

CA

Ovarian Cancer

Robert C. Young, MD

This issue of *CA* focuses on ovarian cancer, and the articles by Teneriello and Park¹ on early detection and Qazi and McGuire² on treatment bring into clear focus the spectrum of issues that face clinicians in managing this difficult disease. While the public focus on women's cancers has increased, breast cancer has received the most attention. Although fewer women develop ovarian cancer, it is a much more commonly lethal malignancy. In 1995, about 26,600 women will develop the disease in the United States and about 14,500 women will die.³

As Qazi and McGuire² emphasize, proper surgical staging and evaluation coupled with appropriate use of adjuvant therapy in early disease and platinum-based combinations and the new drug paclitaxel in advanced disease have steadily improved the outcome for ovarian cancer. Clearly, techniques are presently available to achieve long-term survival in most patients who present with early disease,⁴ and the use of optimal surgical cytoreduction coupled with platinum-containing combinations and paclitaxel enable 25 to 30 percent of women with advanced ovarian cancer to survive five years or longer.⁵ Nevertheless, most women with advanced ovarian cancer will ultimately succumb to their disease, and this is not likely to be altered dramatically by small changes in present treatment.

It is worth emphasizing that stage for stage, the long-term survival in ovarian cancer is similar to that of endometrial

cancer. The overall outcome for endometrial cancer is so much better simply because the vast majority of patients can be diagnosed with early disease. This has led to a renewed focus on screening techniques to detect disease in its early stages and the biologic and genetic underpinnings that predispose certain women to this disease. The article by Teneriello and Park¹ thoroughly reviews this subject and provides the scientific information available about the relative contributions of transvaginal ultrasonography, CA 125, and color flow Doppler imaging to ovarian cancer screening. At present, one must reluctantly conclude that routine screening for patients with no known risk factors is neither particularly successful nor cost effective.⁶ Whether refined screening techniques, additional tumor markers, and a focus on genetically defined high-risk populations will improve the utility of screening is under active investigation.

The explosion of information on the molecular biology of cancer is certain to make a substantial impact on ovarian cancer diagnosis and management. The identification of the *BRCA1* gene on chromosome 17 and the subsequent evidence for a family of genes that may play a role in both the breast-ovarian syndrome and familial ovarian cancer offer the promise of identifying populations that are truly at risk for this disease.⁷⁻⁹ When screening can be applied in a more focused fashion on populations of women truly at risk, it will simultaneously improve the yield and make screening more cost effective. Although this is likely to be the first application of the genetic infor-

Dr. Young is President of the Fox Chase Cancer Center in Philadelphia, Pennsylvania.

mation, it is unlikely to be the last. As we discover more about the function of tumor suppressor genes, such as *BRCA1* and *p53*, it becomes apparent that many are involved with control of the cell cycle and are crucial to the regulation of cancer-cell proliferation. In addition, it has become increasingly clear that many of these genes are involved in a process known as apoptosis or programmed cell death.¹⁰ Clearly, gene defects that disrupt control of cell growth and stop normal programmed cell death must be central to the cancer process. It is likely that future cancer strategies will not only employ the nonspecific anticancer effects of current oncologic pharmaceuticals, but will also produce anticancer drugs that are targeted to these defects in gene regulation. The active search for the genes involved with ovarian cancer will likely produce novel therapeutic strategies for the future.

However, it is inappropriate to conclude that progress cannot continue unless new genetic discoveries are forthcoming. The application of careful surgical staging, appropriate use of adjuvant chemotherapy, and development of better drugs and combinations for advanced disease have already altered nationwide mortality in ovarian cancer. Data from the National Cancer Institute's Surveillance, Epidemiology, and

End Results program indicate that between the years 1973 and 1987, there has been a decrease of 25 percent in overall mortality in women younger than 65 years and a reduction of 15 percent in mortality across all ages. While some of the decrease in the younger age group can be attributed to the widespread curability of the relatively rare germ-cell tumors, some of this decrease is related to better management of epithelial ovarian cancer.

Finally, it is clear that despite progress in managing virtually all stages of ovarian cancer, present therapies are incomplete and inadequate. The search for better treatments of this common cause of cancer death in women will require continued prospective clinical trials. It will also require the continued evaluation of experimental therapies in our rapidly changing health care system with its increasing focus on cost effective and efficient application of standard care. It is not clear that the capacity of the health care system to innovate will be preserved. One of our challenges for the future will be to make certain that the health care system that emerges will allow clinical trial research so that the ovarian cancer therapy of this generation will not be the therapy available to subsequent generations.

References

1. Teneriello MG, Park RC: Early detection of ovarian cancer. *CA Cancer J Clin* 1995;45:71-87.
2. Qazi F, McGuire WP: The treatment of epithelial ovarian cancer. *CA Cancer J Clin* 1995;45:88-101.
3. Wingo PA, Tong T, Bolden S: Cancer statistics, 1995. *CA Cancer J Clin* 1995;45:8-30.
4. Young RC, Walton LA, Ellenberg SS, et al: Adjuvant therapy in stage I and stage II epithelial ovarian cancer: Results of two prospective randomized trials. *N Engl J Med* 1990;322:1021-1027.
5. Neijt JP, ten Bokkel Huinink W, van der Burg ME, et al: Long-term survival in ovarian cancer: Mature data from The Netherlands Joint Study Group for Ovarian Cancer. *Eur J Cancer* 1991;27:1367-1372.
6. Creasman WT, DiSaia PJ: Screening in ovarian cancer. *Am J Obstet Gynecol* 1991;165:7-10.
7. Miki Y, Swensen J, Shattuck-Eidens D, et al: A strong candidate for the breast and ovarian cancer susceptibility gene *BRCA1*. *Science* 1994;266:66-71.
8. Steichen-Gersdorf E; Gallion HH, Ford D, et al: Familial site-specific ovarian cancer is linked to *BRCA1* on 17q12-21. *Am J Hum Genet* 1994;55:870-875.
9. Godwin AK, Vanderver L, Schultz DC, et al: A common region of deletion on chromosome 17q in both sporadic and familial epithelial ovarian tumors distal to *BRCA1*. *Am J Hum Genet* 1994;55:666-677.
10. Green DR, Bissoinette RP, Colter TG: Apoptosis and cancer. *PPO Updates* 1994;8:1-14.