Estrogen Replacement Therapy in Patients with Endometrial Cancer: A Survey of Prescription Intention of Belgian Gynecologists

To the Editor:
In his article, “Contemporary Issues in the Management of Endometrial Cancer,” in the September/October issue (page 299), Dr. Richard R. Barakat reviewed the place of estrogen replacement therapy (ERT) in women with a history of endometrial cancer. As only retrospective data exist, a multicenter randomized trial was designed to resolve the question of whether ERT is safe for these patients. In the meantime, opinion leaders have stated that individual clinical judgment must be used to assess the risk of cancer recurrence balanced against the indications for ERT, such as climacteric symptoms and increased osteoporosis risk.

We have conducted a survey to evaluate the prescription attitude of gynecologists in Belgium toward a patient (see case, below) who presents with indications for ERT and a history of early-stage endometrial cancer.

CASE
A 57-year-old woman was treated by total hysterectomy and bilateral salpingo-oophorectomy with lymphadenectomy at age 54 for a well-differentiated endometrial cancer (stage IA). Since then, cytological smears of the vagina have never shown signs of recurrence. The patient has hot flashes, hair loss, skin dryness, and loss of libido. Other clinical findings (e.g., blood pressure, cholesterol, mammogram) were normal, but a bone density result at the L2-L4 site using a dual x-ray absorptiometer revealed severe osteoporosis (T-score of –3.37).

This case was sent to all 1,363 practicing Belgian gynecologists with the question: “Would you treat this patient with hormone replacement therapy (HRT) — No/Yes.” Respondents could then comment on which type of HRT they would prescribe. A questionnaire requesting demographic data was included in the survey. The gynecologists were assured that their participation would remain anonymous. Statistical analysis was performed using SPSS® software.

We obtained 460 responses, of which 18 were considered invalid after one mailing (i.e., a 32% response rate). There was no difference in response rate between female (27% of total) and male (73% of total) physicians. Neither was there a difference by number of years of practice.

Overall, 67% of the physicians surveyed indicated that they would prescribe treatment. There was no difference in prescription attitude by gender or age of the respondents. Among the physicians who would prescribe HRT, 49% stated that they would prescribe estrogen-only therapy (unopposed estrogens) and 27% would prescribe a combined estrogen-progestin regimen. Other physicians mentioned different options or did not define which type of regimen they favored.

Among those who would prescribe HRT, 75% felt that no other investigations were required to help decide whether HRT was indicated for this patient. In contrast, 84% of those who would not prescribe HRT indicated that they needed more information. The most frequently requested studies were additional tests (e.g., computed-tomography scan, tumor markers, chest x-ray, etc.) to rule out the recurrence of cancer.

In conclusion, this study reports that two of three Belgian gynecologists would accept the concept, at least theoretically,
of prescribing HRT for a woman with a history of early-stage endometrial cancer, no signs of recurrence, and recognized indications for HRT (climacteric symptoms and osteoporosis).

These results contrast with earlier surveys where, respectively, 63% and 25% of general practitioners and 42% and 44% of gynecologists in the United Kingdom considered a history of recurrence-free endometrial cancer as either an absolute or a relative contraindication to HRT. This difference in attitude may be related to changing attitudes over time, or to a variability in prescription intentions or habits between clinicians in different countries.

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Author’s Reply:
I read with interest the findings of Rozenberg and Vasquez regarding their survey of Belgian physicians on the use of estrogen replacement therapy (ERT) in patients with endometrial cancer. Unfortunately, as with many studies involving surveys, this study suffers from a lack of participation, with only 32% of physicians returning the questionnaires.

Physicians who are willing to take the time to respond may be more biased in favor of prescribing ERT for their patients, thereby falsely elevating the percentage of respondents willing to start hormone replacement therapy (HRT) as outlined in the survey.

Unfortunately, the case presented for purposes of the survey does not provide a great deal of useful information. As stated, the authors have selected a 57-year-old patient who underwent hysterectomy and bilateral salpingo-oophorectomy three years ago for a well-differentiated cancer confined to the endometrium and who now has climacteric symptoms. The question presented to the practicing gynecologist is whether or not he or she would initiate hormone therapy in such a case.

The recurrence rate, as defined by studies of the Gynecologic Oncology Group (GOG), for patients with a stage IA endometrial carcinoma is approximately 1%. Further, as the majority of recurrences from endometrial cancer occur within the first three years after treatment, the patient whose history is presented might be assumed, for all intents and purposes, to be cured.

I would suspect that the majority of practicing obstetricians and gynecologists, and certainly gynecologic oncologists, in the United States would have no problem with the decision to initiate estrogen therapy in such a patient.

The question that must be answered, however, is whether estrogen can be prescribed safely to higher risk endometrial cancer patients. Ultimately, that question can be answered only by randomized clinical trials, such as GOG protocol 137, which compares ERT to placebo in clinical stage I and II endometrial carcinoma. Patients entered on study must start ERT within 12 weeks of their surgeries to avoid the bias that occurs by waiting several years, which eliminates potential recurrences.
All practicing obstetricians and gynecologists, and gynecologic oncologists, should be encouraged to enroll their patients in this trial, as it will—it is hoped—finally answer the question as to whether it is safe to give ERT to women with a history of endometrial cancer.

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Reduced Levels of N-acetylaspartate in Malignant Brain Tumors

To the Editor:
I enjoyed the article by Prados, Berger, and Wilson, “Primary Central Nervous System Tumors: Advances in Knowledge and Treatment,” in the November/December 1998 issue. I would like to draw your attention to an error on page 342, under Magnetic Resonance Spectroscopy. In the second paragraph, the authors state that tumors often show elevated levels of the three metabolites, N-acetylaspartate, creatine, and choline-containing compounds.

Almost all tumors of the brain, particularly malignant tumors, show marked decreases in the N-acetylaspartate. While it is true that choline-containing compounds are elevated, the N-acetylaspartate, which is a neuronal marker, is almost always decreased in neoplasms. It may be helpful for the authors to clarify this point.

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Author’s Reply:
Dr. McConnell correctly has noticed an error in our manuscript concerning magnetic resonance spectroscopy. Malignant brain tumors will show elevated levels of choline-containing compounds and reduced-to-absent levels of N-acetylaspartate. We appreciate his comment, agree with it, and apologize for the error.

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