

## SECTION OF UROLOGY

### FACULTY

#### *Professor and Chief of Section*

Robert M. Weiss, M.D. (SUNY-Downstate Medical Center) Donald Guthrie Professor of Surgery

#### *Professor*

Bernard Lytton, M.B., F.R.C.S. (University of London) Donald Guthrie Professor Emeritus of Surgery

Morton G. Glickman, M.D. (Washington University) Uroradiology, Emeritus

Arthur T. Rosenfield, M.D. (NYU School of Medicine) Uroradiology

Stuart Flynn, M.D. (University of Michigan) Uropathology

#### *Associate Professor*

Harris E. Foster, Jr., M.D. (University of Miami School of Medicine)

Kevin R. Anderson, M.D. (University of California, San Diego)

John W. Colberg, M.D. (Washington University)

#### *Assistant Professor*

Edward M. Uchio, M.D. (University of California, Irvine)

#### *Associate Clinical Professor*

Richard P. Lena, M.D. (Tufts University)

#### *Assistant Clinical Professor*

Arnold M. Baskin, M.D. (Albany Medical College)

D. Card, M.D.

Richard J. Dean, M.D. (Georgetown University)

Robert A. Feldman, M.D. (Albert Einstein College of Medicine)

Paul A. Kraus, M.D. (McGill University)

Ralph F. Stroup, M.D. (University of Rochester)

James F. Walsh, III, M.D. (Jefferson Medical College)

#### *Clinical Instructor*

Joseph P. Antoci, M.D. (Georgetown University School of Medicine)

Thomas Buckley, M.D. (Harvard University School of Medicine)

Joseph A. Camilleri, Sr., M.D. (Yale University School of Medicine)

Joseph A. Camilleri, Jr., M.D. (New York Medical College)

Peter Demir, M.D. (New York Medical College)

Ralph J. DeVito, M.D. (Albany Medical College)

Michael Flanagan, M.D. (Rutgers Medical School)

David G. Hesse, M.D. (University of New Mexico School of Medicine)

Thomas V. Martin, M.D. (University of Connecticut Medical School)

James P. Roach, M.D. (New York Medical College)

#### *Instructor (Chief Resident)*

David Shin, M.D. (Cornell Medical School)

Joseph Lee, M.D. (Eastern Virginia School of Medicine)

#### *Resident*

Derek Hausladen, M.D. (Washington University)

Anthony Kim, M.D. (Boston University)

M. Grey Maher, M.D. (Yale University School of Medicine)

Margarett Shnorhavorian, M.D. (University of California, San Francisco)  
Charles Walker, M.D. (Cornell Medical School)  
Joseph Renzulli, M.D. (Boston University School of Medicine)

*Senior Research Scientist*

Jamshid Latifpour, Ph.D. (University of Missouri)

*Postdoctoral Associate*

Wataru Takahashi, M.D., Ph.D. (University of Kumamoto, Japan)  
Makoto Yono, M.D., Ph.D. (University of Kumamoto, Japan)  
Daniel Eisenberg, M.D. (Washington University)  
Frank Tamarkin, M.D. (MCP Hahnemann School of Medicine)

*Research Affiliates*

Piero Biancani, Ph.D. (Yale University)  
George L. Wheeler, Ph.D. (University of Maryland)

*Associate in Research*

Marcia Wheeler, M.S. (University of Maryland)

## **MISSION STATEMENT**

The Section of Urology of the Yale University School of Medicine/Yale-New Haven Medical Center will exploit its areas of competence to maintain its position as one of the leading academic urologic units in the nation. We will offer the Southern New England Community a balance of expertise in the following urologic subspecialties: oncology, pediatrics, neurourology and female urology, the management of stone disease, and minimally invasive urologic surgery. Our main strength is our ability to focus our attention on these specific target areas in which we can channel our portfolio of assets into both the training and the performance of surgical procedures and into providing continuing education in developmental areas, both in the clinical and research arena. Our benchmark studies on signal transduction in urinary tract smooth muscle, and in inflammatory and neoplastic conditions affecting the urinary system, and the skill sets of a strong investigational team of basic scientists and clinicians will permit us to achieve our goal. That is, to improve our understanding of normal urinary tract function and the changes which occur with aging and pathologic processes, i.e., diabetes, cancer, and inflammatory processes involving the urinary tract. Our vision includes the ultimate development of new and innovative therapeutic protocols for the management of these disorders. Our guiding values will be effective communication, high ethical conduct, scientific excellence, clarity of direction and the recognition of the value of our personnel. By interfacing with other strong divisions and departments in the Yale community, i.e., pediatrics, nephrology, pathology, anesthesiology, radiology and pharmacology we will maintain and improve our ability to keep up with the advancements in urology which in turn will be of benefit to our patients. The overarching goal is an advancement and formation of a strong department of urology that will be at the forefront of clinical and laboratory research and that will be a leader in the development of innovative clinical programs.

## **OVERVIEW**

During the past academic year the Section of Urology has continued to maintain its position as one of the leading academic urologic units in the nation as evidenced by its being listed as one of the best urologic programs in the United States in US News and World Reports. The section continues to make contributions to Education, Research and Clinical Care. The teaching mission of the section continues to be considered one of the best by Yale medical students and the faculty, both university and community, and residents consider this to be a most important mission. Members of the section maintain active NIH supported research projects. The section continues from a clinical standpoint to focus its efforts in specific urologic subspecialties: oncology, pediatrics, neurourology and female urology, the management of stone disease and minimally invasive surgery. The efforts of the section have been rewarded by recognition of its

members on numerous editorial boards, on NIH research committees, on the American Board of Urology, and by publications in well peer-reviewed journals.

## ACCOMPLISHMENTS

**Robert M. Weiss, M.D.**, Donald Guthrie Professor of Surgery, is a trustee of the American Board of Urology. He is a member of the Editorial Board of the Investigative Urology Section of the Journal of Urology. Robert Weiss is a member of a NIH Advisory Panel on, "Future Directions in Clinical Research in Interstitial Cystitis," Chair of the External Advisory Committee of the NIDDK on Interstitial Cystitis and a fellow of Timothy Dwight College at Yale. During the last year he chaired two NIH program project grant site visits, one at the University of Maryland and one at the Albert Einstein School of Medicine. Dr. Weiss is President-Elect of the Medical Board of the Yale-New Haven Hospital.

**Bernard Lytton, M.D.**, Donald Guthrie Professor Emeritus of Surgery, is the Director of The Pierpont Center for Emeritus Faculty at Yale University.

**Harris E. Foster, Jr., M.D.** is Director of Neurourology and Female Urology, Chairman of the National Institutes of Health Interstitial Cystitis Clinical Research Network (ICCRN), and is Principal Investigator on a multicenter NIH grant to study the effects of phytotherapy on benign prostatic hypertrophy. His co-investigator is Kevin R. Anderson, M.D., and Terry Martin, R.N. is the nurse coordinator. He is also a co-investigator on a NIH grant studying the effects of diabetes on bladder function and prostatic growth with Dr. Jamshid Latifpour. Dr. Foster has been a faculty member for the American Urological Association sponsored urodynamic course for the past several years. Harris Foster is a fellow at Berkeley College at Yale.

**Kevin R. Anderson, M.D.** continues to serve as the Director of Urologic Laparoscopy and Endourology. Under his direction as the Chief of Urology at the Veterans Administration Medical Center, West Haven, the service has been expanded to include the Newington campus. Clinical activities have expanded to include hand-assisted laparoscopic radical nephrectomies as well as laparoscopic orchidopexy and laparoscopic cryoablation of renal tumors. He is responsible for lectures to the first, second and third year medical students and is on the curriculum committee for anatomy and human sexuality. He is coordinator for the genitourinary exam for second year students. Dr Anderson serves on the OR Committee and is Chairman of the OR Formulary Committee of the Yale-New Haven Hospital. His clinical research efforts include studies on helical CT as a diagnostic tool, and a NIH study of medical management for BPH with Dr. Foster.

**John W. Colberg, M.D.** is the Director of Urologic Oncology and has an active clinical practice dealing with all aspects of urologic oncology and reconstructive urology. He is the Principal Investigator on two grants dealing with prostate cancer and one grant dealing with bladder cancer.

**Edward M. Uchio, M.D.** has been recruited to take over as Chief of Urology at the VA beginning in July 2003. Dr. Uchio took his urology residency at the University of Washington in Seattle and subsequently spent two years as a urologic oncology fellow at the NIH, National Cancer Institute, where he worked with W. Marston Linehan. He will develop a basic urologic oncology laboratory to study molecular pathways of the von Hippel Lindau (VHL) tumor suppressor promoter. Dr. Uchio brings to Yale laparoscopic expertise as it pertains to oncologic pathology.

## RESEARCH PROGRAMS

A research group, headed by Robert Weiss, Jamshid Latifpour, and Marcia Wheeler, possesses a NIH research grant on, "Age-dependent factors in ureteral-vesical function." This grant previously received the first merit award given by the NIH to a urologist. Jamshid Latifpour has a NIH research grant on, "The effects of diabetes in the urinary tract: biochemical and functional changes in diabetic bladder." In association with Dario Altieri, Professor of Pathology, the group has demonstrated the expression of survivin, an anti-apoptotic gene, in transitional cell bladder cancers and showed its potential as a urinary

marker for bladder cancer. Based on this, Marcia Wheeler and Robert Weiss are involved in studies as to how bladder inflammation regulates survivin and apoptosis. Edward Uchio is starting studies of RNAL, based knockdown of the von Hippel Lindau Gene in angiogenesis and tumorigenesis. During the past year, the following individuals contributed to these studies: Harris Foster, M. Grey Maher, Piero Biancani, Mehdi Pouresmail, Derek Hausladen, Walter Kang, Wataru Takahashi, Daniel Eisenberg, Frank Tamarkin, Makoto Yono, Parviz Afiatpour, Justin Cohen, Christopher Cutie, and George Wheeler. The Section of Urology has a slot in a NIH Training Grant in which Dr. Peter Aronson, Professor of Internal Medicine, Section of Nephrology, is the Principal Investigator. The trainees are Daniel Eisenberg and Frank Tamarkin.

**Jamshid Latifpour** leads a group whose primary interests are in receptor mechanisms in urinary tract smooth muscle. They continue their work on the effects of aging and diabetes on receptor mechanisms and receptor G-protein coupling in urinary tract smooth muscle. A specific emphasis has been directed toward the role of endothelins and polypeptide growth factors in diabetic vesicle dysfunction and in prostate growth.

**Marcia Wheeler and Robert Weiss** continue their studies of the role of nitric oxide in inflammatory processes affecting the urinary tract. They were the first to document nitric oxide synthase (iNOS) activity in human inflammatory cells (neutrophils). In association with Dario Altieri, Professor of Pathology, they have showed that survivin, an anti-apoptotic gene, can serve as a marker of bladder carcinoma. Marcia Wheeler and Derek Hausladen have shown that urinary survivin levels correlate with prognosis in patients with transitional carcinomas of the bladder treated with intravesical BCG or mitomycin C.

To determine how bladder inflammation regulates survivin and apoptosis, Dan Eisenberg, using an uroplakin promoter, has established colonies of mice that over-express human survivin or a phosphorylation defective mutant survivin. A small percentage of the mice who express large amounts of survivin have died of bladder cancer. This is an exciting finding since over-expression of an oncogene usually does not cause overt cancer.

**Bernard Lytton**, with the collaboration of Harris Foster and John Colberg, continues his clinical studies of continent urinary diversion. Harris Foster and Bernard Lytton are investigating the mechanism of micturition in patients who have undergone orthotopic neobladders to the urethra.

**John Colberg** is engaged in two double-blind studies involving Casodex funded by Astra-Zeneca Pharmaceuticals and a national phase II trial of interferon alfa 2B plus BCG for treatment of superficial bladder cancer funded by Schering Pharmaceuticals.

**Harris Foster** is involved with research evaluating the effect of phyto therapy on the progression of benign prostatic hyperplasia. He is a Principal Investigator on this NIH sponsored multicenter clinical trial. He also is collaborating with Jamshid Latifpour to identify changes in autonomic and hormone receptors in the prostate, particularly their response to medical therapy for benign prostatic hyperplasia. They are studying the effects of alpha adrenergic antagonists on alpha-1 adrenergic receptors in the rat prostate with hopes of furthering knowledge on how these agents affect progression of BPH in humans.

**Kevin Anderson** is a co-investigator with Dr. Foster on the NIH grant to study the medical management of BPH. He is also involved in studies of clinical outcome in laparoscopic surgery in adults and children.

## GRANTS

AGE DEPENDENT FACTORS IN URETERAL-VESICAL FUNCTION  
U.S.P.H.S. Grant 5 R37 DK 38311 (21-25)  
9/15/99 – 6/30/04  
Institute of Diabetes and Digestive Diseases and Kidney Diseases  
P.I.: Robert M. Weiss

**BIOCHEMICAL AND FUNCTIONAL CHANGES IN DIABETIC BLADDER**

NIH Grant R01-DK-42530 (09-12)

9/15/01-8/31/05

P.I.: Jamshid Latifpour

**NITRIC OXIDE TRANSDUCTION MECHANISMS IN UTIS AND IC**

NIH Grant 1R01 DK 47648 (05-08)

3/01/98-2/28/03

P.I.: Robert M. Weiss

**URINE & BLADDER MARKERS OF INTERSTITIAL CYSTITIS**

NIH RFA Grant # RO3469

P.I.: Deborah Erickson

Penn State University

Investigator: Marcia Wheeler

**PHYTOTHERAPY FOR THE TREATMENT OF BPH SYMPTOMS**

NIH/NIDDK5 U01 D063862

P.I.: Harris Foster

9/03-3/10 Total award \$2,288,000.

**A RANDOMIZED DOUBLE-BLIND COMPARATIVE TRIAL OF BICULATAMIDE (CASODEX) VERSUS PLACEBO IN PATIENTS WITH EARLY PROSTATE CANCER**

Astra-Zeneca Pharmaceuticals

P.I.: John W. Colberg, M.D.

**A RANDOMIZED DOUBLE-BLIND COMPARATIVE TRIAL OF BICULATAMIDE (CASODEX) 150 MG VERSUS PLACEBO EACH IN COMBINATION WITH CASTRATION AS SECOND-LINE THERAPY FOR PATIENTS WITH ASYMPTOMATIC METASTATIC PROSTATE CANCER**

Astra-Zeneca Pharmaceuticals

P.I.: John W. Colberg, M.D.

**A NATIONAL PHASE II TRIAL OF INTERFERON ALFA 2B (INTRON A) PLUS BCG FOR TREATMENT OF SUPERFICIAL BLADDER CANCER**

Schering Pharmaceuticals

P.I.: John W. Colberg, M.D.

**CLINICAL PROGRAMS**

Dr. John Colberg heads a Prostate Disease Center to deal with all aspects of malignant and benign disease affecting the prostate at Yale. This is a multidisciplinary program. Dr. Colberg heads up the arm dealing with prostatic carcinoma. This aspect of the program is closely associated with the Yale Cancer Center. Dr. Harris Foster heads the arm dealing with benign prostatic hypertrophy, and Dr. Kevin Anderson heads the arm dealing with non-pharmacologic alternative managements in the therapy of prostatic disease. The center is involved in clinical trials and brings forth the latest developments in the diagnosis and therapy of prostatic disease to the community. Multidisciplinary groups deal with the diagnosis and management of prostatic carcinoma, and a NIH-sponsored has just been completed comparing the efficacy of alpha blockers, 5 alpha reductase inhibitors, or a combination of both in the management of benign prostatic hypertrophy. Dr. Foster is currently involved in an NIH sponsored multicenter clinical trial designed to investigate the effectiveness of phytotherapies on the progression of BPH.

A clinical program dealing with endourologic and extracorporeal shock wave treatment of urinary calculi remains an important endeavor of the urology section. Dr. Kevin R. Anderson, who received his endourologic and laparoscopic training with Dr. Ralph Clayman at Washington University in St. Louis, is the director of this program. Dr. Anderson is involved in advancing minimally invasive surgery in urologic patients. In 2001 performed the first laparoscopic donor nephrectomy at Yale.

Dr. John W. Colberg, Director of Uro-oncology, took his urology residency at Yale and returned to the Yale faculty after spending eight years at the Washington University in St. Louis. Drs. Bernard Lytton, John Colberg, and Harris Foster are actively involved in the reconstructive urologic aspects of the section.

Dr. Kevin Anderson together with Dr. Ervin Jones in Reproductive biology participate in a multidisciplinary program to treat men with severe male factor infertility. Using percutaneous epididymal sperm aspiration and testis biopsy, intracytoplasmic sperm injection has been successful in achieving fertilization in infertile couples.

The pediatric urologic aspect of the section is headed by Dr. Robert Weiss. Dr. Weiss was one of the first to use laparoscopy in the diagnosis of the non-palpable testis and he assists Kevin Anderson in expanding the role of laparoscopy in the management of pediatric urologic disease.

Dr. Harris Foster continues his involvement with the Gaylord Rehabilitation Hospital in assisting them with the evaluation and management of patients with vesicourethral dysfunction. He and Dr. Weiss also are involved in a program providing urologic care to spina bifida patients. Dr. Foster provides the majority of urologic care at the Yale Health Plan.

## **EDUCATIONAL PROGRAMS**

The Section of Urology has five full-time and seventeen part-time urologic members of the faculty who provide an in-depth educational program for both the medical students and residents-in-training. In addition, there are two Professors of Radiology and one Professor of Pathology who have joint appointments in Urology, and there is an active research staff. Close affiliations with the Veterans Administration Medical Center, staffed by the full-time faculty, and with the Waterbury Hospital, staffed by part-time members of the faculty, continue to be an integral and valuable part of the residency training program.

In addition to the regular weekly clinical and radiologic conferences, there is an active journal club, which meets each month, a series of basic science lectures, a monthly pediatric urology conference, a bi-weekly uro-oncology conference, monthly urodynamic and urolithiasis conferences. There is also a pathology course for the residents, with lectures given monthly throughout the academic year by Dr. Stuart Flynn, Professor of Pathology and Surgery/Urology. Morbidity and Mortality Conferences are held each month. The ongoing undergraduate course is a two-week elective which is always well attended and extremely popular with the medical students. Longer sub-internships also are available for medical students from Yale and other institutions.

The urology residency program accepts two residents each year for three years of clinical urology training. This follows two years of a basic surgical program. There also is a two-year NIH sponsored research training grant slot available on an elective basis. Opportunities for research are available either with the full-time members of the urology faculty or with investigators in other departments in the medical school. One resident spends a preliminary six months in laboratory research prior to beginning the clinical assignments. The other resident spends the first six months on the University service at the Yale-New Haven Hospital and the second six months at the West Haven Veterans Administration Medical Center. The resident who elects six months of laboratory research follows at the Yale-New Haven Hospital in the second six months of the year and then follows the same stepwise progression through the training program as his or her predecessor. During the second year of clinical urologic training, the first six months are spent on the community service at the Yale-New Haven Hospital and the second six months at the Waterbury Hospital, where the resident gains a wide experience with common urologic problems. The final year as Chief Resident is divided between the Veterans Administration Medical Center for the first six months, followed by six months on the university service at the Yale-New Haven Hospital.

## **Graduates of the Program**

### Clinical Trainees

Ithaar Derweesh, M.D., Fellow, Cleveland Clinic, Cleveland, Ohio  
Anthony Acquaviva, M.D., Private Practice, Tampa, Florida  
David Shin, M.D., Fellow in infertility, Baylor College of Medicine, Houston Texas  
Joseph Lee, M.D., Kaiser-Permanente, San Francisco, California

## **VOLUNTEER AND COMMUNITY ACTIVITIES**

### Dr. Bernard Lytton

Director of Pierpont Center, Yale University  
Member of Leadership Council, United Way  
Member of Yale Hillel Board

### Dr. Kevin Anderson

Boy Scouts of America (Organization Representative)  
Church of Jesus Christ, Latter Day Saints (Stake Presidency)  
Habitat for Humanity

### Dr. Harris E. Foster, Jr.

NAACP/Y-NHH Inner City Annual Health Fair  
Southern Connecticut Regional Sickle Cell Foundation

## **PUBLICATIONS**

### **Original**

Afiatpour P, Latifpour J, Takahashi W, Yono M, **Foster HE Jr**, Ikeda K, Pouesmail M, **Weiss RM**. Developmental changes in the functional, biochemical and molecular properties of rat bladder endothelin receptors. *Naunyn-Schmiedeberg's Arch. Pharmacol.* 367:462-472, 2003

**Foster HE Jr**. Urinary tract infections (UTIs) and multiple sclerosis: Connection Between UTIs and Neurological Progression. *Multiple Sclerosis Quarterly Report* 21 (2): 1-4, Summer 2002

Hausladen, DA, Wheeler, MA, Altieri, DC, **Colberg, JW, Weiss, RM**. Effect of Intravesical treatment with Bacillus Calmette-Guerin and mitomycin C on urinary survivin levels and outcome. *H. Urol.* 170:230-234, 2003.

McConnell JD, Roehrborn CG, Barutista OM, Andrioloe GL Jr, Dixon CM, Kusek JW, Lepor H, McVary KT, Nyberg LM Jr, Clarke HS, Crawford ED, Diokno A, Foley JP, **Foster HE Jr**, et al. The Long-Term Effect of Doxazosin, Finasteride, and Combination Therapy on the Clinical Progression of Benign Prostatic Hyperplasia. *NEJM* 349 (25) 2385-2396, 2003.

Sheryka E, Wheeler MA, Hausladen DA, **Weiss RM**. Urinary interleukin-8 levels are elevated in subjects with transitional cell carcinoma. *Urology* 62:162-166, 2003.

Swana J, Phillips JL, Wheeler MA, **Weiss RM**. Changes in nitric oxide synthase activity, immunoreactivity and NO induced relaxation in the fetal, young and adult pig urinary tract smooth muscle (pending publication).

Takahashi W, Yono M, Wada Y, Ikeda K, **Weiss RM**, Latifpour J. Regulatory effect of castration on endothelins, their receptors and endothelin converting enzyme in the rat seminal vesicle. *BJU Int.* 92: 803-809, 2003.

**Weiss RM**. Urinary Obstruction: Mechanism and Diagnosis. *Nishnihon J. Urol.* (in press)

Wheeler MA, Hausladen DA, Yoon JH, **Weiss RM**. Prostaglandin E<sub>2</sub> production and cyclooxygenase-2 induction in human urinary tract infections and in bladder cancer, *J. Urol.* 168:1568-1573, 2002.

Yono M, Takahashi W, Pouresmail M, Johnson D, **Foster HE Jr**, Ikeda K, **Weiss RM**. Developmental changes in the functional, biochemical and molecular properties of rat bladder endothelin receptors. *Naunyn-Schmiedeberg's Arch Pharmacol Methods* 48:87-95, 2003.

### **Book chapters**

**Foster HE Jr**: Transurethral Resection of the Prostate. In: *Management of Benign Prostatic Hypertrophy*. Kevin T. McVary, M.D. (Editor). Humana Press, Totowa, NJ, 2003, pp. 163-193.

**Anderson, K.R.:** In *Stone Disease: Ureteral Calculi*. Pp 153-172 Sequera J, Conort P, Khoury S, Pak C, Preminger GM, Tolley D. (eds), Health Publications 2003.

**Weiss RM**. Physiology and Pharmacology of the Renal Pelvis and Ureter. In: Walsh, P.C., Retik, A.B., Vaughan, E.D., Jr., and Wein, A.J. (Eds.): *Campbell's Urology*, 8<sup>th</sup> Edition. Philadelphia, Pennsylvania, W.B. Saunders Company, 2002, pp. 377-409.

### **Reviews**

Sharp JD, Hausladen DA, Maher MG, **Wheeler MA**, Alteri DC, **Weiss RM**. Bladder cancer detection with urinary surviving, an inhibitor of apoptosis. *Frontiers in Bioscience/ 7:e36-41*, 2002 Feb 1.