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ogists, it has become ever more important to use intraoperative cystoscopy to ensure that the bladder and ureters remain undamaged and unobstructed. In fact, we have reached a point where cystoscopy should be performed routinely for most advanced pelvic reconstructive procedures, whether the procedures are done vaginally or abdominally.

It is absolutely imperative that cystoscopy be performed with every retropubic sling that uses the tension-free vaginal tape (TVT) procedure.

With transobturator tape (TOT), its necessity is more debatable because needles don't pass as close to the bladder. Surgeons who have comfortably and successfully performed a significant number of TOT procedures can probably forego cystoscopy.

There is one exception, however: cases in which TOT is performed before the prolapse is repaired. In this case, cystoscopy remains imperative.

Intraoperative cystoscopy has a fringe benefit as well, in that it sometimes leads to the identification of pathology—bladder stones, for instance—that went undiagnosed during the preoperative work-up.

Cystoscopy can also be used to guide the placement of suprapubic catheters intraoperatively, although its most sig-

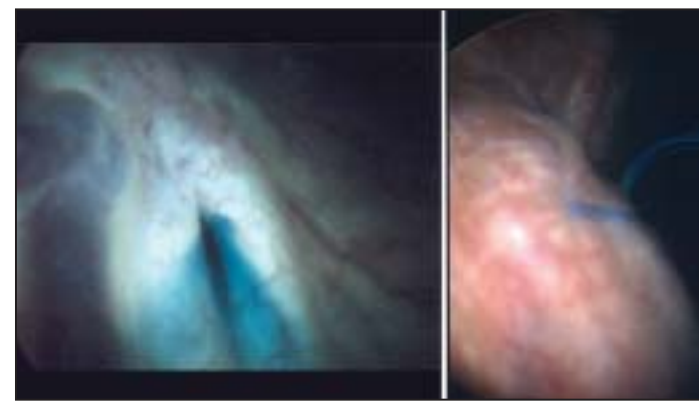
nificant purpose is to document ureteral patency. When examining for patency, most surgeons inject indigo carmine intravenously and examine the bladder approximately 10 minutes later to document flow of the dye through both ureteral openings.

#### Instruments and Training

A urethroscope with a 0-degree lens allows appropriate examination of the urethra; however, a 70-degree lens is preferable for examination of the bladder because it enables visualization of the entire circumference of the bladder in more detail.

Some surgeons are using flexible cystoscopes—the optics of flexible cystoscopy have improved significantly in recent years—but the 70-degree rigid scope is sufficient in the vast majority of procedures.

Gynecologists who perform trans- or periurethral bulking agent injections for intrinsic sphincteric deficiency must be comfortable with using a 0-degree scope in the office. In this process, which typically is done under cystoscopic guidance, a needle is placed either through the cystoscope or lateral to the urethra, and the agent—collagen (Contigen), silicone (Macroplastique), carbon beads (Durasphere), or another agent—is injected to add bulk around



Ureteral opening is shown via cystoscopy, after injection of indigo carmine dye to document ureteral integrity.

PHOTOS COURTESY DR. G. WILLY DAVILA



Tension-free vaginal tape mesh is shown in the urethra.

## Trastuzumab May Aid in Some HER2-Negative Breast Cancers

BY JANE SALODOF MACNEIL  
Senior Editor

CHICAGO — Provocative findings from two studies presented at the annual meeting of the American Society of Clinical Oncology suggest that some patients with HER2-negative breast cancer may benefit from trastuzumab.

A retrospective analysis of the phase III Cancer and Leukemia Group B (CALGB) 9840 trial revealed that human epidermal growth factor 2 (HER2)-negative metastatic breast cancer patients with multiple copies of the chromosome carrying HER2 had significantly better response rates (63% vs. 26%) when they were treated with trastuzumab (Herceptin) in addition to paclitaxel.

In the adjuvant setting, another retrospective analysis showed that a small group of HER2-negative patients in the phase III National Surgical Adjuvant Breast and Bowel Project (NSABP) B-31 trial had significantly better disease-free survival with a relative risk of 0.40 when given trastuzumab after completing treatment for early breast cancer.

Both studies drew considerable attention, with investigators and discussants discouraging attendees from using findings in the clinical setting before they can be verified.

"We emphasize that additional study is needed. At the moment we don't feel that these data should be used clinically," Dr. Peter A. Kaufman concluded in his presentation of the CALGB data.

He stressed that only a small number of patients were analyzed and noted that trastuzumab did not improve progression-free survival or overall survival for the HER2-negative patients with polysomy of chromosome 17.

Dr. Soonmyung Paik of the NSABP called for a randomized clinical trial to test adjuvant trastuzumab in HER2-negative women.

A favorable outcome might lead to expansion of trastuzumab's indication from 20% to about 60% of breast cancer patients, he said.

"The major question raised by this paper is, what now?" Dr. James H. Doroshow said, advising that the NSABP study needs to be confirmed before new standards for HER2 positivity can be developed.

"It is critical that all appropriate adjuvant breast cancer sets be reevaluated, so that a new consensus can be established for HER2 testing," said Dr. Doroshow, director of the National Cancer Institute's division of cancer treatment and diagnosis.

After a lengthy audience discussion in which one physician demanded a reason not to expand use of trastuzumab, Dr. Vered Stearns advocated further investigation of HER2 copy number in available data sets from large clinical trials in the metastatic and adjuvant settings.

"Until additional information is available, HER2 copy number and proteomics are not ready for prime time," said Dr. Stearns of the cancer center at Johns Hopkins University, Baltimore.

Investigators were limited to available tissue blocks in the two retrospective studies of completed trials. They also grappled with disparities between local and central laboratories testing for HER2 positivity, and with standards for making the determination by immunohistochemistry (IHC) and/or fluorescent in situ hybridization (FISH).

The original report from the CALGB 9840 trial indicated that weekly paclitaxel was superior to paclitaxel taken every 3 weeks in metastatic breast cancer. Although more HER2-negative women responded when trastuzumab was added to paclitaxel, the difference was not significant.

For the new report (CALGB 150002), a laboratory correlative science study associated with CALGB 9840, Dr. Kaufman and his associates found that 303 tissue blocks were available from the original 585 patients.

These included samples from 129 patients whom local pathologists and/or

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central testing had classified as HER2-negative at the time that the data were collected.

Within this group, the new investigation determined that 25 patients (19%) had polysomy (defined as 2.2 copies or more per cell) of chromosome 17.

Because the HER2 gene is located on chromosome 17, polysomy is typically associated with increased copies of the HER2 gene as well, according to Dr. Kaufman of the cancer center at the Dartmouth-Hitchcock Medical Center, Lebanon, N.H.

Retesting all the available samples, the investigators classified 192 patients as FISH-negative and identified 38 patients with extra copies of the chromosome. This group included the original 25 HER2-

negative patients plus 7 patients who had been classified previously as HER2-positive and 6 whose original HER2 status was unknown.

New central IHC testing of 37 of the 38 cases determined that only 3 (8%) were HER2-positive based on an IHC count of 3+. The remaining 34 (92%) were HER2-negative with IHC counts of 0-2+.

Although trastuzumab significantly increased response in the 38 women, Dr. Kaufman reported that it added no benefit for 103 women who were HER2-negative and did not have polysomy of chromosome 17. An identical proportion (36%) responded to paclitaxel with and without trastuzumab.

Reporting on the reevaluation of the NSABP trial, Dr. Paik noted that the protocol was changed during the trial to require that IHC testing for HER2 be done by qualified laboratories. He said the proportion of patients classified as HER2-negative by IHC and FISH fell from 16.4% before the amendment to 6.8% afterward. Of the trial population, 9.5% (171/1,795) was negative by both measures.

"This is the bottom line. We couldn't find any subset that didn't benefit from trastuzumab," he said, acknowledging the subsets were small.

In patients deemed negative by both IHC and FISH, the relative risk of recurrence was 0.34.

Noting that the parameters of HER2 positivity originated in the metastatic setting, Dr. Paik and his associates concluded that the "current definition of HER2 overexpression/gene amplification based on data from advanced disease may need to be modified for the adjuvant setting."