Testimony
Before the Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies
United States Senate

Activities at the National Cancer Institute Concerning Gynecological Cancers

Statement of

Andrew C. von Eschenbach, M.D.

Director,
National Cancer Institute
National Institutes of Health
U.S. Department of Health and Human Services

For Release on Delivery
Expected at 9:00 a.m.
Wednesday, May 11, 2005

Senator Specter and members of the Subcommittee, thank you for the opportunity to testify on the topic of gynecological cancer on behalf of the National Cancer Institute (NCI). Ovarian, cervical, and endometrial (also known as uterine) cancers are grouped as gynecological cancers. One hundred years ago, gynecological cancer, specifically cervical cancer, was the leading cause of cancer deaths among women in the United States. Over the past century, we have made major progress toward the defeat of this dreaded disease in our Nation. Today, I would like to talk to you about some of the exciting work NCI is doing to eliminate the suffering and death due to gynecological cancers in the United States and around the world.

Cervical cancer is the most common of cancers among women worldwide. Over 400,000 new cases are diagnosed each year, resulting in about 200,000 deaths. With the continuing education and application of early detection through pelvic examinations and Pap smears, the frequency of advanced or recurrent cervical cancer has diminished in the United States. However, advanced cervical cancer is still observed and has a poor prognosis. We recognized that a better preventive strategy against cervical cancer is needed, and NCI investigators have developed a new vaccine approach to prevent the transmission of the human papillomavirus, the virus responsible for most cases of cervical cancer. We have licensed this technology to two large pharmaceutical companies, Merck and Glaxo Smith Kline, who have recently reported that results of clinical trials indicate that the vaccines were almost 100% effective in preventing the acquisition of the virus types 16 and 18, which together account for nearly 70% of cervical cancer worldwide.

We have also been working to make screening for cervical cancer less expensive, more reliable, and more available. Even with the arrival of potential vaccines, we will need to continue screening for many years to come. An effective vaccine in combination with cervical cancer screening is expected to reduce cervical cancer rates by 90% in the United States.

NCI is working to bring state-of-the-art cervical screening to geographic regions of excess mortality. In one of our most exciting projects, NCI is collaborating with the Centers for Disease Control and Prevention (CDC), the Department of Agriculture, and State health departments to improve screening for cervical cancer among poor, rural women in the Mississippi Delta, who have had some of the highest rates of cervical cancer in the U.S. for the last 50 years. We know that cervical cancer disproportionately affects members of particular racial and ethnic minority subgroups and other underserved women.

If successful in Mississippi, we hope to promote region-specific programs with collaborators in other underserved regions like Appalachia, the Mexican-U.S. border, urban clinic populations, and centers serving migrant workers. This initiative also falls within the Health and Human Services Secretary Leavitt's 500-day plan to support community-based approaches to close the health care gap, particularly among racial and ethnic minority populations. Later this month, the NCI Center to Reduce Cancer Health Disparities will publish a report titled, "Excess Cervical Cancer Mortality: A Marker for

Low Access to Health Care in Poor Communities." This report will explore the components of the problem of excess cervical cancer mortality and identify critical needs.

Ovarian cancer remains the most deadly of the gynecologic cancers. Reasons for this continuing poor outcome include the nonspecific and late clinical presentation of ovarian cancer and the lack of reliable and cost efficient methods of early detection. Through the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial, the NCI is carrying out a major evaluation of CA125 blood tests and trans-vaginal ultrasounds as screening procedures for early ovarian cancer detection. Currently, 70,000 women are receiving these screening methods through this trial. When we are able to validate a screening method for ovarian cancer, the early detection alone – even without changes in current standards of treatment - will have a substantial impact on public health.

Through the NCI Director's Challenge project, we have undertaken major studies into the molecular classification of ovarian cancer. This research, being conducted at the University of Pennsylvania, the University of Michigan, Memorial Sloan-Kettering Cancer Center, and the intramural Center for Cancer Research at NCI, has helped us begin to understand the biology of ovarian cancer. In addition, we have established five Specialized Programs of Research Excellence, also known as SPOREs, to foster translational research in ovarian cancer, at the Fox-Chase Cancer Center in Philadelphia, the University of Texas MD Anderson Cancer Center in Houston, the University of Alabama at Birmingham, Harvard University (Brigham and Women's Hospital, Boston), and the Fred Hutchison Cancer Research Center in Seattle. One of the standard drugs

used to treat ovarian cancer worldwide, Taxol®, was discovered and developed by NCI in collaboration with investigators across the United States and five other international partner countries.

NCI has also begun the Proteomics Ovarian Cancer Recurrence Monitoring Prospective Trial. Among the outcomes of this trial will be a repository of tissue samples for proteomic and other biomarker validation mechanisms for the determination of ovarian cancer recurrence and will begin accrual of patients this June. This is a multi-institutional partnership led by NCI's intramural Center for Cancer Research in collaboration with the SPOREs. This trial will explore the opportunities of the emerging field of proteomics as a way to detect early stages of ovarian cancer. Other collaborative ovarian cancer trials supported by NCI are studying the molecular characterization of newly diagnosed patients, prophylactic surgery for women at high risk for ovarian cancer, monitoring of breast cancer patients for BRCA1 and BRCA2 gene mutations, as well as several trials that are looking for specific diagnostic signatures for malignancy versus benign or unaffected samples. In addition, NCI is currently sponsoring a national clinical trial aimed at evaluating a novel approach to ovarian cancer screening in women at increased genetic risk of ovarian cancer. While we recognize that more women diagnosed with this disease today are living longer, with a higher quality of life than they were twenty years ago, we also acknowledge that more work is needed to end the suffering and death that too many women still face. For women who have a high risk of ovarian cancer, which includes a family history of breast, ovarian, endometrial, or colon

cancer and a known BRCA1 or BRCA2 mutation, we recommend that they receive two yearly exams plus CA125 monitoring as well as a yearly trans-vaginal ultrasound.

Endometrial cancer is the most common gynecologic cancer in the United States, though not the most lethal. Around 90% of endometrial cancers are diagnosed in the early stages of cancer with an overall 85% survival rate. Population studies indicate that endometrial cancer is one where incidence and mortality are most affected by being overweight or obese, as measured by having a high body mass index (BMI). These data suggest that maintaining a normal body weight could prevent about one-half of endometrial cancers. However, the alarming trends of increasing BMI in the United States suggest that endometrial cancer may become more common.

NCI is able to utilize the latest technology to examine the genetic differences in endometrial cancers from women of normal and high BMI. The ability to monitor gene expression is at the heart of many research projects. This allows scientists to better understand the biology of risk, the knowledge of which will enable them to design and implement personalized preventive and therapeutic strategies. Through NCI's Clinical Trials Cooperative Groups, specifically the Gynecology Oncology Group (GOG), NCI has sponsored major anatomic and molecular staging studies of endometrial cancer. Additionally, the GOG has conducted landmark studies evaluating the roles of radiation, hormone therapy, and chemotherapy in women with endometrial cancer.

The NCI budget for gynecological cancers in FY 2004 was $212,527,000. This funding supports NCI's ongoing multi-pronged, multi-disciplinary effort in molecular biology, epidemiology, prevention, treatment, and survivorship issues of gynecologic cancers. Substantial advances have been made intramurally in the NCI Center for Cancer Research and the Division of Epidemiology and Genetics, and through collaborations with extramural colleagues who participate in the SPOREs network, the Cancer Genetic Network (CGN), and GOG clinical trials cooperative groups. Research advances made at NCI are also complemented by collaborations with private industry. In addition to the clinical trials done through the cooperative groups, NCI also sponsors Phase I and II trials in gynecologic cancer through the NCI-designated Comprehensive Cancer Centers and a consortium of Canadian hospitals organized by the Princess Margaret Hospital in Toronto. NCI also co-sponsors the Gynecologic Cancer Intergroup (GCIG), which brings together investigators from all the clinical trials cooperative groups conducting trials for women with gynecologic cancers from around the world. The GCIG meets twice a year and under its umbrella, member groups have joined together to develop joint protocols and develop strategies for future research.

Eliminating the suffering and death from gynecologic cancer is a priority for the NCI. We are working to implement the recommendations of the Gynecological Cancer Progress Review Group, which will further strengthen our research in this area. We have also undertaken, in partnership with the American Cancer Society, the International Agency for Research on Cancer, the International Gynecologic Cancer Society, the International Union against Cancer, and the World Health Organization, a Global

Initiative on Women's Cancer (GLOW) so that we can lift the burden of gynecologic cancer from around the world. This international partnership will focus on reducing the global burden of gynecological cancer, breast cancer, and tobacco use among women. GLOW will include public and professional education, the development of a needs-assessment database, and technical assistance to countries in the developed and developing world as they work to strengthen cancer control efforts, including prevention, screening, diagnosis, treatment, palliation, and end of life care.

NCI is also collaborating with the CDC on education and outreach efforts regarding gynecological cancers. Earlier this year we printed a new publication, *"Understanding Cervical Changes,"* which is intended to assist women and their clinicians to understand the treatment decisions involved with abnormal Pap tests. The same brochures in both Vietnamese and Spanish are currently under development.

There is no single approach, organization, or act that will bring about an end to each of these diseases. It will require a collaborative effort between Federal agencies, private industry, States, health professionals and patients. Efforts to increase healthy life potential through interdisciplinary and interagency collaboration are well underway. Public outreach efforts, comprehensive and novel prevention and early detection strategies, and scientific pursuits to improve the standard of practice will yield the end of suffering and death due to gynecological cancers.

Thank you, Mr. Chairman, for giving me the opportunity to present this information to the Subcommittee. I will be happy to answer any questions you may have.