond to medical therapy or have severe symptoms or complications of BPH, such as urinary retention. Surgery offers the best chance for symptom improvement, but also has a higher risk of complications. A transurethral resection of the prostate (TURP) is associated with the highest degree of symptom improvement (75 percent to 96 percent). A TURP is performed under general anesthesia, and the urologist resects the prostate tissue endoscopically through the urethra. Generally, a same day discharge or one-day hospital stay is needed. Associated complications include retrograde ejaculation and incontinence.

Newer bipolar technology incorporated in standard resectoscopes is showing promise in recent clinical outcome evaluations at our institution. Open prostatectomy is a much more invasive surgery and in turn has a higher complication rate. It is usually reserved for men with severe BPH symptoms and very large prostate glands (> 100 grams).

Numerous technologies have emerged for treating BPH. These include urethral stents, coils, laser ablation, transurethral microwave therapy (TUMT) and transurethral hyperthermia (TUNA). In addition, GreenLight Laser technology is often used for ablation of the prostate adenoma. The risks and benefits of these options are widely varied and certainly surgeon-dependent. Partnership between the primary care provider and the urologist continues to prove efficacious in the management of BPH.

References


Urinary incontinence, predominantly stress or urge incontinence, is a common complaint for many female patients, with prevalence rates of daily incontinence ranging between 5 percent and 15 percent for middle-aged and older women. Both stress and urge urinary incontinence have generated significant discussion in the past 18 months amongst physicians and patients and merit greater in depth coverage.

Urge incontinence has just benefitted from several new advances, including FDA approval of a new drug class, first time over-the-counter availability of a transdermal antimuscarinic and FDA approval of Onabotulinum toxin A for refractory overactive bladder and urge incontinence. Furthermore, patient education on overactive bladder is the American Urological Association’s campaign mission for 2014. Discussions on stress incontinence recently have touched on the surgical use of synthetic mesh for the treatment of this type of incontinence and have arisen largely from the controversy and complications involving use of vaginally placed synthetic mesh for the treatment of a different condition, pelvic organ prolapse. Since most patients first broach the topic of incontinence with their internist or primary care physician, it is worth taking a closer look at the different facets of these recent issues.

Urge Urinary Incontinence

Urge urinary incontinence (UUI) is defined as the involuntary leakage of urine accompanied by or immediately preceded by urgency. Overactive bladder (OAB) is characterized by symptoms of urgency, with or without urge incontinence, usually with frequency or nocturia. Basic evaluation includes obtaining a history and physical, including assessment of symptom severity, bother and duration, environmental and social factors, mental status and physical abilities of the patient. Other associated symptoms that may require further evaluation (e.g. weight loss, hematuria, flank pain, dysuria) should also be queried.

A urine analysis, ranging from dipstick to microscopy and culture, is recommended to rule out infection, microscopic hematuria and sterile pyuria. An assessment of a post-void residual can be helpful (obtained with a bladder scanner or in and out catheterization) when voiding dysfunction is suspected. The measure of post-void residual is actually a component, along with H&P and urinalysis, of measure #48 on the Urinary Incontinence Assessment of the Physician Quality Reporting System (PQRS) for Medicare services. A voiding diary (three-day recording of measured “ins and outs” and types of fluid consumed) allows a physician to tailor behavioral therapy, assess a patient’s functional bladder capacity and also rule out nocturnal polyuria, which may be due to other medical comorbidities (e.g. obstructive sleep apnea or congestive heart failure).

Treatment of Urge Urinary Incontinence

First line: Behavioral therapy

First-line interventions can include behavioral therapy, such as fluid restrictions, bladder drills, timed voiding, management of constipation, diet modification including limiting known diuretics and caffeine, as well as urge suppression techniques using kegel exercises. Pelvic floor muscle training for urge incontinence can be a useful approach in a motivated patient who wishes to avoid medications, and several pelvic floor physical therapists are available in the metro Atlanta area.

Second line: Oral and transdermal Pharmacotherapy

For patients failing first-line therapy, medications are the mainstay in treatment of OAB and UUI. Antimuscarinics...
can reduce daytime and nighttime frequency of urination, urgency and urge incontinent episodes by targeting M2 and M3 receptors in the bladder. Some commonly associated side effects with these medications, mediated by M1-M5 receptors throughout the nervous system, include dry mouth (8-60 percent), dry eyes or blurry vision, constipation (3-10 percent) and somnolence (highest with oxybutynin 12 percent).2

Although extended release and immediate release preparations of oxybutynin and tolterodine are equally effective at reducing the number of UII episodes and voids per day, extended release formulations have significantly lower rates of dry mouth than immediate release preparations2. Antimuscarinics should not be used in patients with narrow-angle glaucoma or gastroparesis and used with caution in certain populations (physically active patients, due to possible risk of anhidrosis; elderly or cognitively impaired patients due to affinity for the M1 receptor in the central nervous system, causing dizziness, memory impairment and somnolence). Due to its polar structure, trospium chloride, a quaternary amine, has limited penetration across the blood brain barrier and may be a safer antimuscarinic in elderly or cognitively impaired patients.2

The antimuscarinic oxybutynin can be delivered transcutaneously (available in patch and gel) in addition to oral immediate and extended-release formulations. Transcutaneous oxybutynin avoids first pass gastrointestinal and hepatic metabolism of oxybutynin, producing less N-desethoxybutynin. (This compound is responsible for anticholinergic side effects such as dry mouth.)2 Last year, transcutaneous oxybutynin became the first antimuscarinic available over the counter. The patch, placed twice a week, releases 3.9mg/day.

Patients should nonetheless be counseled regarding known contraindications to anticholinergics (gastric or urinary retention, uncontrolled narrow-angle glaucoma) and be advised to read the package insert before starting themselves on an anticholinergic. Antimuscarinics should be used with caution in elderly patients. Additionally, patients with conditions that may cause incomplete bladder emptying, including diabetes, lumbar spine problems, extensive pelvic surgery or neurologic conditions, may benefit from assessment of a post-void residual to avoid urinary retention with an anticholinergic. Depending on a patient’s prescription drug plan, an over-the-counter option may be financially advantageous.

In addition to making oxybutynin available over the counter, in 2012 the FDA approved the first new oral drug class in management of overactive bladder since anticholinergics were launched 30 years ago. Mirabegron is a beta-3 adrenergic agonist that targets beta-3 adrenoreceptors in the bladder, modulating the filling phase of the bladder (a sympathetic mediated process). Advantages of the medication include daily dosing and avoidance of common side effects associated with antimuscarinics, including dry mouth, constipation and dry eyes or cognitive impairment.

In studies, the medication can take up to eight weeks to demonstrate benefit, and common side effects include hypertension (11 percent at 25mg daily dosing, 7 percent – equivalent to placebo – at 50mg daily dosing), nasopharyngitis (3 percent) and headache (3 percent).3 It is not recommended in severe uncontrolled hypertension (systolic BP ≥180mmHg and/or diastolic ≥110mm Hg). Additionally, since mirabegron is a moderate CYP2D6 inhibitor, the systemic exposure to CYP2D6 substrates such as metoprolol and desipramine is increased when co-administered with mirabegron.

With no associated cognitive side effects, mirabegron may also have a significant impact on OAB and UII treatment in the elderly. Dual therapy will also likely be an area of interest in the future for beta-3 agonists. A recent Phase II study has already assessed a dual therapeutic approach, combining beta-3 adrenergic mirabegron (25mg and 50mg daily) and antimuscarinic solifenacin (≥5mg daily), which have different mechanisms of action. Initial results have demonstrated combination therapy to be safe and well tolerated, with combination therapy more efficacious than solifenacin alone.4

**Third-line therapy: Neuromodulation (PTNS and InterStim) and Onabotulinum toxin A**

Patients who are refractory to oral pharmacotherapy or unable to tolerate adverse events may consider third-line options. Some patients may need further evaluation at the discretion of their urologist or urogynecologist,
including cystoscopy and/or urodynamics (assessment of bladder storage and emptying on multichannel transducing system) prior to proceeding with these interventions to assess for other functional or anatomical causes for their symptoms.

Percutaneous tibial nerve stimulation (PTNS) is a non-surgical, non-pharmacologic, office-based neuromodulation of the tibial nerve for the treatment of OAB and UUI. Stimulation of the tibial nerve modulates afferent signals through the sacral nerve plexus, resulting in decreased episodes of frequency, nocturia and UUI. Through 12 weekly 30-minute office sessions, a slim needle electrode is inserted by the ankle and connected to the battery-powered stimulator. This process is also referred to as neuromodulation. Voiding diaries are completed at six and 12 weeks. Responders then complete maintenance therapy, typically one 30-minute session once a month. Presence of a pacemaker is a contraindication. Side effects and disadvantages are minimal other than inconvenience to the patient for weekly treatment visits.

Onabotulinum toxin A received FDA approval in 2013 for treatment of OAB and UUI. This specific formulation of botulinum toxin type A inhibits docking and fusion of vesicles within the nerve terminal of the bladder detrusor muscle, inhibiting acetylcholine release from efferent nerves. It is typically an office-based procedure performed under direct vision cystoscopically with 100 units of the toxin injected at 20 different sites in the bladder.

Disadvantages include duration of efficacy (six to nine months), 5 percent risk of temporary urinary retention and 30 percent risk of urinary tract infection. In initial studies, 30 percent of patients achieved continence, and the majority of patients improved on therapy.

Sacral neuromodulation (Interstim)

Stimulation of the sacral nerves to modulate the neural reflexes that affect the bladder is a surgical therapy FDA approved in 1997 for the treatment of refractory urge incontinence, urgency and frequency as well as non-obstructive urinary retention. Implantation consists of two steps. A trial stage, which can be performed in the office under local anesthetic, involves placement of a lead next to the dorsal root of S3. When symptom improvement exceeds 50 percent, the patient undergoes a second stage with permanent implantation of the lead and stimulator in the soft tissue of the buttock. The treatment has cure rates of more than 40 percent and >50 percent improvement in UUI and OAB symptoms in another third of patients. Side effects include pain at the stimulator or lead site (<15 percent) and infection (6 percent). MRIs (except of the brain) are contraindicated in patients with an Interstim device. Duration of the battery is upwards of five years.

Stress Urinary Incontinence: Evaluation and Treatment

Stress urinary incontinence (SUI) is the complaint of involuntary leakage on effort or exertion, or on sneezing or coughing1. Basic evaluation is similar to urge urinary incontinence and includes a thorough obstetric and gynecologic history as well as a pelvic exam assessing for mobility of the urethra, quality of the vaginal tissue, associated pelvic organ prolapse, presence of leakage with cough or exertion on exam and can include assessment of post-void residual.

Non-surgical treatment of SUI

Treatment options for stress incontinence are generally aimed at restoring support to the urethra and anterior vaginal wall to decrease mobility of the urethra, or increased resistance and compression on the urethra during episodes of exertion. This sometimes can be achieved through conservative measures but, depending on the severity of the leakage, may also require other options including surgery. Behavioral therapy can include fluid restriction, pelvic floor muscle training using kegel exercises, defensive voiding and weight loss. Weight loss of 5-10 percent has similar efficacy to that of other non-surgical treatments and should be offered as a first-line therapy. For women who fail conservative measures, further evaluation and treatment with a urologist or urogynecologist may be appropriate.

Office-based measures for stress incontinence include pessaries (silicone ring placed in the vagina by the patient) designed specifically for the treatment of SUI. Pessaries offer patients a non-surgical, reversible option with immediate efficacy, but do not cure the SUI and require periodic removal and cleaning of the pessary.

Urethral bulking agents are a useful treatment modality in patients with stress incontinence seeking less invasive treatment. Most agents are injected transurethrally in retrograde fashion under direct cystoscopic guidance between the mid-urethra and bladder neck and can be performed in the office with local anesthetic or in an operating room.
Though initially felt to benefit patients with intrinsic sphincteric deficiency, reports have demonstrated efficacy in patients with urethral hypermobility. Patients should be counseled that repeat injections are likely required to achieve efficacy, outcomes are inferior to surgical interventions and that efficacy diminishes with time.1

Surgical treatment of SUI and mesh mid-urethral slings

Surgical approaches for SUI have evolved over the years and more recently have included mid-urethral mesh slings, pubovaginal slings using autologous (native) fascia, burch colposuspensions and needle urethropexies. It is not necessary to go into the details of different surgical techniques, but in the last 10 years, the mid-urethral sling (MUS) has become the most commonly performed surgery for the treatment of SUI. It is equally effective and durable as other techniques with the advantage of being less invasive.

Benefits of synthetic mid-urethral slings compared to the Burch procedure and fascial slings include shorter operative times, the procedure is outpatient and has decreased incidence of postoperative voiding dysfunction.9 The sling is placed transvaginally, tension-free, under the mid-urethra and can be placed via a retropubic or transobturator approach. Overall, complications for both approaches for MUS are low and include bladder perforation (<5 percent), bleeding (2-4 percent), nerve injury (1-2 percent), voiding dysfunction (2-9 percent), UTI (7-12 percent) and mesh erosion (0.5-1 percent).10

The use of knitted synthetic polypropylene mesh in the MUS for stress urinary incontinence has generated significant discussion amongst patients, physicians and the legal community due to the recent FDA public health notifications on complications of transvaginal mesh. Since its initial notification in 2008, this has further narrowed its notification to transvaginally placed prolapse mesh solely for pelvic organ prolapse (bulge or herniations of pelvic organs into the vagina) and in 2013 updated its stance stating that “the safety and effectiveness of multi-incision slings is well established in clinical trials that followed patients up to one year.” There has been no recall of mesh mid-urethral slings. The American Urogynecologic Society (AUGS) and the Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (SUFU), released a joint position statement on mid-urethral slings and have created statements and a website covering frequently asked questions by providers and patients on mid-urethral slings to help navigate this area. The following is an excerpt:

“A mid-urethral sling is used to treat stress urinary incontinence. A vaginal prolapse mesh is placed through a vaginal incision to correct a vaginal bulge (ex. cystocele, rectocele or dropped uterus). Vaginal prolapse mesh is larger and placed in a different location than the mid-urethral sling mesh. After the FDA issued its initial statements, additional information appeared in the media, including some lawyer advertisements. The media has also reported issues related to transvaginal mesh. Because mesh is used in both procedures (transvaginal mesh for prolapse and the mid-urethral sling for stress urinary incontinence) there may be some confusion about the use of mesh. As we have noted, transvaginal mesh is currently under further study by the FDA, but with respect to the mid-urethral sling, the FDA has determined that no further study is necessary.”

AUGS and SUFU position statement on safety of mesh mid-urethral slings, 2014

Nonetheless, patient preference or host factors (e.g. radiation, immunosuppression, tobacco use) may steer treatment away from any synthetic material for surgical treatment of stress incontinence. In these instances, alternate surgeries exist, including pubovaginal slings using a patient’s native fascia (rectus fascia or fascia lata).

Regardless of the type of incontinence, the underlying theme in treatment is a personalized approach addressing individual patient needs. Whether it is SUI and the decision for a sling or choosing the best OAB therapy for a frail, elderly woman, multiple safe and effective treatment options are available to improve quality of life in these patients.

Related links:

- For providers: http://www.sufuorg.com/docs/news/Provider-FAQs.aspx
- American Urological Association’s Urology Care Foundation website on overactive bladder (OAB) for patients and physicians: http://www.urologyhealth.org/OAB/

References:

Through research and minimally invasive testing and surgical techniques, Atlanta physicians are making a difference for patients with high-risk pregnancies, gynecological cancers and more.

Non-Invasive Prenatal Testing Moves Toward Becoming Standard of Care

Non-Invasive Prenatal Testing (NIPT) is used to analyze cell-free fetal DNA circulating in maternal blood. It allows for earlier and more accurate detection of chromosomally abnormal pregnancies. Over the past two years, NIPT has become an increasingly popular option for women who desire aneuploidy screening during pregnancy in North America and Europe.

Cell-free DNA (cfDNA) fragments are present in the bloodstream. In pregnant women, cfDNA from both the mother and the pregnancy circulates in the maternal blood. NIPT is able to isolate and analyze the fetal fraction of the cfDNA and detect fetal trisomies such as Down syndrome (trisomy 21) with >99.9 percent accuracy with less than 0.1 percent (1/1000) false-positive rate.

According to Genevieve Fairbrother, M.D., M.P.H., with Obstetrics & Gynecology of Atlanta, the high accuracy of NIPT, along with the additional benefit of a decreased false-positive rate, has made this new approach a “game changer.”

“Prior to NIPT, the most accurate non-invasive, low-risk option had a 1/20 false-positive rate. These older tests could detect affected pregnancies 90 percent of the time, but out of a thousand women, there would be 50 false-positives and maybe only three true-positives,” she explains. “With a false-positive rate this high, it is difficult to counsel a woman when her ‘positive screen’ is correct less than 5 percent of the time.”

A non-invasive prenatal screen, NIPT requires only two vials of the patient’s blood and can be performed as early as the 10th week of pregnancy. From this blood sample, the test distinguishes between the mother’s cell-free DNA and that of her fetus. It determines normal levels of chromosomes using reference chromosomes, and then, with specialized probes, evaluates chromosomes of interest, such as chromosome 21, to determine if the pregnancy is affected.

“We’re so happy to have the ability to detect chromosomal abnormalities with this kind of accuracy and at the same time limit our patients’ exposure to unnecessary invasive tests such as CVS or amniocentesis. The advances that this technology has made in dramatically decreasing the false-positive rate are creating a paradigm shift in our approach to aneuploidy screening in pregnancy,” Fairbrother says. “The majority of insurance companies have agreed to cover this test for women who are age 35 and older at delivery. We have high expectations that an upcoming
Can Diet and Exercise Modulate Ovarian, Fallopian Tube and Primary Peritoneal Cancer Progression-free Survival?

A clinical trial, overseen by John McBroom, M.D., at Piedmont Atlanta Hospital, is exploring whether or not a change in diet and exercise in women with ovarian, fallopian tube or primary peritoneal cancer has an effect on the length of time the patient is cancer-free following their initial treatment. Some studies suggest diet and exercise may improve survival for cancer patients, but no studies have been done to show if changes in diet and exercise can have an effect on cancer returning in women treated for ovarian, fallopian tube or primary peritoneal cancer.

Other goals include finding out if the changes in diet and exercise will improve overall quality of life and the ability to be physically active. In addition, the first 200 patients to enter the study will have their blood and carotenoid levels tested, which will tell them about the kind of foods the patient is eating.

Patients are being sought for the trial. Among the criteria are:

- Histological diagnosis of epithelial ovarian cancer, fallopian tube or primary peritoneal carcinoma, clinical stage II, III or IV at diagnosis
- Completion of all primary chemotherapy and consolidation therapy at least six weeks ago, and no more than six months and two weeks, prior to enrollment and must be in complete remission
- Documented complete response to treatment based on normal CA-125 and CT scan or MRI with contrast
- GOG Performance Grade of 0, 1, or 2
- Not currently enrolled in an ongoing medically prescribed diet or physical activity regimen
- No other chronic disease that would preclude randomization into a lifestyle intervention trial

For more information, contact Franca Cenciarelli, 404-425-7927, franca.cenciarelli@piedmont.org

Breakthrough New Fibroid Surgery

Physicians at WellStar Kennestone Hospital are the first in Georgia to treat women with symptomatic fibroids using the Acessa™ Procedure. Kevin Windom, M.D., recently performed the first of these procedures.

The minimally invasive procedure is highly effective and less invasive than most surgical alternatives, with faster recovery time and symptom relief. Additionally, the need for further fibroid treatment is reduced, as demonstrated by clinical studies in which 90 percent of patients three years after the procedure did not require further medical or surgical treatment.

Fibroids are benign, non-cancerous tumors in a woman’s uterus that, when symptomatic, can be very painful and cause heavy bleeding, pressure on the bladder or rectum, and abdominal discomfort and distention. The laparoscopic Acessa™ procedure allows the surgeon, using a small scope and ultrasound guidance, to locate the patient’s fibroids and treat them individually with radiofrequency energy to destroy them. The surrounding healthy tissue is left intact and unharmed.
Treating Melanoma and Sarcoma: A Comprehensive, Multidisciplinary Approach is Effective for Patients With These Rare Cancers

By Helen K. Kelley

According to American Cancer Society statistics, melanoma will account for more than 76,600 cases of skin cancer in 2014. Additionally, more than 12,000 sarcomas, a cancer that develops from certain tissues, will be diagnosed this year.

A team of experts who comprise the Northside Hospital Cancer Institute’s Melanoma and Sarcoma Program are providing a full continuum of care for patients with these rare and deadly types of cancer. The multidisciplinary approach has contributed to making it one of the fastest growing such programs in the state.

Jonathan Lee, M.D., surgical oncologist and Medical Director of the Melanoma and Sarcoma Program, says that providing an approach that addresses all facets of the patient’s experience — education, screening, diagnosis, treatment, research, support and survivorship — fits in well with Northside’s mission as a community cancer center.

“We are in the unique position of building this program from scratch and we have had the luxury of going back to the basics and forming it in a comprehensive and robust fashion. This is a great opportunity for a physician!” Lee says. “While we already had the resources for diagnosis, treatment and surveillance of patients, we wondered, ‘What more can we deliver?’ The answer to that question included screening, education, counseling, survivorship and patient-oriented research. The goal of our program is to provide a combination of clinical care and research that delivers a full spectrum of care, all integrated into a seamless package for our patients.”

To accomplish that goal, the Melanoma and Sarcoma Program draws on the knowledge and experience of a team of experts that include:

- Dermatology
- Dermatopathology and Sarcoma Pathologist
- Medical Oncology
- Surgical Oncology
- Radiation Oncology
- Plastic and Reconstructive Surgery
- Nuclear Medicine and Radiology
- Nurse Navigation
- Researchers
- Extended healthcare professionals

These combined specializations, incorporating the latest in technology and research, allow for the provision of highly personalized care for each patient. A melanoma and sarcoma specific tumor board, comprised of representatives from all of these areas, meets regularly to discuss individual cases, share information and co-manage the patients.

Education also plays a large role in the Melanoma and Sarcoma Program’s comprehensive approach to patient care. Patients learn about the concept of their disease, what their treatment options are and what they can expect once they begin treatment. They also learn what to expect and what to do after treatment. Nurse navigators are on hand to guide patients through the entire process and facilitate the patients’ access to this full spectrum of care, including Palliative Care, Genetic Counseling and Behavioral Health.

“It’s important to follow patients through the entire treatment process, including their progress afterward. As part of our survivorship initiative, patients can take part in support groups and we continue to monitor them,” Lee notes. “Also, we know so much about other types of cancer due to the wealth of research and data available for those cancer types. Therefore, we’re actively collecting melanoma and sarcoma biospecimens, and are in the process of building melanoma and sarcoma databases that will be helpful in future research and in finding the most effective treatments for these cancers.”
Addition to program brings comprehensive help for sarcoma patients

The Melanoma and Sarcoma program, which was launched in 2012, initially focused solely on melanoma. Despite the fact that it’s still a very young program, Lee says the response from the community has been overwhelming so far.

And the recent addition of more specialists to the program has expanded the ability to treat patients with an even more rare form of cancer — Sarcoma.

“Only 1% of all cases will be sarcomas,” explains B. Scott Davidson, M.D., a surgical oncologist with Northside’s Melanoma and Sarcoma Program. “So it is important to assemble practitioners who have experience and expertise in handling this rare cancer.”

“Medical, radiation and surgical oncologists are not able to manage these patients alone. We also need plastic surgeons, nurse navigators, researchers, geneticists and more,” he states. “A multidisciplinary approach is crucial in the management of these complex cancer cases.”

Progress in treatment and research

Melanoma is an aggressive form of cancer that carries a high risk of metastasis to lymph nodes or other parts of the body. While the best possible treatment for melanoma is surgical removal, patients with advanced stages of the disease may require other forms of treatment.

Lee cites the use of lymphoscintigraphy (sentinel lymph node mapping) — an imaging technique used to find the sentinel lymph node (the first node to receive lymph from a tumor), which can be removed and checked for tumor cells — as an advancement that could help determine patient’s risk and additional therapies from which an individual patient could benefit.

“We’re looking to provide better diagnostic capability,” he says. “By using this type of lymphatic mapping and
then a biopsy of the sentinel lymph node, we can determine whether or not the regional lymph nodes contain cancer. And that helps us determine which therapies — surgery, radiation or drugs — are most appropriate for the patient and can improve his or her outcome.”

For patients with late stage melanoma, progress is being made in immunotherapy and targeted-therapy treatments. “There are several new agents that have been approved in the past year, and there are several more that will be approved in the near future that have increased activity in advanced melanoma,” states Davidson. “Additionally, there are clinical trials now underway that are examining the use of these newer immunotherapies for patients with Stage III melanoma.”

While sarcoma is largely treated with surgery, it can also be treated with a combination of radiation and surgery or with systemic therapy. And because sarcomas originate in the soft tissues — muscle, fat, blood vessels, nerves, tendons and synovial tissues that connect, support and surround other body structures — limb preservation is an important consideration.

“The addition of radiation therapy in the treatment of extremity sarcomas allows for limb preservation,” explains Davidson. “For example, if a patient has a sarcoma on the thigh that is intimate with the femoral or sciatic nerve, we can add radiation therapy followed by surgery and preserve nerve function: brachytherapy catheters are placed at surgery around the nerve to eradicate any remaining microscopic tumor cells. Obviously this avoids amputation of the affected limb but maintains solid oncologic principles of treatment.”

Davidson adds that IMRT (Intensity-Modulated Radiation Therapy) is another effective treatment for sarcoma because it allows for a very specific dose of radiation to be administered to challenging anatomic sites without increasing the deleterious effects of radiation on normal, adjacent tissue.

“IMRT reduces morbidity of the treatment, but it doesn’t reduce its effectiveness,” he notes.

**Multidisciplinary architecture is key**

Lee stresses the importance of the team approach in treating patients effectively, successfully and wholistically.

“One of the biggest advances that the oncology community has made, and that we have adopted in our program, is the concept of multidisciplinary and multi-modality care,” he says. “By gathering specialists — not just doctors, but the extended medical disciplines as well — in the same room to discuss individual cases in a team approach, we have made huge advances in patient care and created a tangible defense in patient management.”

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**Melanoma Facts**

Melanoma occurs in melanocytes, the cells that color the skin and make moles, or nevi. Melanoma is the most serious type of skin cancer because it can spread to lymph nodes and distant organs. Although it accounts for less than 5% of all skin cancers, it is responsible for about 80% of skin cancer deaths.

**Melanoma is classified in a few different ways:**

- Cutaneous melanoma, which occurs on the skin and is the most common type of melanoma
- Mucosal melanoma, a rare form of melanoma that occurs in the mucous membranes, such as the nasal passages, throat, vagina, anus or mouth
- Ocular melanoma (or uveal melanoma), a rare form of melanoma that occurs in the eye
- Metastatic melanoma, not a type of melanoma, but a term used for melanoma that has spread beyond the original site to the lymph nodes or to distant organs

—Melanoma Research Foundation

**Sarcoma Facts**

Sarcoma is a cancer of the connective tissues, such as nerves, muscles, cartilage, joints, bone or blood vessels. It can arise anywhere in the body, frequently hidden deep in the limbs.

- About 1% of all adult cancers are sarcomas.
- Between 15-20% of all children’s cancers are sarcomas.
- When possible, sarcoma patients have surgery to remove the cancer. Surgery is often combined with chemotherapy and/or radiation.
- Sarcomas are often misdiagnosed. Sometimes they are thought to be sports injuries. When they are diagnosed, they may be large and difficult to remove surgically and they may have metastasized.
- Because sarcoma is so rare, many physicians have never seen a case.
- Many sarcomas resist current treatments.

—Jim Hauser Sarcoma Foundation
The Ultimate Guide to Ovarian Cancer
Everything You Need to Know About Diagnosis, Treatment and Research

By Barry Silverman, MD

The Ultimate Guide to Ovarian Cancer is a new book by Dr. Ben Benigno. Ben is an experienced, knowledgeable senior physician who specializes in gynecology oncology. The book is informative, supportive and interesting. It is an outstanding patient education guidebook for ovarian cancer, but, more than that, it is a guide for physicians on how to manage patients faced with a diagnosis of cancer. The book has wisdom, practical advice and empathy. It speaks to patients, nurses and physicians.

Ben brings experience and knowledge to this guidebook as well as considerable insight into the plight of an ovarian cancer patient. He is a graduate of Georgetown University Medical School and trained in obstetrics and gynecology at St. Vincent’s Medical Center in New York City. Following residency, he completed two fellowships in gynecologic oncology, one at Emory and the other at MD Anderson in Houston. Following his training, he spent three years in Vietnam as visiting professor at the University of Saigon, where he started a residency training program in obstetrics and gynecology. After Vietnam, he was on the Emory faculty for eight years directing the gynecologic oncology program. He then moved to Northside Hospital, where he is currently the director of the gynecologic oncology program. Ben is the founder of University Gynecologic Oncology; this program is a world leader in the oncology care of women with cancer of the reproductive tract.

The book is not only a compilation of statistics, therapies, complications and outcomes, but also patient stories about living with a diagnosis of cancer told by a talented storyteller. In discussing how a patient with ovarian cancer would feel, Ben relates the story of Philoctetes from a play by Sophocles. "Philoctetes is the Trojan war hero who prior to his involvement in the conflict was bitten by a snake. This produced such a horrible festering wound that no one could abide his presence and he was banished to the uninhabited island of Lemnos."

When the patient has been diagnosed with stage III ovarian cancer, he is invariably asked how long has it been there and why wasn’t it picked up sooner?

Ben describes how the ovarian cancer patient feels like an outcast; her life is coming to an end. She is enveloped by a strange sense of unworthiness; frequently this includes a loss of her perception of herself as a sexual being. He then discusses his techniques to reduce fear and build confidence. He uses simple techniques that we were not taught in medical school, such as being sure that a new patient is brought directly into his office and does not have to wait alone and frightened in the waiting room.
He introduces himself without the title of doctor and sits down next to the patient. He listens to her story about how she was diagnosed with ovarian cancer; a story that he has heard many times but knows, for this patient, is unique.

Ben describes in detail the process of doctoring, communicating, working to gain the patient’s confidence for what will be a long and difficult road to recovery. Then he tells the patient to plan something really special in one year to celebrate her one-year anniversary of the treatment to cure her cancer.

Ben understands his patients and the impact of cancer and chemotherapy. In this passage he discusses helping a patient through chemotherapy.

“A darkened savage road is a phrase borrowed for Robert Pinsky’s magnificent translation of Dante’s Inferno and I can think of no better way to describe the experience of patient undergoing chemotherapy for ovarian cancer. Of all of the many and varied duties of the oncologist the obligation to transport the patient from the arena of darkness to a place of light! This cannot be accomplished in one visit. Constant attention to this issue on the part of the physician is mandatory; the darkness begins to fade when the patient starts to believe that it’s possible to put this mess behind her. I found that one of the best ways to massage the anxiety and fears of the newly diagnosed patient is to put her in contact with patients who have made a similar journey many years ago and are now doing well and are completely restored to normal life as though nothing had ever happened.”

The book has a chapter on the most frequently asked questions by patients with ovarian cancer. Examples include: Why does a woman get cancer of the ovary? Ben comments there is no good answer to this question. Unlike the relationship of cigarette smoking to cancer of the lung, there is no specific carcinogen related to this disease. There are risk factors and these include: having your first child after the age of 35, obesity, a family history of ovarian cancer and deleterious mutations on the BRCA 1 AND BRCA 2 genes.

When the patient has been diagnosed with stage III ovarian cancer, he is invariably asked how long has it been there and why wasn’t it picked up sooner? His response is if you had a surgical procedure six months earlier and the ovary was visualized and normal, you would be able to say the cancer occurred after that. However in the vast majority of cases, no one is ever able to know how long cancer has been present. Questions regarding whether or not the tumor is fast growing are equally unanswerable.

After treatment when the patient is in remission the patient always asks: If cancer of the ovary comes back when is it likely to appear? What will the cancer do to me and how it be treated? The answer is that ovarian cancer can reoccur more than 10 years after treatment has been stopped. The most likely location is within the abdominal cavity. Although sometimes there are no symptoms at all, when symptoms are present the most common are cramping abdominal pain and bloating, the mirror image of the initial presentation. The treatment will depend on the extent of disease. The patient will go through PET and CT scans of the chest, abdomen and pelvis. This will determine whether surgery is necessary; however, chemotherapy is always mandatory.

I lost my uterus, tubes and ovary and just finished chemotherapy for cancer of the ovary. Is my sex drive also finished? The answer is absolutely not! The sensitivity of the clitoris is unchanged and sexuality frequently returns to its pretreatment level, but sometimes it requires counseling for the patient as well as the partner.

The book is full of interesting and thoughtful quotes. My favorite is from Sir William Osler: Be calm and strong and patient. Meet failure and disappointment with courage. Rise superior to the trials of life, and never give in to hopelessness or despair. In danger, in adversity, cling to your principles and ideals. Good advice for every patient and physician. The book is informative on many levels to many different audiences. I encourage you to read it and if appropriate to your practice place a copy in the waiting room.
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The Medical Association of Atlanta (MAA) is a non-profit association dedicated to the advancement of organized medicine in Atlanta.
Brian E. Hill, M.D.

Dr. Brian Hill is a urologist with Urology Specialists of Atlanta at St. Joseph’s Hospital. He obtained his undergraduate degree at Eastern Mennonite University and graduated from the Medical College of Virginia. He completed his residency at the University of Maryland Medical System before joining his current practice.

Dr. Hill is on the board of the Medical Association of Atlanta. He also serves on the Executive Board of the Emory Healthcare Network (EHN) and the local board of the EHN at St Joseph’s Hospital. He is a member of the Southeast Regional Physician Advisory Committee for Coventry Health Care, the American Urologic Association, the Southeastern Section of Urology, the Medical Association of Georgia and Docs4PatientCare.

Brian has been involved in the healthcare reform debate at the national level. He has written a book, Stop the Noise: A Physician’s Quest to Silence the Politics of Health Care Reform, along with multiple articles assessing the ability of the current reform model to reach its stated end while also presenting alternative treatment options.

Albert F Johary, M.D.

Dr. Albert Johary has been practicing internal medicine in metro Atlanta since 1990. After working in one of the largest multispecialty groups in Atlanta, Atlanta Medical Associates, LLC, Dr. Johary decided to start his own solo internal medicine practice in Dunwoody in 1998. Dr. Johary continues to enjoy a thriving solo practice with offices in Dunwoody Village and at the Emory Johns Creek Hospital. He also does some work at Peachford Behavioral Health System and serves as a Clinical Associate Professor of Medicine for the Medical College of Georgia.

Dr. Johary was one of the founding members of the Emory Johns Creek Healthcare Association. He has served as “Doctor of the Day” at the Georgia Capitol and recently served as Chairman of the Healthcare subcommittee for Congressman Tom Price (District 6- GA).

A graduate of the University of Florida, he received his medical degree from the University of South Florida College of Medicine in Tampa and completed his internship and residency at the Emory University Affiliated Hospitals in Atlanta.

Steven M. Walsh, M.D.

Dr. Steven Walsh is a graduate of Emory University and the Medical College of Georgia. He currently resides in Roswell and is a managing partner of North Fulton Anesthesia Associates, P.C. This 30-member practice provides both surgical and pain management services in the hospital, ambulatory surgical center and clinic settings.

Dr. Walsh is past president of the Medical Association of Atlanta and the Georgia Society of Anesthesiologists, and he currently serves as treasurer of the Medical Association of Georgia. His areas of interest include financial planning, the tools of modern quality management and implementation, and the use of electronic tools for improving medical decision-making and medical care.
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