Cleveland Clinic

GLICKMAN UROLOGICAL & KIDNEY INSTITUTE

2021 Year in Review

CONTENTS

ON THE COVER

Byron Lee, MD, PhD, during a robotic radical cystectomy.

AT A GLANCE

Glickman Urological & Kidney Institute

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.

BY THE NUMBERS

(2021)

150,997
OUTPATIENT VISITS

14,466
SURGICAL CASES

29,032
DIALYSIS TREATMENTS

3,095
ADMISSIONS

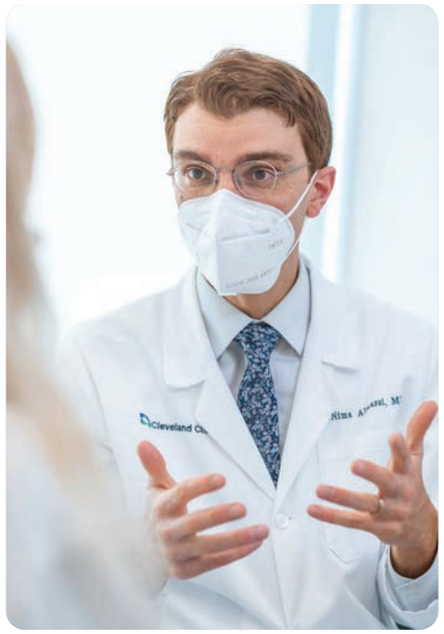
13,717
PATIENT DAYS

4.43
AVG. LENGTH OF STAY (DAYS)

VITAL STATISTICS & RANKINGS

INSTITUTE VITAL STATISTICS	
61	Urologists
35	Nephrologists
414	Total Caregivers
29	Urology Advanced Practice Providers
20	Nephrology Advanced Practice Providers
30	Urology Residents
21	Urology Fellows
11	Nephrology Fellows

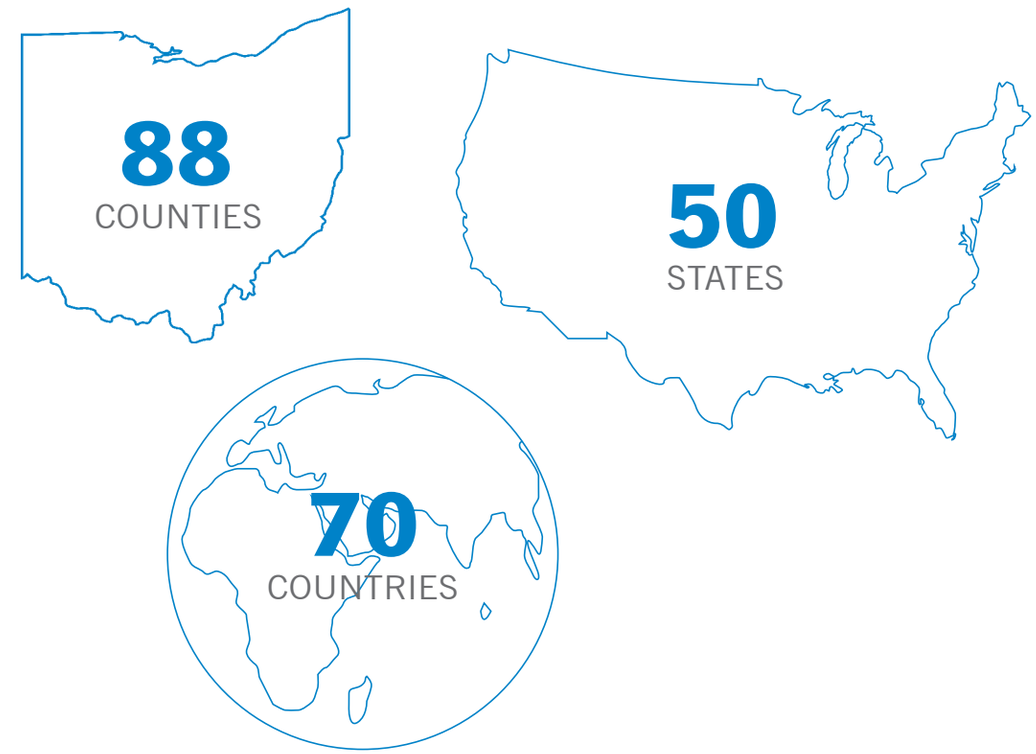
SURGICAL CASES	
810	Benign Prostatic Hypertrophy
1,592	Endourology and Stone Disease
1,246	Female Pelvic Medicine and Reconstructive Surgery
307	Male Fertility
564	Pediatric Urology
570	Genitourinary Reconstruction
324	Renal and Pancreas Transplant
2,988	Urologic Oncology



BEST HOSPITALS U.S.News & WORLD REPORT UROLOGY 2021-22

U.S. News & World Report has consistently ranked Cleveland Clinic urology and nephrology among the country's top programs for the past two decades.

PATIENT ORIGINS



CENTERS

DEPARTMENT OF KIDNEY MEDICINE

- Blood Pressure Disorders
- Chronic Kidney Disease
- Dialysis
- Multicultural Kidney and Hypertension
- Onco-Nephrology
- Kidney and Pancreas Transplant
- Renal Diseases
- Renal Genetics

DEPARTMENT OF UROLOGY

- Endourology and Stone Disease
- Female Pelvic Medicine and Reconstructive Surgery
- Genitourinary Reconstruction
- Male Fertility
- Men's Health
- Minority Men's Health
- Pediatric Urology
- Robotic and Image-Guided Surgery
- Urologic Oncology

DEAR COLLEAGUES,

Despite the challenges of the COVID-19 pandemic, it's been an exciting year within the Glickman Urological & Kidney Institute.

Alongside Cleveland Clinic, the Department of Urology celebrated its centennial year — a milestone moment for the program and a reminder of the incredible advancements we've made in urology over the past 100 years.

Over the course of the last century, caring for our patients and their evolving needs has been our greatest privilege.

This was a milestone year for transitioning leadership as well. I would like to humbly thank Dr. Eric Klein, Chairman Emeritus of the Institute, for over 13 years of inspirational leadership. His contributions to the field of prostate cancer will leave a lasting legacy for patients, colleagues and trainees. So, too, we thank Dr. Robert Heyka, an esteemed nephrologist and Chairman Emeritus of the Department of Kidney Medicine, for his leadership.

With his departure, we welcomed Dr. Crystal Gadegbeku to lead our newly named Department of Kidney Medicine. Prior to joining Cleveland Clinic, she served as Section Chief of Nephrology, Hypertension and Kidney Transplantation at the Lewis Katz School of Medicine at Temple University. While there, she expanded the clinical, research and fellowship programs and was active in National Institutes of Health-funded clinical and translational studies. Dr. Gadegbeku brings an incredible depth of knowledge and expertise to her new role. As a field, kidney medicine is ripe for transformation — and she is at the helm of that change.

I'm proud to announce that our urology and nephrology teams competed successfully for federal funding from the NIDDK/NIH. Urology was awarded a five-year U01 grant that will support the generation of a high-resolution transcriptome and gene regulatory dataset of the human lower urinary tract across the lifespan. Data from this study will be invaluable for efforts in urologic organ repair and regeneration. Nephrology received a U2C/TL1 grant that supports scientific training and professional development for trainees pursuing research in kidney medicine and benign urinary and blood conditions. Training the next generation of scientists is an important part of our mission.

We hope you will take a moment to read through our annual *Year in Review* publication. One of our greatest strengths as an institute is our propensity to innovate within urology and kidney medicine and across our diverse subspecialty areas.

From developing new ways to screen for and treat genitourinary cancers and establishing new standards of care in outpatient and acute kidney care settings, to leveraging robotic and artificial intelligence platforms that improve and individualize care — we are always looking for better ways to serve our patients.

Peter Drucker said the best way to predict the future is to create it, and we are well on our way. With emphasis on screening, prevention and patient-centered wellness alongside disruptive thought, high-impact research and therapies, and a commitment to training, we will define the next 100 years of care.

Georges-Pascal Haber, MD, PhD

Interim Chair, Glickman Urological & Kidney Institute
Chair, Department of Urology

LEFT — Georges-Pascal Haber, MD, PhD

2021 HIGHLIGHT

WOMEN PHYSICIANS ARE INCREASINGLY ENTERING UROLOGY AND NEPHROLOGY

The male-dominated specialties are attracting more women thanks to institutional and peer support.

As a nephrology fellow in the mid-1990s, Crystal Gadegbeku, MD, attended her first American Society of Nephrology (ASN) Kidney Week. "I clearly remember coming down the escalator after a plenary session, looking around the crowd in the lobby and thinking, 'My goodness, this is a male-dominated specialty,'" recalls Dr. Gadegbeku, Cleveland Clinic's Chair of Kidney Medicine. "I was in a sea of people who didn't look like me. But over the 20-something years I've been in the field, I've seen that change dramatically."

In 1995, less than 20% of nephrology fellows were women; that figure rose to 36% by 2019, according to ASN data. Women are making strides in urology too, with the number of women practicing in the specialty increasing nearly 50% in five years, according to the 2020 Annual Census report from the American Urological Association.

"Diversity is important," says Dr. Gadegbeku. "People come with different perspectives, and all together we create better solutions toward a better world."

Resident class is 80% women

Cleveland Clinic's Glickman Urological & Kidney Institute values diversity. It welcomed five residents to the Urology Residency Training Program's class of 2027, four of whom are women.

"Our incoming class is our first one that is female predominant, which will greatly improve gender diversity in our residency," says Steven Campbell, MD, PhD, Residency Program Director. "All five new residents are outstanding and will likely make important contributions to the field in the coming years."

The next generation of urologists who are already making a difference includes Emily Slopnick, MD. She joined Cleveland Clinic's Urology Department in 2020 after completing a fellowship in female pelvic medicine and reconstructive surgery.

Facing the challenges

Dr. Slopnick agrees that while the number of women in urology and nephrology grows, female physicians still face challenges. Topping the list are decisions about having and raising children.

"The hardest thing is balancing the expectations — some that we put on ourselves and some external," she says. How much time should you take off? When you return, how will you handle taking call?

Work-life balance is a well-documented challenge, but female urologists and nephrologists cite other subtle hurdles, including the type of patients they see within their practices.

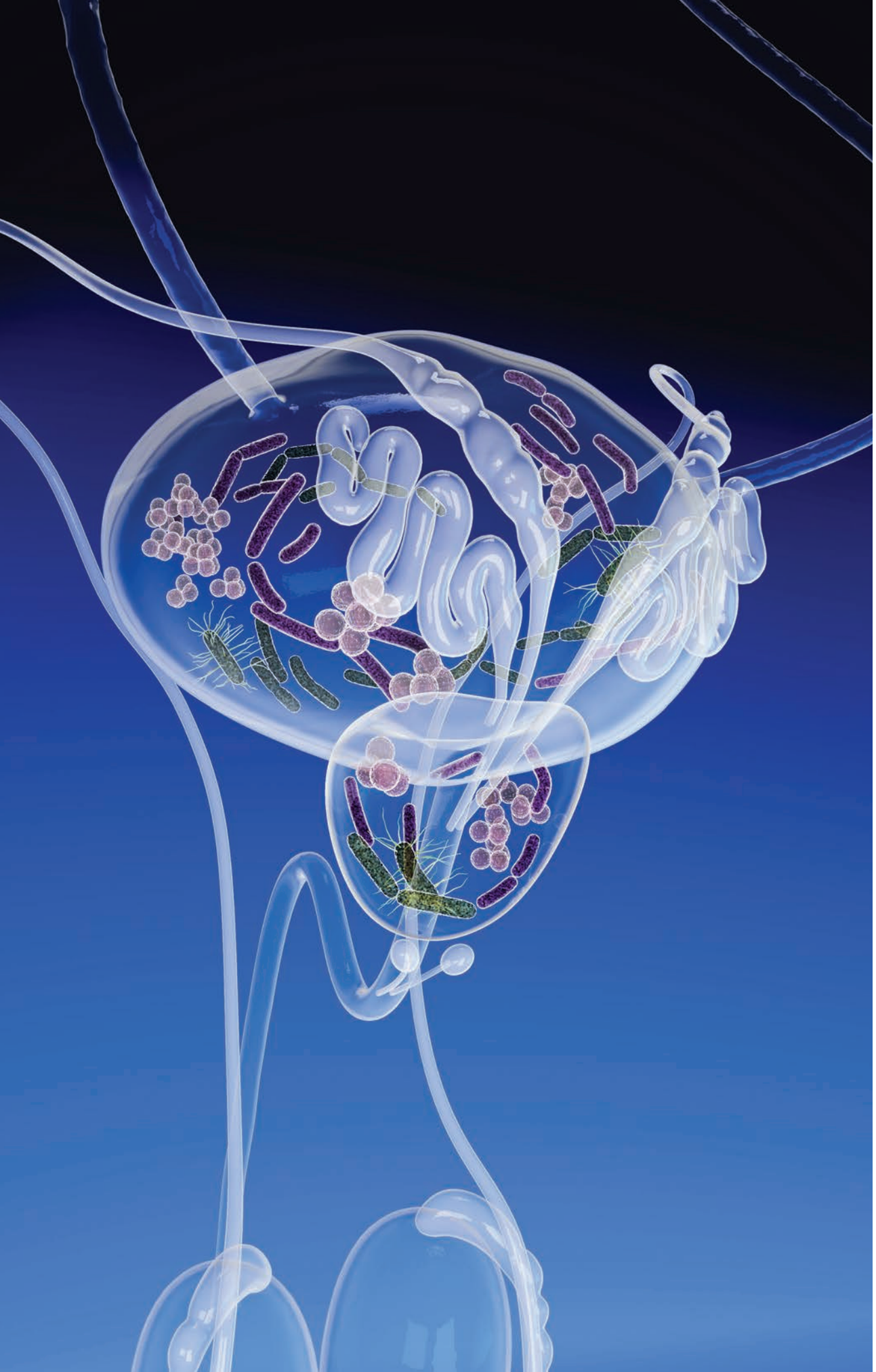
"I think there's an expectation that women patients want to see a woman doctor, so in some practices female urologists might get patients who don't necessarily align with their career interests," says Dr. Slopnick. "A male physician might get more surgical cases, while a woman might see more patients with urinary tract infections, for example." She adds that some women urologists do fellowships in oncology or other specialties to avoid that scenario.

Peers and leaders provide support

Having peer support is key for women working in specialties traditionally dominated by men.

It's also important for young physicians to see diversity in leadership. "I have had the pleasure of meeting so many hospital leaders who are women here at Cleveland Clinic who naturally serve as role models for women coming in, like me," says Dr. Gadegbeku, who joined the healthcare system in July 2021. "As department chair, I hope to inspire more women and more diversity in nephrology and throughout the Glickman Urological & Kidney Institute."

RIGHT — Crystal Gadegbeku, MD, Chair of Kidney Medicine, with a patient in her clinic.



2021 HIGHLIGHT

MAPPING OUT THE GENITOURINARY MICROBIOME

Researchers in the Department of Urology are exploring interactions between the human genitourinary and gastrointestinal microbiomes to tease out possible pathological pathways.

Male infertility and the seminal microbiome

Scott Lundy, MD, PhD, urology fellow, and Sarah Vij, MD, Director of the Center for Male Fertility at Cleveland Clinic, led a study to better understand whether gut and urinary microbiomes are linked with male infertility. "No other studies to date have looked into the role of the human gut in male reproductive health or explored potential pathways using metagenomics," remarks Dr. Vij.

Drawing on the expertise of Charis Eng, MD, PhD, Chair and Inaugural Director of the Genomic Medicine Institute at Cleveland Clinic, the team set out to investigate the differences in the microbiome between fertile and infertile men.

They discovered that not only did the semen of infertile men contain differences in bacteria diversity and quantity, but the gut microbiome was also significantly different. Dr. Lundy says he was "surprised by these findings and optimistic that future diagnostic tests and treatments for male infertility could be designed around this."

Using metagenomics data, they also identified seven differentially expressed pathways, the most common of which between fertile and infertile males was the S-adenosyl-L-methionine, or SAM, cycle. This was confirmed independently in a subanalysis of semen and urine samples.

SAM is a common metabolite with established roles in methylation, oxidative stress and aminopropylation. Dr. Lundy notes, "It's not clear whether one or all of these mechanisms play a role in microbiome-mediated male infertility, but these data are nevertheless important."

In a separate study, researchers tested the hypothesis that a clinical varicocele, a dilation of the testicular veins associated with infertility, is also associated with differences in the seminal microbiome. They compared semen samples of infertile men with or without a clinical varicocele and identified significant differences in pathway expression.

Further prospective studies stemming from both of these investigations are planned.

Urolithiasis and the urinary tract microbiome

Several years ago, Aaron Miller, PhD, a staff scientist in Cleveland Clinic Lerner Research and Glickman Urological & Kidney Institutes, and his research team established the urinary tract microbiome — and not the gut microbiome as previously assumed — as a potential pathogenic target to treat urinary stone disease (USD).

To build on this work and to identify consistent risk factors or bacteria linked to microbiome-associated USD, the team analyzed all published clinical data from microbiome-wide association studies involving USD.

They found that the most significant driver of variables among the studies was the lab where the data originated — and not individual clinical data. Dr. Miller and his team have several ongoing studies to determine the underlying mechanisms that connect the urinary tract microbiome to kidney stone formation and other urologic pathologies.

Is there biological crosstalk?

There is no evidence to suggest biological crosstalk between these two pathologies; however, patients with either USD or male infertility do have different urinary microbiomes from healthy control subjects. How the dysbiosis manifests is likely very different, but mapping out the genitourinary microbiome could be revelatory.

"Based on what I've seen so far, I do suspect that there are some common players involved that either promote or inhibit pathology," says Dr. Miller.

LEFT — Conceptual rendering of the microbiome of the male genitourinary system; pictured are bacteria bacilli and cocci (not to scale) in the bladder and prostate. Most of the bacteria found in the microbiome are in the Firmicutes, Proteobacteria, Actinobacteria or Bacteroidetes phyla.

2021 HIGHLIGHT

TUNNELED HEMODIALYSIS CATHETERS FOR ACUTE KIDNEY INJURY IN THE MEDICAL ICU

Cleveland Clinic physicians Tushar Vachharajani, MD, interventional nephrologist and Director of Interventional Nephrology, and Eduardo Mireles-Cabodevila, MD, critical care physician and Director of the Medical Intensive Care Unit (MICU), are reimagining the dialysis vascular access strategy in an acute care setting.

Managing hemodialysis vascular access in the MICU

Conventionally, acute hemodialysis therapy in the ICU is initiated by intensivists with a temporary nontunneled dialysis catheter placed at the bedside. However, explains Dr. Vachharajani, "If the anticipated need for dialysis therapy is beyond seven to 10 days, a tunneled dialysis catheter (TDC) is preferred over a nontunneled catheter to minimize the risk of bloodstream infection and catheter dysfunction, which can result in suboptimal dialysis treatment."

Early transition to a TDC in the critically ill population can be challenging for a multitude of logistical reasons. As such, the MICU and Interventional Nephrology teams at Cleveland Clinic established a collaborative service to place TDCs and other small bore tunneled central venous catheters in the ICU setting.

A product of the pandemic with lasting implications

Early in the coronavirus pandemic, delivering TDCs efficiently while also minimizing the risk of exposure became critical. This was particularly germane given the high incidence of acute kidney injury in patients with severe cases of COVID-19.

The placement of a TDC is time and resource intensive; it requires a specialized procedure room or an interventional radiology suite with access to fluoroscopy to guide catheter placement, per the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines. It also involves coordination among different clinical and patient transport teams, which poses a greater risk for viral spread.

The physicians developed a protocol to guide internal jugular TDC placement at the bedside without compromising patient safety. The placement is done under the direction of an experienced provider using ultrasound guidance, continuous cardiac monitoring and anatomical landmarks.

An early pilot study using this approach in 10 patients with COVID-19 was presented at the World Congress of Nephrology in Canada in 2020 and published in *Kidney International Reports*, establishing its safety and effectiveness in select patients.

Since then, the team has placed a total of 425 tunneled central venous catheters, with 120, or nearly one-third, at the bedside — in patients with and without COVID-19.

A cross-discipline innovation becomes a best practice

The collaboration between Interventional Nephrology and critical care services leverages skill sets from both disciplines. Says Dr. Mireles-Cabodevila, "The interventional nephrologists are experts on how and when to place the long-term catheter while the intensivists manage acute care. This partnership truly represents a new paradigm in care for our patients."

Dr. Vachharajani says they have also begun cross-training efforts, enabling critical care physicians to place TDCs; they have also developed a regional training center.

Though bedside placement of TDCs began as a COVID-19-era innovation, the physicians agree that with the appropriate resources it's a best practice in select patients.

"We are seeing select, high-risk patients benefit from getting a long-term catheter earlier and without having to move them out of ICUs," says Dr. Vachharajani.

RIGHT — Tushar Vachharajani, MD, and Eduardo Mireles-Cabodevila, MD, having a conversation in the MICU.

2021 HIGHLIGHT

LEADING THE WAY IN PROSTATE CANCER CARE

Experts at Cleveland Clinic have invested in research and technology designed to improve outcomes and patient experience. From diagnosis and biopsy to surgical approaches and longer-term management — learn more about how the team is leading the way in prostate cancer care.

IsoPSA: A more accurate screening test

Most prostate cancers are discovered through screening for prostate-specific antigen (PSA). However, the test has several shortcomings. For example, it is not prostate-cancer specific; an elevated PSA level is often caused by benign prostate hyperplasia.

Cleveland Clinic partnered with Cleveland Diagnostics to develop a blood test that detects and measures PSA-related proteins in the blood. The test, called IsoPSA™, is more accurate in predicting high-grade prostate cancer, potentially reducing unnecessary biopsy.

A more patient-friendly biopsy

Use of MRI in performing prostate biopsy allows precise targeting of areas of concern where cancer is most likely to be present. In the past, these biopsies were generally done transrectally, which is uncomfortable for patients and carries some risk of bacteremia and infection.

Cleveland Clinic urologists have found that passing the needle through the perineum targets the prostate more accurately, carries a negligible risk of infection, and can be done under local anesthesia, sedation or general anesthesia. Importantly, patients report no discomfort.

"Transperineal biopsies require dedicated equipment, special expertise and some experience, but I think the whole field will move this way in the next few years," says Eric Klein, MD, urologic oncologist and Chairman Emeritus of the Glickman Urological & Kidney Institute.

"We have preliminarily shown that micro-ultrasound is as effective as MRI at finding high-grade cancers, and it may be better than MRI at finding tumors," says Dr. Klein. "In the future, it may be possible to obtain an accurate prostate biopsy without MRI."

Identifying candidates for active surveillance

Cleveland Clinic helped develop several assays that use high-end genomic technology to identify which men may be good candidates for active surveillance and which need closer follow-up, early re-biopsy or immediate treatment. These tests allow assessment of tumor aggressiveness that is not visible using standard microscopes, and they serve as adjuncts to routine pathologic assessment.

Outpatient, noninvasive treatment of low-risk cancers

Cleveland Clinic is one of the first sites in the country to offer an improved form of high-intensity focused ultrasound (HIFU) using the Focal One® system. The technology combines imaging and ablative techniques to target prostate tumors in a short, noninvasive outpatient procedure performed under MRI guidance. Unlike radical prostatectomy and radiation therapy, HIFU does not increase the risk for urinary or fecal incontinence. Since only part of the prostate is treated, HIFU is better able to preserve potency. Patients return to normal activities in a few days.

At this time, HIFU is reserved for patients with a single tumor that is easily visible on MRI and located in a favorable anatomic position.

Single-port robotic radical prostatectomy

Robotic radical prostatectomy at Cleveland Clinic can be done through a single incision using a single-port robot. Performing the procedure extraperitoneally avoids bowel-related complications and adverse events that can occur during surgery, including optical nerve edema, congestion and respiratory problems. In select patients, this approach has become an outpatient procedure with minimal need for opioids to manage pain.

LEFT — Microscopic view of the cellular structure of a prostate gland adenocarcinoma.

2021 HIGHLIGHT — CASE STUDY

ONCO-NEPHROLOGY: A NOVEL APPROACH TO KIDNEY CARE FOR PATIENTS WITH CANCER OR CANCER TREATMENT

Onco-Nephrology, kidney care for patients who have had cancer or cancer treatment, is a nascent field. Roman Shingarev, MD, Director of the Center for Onco-Nephrology, discusses a case that highlights the complexity of managing kidney disease for patients receiving oncologic treatment.

A 62-year-old female presented to the onco-nephrology clinic with worsening proteinuria while receiving bevacizumab for nonsquamous, non-small cell lung cancer that was diagnosed one year prior. No somatic driver mutation was found upon tumor tissue assessment following complete tumor resection.

Her initial treatment included cisplatin and pemetrexed. Following the sixth round of chemotherapy, the patient developed acute kidney injury (AKI), characterized by bland urine sediment, partial Fanconi syndrome and peak creatinine of 2.0 mg/dL.

The AKI and most of her electrolyte abnormalities resolved one month following discontinuation of chemotherapy. Positron emission tomography (PET) scans demonstrated significant radiotracer uptake in two hilar nodes, and the patient was started on bevacizumab at 15 mg/kg every three weeks, resulting in improved PET parameters.

The patient developed hypertension and then new proteinuria at two and three months, respectively, into the treatment. Initially, her blood pressure (BP) improved with amlodipine, and the proteinuria was monitored until her urine protein-to-creatinine (UPC) ratio increased to 3.4 g/mg.

Vascular toxicities of vascular endothelial growth factor (VEGF) inhibitors

Both hypertension and proteinuria are common adverse effects of VEGF inhibitors, affecting approximately 50% of patients. These are considered class side effects of this targeted therapy and are sometimes associated with higher antitumor efficacy. If left untreated, hypertension may become severe and result in a stroke; proteinuria may lead to nephrotic syndrome and substantially increase the risk of venous and arterial thromboembolism, also common in these patients.

A gap in clinical guidance

No evidence-based guidelines exist on management of these conditions. The American Society of Clinical Oncology recommends discontinuation of treatment when nephrotic syndrome develops. KDIGO guidelines covering proteinuria treatment may not be applicable to this patient population. Nevertheless, inadequate control of these toxicities may lead to premature treatment termination and decreased patient survival.

A lesson in individualizing treatment approach

The patient presented with nephrotic-range proteinuria, and we started her on lisinopril, titrated to maximum dose. This led to a transient decrease in UPC and better BP control. However, as bevacizumab was continued, the proteinuria worsened again. The addition of spironolactone was not beneficial, and bevacizumab was held.

Although the addition of angiotensin receptor blockers to angiotensin converting enzyme inhibitors has a moderately greater impact on proteinuria in patients with chronic kidney disease, their combined use is discouraged by KDIGO because of a significant risk of AKI and hyperkalemia.

Because the patient's cancer was being effectively controlled by bevacizumab, we decided to restart the treatment and attempt to control proteinuria with lisinopril and losartan after counseling the patient on lifestyle modifications to minimize the risks of hyperkalemia and AKI.

The patient has been closely monitored and has maintained normal potassium levels. Her creatinine fluctuated between 0.8 and 1.5 mg/dL, improving with intermittent losartan stoppage.

Importantly, her UPC has decreased from the peak of 6.5 g/mg to 2 g/mg, allowing safe continuation of the VEGF inhibitor. It has been two years from the time of initial presentation to onco-nephrology, and the patient has remained in stable condition.

RIGHT — Roman Shingarev, MD, talks with a patient in the onco-nephrology clinic.

2021 HIGHLIGHT

THE UROMONITOR ADVANCES TO IN-HUMAN TRIALS

The UroMonitor, a wireless, insertable pressure sensor to assist in the diagnosis of urinary incontinence and other bladder disorders, is safe, feasible and well tolerated in women with refractory overactive bladder (OAB), according to the results of a Cleveland Clinic-led proof-of-concept study.

This is the latest report about the device that has been more than a decade in the making. But, up until now, its clinical safety and feasibility have been untested.

Telemetric ambulatory monitoring represents a paradigm shift in traditional clinical urodynamic studies (UDS), which have some significant drawbacks, including physical and emotional discomfort, artificial test conditions with catheters, and rapid retrograde filling of the bladder, which can result in variable diagnostic accuracy.

More than 50% of patients experience test-related anxiety and difficulty with in-office monitoring. UDS has been described as invasive and very different from how the body functions in everyday life. The UroMonitor may obviate these issues.

Margot Damaser, PhD, a biomedical engineer in Cleveland Clinic's Lerner Research Institute who created and oversees the development of the UroMonitor, has previously referred to it as a "Fitbit® for the bladder."

"Our vision is to take the monitoring out of the clinic and take the catheter out of the monitoring."

She works closely with a team of urologists, including Howard Goldman, MD, Vice Chair of Quality and Patient Safety in the Glickman Urological & Kidney Institute, to test the device in a clinical setting. They say the results so far are promising.

UroMonitor: First-in-human trial

Eleven adult female patients, all of whom were evaluated for refractory OAB, were included in this study. Investigators first performed a baseline assessment using standard multichannel UDS.

Next, they inserted the device transurethrally as would be done in cystoscopy or catheter placement, with a silk suture attached to one end of the device, and taped it to the patients' thigh for easy retrieval from the bladder.

UroMonitor's medical silicone-coated sheath that houses the pressure-sensing technology curls into a pigtail shape upon insertion to remain within the bladder, explains Dr. Goldman. The device transmits vesical pressure data at 10 Hz to a device taped to the patient's abdomens.

Once the UDS catheters were removed, leaving only the UroMonitor in place, the patients were encouraged to ambulate and void. The team assessed patient discomfort at every stage using visual analog pain scales, and overall comfort and safety during testing were also assessed.

Results so far

The researchers recently reported the results of the completed study at the 2021 American Urological Association meeting and are preparing to publish their findings.

"The device is easy to insert and extract; it reliably reproduced vesical pressure data patterns during both filling cystometry and ambulatory measurements. And patients were able to void freely with the device in place," Dr. Goldman says.

Patients reported minimal discomfort during the insertion phase but "nothing unexpected," he says. There were no post-procedure complications to report and, anecdotally according to Dr. Goldman, physicians and patients are pleased with the experience.

LEFT — Margot Damaser, PhD, holding the UroMonitor device.

2021 HIGHLIGHT

RESEARCH GRANTS AIM TO IMPROVE AND PERSONALIZE KIDNEY CARE

The principal investigators of two recently awarded National Institutes of Health-funded multicenter grants discuss how these projects are designed to better manage care for patients with acute kidney injury (AKI) following discharge and also set the stage for more personalized care.

Managing acute kidney injury after discharge

Survivors of acute kidney injury (AKI) are at increased risk for developing long-term major adverse kidney events (MAKE), progressive chronic kidney disease (CKD) and end-stage kidney disease (ESKD), and have a higher risk of all-cause mortality.

However, there is no clear outpatient protocol to prevent rehospitalization and/or subsequent CKD for these patients following discharge.

Cleveland Clinic and MetroHealth have teamed up as one of three national sites for the Caring for Outpatients with Acute Kidney Injury (COPE-AKI) trial. This five-year trial will compare outcomes between the standard of care and an intensive protocol, where patients will be followed closely through virtual and in-person visits.

"It's an opportunity to fill a gap in our knowledge about optimal care for patients with AKI as they transition from hospital to outpatient care," says Emilio Poggio, MD, principal investigator of the trial.

The study is set to begin in late 2021 and will utilize novel strategies for remote monitoring of risk factors among AKI survivors. Patients will also participate by reporting their blood pressure, weight, kidney function and albuminuria data for the first three months after hospital discharge and then at predefined intervals for two years thereafter.

Leveraging datasets to inform novel biomarkers, therapeutic options

Researchers have analyzed traditional and nontraditional clinical risk factors to examine the progression of CKD and cardiovascular disease in patients with CKD using data and biosamples from the Chronic Renal Insufficiency Cohort (CRIC) Study.

The longitudinal observational study has followed 5,499 patients at 13 U.S. recruiting sites since 2003 and includes a racially and ethnically diverse study population with extensive clinical CKD phenotypes and associated cardiovascular and metabolic comorbidities.

The information gained from this cohort has been incredibly helpful in advancing knowledge of CKD. For example, data from this cohort were used to assist the National Kidney Foundation-American Society of Nephrology Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Diseases in its final recommendations.

Cleveland Clinic nephrologists are now leveraging this rich dataset, alongside the clinical and molecular phenotyping data from the Kidney Precision Medicine Project (KPMP), a multicenter trial, to make advancements toward precision kidney medicine.

Jonathan Taliercio, DO, is leading this effort as principal investigator. He says the Cleveland CRIC-KPMP study combines the strengths of these landmark trials by recruiting CRIC participants from Cleveland Clinic, University Hospital and MetroHealth to undergo research kidney biopsies using KPMP protocols.

"We hope to identify novel biomarkers and therapeutic options that lead to a cure for kidney disease attributed to diabetes and hypertension, the two leading causes of CKD and progression to ESKD," he says.

RIGHT — Dialysis is often referred to as an expensive, outdated intervention; research efforts underway aim to improve therapies.

2021 HIGHLIGHT

IMPROVING OUTCOMES AND EXPANDING OPTIONS FOR BLADDER CANCER PATIENTS

For patients with muscle-invasive bladder cancer, neoadjuvant chemotherapy followed by radical cystectomy remains the mainstay for treatment.

Robotic radical cystectomy has steadily gained popularity as a minimally invasive alternative to open radical cystectomy. Currently, most urinary diversions after robotic cystectomy are performed using an open (extracorporeal) approach where an incision is made to exteriorize the bowel.

Cleveland Clinic surgeons, however, have increasingly standardized the use of intracorporeal urinary diversion. After robotic radical cystectomy, the urinary diversion is performed entirely using the surgical robot without any additional incision to exteriorize the bowel. While it is more technically challenging, the team adopted this approach as a way to make robotic radical cystectomy even less invasive for this frail patient population.

Assessing outcomes among surgical approaches

In 2020, a team led by Byron Lee, MD, PhD, published a study that examined perioperative outcomes at Cleveland Clinic for open radical cystectomy, robotic radical cystectomy with extracorporeal urinary diversion and robotic radical cystectomy with intracorporeal urinary diversion.

The study found that robotic radical cystectomy with intracorporeal urinary diversion outperformed the other approaches with respect to blood loss, length of stay and complication rates.

"These findings underscore the perioperative benefits of this technique, which we have understood anecdotally for years," says Dr. Lee, "but there were still questions regarding oncologic outcomes since robotic cystectomy is a relatively newer surgical approach, and muscle-invasive bladder cancer can exhibit very different biological behavior compared with other urologic cancers that we routinely manage robotically."

Dr. Lee and his team once again examined the experience at Cleveland Clinic to evaluate the center's oncologic outcomes of radical cystectomy as they relate to surgical approach. They found no differences in rates or patterns of cancer recurrence.

"These studies demonstrate that robotic cystectomy with intracorporeal urinary diversion is just as effective at cancer control as the other approaches but has significant perioperative benefits for the patient," says Dr. Lee.

Bladder preservation options for patients with muscle-invasive bladder cancer

Recognizing that bladder preservation may play an increasing role in the management of muscle-invasive bladder cancer, Nima Almassi, MD, is leading research to improve patient selection for this approach. One such option is partial cystectomy, a surgical treatment in which only the portion of the bladder that contains cancer is removed, often in conjunction with chemotherapy.

"Right now, only a very select group of patients qualify for this procedure, but we are actively investigating clinical characteristics and outcomes that may allow us to broaden the selection pool and offer a less-invasive approach to more patients," he says.

Cleveland Clinic is participating in a multicenter clinical trial examining the safety of bladder sparing in select patients with muscle-invasive bladder cancer who have a complete response to chemotherapy.

Studies have shown that patients with specific genetic changes in their bladder cancer respond very well to chemotherapy, many with no residual cancer identified after chemotherapy. In this trial, patients who have one of these specific genetic changes and a full response to chemotherapy are managed with surveillance, rather than undergoing cystectomy.

"Our goal is to provide as many novel options as possible to provide the best care for our patients," Dr. Almassi concludes.

LEFT — Byron Lee, MD, PhD, and team performing robotic radical cystectomy, bilateral pelvic lymphadenectomy and ileal conduit diversion.

TAKE A CLOSER LOOK

Our surgeon's view at the console during a robotic radical cystectomy. Cleveland Clinic has been at the forefront of robotic and image-guided surgeries as a technique to treat and improve outcomes for urologic, kidney and bladder cancers, kidney and pancreatic transplant, and other urologic procedures.

2021 UPDATES

The following updates from our subspecialty centers represent just a few highlights and accomplishments from 2021.

CENTER FOR RESEARCH IN KIDNEY DISEASE

The center is a major site for seven active multicenter trials in nephrology:

KPMP is designed to better understand and personalize treatment for chronic kidney disease (CKD) and acute kidney injury.

FIND-CKD is a randomized, double-blind, placebo-controlled, parallel-group, multicenter phase 3 study to investigate the efficacy and safety of finerenone to control CKD in select patients.

EMPA-KIDNEY is a randomized, double-blind, placebo-controlled trial to assess the effect of empagliflozin on cardio-renal outcomes in patients with CKD.

CRIC, now in its 4th phase of investigation, is a cohort study designed to understand the progression of CKD and its associations with cardiovascular disease.

NEPTUNE and **CureGN**, both focused on the multidisciplinary investigation of primary glomerular diseases, aim to discover molecular mechanisms associated with the disease and use this information to revolutionize classification and guide targeted therapies.

APOLLO is designed to investigate the impact of renal-risk variants in the APOL1 gene on outcomes in kidney donors and recipients with African ancestry.

CENTER FOR ENDOUROLOGY AND STONE DISEASE

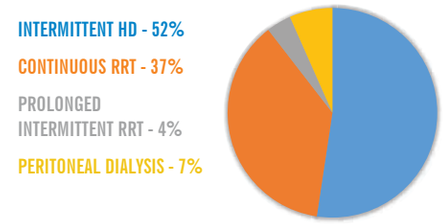
The center recently evaluated the role of smart technology in patient adherence and fluid management. The authors say their findings underscore the impact of patient-specific guidance for metabolic kidney stone management and reinforce the value of direct counseling for patients.

One of eight national centers that are part of the Urinary Stone Disease Research Network, the team continued enrollment efforts for the PUSH study (Prevention of Urinary Stones with Hydration).

CENTER FOR DIALYSIS

The Center for Dialysis has performed record numbers of procedures in 2021. To date, at main campus alone, the team of nephrologists, dialysis nurses and dialysis technicians have performed >20,500 procedures, including a variety of therapeutic modalities. In addition, the center has worked with Cleveland Clinic hospitals throughout the region to share expertise, devices and supplies during a time of nationwide shortages and increasing demands.

Dialysis Activity



CENTER FOR FEMALE PELVIC MEDICINE AND RECONSTRUCTIVE SURGERY

Center members are leading a multicenter, prospective trial examining aspects of pelvic floor support and sexual function in women undergoing female cystectomy.

"Most studies that are currently available focus on post-cystectomy function and disorders in male patients," says center Director Sandip Vasavada, MD. "We are hopeful that these outcomes will inform future patient counseling on these important aspects of women's health and quality of life following cystectomy."

Additional studies within the center are exploring microbial and metabolite byproduct composition of biofilms on implanted urologic devices, including sacral nerve stimulators, and how this composition is associated with clinical factors, including device-associated infection and pain.

CENTER FOR GENITOURINARY RECONSTRUCTION

The center is committed to being a resource for patients both regionally and nationally with routine and complex urological problems requiring reconstructive surgery. Center members are involved in leadership and teaching roles at national and international levels and place considerable emphasis on the training experience.

CENTER FOR MALE FERTILITY

Center Director Sarah Vij, MD, received a VeloSano Impact Award to fund a research project supporting fertility preservation in prepubertal males undergoing gonadotoxic treatments.

This is the only pediatric cancer patient population with no option for fertility preservation. The award will fund testicular tissue biopsy and storage at no cost to patients. "We are really excited about this and hope that we can offer it soon," says Dr. Vij.

Additionally, center members published a paper in *European Urology* exploring interactions between the gut and urinary microbiomes and male infertility.

CENTER FOR PEDIATRIC UROLOGY

The center continues to provide a full range of diagnostic and therapeutic interventions to our pediatric population, including more progressive and cutting-edge procedures:

- Testicular tissue cryopreservation for prepubertal males prior to undergoing gonadotoxic therapies.
- Single-port robotic reconstructive cases, such as pyeloplasties, in select patients.

Pain management in pediatric urology is an area of interest for the team, as they continue to partner with anesthesia colleagues to explore optimal care pathways and limit narcotic exposure in patients.

CENTER FOR MINORITY MEN'S HEALTH

The center's Minority Men's Health Fair has provided health and wellness information and health screenings to more than 35,000 men since 2003.

CENTER FOR MEN'S HEALTH

Two papers, led by center Director Petar Bajic, MD, were published in high-impact journals. One paper examined healthcare disparities risk factors for men presenting to the emergency room with ischemic priapism; the other proposed a surgical ergonomics guide for urologists.

Members have been recognized by the Sexual Medicine Society of North America and selected to investigate emerging research areas in men's sexual health, including the microbiome of penile prosthesis biofilms and the role of the gut microbiome in erectile dysfunction and PDE5 inhibition.

CENTER FOR RENAL DISEASES

Survivors of acute kidney injury (AKI) are at increased risk for developing long-term major adverse kidney events, but there is no clear protocol to prevent rehospitalization after discharge.

To address this, Emilio Poggio, MD, is leading the Cleveland COPE-AKI Clinical Centers trial, a five-year trial comparing outcomes between the standard of care and an intensive protocol. The goal is to enroll 500 patients between Cleveland Clinic and MetroHealth.

CENTER FOR ROBOTIC AND IMAGE-GUIDED SURGERY

The team performed more than 70 transvesical prostatectomies using the single-port robot, a first-of-its-kind approach. Patients are typically discharged a few hours after surgery with no narcotic required postoperatively.

The approach has decreased Foley catheter duration by almost 50%, and most patients have urine control immediately following prostate removal.

+11%

CENTER FOR KIDNEY AND PANCREAS TRANSPLANT

The team completed 300 kidney transplants in 2021, exceeding the program's 2020 record by 11% for highest transplant activity.

CENTER FOR UROLOGIC ONCOLOGY

The Genitourinary Malignancies Research Center published over 100 articles focused on advancing discoveries to better understand, diagnose and treat cancers of the prostate, bladder and kidney.

The team has treated its first 10 patients using high-intensity focused ultrasound (HIFU), a type of focal therapy for treating localized prostate cancer. The center acquired a Focal One system in 2021, making it one of very few sites locally and nationally to offer this technology.

In bladder cancer news, Byron Lee, MD, PhD, led the largest single-institution study comparing oncologic outcomes in patients undergoing three different surgical approaches to cystectomy.

Christopher Weight, MD, center Director, is the clinical lead for the International Kidney and Kidney Tumor Segmentation Challenge

NEW STAFF

In 2021, Cleveland Clinic welcomed Crystal Gadegbeku, MD, as the Department Chair of Kidney Medicine. Her strong academic and clinical leadership, activism in kidney disease research, and work to improve healthcare access for patients of color has positioned the department to lead a new era of innovation in kidney care.

"We are at a point where the field of nephrology needs disruptive thought and action for advancement," asserts Dr. Gadegbeku.

FAREWELL FROM ERIC KLEIN, MD

Author and biochemist Isaac Asimov said, "Education isn't something you can finish."

To which I would add, education is not something one should *want* to finish. This is the sentiment I take with me as I move on to the next phase of my life as a Fellow in the Distinguished Careers Institute of Stanford University, an opportunity that affords me the chance to continue a lifelong journey of academic pursuit.

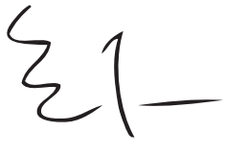
This is not the first time my wife and I have left Cleveland Clinic. In 1986, we headed to New York City after residency to begin our fellowship training. Reflecting on my training and looking ahead, literally and figuratively, as we crossed state lines, I told her I hoped to return and work at Cleveland Clinic one day. That day came several years later in July 1989. And now I can look back at 32 years of tenure with pride and appreciation.

I am grateful for the opportunity to have led the Glickman Urological & Kidney Institute and am incredibly proud of its success in all aspects of the program: clinical care, education, research, philanthropy — and of all the individuals who contribute to the culture of each.

I am particularly proud of our nephrology and urology trainees, all of whom have gone on to successful careers and many of whom have joined our team as faculty. I would also like to thank all the patients who placed their trust in me and my team—what an extraordinary privilege.

Moving on from a fulfilling decadeslong experience in Cleveland is very difficult, but I recognize how lucky that makes me. I will remain engaged with the institute during my sabbatical and look forward to its future success.

Gratefully,



Eric A. Klein, MD
Professor and Chair Emeritus

NEW STAFF

Glickman Urological & Kidney Institute welcomed these new staff members in 2021.

UROLOGY

Jorge Gutierrez-Aceves, MD
Hannah Kerr, MD
Ramesh Krishnamurthi, MD
Fernando Pablo Secin, MD
Zeyad Schwen, MD
Paul Chialastri, DO

KIDNEY MEDICINE

Liza Cholin, MD
Crystal Gadegbeku, MD

RESOURCES FOR PHYSICIANS

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CME Opportunities
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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. 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.

Year in Review

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