Gynecologic Cancer: Screening, Treatment Options, and Quality-of-Life Considerations

This issue of Cancer Control highlights cancers unique to women with emphasis on gynecologic cancers. Gynecologic cancers are diagnosed in approximately 77,000 women per year in the United States. The most common sites of gynecologic carcinomas, in order of increasing incidence, are the cervix, the ovaries, and the endometrium, all of which are profoundly affected in both the normal and malignant state by endogenous as well as exogenous female sex hormones. Estrogen generally has a proliferative effect on both benign and malignant gynecologic tissues, which suggests that patients treated for gynecologic cancer would benefit from a chronic hypoestrogenic state. However, this hypothesis does not consider the effect of the hypoestrogenic state on the rest of the body.

Until recently, patients treated for breast cancer or gynecologic cancer were not offered hormone replacement therapy for fear of activating quiescent cancer cells. Our current knowledge regarding the numerous benefits of hormone replacement therapy suggests that this strategy be reexamined. In the lead article, Philip DiSaia, MD, summarizes the evidence for and against hormone replacement therapy in patients treated for breast, endometrial, and ovarian cancer. It becomes evident that there is little or no evidence that estrogen replacement therapy increases the recurrence rate or decreases survival in these cancers, and indirect evidence exists that estrogen replacement therapy is safe in breast and endometrial cancers. Prospective, randomized trials are needed to address this significant public health problem. Even if estrogen replacement therapy is found to adversely affect disease-free survival in these cancer survivors, a risk-benefit analysis needs to be employed. It is conceivable that overall survival in patients who receive hormone replacement will be superior as a result of fewer deaths due to ischemic heart disease or osteoporosis. Beneficial effects of estrogen replacement therapy on severe vasomotor and genitourinary atrophy symptoms also must be considered. Until prospective, randomized studies are completed, patients treated for these cancers should be offered the option of estrogen replacement after candid discussions of its benefits and risks.

Tamoxifen is used in breast cancer therapy for its so-called antiestrogenic effects. Paradoxically, it has an estrogen-agonist effect on the endometrium. Unopposed estrogen administration has been shown to significantly increase the risk for the development of endometrial cancer. In his discussion of the association between tamoxifen and endometrial cancer, Richard Barakat, MD, examines several large studies documenting the increased relative risk (from 4.1 to 7.5) of developing endometrial cancer in breast cancer patients taking tamoxifen. Since breast cancer patients taking tamoxifen are at high risk for the development of endometrial cancer, is screening appropriate? Dr. Barakat presents an excellent discussion on this issue and concludes that screening is not warranted. This conclusion seems appropriate, given an estimated annual risk of 2,000, a generally good prognosis at the time of discovery in symptomatic patients, and his estimate of a decrease in mortality of only 0.03% of tamoxifen-treated patients who are screened. These patients should have an annual gynecologic examination, and for those who report abnormal vaginal bleeding or spotting, an endometrial biopsy should be performed on an outpatient basis. Patients for whom this would not be technically possible can be further evaluated with vaginal ultrasonography rather than with dilation and curettage in the operating room. If the endometrial thickness on ultrasonography is 5 mm or less, then the risk of endometrial cancer is negligible. If the endometrial thickness is more than 5 mm, then a dilation and curettage should be performed in symptomatic patients. However, vaginal ultrasonography can be falsely alarming at times, frequently due to the misinterpretation of subendometrial structures as endometrial pathology.

Indications for the use of tamoxifen are expanding, and the drug eventually may be used to prevent the development of breast cancer in women. The incidence of endometrial cancer will likely increase as a result. Routine screening, however, will have to await simpler and less expensive methodology.

Changes in sexual function following treatment for cancer is a critical quality-of-life aspect that is often neglected. As Barbara Andersen, PhD, discusses in her article on the development and treatment of sexual dysfunction, this issue is particularly relevant in the treatment of gynecologic cancers, which often result in anatomically or functionally altered sex organs. This aspect of the patient's recovery after gynecologic cancer treatment is too often neglected. Dr. Andersen points out that the development of sexual dysfunction is most closely related to the extent of disease and treatment and to baseline psychologic/behavioral functions. Dr. Andersen uses the term “sexual self-schema” to identify women at greatest risk for the development of sexual dysfunction. Patients with a low sexual self-concept are at greatest risk. Treatment of sexual dysfunction in this setting can be difficult. Dr. Andersen makes an elegant case for intervention in high-risk patients prior to their resuming sexual activity after treatment. The psychologic and behavioral processes that result in sexual dysfunction also are described. Both the patient and the health care team would benefit from education in this area.

As the fourth leading cause of cancer deaths in women in the United States, ovarian cancer is most important of all the gynecologic cancers from a public health standpoint. The annual deaths attributable to this disease comprise more than that of all other gynecologic cancers combined. This excess mortality is a consequence of the fact that 70% of patients are initially diagnosed with disseminated disease with an overall 10-year survival of approximately 10%. In the rare cases when ovarian cancers are diagnosed at an early stage, survival reaches 90%. Given these circumstances, screening for ovarian cancer in asymptomatic women would appear to be a worthwhile effort. James Fiorica, MD, reports on ovarian cancer screening methods and the feasibility of screening in various populations. While measurement of serum CA 125 levels appears to be an ideal screening method for ovarian cancer, only 50% of patients with early ovarian cancer have an elevated serum CA 125 level, and many benign conditions result in elevated levels. Pelvic ultrasonography suffers from a low positive predictive value that results in many operations in order to discover just one case of ovarian cancer. A combination of CA 125 measures and pelvic ultrasonography might accomplish the sensitivity, specificity, and positive predictive value necessary for cost-effective screening in the general population. The PLCO study initiated by the National Cancer Institute is testing this hypothesis, although an answer will not be forthcoming for many years. Dr. Fiorica points out that although screening for ovarian cancer in the general population is not warranted at this time, it is indicated in certain high-risk groups, including women in families with an identified hereditary ovarian cancer syndrome and women with a very strong family history of ovarian cancer (two first-degree relatives with ovarian cancer or one first-degree relative with ovarian cancer diagnosed before the age of 45 years). The discovery of the BRCA1 gene represents the dawn of genetic screening that can identify individuals at greatest risk for ovarian and other cancers.

The value of cytoreductive surgery in the management of ovarian cancer also is presented in this issue. This aggressive and potentially morbid procedure has never been evaluated in a prospective, randomized study except in the interval debulking setting. The single randomized study showing the value of interval debulking was published recently in the New England Journal of Medicine (1995;332:629-634). I believe that an extrapolation of the result of this study to the primary debulking setting is reasonable, and I doubt that primary cytoreductive surgery will ever be evaluated in a prospective, randomized fashion.

Finally, John Kavanagh, MD, and colleagues from the M.D. Anderson Cancer Center succinctly review some of the exciting advances that are being made in the systemic therapy of ovarian cancer. New approaches are already being tested in the clinic, and we will hear more about these developments soon.

William S. Roberts, MD  
Program Leader, Gynecologic Oncology Program  
Chief, Gynecologic Oncology Service  
H. Lee Moffitt Cancer Center & Research Institute