Researchers Experiment With Novel Approaches for Treating Bladder Cancer

NewYork-Presbyterian Hospital has developed a 2-pronged strategy for the treatment and cure of bladder cancer that integrates the use of novel medical therapies with state-of-the-art surgical techniques. The ultimate goal of the new strategy is to preserve bladder function.

As part of the medical approach to care, James M. McKiernan, MD, and Mitchell C. Benson, MD, are studying the efficacy of the direct delivery of docetaxel to the bladder in patients who do not respond to first-line therapies such as vaccination with bacille Calmette-Guérin (BCG). BCG vaccine, made from an attenuated strain of Mycobacterium bovis, stimulates a cell-mediated immune response. Before this research, the only option for people with bladder cancer that did not respond to BCG was to remove the bladder.

The origins of docetaxel: One of the most successful novel treatments for bladder cancer is derived from yew tree needles.

Renal Cancer: Evaluating Lap Approaches

Today, laparoscopic surgery for renal cancer provides equal cure rates to open radical or partial nephrectomy. But only a few institutions have the expertise to offer the alternative. NewYork-Presbyterian Hospital is among them.

In 1990, surgeons performed the first laparoscopic radical nephrectomy (LRN). Next came laparoscopic partial nephrectomy (LPN), a technique that removes the neoplastic section of the kidney, sparing healthy tissues. Laparoscopy requires smaller incisions (5 to 12 mm) than open procedures, reducing pain and recovery time.

“We have taken what is theoretically possible in minimally invasive procedures, and shown that it can be effective and safe in many cases,” noted Peter Schlegel, MD.

“At our institution, there is almost no patient who is not a candidate for laparoscopic rather than open nephrectomy,” added Mitchell C. Benson, MD. “I tell people that, before you sign a consent form elsewhere for an open procedure, seek a second opinion here.”

Hospital physicians have published numerous articles on their evolving experience in LRN and LPN. Published data show that, since 2000, LRN has been used in more patients with larger tumors (Scherr DS, et al. *Urology*. 2003;62:1007-1011).

From January 2000 to April 2004, see Laparoscopy, page 6
To date, data are limited, but Columbia and Weill Cornell researchers at New York-Presbyterian Hospital are actively pursuing the development of tools such as tumor genetic profiling along with assessment of blood and bone marrow to better predict a breast cancer patient’s risk for recurrence.

“We’re going to get a lot of information from needle biopsy and genetic profiling [for breast cancer],” said Rache Simmons, MD.

While waiting for new approaches to emerge, researchers are evaluating bone marrow aspiration at the time of surgery. In this approach, developed by Michael Osborne, MD, physicians draw approximately 5 cc of bone marrow from each of the hip bones, which is then evaluated by pathologists who use a monoclonal antibody stain to look for breast cancer cells. The presence of metastatic cells in the bone marrow is associated with an increased risk of relapse and decreased survival. Performing the bone marrow aspiration in conjunction with lymph node biopsy to determine axillary status helps physicians assess patient risk and recommend therapeutic options such as chemotherapy. Eight years of research by investigators at New York-Presbyterian Hospital has shown the bone marrow procedure to be a good prognostic indicator.

“The presence of breast cancer cells is a negative prognostic indicator independent of axillary node status,” Dr. Simmons explained.

In a related study (Journal of the American College of Surgery 2005;200:720-725), Dr. Simmons and her colleagues examined whether sentinel lymph node biopsy and bone marrow micrometastases are associated. Researchers performed a retrospective analysis of 124 breast cancer patients, stages I to III, treated with mastectomy or lumpectomy, sentinel lymph node biopsy, and bone marrow aspiration between 1997 and 2003.

In this study population, 36 patients (29%) had micrometastases detected in their bone marrow, and 51 patients (41%) had positive sentinel lymph nodes. Of the patients with positive bone marrow micrometastases, 19 (53%) had positive sentinel lymph node biopsy. In the 88 patients with negative bone marrow micrometastases, 32 (36%) had a positive sentinel lymph node biopsy. Researchers concluded that there was a poor correlation between axillary metastases and micrometastases detected in the bone marrow.

Dr. Simmons and her colleagues are also investigating the use of heat sensors to detect breast cancer, a technology that they hope will eventually replace mammograms. This technique involves blowing a puff of air on the breast, while measuring tissue temperature. Temperatures remain warm around cancerous tumors, even in the presence of a cooling air puff, due to hypervascularization. Researchers are currently comparing heat sensor technology with mammography and patients’ biopsy results. “There’s no discomfort, no compression, no radiation, and it’s completely safe and comfortable,” said Dr. Simmons. “It’s a matter of determining if the technique is as good as mammography.”

Another approach that has been investigated in the laboratory of recent New York-Presbyterian/Columbia recruit Brett Tabaek, MD, is the use of novel molecular techniques for the detection of circulating tumor cells in

---

**Dr. Taback et al’s identification of tumor-specific DNA in breast cancer patients may permit detection of tumor spreading.**

---

**Eight years of research by investigators at New York-Presbyterian Hospital has shown the bone marrow procedure to be a good prognostic indicator.**
the blood and bone marrow of breast cancer patients. Using a multimolecular marker assay, Dr. Taback and colleagues were able to identify occult tumor cells circulating in the blood of early-stage breast cancer patients (Cancer Research 2001;61:8845-8850). Furthermore, they demonstrated correlation with increasing tumor size and patient disease stage. These results provide support for potential clinical implications of their basic science research.

Dr. Taback and colleagues are also in the process of identifying unique surrogate markers in the blood and bone marrow of breast cancer patients (Table) that may be used for surveillance of occult disease progression, monitoring response to therapy and patient prognosis (Annals of the New York Academy of Sciences 2001;945:22-30, Cancer Research 2003;63:1884-1887, Proceedings of the American Association for Cancer Research 2004;45:772). Their identification of tumor-specific DNA in the circulation of breast cancer patients may eventually permit detection of tumor spreading before it can be identified with currently available imaging studies.

“With improved imaging studies for early breast cancer detection, more sophisticated techniques with greater sensitivity will be needed to identify those patients at greatest risk for relapse early in their disease course,” said Dr. Taback. “Alternatively, these approaches may permit better selection of patients who do not need additional systemic therapy and thus avoiding potential toxicities associated with such treatments.”

Dr. Taback’s current research will focus on the development of a novel approach to detect micrometastases before they can be identified by conventional imaging as well as the genetic events associated with tumor progression and the efficacy of circulatory nucleic acids as diagnostic markers for disease.

Rache Simmons, MD, is Associate Attending Surgeon, Weill Cornell Breast Center at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, and is Associate Professor of Surgery at Weill Medical College of Cornell University. E-mail: rms2002@med.cornell.edu

Bret Taback, MD, is Assistant Attending Surgeon at NewYork-Presbyterian Hospital/Columbia University Medical Center, and is Assistant Professor of Surgery at Columbia University College of Physicians and Surgeons. E-mail: bt2160@columbia.edu

NewYork-Presbyterian Oncology
is a publication of the Cancer Centers of NewYork-Presbyterian Hospital. The Cancer Centers are at the forefront of cancer screening and diagnosis, basic science, and clinical research. The Cancer Centers serve over 6,500 new cancer patients each year, who receive state-of-the-art multidisciplinary care. The Cancer Centers include the Herbert Irving Comprehensive Cancer Center at NewYork-Presbyterian Hospital/Columbia University Medical Center and the Weill Cornell Cancer Center at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, which are respectively comprised of faculty from the Columbia University College of Physicians and Surgeons and the Weill Medical College of Cornell University.

NewYork-Presbyterian Oncology Editorial Board

Nasser Altorki, MD
Director, Division of Thoracic Surgery
NewYork-Presbyterian/Weill Cornell
Professor, Cardiothoracic Surgery
Weill Medical College of Cornell University
naltork@med.cornell.edu

Mitchell C. Benson, MD
Urologist-in-Chief
Herbert Irving Comprehensive Cancer Center
NewYork-Presbyterian/Columbia
George F. Cahill Professor and Chairman of Urology
Columbia University College of Physicians and Surgeons
mcb2@columbia.edu

Andrew J. Dannenberg, MD
Co-Director, Cancer Prevention Program
NewYork-Presbyterian/Weill Cornell
Henry R. Erle, MD–Roberts Family Professor of Medicine
Weill Medical College of Cornell University
ajdannen@med.cornell.edu

Howard Kaufman, MD
Attending Surgeon
NewYork-Presbyterian/Columbia
Edwin C. and Anne K. Weiskopf Associate Professor of Clinical Surgery and Vice Chairman, Surgical Oncology
Columbia University College of Physicians and Surgeons
hkk2003@columbia.edu

John Leonard, MD
Associate Attending Physician
NewYork-Presbyterian/Weill Cornell
Associate Professor of Medicine
Weill Medical College of Cornell University
jpleonar@med.cornell.edu

David Nanus, MD
Co-Division Chief, Hematology and Medical Oncology
NewYork-Presbyterian/Weill Cornell
Mark W. Pisters Professor of Hematology and Oncology in Medicine
Weill Medical College of Cornell University
dnanus@med.cornell.edu

Alfred I. Neugut, MD, PhD
Co-Director, Cancer Prevention Program
Acting Chief, Division of Medical Oncology
Herbert Irving Comprehensive Cancer Center
NewYork-Presbyterian/Columbia
Myron M. Studner Professor of Cancer Research
Columbia University College of Physicians and Surgeons and Mailman School of Public Health
a1l1@columbia.edu

Dattatreyyudu Nori, MD, FACR
Radiation Oncologist-in-Chief, Department of Radiation Oncology
NewYork-Presbyterian/Weill Cornell
Professor of Clinical Radiology
Weill Medical College of Cornell University
dnor@nyp.org

Alexander J. Swistel, MD
Director, Weill Cornell Breast Center
NewYork-Presbyterian/Weill Cornell
Associate Professor of Clinical Surgery
Weill Medical College of Cornell University
aswistle@med.cornell.edu

Michael Weiner, MD
Chief, Pediatric Oncology
Herbert Irving Child and Adolescent Oncology Center at Morgan Stanley Children’s Hospital of NewYork-Presbyterian/Columbia
Hettinger Professor of Clinical Pediatrics
Columbia University College of Physicians and Surgeons
mw216@columbia.edu

Researchers Approach Angiogenesis From Multiple Directions

Basic research at both the Herbert Irving Comprehensive Cancer Center of Columbia University College of Physicians and Surgeons and Weill Medical College of Cornell University is focused on isolating the key molecular steps in angiogenesis; clinical research at NewYork-Presbyterian Hospital is putting this basic science to work.

In the Division of Pediatric Oncology at Morgan Stanley Children’s Hospital of NewYork-Presbyterian/Columbia University Medical Center, basic and clinical investigators are collaborating in identifying combinations of inhibitors of angiogenesis with the potential to shrink tumors rather than inhibit their growth. At the same time, Weill Cornell researchers are evaluating the mechanisms of angiogenesis, not only to inhibit blood supply to malignancies but to increase blood supply for such conditions as cardiovascular disease.

Shahin Rafii, MD, has been active in assessing the biologic significance of novel pro-angiogenic factors that promote tumor angiogenesis. He noted that vascular endothelial growth factor, one of the most well-known vascular mediators, is just one of several in a series of factors that modulate neo-angiogenesis. Darrell Yamashiro, MD, PhD, who has also been involved in isolating the mechanisms of angiogenesis, has been collaborating with Julia Glade Bender, MD, to translate work in the laboratory into new treatment regimens for pediatric cancer patients.

“We have become interested in combining anti-angiogenic agents to improve on the activity we see with 1 agent alone,” noted Dr. Glade Bender. “We have a lot of evidence that these drugs are effective at inhibiting tumor growth, but, when used alone, they have not been very effective in bringing about tumor regression. However, there are preliminary data to suggest that combinations of these agents may yield the objective responses important to tumor eradication. We have already designed a trial that will combine the anti-angiogenic agents bevacizumab and erlotinib for pediatric cancer.”

“There are preliminary data to suggest that combinations of these agents may yield the objective responses important to tumor eradication.”

—Julia Glade Bender, MD

Indeed, Dr. Glade Bender was the principal investigator of the first clinical study of bevacizumab in children. Conducted in a limited number of children with a variety of cancer types, the Phase I study demonstrated tolerability similar to that seen in adults. In combination with standard chemotherapy, this agent has been shown to add survival benefit in several adult cancers including cancer of the colon, for which the drug was approved in 2004. The favorable Phase I results in children have paved the way for more studies, which will be designed to look at the potential for these drugs in cancer diagnoses unique to children. One of the first studies will focus on recurrent Ewing’s sarcoma, a pediatric bone and soft tissue cancer, and will compare a triple-drug chemotherapy regimen (vincristine, topotecan, and cyclophosphamide) with and without bevacizumab.

In addition to a unique mechanism of action, one of the most attractive features of anti-angiogenic drugs is their relative tolerability. Although these drugs often cause significant rash and some nausea, they are associated with very low rates of the most feared side effects of cytotoxic agents, such as low blood counts and alopecia. However, as their ability to shrink tumors as single agents has been limited, there has been increasing interest in using these drugs to transform terminal malignancies into chronically managed diseases in which the goal is not to cure but to prevent a tumor from progressing. Yet, the focus in children has remained on the potential for these drugs to cure disease. This is an area in which Dr. Yamashiro has focused some of his research.

“In the animal models, like in patients, we can see very effective control of tumor growth, but eventually the cancer begins to progress,” he said. “The question we are asking ourselves is, how can we make this therapy better.”

One of the strategies being considered is to implement metronomic scheduling for combinations of cytotoxic agents and anti-angiogenic drugs. Metronomic scheduling involves providing small doses of cytotoxic agents on a daily basis rather than large doses on an every-3-week schedule. Many anti-angiogenic drugs are already administered on a daily schedule, but the combination of the chemotherapies and the antiangiogenic agents on a daily basis might reduce the side effects of chemotherapy while providing their cytotoxic effects in context with inhibitors of signals for new blood supply.

Meanwhile, Dr. Rafii has been working on both sides of angiogenesis. He has been pursuing inhibition of new blood supply by targeting a variety of novel molecular targets that participate in proliferation and differentiation of
New HPV Vaccine Could Alter Course of Treatment for Gynecologic Cancers

Columbia researchers at NewYork-Presbyterian Hospital are furthering recent efforts to develop vaccines for the prevention of human papillomavirus (HPV) infection.

Although a study published in the fall of 2005 demonstrated that a vaccine can indeed prevent HPV infection, thereby reducing a woman’s risk for cervical intraepithelial neoplasia (CIN), the study excluded women older than 25 years of age. NewYork-Presbyterian/Columbia is participating in a new trial designed to demonstrate that the protective effect extends to older women.

“We should not forget that most women over 25 will have new sexual partners during their lifetimes and will continue to have exposure to sexually transmitted diseases,” noted Thomas Wright, MD. “They are still at risk for HPV infection and its consequences. There is substantial potential for major health benefits if vaccination against HPV-16 and HPV-18 in older women is shown to be safe and effective.”

Neither of the 2 vaccines currently being studied has yet been approved by the FDA, but early results of clinical trials have been encouraging. Both of the vaccines have been designed to provide protection against HPV-16 and HPV-18. One of the vaccines is bivalent and targets only these HPV types, whereas the other is quadrivalent and also provides protection against types 6 and 11.

In the trial that is enrolling patients at NewYork-Presbyterian/Columbia, sexually active women older than 25 years with no known previous HPV infection will be randomized to the bivalent vaccine or placebo. They will then be followed for 3 years.

“We expect to enroll about 150 women at our site,” Dr. Wright said. A higher proportion of women older than 25 is likely to have had a previous exposure to HPV. The vaccine may still provide clinical benefit by preventing infection in those not yet exposed; reinfection in those without persistent disease; or even reactivation of a dormant infection.

Results of the first Phase III randomized trial of the HPV vaccine have generated considerable excitement. Performed with the quadrivalent vaccine, this placebo-controlled trial enrolled 5,455 women between the ages of 16 and 24 years (mean age, 20.2 years). The primary end point was the presence of any lesions related to HPV-6, -11, -16, or -18, including genital warts, CIN of any grade, and cancer of any kind. The study demonstrated a high degree of protection against both genital warts and CIN after 18 months of follow-up. On per protocol (PP) analysis, which meant analysis of the patients who received all 3 doses of the vaccine, there were no cases of CIN in the vaccinated group versus 37 in the placebo group (P<0.001). Protection against genital warts from the vaccine on the PP analysis was also 100%. On the modified intention-to-treat analysis, there were 3 cases of genital warts or CIN in the vaccinated group versus 57 in the placebo group (P<0.001). This translated into 97% protection against CIN. The vaccine was well tolerated, with no patients discontinuing therapy because of adverse events.

An upcoming study at NewYork-Presbyterian/Weill Cornell is looking at a new heat-shock protein vaccine that may eliminate the need for cone biopsy in young women with known dysplasia.

“Ideally, this vaccine will decrease the number of surgical procedures in young women and protect fertility while avoiding the complications of surgery,” said Thomas Caputo, MD. According to the National Cancer Institute-approved study protocol, diagnosis of dysplasia will be established in subjects by cone biopsy, after which they will receive 3 doses of the vaccine. At either 4 or 6 months after administration of the vaccine, another cone biopsy of the cervix will be done to determine whether precancerous cells are still present.

HPV infection is enormously prevalent, with the majority of sexually active women demonstrating at least 1 previous exposure when sensitive testing is performed. However, persistent infection, which is a risk factor for cervical cancer or its precursor lesions, develops in only approximately 5% of women. Although the effect of the vaccine in preventing cervical cancer may not be known for a decade or more after it becomes available, because of the long latent phase before malignant transformation, its more immediate clinical benefits may be more important. The vaccine does not eliminate the need for Pap smear screening, but it should dramatically reduce the number of abnormal results and thus the attendant stress, discomfort, and cost of additional diagnostic studies and treatment.

“Although the ideal is to provide protection before risk of infection, we still have to recognize that older women are engaging in the activities that lead to HPV exposure,” said Dr. Wright. “In addition, prior exposure to HPV does not rule out benefit from vaccine. In the Phase III trial just completed, it is...”

see HPV, page 6
**Laparoscopy**

continued from page 1

mean operative duration for LPN versus open partial nephrectomy was significantly shorter, 144 versus 239 minutes, respectively (Schiff JD et al. BJU Int. 2005;96:811-814). Clear fluids were started at a mean of 24 hours after LPN, compared with 41 hours after the open procedure. LPN patients were discharged after a mean of just 3.4 days, compared with 5.4 days for those receiving open partial nephrectomy.

NewYork-Presbyterian Hospital boasts a high annual number of laparoscopic procedures performed for renal cancer (more than 250 in the past year). Meanwhile, surgical teams led by Joseph del Pizzo, MD, and Jaime Landman, MD, are constantly improving their laparoscopic techniques. Surgeons now use hand-assisted laparoscopy, in which that most versat¬ile tool, the surgeon’s hand, reaches into the laparoscopic field. In general, according to researchers, laparoscopic technique increasingly includes elements of open surgery, such as clamping of arteries and suturing the urinary collecting system after tumor removal. Mimicking open surgery in these ways improves control of bleeding and closure of the collecting system.

Use of laparoscopic ultrasound imaging has enabled surgeons to minimize bleeding complications and positive margins. Cosmesis is enhanced by laparoscopic incisions in the lower abdomen. Vast improvements in laparoscopic hemostasis have enabled surgeons to employ laparoscopic techniques more liberally. Optimal control of bleeding can be achieved by combining the surgeon’s technique with coagulative technologies such as pharmaceutical hemostats and electromechanical devices like the argon-beam coagulator.

These advances have expanded the candidate pool for laparoscopy to include patients with only 1 kidney and a deep central tumor, or cases where a kidney must be cooled to facilitate surgery. It remains difficult to cool a kidney laparoscopically, although techniques are being developed.

“If the incision you need for tissue removal laparoscopically is as large as the incision you would make for an open procedure, it makes sense to do the procedure openly,” explained Dr. Benson. “Typically these are large incisions—something on the order of 6 inches or more.”

The future promises further advances. The next step is expanded use of ablative techniques, which target the cancer and spare a greater amount of healthy tissue. Two techniques, cryoablation and radiofrequency (RF) ablation, represent viable clinical alternatives for some patients. Ablation can be applied laparoscopically, in open procedures, or percutaneously—an option useful for patients who cannot tolerate surgical anesthesia. Currently, however, ablative techniques cannot match the low cancer recurrence rates associated with LPN—2.7% for LPN versus 4.6% for cryoablation and 7.9% for RF ablation.

“The laparoscopic approach is cost neutral for the healthcare system,” noted Dr. Schlegel. “The procedure costs more, but hospital stays are shorter.”

“Laparoscopic procedures are more expensive for our institution because the equipment is more expensive,” added Dr. Benson. “But it’s an investment in our patients that is well worth it.”

**HPV**

continued from page 5

reasonable to speculate that a proportion of women were also exposed to HPV before they received the vaccine, and still the protection was near 100% in that study.”

If the trial in older women does demonstrate protection against CIN, it will suggest that the vaccine can be considered for any woman who is sexually active. Importantly, although the vaccine should reduce the rates of cervical cancer, the most important effect in countries where Pap smears are widely performed will be a reduction in CIN lesions rather than in malignancy. This alone may have a notable effect on women’s health.

**Thomas Caputo, MD,** is Director, Division of Gynecologic Oncology, NewYork-Presbyterian Hospital/Weill Cornell Medical Center, and is Professor and Vice Chairman of Obstetrics and Gynecology at Weill Medical College of Cornell University. E-mail: tacz001@med.cornell.edu.

**Thomas Wright, MD,** is Director, Gynecological Pathology and Colposcopy Services at NewYork-Presbyterian Hospital/Columbia University Medical Center, and is Associate Professor of Pathology at Columbia University College of Physicians and Surgeons. E-mail: tcw1@columbia.edu.

**Mitchell C. Benson, MD,** is Urologist-in-Chief, NewYork-Presbyterian Hospital/Columbia University Medical Center, and is George F. Cahill Professor and Chairman of Urology at Columbia University College of Physicians and Surgeons. E-mail: mcb2@columbia.edu.

**Joseph del Pizzo, MD,** is Director, Laparoscopic and Robotic Surgery, Urologic Surgery, NewYork-Presbyterian Hospital/Weill Cornell Medical Center, and is Assistant Professor of Urology at Weill Medical College of Cornell University. E-mail: jod2009@med.cornell.edu.

**Jaime Landman, MD,** is Director, Minimally Invasive Urology, Department of Urology, NewYork-Presbyterian Hospital/Columbia University Medical Center, and is Assistant Professor of Urology at Columbia University College of Physicians and Surgeons. E-mail: jl2674@columbia.edu.

**Peter Schlegel, MD,** is Urologist-in-Chief, NewYork-Presbyterian Hospital/Weill Cornell Medical Center, and is Professor and Chairman of Urology at Weill Medical College of Cornell University. E-mail: pnschleg@med.cornell.edu.
Bladder
continued from page 1

“We asked what would happen if we gave treatment one more try with docetaxel to preserve people’s bladders,” said Dr. Benson. This approach appears to be effective for early-stage superficial or noninvasive bladder carcinoma, thus delaying surgical removal of the organ. So far, the therapy has been effective in 60% to 70% of patients in the study.

Medical treatments are being evaluated in preclinical laboratory and animal studies. Douglas S. Scherr, MD, and his colleagues have found that imiquimod, an immune response modifier, could help kill bladder cancer cells with no side effects. Phase I trials are scheduled for this spring or summer, he said.

Generally, if only 1 growth is present in the bladder, the standard therapy is for the physician to scrape out the cancer and administer chemotherapy such as mitomycin-C, noted Dr. Benson. However, if a patient has multiple or recurrent polyps, it may be necessary to administer a series of chemotherapeutic agents or treat with an immunotherapeutic agent such as BCG, which is also instilled directly into the bladder.

If chemotherapy is not effective or if the cancer cells appear aggressive historically, urologists often use BCG as a first-line therapy. This treatment is initially effective in 50% to 70% of patients but then fails in at least half of them as therapy progresses. For patients whose disease is refractory to BCG, the direct placement of docetaxel into the bladder with a catheter offers a new treatment option. However, the research is preliminary.

“People who would have otherwise lost their bladder can keep it longer,” explained Dr. Benson. “We’ve had very promising results, with no toxicities.”

Dr. Benson and his colleagues will continue to follow patients and enlarge the study to obtain conformational data. Dr. McKiernan and medical student Puneet Masson of the Doris Duke Fellowship Program were both instrumental in conducting this research.

Columbia and Weill Cornell researchers at NewYork-Presbyterian Hospital are also evaluating systemic I.V. chemotherapy in selected groups of patients with bladder cancer in an effort to avoid removal of the bladder. Both docetaxel and other forms of chemotherapy are being tested.

“You have to tailor the right drugs to the right person,” said Dr. Benson. “Our goal is to avoid bladder removal whenever possible.”

“Patients are returning to a normal quality of life and voiding better than prior to surgery.”
—Douglas S. Scherr, MD

For those patients who do not respond to medical treatment, Dr. Scherr’s group is evaluating new surgical approaches that preserve bladder function. “We’re working on new ways to create a neobladder,” Dr. Scherr explained. Most bladders reconstructed after cystectomy are made from the patient’s intestine. However, in animal studies, researchers are evaluating use of the gallbladder and other internal tissues to create neobladders in an effort to improve the patient’s quality of life.

“Patients are returning to a normal quality of life and voiding better than prior to surgery,” said Dr. Scherr. A highly skilled pelvic reconstruction team makes urinary continence after bladder cancer a possibility.

Perfecting bladder reconstruction will make cystectomy a more attractive option, according to M. Mendel Shemtov, MD. Additionally, the use of robotics for the surgical removal of the bladder, a minimally invasive technique, is being evaluated in humans, said Dr. Scherr. “We are able to apply aggressive surgical tenets while limiting the insult to the patient,” he added. “Patients are able to leave the hospital sooner, and return to daily activities.”

Researchers are working closely with medical oncologists to administer multimodal therapy for bladder cancer, including systemic chemotherapy, before performing cystectomy in patients with invasive disease. One of the biggest challenges a clinician faces is treating patients with superficially invasive bladder cancer, noted Dr. Shemtov.

“The goal is to try to preserve the bladder, but there is often a fine line between performing the surgery too early and too late,” said Dr. Shemtov. Physicians need to have comprehensive discussions with their patients about the risks and benefits of various treatment options, he explained.

In addition to the research on new treatments and efforts to improve techniques for cystectomy and reconstruction, the development of more precise clinical markers of the recurrence of bladder cancer is an area requiring further investigation, noted Dr. Shemtov.

“But none of them have really caught on, primarily because of inadequate specificity or sensitivity,” he said. However, some physicians use these markers as an adjunct to cystoscopy.

Mitchell C. Benson, MD, is Urologist-in-Chief at NewYork-Presbyterian Hospital/Columbia University Medical Center, and is George F. Cahill Professor and Chairman of Urology at Columbia University College of Physicians and Surgeons.
E-mail: mcb2@columbia.edu.

James M. McKiernan, MD, is Director, Urologic Oncology at NewYork-Presbyterian Hospital/Columbia University Medical Center, and is Assistant Professor and Vice Chairman of Urology at Columbia University College of Physicians and Surgeons.
E-mail: jmm23@columbia.edu.

Douglas S. Scherr, MD, is Clinical Director of Urologic Oncology at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, and is Assistant Professor of Urology at Weill Medical College of Cornell University.
E-mail: dss2001@med.cornell.edu.

M. Mendel Shemtov, MD, is Assistant Attending Urologist and NewYork-Presbyterian Hospital/Weill Cornell Medical Center, and is Assistant Professor of Urology at Weill Medical College of Cornell University.
E-mail: mshemtov@med.cornell.edu.
stem cells into endothelial cells. At the same time, he has been pursuing methods of delivering pro-angiogenic factors to improve blood supply in patients with cardiovascular disease.

“These fields are very closely related,” he explained. “The same angiogenic factors being targeted to block tumor growth could be exploited to promote generation of blood supply in patients with advanced atherosclerosis.” However, Dr. Rafii’s molecular studies are not limited to the control of signaling of mature cells; they also include the signaling that permits stem and progenitor cells to participate in the rebuilding of damaged vascular endothelium. He emphasized that the progress in stem cell research would move even more rapidly with greater support from the federal government.

“We have preclinical data demonstrating that both human and embryonic vascular stem and progenitor cells could be used to revascularize damaged heart or brain in rodent models,” he said. “These stem cell therapy strategies are ready for prime time, and, after Phase I trials to assess therapeutic efficacy and safety, could potentially be delivered to treat patients with life-threatening heart attacks or strokes.”

Columbia and Weill Cornell researchers are now attempting to unravel the mechanisms by which the body controls its own blood supply. The studies are indicative of the novel initiatives to approach disease by deciphering the secrets of fundamental physiologic processes that have the potential to be exploited for clinical benefit.

Julia Glade Bender, MD, is Associate Director, Phase I and Experimental Therapeutics, and Director, Pediatric Cancer Foundation Clinical Research Program, Herbert Irving Child and Adolescent Oncology Center at Morgan Stanley Children's Hospital of NewYork-Presbyterian/Columbia University Medical Center and is Assistant Professor of Clinical Pediatrics at Columbia University College of Physicians and Surgeons. E-mail: jg589@columbia.edu.

Shahin Rafii, MD, is Director, Ansary Center for Stem Cell Therapeutics at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, and is Arthur Belfer Professor of Genetic Medicine and Professor of Medicine in the Division of Hematology–Oncology at Weill Medical College of Cornell University. E-mail: srafii@med.cornell.edu.

Darrell Yamashiro, MD, PhD, is Assistant Attending Physician in Pediatrics, Herbert Irving Child and Adolescent Oncology Center at Morgan Stanley Children's Hospital of NewYork-Presbyterian/Columbia University Medical Center, and is Herbert Irving Assistant Professor of Pediatrics and Pathology (in Surgery) at Columbia University College of Physicians and Surgeons. E-mail: dy39@columbia.edu.