

Restoring Sexual Function

Arthur Burnett, surgeon and neurourologist, is a pioneer in the area of sexual medicine. Many of his patients are men with prostate cancer who are worried about impotence after radical prostatectomy. But other men of all ages come to see Burnett for help with issues ranging from ejaculatory disturbances to libidinal problems, and may need treatment ranging from pharmacotherapy, to injection therapy, to prosthetics, to genital reconstruction following injury or cancer.

Protecting nerves: Burnett's discovery with Johns Hopkins neuroscientist **Solomon Snyder** that nitric oxide plays a crucial role in erection led to development of the drug Viagra. For nearly three decades, much of his lab and clinical work has focused on protecting the integrity of the neurovascular bundles responsible for erection, easily damaged even in the "nerve-sparing" radical prostatectomy developed by Johns Hopkins urologist **Patrick Walsh**. "It may be from traction, or even that the adjacent dissection somehow exposes the nerves to injury," Burnett

says. "Something causes them to sustain an inflammatory setback."

In groundbreaking studies of rats with nerve injury and erectile dysfunction similar to that found in men after radical prostatectomy, he has tested many inflammation-fighting agents and growth factors designed to "preserve, nourish, regenerate and restore nerves to normal function." One of these is an agent used to combat anemia, erythropoietin (EPO). In a randomized, controlled clinical trial, still actively enrolling patients, Burnett is studying EPO's ability to enhance nerve function. EPO is injected the day before, the day of, and the day after radical prostatectomy.

In other work, Burnett has targeted the fragile network of blood vessels and chambers within the penis. Even though they're not directly traumatized by surgery, "these structures may degenerate or shrivel," he says, "and thus contribute to poor recovery of erectile function in some men after surgery." To fight this, Burnett is testing such blood vessel-strengthening agents as angiotensin II type 1 receptor antagonists. In another clinical trial, he is testing an external vibration nerve-stimulatory device, which he helped develop, that may be applied under a specific protocol after surgery.

Help for incontinence and impotence: Having both urinary incontinence and impotence after radical prostatectomy should be a rare complication, but some men find themselves in this situation and need help. For the last 13 years, Burnett has offered a successful operation that restores both urinary continence



Arthur Burnett directs the Sexual Medicine Fellowship Program and the Basic Science Laboratory in Neurourology: "We are very serious in providing help and restoration of function in all areas of male sexual health."

FOR THE LAST 13 YEARS, BURNETT HAS OFFERED A SUCCESSFUL OPERATION THAT RESTORES BOTH URINARY CONTINENCE AND POTENCY AT THE SAME TIME.

and potency at the same time—implantation of an inflatable penile prosthesis and an artificial urinary sphincter. "It provides efficient and rapid resumption of both functional disorders," he says.

Burnett is also conducting further research into utilization and predic-

tion modeling for penile prosthesis surgery. "Our goal," he explains, "is to approach everything we do thoughtfully and rigorously, so that we can make advances based on what is scientifically meaningful." ■



WELCOME

to our first issue of *Johns Hopkins Urology*. Our goal is not to provide a complete look at everything we're doing, because we would need a much bigger publication. Instead, we're highlighting some of our research and clinical efforts here at the Brady Urological Institute in a variety of areas, including:

- * Brian Matlaga's work to treat stone disease in children and adults, and to minimize odds of recurrence
- * Phillip Pierorazio's active surveillance program for small renal masses, which is allowing many patients to be safely followed without surgery
- * Arthur Burnett's comprehensive program to restore function in all areas of male sexual health
- * Ming-Hsien Wang's protocol to keep young children with UTIs from getting DMSA scans they don't need
- * Stephen Schatz's work with vaporization techniques, robotic surgery and other novel approaches for BPH

Come visit us on social media: Phil Pierorazio is blogging at <http://bradyurology.blogspot.com>. We are also on Twitter: @brady_urology, and on Facebook at Brady Urology, working to get the word out about what we do and how we can help.

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Vaporization Challenges TURP as Gold Standard for BPH

Good news for men with BPH seeking surgical relief for their symptoms: There have never been so many excellent, minimally invasive options.

There's still traditional transurethral resection of the prostate (TURP)—long the “gold standard” for symptom relief. But now, instead of chipping away at the prostate, says urologist **Stephen Schatz**, “we are doing far more procedures using either bipolar electrosurgical vaporization or laser vaporization techniques. Essentially, vaporization is safer than traditional TURP, with results that are entirely comparable” in terms of the durability and degree of symptom relief, and retreatment rates are quite low.

Schatz and colleagues are even able to use vaporization on men with low-risk prostate cancer in Johns Hopkins' active surveillance program who are significantly bothered by lower urinary tract symptoms. “We continue to follow them regularly with biopsies and PSA tests,” he says, “but the cancer doesn't get in the way of their treatment.”

With vaporization, the only significant downside is temporary worsening of irritative urinary symptoms (frequency, urgency and burning) immediately afterward. But, Schatz says, “I have found this always gets better, and the long-term improvement is profound in most men. It's a great alternative to long-term medical treatment,” which takes longer to achieve an effect and does not provide as great a relief of symptoms.

Although Schatz performs all the surgical procedures, he prefers bipolar vaporization. “I can see the prostate clearly as I work, without bleeding obscuring my view,” he says. Immediately afterward, he adds, “the urine is almost always clear.” Only about 5 percent of patients stay overnight. In addition, the rates of erectile dysfunction are lower than with TURP because there's no electricity arcing outside the prostate and potentially injuring the cavernosal nerves.

For men with very large prostates, Schatz performs a simple prostatectomy—nucleation of the prostate, going in through the bladder—robotically. In a case series of more than 50 patients, Johns Hopkins urologists have reported urinary outcomes that are comparable to the results from open surgery, but with clear decreases in perioperative blood loss.

For men who are poor candidates for surgery, Schatz and interventional radiologist Mark Lessne are conducting a multicenter trial comparing prostatic artery embolization with traditional TURP,



Vaporization, says Stephen Schatz, offers many of the advantages of TURP, but most patients go home the same day, and there is much less associated bleeding. Like TURP, vaporization improves urinary flow by significantly reducing prostate size, as reflected in a reduction in serum PSA and ultrasound measurements of prostate volume.

using very rigorous outcome measures, measuring prostates and performing urodynamics before and after, and tracking quality of life indices to see how patients respond. This angiography procedure, done through the femoral artery, takes less than three hours and has “essentially no blood loss and no absorption of any fluids,” Schatz says. Symptom improvement comes gradually as prostate tissue dies back.

Schatz suspects that within a few years, this treatment will be offered to men who “may not be candidates for even minimally invasive surgery, but who have significant symptoms not helped all that much by medications.” ■

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Active Surveillance Proving Safe for Small Renal Masses

Although the incidence of kidney cancer has increased dramatically over the last few decades, John Hopkins research is showing that many patients can be safely followed without the need for surgery.

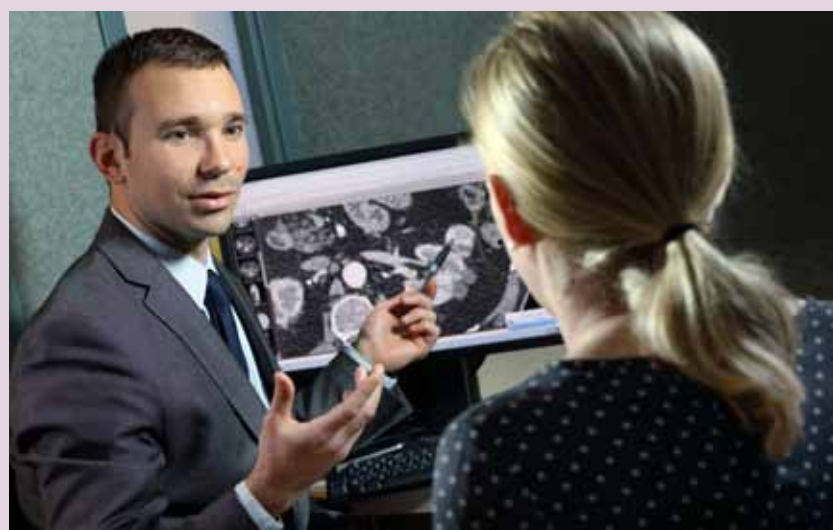
For more than five years, urologist **Phillip Pierorazio** has run the Delayed Intervention and Surveillance for Small Renal Masses Registry, following patients with small, localized kidney tumors (stage T1a, 4 cm or smaller) who choose either active surveillance or immediate surgery. “Patients undergoing surveillance have done incredibly well,” he says. “None have died of kidney cancer.” About 500 patients at Johns Hopkins, Columbia University and Beth Israel Deaconess Medical Center are in the registry; of those, nearly 200 have chosen surveillance. About 30 patients in the surveillance group later opted for surgery, either because their tumor grew or “they didn’t want to worry about it anymore, or because they had a medical issue that resolved,” says Pierorazio.

In the 1970s, about 30,000 Americans were diagnosed yearly with kidney cancer; that number has jumped to about 60,000 today, in large part because of increasing use of CT scans. Still, the number of annual deaths—between 10,000 and 13,000—has remained unchanged, Pierorazio notes. “We’re operating on all these people, but we have not significantly changed the mortality of this disease. Which begs the question, are all of these tumors of consequence?” Although several institutions have studied surveillance, the studies have been mainly retrospective. Johns Hopkins is one of three institutions worldwide with this kind of prospective protocol.

Once it escapes the kidney, cancer is fatal. Surgical cure rates for kidney-confined tumors are excellent—about 95 percent. “If you took everybody in this country with a small kidney tumor, anything 4 cm or less,” says Pierorazio, “upwards of 30 percent are benign lesions. Of the 70 percent left, half are low-grade, indolent tumors that are never going to cause a problem. That leaves about a third that are potentially aggressive.”

Who can safely avoid surgery? Pierorazio and colleagues have come up with a score based on some key clinical factors. For example, tumors that are close to the renal hilum tend to be more aggressive. Women are more likely to have benign tumors, and older people are more likely to have indolent tumors. The risk of metastasis is extremely low in tumors under 2 cm. Surveillance is better for people with heart problems, particularly congestive heart failure.

With urologist **Mohamad Allaf**, Pierorazio runs a clinic for people with small kidney tumors. All in one day, patients get an ultrasound and lab work, then meet with a physician. “For patients who want surgery,” says Pierorazio, “we offer every option,” including complex partial, open-incision and robotic procedures. Patients who choose surveillance receive ultrasound every six months for the first two years, then annually. ■



Phillip Pierorazio recently received a Young Investigator’s Award from the National Comprehensive Cancer Network and will present several abstracts summarizing data from the renal masses registry at the American Urological Association meeting in May.



Brian Matlaga and colleagues were the first to describe the increasing prevalence of pediatric stone disease and among the first to use large-scale epidemiologic data sets to characterize co-morbidities such as diabetes, obesity and hypertension as they relate to stone disease.

A Comprehensive Approach to Stone Disease

Stones run in families. They also tend to recur, which is why urologist **Brian Matlaga**, who directs stone disease at Johns Hopkins, views surgery as merely the first step.

“If you have one stone, you have a 50 percent lifetime recurrence risk, which is pretty high,” he says. “Patients with a stone really have two problems.” The first priority is to get the stone out. Then, Matlaga says, “we need to figure out why the stone formed and how to lower those risk factors, because if we don’t do anything, we’re going to see half of these people back again with the same problem. So we attack stones with a multidisciplinary approach, focused on adult and pediatric stone formers.”

For children, the Comprehensive Stone Clinic offers patient-friendly one-stop shopping.

“We’re used to taking care of complex surgical problems, we have a pediatric nephrologist who is used to taking care of complex medical problems, and the nutritionist manages the dietary issues,” says Matlaga. Using 24-hour urine studies, he says, the team “back-calculates” a patient’s metabolic risk factors to see whether “it’s too much calcium, too much oxalate or not enough inhibi-

tors of stone formation, and then we can say, *Your recurrence risk is now 50 percent; let’s try to get it down to about 10 percent*, which is the general population’s risk.”

Surgically, Matlaga and colleagues specialize in complex procedures such as percutaneous operations for larger stones. “We make a little incision in the back and pass a scope directly into the kidney to remove the stone,” he says. “It’s more difficult and time-consuming, and the risk profile is different than for blasting a stone” with lithotripsy. Most procedures involve overnight hospitalization. “Percutaneous stone surgery requires a myriad of equipment and devices” says Matlaga, “but our operating room staff is so familiar with the procedure—we do it every day—it’s actually amazing how smooth it is.”

Many of the procedures are done with X-ray guidance, and afterward Matlaga studies the images looking for incremental improvements. With the large volume of procedures, he says, “you’re able to identify subtleties, you begin to see things just because you’re looking at it over and over again. I’m always thinking, how can we do this better?” ■

Rethinking the DMSA Scan

She's a 3-year-old with a culture-proven urinary tract infection and fever. You're treating her. What should you do first? Order a DMSA scan to check for a renal scar?

Not so fast, says pediatric urologist **Ming-Hsien Wang**, who has studied this issue at Johns Hopkins and is also co-principal investigator for an ongoing NIH study of urinary tract infection in these children.

"A baseline ultrasound can tell you whether there's a significant scar," she says, "and it can do so without exposing children to the side effects of a test that has minimal clinical benefits." Today, Wang adds, because UTIs are being diagnosed earlier, "it's pretty rare for a kid to come in with a

scar." Yet many children are still being put through a DMSA scan even if an ultrasound is normal; further, many children are given one or more repeat DMSA scans as a follow-up.

In Wang's retrospective study of 126 Johns Hopkins patients between the ages of less than 1 month and 5 years, DMSA scanning added nothing to the diagnosis when a kidney ultrasound was normal. "With the DMSA scan, children are getting exposed to radiation from the nuclear tracer, and we don't know how long it actually stays in their system," she says. Also, because a DMSA scan takes about three hours, "these young children wind up getting general anesthesia," which can cause respiratory

problems and the need for an overnight hospital stay. There is a significant cost difference, too, between ultrasound alone and DMSA.

At Johns Hopkins, Wang and colleagues see about 200 children with a fever and culture-proven UTI every year. "Our protocol for these children is a baseline ultrasound," she says, "and we do not order a DMSA unless the ultrasound shows evidence of a scar." In upcoming research, Wang plans to see if there is a difference in clinical outcome in children who are followed with DMSA scans versus renal ultrasounds. She also hopes to develop evidence-based clinical decision rules to help improve diagnosis and avoid unnecessary tests. ■



Ming-Hsien Wang will present abstracts of her findings at meetings of the American Urological Association and the European Society for Pediatric Urology.

JOHNS HOPKINS Urology

This newsletter is one of many ways the Johns Hopkins Brady Urological Institute seeks to recognize and enhance its partnership with its referring physicians. Comments, questions and thoughts on topics you would like to see covered in upcoming issues are always welcome.

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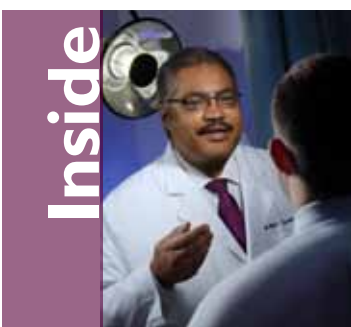
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