AUA News

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Inside THIS ISSUE

HEY *Bob!*

Comparison of NCCN and AUA Prostate Cancer Treatment Guidelines

NCCN Guidelines

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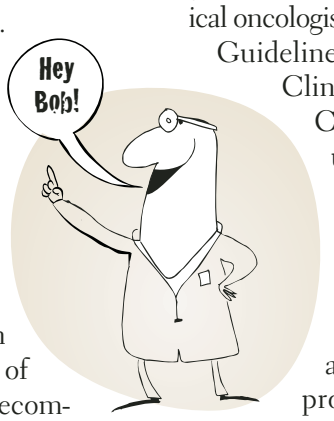
The National Comprehensive Cancer Network (NCCN) issued updates to the Clinical Practice Guidelines on Oncology-Prostate Cancer in January 2010 and revised the web version on May 27, 2010 to incorporate PROVENGE® (sipuleucel-T) for the treatment of advanced prostate cancer.[1,2] These guidelines were created to assist urologists in caring for patients with prostate cancer based on various levels of medical evidence. New to the 2010 guidelines is the recommendation of active surveillance as the only option for men with 1) low risk prostate cancer with an estimated life expectancy of less than 10 years and 2) very low risk prostate cancer with an estimated life expectancy of less than 20 years. These recommendations for active surveillance have increased the focus of urologists on guideline use, and called attention to the differences between the NCCN and the AUA guidelines.



Both guidelines originated in 1995. The missions of the NCCN and the AUA are similar in setting forth recommendations for optimal treatment based on current evidence and expert consensus. Both guideline panels advocate a multidisciplinary approach, and are composed primarily of urologists, radiation oncologists and medical oncologists. The AUA revised their Guideline for the Management of Clinically Localized Prostate Cancer in 2007 and updates were contained in the 2009 Prostate Specific Antigen (PSA) Best Practice Statement.[3,4] The NCCN has issued updates at least annually, and considers all stages of prostate cancer including locally advanced and metastatic disease.

Choice of therapy is influenced by

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FROM THE *Office of Education*

Urological Ultrasound Education

Dr. Pat Fulgham
Chair, Urologic Diagnostic and Therapeutic Imaging Committee
Dallas, Texas

The AUA Office of Education continues to demonstrate its dedication to providing ultrasound education to its members. This year the AUA conducted 7 hands-on courses on urological ultrasound, and sold hundreds of self-study DVDs covering the basic principles of ultrasound, as well as site specific modules on renal, bladder, male genitalia and prostate ultrasound.

We offer urologists several opportunities to expand their skills in urological ultrasound. Our 2 weekend courses on hands-on urological ultrasound, one of which is held at AUA headquarters in Linthicum, Maryland and the other is held in Dallas, Texas, are the most comprehensive offered. We also provide a full day hands-on course the Friday preceding the AUA meeting and 4 hands-on lab courses on Saturday, the first day of the AUA meeting.

A hands-on module on Advanced Urologic Ultrasound has been added to the 2011 AUA annual meeting in Washington, D. C. This advanced course will offer urologists the opportunity to improve their skills with Doppler ultrasound and other advanced techniques. In addition, site specific urological ultrasound training modules have been offered as part of the AUA Courses of Choice available at AUA Section meetings.

Before enrolling in an AUA ultrasound course, it is recommended that registrants purchase the Basic Urologic Ultrasound DVD and complete the online test. For a complete listing of ultrasound course offerings, visit the course calendar on the AUA web site at www.auanet.org.

To ensure the provision of high quality patient care, the Office of Education has established a skills verification program for urological ultrasound. The AUA has funded and trained 40 instructors with expertise and interest in urological ultrasound to teach AUA courses throughout the country. This team of instructors, also known as the National Urologic Ultrasound Faculty (NUUF), has created and delivered educational modules on renal, bladder, scrotal, transrectal and pediatric ultrasound. These modules focus not

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a combination of factors, balancing the probabilities of cure based on clinical and pathological parameters, and patient estimated life expectancy, comorbidities, potential side effects and preference. Both guidelines advise the practitioner to estimate life expectancy but only the NCCN guidelines provide specific instructions and specify adjustment based on patient quartile of health. Bone scans and pelvic computerized tomography (CT) are incorporated in the staging evaluation in both guidelines.

According to the AUA guideline these staging studies are unnecessary in low risk cases, defined as PSA 10 ng/ml or less, cT1-2a disease and absence of Gleason score 4 or 5. However, bone scans should be considered in patients with PSA greater than 20 ng/ml, history or examination suggestive of bony involvement, Gleason score 8 or greater, or clinical stage T3 or greater. CT or magnetic resonance imaging (MRI) should be considered in men with PSA greater than 20 ng/ml, Gleason score 8 or greater, or locally advanced disease.

"Both guidelines advise the practitioner to estimate life expectancy but only the NCCN guidelines provide specific instructions and specify adjustment based on patient quartile of health."

In contrast, the NCCN recommends determining if life expectancy exceeds 5 years before considering imaging. Bone scans are recommended for patients with T1-T2 disease, PSA greater than 20 ng/ml and Gleason score 8 or greater, those with T3, T4 disease or those who are symptomatic. Pelvic CT or MRI is recommended for patients with T3-T4 disease or T1-T2 disease with a nomogram probability of lymph node involvement greater than 20%. In all other patients no additional imaging is recommended.

Once staging is completed, patients are placed into risk stratification groups. The AUA guideline was written for clinically localized disease, and so the risk strata discussed are low, intermediate and high risk based on PSA, Gleason score and clinical T stage. The NCCN guidelines risk strata differ from those of the AUA in 3 ways. 1) T2c is considered intermediate risk in the NCCN guidelines but high risk in the AUA guideline. 2) Locally advanced, very high risk and metastatic are included in the NCCN guidelines. 3) The 2010 NCCN guidelines include the new risk category of very low risk.

The very low risk category is based on a modification of the Epstein criteria for clinically insignificant prostate cancer. To qualify as very low risk, specific criteria must be fulfilled including T1c, Gleason score 6 or less, PSA less than 10 ng/ml, fewer than 3 positive biopsy cores, 50% or less cancer in each core and PSA density less than 0.15 ng/ml/gm. For the first time active surveillance is the only option recommended for men in this category whose life expectancy is less than 20 years. Active surveillance is also the only recommendation for men with low risk prostate cancer whose estimated life expectancy is less than 10 years.

In-depth counseling must highlight the pros and cons of this option. Disadvantages, such as the chance of missed opportunity for cure, increased anxiety of living with untreated cancer, the risk that subsequent treatment may be more complex with increased side effects and nerve sparing at subsequent prostatectomy may be more difficult, must be discussed. Similarly the benefits must be reviewed, such as the avoidance of treatment related side effects from definitive therapy that may not be necessary, as with small indolent cancers. Concerns that men with prostate cancer are being over treated, especially older men with favorable prostate cancer, in addition to the

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prostate cancer specific mortality results from American and European randomized screening studies, have driven the NCCN to make these recommendations.[5, 6]

The AUA guideline lists active surveillance as an option for all patients but it does not recommend active surveillance for any specific group. However, the guideline emphasizes that patients with high grade tumors are not suitable candidates given the high recurrence rates and worse survival. Both guidelines state that active surveillance entails actively monitoring the course of the disease with the expectation of intervention for obvious biochemical and/or evidence of histopathological progression. However, the NCCN defines specific progression parameters as Gleason grade 4 or 5 on repeat biopsy, prostate cancer in a greater number of cores or occupying a greater extent of the biopsy tissue, or PSA doubling time less than 3 years.

Patients requiring intervention can be treated with various modalities. According to the AUA guideline brachytherapy is listed as an option for all risk strata, whereas the NCCN recommends brachytherapy as an option only in cases of low risk or intermediate risk disease. The NCCN guidelines also specify the regimen doses for monotherapy vs combination therapy. Candidates suitable to receive external beam radiation therapy and recommendations for androgen deprivation therapy to be used in those with intermediate and high risk cancers are similar in both guidelines.

Both guidelines also use the new Radiation Therapy Oncology Group-American Society for Therapeutic Radiology and Oncology-Phoenix Consensus definition of biochemical failure after radiation therapy. However, NCCN guidelines require a minimum of 75 Gy radiation for monotherapy, and daily image guided radiation therapy is mandatory for radiation doses greater than 78 Gy. Patients with low risk cancers and 10-year or longer life expectancy should not

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receive pelvic lymph node radiation or androgen deprivation therapy. Furthermore, NCCN guidelines state that neither proton therapy nor cryotherapy is recommended as primary treatment except in a clinical trial.

Radical prostatectomy with or without pelvic lymph node dissection via the open or robotic assisted approach is the surgical treatment of choice for men with low, intermediate and selected high risk cancers. Suitable candidates for pelvic lymph node dissection differ between the guidelines. The AUA guideline states that the procedure may not be necessary for clinically localized prostate cancer if PSA is less than 10 ng/ml and Gleason score is 6 or less, although it emphasizes that patients with higher risk disease would benefit.

The decision to perform pelvic lymph node dissection should be guided by the probability of nodal metastases according to NCCN guidelines. The NCCN panel chose a 2% cutoff based on a nomogram, thereby avoiding 47.7% of pelvic lymph node dissections at a cost of missing 12.1% of positive lymph nodes. The NCCN also specifies that only an extended technique should be performed.

Lastly, the definition of biochemical recurrence differs between the guidelines. The AUA guideline defines biochemical recurrence as an initial PSA of 0.2 ng/ml or greater followed by a subsequent confirmatory PSA of 0.2 ng/ml or greater. This definition is in contrast to the NCCN definition of either failure of PSA to decrease to an undetectable level or a detectable PSA that increases on 2 subsequent

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measurements.

The NCCN panel held an interim update teleconference in May 2010 to review the Food and Drug Administration approval of the immunotherapeutic agent sipuleucel-T for the treatment of advanced prostate cancer. The panel discussed the 2 phase 3 trials published for asymptomatic or minimally symptomatic, metastatic, castration recurrent prostate cancer.[7,8] Median survival was improved by 4 months and a 22% reduction in the risk of death from prostate cancer was reported for sipuleucel-T vs placebo. Based on these results the panel supported inclusion of sipuleucel-T for systemic salvage therapy in patients with ECOG (Eastern Cooperative Oncology Group) performance status 0-1, estimated life expectancy greater than 6 months, no visceral disease and no or minimal symptoms.

The 2 guidelines are more similar than different. The NCCN guidelines are more inclusive and more detailed. Both guidelines assist the clinician and patient in choosing therapy using evidence-based medicine, and acknowledge that therapy is determined on an individual basis.

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AUA Guideline

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We appreciate the efforts of Drs. Seixas-Mikelus and Mohler to outline the differences between the NCCN and the AUA prostate cancer guidelines. However, it is important to provide potential reasons for the differences in the recommendations between the documents.

It should be noted that both guidelines were created using different methodologies. The AUA guideline was published in 2007. The prostate cancer literature review panel surveyed all peer reviewed studies on that topic since publication of the guideline and determined that there was no need to revise or update the current document. Additionally, AUA guidelines are living documents that are reviewed annually to determine whether a guideline should be revised or a full panel reconvened and the guideline updated.

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The AUA Prostate Cancer Guideline Panel convened with directions from the AUA Practice Guidelines Committee to create an evidence-based document to direct practicing physicians treating clinically localized prostate cancer. Emphasis in the AUA guideline process has always been to base the conclusions and recommendations on the highest level of evidence from the literature and not on the opinions of the panel.

Although AUA guideline participants comprise an international group of prostate cancer experts in the areas of medical oncology, radiation oncology, urological oncology and outcomes research, document conclusions are based on peer reviewed articles using strict criteria for data review and extraction. The reader is encouraged to review figure 2 and the appendix in the primary guideline document, both of which demonstrate why reaching definitive conclusions regarding the best treatment for any patient was not possible after a comprehensive review of available evidence (http://www.auanet.org/content/guidelines-and-quality-care/clinical-guidelines.cfm?sub=pc).

Given the different methodologies (highly proscriptive, evidence-based recommendations vs consensus-based recommendations), it is not surprising that there are differences in the NCCN and AUA guidelines. The AUA guideline focused on only clinical stage T1 and T2 disease with elimination of cross-contamination from T3 disease. This strict requirement eliminated some studies from consideration as well as changed the spectrum of patients considered. There are also other noteworthy differences.

Published Active Surveillance Studies

References	No. Pts	Median Pt Age	Median Mos Followup	(%) Overall Survival	(%) Ca Specific Survival	% Remaining on Surveillance
Klotz et al[1]	450	70.3	82	78.6	97.2	70
Carter et al[2]	407	66	41	98	100	59
Soloway et al[3]	99	66	45	100	100	92
van den Bergh et al[4]	616	66	47	77	100	43
Khatami et al[5]	270	64	63	NR	100	61
van As et al[6]	326	67	22	98	100	73
Overall	2,168	68	43	90	99.7	64

The new NCCN recommendation lists active surveillance as the only option for the patient with low risk prostate cancer whose estimated life expectancy is less than 10 years and very low risk disease with an estimated life expectancy of less than 20 years is not supported by the literature. The available studies in the literature on active surveillance are listed in the table, all of which suffer from small numbers of patients, nonrandomized design and short followup.[1-6] The AUA guideline mentions this option for patients with low risk disease but in the absence of randomized trials comparing this option to currently available standard treatments, the panel did not believe this should be the only available recommended option.

"Given the different methodologies (highly proscriptive, evidence-based recommendations vs consensus-based recommendations), it is not surprising that there are differences in the NCCN and AUA guidelines."

Additionally, predictions of life expectancy spanning 2 decades are fraught with inaccuracies and potentially deny the chance for cure of a disease for which one treatment option has not proved superior to another in a randomized study. However, active surveillance has been shown in a single randomized trial, mentioned in the AUA guideline to be inferior to radical prostatectomy.[7] Also, the AUA guideline gives weight to patient preferences. As a result, it is probably premature at this time to tell a man with a low grade tumor and whose father died of prostate cancer that he cannot opt for curative treatment.

The NCCN guidelines also do not recommend brachytherapy as an option for patients with high risk prostate cancer. While it is true that the outcomes of brachytherapy for high risk disease are poor, this could also be said of all types of treatment. In the absence of high level evidence proving this specific treatment to be inferior, the AUA Practice Guidelines Committee thought that all available options should be discussed with the high risk patient.

The NCCN considers cryotherapy and proton beam radiation experimental. These treatment options were not experimental in the AUA guideline because cryotherapy has been approved by the Food and Drug Administration as a treatment option for clinically localized prostate cancer and the efficacy of proton beam radiation appears to be similar to other forms of external beam radiation.[8] An AUA Best Practice Policy Statement has also been published on the use of cryosurgery for localized prostate cancer (http://www.auanet.org/content/media/cryosurgery08.pdf).

Finally, the AUA Prostate Cancer Guideline Panel recommended that only the highest level of evidence in the literature, preferably randomized controlled trials, be used for future guideline updates and revisions. The AUA panel reviewed 6 years of available literature on clinically localized prostate cancer and, unfortunately, found few randomized trials for inclusion.

Given the poor level of evidence in the literature evaluating available treatment options, it is risky to make single, concrete recommendations regarding excluding any treatment from consideration or selecting a single best treatment for any given patient. While this may be unsatisfactory for patients and physicians, it accurately reflects the data. These conclusions also allow patient priorities and physician insight to determine individualized treatment and provide impetus to the development of randomized clinical trials. These studies ultimately will help determine the truly best treatment for an individual patient. ◆

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From the Office of Education

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only on the clinical aspects of scanning, but also on the physics of ultrasound, image quality, patient safety and appropriate documentation of imaging studies. The educational modules ensure that comprehensive standardized content is presented at all AUA sponsored ultrasound courses.

The key feature of our educational program in ultrasound is the verification of skills. Course participants are assessed for the ability to complete the learning objectives of each course. All participants who complete an AUA sponsored ultrasound course are eligible for AMA PRA New Procedures and Skills level 1 classification. Participants who successfully complete the posttest for a live course and a DVD module are eligible for AMA PRA level 2 classification for satisfactorily meeting all specified learning objectives. Each DVD module has an associated online didactic test available via the AUA web site.

For courses with a hands-on component, each candidate is personally evaluated by a qualified NUUF instructor. This verification of skills has the additional value of providing to third parties and hospitals a justification for granting credentials in ultrasound imaging. It should be emphasized that skills level verification does not constitute a separate certification by the AUA or any other body. Currently the American Board of Urology certification examination includes test questions related to all forms of urological imaging including ultrasound.

As part of its ongoing mission to provide the highest quality training for urology residents, the AUA Board of Directors and the American Board of Urology have updated the Urology Core Curriculum with a section on imaging, In the updated curriculum greater emphasis has been given to the basic underlying physics of ultrasound as well as machine characteristics, interpretation of artifacts, documentation and patient safety. It is hoped that by standardizing the recommended reference materials, all residents will have a similar experience with regard to urological ultrasound training.

Urology residents who become acquainted with ultrasound early in training are more likely to perform ultrasound. Several initiatives are under way to promote a more cohesive ultrasound experience for urology residents. Some program directors have adopted the AUA Ultrasound DVDs as part of their training programs. The hands-on courses have been offered to residents in the New York Section and are popular. An objective of the NUUF, now chaired by Dr. Bruce Gilbert, is to extend ultrasound training into residency training in a more structured manner. An integrated and standardized approach to ultrasound education will ensure that urology patients continue to benefit from high quality examinations provided by their urologist.

For more information on the ultrasound DVD modules and upcoming AUA ultrasound courses, please visit the AUA web site at www.auanet.org. ◆

FROM THE *Secretary*

Quality

Dr. Robert C. Flanigan
***AUANews* Editor in Chief**
Maywood, Illinois

Quality is a word that we hear nearly each and every day in our professional lives. The pure and simple fact is that the initiatives to make medicine safer and more effective have continued to grow, and have captured the attention of government leaders, hospital boards of trustees, hospital administrators, physicians and other health care providers. Patients are also increasingly aware of, and have greater access to, quality data compiled for our institutions and practices.

"My appeal to you as urologists and urology caregivers is to be leaders in this area of medicine called quality improvement."

At a recent quality forum at my institution I heard many examples of how health care professionals have successfully ended or significantly decreased some of the side effects of the procedures they do and have always accepted the idea that they must have a risk associated with them that could not be changed. This appears just not to be true. The fact is that the more carefully we look at unwanted outcomes, the more it seems that the unavoidable is actually avoidable if we can only take the steps to find ways to do so.

Another truism is that if changes to improve quality are to be successful, it will likely be because physicians, nurses and other patient care providers have a key role in examining the problems that are detected and finding structural ways to resolve them. Physicians interested in improving quality of care must not only keep current with the science of their field, but also must begin to understand how systems work, and how practice variation and human psychology impact the results of their work. As Dr. Paul Batalden said, "Every system is perfectly designed to get the results it gets." Unfortunately this concept holds true whether these results are good or bad.

As urologists interested in quality improvement we need to look carefully at the enormous amounts of quality data being generated (and reported) daily by our institutions and our practices. Within that data set it is likely you will find that the rates of some adverse event at your institution (for example postoperative deep venous thrombosis, surgical site infection etc) are higher than should be expected, higher than is experienced at institutions like your own or simply seem unacceptable to you.

What do you do next? What seems to be the best course is to gather the entire team responsible for the care of the patient (as it relates to that problem) and get out of the conference room and on to the floors and care units to see exactly what is being done, and if it is being done reliably and consistently. Then, and perhaps only then, can the team make real changes in care patterns which may improve patient quality outcomes. My appeal to you as urologists and urology caregivers is to be leaders in this area of medicine called quality improvement. It is truly amazing what can be accomplished if we not only embrace this word, quality, but actually do something tangible to improve it. ◆

Do the Outcomes of Radical Prostatectomy Vary Among Surgeons?

Dr. Andrew Vickers

Dr. James Eastham

New York, New York

Answers to questions of surgeon variability are in many ways self-evident. Humans vary in their ability in any technical skill. We do not expect all surgeons to have identical results in the same way that we do not expect Mets position players to share the same batting average. Therefore, the interesting question is not whether surgeons vary but the degree to which they do so.

There is accumulating evidence that the results of radical prostatectomy vary widely among surgeons. Indeed the extent of this variation is so great as to have led to calls for radical changes in the practice of urology. By way of comparison, the lowest batting average of the 2010 Mets is 0.192 with the highest being 0.293, which is about a 50% difference. In contrast, rates of many radical prostatectomy outcomes vary 10-fold or more across surgeons.

Variation Types

One of the first studies on surgeon variation in radical prostatectomy was conducted by Begg et al, who used SEER (Surveillance, Epidemiology and End Results)-Medicare data to examine complication rates.[1] In their first analysis they demonstrated that complications varied systematically with surgeon volume. Surgeons in the lowest 25% of annual caseload had a complication rate of 6% to 8% greater than that of surgeons in the highest 25% of surgical volume. There was also important variation within the group of highest volume surgeons, with complication rates ranging from less than 5% to more than 50%. This variation was far greater than expected by chance in that 8% of high volume surgeons had postoperative complication rates greater than the predicted 99th percentile, whereas 3% had rates below the 1st percentile.

A key aspect of this study is that 2 different types of variation were analyzed separately. The first type of variation was associated with measurable characteristics of a surgeon such as training, experience or type of institution. The second type of variation was associated with unmeasured aspects of technique, and is described as heterogeneity or extra-binomial variation.

Experience or Volume?

Begg et al, like many other investigators going back to the 1970s, found an association between outcomes and annual case volume. This association raises the question of exactly what it is about high volume that leads to better patient care. Our work focuses on surgeon experience (total number of cases that a surgeon has performed in his or her career) which is different from volume (the number of cases in the previous year), although both figures are obviously correlated.

For example, a low volume surgeon can never gain significant surgical experience. It seems self-evident that experience would be a better predictor than volume. Most of us would prefer to be treated by an experienced surgeon who had cut back caseloads due to administrative work than by a surgeon who had been treating several cases a week in the 3 months since qualifying.

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A Message from Amgen

RANK Ligand: an essential mediator of bone destruction in patients with prostate cancer and bone metastases

Studies suggest 65%–75% of patients with advanced prostate cancer can develop bone metastases over the course of their disease[6]

Recognizing the central role of RANK Ligand is pivotal to understanding the underlying mechanism of bone disease in patients with prostate cancer and bone metastases.[4,5]

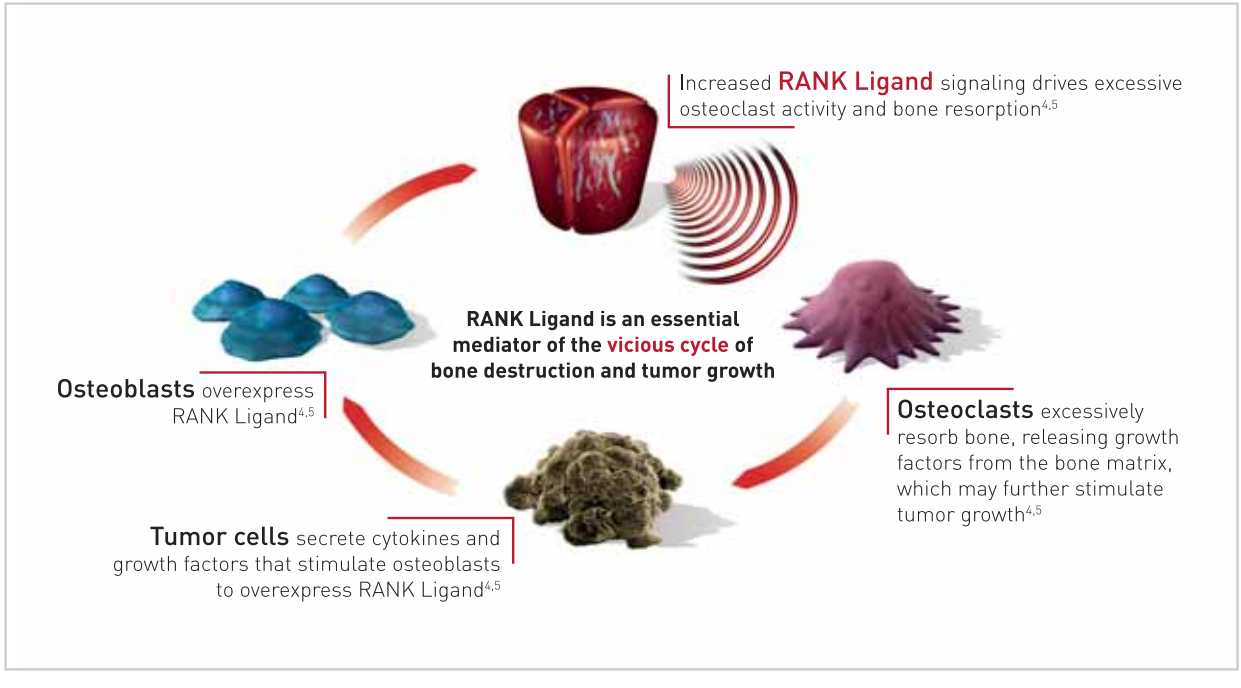
What is RANK Ligand?
RANK Ligand is a protein expressed by osteoblasts, the cells responsible for bone formation. RANK Ligand promotes the differentiation, activation, and survival of bone-resorbing osteoclasts.[1,4,7,8] In healthy bone, the body regulates RANK Ligand activity to balance bone formation and bone resorption.[1,2]

RANK Ligand in metastatic prostate cancer
When tumor cells invade the bone microenvironment, they secrete cytokines and growth factors that stimulate osteoblasts to overexpress RANK Ligand. This increased RANK Ligand signaling disrupts the natural balance of bone remodeling by driving excessive osteoclast activity and perpetuates the vicious cycle of bone destruction and tumor growth that can lead to devastating skeletal-related events (SREs).[4,5] In preclinical models, data suggest that RANK Ligand may act as a signal for RANK-expressing prostate tumor cells to preferentially metastasize to bone.[9,10]

RANK Ligand overexpression and skeletal complications
Data have shown that SREs are common in patients not treated for bone metastases from prostate cancer, with 49% (101/208) of patients experiencing an SRE within 2 years.[11]

SREs, which include pathological fracture, palliative radiation therapy, surgery to bone, and spinal cord compression, can lead to intractable pain and impaired mobility.[6,11]

Image courtesy of the Tel Aviv Sourasky Medical Center. www.tasmc.org.il/e/



Amgen is committed to understanding the role of **RANK Ligand** in cancer-induced bone disease. To learn more about **RANK Ligand**, please visit **www.rankligandincancer.com.**

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Surgical Outcomes and Surgeon Variability

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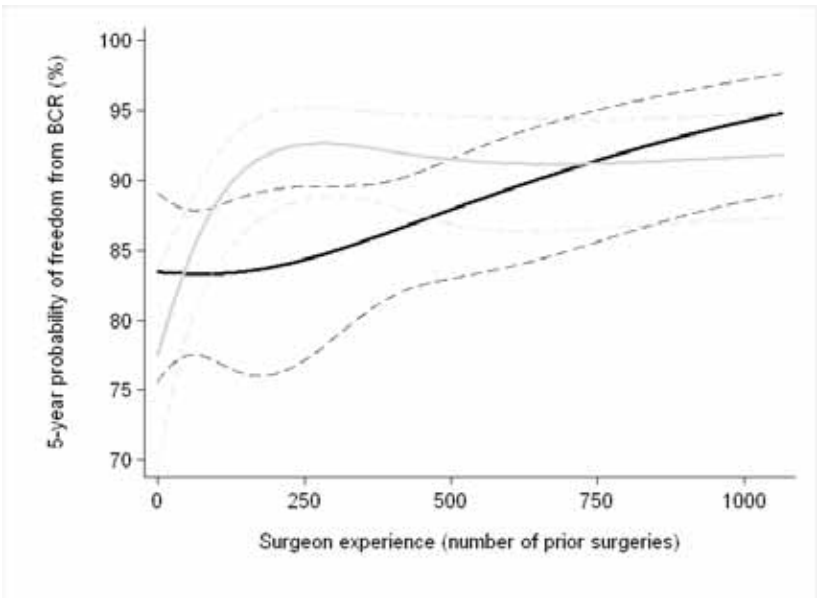
Indeed the wealth of articles on volume is not because researchers prima facie defined volume as an important predictor variable, but because the structure of databases like SEER-Medicare is such that only research on volume and not experience is possible.

Our initial study on surgeon experience included 7,765 patients treated with open radical prostatectomy at 1 of 4 United States academic centers.[2] After adjusting for tumor characteristics, the risk of biochemical recurrence at 5 years decreased from approximately 18% for a typical patient treated by an inexperienced surgeon (10 radical prostatectomies) to 11% for those treated by more experienced surgeons (250 cases).

This result was independently replicated using a data set of 4,702 patients with prostate cancer treated laparoscopically by 1 of 29 surgeons from 7 institutions in Europe and North America.[3] The patients in the latter series were all treated after the stage shift, and there was no important association between surgeon experience and patient characteristics. Thus, it is unlikely that the findings could be explained by patient selection.

In a subgroup analysis recurrence rates for organ confined disease decreased from close to 15% for inexperienced surgeons to less than 1% for the most experienced surgeons with 1,500 or more prior cases.[4] This constitutes a greater than 10-fold difference in recurrence rates across surgeons. Improving outcomes with experience is what is commonly referred to as a learning curve (see figure).



Learning curve for open (gray) and laparoscopic (black) radical prostatectomy. Broken lines indicate 95% CI.

Recurrence rates differ even after adjusting for experience,[5] that is the chance of cure can vary depending on which of 2 surgeons a patient sees even if they are similarly experienced. We have also recently studied important variation in outcomes for erectile and urinary dysfunction (unpublished data). Even within a small group of surgeons at 1 academic center rates of full potency at 1 year ranged from less than 10% to more than 50%, and urinary dysfunction rates ranged from less than 5% to more than 35%.

What is to Be Done?

Gross variations in patient outcomes after radical prostatectomy are unacceptable, and steps must be taken to ensure that patients receive more uniform and high quality care. If there was similar variation in baseball some position players would be hitting 0.030, and it is hard to believe that many managers or fans would put up with such dismal performance.

The first step in improving outcomes is surely the monitoring of outcomes. Surgeons need to know how their results compare to those of their peers, which leads to an interesting spin on the volume-outcome debate. Some have argued that volume is not a surrogate for quality. In other words, it is perfectly possible for a low volume surgeon to have good results while a high volume surgeon performs poorly.

The problem with this argument is that if you do not have volume, you will never know about outcome. We cannot be sure that a surgeon who operates on only a handful of cases per year offers effective treatment any more than we can assess whether a baseball player with only 10 lifetime at bats is a good hitter. Thus, we should insist that surgeons choosing to perform radical prostatectomy conduct a high volume of cases and we should carefully monitor their outcomes. ◆

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Impact of Shock Wave Delivery Rate on Stone-Free Outcome and Treatment Cost

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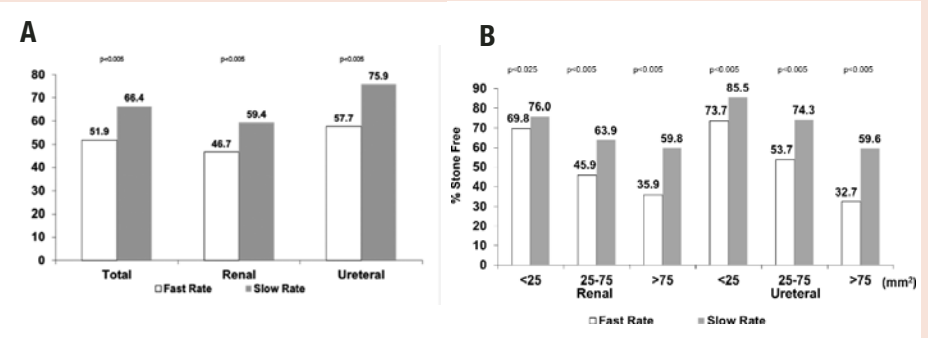
Since the 1980s extracorporeal shock wave lithotripsy (SWL) has been a standard of treatment for urinary calculi, and during the last 25 years the technique has been refined to improve effectiveness and efficiency. A recent change in technique has been to slow the rate of shock wave delivery, which has been reported to improve treatment efficacy by increasing the stone-free rate.[1,2]

The impact of slowing the shock wave delivery rate was evaluated in a cohort of 1,745 consecutive cases. All treatment was performed with a single lithotripter (Lithotron®) by more than 20 urologists at a freestanding urology surgery center. The procedures were standardized by the number of shocks delivered (3,000 per treatment), kV settings, imaging technique and use of general anesthesia. The evaluated treatments were divided into a fast rate (FR) of 120 shocks per minute in 872 cases and a slow rate (SR) of 60 shocks per minute in 873 cases. There was no statistical difference between the groups in terms of stone size or location in the urinary tract. The stone-free rate was determined 4 to 6 weeks postoperatively by plain film of the abdomen.



Stone-free rates by location *(A)* and size *(B)*

A comparison of the stone-free rates of the FR and SR groups revealed a significantly higher rate (overall 14% increase) in all stone categories except for stones smaller than 25 cm^2 for the SR group (see figure). This improvement resulted in a marked decrease in the need for a second procedure (SWL or ureteroscopy) to render the patient stone-free. The second procedure rate in the FR group was 35.4% whereas it decreased to 18.2% in the SR group.

The decrease in shock wave delivery rate resulted in an increased procedure time. Each SR procedure was 24 minutes longer than the FR procedure (50 vs 26 minutes), which resulted in fewer procedures that could be performed daily at the ambulatory surgery center.

To estimate the economic impact this change in SWL technique would have on the payer, the results were

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Shock Wave Delivery Rate

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compared using the 2009 Medicare reimbursement schedule. The increase in SR procedure time resulted in an increase in anesthesia related payments of $28,294. However, the significant decrease in secondary procedures resulted in a payment decrease of $264,989. Thus, there was a total estimated savings of $236,695 with the SR technique. This change in technique resulted in savings of $271.13 per SWL treatment. However, this estimate of decrease in payment may be understated considering 70% of these patients were privately insured, which generally indicates a higher payment schedule than Medicare.

In this study of a community general urology practice the SR technique for SWL resulted in a higher stone-free rate, which decreased the need for secondary procedures, thereby decreasing payer cost. The quality of patient care was likewise improved by decreasing the risk and morbidity associated with secondary procedures.

Slowing the SWL rate is an example of scientific research leading to a change in the practice patterns of clinical urologists, which translates into improved quality of patient care at a lower cost. ◆

Awarded best poster at annual meeting of the American Urological Association, San Francisco, California, May 29–June 3, 2010.

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Management of Overactive Bladder. Part II: How to Use Medications

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In part I of this series on behavioral therapy 3 major points were emphasized. 1) The clinical manifestation of urge incontinence is due to bladder dysfunction and behavioral/pelvic floor factors. 2) The bladder diary provides a simple, inexpensive assessment of the degree of bladder dysfunction. 3) The goals of the patient should be incorporated in the decision making process because many nonmedical treatments are available and are often preferred.

Nevertheless, pharmacological therapy retains a primary position in the treatment of the overactive bladder (OAB), and most clinicians agree that medications, behavioral therapy and pelvic floor rehabilitation are complementary tools best used in combination. Patient goals are of great importance, and some prefer medical therapy alone while others prefer an

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Management of Overactive Bladder: Part II

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aggressive approach using all modalities together from the outset.

Similarly clinicians have different viewpoints, with some preferring to start every patient on medical therapy. The idea is that patients will more likely see early improvement, which will create confidence. On the other hand, others believe that medications should always be second line therapy because of the significant side effects that may cause patients to lose confidence if they experience a bad reaction. These different styles are best negotiated openly with the understanding that there is no single best approach.

I advocate selective use of early medical therapy and try to identify patients who are particularly good candidates for treatment with drugs. Patients with a low functional capacity (less than 150 to 200 ml) typically have more severe bladder dysfunction and those with high volume urine loss are less tolerant of the condition.

Patients with a low total 24-hour urine output are already practicing fluid restriction and have less opportunity to respond to behavioral change. Those with strong pelvic floor muscle contraction on examination have less chance of improving with pelvic floor rehabilitation. Patients in whom OAB has a neurogenic cause are less likely to achieve and maintain complete remission. All of these groups are more likely to require medication to achieve an adequate response and, thus, early use of drug therapy is recommended.

The medications currently available for the treatment of OAB are listed with the usual dosing in the Appendix. All of the medications have a similar mechanism of blocking muscarinic cholinergic receptors in the bladder. There is little doubt that all medications are superior to placebo in reducing urgency and urge incontinence episodes.

Similarly the medications can cause anticholinergic side effects in other organ systems such as dry mouth and eyes, heartburn, constipation, blurry vision, palpitations etc. All drugs should be used with caution in patients who have associated difficulty emptying the bladder, although even documented bladder outlet obstruction is not an absolute contraindication. The newer once daily medications are consistently superior to short-acting generic oxybutynin due to the reduced incidence of adverse effects. Otherwise there is little evidence of meaningful differences among medications in efficacy or side effects. When deciding on the approach some important principles of medical therapy should be considered.

1. There is no best drug. Many insurance companies currently require that patients begin therapy with generic oxybutynin ER and I use a starting dose of 10 mg. All medications should be combined with timed voiding and urge inhibition strategies.
2. Although most patients see a response within 2 weeks, it is best to give a drug a full month before assessing response. A followup bladder diary collected while the patient is taking medication is helpful in evaluating treatment response.
3. Patients who experience improvement but are not dry should be encouraged to try a higher medication dose. Similarly those who are dry but still have a low functional capacity based on bladder diary should work on normalizing function using a combination of higher medication dose and/or behavioral techniques.
4. Before changing to a new medication the dose of the current drug should be increased until the patient experiences limiting side effects.
5. Patients who do not respond to a maximally tolerable dose of a medication can be given a trial of a different drug. However, when a patient does not respond to 2 different drugs there is a markedly lower chance that other drugs will be effective.
6. There is some evidence that patients who experience anticholinergic side effects with oral medications, particularly dry mouth, may find transdermal preparations more tolerable.
7. There is no rationale for combining standard anticholinergic medications, and titration to a maximum dose of a single agent is preferable. There is a rationale for combining the standard agents with imipramine, particularly if the patient has mixed incontinence, but this theoretical advantage must be balanced against the risk of cardiac toxicity from imipramine, which has significant arrhythmogenic properties.
8. Patients limited by side effects might still be treated on an as needed basis with 0.125 mg sublingual hyoscyamine, which has a rapid onset and short duration of effect.
9. Attention should be given to the cumulative anticholinergic load and the risk of central nervous system (CNS) side effects that can be significant for patients on multiple medications. While the evidence is inadequate, theoretical arguments can be made for the use of trospium (a quaternary amine that should not cross the blood-brain barrier), darifenacin (M3 over M1 receptor selectivity limiting CNS toxicity) and solifenacin (a large molecule less likely to cross the blood-brain barrier) in such cases.

Whether drugs are used in all patients or selectively, consideration should always be given to the ultimate goal of bladder retraining. Patients who become completely continent with good capacity on the voiding diary probably have approximately a 50% chance of being able to go off medication and stay dry a long time. Titration off medication should be suggested after 3 to 6 months when drug therapy is successful. ◆

**Financial interest and/or other relationship with Afferent Pharmaceuticals, Allergan, AMS, Astellas, Celgene, Coloplast, Curant and Medtronic.*

Appendix

Oral products

Generic drugs:
- Oxybutynin immediate release (5 mg up to 3 times daily)
- Oxybutynin ER (5, 10 and 15 mg once daily)

Proprietary drugs:
- Oxybutynin ER (Ditropan XL® 5, 10 and 15 mg once daily)
- Tolterodine (Detrol® LA 4 mg once daily)
- Solifenacin (VESIcare® 5 and 10 mg once daily)
- Darifenacin (Enablex® 7.5 and 15 mg once daily)
- Trospium (SANCTURA XR® 60 mg daily)
- Fesoterodine (Toviaz® 4 and 8 mg once daily)

Transdermal products

Oxybutynin patch (OXYTROL® 36 mg patch twice weekly, 3.9 mg daily)

Oxybutynin gel (Gelnique® 10% gel 100 mg/gm, 1 mg gel daily)

Nonstandard products

Hyoscyamine (Levsin® 0.125 mg SL as needed)

Imipramine (Tofranil® 10 to 25 mg up to 3 times daily)

Do Mixed Histological Features Affect Survival Benefit of Chemotherapy for Bladder Cancer?

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Level 1 evidence indicates that cisplatin based multidrug chemotherapy regimens given before cystectomy improve overall survival from muscle invasive urothelial cancer (UC) and significantly improve pathological down staging to stage pT0 (no cancer in the cystectomy specimen).[1,2] However, 20% to 40% of muscle invasive UCs contain other histological types, primarily squamous cell and adenocarcinoma elements,[3] and it is not known if these mixed histology (MH) cancers are as responsive as pure UC to these chemotherapy regimens.

In clinical series metastatic MH cancers respond to these chemotherapy regimens, although less well than does pure UC.[4, 5] It is not known whether MH cancers would also respond to these combination regimens in the nonmetastatic setting and, if so, how survival would be affected.

To answer these questions we performed a secondary analysis of the SWOG (Southwest Oncology Group) trial S8710/Intergroup INT0080 of neoadjuvant methotrexate, vinblastine and cisplatin (MVAC) plus radical cystectomy (RC) vs RC alone for stage cT2-4+, N any, M0 bladder UC. Tumors were classified as pure UC (236) or MH (59). More than half of the patients with MH or pure UC in each treatment arm had clinical stage cT3-4 (ie extravesically extending) cancer.

The chi-square and Fisher's exact tests were used to compare the proportions of cases down staged to pT0 with MH and those with pure UC in the MVAC plus RC and RC only arms. Cox regression models were used to estimate the effect of neoadjuvant MVAC on all cause mortality for patients with pure UC and those with MH tumors, with adjustment for age and clinical stage.

Down staging to pT0 was seen in MH and pure UCs using MVAC plus transurethral resection (TURBT) vs TURBT alone (RC only groups) (table 1). The additive down staging effect (ADE) when adjusted for stage was almost twice as great in patients with MH cancer as in those with pure UC (tables 1 and 2).

The overall survival benefit from chemotherapy was greater in patients with MH tumors (HR 0.46, p = 0.02) than in those with pure UC (HR 0.90, p = 0.48), and occurred equally in patients with clinical stage T2 and those with extravesical disease (tables 2 and 3). There was marginal evidence of statistical interaction between the use of neoadjuvant chemotherapy and histology status (p = 0.09).

The effectiveness of neoadjuvant MVAC in the MH group was not anticipated based on the limited data from series of patients with metastatic disease.[4, 5] Indeed it was our initial hypothesis that if MH cancer responded less well than pure UC to neoadjuvant chemotherapy, withholding this treatment in such patients might be advisable to avoid unnecessary toxicity and prevent potentially harmful delays in performing surgery if necessary.[6] However, while a primary purpose of neoadjuvant chemotherapy is to eradicate micrometastases because they are assessed radiographically rather than histologically and because survival rates are much poorer in patients with metastases than in those with localized disease, responses in the metastatic setting might not accurately predict

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Survival Benefit of Chemotherapy for Bladder Cancer

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responses in the local and regional setting.

There are numerous limitations to our study including the relatively small number of MH cancers, possible disagreement among pathologists in classifying MH status despite central histology review and the inability to determine the proportion of nonUC components in MH cancers. These limitations made it impossible for us to determine whether this proportion affects the response to MVAC. Also, we could not address whether other chemotherapy regimens now commonly used for UC (eg gemcitabine-cisplatin) are as effective as MVAC on MH tumors, or whether other mixed histologies such as micropapillary differentiation or UC plus small cell carcinoma respond similarly to MVAC as UC plus squamous or adenocarcinoma.

However despite these limitations, we believe that MH bladder cancer is at least as responsive to neoadjuvant MVAC chemotherapy as is pure UC. The presence of squamous or glandular differentiation in locally advanced bladder UC is a strong indication for the use of neoadjuvant chemotherapy before cystectomy. ◆

Awarded best poster at annual meeting of the American Urological Association, San Francisco, California, May 29–June 3, 2010.

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Table 1. Patient characteristics for treatment combinations

	Mixed Tumors		Pure UC	
	MVAC + RC	RC Alone	MVAC + RC	RC Alone
No. pts	32	27	115	121
Mean pt age	60	65	63	62
% cT3-T4a disease	59	70	59	57
% Female	31	15	14	21
% White	+91	78	96	96

Table 2. Patients with pT0 disease and those with unknown pT0 status at RC

Treatment Arm	No. Pts	No. pT0 (%)	No. pT0 Status Unknown (%)
Mixed tumors:			
MVAC + RC	32	11 (34)	4 (13)
RC alone	27	1 (4)	3 (11)
Pure UC:			
MVAC + RC	115	33 (29)	15 (13)
RC alone	121	17 (14)	7 (6)

Table 3. Estimated down staging effects

Subset	No. Pts	Contrast	% ADE*	95% CI	p Value
Mixed tumors	59	MVAC vs RC only	28	11, 44	0.004
Pure UC	236	MVAC vs RC only	15	5, 25	0.004
MVAC + RC	147	Mixed vs pure UC	6	-11, 23	0.51
RC only	148	Mixed vs pure UC	-8	-20, 3	0.27

**Directly standardized to the distribution of clinical stages among all patients in analysis.*

Burning Bridges: Cavernous Nerve Resection

Drs. Parviz K. Kavoussi, Adam C. Straub, William D. Steers,* Raymond A. Costabile,† Brant Isakson and Jeffrey J. Lysiak
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The increased detection of prostate cancer as well as the widespread availability of curative therapies for this and related diseases in which treatment results in neurovascular injury have produced a cohort of men with extended disease-free survival but ultimately with erectile dysfunction (ED).[1] Overall ED affects 25% of men in the United States and is associated with an impaired quality of life.[2]

Normal erectile function requires that several cell types and systems work in concert. This process includes neural input from the cavernous nerves (CNs) to release nitric oxide, coordinated changes in arterial endothelial and vascular smooth muscle cells (VSMCs) for vasodilation, and a corpora cavernosal apparatus through which venous endothelium and vascular smooth muscle interact to trap blood. It is obvious that CNs can be injured during radical prostatectomy and chronically after radiotherapy for prostate cancer, and the more severe the degree of nerve injury the greater the chance of ED. However, the precise mechanisms of how nerve injury ultimately affects erectile function are not well understood.

Coordinated communication between endothelial cells (ECs) and VSMCs is paramount for smooth muscle cell relaxation and resulting tumescence. Myoendothelial junctions (MEJs) are cellular extensions through the internal elastic lamina (IEL) between ECs and VSMCs. At the points of cell-cell contact in the MEJ, gap junctions form pathways for the flow of signaling molecules between the 2 cells.[3,4] ECs cause smooth muscle relaxation byrelease of a number of factors including nitric oxide, prostaglandins and endothelium derived hyperpolarizing factor. There is recent evidence that endothelium derived hyperpolarizing factor requires intact MEJs for its action.

Since to our knowledge MEJs have not been described in the penile corpus cavernosum, the focus of our studies was to 1) determine if MEJs are present between ECs and smooth muscle cells in the corpus cavernosum, 2) use a genetic model of mice that lack MEJs to determine if they have normal erectile function and 3) determine if cavernous nerve resection (CNR) alters the presence of MEJs. All work was conducted in accordance with the Guiding Principles of the Care and Use of Research Animals promulgated by the University of Virginia.

Electron microscopy on murine and human corporal tissue revealed MEJs traversing the internal elastic lamina from the endothelial cell to the vascular smooth muscle cell as well as from the vascular smooth muscle cell to the endothelial cell (fig. 1). In a genetic mouse model that lacked MEJs in other vascular beds (plasminogen activator inhibitor-1 deficient mice) electron microscopy on tissue sections of the corpus cavernosum confirmed the absence of MEJs as well.[5] Interestingly CN electrical stimulation studies to assess erectile function revealed that unlike normal wild-type mice that have MEJs in the corporal tissue, mice lacking MEJs had a significant delay in the time to achieve tumescence, defined as time to reach maximum intracavernous pressure.

Since MEJs are important conduits for heterocellular communication, the data suggest that molecules transported across the gap junctions in the MEJs are important for normal corporal EC and smooth muscle cell signaling during the erectile response. It is also becoming increasingly clear that specific proteins can reside in the MEJ complexes. Thus, disruption of

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Effect of Cavernous Nerve Resection on Erectile Function

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their normal cellular distribution may, in turn, disrupt normal heterocellular communication.

As previously stated, injury to the cavernous nerves which may occur during prostatectomy results in ED. To determine if the MEJs in the corporal tissue are affected after CN injury, 1 group of normal wild-type mice were subjected to bilateral CNR and 1 group underwent sham operations. At postoperative week 4 electron microscopy of the cavernous tissue revealed that the bilateral CNR mice had a significant decrease in the number of MEJs, whereas sham operated mice had numbers similar to those of unoperated control mice (fig. 2). It is intriguing to speculate that a possible mechanism of CN injury induced ED may be due to the loss of MEJs between ECs and VSMCs in the corporal tissue. However, at this time we do not know if the loss of MEJs is a cause of ED, the result of ED or simply correlated with ED. Studies are ongoing to answer these questions.

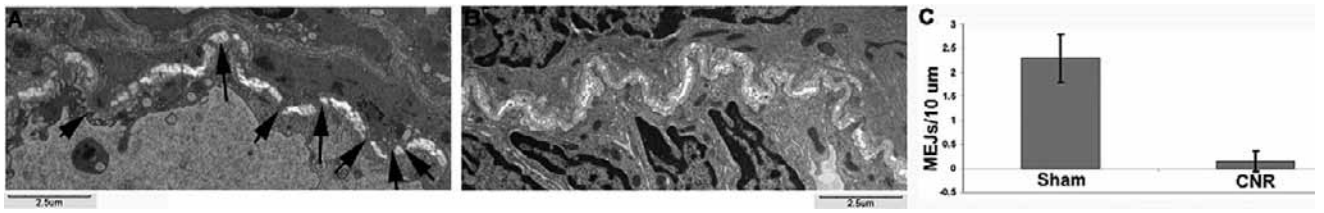

Fig. 2. CNR results in loss of MEJs in corporal tissue. MEJs are observed in sham operated control mice *(A, black arrows)*. CNR results in loss of MEJs in corporal tissue *(B)*. Quantification of MEJs per 10 µm IEL *(C, 3 in each group)*.

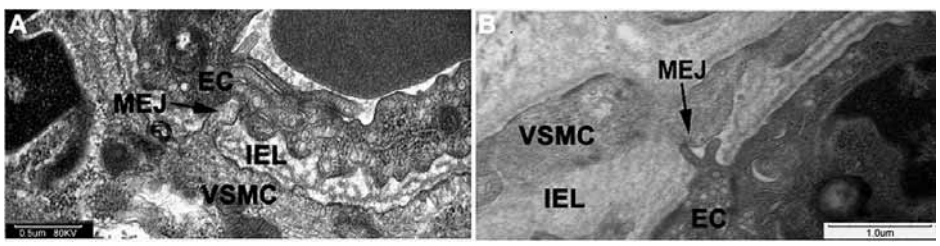

Fig. 1. MEJs in murine *(A)* and human *(B)* corpus cavernosal tissue *(black arrows)*. MEJs can be formed from VSMC traversing IEL to EC as demonstrated in mouse section or conversely from EC to VSMC as demonstrated in human section.

Regardless of the results of our ongoing studies it is clear that MEJs are present in human and mouse corporal tissue, and that their presence is directly correlated with ED. MEJs may have a pivotal role in the coordinated endothelial cell–smooth muscle cell response necessary for normal tumescence. Future studies are also aimed at investigating the presence of MEJs in other pathological states known to cause ED such as diabetes and smoking. ◆

**Financial interest and/or other relationship with Allergan, American Board of Urology, Food and Drug Administration and National Institutes of Health.*

†Financial interest and/or other relationship with Allergan, Lilly, Vivus and Boehringer Ingelheim.

Awarded best poster at annual meeting of the American Urological Association, San Francisco, California, May 29–June 3, 2010.

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Peyronie's Disease. Part II: Surgical Treatment Options

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Surgical reconstruction remains the gold standard for correcting deformities associated with Peyronie's disease (PD). The indications for surgical reconstruction include a stable deformity for at least 6 months and at least 1 year from the onset of symptoms. The deformity should be painless on palpation, and the ability or inability to engage in coital activity should be compromised due to the deformity and/or inadequate rigidity. Certainly patients in whom conservative therapy has failed and those with extensive plaque calcification are candidates for surgery.

Preoperative consent is critical because patients with PD are frequently unhappy and setting expectations regarding outcome can enhance postoperative satisfaction (Appendix 1). Patients should be informed that curvature may persist or recur. I inform patients that the goal is to make the penis functionally straight, which is defined as less than 20 degrees of curvature in any direction. In addition, the length may change. Shortening appears to be more prevalent with plication than with grafting but both techniques should be presented as straightening procedures rather than as lengthening or shortening procedures.

The greatest risk of surgical correction without a prosthesis is decreased rigidity. This outcome has been reported to have a rate of at least 5% in all studies but occurs most often after grafting procedures. Several studies have examined predictors of postoperative erectile dysfunction (ED), and preoperative erectile quality appears to be the most reliable predictor.[1] Lastly, decreased penile sexual sensation has been reported but most patients who experience some sensory loss find that it recovers in the days and months after surgery.

Several surgical algorithms have been published, all of which essentially agree that when preoperative rigidity is adequate with or without phosphodiesterase type 5 (PDE5) inhibitors, a tunica plication technique is best when curvature is less than 60 degrees, there is no hourglass or hinge effect and the predicted loss of length would be less than 20% of the stretched length (Appendix 2). For those men who have more complex curvature of greater than 60 to 70 degrees or have a destabilizing hourglass, then excision or partial excision of plaque and grafting are recommended.[2-4]

"Certainly patients in whom conservative therapy has failed and those with extensive plaque calcification are candidates for surgery."

Multiple plication techniques have been presented during the last 40 years, starting with the Nesbit procedure. This approach involves excising a wedge of tunica on the convex side, opposite the direction of the curvature. The defects are then closed to shorten the longer side. The Yachia procedure is a plication involving use of the Heineke-Mikulicz technique, whereby a longitudinal incision is made on the convex aspect but is closed transversely. Although this procedure is successful, it may exaggerate areas of narrowing.

No incision is necessary for the 16-dot technique, which involves use of extended Lembert applied nonabsorbable sutures on the convex aspect to shorten the convex side. The Duckett-Baskin tunica albuginea plication (my preferred approach) is accomplished with a pair of parallel transverse incisions through the longitudinal fibers without violating the circular fibers or cavernosal tissue. The space between the 2 parallel incisions is thinned to reduce the bulk of the plicated tissue. This procedure can be performed with permanent or absorbable sutures.

Multiple reports have been published in the last decade on these plication procedures, which in general provide an 85% to 100% rate of straightening and a 13% rate of postoperative

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Peyronie's Disease: Part II

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ED. Decreased sensation has been reported infrequently but ranges from 4% to 21%. The recently published recommendations from the International Consultation on Sexual Medicine (ICSM) in 2009 suggest that "there is no evidence that one surgical plication approach provides better outcomes over another but curvature correction can be expected with low risk of new ED" (Appendix 3).[5]

Historically when grafting was used, the assumption was that the entire scar needed to be excised to "get rid" of the disease. This procedure typically left large tunica defects that may have been responsible for the high rate of postoperative ED. With the advent of the incision or partial plaque excision, correction of severe deformity can be accomplished without a penile prosthesis and with a low rate of postoperative diminished rigidity in patients with good to excellent preoperative erections.

The other indications for incision or partial excision and grafting include curvature greater than 60 to 70 degrees and/or significant shaft narrowing resulting in a hinge effect. The incision and partial excision techniques involve a modified H-incision to correct the area of maximum deformity. The corners of the rectangular defect are expanded in a radial fashion to reestablish normal caliber as well as lengthen the shortened aspect of the penis.

A variety of grafts have been used including fat, dermis, fascia lata, dura mater, Dacron® and polytetrafluoroethylene. However, these materials have fallen out of favor as they often require a second incision with added morbidity or in the case of synthetic grafts increase the risk of infection and remain palpable. For autologous grafts, the preferred graft is the saphenous vein but this tissue may be useful as a future coronary graft.

Off-the-shelf products appear to have emerged as the preferred grafts, including Tutoplast® processed human pericardial graft and small intestinal submucosa (SIS). Multiple studies have been published in the last 2 decades on grafting techniques to correct PD. In general, satisfactory straightening rates range from 74% to 100%, and 5% to 53% of patients experience diminished rigidity postoperatively. More recent studies have indicated a 5% to 15% ED rate in patients who had strong preoperative erections.[6]

Rehabilitation is strongly advised following surgical straightening, particularly with grafting.[6] This process begins with massage and stretch therapy 2 weeks postoperatively for 5 minutes twice daily for 4 weeks. PDE5 inhibitors have been recommended in the early postoperative period to enhance nocturnal erections and thereby nourish the graft and reduce the risk of fibrotic changes to the exposed cavernosal tissue.[1] Recently postoperative external traction therapy has been demonstrated to prevent further or recover loss of length.[7] The technique is to apply a penile traction device 2 to 4 weeks after surgery which is worn for 3 to 8 hours daily for 3 months.

For patients with PD who present with ED refractory to medical therapy, a penile prosthesis is recommended.[8] Adequate straightening can occur simply by placing the device, and a high pressure cylinder is recommended. A significant and important advance to simplify the correction of curvature is manual modeling, which must be done with great care so as not to disrupt the corporotomies or extrude the distal tips of the prosthesis through the meatus.[9]

If there is residual curvature after modeling of more than 30 degrees, a tunica releasing incision is recommended. This procedure should be performed with no more than 35 watts of cautery power to reduce the likelihood of thermal injury to the underlying cylinders. If a tunica defect is larger than 2 cm, then applying a biograft such as pericardium or SIS is indicated to reduce the likelihood of cicatrix contracture or cylinder herniation.

Recent experience from our institution has been published on 90 consecutive inflatable penile prostheses (IPPs) placed in men with PD and drug refractory ED.[10] In this series 4% of patients had satisfactory straightening with an IPP alone, 79% required only modeling, 4% had an incision and 12% had grafting over the incision. There was 1 case of infection and the mechanical failure rate for the group was 7% with a mean followup of 49 months. A nonvalidated questionnaire revealed that overall patient satisfaction was 84% but satisfaction with curvature correction was only 73%.

These results suggest that patients may find any residual curvature distressing. If the patient insists on complete straightening, he should understand that further surgical maneuvers such as incision and grafting may be necessary with possible increased risks of postoperative complications.

In conclusion, PD seems to be far more prevalent than previously thought. More men are presenting with PD around the world and are seeking effective treatment options. Nonsurgical therapy as discussed in part I of this series is appropriate for the patient who does not have stable disease or who declines surgery. However for those men who want the most rapid and reliable result, surgical correction remains an option. ◆

**Financial interest and/or other relationship with American Medical Systems, Coloplast, Pfizer, Auxilium and Physiomed.*

Appendix 1: Patient Consent: Set Expectations Regarding Outcome

Persistent/recurrent curvature:
- Goal – "functionally straight," less than 20 degrees
- Ensure stable disease preoperatively

Change in length:
- More likely shorter with plication vs grafting

Diminished rigidity:
- 5% or More in all studies – especially with grafting
- 30% or More if suboptimal preoperative rigidity, dependent on preoperative erectile quality

Decreased sexual sensation:
- Common but rarely compromises orgasm/ejaculation

Appendix 2: Surgical Algorithms

When rigidity is adequate with or without pharmacotherapy

Tunica plication techniques:
- Simple curve less than 60 to 70 degrees
- No hourglass or hinge effect
- When length decrease is less than 20% total erect length

Incision/partial excision and grafting:
- Complex curve greater than 60 to 70 degrees
- Destabilizing hourglass or hinge

Penile prosthesis placement when rigidity is inadequate:
- IPP alone (not Ultrex™/LGX™)
- With modeling
- With incision
- With incision and grafting (defect greater than 2 cm)

Appendix 3: ICSM Recommendations With Regard to Surgery

1. Detailed consent is imperative
2. Follow published algorithms
3. Plication for less severe deformity graded as less than 60 degrees and when borderline ED
4. Grafting reserved for severe deformity greater than 60 to 70 degrees ± hinge, normal erectile function and experienced surgical team
5. Prosthesis placement with additional maneuvers when refractory ED occurs with PD

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Helped over **25 million men** with ED[1]

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*Results taken from an online survey of 772 short- and long-term patients aged 35 to 80 taking Cialis® (tadalafil), Levitra® (vardenafil HCl), or VIAGRA for erectile dysfunction (ED). Patients were asked "How soon after taking a (VIAGRA, Cialis, or Levitra) pill do you typically initiate sexual intercourse?"

† Results from an open-label, flexible-dose study with 979 patients with ED who had previously completed a double-blind trial and an open-label extension study of VIAGRA. At yearly intervals up to 4 years or at discontinuation, patients were asked if they were satisfied with their erections. Only 62 patients discontinued treatment due to insufficient response, and 11 due to adverse events. At year 4 (N=571), 96.3% said they were satisfied.

‡ Data pooled from 26 flexible-dose, placebo-controlled, parallel-group, phase 2, 3, and 4 studies with 6146 patients with ED who responded to Q7 of the International Index of Erectile Function (IIEF). Patients taking VIAGRA for ED (n=3260) reported a 94% improvement from baseline in the frequency of satisfactory sexual intercourse, compared with 22% with placebo (n=2886; $P<.0001$). In the same data set, patients responded to Q3 (N=6144) and Q4 (N=6136), reporting an 81% improvement from baseline in the ability to penetrate ($P<.0001$) and a 104% improvement from baseline in the ability to maintain an erection ($P<.0001$), compared with 19% and 26% for placebo, respectively.[1]

§ Results from a double-blind phase of a placebo-controlled, fixed-dose study (VIAGRA 100 mg) of 228 patients with ED of various etiologies and degrees of severity. The study assessed onset of action (median time to erection hard enough for penetration and to erection that resulted in successful intercourse). The study included previous VIAGRA responders who took 100 mg at least 2 hours after eating. Thirty minutes postdose, 67.8% of patients taking VIAGRA 100 mg had an erection that resulted in successful intercourse versus 36.3% taking placebo. Fourteen minutes postdose, 34.8% of patients taking VIAGRA 100 mg had an erection that resulted in successful intercourse versus 22.1% taking placebo.

VIAGRA is indicated for the treatment of erectile dysfunction (ED).

Important Safety Information

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Before treating ED, physicians should consider the impact of resuming sexual activity and the mild and transient vasodilatory effects of VIAGRA on blood pressure. Physicians should carefully consider whether patients with underlying cardiovascular disease or other more unusual conditions could be adversely affected by vasodilatory effects, especially in combination with sexual activity.

As there have been infrequent reports of prolonged erections lasting more than 4 hours or priapism with all ED treatments in this drug class, patients should be advised to seek immediate medical attention should these occur.

In a controlled interaction study of VIAGRA and amlodipine, the mean additional reduction in supine blood pressure was 8 mm Hg systolic and 7 mm Hg diastolic.

Physicians should advise patients of the potential for PDE5 inhibitors, including VIAGRA, to augment the blood pressure–lowering effects of alpha blockers and antihypertensive medications. In some patients concomitant administration of a PDE5 inhibitor and alpha blocker may lead to symptomatic hypotension. Patients should be stable on alpha-blocker therapy prior to initiating VIAGRA treatment and VIAGRA should be initiated at the lowest dose (25 mg).

Sudden decrease or loss of hearing has been reported in temporal association with the use of PDE5 inhibitors, including VIAGRA. Non-arteritic anterior ischemic optic neuropathy (NAION) has been reported rarely post-marketing in temporal association with the use of PDE5 inhibitors, including VIAGRA. It is not possible to determine if either of these events is related to PDE5 inhibitors or to other factors. Physicians should advise patients to stop use of PDE5 inhibitors, including VIAGRA, and seek medical attention in the event of sudden decrease of vision or hearing.

Use of VIAGRA offers no protection against sexually transmitted diseases, including the human immunodeficiency virus (HIV); therefore, physicians should consider counseling their patients about protective measures.

The most common side effects of VIAGRA were headache, flushing, and dyspepsia.

For more information, visit www.PfizerPro.com/VIAGRA.

Please see brief summary of prescribing information for VIAGRA tablets on the following pages.

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HAVE YOU *Read?*

Dr. Carl A. Olsson
New York, New York

Kumarasamy KK, Toleman MA, Walsh TR et al: Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study. Lancet Infect Dis 2010; 10: 597-602.

Gram-negative enterobacter organisms with resistance to carbapenems are a potential global health threat. These authors identified numerous isolates of Escherichia coli and other Enterobacteriaceae (Klebsiella) containing the carbapenem resistance gene NDM-1 (New Delhi metallo-beta-lactamase-1 gene) in areas of India, Pakistan and the United Kingdom. Most of the U.K. isolates were from patients who had recently traveled to India or Pakistan, often receiving medical treatment in those countries. As of September 14 these superbug infections had been reported in Canada, Japan, France and Belgium. The first 3 cases in the United States were also reported in people who received medical care in India or Pakistan. This information could put a real damper on tourism.

Hurst FP, Abbott KC, Raj D et al: Arteriovenous fistulas among incident hemodialysis patients in Department of Defense and Veterans Affairs facilities. J Am Soc Nephrol 2010; 21: 1571-1577.

In many countries other than the United States hemodialysis is initiated in a higher proportion of patients with an arteriovenous fistula (AVF) already performed and matured. Hurst et al report that the number of patients beginning hemodialysis in the U.S. in 2005 and 2006 with an AVF was shockingly low (14%). If patients had Veterans Affairs or Department of Defense insurance the number was twice as high (27%) due to available pre-transplant kidney care and early vascular surgery consultation. Of patients with employer group insurance only 18.5% started dialysis with a mature AVF, and of those with Medicare and Medicaid the rates were even lower at 15.6% and 13%, respectively.

A Fistula First Breakthrough Coalition working with the Centers for Medicare & Medicaid Services and End Stage Renal Disease Networks is striving to increase these

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Have You Read?

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figures by improving the stance of all insurance types, including Medicare and Medicaid, to allow pre-dialysis nephrology and vascular surgery care. These treatments are not presently covered by most insurance agencies (including Medicare and Medicaid) and, in fact, most agencies do not cover these services until renal failure actually occurs.

Chang SL, Harshman LC and Presti JC Jr: Impact of common medications on serum total prostate-specific antigen levels: analysis of the National Health and Nutrition Examination Survey. J Clin Oncol 2010; 28: 3951-3957.

Total prostate specific antigen (PSA) determinations were correlated with the results of 10 commonly prescribed medication classes in 1,864 men 40 years old or older from the 2003 to 2006 cycles of the National Health and Nutrition Examination Survey. The 3 drug classes that revealed PSA decreases compared to nonuse were nonsteroidal anti-inflammatory drugs (NSAIDs) (p=0.03), statins (p=0.01) and thiazide diuretics (p=0.025). After 5 years of medication PSA decreased by 6% with NSAIDs, 13% with statins and 26% with thiazide. If a man took statins and thiazides for 5 years PSA decreased by 36%. However, calcium channel blockers negated the effects of statins on PSA.

Kachalia A, Kaufman SR, Boothman R et al: Liability claims and costs before and after implementation of a medical error disclosure program. Ann Intern Med 2010; 153: 213-221.

This report reflects the experience of the University of Michigan Health System since they adopted a policy of full disclosure and offered compensation to victims of medical errors in 2001. The authors compared the number of new claims for compensation, number of claims compensated, time to claim resolution and claims related costs from 1995 to 2001 and from 2001 to 2006. After implementing the disclosure-with-offer program, the monthly rate of new claims decreased from 7.03 to 4.52/100,000 patient encounters (rate ratio 0.64). The average monthly rate of lawsuits decreased from 2.13 to 0.75/100,000 patient encounters and median time to claim resolution declined from 1.4 years to less than a year. Rate ratio decreased to 0.41 for average monthly cost rates from all liability, 0.41 for patient compensation and 0.39 for legal costs. These excellent results are clearly achievable given that University of Michigan Health System has a closed staff model and a captive insurance company covering the entire staff. Other large groups should strive for a similar strategy.

Vickers AJ, Cronin AM, Björk T et al: Prostate specific antigen concentration at age 60 and death or metastasis from prostate cancer: case-control study. BMJ 2010; 341: c4521.

Finally, an interesting article that presents a new outlook on prostate cancer screening. Vickers et al studied 1,167 patients in the Malmo Preventive Project, all of whom were 60 years old, gave blood and were followed until age 85 years. The outcome measures were prostate cancer metastasis and death from prostate cancer. The rate of screening during the study course was low in Sweden at that time. A total of 126 patients with prostate cancer were found, of whom 43 had metastatic disease or died of prostate cancer. No man had cancer detected with screening and curative therapy was attempted in only 1 patient treated with radical prostatectomy.

The PSA concentration at age 60 years was associated with prostate cancer metastasis (AUC 0.86) and death (AUC 0.90). Since PSA determinations at age 60 years were as high as greater than 20 ng/ml, the mortality rate from prostate cancer was 66% and many men had metastatic disease at the time of diagnosis, these data do not replace normal screening practices. However, these findings support the notion that if PSA at age 60 years is less than 1.0 ng/ml (83 men in this study, which is a small sampling), patients may be able to avoid further screening because there is a negligible risk of life threatening disease. ◆

FROM THE *Executive Director*

Michael T. Sheppard, CPA, CAE
Linthicum, Maryland

In this month's column Michael A. Pretl, Esq., AUA General Counsel, provides an update on AUA activities associated with the Red Flags Rules, which would require medical practices to implement procedures intended to reduce identify theft. The AUA is challenging implementation of the Red Flags Rules to protect the rights of all U.S. AUA members and is sharing the burden of legal expenses associated with lawsuit. The AUA Board of Directors recognizes the importance of this issue to our members and the AUA will continue to take an active role in the litigation.

Intervention to Protect AUA Members From "Red Flags Rules"

Michael A. Pretl
AUA General Counsel
Linthicum, Maryland

On August 16, 2010 the AUA joined in a motion to intervene in federal litigation seeking to block imposition of burdensome "Red Flags Rules" on all of our members. These Rules have little or nothing to do with the practice of medicine. They seem to do little to protect patients, and impose additional paperwork on busy physicians and their staff.

The Red Flags Rules were devised by the Federal Trade Commission (FTC) in 2007 to implement a 2003 expansion of the federal Fair Credit Reporting Act. The new provisions would compel financial institutions and other creditors to protect consumers against the possibility of identity theft by devising written programs encompassing effective "mitigation plans" to ensure that consumers to whom they extend credit are properly identified.

The statutory definition of "financial institutions" includes anyone who "holds a transactional account … belonging to a consumer." It was originally believed that the Rules did not apply to health care entities as inapplicable or unnecessary in the context of the physician/patient relationship. However, in June 2008 an FTC alert was issued to a large number of "extenders of credit" indicating that the agency had chosen to paint with a broad brush. In March 2009 the government expressly declined to exclude medical practices or other professionals from the scope of these regulatory requirements.

The American Bar Association (ABA) promptly filed suit, asserting that attorneys were not "creditors" of their clients, and that the FTC had failed to follow proper rulemaking procedures. The ABA secured an injunction from a federal judge in Washington, who ruled that lawyers and law firms should be exempted from the Rules. In May 2010 the American Medical Association (AMA) filed a similar action seeking an injunction covering and exempting physicians in private practice. However, the AMA suit applies only to its own members, and to members of its state medical societies.

Therefore, more than 20 specialty groups of physician members of the Council of Medical Specialty Societies (CMSS) have engaged counsel in Washington to represent them in seeking to intervene in the AMA proceeding to broaden the requested injunction to cover all of their members. Only an estimated 30% of AUA members currently belong to the AMA, while a larger number are members of state medical organizations.

AUA and the other specialty organizations are represented by Rob Portman of Powers Pyles Sutter & Verville PC, an experienced Washington attorney who has long advocated for medical specialty groups (including the AUA) in such regulatory matters. The government and the AMA have consented to our intervention in the pending case. However, consideration and final resolution of the medical societies' action will likely be delayed pending resolution of a government appeal of the injunction previously granted to the ABA. The FTC has agreed not to enforce its Red Flags Rules against physicians until 90 days after a final decision in the ABA case so that the court may act in the present (medical society) litigation.

The AUA Board of Directors took prompt action and voted unanimously to authorize this intervention to protect the rights of all U.S. AUA members, many of whom would not be covered by the injunction sought by the AMA. The legal costs of the intervening societies are being shared equitably among participating CMSS members, and the AUA Board believes that the cost of this litigation is well justified. We will continue to take action, singly or in conjunction with other organizations, to resist unwarranted bureaucratic intrusion into our members' ability to serve their patients safely, effectively and compassionately. Additional updates will be provided in future issues of *AUANews*. ◆

HEALTH POLICY/ *Government Affairs*

Health Policy: The Power of Teamwork

Dr. Steven M. Schlossberg
Chair, Health Policy
New Haven, Connecticut

Recently, I had the pleasure of witnessing true teamwork in action with the introduction of a bill in the U.S. Senate and U.S. House of Representatives to improve federal efforts to coordinate prostate cancer research, patient education and treatment. Several important initiatives and 3 key groups came together to make this possible.

1) Several years ago the AUA Board of Directors approved implementation of a plan to improve our advocacy efforts in the capital. Staff was hired and a Washington, D. C. office was opened. A physician led Legislative Affairs Workgroup was created to coordinate physician involvement with the advocacy staff. In 2010 the workgroup became a full-fledged AUA committee. The efforts of the AUA Washington staff and physicians were critical in educating Congressional representatives to develop support for this bill.

2) The AUA Foundation developed the national prostate cancer awareness campaign "Know Your Stats About Prostate Cancer®" in collaboration with the National Football League (NFL) to improve awareness and increase education about prostate cancer. In the last year and especially walking around Washington recently I witnessed firsthand the power of this partnership. The NFL was well represented by Harold Henderson, Executive Vice President and Senior Advisor to the NFL Commissioners, and George Martin, Executive Director and President, NFL Alumni.

"In an era of increasing deficits and public concern about the national debt, this bill does not ask for new money."

The AUA and AUA Foundation owe a special thanks to the NFL alumni and NFL Hall of Famers who have participated in this initiative. Mike Haynes, Hall of Famer who played with the New England Patriots and Oakland Raiders, spearheaded this effort and helped the AUA Foundation recruit other NFL alumni. Each time I listen to Mike his story becomes more powerful. I'd like to thank Mike for all of his hard work. To read more go to http://knowyourstats.org.

3) There would not have been a bill without someone to write it and actively promote it in the halls of Congress. The AUA produced a bill capable of gaining traction through the joint efforts of several AUA staff members. Beth Kosiak, Ph.D., Associate Executive Director for Health Policy, formulated the key ideas; Karen Lencoski, J.D., Government Relations and Advocacy Federal Manager, relentlessly pressed members of Congress to support it; Brian Bailey, States and Sections Manager, and Jennifer Bertsch, Executive Coordinator for Health Policy, conducted the necessary background research; and Sue Ramthun, our external lobbyist from Hart Health Strategies, ensured that the legislative language was in order.

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Health Policy/Government Affairs

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The bill, known as the Prostate Research, Outreach, Screening, Testing, Access and Treatment Effectiveness (PROSTATE) Act of 2010 (S. 3775), requires the creation of a federal interagency task force, convened by the Secretary of Veterans Affairs, in collaboration with the Secretaries of Health and Human Services and Defense, to align current federal programs on prostate cancer to more efficiently and effectively address activities in the areas of 1) education and early detection, 2) research, 3) health care delivery, and 4) underserved populations in inner cities and rural areas. In an era of increasing deficits and public concern about the national debt, this bill does not ask for new money. Rather it asks for the monies currently allocated to be spent more wisely by identifying best practices and eliminating possible duplication. Given that addressing prostate cancer effectively is a priority of the Department of Veterans Affairs and Department of Health and Human Services, it is possible that this bill may attract attention and support.

Now that this bill has been introduced, the next step is to get momentum behind it by obtaining cosponsors from both sides of the aisle, and get it on the legislative calendar for a hearing by the Senate HELP (Health, Education, Labor and Pensions) Committee and the House Committee on Oversight and Government Reform. If each committee passes the bill, it then goes to the floor for a vote. However, with limited time before the November elections, it is unclear whether the current Congress will get to the point of actually voting on this bill before or after the election. We fully expect that the momentum we have achieved with the introduction of the bill during Prostate Cancer Awareness Month and the support of the NFL will continue into January 2011 when the 112th Congress convenes. We will continue to work hard for its passage.

There are several lessons to be learned from these efforts. Legislation has a long lead time, and requires the ongoing (perhaps years) and well coordinated efforts of experienced and articulate urologists, seasoned professional staff, and supporters like the general public, the NFL and patient advocates to be successful. Other areas, such as negotiating to change private insurer reimbursement policies, often have a shorter lead time but still require a comparable, carefully structured, broad effort.

The next major step to implement the Affordable Care Act, previously known as the Patient Protection and Affordable Care Act or the Healthcare Reform Act of 2010, is the writing of regulations by federal agencies such as Centers for Medicare and Medicaid Services which will further articulate such general concepts like Accountable Care Organizations included in the statute. To ensure that the unique needs and perspectives of urology are considered, we will need to call on all of our resources to make sure that the federal government fully understands the implications of the decisions they make in the regulation process. This not only means submitting the comment letters the AUA staff carefully prepares in collaboration with our volunteer physicians, but also arranging targeted in-person visits by urologists and AUA staff with key federal officials at appropriate times.

Perhaps most importantly in this process is the element of teamwork. Because of the massive and complex environment produced by national health care reform, a well orchestrated effort by volunteer urologists, AUA staff, and powerful supporters such as the NFL and patient advocacy groups identified through the AUA Foundation, is essential to all of the activities in which we must be involved. A maximally effective team is one that draws on the expertise of all of its members. I urge you to consider becoming more engaged in AUA advocacy activities to advance and protect the field of urology. ◆

FROM THE *Office of Research*

Increasing the Talent Pool in Urological Research

Dr. Johannes Vieweg
Chair, Research Council
Gainesville, Florida

AUA Foundation Research Scholars Program

Since 1987 the Research Scholars Program of the AUA Foundation (AUAF) has provided funding to approximately 500 young men and women interested in pursuing careers in urological research. These scholarships have allowed young scientists to begin research careers even while many urology departments across the country face serious budget constraints. A major objective of this program is to expand the number of physician-scientists who devote the majority of their professional efforts to seeking new knowledge about urological health and disease through the advancement of research.

Physician-scientists have a critical role in bridging the gap between basic science researchers and practicing health care professionals, thus advancing scientific knowledge and biomedical innovation. Nevertheless, socioeconomic pressures, such as budget constraints, the need for generating clinical revenues and the lack of adequate research mentorship, create the risk of physician-scientists becoming an endangered species. The field of urology appears to be especially affected by a shortage of physician-scientists involved in fundable, patient oriented research.[1]

The National Institutes of Health (NIH) awarded only $59.3M to the field of urology in 2009, resulting in a poor ranking of 14 among 19 clinical science departments.[2] NIH grant submission rates by urological scientists are low, and at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) the number of R01 applications related to urology has been modest, with only approximately 50 applications submitted annually during the last 5 years.[3]

Interestingly, NIDDK data suggest that in urology the number of R01 awards mirrored the number of applications, and R01 success rates were similar to those in other NIDDK funded disciplines such as nephrology or hematology. Therefore, for the urology portfolio of R01s to show a meaningful increase, the number of new investigator applications must increase significantly. In view of these data there is an urgent need to increase the availability of talented researchers and establish a robust pipeline of young scientists who can successfully compete for federal funding.

"…for the urology portfolio of R01s to show a meaningful increase, the number of new investigator applications must increase significantly."

The AUAF Research Scholars Program has refocused its efforts as the premier urology research support program in the United States to address this unmet need by encouraging interest in urological research careers and ensuring that new talent will enter the field of urological research. The value of this program cannot be overstated and it merits the continued support of the entire AUA membership.

Research Support at All Career Stages

A recent evaluation of the AUAF Research Scholars Program revealed that since its inception, funded scholars have gone on to secure more than $373.4M in federal ($320.0M) and private ($53.4M) research dollars to date (cumulative data). However, further analysis indicated that this success is attributable to only 20% of the 493 scholars, and that only this subset of scientists has moved on and attained research independence. So how can we improve the selection process for awarding AUAF Research Scholarships so that future designees will be successful in competing for NIH funding and will make valuable contributions to the field of urological research?

We must address multiple issues to improve this process, including defining more rigorous selection criteria, assuring appropriate mentorship, promoting better comprehension of the grant process and enhancing communications with the NIH. Fortunately many educational programs and workshops provided by the AUAF and other organizations have already begun to address some of these concerns. Other

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From the Office of Research

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mechanisms to increase the availability of scholars with NIH funding potential are to increase the talent pool of young investigators entering urology and support those with research interests during residency.

At present virtually all of the AUAF research support portfolio is awarded to M.D. or M.D./Ph.D. investigators after their residency training, or to Ph.D.s who have already spent a significant amount of time in the research arena. Broadening funding to all career stages would increase the opportunities for attracting top students and residents to urology research, individuals who would otherwise go into different specialties or be unable to pursue research interests during training. In reality 80% to 90% of urology residents do not choose to pursue research careers, not because of a lack of conviction, but because of a lack of appropriate training, encouragement and mentorship as medical students or during urology residency.

Conducting research during residency is a challenge since the Centers for Medicare and Medicaid Services (CMS) restrict time spent on patient oriented research. However, approximately 35% of all U.S. urology residency programs offer a protected research year, although this research year must be performed as a time-out outside the scope of the CMS supported residency program.[4] New research award mechanisms for residents may encourage other urology programs to request these time-outs and grant dedicated research time for select house staff with research interests. At the student level additional educational conferences and workshops would encourage more students to consider a urology career, which could be the catalyst for increased interest in urology research.

In the coming months the Office of Research will be working to enhance our capacity to attract the best and brightest young scientists to pursue careers in urology, thus shaping the future of our specialty through their research contributions. We propose to refine the scholar selection criteria and broaden funding to include earlier career stages. Mentorship guidelines will continue to be improved, as will communications with the NIH and other public and private granting agencies. As this process goes forward your feedback and continued support will have a critical role in ensuring our progress. ◆

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FROM YOUR *Foundation*

Sandra Vassos, MPA
Executive Director,
AUA Foundation
Linthicum, Maryland

New Basic Science Symposium

The AUA Foundation continues to work on renewing and increasing the emphasis on research at the AUA annual meeting. We are proud that the last few years have seen a resurgence of interest in the annual Research Forum and Grantscraft Course, as well as an increase in the number of poster and podium presentations, and sessions led by past scholars and awardees.

The AUA Foundation Office of Research and the Society for Basic Urologic Research leadership have joined with program officers from the National Institute of Diabetes and Digestive and Kidney Diseases to develop an annual Basic Science Symposium to be held the Friday preceding the AUA annual meeting beginning in 2011 in Washington, D. C. This annual symposium will address an overarching area in research that has the transformational potential to impact the practice of urology across the spectrum of urological diseases. Topics will be selected annually based on the expertise available around the host city.

The 2011 Basic Science Symposium will be held on Friday, May 13 (1:00 to 6:00 p.m.) on "Stem Cells in Urologic Development and Disease." A program agenda will be available in early 2011, so you can add this important program to your AUA annual meeting itinerary. For more information contact the Office of Research at research@auafoundation.org or telephone 410-689-3929.

UrologyHealth.org to be Re-Launched

You asked and we listened. So many AUA members have told us how much they appreciate the urologist written and vetted patient information available on our website, www.UrologyHealth.org. However, many are frustrated (as are their patients) with navigating the current online setup. An exciting new look is on the horizon for the AUA Foundation website and we are looking forward to showing it off!

The site will be undergoing a major renovation in early 2011 to increase functionality, provide a hub for research information, grants and updates on funded projects, create a user-friendly experience for patients and physicians, and launch a new portal to generate support for our mission based programs. Look for more information in upcoming issues of *AUANews*. The Foundation is working hard to improve resources for you and your patients. ◆

GRADUATE MEDICAL *Education News*

Resident Education and the AUA Core Curriculum

Dr. Beau N. Dusseault
Residents Committee
Southeastern Section
Representative
Lexington, Kentucky

The American Urological Association (AUA) mission is, "To promote the highest standards of urological clinical care through education, research and in the formulation of health care policy." There are many components to education in urology, including but not limited to basic science research, clinical knowledge and clinical skills.

Not long ago the standardization of urological education for medical students was deemed necessary and, thus, the National Medical Student Core Curriculum was created. This curriculum set the standard for what the urological community, represented by residency directors as well as medical students, believed was vitally important for all physicians to have been taught during their medical school education. This project was well received and a similar effort was undertaken for formal urology training. The AUA Core Curriculum project began in 2006, and was finalized and revealed to the international urological community in San Francisco at the 2010 AUA meeting.

The Core Curriculum is an online tool for education in the areas that constitute the standard knowledge foundation that residents must acquire during training. It is divided into 50 sections that encompass what is considered the whole of urology. This tool not only lists what is deemed important, but it also references every point with a salient article, book chapter or other appropriate reference. In most instances the user of the Core Curriculum can retrieve the original reference with a simple click of the mouse, and how to find information related to the objectives and contents is clearly explained. The Core Curriculum also includes an exhaustive list of references that can be used for further research or clinical publications.

Dr. Stephen E. Strup, a contributing author for the section on Upper Urinary Tract Obstruction and Ureteropelvic Junction Obstruction, stated that "The AUA Core Curriculum was designed to be a comprehensive, yet fluid, source of urological knowledge. It represents the core knowledge in Urology that should be mastered…[The greatest strength is that] the core curriculum can be easily adapted and modified by changing that particular section and updating the links rather than having to wait for a new edition to be printed."

Residency education is a multifaceted charge given to various training

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Graduate Medical Education News

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programs across the nation. This task includes instilling critical thinking skills, laying a large foundation of knowledge, developing surgical technique and knowledge of many procedural interventions, and conveying the fundamentals of research. This massive undertaking must be accomplished while creating a physician who looks to the interest of the patient, and provides efficient, cost-effective and ethical medical care to various populations. The graduating urology resident must be well trained, and able to successfully complete the written and oral certification examinations given by the American Board of Urology. Dr. Strup believes that "by mastering the core knowledge reflected in the curriculum, the urology trainee and practitioner should be well prepared for in-service and board testing that is designed to test this 'core knowledge'."

While education is a cornerstone of the AUA, urology resident education is a uniquely important part of its role in serving the public at large. The training of future urologists sets the stage for the development and continued progress the AUA has seen since its beginnings in 1902. To maintain the highest standards and expect competent, well trained, thoughtful physicians to enter into practice it is vital to be able to clearly identify what is expected of their education. The development of the Core Curriculum has showcased this privilege and responsibility of the AUA in promoting this more fluid and comprehensive educational process. ◆

MANAGING *Your Practice*

Stocks and Bonds—What Mixture is Right for You?

Joel M. Blau, CFP® and
Ronald J. Paprocki, JD, CFP®, CHBC
Chicago, Illinois

Investors have come to realize that choosing the proper basic stock-bond mix is an integral first step in portfolio design. Although the decision may appear simple, it can have a profound impact on future wealth. Portfolio theory explains the value of making a deliberate, strategic decision about the proportion of stocks vs bonds to hold in a portfolio. The premise is that when constructing portfolios all investors face the 2 important issues of 1) how much risk to take, and 2) how to balance a portfolio of risky assets (equities/stocks) and less risky assets (fixed income/ bonds) to achieve that desired level of risk.

Investors willing to take stock risk should begin with a diversified market portfolio. In its simplest form each investor can then dial down total risk in the portfolio by adding fixed income to the mix. The greater the bond allocation relative to stocks, the less risky the portfolio and the lower the total expected return. The greater the stock allocation relative to bonds, the higher the expected return and risk of the portfolio. Investors who want to take even more risk than the market can increase exposure by borrowing on margin and/or adding more aggressive equity asset groups that offer higher expected returns for the higher risk being taken.

So how does one decide how much to allocate between stocks and bonds? A common method is to evaluate model portfolios along the risk-return spectrum. A riskier portfolio holds 100% stocks and the least volatile portfolio holds 100% bonds. Between these extremes lie standard stock-bond allocations such as 80%-20%, 60%-40%, 40%-60% and 20%-80%. You can then compare the average annualized return and volatility (standard deviation) of each model portfolio for periods such as 1, 3, 5, 10 and 20 years. Volatility is one of several risk measures investors may want to consider. With this in mind the analysis should feature average returns as well as best and worst case returns for the various periods.

While this technique relies on historical performance that may not repeat in the future and does not consider various investment costs, it may help you think about the risk-return tradeoff, and visualize and quantify the range of potential outcomes based on the aggressiveness of the strategy.

After establishing the basic stock-bond mix, investors can turn their attention to the stock allocation, where the best opportunities to refine the risk-return tradeoff are found. Investors comfortable with higher doses of equity risk can overweight or "tilt" their allocation toward riskier asset classes that have a history of offering average returns above the market. As an example, researchers have found that small cap stocks have had higher average returns than large cap stocks. By holding a larger portion of small cap stocks in a portfolio, an investor increases the potential to earn higher returns for the additional risk taken.

The final step in refining the stock component is to diversify globally. By holding an array of equity asset classes across domestic and international markets, investors can reduce the impact of under performance in a single market or region of the world. Although the markets may experience varying levels of return correlation, this diversification can further reduce volatility in a portfolio, which may translate into higher compounded returns over time.

Mr. Blau and Mr. Paprocki welcome readers' questions. They can be reached at 800-883-8555, or at blau@mediqus.com or paprocki@mediqus.com. ◆

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HISTORY *Corner*

Cello Scrotum Cured

Dr. Lawrence M. Wyner*
Huntington, West Virginia

Medical ailments of musicians have been described for the last 3 centuries, beginning with the Bernardino Ramazzini, who is now acclaimed as the father of occupational medicine (fig. 1). Ramazzini was a distinguished professor at the University of Padua, Italy, whose early career focused on the diagnosis and treatment of malaria. One day he hired some men to clean out the cesspit at his home, and subsequently witnessed one of them being overcome by fumes.

Fig. 1. Bernardino Ramazzini, 1633–1714

Keen observer that he was, Ramazzini realized that this case of "bad air" was work related, and served as the springboard for his 1713 magnum opus, De Morbis Artificum Diatriba (Diseases of Workers), a monumental effort in which he studied 52 occupations or groups of people, describing the medical ailments peculiar to their role in society. With every patient encounter Ramazzini exhorted his reader to inquire "What do you do for a living?" as a part of taking a medical history. In addition to its watershed effect on the practice of medicine and public health, it also provides us with a window into life in the century preceding the Industrial Revolution.

Buried among the descriptions of ailments of miners, farmers, scribes and manufacturers is a chapter devoted to the trials and tribulations of musicians. Calling on his own observations as well as those of his colleagues, Ramazzini gives examples of hernias and gastrointestinal hemorrhages occurring in singers and players of wind instruments, probably as a result of prolonged and exaggerated diaphragmatic excursion, or perhaps more simply by bad technique. For example, he says,

> In his Observations, Diemerbroeck gives a pitiable case of a flutist who, when certain others were playing the trumpet, was so ambitious to play louder than they that he ruptured a large vein in the lung, had a violent hemorrhage, and died within two hours.[1]

Yet despite these ailments, the musicians of Ramazzini's day had not yet acquired the virtuosic aspirations of their successors. Music performance in the 17th century was rooted in the nobility and the Church, and the idea of an individual superstar performer was still years in the future. However, by the mid 1800s the possibility of a young man or woman becoming a renowned soloist was now a probability, at least for anyone who was willing to work hard enough at it. Musicians of this era were bent on pushing the limits of human ability, and music that had once been heavenly now became fiendishly difficult to play, leading to further challenges.

This set the stage, so to speak, for George Vivian Poore, an internist of the Victorian era in London (fig. 2). Poore was an eminent physician who had many professional interests, not unlike Prof Henry Higgins in *My Fair Lady*. He was especially interested in studying the neuromuscular injuries that may occur following repetitive motions, and the hordes of young people trying to master the music of Beethoven, Chopin and Brahms provided a ready supply of patients.

Fig. 2. George Vivian Poore, 1843–1904

In 1887 the *British Medical Journal* (BMJ) became the first scientific periodical to publish a study of a musician's ailment, a study by Poore of muscle cramping in piano players which he called "pianist's breakdown."[2] He wrote,

> Piano-playing, if not prohibited altogether, must only be practiced to a degree short of that which causes pain or annoyance. It is often difficult to restrain the ardour of these patients in the matter of playing. Directly they feel in a small degree better, they fly to the piano; and I have known the progress of more than one case very seriously retarded by the undoing, as it were, of the good effect of rest by an hour's injudicious and prohibited 'practicing.'

These endeavors spawned the field of performance medicine, which has since grown to encompass multiple textbooks and journals dedicated to this topic. In addition to the hernias and hemorrhages that Ramazzini treated, care of the modern musician is comprehensive, and may range from treatment of musculoskeletal problems and hearing loss to stage fright and stress related illnesses. Recent literature suggests that the majority of modern symphony orchestra players have experienced 1 or more of these conditions during the course of their careers.[3]

For example, in 1935 trumpeter Louis Armstrong hurt his lips from too much playing and had to lay down his horn for a year. His condition was diagnosed as a rupture of the orbicularis oris muscle and was referred to as Satchmo's syndrome. Other musician ailments soon followed, affecting string, woodwind, brass and percussion players alike, ascribed to the vagaries of the various musical instruments. However, perhaps the envelope was pushed a bit too far by Curtis, who reported cystic mastitis in 3 adolescent girls learning to play classical guitar, presumably from pressure on the breast from the edge of the sound box, a condition he called "guitar nipple."[4]

Fig. 3. Dr. Elaine Murphy and Mr. John Murphy, c. 1974

Enter Dr. Elaine Murphy, at the time a young registrar in psychiatry, and her husband John, a businessman, both avid readers of the *BMJ* (fig. 3). Both doubted the authenticity of "guitar nipple," and so they decided to perform a public service by sending in their own spoof to the *BMJ*. They wrote about a condition called cello scrotum, claiming to have seen a cellist patient with chronic groin irritation due to long hours of scrotal contact with the vibrating body of the instrument.[5] Dr. Murphy later explained, "We cooked all this up after reading this letter about guitar nipple. John used to read the *BMJ* too and after dinner one night, I guess after a glass or two of wine, we composed this letter."[6] To their surprise the *BMJ* published the letter, and wire services reported the phenomenon worldwide. Musicians unions in the United Kingdom and Soviet Union lobbied to have the condition declared an industrial disease.[7] Reportedly an entire Russian symphony orchestra cello section was affected.[8]

Cello scrotum would be referenced at least a dozen times in the peer reviewed medical literature during the next 35 years, although skeptics questioned how the body of the cello could contact the scrotum if the instrument were played properly.[9-13] These naysayers pointed out that the cellist would have to be doing something fairly extreme for this to occur. With apologies to Sir Percivall Pott, one wag suggested that the affected cellists were

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History Corner

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moonlighting as chimney sweeps[13] while another implicated the chair rather than the cello itself.[14]

In any case the Murphys decided to come clean after witnessing yet another review article referencing their creation in 2008,[15] and sent a letter of retraction to the *BMJ* later that year, admitting that cello scrotum was indeed a high-brow hoax.[16] By this time they had advanced their careers considerably.

John Murphy had become a successful entrepreneur as chairman of St. Peter's Brewery in Suffolk, where his products have earned international renown. Dr. Elaine Murphy had been elevated in 2004 to the House of Lords, where she sits on the panel overseeing the National Health Service, and advises the Crown on matters pertaining to geriatric mental health and Alzheimer's disease. Although her cello scrotum days are now over, her work still undergoes "peer" review.

In addition to being one of the more ridiculous episodes in the history of urology (the Murphys' revelation garnered the number 2 spot on *Time* magazine's "Top Ten Oddball News Stories of 2009"), cello scrotum may have helped to coin the word "scrotum-gate," which was the moniker bestowed on the affair by *BMJ* staffers, although in reality the term had been used 2 years before the Murphy revelation. It appears that the literary community was in an uproar over the use of the word scrotum on the opening page of a children's book (even an award winning one) and applied scrotum-gate first in reference to this controversy.[17]

In the final analysis the ultimate legacy of cello scrotum is the admission by *BMJ* editors that journalistic fraud is indeed taken seriously but that in this particular case no one was harmed by the lighthearted deception and everyone had a good laugh. They awarded Baroness Murphy the Hoax of the Century award at their annual Christmas party, and vowed that the *BMJ* would continue its pioneering efforts on behalf of musicians' health.◆

**Financial interest and/or other relationship with Novartis and Pfizer.*

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CALENDAR *of Events*

November 2010

November 5–6
Robotic Surgery Beyond the Prostate

Winston-Salem, North Carolina
Wake Forest University Baptist Medical Center
krchrdsn@wfubmc.edu
www.wfubmc.edu/school/urology/CME-credits.htm

November 6–7
AUA Mentored Renal Laparoscopy: A Skills and Knowledge-Based Approach

Houston, Texas
Houston Marriott Medical Center
800-908-9414
registration@auanet.org
www.auanet.org/content/courses/MLAP101/

November 11–14
Sexual Medicine Society of North America Annual Meeting

Miami Beach, Florida
Loews Miami Beach Hotel
847-264-5949
info@smsna.org
www.smsna.org

November 11–14
SBUR Fall Symposium

Atlanta, Georgia
Grand Hyatt Atlanta
847-517-7225
nathan@wjweiser.com
www.sbur.org

November 12–13
AUA Tissue Ablative Course: Kidney and Prostate

Miami, Florida
University of Miami
Miller School of Medicine
800-908-9414
registration@auanet.org
www.auanet.org/content/courses/TAC101/

November 20
AUA Oncology Knowledge Assessment Test

Various sites throughout the U.S. and Canada
410-689-3783
exams@auanet.org

November 20
AUA In-Service Examination

Various sites throughout the U.S. and Canada
410-689-3783
exams@auanet.org

December 2010

December 3–4
LESS in Urology: A Comprehensive Course on Laparoendoscopic Single Site Surgery

Dallas, Texas
University of Texas Southwestern Medical Center
800-908-9414
registration@auanet.org
www.auanet.org/content/courses/LESSF210

December 10–11
AUA Urolithiasis Update

Washington, D. C.
Park Hyatt Washington
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www.auanet.org/content/courses/URU101

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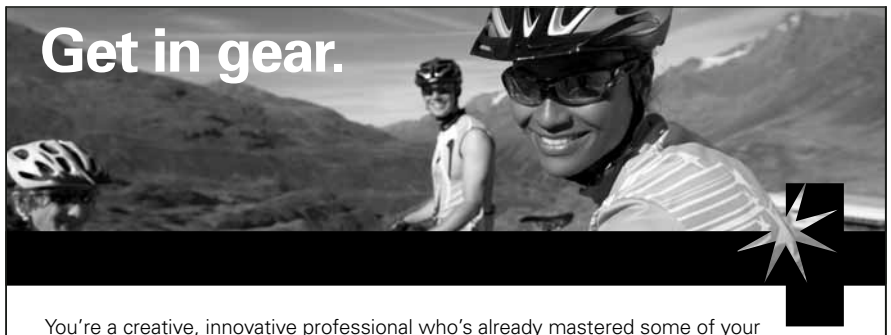

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