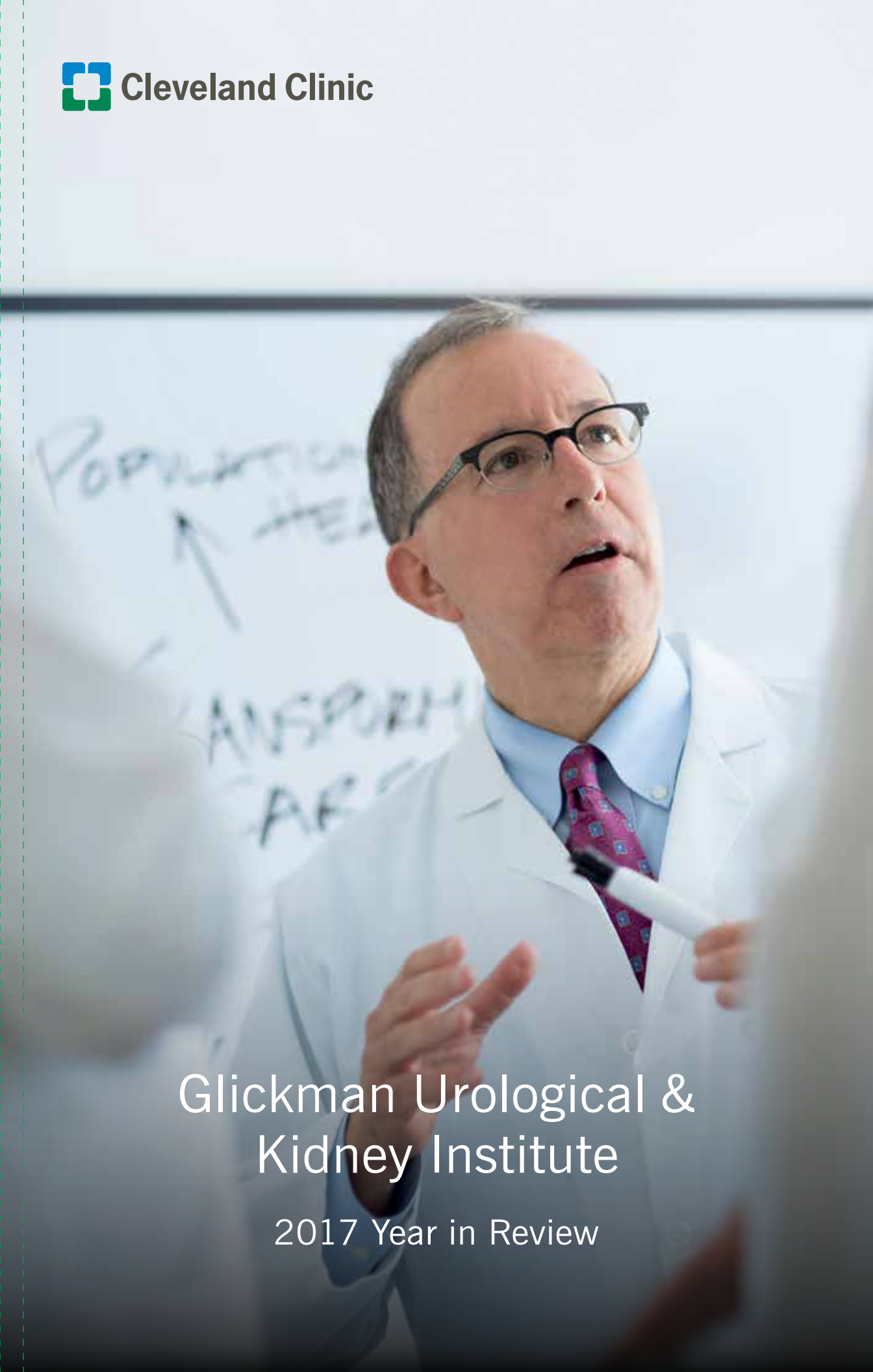


A man in a white lab coat and glasses, holding a white marker, pointing at a whiteboard with handwritten text. The whiteboard has the words "Population", "HEALTH", "TRANSPORT", and "AREA" written on it, with an arrow pointing from "HEALTH" to "Population".

Glickman Urological & Kidney Institute

2017 Year in Review

Contents

- 3 Glickman Urological & Kidney Institute at a Glance
- 7 Message from the Chairman
- 9 Revitalized Research Program in Renal Disease
- 11 New Men's Health Center Correlates Urologic Symptoms and Systemic Health Conditions
- 12 Transformational Initiatives in Bladder Cancer Care
- 14 Advanced Practice Providers' Expanding Roles Boost Efficiency for Physicians and Patients
- 17 Precision Medicine Applied to Prostate Cancer
- 19 Minority Men's Health Center Reaches More Than 35,000 Men
- 20 2017 Achievements

ON THE COVER

Edmund S. Sabanegh Jr., MD, Chairman, Department of Urology, is leading the department's efforts to transform delivery of care through initiatives such as enhanced recovery protocols and expanding the roles of advanced practice providers.

Glickman Urological & Kidney Institute

AT A GLANCE

The Glickman Urological & Kidney Institute’s activities encompass a unique combination of high-volume and challenging clinical cases, extensive basic and translational scientific efforts, and innovative laboratory research conducted in an environment that nurtures the future leaders of its specialties.



INSTITUTE VITAL STATISTICS (2016)	
59	Urologists
22	Nephrologists
29	Advanced Practice Providers
30	Urology Residents
20	Urology Fellows
9	Nephrology Fellows
154	Other Caregivers



U.S. News & World Report ranked Cleveland Clinic’s urology program No. 1 and our nephrology program No. 2 in the nation in 2017. Urology has been ranked No. 1 or 2 for 18 years in a row, while nephrology has achieved No. 1 or 2 rankings for the past eight years.

U.S. NEWS & WORLD REPORT RANKINGS		
YEAR	NEPHROLOGY	UROLOGY
2017	2	1
2016	2	2
2015	2	2
2014	2	1
2013	2	2
2012	1	1

BY THE NUMBERS

(2016)

96,474
OUTPATIENT VISITS

8,991
CASES

19,695
DIALYSIS TREATMENTS

2,060
ADMISSIONS

9,291
PATIENT DAYS

4.51
MEAN LENGTH OF STAY (DAYS)

Jihad Kaouk, MD, FACS



SURGICAL CASES (2016)	
438	Benign Prostatic Hypertrophy
939	Endourology and Stone Disease
934	Female Urology
166	Male Fertility
285	Pediatric Urology
351	Genitourinary Reconstruction
252	Renal and Pancreas Transplant
2,780	Urologic Oncology

EDUCATION

Hernan Rincon-Choles, MD



Glickman Urological & Kidney Institute’s top-ranked residency and fellowship programs provide challenging clinical and research experiences. We offer a urology residency program with a dedicated research year, and fellowships in nephrology, transplant and urology (with nine subspecialty tracks).

CENTERS

DEPARTMENT OF NEPHROLOGY

- › Blood Pressure Disorders
- › Chronic Kidney Disease
- › Dialysis
- › Kidney Stones
- › Renal and Pancreas Transplant
- › Renal Diseases

DEPARTMENT OF UROLOGY

- › Endourology and Stone Disease
- › Female Urology
- › Genitourinary Reconstruction
- › Renal and Pancreas Transplant
- › Male Fertility
- › Men’s Health
- › Minority Men’s Health

- › Pediatric Urology
- › Robotic and Image-Guided Surgery
- › Urologic Oncology

PATIENT ORIGINS (2016)

- › 88 Ohio counties
- › 50 U.S. states
- › 70 countries





Cleveland Clinic

Eric A. Kela, M.D.

MESSAGE FROM THE CHAIRMAN

Dear Colleagues,

Cleveland Clinic’s Glickman Urological & Kidney Institute’s Department of Urology has achieved the No. 1 ranking in this year’s *U.S. News & World Report* survey of Best Hospitals. This is the third time since 2012 that the Department of Urology has received the honor of being ranked No. 1. Our Department of Nephrology ranked extremely well again this year, too, maintaining its No. 2 position for the fifth year in a row.

What’s more, Doximity Residency Navigator — *U.S. News & World Report*’s ranking system for residency programs — has recognized our Urology Residency Program as top-ranked. Our fellowship in Robotic and Laparoscopic Surgery received a No. 1 ranking from the Endourological Society.

Rankings like these are significant in many regards. Most importantly, they reflect our culture of compassion and quality, which is at the root of our growing institute. Everything we do — in patient care, research and education — is because patients come first.

This annual *Year in Review* highlights some of the exciting initiatives that have evolved in the past year.

We attracted four talented clinician-researchers. John Sedor, MD; John O’Toole, MD; and Leslie Bruggeman, PhD, joined the Department of Nephrology, and Byron Lee, MD, PhD, joined the Department of Urology.

Dr. Sedor and Emilio Poggio, MD, were awarded a \$1.5 million grant from the National Institutes of Health to lead a research consortium studying disparities in renal transplant outcomes. Dr. Lee was awarded a Sidney Kimmel Scholar Award (one

of only 15 awarded nationally) as well as a Bladder Cancer Advocacy Network Young Investigator Award.

We opened the Center for Men’s Health, the first such multispecialty center in Northeast Ohio.

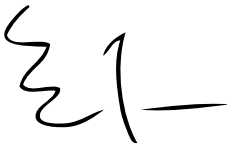
In the area of bladder cancer, we have transformed our approach to cystectomy care, decreasing lengths of stay, costs and readmissions, and improving outcomes. We have significantly expanded the roles of our cadre of advanced practice providers.

In prostate cancer, we are at the forefront of precision medicine, and remain devoted to reducing the disease’s impact by helping to sort out which men need aggressive care and those for whom active surveillance is a perfectly reasonable approach.

In the area of health disparities, our Center for Minority Men’s Health has had a tremendous effect on our community. The center’s origins lie in a father’s sage advice and encouragement for his son (who happens to be on our staff).

Thank you for reading our *Year in Review*. As always, I welcome your feedback and collaboration in patient care, research and education in the year ahead.

Sincerely,



Eric A. Klein, MD

Chairman, Glickman Urological & Kidney Institute
Professor, Cleveland Clinic Lerner College of Medicine



2017 HIGHLIGHT

Revitalized Research Program in Renal Disease

The addition of distinguished researchers John Sedor, MD; Leslie Bruggeman, PhD; and John O'Toole, MD, to the Glickman Urological & Kidney Institute research team has brought renewed vitality and \$3.5 million in National Institutes of Health grants for projects aimed at improving the understanding of chronic renal disease.

"We are aiming to answer the big questions: why kidney disease disproportionately affects minorities, and what drives it in patients with diabetes and hypertension," says Dr. Sedor. "Answers are needed to round out the big picture and help us develop more effective treatments for patients with kidney disease."

More than 40 million U.S. adults suffer from chronic kidney disease (CKD). Not all progress to end-stage renal disease (ESRD), but 35 percent of those who do are African-American.

"It's a major cause of health inequality," Dr. Sedor continues. "It's also an enormous burden on our healthcare system, since the federal government pays for dialysis and kidney transplantation for more than 600,000 patients with ESRD every year. The cost eats up 7 percent of the Medicare budget, yet involves less than 1 percent of Medicare beneficiaries, and outcomes and quality of life remain poor."

Several years ago, *APOL1* was identified as the gene associated with increased frequency of chronic and progressive kidney disease in African-Americans. About 15 percent of this population carries the gene.

Genetic models used in study of *APOL1*

Drs. Sedor, Bruggeman and O'Toole are taking a multipronged approach to studying *APOL1* using several genetic model systems and also investigating the gene's role in HIV-associated kidney disease. They are working closely with colleagues Emilio Poggio, MD; Ziad Zaky, MD; and Jesse Schold, PhD.

"There is some information suggesting kidney recipients from donors with this gene may be at increased risk of developing kidney disease," says Dr. Poggio, Director, Renal Function Lab, Medical Director, Kidney and Pancreas Transplantation.

NIDDK precision medicine project involvement

Drs. Sedor and O'Toole's arrival and collaboration with Dr. Poggio put Cleveland Clinic in the spotlight as one of a select number of U.S. institutions involved in the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Kidney Precision Medicine Project (KPMP).

KPMP aims to evaluate human kidney biopsies from participants with acute kidney injury or CKD, create a kidney tissue atlas, define disease subgroups, and identify critical cells, pathways and targets for novel therapies.

"We are borrowing approaches that were successful in cancer and applying them to kidney disease," Dr. Poggio continues. "Significant advances in cancer care were made possible through the availability of tissue for study. Similarly, we will be conducting kidney biopsies to obtain tissues that can be studied with state-of-the-art methods to better understand the processes that drive kidney diseases in patients with diabetes and hypertension."

"We don't yet understand which patients with CKD are going to progress to ESRD and which ones are not. Our goal is to identify whose disease will worsen early on," says Dr. Sedor. "Our ultimate goal is to offer the best treatment for an individual patient, delivered at the right time with the right drugs."

"Cleveland Clinic offers a large patient volume, high-quality research facilities and outstanding scientists available for collaboration, making it an ideal location for this work."



2017 HIGHLIGHT

New Men's Health Center Correlates Urologic Symptoms and Systemic Health Conditions

Central to Glickman Urological & Kidney Institute's new Center for Men's Health is the recognition that systemic health conditions can have a major impact on urologic conditions and their symptoms, and vice versa. The new center, opened in August, is directed by urologist Daniel Shoskes, MD.

Benign prostatic hypertrophy; lower urinary tract symptoms (LUTS); erectile dysfunction (ED); adult-onset hypogonadism and pelvic pain, including chronic prostatitis/chronic pelvic pain syndrome (CPPS); and chronic orchialgia all can be affected by chronic disease, Dr. Shoskes notes. "Symptoms of LUTS, ED and CPPS are often exacerbated by cardiovascular disease and its treatment, and by low testosterone and diabetes. Furthermore, ED or LUTS can be the first manifestation of cardiovascular disease or poor diabetic control.

"Our goal is to improve the care of men with urologic conditions by bringing together urologists, cardiologists, endocrinologists and other specialists," Dr. Shoskes says. "Patients can see multiple specialists at the same visit, which improves access for men who may otherwise avoid or not have access to care. We have found that providing a 'one-stop shop' also improves compliance."

Other experts participating in the center treat exacerbating comorbidities and include a psychologist/sex therapist, sleep medicine specialist (sleep apnea is associated with LUTS and ED) and pelvic floor physical therapists.

New men's health phenotype deployed

At the heart of the center's approach is a new men's health phenotype. This phenotype, with the acronym ACTIONS, classifies men according to presence and severity of seven conditions:

- › Anxiety/alarm falsification
- › Cardiovascular disease

- › Low testosterone
- › Insulin deficiency/resistance (diabetes)
- › Obesity
- › Neurologic disease
- › Sleep apnea

"Our team has shown a correlation between total burden of systemic disease and severity of urologic symptoms," Dr. Shoskes points out.

"We hypothesize that the greater the systemic comorbidity burden, the less likely specific urologic interventions (medical or surgical) are likely to succeed."

Improved access helps men get needed care

"It is no secret that men could be better at tending to their health and seeking the medical care they need, and we continue to look for ways to improve access for our male patients," Dr. Shoskes notes. Expanding clinic hours into the evening and weekend is one approach. The center also sends staff to regional locations, including Cleveland Clinic's Center for Lesbian, Gay, Bisexual and Transgender (LGBT) Care at the Lakewood (Ohio) Family Health Center; works with oncology colleagues to ensure rapid access to penile injection teaching for cancer patients with ED; and provides testosterone pellet implants (long-acting testosterone pellets inserted into the hip or other fatty area) when endocrinologists do not perform the procedure.

Therapeutic options for complex problems

The center also offers new technology to enhance therapeutic options for these men. For instance, new benign prostatic hyperplasia technologies are offered, along with spermatic cord denervation for chronic orchialgia. More recently, low-intensity shockwave therapy has been made available for men with ED or CPPS, especially those experiencing pelvic floor spasm.

2017 HIGHLIGHT

Transformational Initiatives in Bladder Cancer Care

Historically, radical cystectomy patients faced long hospital stays and complications that could lead to readmissions. “Cystectomy patients are the sickest patients we see,” says Glickman Urological & Kidney Institute urologist Georges-Pascal Haber, MD, PhD.

With this in mind, the perioperative management of patients undergoing radical cystectomy for cancer has undergone a radical change at Cleveland Clinic.

Dr. Haber and colleagues have overhauled their approach to cystectomy care, from presurgical patient education and preparation to recovery and follow-up. The result? Length of stay dropped by 29 percent, costs decreased by 14 percent, postsurgery emergency room visits dropped 40 percent and readmissions went down by 39 percent.

Enhanced recovery protocols impact outcomes

Known as enhanced recovery after procedures, these changes reflect a multidisciplinary, data-driven approach. The program brings together anesthesiologists, surgeons, clinical and administrative fellows, residents, nurses, and administrators. They have created a patient education guide, renounced bowel prep and fasting before surgery, reduced the amount of opioids and fluids given to patients (lowering the risk for developing an ileus), and done away with nasogastric tubes, encouraging patients to ambulate and eat as soon as possible after surgery to expedite the return of bowel function.

“We did a root cause analysis on almost every patient who was readmitted or had complications,” Dr. Haber says. “We audited all the cystectomies we’ve performed and looked at opportunities for improvement.”

Staff members are also studying the biology of bladder cancer and testing new drugs, under the purview of urologist Byron Lee, MD, PhD.

Bladder cancer genomics

Dr. Lee recently received a Sidney Kimmel Scholar Award from the Sidney Kimmel Foundation for Cancer Research and a Young Investigator Award from the Bladder Cancer Advocacy Network. His research involves how chromatin-modifier gene mutations contribute to bladder cancer development, progression and response to therapy.

“These mutations occur in about 70 percent of bladder cancers,” Dr. Lee says, “so we think it’s incredibly important to understand what they do.” Dr. Lee uses CRISPR (clustered regularly interspaced short palindromic repeats) technology to mutate specific chromatin modifiers, then analyzes the effect on the cell’s behavior. He has also bred a strain of mice with chromatin modifiers mutated in their bladder tissue.

The team participates in clinical trials of new therapies, including the latest immunotherapies. Cleveland Clinic investigators were involved in both the IMvigor 210 trial, which found that the checkpoint inhibitor atezolizumab is promising for locally advanced or metastatic urothelial cancer, and KEYNOTE 052, which found a significant response rate when the checkpoint inhibitor pembrolizumab was used as first-line therapy in cisplatin-ineligible patients with metastatic bladder cancer.

Meanwhile, Dr. Haber and his colleagues have improved how they perform cystectomies. Rather than beginning with a robotic approach and switching to open when necessary, they now perform many cystectomies entirely robotically. This minimizes trauma and speeds recovery.

“We are adding to our already strong foundation,” Dr. Haber says, “through enhanced recovery, through a less invasive surgical approach, by focusing on basic research and by evaluating new drugs.”



2017 HIGHLIGHT

Advanced Practice Providers’ Expanding Roles Boost Efficiency for Physicians and Patients

When Dana Longo, CNP, began her career as a nurse practitioner in 2012 at Cleveland Clinic, she stepped into a role where she supported a busy surgeon specializing in robotic procedures. She worked alongside him in the clinic, seeing patients, managing administrative tasks, making patient phone calls, filing documents and performing other nonclinical duties.

A few years later, Edmund Sabanegh Jr., MD, Chairman, Glickman Urological & Kidney Institute’s Department of Urology, realized that having advanced practice providers (APPs) — nurse practitioners and physician assistants — perform supportive roles was an underutilization of talented personnel and a lost opportunity. Instead, Dr. Sabanegh, also Cleveland Clinic’s Associate Chief of Staff, envisioned them practicing at the top of their licensure.

“It’s been a huge culture shift and transformation,” says Ms. Longo. Today, about 75 percent of the institute’s APPs have some level of independent practice, treating patients for a range of nonsurgical concerns such as incontinence, kidney stones and urinary tract infections (UTIs).

Answering nationwide shortage of urologists

With a nationwide shortage of urologists, the shift to using APPs to the full extent of their licensure has lowered costs and improved efficiency, notes James Ulchaker, MD, Vice Chairman, Department of Urology.

“Patient wait times have been drastically reduced,” he says. “For instance, if a patient has a UTI, they can often get same-day care, accessed through our virtual-visit UTI clinic or an in-person visit with an

APP.” APPs are spread out geographically across various Cleveland Clinic sites to increase access.

“If I need to contact one of the doctors, they’re happy to take the call,” Ms. Longo says. “I explain my management plan, we talk things through, and they agree or make suggestions.”

APPs practice at top of their credentialing

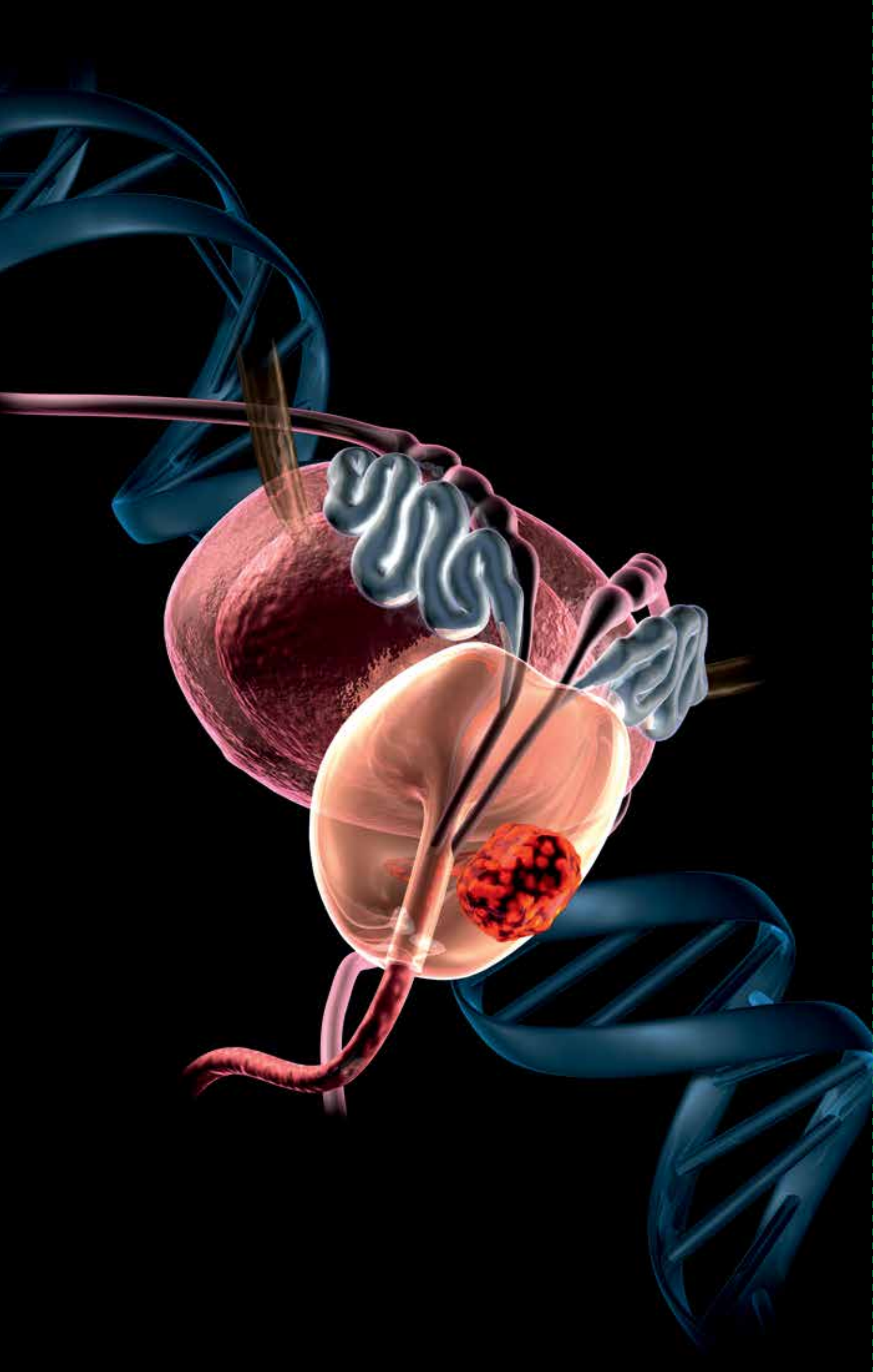
To begin the transition, the Department of Urology analyzed results of an APP survey. It was clear APPs were eager for a change and capable of taking on more responsibility, but many had been working in specialized clinics and needed more training in fundamental areas. So urologist Hadley Wood, MD, created an educational series of readings, assessment and didactic lectures on general urology. The American Urological Association has since accepted the curriculum she developed as the official online education program for the association’s nurse practitioner and physician assistant members.

Referring physicians appreciate their patients being seen more quickly, Ms. Longo adds, especially when a procedure such as a prostate biopsy has been ordered.

Though they focus on nonsurgical care, the APPs do perform some simpler procedures, such as cystoscopy and ureteral stent removal following a kidney stone procedure. They may perform biopsies eventually, Dr. Ulchaker adds.

“We’re working to continue increasing the scope of practice of our APPs,” Dr. Ulchaker continues, “which will help urologists maximize their time in the operative environment. This means surgical wait times are decreased and optimal quality of care is achieved.”





2017 HIGHLIGHT

Precision Medicine Applied to Prostate Cancer

Glickman Urological & Kidney Institute is leading the precision medicine charge against prostate cancer, publishing several milestone studies in 2017.

Exploring tumor resistance to enzalutamide

Researchers discovered that increasing expression of the enzyme 11 β -hydroxysteroid dehydrogenase-2 (11 β -HSD2) can reverse tumor resistance to enzalutamide while sparing healthy tissue after chemical or surgical castration.

Physician-scientist Nima Sharifi, MD, described the effect of enzalutamide on suppressing a metabolic pathway in which 11 β -HSD2 inactivates the tumor-proliferating cortisol hormone into cortisone via increased autocrine motility factor receptor expression and ubiquitin E3-ligase production. His team further showed that restoring 11 β -HSD2 function by restricting AMFR expression restores tumor sensitivity to enzalutamide.

“Our findings reveal a surprising metabolic mechanism of enzalutamide resistance that may be targeted with a strategy that circumvents the need for systemic glucocorticoid receptor ablation,” says Dr. Sharifi.

He has joint appointments in the Lerner Research Institute Cancer Biology Department, Glickman Urological & Kidney Institute and Taussig Cancer Institute. He holds the Kendrick Family Endowed Chair for Prostate Cancer Research.

181 androgen receptor coregulators; 18 that matter

A team led by Hannelore Heemers, PhD, associate staff, Lerner Research Institute Cancer Biology Department, showed that of 181 currently known coregulators of the androgen receptor (AR), at least 18 could theoretically be modulated to interrupt androgen signaling.

“All therapies that target ligand activation of AR eventually fail. We are attempting to target another point in the pathway,” says Dr. Heemers.

The study elucidated several previously unknown interactions between AR, coregulators and other proteins, the most important of which is the one between the androgen receptor, the coregulator WDR77 and the p53 protein. These WDR77-p53-AR interactions are enriched in prostate cancers, including those that do not respond to androgen deprivation therapy, where they promote cancer growth.

The findings lay the foundation to develop new drugs that interfere with these cancer-specific interactions.

Next-generation risk stratification: going beyond PSA

Two new molecular tests — Decipher® and IsoPSA™ — are cornerstones of prostate cancer research and show utility in patient care.

A retrospective study of prostate tissue from men with 3+3=6 Gleason scores showed that up to 20 percent with favorable disease pathology have tumors with molecular alterations that put them at higher risk for metastatic disease.

The Decipher study, led by institute Chairman Eric Klein, MD, showed that the test accurately stratified patients with 3+3 Gleason disease into low-, intermediate- and high-risk categories.

Similarly, a yearlong study of 261 men scheduled for biopsy showed that IsoPSA testing offered a 48 percent reduction in false-positive biopsies and a superior net benefit over no biopsy, all biopsy and the modified Prostate Cancer Prevention Trial Risk Calculator 2.0.

IsoPSA, developed at Cleveland Clinic, is a serum-based assay that predicts prostate cancer risk by partitioning isoforms of prostate-specific antigen (PSA) with an aqueous two-phase reagent.

“Study after study has shown that active surveillance represents the best option for many men with low-grade prostate cancer,” Dr. Klein says. “The important thing is to ensure we select the right patients for deferred treatment to improve overall outcomes, and reduce chances that we miss aggressive disease.”

LEFT — A medical illustrator’s depiction of prostate cancer



2017 HIGHLIGHT

Minority Men's Health Center Reaches More Than 35,000 Men

Cleveland Clinic urologist and kidney transplant surgeon Charles Modlin, MD, MBA, has taken his late father's words to heart: "Nobody cares about black men," his father said decades ago. "It's your responsibility to use your education, that not everyone has had the opportunity to acquire, to help our community."

The first man in his family to graduate from high school, Dr. Modlin began noticing health disparities in minority populations when he was a kidney transplant fellow in the early '90s.

The disparities still exist, he notes. For instance, African-Americans are six times more likely to develop kidney failure from hypertension. They are less likely to receive kidney transplants and more likely to reject the ones they do receive. Hispanic men are more likely than whites to have diabetes and diabetes-related kidney failure, and to die from it.

"In the late '90s, I started going to community centers and churches, talking to men about the importance of screenings and not waiting for symptoms," says Dr. Modlin, who also credits his late mother, an elementary school teacher, for his drive to close the healthcare disparity gap. "Some just weren't educated about preventive care. Others avoided it because of generational distrust of the healthcare system."

Empowering men to adopt healthier lifestyles

Dr. Modlin realized that before they could access preventive care, minority men needed a "friendly portal of entry" to the healthcare system. In 2003, he founded the Minority Men's Health Fair at Cleveland Clinic. That gave rise in 2004 to the Minority Men's Health Center, of which he is the Director.

Among the first of its kind, the center remains one of the nation's only minority men's health programs not in existence due to a grant or research study.

"The Minority Men's Health Center isn't based on a special project," says Dr. Modlin. "It's based on

establishing community connections that empower underserved men to adopt healthier lifestyles."

The center provides screenings, wellness information, primary care at three locations around Cleveland, and referrals as needed. It also spearheads research and education for consumers, physicians and other providers about how certain medical conditions present differently in minorities and require different management.

The Minority Men's Health Fair is the largest clinical community outreach initiative at Cleveland Clinic each year. Dozens of specialists and hundreds of Cleveland Clinic caregivers volunteer to provide free screenings and services. Community groups, corporate sponsors and nonprofits are also represented.

The first year, 35 men came to the fair. Since then, more than 35,000 have received screenings, health consults and more. And for many, the Minority Men's Health Fair has been a lifesaver.

The 15th annual fair in April drew over 1,000 attendees, who received nearly 5,600 health screenings. More than 500 screenings — for chronic kidney disease, hepatitis C, prostate cancer, oral cancer and other conditions — reported abnormalities.

Welcoming an underserved population

"Before he passed away in 2010, my father attended many Minority Men's Health Fairs, standing at my side and watching the men come in," says Dr. Modlin. "My father and I both recognized and felt grateful that Cleveland Clinic and Cleveland Clinic providers do care about black men."

Dr. Modlin expects steeper declines in mortality rates that disproportionately afflict men of color.

"We're headed in the right direction," he says. "Even though the Minority Men's Health Center and fair welcome all men, labeling these programs for 'minority men' motivates this population and stresses the message 'Preventive healthcare is for you.'"

2017 Achievements

Center for Blood Pressure Disorders

An updated analysis from the Systolic Blood Pressure Intervention Trial (SPRINT) in patients with chronic kidney disease (CKD) showed similar results as the main study: In patients with CKD and hypertension without diabetes, targeting a systolic blood pressure < 120 mm Hg compared with < 140 mm Hg reduced rates of major cardiovascular events and all-cause death without evidence of effect modifications by CKD or deleterious effect on the main kidney outcome.

It is important to note that the SPRINT study utilized a standardized blood pressure (BP) measurement protocol involving measurement with an automated BP device that checked three BP measurements automatically after a five-minute period of rest, with the participant alone in the room. The new BP guidelines, largely based on SPRINT, emphasize proper measurement techniques. Otherwise, attempts at intensive control may result in more adverse events. Center Director George Thomas, MD, served as Cleveland Clinic site principal investigator for SPRINT.

New hypertension guidelines also strongly recommend out-of-office BP measurements (home BP monitoring or ambulatory BP monitoring). Lifestyle modifications need to be emphasized and reinforced, with a greater use of combination antihypertensive therapy. A team approach, using pharmacists and nurse practitioners, along with optimal use of best practice algorithms and remote monitoring technology, must be implemented for efficient and effective care.

Participating clinician: George Thomas, MD

Center for Chronic Kidney Disease

We recently conducted the first observational study of the associations of different blood pressure levels with various causes of death in a chronic kidney disease (CKD) population. Using Ohio Department of Health mortality files, we identified 45,412 patients with eGFR 15-59 mL/min/1.73m² with underlying hypertension and who were receiving at least one antihypertensive agent. Over four years, 13,332 of those patients died. We classified their deaths into three categories: cardiovascular, malignancy-related and noncardiovascular-/nonmalignancy-related. We found a J-shaped curve — patients with systolic blood pressures over 150 mm Hg and under 120 mm Hg (versus 130-139 mm Hg) were associated with higher all-cause and cardiovascular mortality. We also found that patients with certain comorbidities — diabetes mellitus, cirrhosis and heart failure — were more likely to die if their blood pressure was less than 120/80 mm Hg.

Our results conflict with the 2015 SPRINT randomized control study, which found fewer overall deaths and fewer deaths from cardiovascular disease in patients who were managed so that their blood pressure was less than 120/80 mm Hg. The SPRINT trial did not include patients with diabetes mellitus or who had had prior strokes. We believe that our findings offer a note of caution for clinicians regarding targeting systolic blood pressure less than 120 mm Hg for higher-risk CKD patients with diabetes and/or heart failure, and that a new trial is needed that includes those populations.

Participating clinicians: Stacey Jolly, MD; Joseph Nally Jr., MD; and Sankar Navaneethan, MD, Baylor University

We found evidence that there's a sweet spot for diabetes control for patients who have both diabetes and CKD. Specifically, patients who maintain a target hemoglobin A1c (HbA1c) of 6 to 6.9 percent are

George Thomas, MD



less likely to die from diabetes-related complications.

Published in the *American Journal of Kidney Diseases*, our observational study involved looking at the records of 6,165 Cleveland Clinic patients with diabetes (both Type 1 and Type 2) and CKD. Among these patients, we found that those with HbA1c levels below 6 percent or greater than 9 percent had a similar risk of death that was higher than the risk for patients who kept their HbA1c levels in the 6 to 7 percent range.

When considered as a continuous variable, HbA1c level was significantly associated with pre-end-stage renal disease mortality. The relationship was nonlinear, with very low and high HbA1c levels having the higher risk for mortality and the risk being lowest at HbA1c levels of about 7 to 8 percent.

Among the primary reasons that lower HbA1c can put diabetic patients with kidney disease at increased risk of death is that having CKD predisposes patients to hypoglycemia, itself a life-threatening and emergent condition.

Participating clinicians: Joseph Nally Jr., MD; Jesse Schold, PhD; Stacey Jolly, MD; and Susana Arrigain, MS

Center for Dialysis

We are educating and training nephrologists to uncover and treat infections in dialysis before they become deadly. Infections are the second leading cause of mortality in dialysis patients, after heart disease.

In conjunction with the American Society of Nephrology (ASN), we led a national webinar in May, “Targeting Zero Infections: Where Do We Begin?” During the program, center Director Leslie Wong, MD, MBA, Director of End-Stage Renal Disease, discussed the case of a hepatitis C outbreak at a dialysis facility and the critical role nephrologists play in such situations.

Dr. Wong serves on the executive committee of the Nephrologists Transforming Dialysis Safety (NTDS) initiative on behalf of the ASN. The NTDS, a three-year project now in its second year, has the aim of reducing the infection rate to zero and is funded by the Centers for Disease Control and Prevention (CDC).

Dr. Wong presented at the Making Dialysis Safer Coalition meeting at the CDC in August, discussing how nephrologists can and should serve as leaders in the area of dialysis infection prevention. He also helped teach a pre-course, “Dialysis Infection Crisis in the United States: A Call to Action,” and a main session, “Nephrologist Infection Prevention Leadership: Why Should I Care?” at the annual ASN meeting in November.

Participating clinician: Leslie Wong, MD, MBA

Center for Endourology and Stone Disease

Computed tomography (CT) scans remain the most accurate imaging modality to detect kidney stones and to direct management, providing a reliable measure of stone burden, stone location, stone density and skin-to-stone distance. “Opportunistic imaging” is a term used for evaluating other conditions using an existing image. We evaluated the ability of the noncontrast CT scan, obtained during a kidney stone work-up, to contribute to a better understanding of patient comorbidities and the potential causes of their stones.

In a collaboration between the departments of Urology and Radiology, CT scans were evaluated for visceral obesity, hepatic steatosis, abdominal aortic calcifications and vertebral bone mineral density. We found that visceral obesity and hepatic steatosis were associated with a low urine pH. Visceral obesity was a better predictor than body mass index when identifying those with a low urine pH and uric acid stones. Indeed, 90 percent of uric acid stone patients had a high visceral fat area on CT scan. Abdominal aortic calcifications were associated with a higher risk of low urine pH and hypocitraturia. Patients with low vertebral bone mineral density on CT were more likely to have large stone volumes, hypercalciuria and hypocitraturia.

In summary, if a CT scan is ordered, we should put it to good use. It can identify potentially significant comorbidities that may require further evaluation and management (e.g., cardiovascular risk, bone health). It can predict underlying metabolic abnormalities, suggest kidney stone preventive strategies and identify those best suited for a trial of dissolution therapy. Our future studies will evaluate the impact of medical approaches to stone prevention (thiazides, citrates) on bone mineral density. The goal is to maximize the “opportunity” our imaging provides.

Participating clinicians: Nishant Patel, MD; Ryan Ward, MD; Juan Calle, MD; Erick Remer, MD; and Manoj Monga, MD

Center for Female Urology

We published the first-ever study using functional magnetic resonance imaging (fMRI) to measure brain activity in women with overactive bladder who had success using sacral neuromodulation (SNM) therapy.

This experiment was a culmination of years of work, including several safety studies we performed in order to receive Institutional Review Board approval for enrolling patients in this type of investigation. Generally, fMRIs are not allowed for patients with implanted electrical devices.

For the study, we turned off patients’ SNM devices for one week, causing their symptoms to return. Then we performed fMRI on each patient while we turned the SNM on and off. Patients underwent three fMRI sessions with their devices operated at a different level of intensity each time: subsensory, sensory and suprasensory.

The data yielded some interesting results. In general, brain activation progressed with increased stimulation levels. However, activation of the inferior frontal gyrus remained stable, and deactivation of the pons and the periaqueductal gray matter only occurred with subsensory stimulation. Sensory stimulation activated the insula, which previous studies have shown is activated upon bladder filling, but deactivated the medial and superior parietal lobes. Suprasensory stimulation activated multiple structures, including sensory regions of the S3 nerve root where the stimulator lead is implanted.

Our study achieved its aim of showing that SNM devices alter brain activity. In the future, we hope to change the parameters, such as performing the fMRI when patients have a full bladder or with different stimulus settings, to tease out more details on how SNM devices affect neural structures and circuits.

Participating clinicians: Bradley Gill, MD, MS; Javier Pizarro-Berdichevsky, MD; Pallab Bhattacharyya, PhD; Sandip Vasavada, MD; Stephen Jones, MD, PhD; and Howard Goldman, MD

Center for Genitourinary Reconstruction

The National Spina Bifida Patient Registry is a multi-institutional registry established by the U.S. Centers for Disease Control and Prevention with a primary goal of understanding the life course and maximizing care pathways for patients with spina bifida (SB). In 2016, the Glickman Urological & Kidney Institute and other participating specialists at Cleveland Clinic joined the registry with both their pediatric and adult multidisciplinary myelomeningocele clinics.

Participation in the registry will permit us to benchmark and compare SB care at Cleveland Clinic with that of other institutions, and also will allow the institute to engage in multi-institutional research focused on outcomes and life course.

The Center for Genitourinary Reconstruction has one of the largest experiences in the country in the management of rectourethral fistula (RUF), an uncommon but often devastating complication most typically seen following treatment for pelvic

malignancy. At the American Urological Association annual meeting in May, we presented an updated review of over 100 patients evaluated at our institution over 10 years. Approximately 85 percent of cases were associated with prior treatments for prostate cancer, and over 25 percent had undergone prior reparative surgery that had failed. After a period of diversion, patients underwent careful evaluation to determine the most appropriate long-term treatment plan based on their anatomy and medical comorbidities. Eighty percent of the patients underwent corrective surgery for RUF at our institution, and ultimately 60 percent of this cohort ended up with no stoma, 30 percent required permanent fecal or urinary diversion (one stoma, 15 percent each) and 10 percent were managed with two stomas.

Although the rate of RUF resolution is high, patients should be counseled on the possibility of permanent diversion and carefully selected for the optimal form of surgical management.

Participating clinicians: Kenneth Angermeier, MD, and Hadley Wood, MD



Hadley Wood, MD, (center) with former urology resident Christina Ching, MD

Center for Men’s Health

MENTion It™, launched in 2016, is an educational campaign designed to influence men to talk about their health issues, be proactive about their health and take action when needed. Based on that successful year, the campaign expanded and focused on father-son communication in 2017.

A survey of men across the country provides key insights and direction for the campaign. The national probability sample consists of approximately 1,000 males age 18 and older.

The initial survey confirmed that men keep their health problems close to home — sharing health issues with spouses or significant others, but not with children, other family members or friends.

In 2017, the survey was expanded to focus specifically on father-son relationships. Findings included:

- About 70 percent of fathers with sons stated that their family has spoken openly with them about health issues and concerns throughout their life. Millennials (79 percent) are significantly more likely than baby boomers (64 percent) to have experienced this growing up.
- About half of fathers with sons say that they didn't know about their family health history until they started to go to the doctor as an adult (47 percent).
- About 43 percent of fathers with sons whose family doesn't currently talk openly about health issues and concerns say they want to break the pattern.
- About 62 percent wish their own father or father figure had talked to them more about health topics.

Communicating is key and knowing family history and genetic predispositions is essential to improving healthcare for men. What better way to start than with a conversation between a father and son?

Participating clinicians: Daniel Shoskes, MD; Edmund Sabanagh Jr., MD; Eric Klein, MD; James Ulchaker, MD; and Ryan Berglund, MD

Center for Minority Men’s Health

More than 500 patients have provided specimens to the African-American Male Biobank, contributing to several basic science studies at Cleveland Clinic Lerner Research Institute. The biobank will allow scientists to study specimens from Minority Men’s Health Center patients, identify the best treatments to address health disparities in African-American males and foster broader research. The biobank is a tremendous resource for advancing scientific discovery that benefits patients not only at an individual level, but also at a population level.

Participating clinician: Charles Modlin, MD, MBA

Center for Pediatric Urology

In the pediatric population, the decision to intervene has an impact on both immediate and long-term outcomes. In the posterior urethral valve (PUV) population, our goal is to preserve overall renal function. There are significant data regarding progression of disease in the pediatric population, but the adult PUV patients are not well-studied. One of the many benefits of working at a pediatric center within a large adult tertiary hospital is that we have the benefit of retrospectively evaluating the progression of disease in these patients.

The Cleveland Clinic team has sought to determine when the renal decline occurs and what factors help delay end-stage renal disease (ESRD). It appears that a significant number of these PUV patients do progress to ESRD after childhood, suggesting that the overall renal failure rate is higher than published studies indicate.

Participating clinician: Audrey Rhee, MD

Center for Renal Diseases

Cleveland Clinic continues its involvement in research into Alport syndrome, a rare genetic disease that causes kidney failure and hearing loss. The ATHENA trial, which collected data on patients with Alport syndrome to improve our understanding of the disease, closed to enrollment this winter. For the first time, treatment trials for Alport syndrome are investigating medications specifically being developed for this patient population. The CARDINAL trial, a phase 3 placebo-controlled trial using bardoxolone, is currently enrolling. HERA, a phase 2 placebo-controlled trial using a miR-21 antibody, is in the final approval process. HERA's sister trial, which includes kidney biopsies following administration of the study medication, is also in the final approval process. James Simon, MD, is site principal investigator for all three trials.

Participating clinician:
James Simon, MD

Center for Renal and Pancreas Transplant

African-Americans may carry a genetic mutation, *APOL1* on chromosome 22, that predisposes them to developing chronic kidney disease (CKD). Recent studies report strong associations between CKD and the presence of the *APOL1* mutation. Researchers, however, are unsure how this mutation affects the outcomes of African-American kidney transplant recipients. They also don't know how a high-risk variant of the *APOL1* mutation affects African-American kidney donors.

The National Institutes of Health recently allocated funding to 13 clinical consortiums, including Cleveland Clinic, to form an *APOL1* Long-Term Kidney Transplantation Outcomes (APOLLO) Network to investigate these questions. Emilio Poggio, MD, transplant nephrologist, will serve as the primary investigator for the Cleveland Clinic-led consortium, which includes transplant centers from Ohio, Michigan, Indiana, New York, New Jersey, Kentucky and West Virginia.

The APOLLO Network will prospectively study the impact of *APOL1* genetic variants as susceptibility factors in kidney transplant patients who receive kidneys from living or deceased donors with African ancestry. The goals of the study are to evaluate the rate of change of kidney function in recipients, as well as rates of acute rejection of the kidney transplant, graft failure and return to maintenance dialysis. African-American kidney donors will also be followed for five years to determine whether there are any potential implications of *APOL1* genetic mutations on their long-term outcomes.

Participating clinicians: Emilio Poggio, MD; Ziad Zaky, MD; and Jesse Schold, PhD



Alvin Wee, MD, Director, Center for Renal and Pancreas Transplant, (center) with transplantation fellow Mohamed Eltemamy, MD, (left) and urology resident Nitin Yerram, MD, (right)

Center for Robotic and Image-Guided Surgery

Robotic technology continues to transform urological surgeries, shifting operations from open to minimally invasive approaches and improving safety. For instance, robotic prostatectomy, which we performed more than 3,000 times this year, has improved success rates and reduced postoperative complications by reducing morbidities and improving outcomes.

We are adopting newer procedures to make minimally invasive surgery even less intrusive. Perineal prostatectomy was an open surgery with poor exposure that could damage the perineum and was difficult to teach. With robotics, we can access the prostate through a small incision rather than through the belly, which required moving the bowel and bladder. The results are minimal postoperative pain and almost immediate urine control postsurgery. We also perform partial nephrectomy for solitary kidneys, large tumors and multiple tumors using robotics.

We developed an intracorporeal kidney cooling technique using ice slush to provide a consistent cold ischemia of 14 degrees Celsius to extend the safe operative time. In addition, we developed several first-ever procedures for single-port robotic surgery, transvaginal nephrectomies and robotic perineal surgery, reports center Director Jihad Kaouk, MD, FACS.

Finally, we have refined ileal conduit and Studer neobladders, both intracorporeal urinary diversion procedures, completing them inside the body cavity without a large laparotomy incision.

Our fellowship program was ranked No. 1 by the Endourological Society. We train two clinical and two research fellows per year with a volume load of more than 1,000 robotic surgeries, spanning the entire spectrum of robotic applications and urology.

Our team produces more than 30 peer-reviewed publications in top urology journals per year. We present lectures and broadcast live surgeries worldwide and collaborate in multicenter studies on five continents.

The center strives to provide the least invasive surgeries with the most precise treatment to achieve the best possible outcomes and to shape the future of surgery.

Participating clinician: Jihad Kaouk, MD, FACS

Center for Urologic Oncology

Center members were very active at the American Urological Association (AUA) 2017 Annual Meeting, presenting a number of abstracts that were later turned into journal articles. Several of those studies examined the value of genomics and MRI-guided biopsy to help select and monitor patients on active surveillance for prostate cancer. For instance, one study found that if a confirmatory biopsy shows an absence of cancer, that result is associated with a significant decrease in prostate cancer grade and volume reclassification among men on active surveillance.

Also at the meeting, urologist Steven Campbell, MD, PhD, presented on new AUA guidelines for localized kidney cancer, and urologist Andrew Stephenson, MD, Director, Center of Urologic Oncology, presented on new AUA guidelines for testes cancer.

On the translational medicine front, we are working closely with researchers at Cleveland Clinic Lerner Research Institute on several novel and exciting initiatives. For instance, we are focusing on new adjuvant protocols looking at antigen receptor-targeted therapy assessing response in prostatectomy specimens based on specific genotypes of patients for androgen metabolism.

Finally, we are investigating renal dysfunction after kidney cancer surgery. Specifically, we are attempting to identify the role of coexisting renal disease and surgical techniques and how they impact renal function after surgery.

Participating clinicians: Steven Campbell, MD, PhD; Andrew Stephenson, MD; Yaw Aninakwa Nyame, MD, MBA; Eric Klein, MD; and Charles Dai, MD

Resources for Physicians

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Glickman Urological & Kidney Institute

The Glickman Urological & Kidney Institute is a world leader in treating complex urologic and kidney conditions in adults and children. It is ranked No. 1 in America for urology and No. 2 in nephrology by *U.S. News & World Report*. Our internationally recognized staff has pioneered laparoscopic and robotic surgical techniques and developed innovative procedures for urologic cancers and transplantation. We provide advanced management of kidney disease, hypertension, infertility and congenital malformations to help patients worldwide.

About Cleveland Clinic

Cleveland Clinic is a nonprofit, multispecialty academic medical center integrating clinical and hospital care with research and education for better patient care. More than 3,500 staff physicians and researchers in 140 medical specialties provide services through 27 clinical and special expertise institutes. Cleveland Clinic comprises a main campus, 10 regional hospitals and more than 150 outpatient locations, with 18 family health centers and three health and wellness centers in northern Ohio, as well as medical facilities in Florida, Nevada, Toronto and Abu Dhabi, and opening in 2020, in London, England. *U.S. News & World Report* ranks Cleveland Clinic as the No. 2 hospital in the nation.

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Year in Review

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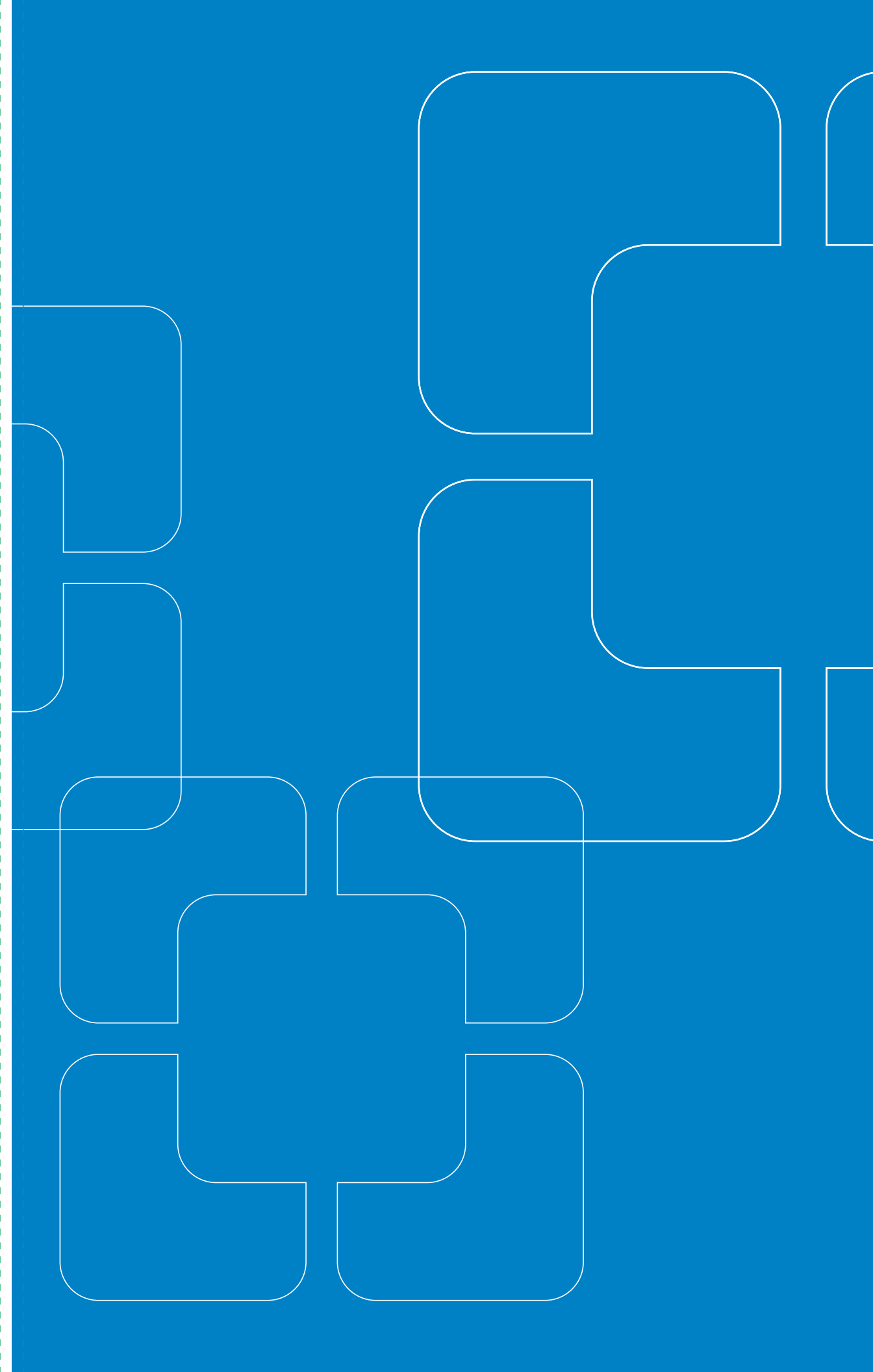
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