In the United States, bladder cancer is the fourth most diagnosed malignancy for men, and the tenth most common for women. Despite the fact that diagnosis rates have leveled off over the past decade, bladder cancer is still of great concern to the 60,000 people who are estimated to be diagnosed with the disease this year. Yet, the disease rarely receives the high-profile attention of other statistically similar cancers, such as melanoma.

There are three main types of bladder tumors, identified by the way they appear under the microscope:
- urothelial carcinoma (also known as transitional cell carcinoma or TCC);
- squamous cell carcinoma; and
- adenocarcinoma.

These same types of cancer, can also grow in the ureter and the urethra, which is why a complete evaluation of the urinary system is recommended for patients diagnosed with a cancer of the bladder, ureter, or urethra.

Cancer in the urothelial cells lining the bladder (also known as urothelial or transitional cell carcinoma) is the most common form of bladder cancer, accounting for 90% of diagnosed cases. Only about 2% of bladder cancers are squamous cell carcinomas, which look much like skin cancer under the microscope, and only about 1% to 2% of bladder cancers are adenocarcinomas. While nearly all squamous cell cancers and adenocarcinomas of the bladder are invasive, urothelial tumors can be categorized as noninvasive or invasive. In noninvasive cases, the cancer has not spread further than the urothelium, which is the innermost layer of the bladder. In invasive cases, however, the malignancy spreads through the lining of the bladder into the deeper tissues of its wall, and even into the thick, deep bladder muscle called the muscularis propria. These invasive cases are often far more serious, and outcomes are much less certain.

New advances

Three recent scientific advances are providing good news to doctors and patients dealing with bladder cancer. The first confirms that a novel, noninvasive test can detect bladder cancer with unprecedented accuracy. The second reveals the discovery of the “bladder-cancer gene,” which is expected to lead to more effective, individualized treatments of the disease, particularly in its recurrent form. The third discusses a connection made between a specific oncogene and the development of bladder cancer. All three discoveries are poised to provide laboratories with better tools to help doctors and their patients make the best possible treatment decisions.

FISH technology

In the first study, reported in the February 2004 journal Urology, researchers found that utilizing fluorescence in situ hybridization (FISH) technology when testing urine specimens for bladder-cancer markers was 92% effective in detecting those markers, compared with a sensitivity of only 64% for traditional cytology screenings. FISH technology works on voided urine by determining the absence or corruption of certain chromosomes in it — namely numbers 7 and 9, among others. Numerous scientific studies over the past decade have linked the deletion or corruption of these two chromosomes to a high likelihood of bladder cancer.

The British Institute for Cancer Research identified E2F3, a gene they call “the missing link in our understanding” of bladder cancer.

Through FISH analysis, laboratories will be able to provide initial analysis more quickly, and with a higher degree of accuracy, to physicians, so that they and their patients can make an informed biopsy decision and begin designing potential treatment protocols much sooner. Not surprisingly, recent therapeutic studies have concluded that early diagnosis, coupled with a combined treatment regimen, leads to the highest survival rate among bladder-cancer patients.

The “missing link”

In the second study, reported in the April 2004 issue of the journal Oncogene, scientists at the British Institute for Cancer Research identified E2F3, a gene they call “the missing link in our understanding” of bladder cancer. Researchers found a direct correlation between the overexpression of the gene and the proliferation of bladder-cancer cells. Addi-
tionally, they noted that the amount of E2F3 proteins present was a significant indicator of the seriousness of the cancer. Higher amounts were associated with larger tumors, while smaller amounts indicated smaller, Stage I malignancies. The study authors expect their work will lead to more targeted treatment and better disease-progression prediction in individual patients.

Oncogene CDC91L1

The third discovery, made by a group of scientists from Johns Hopkins University Medical Center in Baltimore and the National Institutes of Health in Bethesda, MD, and reported in the April 2004 issue of the journal Nature Medicine, is of an oncogene called CDC91L1. Researchers theorize that the overexpression of this gene is a major culprit in the development of primary bladder cancer.3 Relying on the knowledge that cancer begins by an activation or amplification of these oncogenes, the scientists traced what is known as a germline translocation, or break, in the DNA of a bladder-cancer patient, and found that the overexpression of CDC91L1 was the only consequence of that break. Researchers confirmed their theory through a subsequent in vivo study using 61 nude mice.

Promising advances

These genetic discoveries are perhaps the most promising in the quest for faster, more accurate laboratory diagnosis, which can then lead to more successful treatment of disease. Moreover, these recent advances are likely to spur more interest in further research, promoting a higher level of understanding among clinicians about the development and progression of bladder cancer and other malignancies.

Such further advances are clearly critical, as the sobering facts about this often-overlooked disease continue to be confirmed and expanded by researchers. Bladder cancer is the ninth most common form of cancer in the world today, accounting for 330,000 new cases — and 100,000 deaths — each year. Bladder cancer is also one of the most chronic cancers, recurring in almost 70% of patients.

Preventive Strategies

On the preventive front, previous research identifying smoking as a chief cause of the disease has been corroborated in numerous medical journal reports over the past several years. The International Agency for Research on Cancer (IARC) estimates that 65% of male bladder-cancer patients and 30% of female bladder-cancer patients are smokers. In fact, two studies — one in the Canadian Journal of Urology and one in the Journal of the National Cancer Institute — found that smokers are more than twice as likely to develop bladder cancer than nonsmokers, and that the rate at which female smokers develop bladder cancer is “significantly higher” than the rate of male smokers.5,6

Clearly, bladder cancer is a disease that is troubling in its prevalence, yet the advances in our understanding of the disease bode well for patients and clinicians alike. From our knowledge about preventive strategies, to our ability to detect the disease earlier, easier, and more accurately than ever, to the prospect of new, effective gene-therapy treatments, to the prospect of even more advancements in research and development, there are many reasons to be optimistic about the future for those affected by bladder cancer.

References


George Hollenberg, MD, an authority in the fields of pathology, clinical pathology, and dermatopathology, has expertise in the areas of dysplastic nevi, melanoma, prostate, and gastrointestinal cancer. As founding director of Acupath Laboratories Inc., he supervises the analysis of tens of thousands of biopsies per year, using cutting-edge technology in histology and immunocytochemistry, as well as the latest advances in computerized report preparation.

Stages of Bladder Cancer

Generally, bladder cancer is divided into four stages, indicating its spread from small and localized to metastatic, or secondary bladder cancer, in other parts of the body.

Stage 0 — Carcinoma in situ or pre-cancerous change means the bladder-cancer cells are completely contained within the inner surface of the bladder lining, and have not begun spreading into its deeper layers.

Stage I — Cancer cells exist only in the bladder lining, sometimes appearing as a warty or mushroom-like lump protruding out into the bladder cavity.

Stage II — Cancer cells have spread into the inside layer of the muscle in the bladder wall.

Stage III — Cancerous tumor has grown through the muscle wall into the surrounding fat, and may have spread into the fibrous capsule surrounding the bladder, as well as into nearby organs (prostate gland, vagina, or bowel).

Stage IV — Cancerous tumor has spread beyond the bladder into other organs in the abdomen or into lymph glands in the bladder area — and may have spread into other parts of the body quite distant from the bladder.

Smokers are more than twice as likely to develop bladder cancer than nonsmokers.