Klinefelter syndrome is the most common genetic cause of male infertility, and new fertility preservation strategies are critically important for these patients. Klinefelter syndrome – which affects 1 out of every 650 males born – is characterized by a masculine phenotype, supernumerary sex chromosomes (usually XXY), and spermatogonial stem cell loss in early development.

The Urology Department's Male Fertility Research Group, in cooperation with the Wake Forest Institute for Regenerative Medicine, utilized an XXY mouse model for a recent study of Klinefelter syndrome. Testicular cells from frozen-thawed testes of a prepubertal animal model were used. The data demonstrated that spermatogonial stem cells survived and were able to be propagated with testicular somatic cells in culture for up to 120 days. DNA fluorescent in situ hybridization showed the presence of XXY spermatogonia at the beginning of the culture and a variety of propagated XY, XX, and XXY spermatogonia at the end of the culture.

“We have published the first evidence that an extra sex chromosome was lost during innate spermatogonial stem cells in vitro propagation, a crucial finding in treating Klinefelter syndrome patients for preserving and propagating spermatogonial stem cells for future sperm production, either in vitro or in vivo,” said Hooman Sadri, MD, PhD, lead scientist on the paper. “This in vitro propagation system can someday be translated to clinical fertility preservation for Klinefelter syndrome patients.”

Sadri said the team hoped this latest research will open the door to pursue new cell-based therapies to treat infertility in Klinefelter syndrome patients. The growing mosaicism observed in the cells in culture may lead to a better understanding of the stem cell selection dynamics in the Klinefelter patient's testes.

This study, “In Vitro Propagation of XXY Undifferentiated Mouse Spermatogonia: Model for Fertility Preservation in Klinefelter Syndrome Patients,” was recently published in the International Journal of Molecular Sciences, doi.org/10.3390/ijms23010173.

Authors include: Guillermo Galdon, Nicholas A. Deebel, Nima Pourhabibi Zarandi, Mark J. Pettenati, Stanley Kogan, Christina Wang, Ronald S. Swerdloff, Anthony Atala, Yanhe Lue, and Hooman Sadri-Ardekani.
Optimal timing of a second postoperative voiding trial in women with incomplete bladder emptying after vaginal reconstructive surgery: a randomized controlled trial
Schachter S, Draelos P, Plair AR, Hurstado EA, Parker-Austen B, Baillie G, Davila GR, Matthews CA

The optimal length of time for postoperative catheter drainage has not been clearly established. This study aimed to compare the outcomes of a second postoperative voiding trial at 2-4 vs. 7 days after vaginal reconstructive surgery in women with incomplete bladder emptying after vaginal prolapse surgery.

Results showed that women with incomplete bladder emptying after multiparametric complicate repair had a 7-fold higher risk of an unsuccessful repeat office voiding trial if performed within 4 days of surgery than when performed within 7 days. In addition, requiring additional prescriptions for analgesia increased the risk of an unsuccessful follow-up office voiding trial.


Pulsed electromagnetic field as an adjuvant therapy for pain management in interstitial cystitis/bladder pain syndrome

Patients with interstitial cystitis/bladder pain syndrome (IC/BPS) often experience pelvic and even systemic pain that can be difficult to manage. Pulsed electromagnetic field (PEMF) therapy, a non-invasive strategy that has shown significant efficacy for pain reduction in other chronic pain conditions, was evaluated. The present discovery that a subset of IC/BPS and fibromyalgia patients has underlying PEMF-responsive pain is significant. PEMF represents a low-risk high-reward discovery that a subset of IC/BPS and fibromyalgia patients that has shown significant efficacy for pain reduction in other clinical trials.


Chemokine therapy in cats with experimental renal fibrosis and in a kidney disease pilot study
Bennetton contracted study PI: Catherine Paré, MD

Permanently compared with absorbable suture for vaginal mesh fixation during total hysterectomy and sacrocolpexy: A meta-analysis

Across five US centers, 204 women were randomized to permanent or absorbable suture for vaginal attachment of a ‘Y’ mesh during hysterectomy and sacrocolpexy for stage II prolapse and worse. The primary outcome was mesh or permanent suture exposure in the first 24 weeks. The second outcome was to compare a composite measure for success defined as leading edge of prolapse not beyond the hymen and apex not descended more than one third vaginal length, and no subjective bulge and no prolapse retreatment. Results found that suture type did not influence mesh or permanent suture exposure rates.


Sustained glycinergic control observed in diabetic men who improve hemoglobin A1c values to allow for elective penis prosthesis placement
Guthery KA, Thomas GM, Cowper M, Chouhan JD, Thakker PJJ, Patila ET, Dutta R, Terlecki RP

This study sought to determine that men with diabetes mellitus whose inflatable penile prosthesis (IPP) implantation is delayed for unacceptably high hemoglobin A1c (HbA1c) will have durable improvements in their glycemic control after achieving acceptable HbA1c levels for surgery. Our results suggest requiring men to meet health-related targets prior to elective IPP surgery may contribute to a durable health benefit. It is conceivable that regulating the potential for ventilatory and performance improvements in activity (sexual or otherwise), potentially improved confidence/self-image, and an improved overall health. IPP implantation appears safe in diabetic men with periporative HbA1c values <9%.

Urology. 2020 Dec; 141-142.144.

Salve penile plication is an effective strategy for resolving residual curvature after surgery for Peyronie’s Disease
Deebel NA, Scarberry K, Dutta R, Matz E, Terlecki RP

Patients with residual or delayed recurrence of curvature after plication can be effectively managed with salve plication. Care should be provided to help patients set reasonable preoperative expectations and to identify risk factors for surgical care including severe and/or multiplanar curvature, as well as baseline erectile dysfunction.


Administration of secreton from human placental stem cell-conditioned media improves erectile function in the pelvic neurovascular injury model

We tested the hypothesis that bioactive factors secreted by human placental stem cells (PSCs) could mediate functional recovery and that acellular-conditioned media (CM) from PSC culture (PSC-CM) could be used to improve oxidative stress in injured and histological recovery. To identify factors secreted to efficacy of PSC, a comparison of CM from PSC conditioned and unconditioned cell populations was performed. Injection of the secreton isolated from human PSC improves erectile functional recovery and histological structure in a rat model of chronic spinal injury and histological recovery. To identify factors secreted to efficacy of PSC, a comparison of CM from PSC conditioned and unconditioned cell populations was performed. Injection of the secreton isolated from human PSC improves erectile functional recovery and histological structure in a rat model of chronic spinal injury.


RARP: Prospective trial evaluating return to continence and quality of life for patients using umbilical cord allograft - PI: Askii L, Hemal, MD

The goal is to determine the effectiveness of using human umbilical cord allograft to help improve return to erectile function and bladder control in patients following robot-assisted radical prostatectomy.

The effect of Tamsulosin on Postoperative Urinary Retention - PI: Majid Mirzazadeh, MD

Postoperative urinary retention is a significant postoperative complication in 14-15% of all surgeries and 21-50% following radical prostatectomy. The purpose of this research is to help determine if starting Tamsulosin 5 days prior to addressing for complications, specifically with the native tissue repair, will help decrease the chances of going home with a bladder catheter, same day of surgery, and continuation for 5 more days after surgery to reduce retention of urine in the near future.

The SIAP Study - PI: Candace Parker-Autor, MD

The purpose of this trial is to apply gold-standard randomization to evaluate concomitant perineumorrhaphy during a vaginal reconstructive pelvic organ repair surgery to understand its impact on female sexual function and the heterosexual sexual relationship counseling for the unique complexity of female and male sexual dysfunctions.

ROSII - PI: Hooman Sadri, MD

Round Spermatic Injection (RSI) to fertilize oocytes is not a brand-new technology; however, it is plagued with notoriously low efficacy. Despite this report of positive results from most of these patients still desire to have the RSI procedure performed. The purpose of the study is to provide detailed information on clinical outcomes and injection of round spermatic into activated oocytes.
Female Pelvic Medicine — a Truly Collaborative Effort to Benefit Patients

Wake Forest Baptist was the first medical center to create a combined service unit that brings together both urologists and gynecologists with their primary faculty appointments in the Department of Urology, allowing the team to be fully aligned in terms of its mission and scope, treating patients in the same physical space — a center of excellence focused on female pelvic medicine and reconstructive surgery.

“Very few departments are set up the way we are, with both urologists and gynecologists together in the same physical space, utilizing the same staff. Each one of us brings something different,” said Gopal Badlani, MD, professor of urology who serves as co-director of the joint service line for Female Pelvic Medicine.

The clinical infrastructure of Female Pelvic Medicine is made up by two board certified urogynecologists from ob/gyn, two board certified urologists in female pelvic medicine — one of whom had expertise in in neuro-urology and one in bladder pain syndrome — and a urologist with expertise in recurrent urinary tract infections. The team provides coverage in all breadth of disease states, as well as different aspects of surgery - vaginal, robotic, open, and endoscopic. Major conditions treated include:

- Incontinence
- Fecal incontinence/bowel incontinence
- Pelvic organ prolapse
- Painful bladder/badder syndrome
- Overactive bladder
- Recurrent urinary tract infection
- Vaginal mesh complications
- Pelvic pain
- Viscovaginal fistula
- Rectal vaginal fistula

The team of providers, who have different areas of subspecialty expertise, is uniquely qualified to manage female pelvic health for patients who need true multidisciplinary care. The team performs a full array of diagnostic and therapeutic interventions including video urodynamic testing, anorectal manometry, pelvic floor ultrasound, flexible cystoscopy, intravesical injections and installations, vaginal laser therapy and pelvic floor physical therapy.

“While our structure is unusual, it is beneficial to patients,” said Catherine A. Matthews, MD, professor of urology and gynecology, who serves as director of the joint service line. “We are able to really push the envelope in terms of clinical care of stress incontinence, bladder pain syndrome and recurrent urinary tract infection. Because of our strengths in these areas and the attraction of patients, we have also been able to build a robust clinical trial division where we’re able to study the success of different surgical procedures.”

Female Pelvic Medicine is expanding its clinical operations across the region and continued growth will be supported with the addition of providers in neurourology and female reconstruction with urinary diversion. Matthews and Badlani are intent on strengthening Wake Forest Baptist as the premier referral site in the south Atlantic for complex patients with pelvic floor disorders.

The collaborative structure of the unit has also enhanced the general urology residency training program in regards to female urology, said Candace Parker-Autry, MD, assistant professor of urology. “We feel it’s a huge strength that urinary tract infections, bladder pain syndrome and recurrent urinary tract infection. Because of our strengths in these areas and the attraction of patients, we have also been able to build a robust clinical trial division where we’re able to study the success of different surgical procedures.”

The construction of the fellowship is complimentary to the mission of the medical center – to advance knowledge, promote secondary education, and develop new treatments and cures.

“One of the benefits of a fellowship training program is that we can advance the knowledge of the next generation of physicians who are going to be taking care of these highly specialized patients,” said Matthews, who directs the fellowship program. “We can provide a very comprehensive training experience, as well as a unique research opportunity. These two experiences together give the fellows the opportunity to help advance the science with us and provide excellent patient care.”

The program also offers a fellowship program. The Female Pelvic Medicine and Reconstructive Surgery Fellowship is a three-year subspecialty-training program for obstetrics and gynecology physicians and a two-year program for urology physicians who wish to specialize in urogynecology and reconstructive pelvic surgery. The program offers unprecedented training experiences for complex pelvic floor re-constructors - under the guidance of faculty experts in female urology, urogynecology, and colorectal surgery - and opportunities to conduct cutting edge translational research.

The program includes 12 months of research at the Wake Forest Institute for Regenerative Medicine, a leader in translating scientific discovery into clinical therapies.

Wake Forest Institute for Regenerative Medicine, a leader in translational research, is a critical component of the fellowship program. The Female Pelvic Medicine and Reconstructive Surgery Fellowship is made possible by a $5 million grant from the National Institutes of Health's National Institute on Aging. The fellowship program is designed to train fellows in the areas of translational research and clinical expertise.

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Clinical Expertise + Translational Research + Interstitial Cystitis (IC)

Long before there was a Female Pelvic Health service unit, there was a pelvic health research group. Dr. Badlani represented the clinical side and worked with faculty researchers at the Wake Forest Institute for Regenerative Medicine (WFIRM) on a number of pelvic health projects. Following the arrival of Dr. Robert Evans, one of the country’s leading clinical experts for IC, the group won a small grant from the Interstitial Cystitis Association, and from there, the IC research activities have expanded even further as more substantive grants have been awarded from the National Institutes of Health and the Veterans Administration.

“It’s an interesting disease to study because it’s very complex. It is not well defined,” said Dr. Robert Evans, professor of urology and gynecology. “You rule out everything else and you end up with a diagnosis of IC, which unfortunately is a lifelong, chronic condition that varies in severity depending on the person.”

Evans’ IC expertise results in Wake Forest Baptist’s Female Pelvic Medicine program being a tertiary referral center with a very large database and patient tissue bank with more than 550 bio samples and database. This resource enables the team to conduct a variety of analyses on the patients they already have. From basic science projects to clinical trials, the IC research is looking for answers on how to treat the disease and perhaps cure it.

“Conditions such as peripheral neuropathy and cryptic bacteria embedded in the bladder wall may be triggers of some sort,” Evans explained. “We are trying a wide range of treatments, from acne vera formulations to the use of pulsed electromagnetic field therapy to reduce pain.” (see study summary on pg 22)
Meet Our Faculty

Anthony Atala, M.D., FACS, professor and chair, is section editor for Urological Surgery, for the Journal of Urology, and a fellow of the Transplantation Society. He is a recipient of the Gold Cystoscope Award, the Raymond and Ruth Ackerman Award, and the Barringer Medal from the American Urological Association. His work in tissue engineering and the creation of organ tissues has impacted his contributions to the field of urology. He is a member of the National Academy of Medicine and is one of 98 innovators named a charter fellow of the National Academy of Inventors. He is editor of 30 books and has published over 700 journal articles.

Robert J. Evans III, M.D., FACS, professor of urology and gynecology, directs the department's clinic operations. He specializes in genitourinary surgery, including the medical advisory boards of the Interstitial Cystitis Association and the International Bladder Support Network. He is involved in several clinical trials and NIH-funded studies evaluating the role of biofeedback therapy and pelvic floor dysfunction. In addition, he is part of a genomics study to identify biomarkers for the diagnosis of colorectal cancer. The Foundation selected him to provide oversight on patient education materials related to bladder pain, and he is named the UBCB Department of Urology's 2018 urology chair.

Laura Foster, M.D., practices general urology and has special interests in treating voiding dysfunction/inefficiency, urinary tract infections and kidney stones. She earned her medical degree from the University of Florida College of Medicine, Chapel Hill, and completed her residency in General Surgery and also Urology at UNC.

Ashok K. Hemal, M.D., MCH, FACS, professor, serves as director of the Robotics and Minimally Invasive Surgery Program and chairs the Section of Urology. He is known for his pioneering work in the field of uro-urology, robotic and pure laparoscopic surgeries, developing several surgical techniques. He is principal or co-investigator on several research projects at the Wake Forest Comprehensive Cancer Center and the Institute for Regenerative Medicine. He has published more than 400 scientific papers in peer-reviewed journals and edited seven books, including the second edition of Robotics in Genitourinary Surgery. He is the recipient of many academic distinctions currently serving as associate editor of the Journal of Endourology, the editorial board of Urologic Robotic Surgeons.

Steve Hodges, M.D., associate professor, specializes in pediatric urology and is recognized for the prevention of urinary infection and scar disease throughout the urinary tract, and dysfunctional elimination. He has developed several new treatments, including drug-coated catheters and stents designed to prevent or treat urethral strictures, and drug-coated wires to prevent vesicoureteral reflux and urinary tract infections in females. He has co-authored 10 books on toilet training and voiding dysfunction.

Stuart Howard, M.D., FACS, professor, is nationally recognized expert in male infertility. He specializes in microsurgical and assisted reproduction and female pelvic medicine and sperm retrieval. He has served on the editorial board of Human Reproduction since 1988, and has more than 1,500 scientific review papers. Howard serves as executive secretary of the American Board of Urology for 15 years, and at the NIH as the urologic advisor to the director of the National Institute of Diabetes and Digestive and Kidney Diseases. In 2011, he was elected as president of the Society for Urologic Robotic Surgeons.

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John D. McConnell, M.D., FACS, is the Gordon Hanes Professor and Residency Program Director. He is a recipient of the AUA Gold Cystoscope Award and the American Association of Genitourinary Surgeons' Barringer Medal for his contributions to the urology field. McConnell's research in the field of prostate disease and related health policy contributions led to his 2004 election to the National Academy of Medicine. He has served on the board of directors of the American Urological Association, an interest that led to the Medical Advisory Board. He is a fellow of the American College of Surgeons.

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In a course designed for the practicing urologist and healthcare provider, thought leaders in urology discuss the latest evidence-based approaches to managing a wide range of urologic conditions, from stone disease to incontinence, pelvic health, sexual dysfunction, infertility, common pediatric conditions, and cancer. A presentation of practical topics, patient cases, and panel discussions, mixed with networking and the beautiful setting of the North Carolina mountains with its renowned foliage.

Asheville is a city known for a vibrant arts scene, historic architecture, the Biltmore Estate, premier golf courses, breathtaking scenic vistas and the highest peaks of the Appalachian mountains, making for an outdoor destination perfect for all-season exploration.

Social Media Keeps Us Connected
Please check us out on Twitter and Facebook.

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To learn more about our clinical trials or to refer patients, please contact BeInvolved at www.wakehealth.edu/BeInvolved.