

President's Cancer Panel Meeting  
Meeting Minutes

*Cancer and the Aging Population*  
**Meeting Summary**  
**From the President's Cancer Panel Meeting**  
**July 31, 1997**  
**Ann Arbor, Michigan**

## Overview

The President's Cancer Panel was chartered to monitor and evaluate the development and execution of the National Cancer Program and to report to the President on barriers to Program implementation. The purpose of this meeting, the second in a series of four meetings focusing on the concerns of special populations in the National Cancer Program, was to consider the particular issues and concerns of older Americans.

Twenty-three speakers representing varied disciplines presented testimony to the Panel on current activities of the National Cancer Institute and the National Institute on Aging related to cancer and aging, reviewed current statistics on cancer in older Americans, outlined epidemiologic issues related to cancer and aging, and considered health research questions for older Americans. Cell culture and animal models for studying molecular biologic questions of aging were described, as were pharmacologic issues in aging. Prevention, detection, behavioral, treatment, management, access, and outreach issues specific to aging populations were discussed. In addition, issues of survivorship, supportive care, and education of the public and health professions on issues of aging and cancer were reviewed. Speakers offered specific recommendations for better addressing the issues of the older person with cancer or at risk for cancer for consideration by the Panel.

## Meeting Participants

**President's Cancer Panel:** Harold P. Freeman, M.D., Chairman; Paul Calabresi, M.D.

**National Cancer Institute:** Alan S. Rabson, M.D., Deputy Director, NCI; Maureen O. Wilson, Ph.D., Assistant Director, NCI, Executive Secretary, President's Cancer Panel

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## Opening Remarks - Dr. Harold Freeman, Chairman

In opening the meeting, Dr. Freeman stated that:

- This is the second of four meetings to pursue the concerns of special populations in the National Cancer Program. The Panel held its first meeting on this subject in April 1997 on the meaning of race in science and related considerations for cancer research. The two upcoming meetings will examine the real impact of the reduction in cancer mortality, and will review the responsiveness of the health care system to special populations.
- Addressing cancer issues related to the aging population has become increasingly critical as the numbers of young-old (those aged 65-74 years), older-old (aged 75-84 years), and oldest-old (85 years and older) continue to grow.
- The population aged 65 and older increased eleven-fold (to 33.5 million or one in eight Americans) from 1900 to 1995. During the same period, the under 65 population grew only three-fold. Further, since 1900, the percentage of Americans over age 65 has tripled from 4.1 percent in 1900 to 12.8 percent in 1995. In 1995, persons reaching age 65 had an average life expectancy of an additional 17.4 years. The growth in the older population is expected to continue, with the most rapid increase between 2010 and 2030, when the "baby-boom" generation reaches age 65. By 2030, there will be an estimated 70 million older persons, more than twice the number in 1900, comprising about 20 percent of the U.S. population. It also is projected that in the coming decades the older population will be much more racially and ethnically diverse than it is today.
- Overall, 58 percent of all cancer incidence is in the older segment of the population. Older persons have a risk of developing cancer 10 times that of individuals younger than age 65.
- These data suggest an urgent need to address the special concerns of the aging population within the National Cancer Program. The need for prevention and control strategies and cancer treatment and care for the elderly is already great, and is likely to increase.
- Among the potential age-related factors that may be involved in the etiology of cancer in this population are decreased cancer surveillance, longer duration of exposure to carcinogens, increased cell susceptibility to carcinogens, decreased DNA repair function, amplified oncogene activation, and defects in tumor suppressor genes. Detecting cancer in the elderly is often complicated by nonspecific presentation of a malignancy, and treatment often must take into account comorbidities, decreased physical and psychologic functioning, differences in drug metabolism, and the potential for secondary complications.
- Other relevant concerns for the aging population are issues in understanding medical procedures and options, diminished social support, limited financial resources, and quality of life. The Panel believes quality of life is a particularly important consideration for aging Americans, who must measure the risk of treatment against the benefits of survival (or perhaps, the benefits of treatment against the risk of survival).

### Welcome – Dr. Max S. Wicha

Dr. Wicha welcomed the Panel, speakers, and other attendees, adding that:

- The establishment of centers for geriatric medicine and cancer at the University of Michigan, now co-located at a newly opened facility, reflects a recognition of aging and cancer (and their relationship to each other) as priority areas in medicine for the next decade.
- Further, housing together both research laboratories and patient care facilities is expected to facilitate understanding of the impact of changes in aging cells on cancer development and the special clinical problems of the elderly.

### Welcome – Dr. Jeffrey B. Halter

Dr. Halter posed several questions that he hoped would be addressed at least in part during the meeting:

- Why do so many older people develop cancer?
- What is the current level of funding nationally for the study of cancer and aging?
- Why is there such a large gap between what is known about cancer prevention, screening, and detection, and what is applied in general practice in the care of older people?
- Why are so many older patients with cancer referred rapidly to hospice instead of being entered into treatment programs?
- Why are there few treatment programs designed for older patients with cancer? What are the limiting factors for designing such regimens?
- Why is so little known about treatment outcomes in older adults?
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Dr. Halter expressed his optimism that through activities of the President's Cancer Panel, some of these issues will be brought forward and more fully addressed.

### Director's Remarks

Representing Dr. Richard Klausner, Director, NCI, Dr. Rabson indicated that:

- Dr. Klausner was unable to attend because of activities related to the NCI's Congressionally mandated study of radioactivity exposures following nuclear tests conducted in the 1950s and 1960s. The study, employing computer modeling based on the scant available data, identified 24 counties in the United States most heavily exposed to radioactive fallout. A briefing and press conference on the study are scheduled.

## NATIONAL INSTITUTE ON AGING REPORT

### Key Points

- Age is the single greatest risk factor for cancer; old people are disproportionately affected by cancer in terms of its incidence, and to an even greater extent, in cancer deaths. The median age of cancer patients in the United States is 70 years.
- It is unclear why cancer occurs more frequently in the elderly. Key issues may include exposure to carcinogens, greater cellular susceptibility to cancer over time, greater opportunities for mutagenesis and transforming events in older cells, decreased DNA repair capability with age, a favorable microenvironment, and failures of immune surveillance.
- Several areas of biology are of interest both in cancer and aging. Growth regulation by a cell or organ in response to environmental stimuli is influenced by proto-oncogene expression, oncogene expression, and tumor suppressor gene mutation. The processes that affect cell replication are important both in cancer and in aging, however, there are anti-carcinogenic elements of the aging process that require further exploration. One such process involves the preservation of telomeres through inappropriate expression of telomerase, allowing cells to escape normal cell death.
- Free radical damage is an important partial contributor to the aging process and is also thought to play a role in carcinogenesis.
- Immune system decline with age may allow cancer cells to develop without immune surveillance. It is also possible that decreased immunity is responsible for what appears to be slower tumor growth in older people, however, certain immune system products can enhance tumor growth.
- Considerable common ground exists between medical oncology and geriatrics: both specialties provide care for predominantly older people, involve multi-disciplinary approaches, and involve end of life care, including hospice. It is important, however, to acknowledge the fundamental cultural and training differences between the two disciplines. For example, geriatricians may tend to be risk and toxicity averse compared with oncologists as a group, who may tend to be more aggressive, except in treating older patients.
- Two joint NIA/NCI program announcements have been issued. One is intended to foster research on the issues of aging, women, and breast cancer; breast cancer incidence clearly is influenced enormously by age. The second announcement focuses on aging, race, and ethnicity in prostate cancer; prostate cancer mortality is quite high in older men, and is twice as high in African American men as in white men. Applications submitted under these program announcements will be reviewed through the usual peer-review process. The importance of these areas may justify fostering research with more targeted funding.
- In response to environmental stimuli, an individual cell may grow, differentiate, stop dividing reversibly, stop dividing irreversibly (senescence), or undergo transformation and become immortalized. Understanding the process by which these manifestations are regulated is extremely important. There is a great deal of debate as to whether or not the aging of individual cells equates to aging of the

organism. It is known that different organs age at different rates, but these different rates may not be related to the replicative capacity of the cells in the organ. Cellular proteins change in conformation and function, which may be related to aging, but not to replication. A better understanding is needed of the relationship between senescence in cells in vitro and aging in vivo in organs and in people.

- Older cancer patients experience differences in drug metabolic activation and clearance compared to younger patients; these differences impact the treatment regimens given older patients and the toxicities they experience. Prognostic indicators also are likely to be different in older people, and cancers may present differently in the elderly.
- Comorbidity, including previous illness, disability, and degenerative conditions, have been used as a justification for not treating older people with cancer aggressively. We need to know which conditions actually influence anticancer drug toxicity, and which do not. The NCI Cooperative Groups could be an excellent vehicle for addressing treatment questions in older people, such as pharmacology evaluations or comparing the usefulness of the geriatric method of patient assessment to that of the Karnofsky index used in oncology as a measure of a patient's physiologic reserve to tolerate treatment.
- Evidence exists that even when older people are treated with surgery alone, their incidence of second and third cancers is higher than would be expected. This suggests that intrinsic aspects of aging create susceptibility, and there may be undiscovered multiple tumor syndromes that affect older people most frequently.
- Epidemiologic evidence also suggests that cancer incidence may be decreased in the oldest old (i.e., those aged 85 years and older).
- The NIA intramural program is conducting pilot trials to determine whether the in vitro DNA repair capability of bone marrow cells or lymphocytes from an individual patient can predict the toxicity that person will experience from chemotherapy. Pharmacology and vaccine development are also under study.

#### Additional Research Needs and Other Recommendations

- It is incumbent upon the NIA and the NCI to work together to develop jointly funded research programs dealing with the interrelationship of aging processes and cancer development. Because fundamental differences exist in the culture and the body of knowledge in geriatrics and oncology, joint training initiatives are also needed. The Hartford Foundation is currently conducting geriatric education retreats with various medical subspecialties. There should be geriatric oncology fellowships, which could be expected to give rise to new geriatrics requirements for medical oncology training universally and requirements for board certification.
- Funds should be set aside for research on high priority questions in cancer and aging.
- We need to become better educated about the real issues of aging and cancer so that effective treatment programs can be developed that accommodate the decreased physiologic reserve of the elderly.

- Outcomes research focusing on the older cancer patient population is needed. Little longitudinal data exist on survivorship issues of older aged cancer survivors. Research is also needed on health care access issues of older cancer patients and their families.

## **History and Identification of Older Americans as a Special Population**

### **Opening Remarks**

#### Key Points

- Many definitions of aging exist; Dr. Kennedy prefers to define the aged as those who are chronologically gifted. In the past century, we have seen a remarkable increase in survival. For example, according to Minnesota cancer surveillance data, 25 percent of Minnesota women born today can expect to live to age 92, and an equal percentage of Minnesota men can expect to achieve age 86 years, assuming current conditions. However, aging typically precedes the development of cancer, therefore, an increasing elderly population with a high incidence of cancer may prove to be a factor that limits the continued extension of the average lifespan.
- The older population receives less cancer screening, less staging of disease, and less aggressive therapies (often, no therapy at all), simply because they are older. Little research has been done on people over age 65-70. The primary reasons cited have been unacceptable toxicity, comorbidity, lack of benefit from treatment, limited financial resources, lack of support, other social factors, and transportation problems.
- Some research has been done; for example, a national study of Hodgkin=s disease showed that older people (at diagnosis) do less well, stage for stage, than do younger people, and suggested that Hodgkin=s disease in older people differs biologically from the disease in younger individuals.

#### Additional Research Needed and Other Recommendations

- Older cancer patients should be offered more aggressive primary surgery, and more aggressive chemotherapy (particularly for those with tumors known to be responsive).
- Older cancer patients need to be involved in setting goals for their care, and physicians need to become more expert in caring for patients who are dying of cancer.
- Economic, social, and bioethical issues related to cancer in the older population will be a part of our future and must be addressed.

## Cancer in Older Americans

### Key Points

- The Surveillance, Epidemiology, and End Results (SEER) program monitors cancer incidence and survival in approximately 14 percent of the United States population. For the period 1990-1994, the median age at cancer diagnosis was 68 years, with 60 percent of cases occurring in persons 65 years and older. The median age for cancer mortality was 71 years, with 69 percent of cancer deaths occurring in people over age 65.
- The cancer incidence rate in the over age 65 population is more than 10 times that of the under 65 population (all cancer sites). Two in every 100 Americans aged 65 and older will be diagnosed with cancer each year.
- Between 1973 and 1994, the cancer incidence and survival rate for all sites combined has gone up 15 percent among those under age 65; for those 65 years and older, it has increased more than 31 percent. For the same period, cancer mortality (all sites) has declined by almost 10 percent for those under age 65, but has increased almost 17 percent for those 65 years and older.
- Different racial and ethnic groups have differing cancer patterns. For all cancers combined, incidence is lowest among American Indians, and highest among African Americans. For every ethnic and racial group, however, cancer rates increase with age.
- Among women, breast cancer incidence peaks around age 80 years, but colorectal cancer rates are higher than breast cancer rates in the 85 years and older group. Lung cancer in women peaks in incidence around age 70, then declines.
- Among men, prostate cancer overwhelms the age curve (1,400 cases per 100,000 men) at ages 70-74; incidence rates for colorectal and lung cancer show patterns similar to those in women.
- Although breast cancer incidence is 74 per 100,000 for those under age 65 and 443 per 100,000 for those 65 and older, survival is worst for the youngest age group. Median age at diagnosis is 64 years. Between 1973 and 1994, breast cancer mortality declined in the population under 65 years old (by 15 percent) and increased almost 12 percent among those 65 years and older.
- Colorectal cancer incidence (median age 72 years) among men and women has been declining for both the under 65 and 65 and older age groups, but the decline has been steeper for the younger age group. The same is true for mortality from this disease.
- The risk of developing lung cancer is much lower in those under age 65 (approximately 27 per 100,000) than for those 65 and older (346 per 100,000). Median age at diagnosis is 68 years (men and women). The trend in incidence between 1973 and 1994 shows a less than five percent increase in those under age 65, but a nearly 60 percent increase among those 65 years and older. Survival is worst for the oldest age groups. Between 1973 and 1994, mortality increased by almost 73 percent among those 65 and older, but increased less than nine percent for those under age 65.

- Prostate cancer is clearly a disease of older men. The median age at diagnosis is 71 years. The risk of developing prostate cancer is 43 per 100,000 for men under age 65, but 1,236 for those 65 and older. One in 100 men aged 65 and older will develop prostate cancer. Although the trend in incidence of prostate cancer in men under age 65 has increased more rapidly between 1973 and 1994 than for men 65 years and older, since 1993/1994, there has been a substantial decrease in the disease; this decrease, or at least a leveling off, is expected to continue and should be demonstrated in final data for 1995. Between 1973 and 1994, prostate cancer mortality (median age 78 years) has been virtually unchanged in the under 65 age group, but has risen over 23 percent for men 65 years and older.
- The data presented above are from the SEER Cancer Statistics Review and Racial/Ethnic Patterns of Cancer; both documents are available from the Cancer Information Service (1-800-4-CANCER), by order, and from the SEER Web page under "Publications."

## Epidemiology and Aging

### Key Points

- Generally, we define "older age persons" as those 65 years and older; this is a point of reference that has been used traditionally, but does not reflect the heterogeneity of aging.
- Although 60 percent of cancers (all sites combined) occur in the 65 and older age group, many cancers (lung, rectum, stomach, bladder, pancreas, colon, prostate) occur even more frequently in this age group. At least half of certain other cancers (leukemias, ovarian cancer, non-Hodgkin=s lymphoma) occur in those 65 years or older.
- For all cancer sites combined, 69 percent of cancer deaths occur in the 65 years and older age group. However, mortality rates for various cancers vary significantly by age and gender, with progressive increases by five-year age cohort for the major cancer sites. The exception is lung cancer, in which mortality for the oldest age groups declines; this difference is associated with smoking patterns in the various cohorts.
- The population aged 65 years and older, estimated at 13 percent of the U.S. population for the period 1990-2000, is expected to rise to 70 million people (20 percent) in 2030, or one in five persons. In addition, the older population will be older (i.e., the older age segments of this population will comprise larger fractions of the population aged 65 and older). Moreover, the numbers of older Americans will continue to swell through 2050, resulting in a rectangularization of the population age structure that was distinctly pyramidal until 1982.
- Since cancer is primarily a disease of older age persons, these population trends mean that, absent major treatment and/or prevention breakthroughs, we will have a growing population that is highly vulnerable to cancer.
- The NIA/NCI SEER Collaborative Study on Comorbidity and Early Diagnosis of Cancer in the Elderly, a retrospective medical records review of more than 7,600 patients with any of seven tumor types (identified through six of the SEER

registries), demonstrates the heterogeneity of older cancer patients with respect to comorbid conditions. The study data have shown that as age increases, greater numbers of comorbid conditions are likely to be present, though many comorbid conditions are not life threatening. The data have also demonstrated that some older individuals, even in the older age groups, may have no comorbid conditions at the time of their cancer diagnosis.

### Additional Research Needs and Other Recommendations

Research is needed to address the following questions:

- How do the pathophysiology of aging, the interaction of aging with normal physiologic processes, and comorbidities impact cancer, cancer treatment, and cancer prevention?
- Do the various forms of cancer present differently in older persons?
- How can the complications inherent in the management of older patients be anticipated? What tools can be used as prognostic indicators?
- What are the potentialities, hazards, and limitations of surgery, radiation therapy, and chemotherapy in the older cancer patient? To what adverse reactions related to cancer treatment drugs and drug interactions are older patients at increased risk?

### Health Research Questions for Older Americans

#### Key Points

- Though often perceived as being the same, gerontology and geriatric medicine are distinct disciplines. Gerontology is the study of aging, a dynamic process that may be considered to begin before conception and end at, or perhaps after, death. It includes the programming and development of the entire life cycle and how it is played out in humans in the real world. In part, being old can be viewed as a process of having escaped certain other problems.

Geriatrics is the science and art of caring for people who are old; it shares with gerontology the challenges of prevention, understanding the maintenance of health, vigor, and the social, psychological, and other aspects of robust life as an individual ages.

- The study of aging potentially has much to gain from collaboration and dialogue with those studying oncology and the processes involved in aberrant cellular replication, regulation, and death.
- As previous presenters have shown, we are seeing a growth in the older population and a decline in age-specific mortality rates at all ages across adulthood; this is particularly the case among those aged 85 years and older. The functional spectrum of this group is likely to range from those who are robust, well-educated, financially secure, and socially engaged to individuals who are

dependent, educationally and financially disadvantaged, and in need of enormous amounts of care and support.

### Additional Research Needs and Other Recommendations

- Our challenge today is to plan for the needs of the aging population. Scholars and scientists concerned with aging have an obligation to inform public policy debate.
- Some of the barriers to optimal care of the older person stem from traditional politics, practices, and economic considerations. For example, although the majority of cancers and cancer deaths occur in people over age 70 years, this is not reflected in the budget of the National Institute on Aging, which is one-third that of the NCI. This disparity also reflects a societal preoccupation with youth and, more recently, with middle age, rather than with the future when most people will be older. Continuing shifts in priorities can be expected as the population ages; this should be anticipated and acted upon.
- Geriatricians care for the cancer patients whose multiple comorbidities cause oncologists to reject them as candidates for cancer care. Collaborative education in aging and oncology can help to overcome this barrier to optimal care for older patients.
  
- One of the historical areas of acceptance of geriatricians is their understanding of the complexity of life and the need for multidisciplinary collaboration involving not only physicians, but non-physicians, therapists, psychologists, and public agencies. Oncologists will need to join forces with gerontologists to expand some of their approaches to patient care to best serve the very old, most of whom are women with multiple health problems.
- The hospice philosophy should be extended to people who have multiple health problems.

### Discussion

#### Key Points

- Multidisciplinary approaches have been acknowledged in both geriatrics and oncology as the best way to care for patients, however, these multidisciplinary approaches differ. The challenge is to integrate these two approaches, both logistically and educationally, to the best advantage of patients.
- An oncology-geriatrics retreat held in February 1997 included discussion, now leading to a formal proposal, for joint fellowship training of geriatricians and oncologists. Development of this proposal has also been one activity of a joint task force established by the American Society of Clinical Oncology and the American Geriatric Society; the task force is also discussing possibilities for joint research and clinical initiatives. At a later point, curriculum and clinical practice

guidelines might also be developed for distribution to the geriatrics and oncology communities.

- It has been estimated that approximately 20 percent of the gender differential in life expectancy--currently about seven years--is attributable to gender differences in cancer incidence and mortality. Research is needed to better understand the complex mediating influences of lifestyle and behavior on this difference. Similarly, gender-related genetic and hormonal influences on processes such as inflammation and immune function (e.g., immune competence related to oncologic surveillance) are areas for further study. Gender-related differences become apparent to those treating the very old, the vast majority of whom are women.
- It was suggested that to some extent, medical oncologists have been key players in promoting interdisciplinary approaches to oncology. Other efforts that have supported this trend include the Geriatric Education Retreats noted previously and a companion program sponsored by the Hartford Foundation to encourage the incorporation of geriatric content in surgical subspecialty, emergency medical, and certain nonmedical specialty training. It was noted that creating a formalized focus on geriatric oncology within institutions attracts the interest and participation of health professionals from diverse disciplines. Having a geriatrics-oriented member on the treatment team helps to raise the awareness of all team members to the aging-related issues associated with care of older patients and can be particularly important when treatment options are being considered. In fact, it has been proposed that the geriatrician should now be included routinely on tumor boards.

## NEEDS OF OLDER AMERICANS

### Background

The American Association of Retired Persons (AARP), a consumer organization dedicated to the needs of older adults, operates a number of educational programs under the auspices of its Health and Long-Term Care Issue Section. Two of these are cancer education programs, a prostate cancer education program for older men, and the Breast Care Campaign to encourage older women to perform breast self-examinations and be screened for breast cancer, being conducted in partnership with the NCI and the American Cancer Society.

### Key Points

- In conjunction with the Breast Care Campaign, AARP conducted surveys of its membership and the general public, and also conducted focus groups with older women. Seventy-four percent of surveyed women over age 65 were aware of (had seen or heard something about) mammography in the preceding year. Older women in the western United States were found to be most aware of mammography; those in the South were least aware. Women aged 80 years and older were found to be less aware of mammography than were younger women in

- the survey. As expected, those with higher incomes and educational levels were found to be more aware of mammography than those with lower incomes and educational levels. The largest percentage of women surveyed learned about mammography from television; substantial percentages received information about mammography from doctors or newspapers.
- The focus groups revealed that among women who had had mammograms, the most important motivator had been their physician's recommendation. Conversely, lack of physician recommendation was found to be a major reason why older women failed to obtain mammograms. The survey findings also suggested that physicians other than obstetrician/gynecologists (whom older women tend to see infrequently) should be encouraged to recommend breast cancer screening to their patients; such physicians might include rheumatologists, cardiologists, and others.
  - Most of the surveyed women (64 percent) were unaware that Medicare pays for a screening mammogram every two years. Seven percent believed Medicare paid for mammography only if a woman had symptoms. In addition, women surveyed expressed confusion as to the deductible and copayment requirements associated with Medicare mammography coverage, the distinctions between coverage for screening and diagnostic mammograms, and uncertainty as to how to locate a certified facility. These findings suggest that the Health Care Financing Administration (HCFA) needs to more aggressively promote this benefit.
  - Data collected on the Breast Care Campaign indicated the need for education about breast cancer screening, particularly for ethnically diverse populations, widows, those with low income, and those over age 80 years. The educational efforts should be designed to raise awareness that breast cancer risk increases with age, emphasize the importance of early detection, promote the three-pronged approach (breast self-examination, clinical breast examination, and mammography), and raise awareness of the Medicare mammography benefit. Strategies for achieving these objectives include advocacy efforts, use of media (e.g., video news releases, public service announcements, radio spots), and distribution of print materials such as brochures.

## Discussion

### Key Points

- The data are insufficient and inconclusive concerning the benefit of screening women over age 80; breast cancer screening studies have typically excluded women over age 74 years. As a result, it is difficult to achieve consensus about screening recommendations for this age group. At the same time, it must be recognized that a randomized control trial of breast cancer screening in women over age 80 will never be conducted, since there are not enough women in this age group in the country to provide the necessary statistical power needed to generate a definitive answer to the question of screening efficacy in these women. Therefore, we need to find better ways to use existing data to develop sensible screening recommendations for women aged 80 and older.

- Physician-related reasons why older women do not receive screening mammography include incorrect but seldom tested assumptions that patients cannot afford the cost of mammography, do not want to be screened, or do not wish to be screened on a regular basis. Patient-related issues include the tendency for older patients to be less aggressive and assertive in asking questions of their physicians, or asking for screening. It was noted, however, that physicians generally respond positively to prompting.
- Although data on screening mammography in women above age 74 are not available, every study that has included women up to that age group has demonstrated that a significant difference in mortality results when screening is applied to the population. Therefore, in conjunction with publication of its revised mammography screening guidelines, an ACS consensus conference recommended that if a woman has a good quality of life with an estimated five year survival, she can be assumed to benefit from screening mammography. The guidelines for women in other age groups refer to essentially healthy individuals.
- Currently, women aged 65-70 years have the highest risk for breast cancer, yet less than half are receiving regular mammograms, the benefit of which is uncontested in this age group. A key question for the Panel is how to change this behavior. By contrast, 65-70 percent of women in their forties are being screened regularly, although some disagreement remains as to the mortality benefit of screening this population.
- Colorectal cancer incidence trends are declining, especially in the younger age groups. The decline in older age groups, however, has been slower. Colorectal cancer mortality among women has been declining for a longer period of time and to a greater extent than has the rate for men.
- The point was raised that while presenters and others have indicated that treatment for elderly cancer patients should be more aggressive, it has also been argued that health care expenditures in the last six months of life are often not justified by their benefit. The difficult issue of determining how to strike a balance between these conflicting views has complex bioethical, social, and economic components that will require ongoing discussion.

## **Research Findings and Issues Among the Aging**

### **Opening Remarks**

#### Key Points

- Common ground between cancer and aging exists at a variety of levels; chief among these is at the molecular level. We now have a fairly good understanding of the antecedents of clinical cancer and the genes that are overexpressed, underexpressed, or mutated in the development of cancer.
- Gerontologists investigating cellular senescence have been studying these same genes, which they believe are also relevant to the biology of aging. Yet the distinction between cellular senescence and whole body aging is incompletely

understood, and the relationship of cellular senescence and oncogenesis is not well understood.

## Molecular Biologic Questions

### Key Points

- In vertebrates, aging can be considered to take place in post-mitotic cells, mitotically competent cells, and the extracellular components (the source of elasticity and support for many body organs).
- Post-mitotic cells (principally neurons, muscle, and fat cells) never divide throughout an individual's life. Cell division is prevented by complex molecular mechanisms. Although tumors of the precursors of these cells may occur, when mature, post-mitotic cells never give rise to cancer. It is possible that these cells age by a fundamentally different mechanism than mitotically competent cells.
- Mitotically competent cells can divide in vivo; they are the source of tumors in people and animals. It has been recognized for about 40 years that noncancerous cells do not divide indefinitely. In a sample of normal cells, the ability to divide declines approximately exponentially until all cells have ceased dividing; at this point, the cells resemble post-mitotic cells. The number of cell doublings varies between 10 and 80 depending upon the age and species of the sample donor and the tissue type. Over time, the idea has developed that this process, referred to as cellular or replicative senescence, constitutes a tumor suppressive mechanism.
- Three exceptions to the replicative behavior of normal cells are believed to exist: germ cells, tumor cells, and perhaps, primitive stem cells. Tumor cells= replicative capacity does decline eventually, but essentially, they divide without any intrinsic limit. It is possible that stem cells of the hematopoietic system may not exhibit replicative senescence.
- The notion of replicative senescence, and its relationship to the aging of the organism, has only recently achieved legitimacy, particularly among cell and molecular biologists.
- Evolutionary theories of aging may be useful in understanding how the same cellular process can be involved in aging and cancer. It appears that the force of natural selection (the process that selects for genes that maintain reproductive fitness) declines with age. The processes associated with maintaining fitness while we reproduce (the sole concern of evolution) may have unselected adverse effects, but since these negative phenotypes only manifest at post-reproductive ages, the evolutionary process will never correct them. Thus, the process of replicative senescence may act to keep us relatively cancer free for about the first 50 years of our lifespan, but may have negative repercussions in later age, particularly in tissues that have mitotically competent cells.
- Replicative immortality (i.e., escape from replicative senescence) places cells at extremely high risk for developing the malignant phenotypes that can be fatal. The replicative lifespan of a typical neonatal human cell (human fibroblast) is approximately 50 doublings, but this division potential is insufficient to accumulate mutations in all of the critical genes necessary to achieve aggressive

malignant phenotypes and metastasis. Many tumor cells do not undergo replicative senescence, and it appears that there is a selection process associated with tumorigenesis to introduce mutations that allow cells to overcome normal senescence.

- It also appears that cells may achieve replicative immortality through the action of viral (and some cellular) oncogenes (i.e., normal proto-oncogenes converted to oncogenes by virtue of mutation). For example, we now know that some of the genes encoded by the human papillomavirus act primarily to get cells beyond the point at which they would naturally senesce.
- Another line of evidence for the relationship between cancer and replicative senescence is our current understanding that two tumor suppressor genes, p53 and retinoblastoma (RB), are critical for maintaining the senescent phenotype and signaling cells to cease replication. If either of these genes is inactivated in a normal cell, the cell will not senesce on schedule. If both genes are inactivated, the cell has a very high probability of becoming replicatively immortal and eventually becoming tumorigenic. It is estimated that 80 percent of naturally occurring human cancers have mutations in p53, RB, or both. Thus, tumorigenesis and the genes that control replicative senescence are intimately related in that they both rely on the activity of these two tumor suppressor genes. There are now at least two genetically engineered mouse strains (the p53 and p16 knockout mice) with complete knockouts of these tumor suppressor genes. Cultured embryonic cells from these mice do not senesce; in vivo, these mice develop cancer at an extremely accelerated rate.
- The idea that replicative senescence has a role in aging derives primarily from correlative molecular and cell biological data. It has been demonstrated repeatedly (though there are inconsistencies in the data) that there is a relationship between when a cell culture senesces and the age of the cell donor; in general, the older the donor, the fewer replications the cells have remaining. Interspecies comparisons demonstrate that the longer-lived the species, the greater the number of doublings a particular cell type is likely to have when measured in culture. For example, fibroblasts from the Galapagos tortoise undergo more than 100 population doublings; in humans 50-60 doublings are common; in the mouse 10-15 doublings are typical. The most optimistic interpretation of these data is that there may be an overlap between the genes that control life span and the genes that control the senescence of individual cells.
- Studies of premature aging syndromes in humans provide additional evidence for the relationship between aging and replicative senescence. In Werner's syndrome, an adult onset aging syndrome, affected individuals experience relatively normal development and puberty, but begin to age rapidly when the disease manifests itself in the person's twenties, thirties, or forties. People with Werner's syndrome do not get all of the diseases typically associated with aging, but frequently die from early cardiovascular disease. The second most common cause of death is cancer. Cells isolated from people with this disease senesce much more rapidly than those from age-matched controls. The gene for Werner's syndrome has been cloned and is providing new insights into the relationship between aging and DNA repair transcription in cancer.

- Senescent cells produce an enzyme that causes the cells to stain differently from mitotic cells. In samples of young skin, staining reveals no senescent cells. In stained samples of skin from old donors, accumulations of senescent cells are apparent. There is reason to believe, therefore, that senescent cells not only exist, but accumulate in vivo.
- Many laboratories over the last several decades have shown that senescent cells express molecules that can act at a distance, some of which can pose a danger to healthy tissues. For example, senescent fibroblasts express enzymes that can destroy stromal portions of epithelial organs. This destruction may affect the basement membrane that contains the fibroblasts and supports and organizes the epithelial cells of the organ. These senescent cells also express molecules that are pro-inflammatory, prevent angiogenesis (causing tissues to be deprived of blood supply), and produce a number of growth factors with the capacity to stimulate growth. A testable hypothesis is that with age, accumulating senescent fibroblasts and senescent epithelial cells produce molecules that cause dramatic changes in the local microenvironment of the organ.
- The exponentiality with which cancer rates increase with age varies enormously by organ. In addition, it is known that multiple "hits" (exposures or other mutation-causing events) are required for an epithelial cell to be transformed to a fully malignant state. It is possible that during aging, molecular products of accumulating senescent cells are disrupting the microenvironment, which in turn may cause a given cell, mutated but previously controlled in the young organism, to begin to grow inappropriately. In this way, replicative senescence may contribute to the initiation of carcinogenesis. This hypothesis suggests that the relationship of cancer and aging is far more intimate than has been imagined previously; further, that the process of replicative senescence, which is critically important to keeping us cancer free, may actually be pro-carcinogenic within the atmosphere of the aged organism.

## Molecular Biologic Questions – Animal Models

### Key Points

- There are important species differences in cancer risk. Although the lifetime risk of a lethal cancer is approximately 30 percent for mice (two to three year lifespan) and humans (75 year lifespan), the mouse has an average 10 percent per year risk of cancer, while a human has a 0.4 percent risk. Considering that the population of mouse cells susceptible to the cancer-forming process is far smaller than that of humans by weight, the cancer risk of mouse cells is 55,000 times higher than that of human cells.
- Scientists studying the biology of aging are in fact studying the biology of cancer. When we understand the biology of aging, we will solve the cancer problem because we will understand the fundamental biology of cancer and how it is linked to the genetics that exert evolutionary pressures.
- A major evolutionary challenge in developing a large, long-lived animal was to reduce cancer risk substantially enough and long enough to ensure the survival of

breeding individuals. It is reasonable to believe that this was accomplished by making use of the pathways that also delay aging in a wide range of tissues. Thus, the genes that control species differences in aging must also control species differences in cancer risk. One of the central problems for experimental aging research is to determine the location of these genes, their function, and the mechanisms by which they act.

- Studies in non-mammalian animal models are providing clues to the genetic regulation of aging and cancer. For example, the worm *C. elegans* normally has a lifespan of about 10 days; by changing a single gene, its lifespan can be doubled or tripled, even extended up to four-fold in the case of double mutations. Although the same genes regulating the worm's lifespan are not the same genes controlling human lifespan, the findings of this research suggest ways in which the genetics of aging in humans might also be linked through physiological processes. Other studies have shown that most of these long-lived *C. elegans* mutants share an unusual resistance to heat, ultraviolet light, and other stressors that typically damage cells. These studies and our current understanding of how humans alter their response to stressors suggest that longevity may be increased by raising resistance to certain kinds of cell stress.
- Mouse and rat studies have shown marked survival gains in animals placed on a calorie-restricted diet (40-60 percent of an average ad libitum diet). Not only is death delayed, but many age-associated changes (e.g., kidney disease, muscle failure, immune failure) are also retarded significantly. Further, calorie-restricted mice in these studies developed cancer at a delayed rate. It seems clear that the process timing the aging process and disease processes can be controlled by environmental manipulation.
- Studies of differences in longevity among various breeds of dogs suggest that more than half of the variation in their lifespans is associated with weight-determining genes. Similar studies are now being conducted with breeds of mice of different body sizes to assess weight-related differences in aging and cancer development rates.
- Other mouse studies suggest that lifespan may be predicted by testing the strength of immune response. Although the relationship demonstrated (that young mice with the lowest immune function die soonest) does not prove in any sense that the immune system controls the aging process, it provides hints that the genes that regulate aging may also have something to do with controlling the strength of an individual's immune response.
- Understanding the underlying principles that separate long-lived from short-lived animals can be of great help to gerontologists. For example, it is unexplained why certain sea birds that use enormously more glucose and generate far more free radicals than do animals such as rats or opossums nonetheless live 30-50 times longer than those mammals. To test specific questions about the aging process--such as the roles of DNA methyltransferase, brain plasminogen, the gene for Werner's syndrome, or glucose transporter genes--transgenic mice are being developed. To date, these animals have not been studied by oncologists, but it is likely that the strains of mice that are long-lived also have delayed cancer rates.

- To try to identify mouse genes involved in regulating aging and cancer rates, Dr. Miller and a colleague are studying approximately 600 animals (which are all genetically related though not genetically identical) that will be followed until death. Data are being collected on how long they live, what they die of, and their immune function at different ages. It is hoped that genetic differences associated with various outcomes will be discernable, although the principal interest is in genetic loci that regulate the age at death (i.e., the all-cause mortality risk). Preliminary results already indicate an allelic difference related to certain immune cell levels and cause of death from diverse causes including cancers, and specific allelic differences related to fibrosarcomas, pituitary adenoma, and liver, breast and lung cancers. Some of the loci identified to date appear to be gender specific. Similar human studies by other researchers are beginning, but will take decades to complete.

## Discussion

### Key Points

- Concern was expressed about extrapolating too liberally from mouse to human regarding cancer rates; the majority of cancers in mice have an endogenous etiology influenced by retroviruses, whereas the pathogenesis of human cancers is more frequently related to environmental exposures that accumulate over many years, resulting in the multiple genetic "hits" that lead to malignant transformation. Dr. Miller indicated that retroviral etiology was established for leukemias and certain mammary tumors in mice, but that the etiology of other mouse tumors was not well characterized. He agreed that resolving the retroviral problem was probably important in the evolution of long-lived animals, but suggested that diseases with and without retroviral etiology seem to be regulated in common by speciation and by caloric restriction.
- Concerning the heterogeneity of rats, Dr. Miller suggested that rats that appear to be resistant to cancer often have genes that predispose them to die earlier of kidney disease, pituitary adenoma, or other lethal late-life pathologies. In humans, and in other animals, the onset of lethal syndromes is influenced by one's genes and by environmental factors. Learning about environmental influences is important for understanding disease etiology, but distracts us from understanding the fundamental influence of how aging increases the risk of all of these cancer and non-cancer diseases as a whole.
- When cells reach the point of replicative senescence, they cease to divide, begin to produce molecules that can act at a distance, and become resistant to apoptosis (programmed cell death). Preliminary data suggest that resistance to apoptotic death involves an up-regulation or stabilization of bcl-2 gene expression. It is known that circumvention of the apoptotic program increases cancer risk, however, while senescent cells resist apoptosis, they cannot divide and so virtually never give rise to tumors.
- It was suggested that the mutagenic and carcinogenic effects of low-dose ionizing radiation are not being adequately investigated. It was pointed out that the

- Department of Energy supports substantial research in this area, and that the National Institutes of Health supports a study section devoted to radiation biology.
- It was clarified that while mouse cells have far less replicative capacity than do human cells, mouse cells are notorious for the rate at which they escape replicative senescence, which human cells rarely do. This accounts for the higher rates of malignant transformation in mouse cells compared with human cells. It may indicate that mice have a more unstable genome and a greater propensity for escaping one of the anti-tumor mechanisms nature has provided.
  - For species other than humans, the association of replicative capacity and life span disappears when the influence of weight (i.e., cell divisions needed to create a large animal) is factored out.
  - In the dog studies cited, the influence of dietary fat was not studied; data of this type are not known to be available at this time.
  - Concerning relationships among animal size, longevity, and reproductive efficiency, it was noted that small species tend to reproduce rapidly, while large species reproduce relatively slowly. Within species, however, there is an inverse relationship relative to size--selection pressures lead to larger animals that have larger litters. Smaller animals within a species have smaller litters but may live longer and perhaps reproduce more frequently.
  - The Nurse's Health Study has demonstrated an association between body mass and higher cancer rates.

## Pharmacology and Aging

### Key Points

- Older persons currently comprise about 12 percent of the population, yet they account for 25 percent of physician visits, 30 percent of all drug mentions in various surveys, and about 35 percent of drug expenditures. More than 90 percent of ambulatory older persons take at least one medication; the average is four medications.
- Nursing home patients are at particular risk for high drug use. One study in Philadelphia showed that patients over age 80 years took an average 9.3 drugs per patient and had nearly 10 distinct diagnoses per patient.
- Age-related physiological changes can affect drug disposition in the body. Little difference in drug absorption (the passage of the drug from the site of administration into the plasma compartment) has been observed in clinical investigations. Similarly, little difference in drug bioavailability (the fraction of the drug dose administered that reaches the systemic circulation) has been observed. Drug distribution in the body, however, is affected by age-related increases in body fat (influencing the distribution of fat soluble or liquid soluble drugs) and accompanying decreases in lean body mass and in total body water (10-15 percent, affecting the distribution of water soluble drugs). The information about changes in proteins relevant to the binding of drugs in plasma is unclear; serum albumin levels (involved in binding acidic drugs) have been shown to be unchanged or decreased, while alpha-1 acid glycoprotein (involved in binding

basic drugs) has been shown to be increased or unchanged. It seems clear, however, that in individuals with poor nutrition (e.g., cancer patients), serum proteins are likely to be depressed, affecting the plasma protein binding of some drugs.

- Animal studies of drug metabolism suggest clear age-related differences in liver drug metabolism, but may not reflect equivalent changes in humans; alterations in plasma clearance in humans are more likely related to changes in hepatic mass than to intrinsic enzyme activity. For example, available data in primates and humans do not suggest that intrinsic cytochrome P-450 activity is altered significantly with aging. Autopsy and ultrasound liver volume studies show, however, that hepatic mass decreases across the lifespan by 23-30 percent; hepatic blood is estimated to decrease by about 35 percent. These liver mass changes influence the amount of enzyme available for drug metabolism and, therefore, the clearance of drugs from the body. Studies of Warfarin (an anti-coagulant metabolized in the liver) dose requirements showed an association of decreased dose requirements and reduced liver size with advancing age.
- Environmental factors, including nutrition and exposure to cigarette smoke, can affect drug metabolism. Cigarette smoke is a potent inducer of certain P-450 enzymes, including P-450-1A2 and 1A1; the latter in particular has been implicated in carcinogenesis.
- Little is known about genetic polymorphisms influencing the expression of P-450 and other conjugation enzymes, nor are there indications of significant age differences in the expression of those enzymes.
- In addition, little is known about stereospecific or stereoselective drug metabolism. For example, it is known that oral clearance of the l-enantiomer of hexobarbital is depressed in the elderly, but there is no age difference in oral clearance of the d-enantiomer. Similar studies of propranolol and ibuprofen have not shown age differences. More research is needed in this area.
- Many cancer drugs are excreted by the kidney. Kidney mass decreases by 25-30 percent between the ages of 30 and 80 years, and renal blood flow decreases about one percent per year after age 50. In addition, tubular function (PAH secretion, concentrating and diluting ability) and glomerular filtration rate (resulting in reduced creatinine clearance) are decreased with age.
- Drug response can be evaluated at the systemic, organ, receptor, and intracellular levels; and can also be assessed at the level of molecular genetic regulation of receptor and enzyme expression. Studies have shown that elderly patients are more sensitive to medications such as analgesics and anesthetics, and this population is at higher risk for adverse drug events (two- to three-fold higher regardless of setting) than are younger populations. Epidemiologic data show that adverse drug events in the elderly have more to do with the total number of drugs taken by the individual and number of diagnoses than with age. Evidence indicates that approximately 50 percent of drug-induced deaths occur in individuals over age 60 years.
- Other age-related physiologic changes that may affect older cancer patients include homeostatic impairments such as decreased blood pressure regulation, decreased thermoregulation (resulting in increased susceptibility to hypothermia

and hyperthermia), and impaired volume regulation (e.g., decreased thirst, impaired excretion of water load).

- Drug interaction is a significant issue in individuals taking many drugs. These problems can include drug-disease interactions (i.e., a drug makes a pre-existing condition worse), drug-food interactions (e.g., foods causing impaired drug absorption, drugs causing malnutrition, including use of herbal and botanical preparations), and drug-drug interactions that can result in impaired drug absorption and induction/inhibition of drug metabolism. Smoking may induce drug metabolism to a lesser extent in older individuals than in younger people, however, studies of enzyme inhibition with various agents have tended not to show age differences in the susceptibility to inhibited drug metabolism; thus, the elderly will be just as vulnerable to inhibited metabolism of a highly toxic anti-cancer agent as would younger individuals.
- A New Mexico study indicated that 70-80 percent of the Hispanic population and 50 percent of the non-Hispanic population studied in the Albuquerque area used botanicals.
- Factors predisposing the elderly to polypharmacy include: multiple prescribing physicians, multiple filling pharmacies, propensity of physicians to prescribe, patient expectations, use of medications for symptoms rather than diagnoses, reluctance by physicians and patients to discontinue drugs, automatic prescription refills, use of multiple over-the-counter medications, and borrowing medications from family and friends.
- Age is not an independent risk factor for non-adherence to treatment. Rates of unintentional non-adherence range from 25-50 percent; omission is the most common form (up to 90 percent of all non-adherence). Factors predisposing to non-adherence include: dosing schedule complexity, frequent changes in medication or brands, multiple medications, unpleasant side effects, containers that are difficult to open, medication cost, difficult routes of administration, inadequate patient education and understanding, and cognitive, visual or physical impairment.
- Responsible prescribing is based on common sense: obtaining a complete history of medications, habits, and diet; evaluating the need for drug therapy; knowing the pharmacology of drugs prescribed; titrating from smaller initial doses to reach therapeutic levels; simplifying therapeutic regimens; encouraging treatment adherence and use of home health services; revising treatment plans regularly and discontinuing drugs no longer needed; using new drugs with caution; and monitoring for adverse effects.
- In conducting clinical cancer research with older populations, ethical considerations related to patients' ability to understand consent forms and complex clinical trial protocols must be addressed. Other clinical issues include those related to study population selection, population sampling, study design, and pharmacokinetic-pharmacodynamic relationships.

## Additional Research Needs and Other Recommendations

- The literature on aging and cancer chemotherapy is exceedingly scant; research is needed on the complex issue of aging and the disposition of cancer drugs. There are opportunities for collaborations between medical oncologists and clinical pharmacologists interested in aging to uncover insights that will enhance the care of the geriatric cancer patient.

## Discussion

### Key Points

- Thoughtful investigators, given appropriate resources and motivation, will be able to design study protocols to answer key questions about aging and cancer that accommodate the issues of polypharmacy among these study subjects. Recent attention to the relationship between aging and cancer, and the interest of the President's Cancer Panel, may help to make resources available to further research in this area.
- Older cancer patients are rarely enrolled on early-phase drug studies. Those who do come to cancer centers tend to have fewer comorbidities (and take fewer medications) than patients being treated by community physicians in local hospitals; this reflects a selection bias common to the cancer centers. In addition, many research protocols require adherence to strict physiological function thresholds that exclude participation by older patients. It will require concerted effort to enroll older patients representative of the population in studies that will address the questions of treating cancer in older individuals. There is a need to develop clinical trials that will not exclude older people with comorbidities.
- Interactions among the multiple medications taken by many patients can cause unclear thinking and slowed reaction times. These effects in turn affect patient adherence. In addition, many patients are apathetic and depressed; older women in particular are nonassertive and may hesitate to ask questions or relate to their physician all of the problems they are experiencing.
- The U.S. Pharmacopeia is in the process of setting standards for the manufacture of the 12-20 most commonly used botanicals and evaluating the existing (poor quality) data on their use.
- In the same way we have extrapolated from studies done in middle aged or young males the drug regimens appropriate for children and women, we are basing drug treatment for older patients on studies done in younger populations. Pharmacologic research as suggested by Dr. Vestal might be best conducted by the pharmaceutical companies rather than the NCI or NIA. It was noted that New Drug Applications (NDAs) being submitted to the Food and Drug Administration (FDA) now usually include information about older populations. Based on guidance issued by the FDA in the late 1980s, the pharmaceutical industry is conducting small studies with older subjects in cases in which aging-related effects are potentially relevant. In addition, aging-related issues are being monitored more closely than previously in post-marketing surveillance.

## Additional Research Needs and Other Recommendations

- Currently, physician ambivalence, indecision, and inaction regarding treatment selection and advice to older patients is founded in a lack of knowledge. Research is needed to answer questions on the issues of aging and cancer so that clear answers and advice can be provided to patients. Dr. Vestal reiterated that molecular techniques are becoming more useful as tools for individualizing drug therapy; these techniques can help identify older cancer patients who may be at particular risk for bone marrow suppression, neurotoxicity, or other adverse side effects of cancer chemotherapies.
- Each drug used in oncology needs to be studied for its toxicity in the older patient. It should not be assumed, however, that a drug will not be well-tolerated by elderly patients. For example, a study found that although creatinine clearance in older people is decreased, platinum drugs are well-tolerated. It was noted, however, that studies such as these are relatively mundane and fail to attract the attention and support of study sections. A commitment of resources through the Cooperative Group program or a special initiative may be needed to begin systematic investigation of cancer drug toxicity in the elderly.
- The informed consent process and documentation must be made more understandable and less frightening to older patients; advocacy groups may have an important role to play in helping older cancer patients understand the benefits of participating in clinical studies.
- Polypharmacy in the elderly is a fact of modern medical practice. There is a need to better educate medical students in clinical pharmacology for the elderly; in most institutions, this is rarely addressed except in the context of general medical training on hospital wards.

## **Clinical Findings and Issues Among the Aging**

### **Opening Remarks**

#### Key Points

- Among the distinguishing features of the older patient are: marked health status heterogeneity, physiologic changes, increased prevalence of disease and multiple comorbidities, underreporting of symptoms, atypical presentation of common diseases, increased importance of social support, greater rates of adverse drug and treatment effects, and varied goals of treatment.
- The goals of care in geriatrics need to be refined. Guiding principles include considering the issues of cure versus care which should not be mutually exclusive; recognizing the heterogeneity of health status to ensure appropriate treatment to improve or maintain function and quality of life; including prevention in routine care; and providing comfort for the terminally ill.
- Clinical priorities for providing better care to the older cancer patient include developing a better understanding of disease behavior, comorbidity, and treatment response in this population; identifying and using biomarkers (including

biochemical markers and physical assessment markers) for treatment vulnerability; developing new approaches to pharmacotherapeutics; and developing improved approaches to symptom control and supportive care. Funding increases are needed to both discover and disseminate knowledge in these areas.

## Prevention/Detection

### Background

Cancer prevention and control, which targets multiple populations, is the application of the public health sciences (e.g., epidemiology, behavioral science, biostatistics, health services, environmental health sciences) to the cancer problem. Healthy individuals need screening to detect disease at its earliest stages and minimize cancer-related morbidity. High risk individuals (e.g., older women whose breast cancer risk is rising; individuals who have had a polyp removed from the colon and are at risk for subsequent polyps and invasive colon cancer) are potential subjects for chemoprevention or dietary intervention studies that may reduce their risk of future cancers. Cancer patients are also the subject of cancer control research, particularly related to issues of access to care, health services delivery, and quality of care. We know, for example, that the elderly are often under-diagnosed with many of the common cancers and are often undertreated. The growing community of cancer survivors suffer from the sequelae of cancer treatment and from psychosocial concerns such as fear of recurrence.

The cancer control research continuum includes prevention (e.g., primary prevention interventions to reduce smoking exposure or improve nutrition), detection (e.g., screening for common cancers), diagnosis and treatment (e.g., studies of patterns of care, access to state-of-the-art and standard care, stage at diagnosis), management (research on strategies for improving survival, quality of life issues, rehabilitation and continuing care, pain and symptom control), dissemination of information through public and professional education, and outcomes research (e.g., non-mortality outcomes such as quality of life, cost of treatment, quality of adjusted life years studies).

With a P-20 developmental grant from the National Institute on Aging, the University of Southern California (UCLA) Jonsson Comprehensive Cancer Center has established a program on breast cancer prevention and control in older women.

### Key Points

- Elderly cancer patients typically are in community settings and are not usually treated at cancer centers. In addition, geriatric researchers are not usually part of the cancer center. This poses fundamental difficulties for studying the cancer problem in the geriatric population. Geriatricians and others who treat the elderly are aware that cancer is a leading cause of death and morbidity in the elderly. Screening tests such as mammography have a demonstrated impact on mortality

and morbidity in the elderly population, who in fact comprise a large underserved community of patients.

- To develop the breast cancer prevention and control program for older women, Dr. Ganz and co-principal investigator David Rubin developed a leadership group of geriatricians, cancer control researchers, and other breast cancer experts. They also actively recruited new members to the Cancer Center through this program funding and workshops; the work of some of these individuals had not previously involved cancer. In addition, Ganz and Rubin sought to encourage established investigators at the Cancer Center to focus on older women. Established seed grant funding was also used to support pilot studies by junior and established investigators across the prevention and control research continuum, emphasizing breast cancer in older women. Faculty development awards have been used to attract geriatricians and health services researchers to cancer research, and annual workshops have been conducted with the participation of external advisors who are leaders in the field of geriatric oncology. The workshops have provided the opportunity to focus on the special issues of elderly women and present research to the center's geriatrics and cancer communities. Participation by the external advisors has added a noninstitutional perspective that has been of great value to the program leaders and funding recipients.
- To date, five of 16 research applications submitted have been funded. Study topics have included breast cancer screening in older Filipino women, diet and estrogen metabolism in postmenopausal women with breast cancer, multiple breast cancer markers in fine needle aspiration (FNA) specimens, breast cancer screening in elderly care givers, and quality of life in elderly breast cancer patients. One goal of supporting these pilot efforts was to develop and legitimize research activity on this area of cancer control at the cancer center. One of the pilot projects has since achieved NCI funding.
- To develop a robust geriatric oncology program of the type initiated at UCLA, it is necessary to establish a critical mass of investigators. After three years of operation, it has become clear that a sustained funding opportunity (not just a single RFA) is needed to develop a multidisciplinary group of people who will work together on a continuing basis. The Cancer Center has provided an excellent framework for establishing and operating this initiative. In addition, the collaborations with geriatricians have now expanded to include other cancer sites (e.g., colon cancer) and has increased geriatric focus on cancer.

#### Additional Research Needs and Other Recommendations

- There is a need for joint training opportunities in geriatrics and oncology. Many of the areas of interest to geriatricians are common to clinical interests in cancer prevention and control. We also need to build the research infrastructure and improve the limited data base that exists in many areas. For example, strategies that have been demonstrated to motivate younger people to obtain screening tests may not be appropriate for the elderly.
- It is a moral imperative that we provide access to high-quality prevention, detection, and state-of-the-art treatment to the elderly. Doing so simply means

- providing them with interventions we already know to be effective, and learning more about how to modify other strategies for this population.
- Developing strategic alliances among all of the health care professionals and researchers involved in caring for the elderly is essential. The breast cancer prevention and control program for older women at UCLA provides a successful model for initiating such activities.

## Health and Behavior

### Key Points

- For the population over age 55 years, we have few approved cancer screening tests that meet the criterion of reducing mortality. As of 1996, the only screening tests approved for this population by the U.S. Preventive Services Task Force are for breast, colorectal and cervical cancer. For breast cancer, the guidelines specify mammography alone or mammography plus annual clinical breast examination (CBE) every one to two years for women aged 50-69 years, continuing at age 70 and older if the woman has a reasonable life expectancy. Pap smears for cervical cancer are recommended every three years until age 65. Recommended colorectal screening, recently approved by the Task Force, does not specify an upper age limit; fecal occult blood testing (FOBT) is recommended annually and sigmoidoscopy frequency is not specified.
- 1992 National Health Interview Survey (NHIS) data indicated that approximately 60 percent of women aged 60-69 years receive Pap smears; screening rates for other tests (CBE, mammography, colorectal cancer screening) are lower, as are rates for all tests among women and men aged 70 and older. NHIS data also show that between 1987 and 1992, gains in screening rates for Pap tests and CBE were slow for both the 60-69 year old age group and for those 70 years and older. Mammography screening, however, rose rapidly during this period.
- Although NHIS data indicate that about half of women are getting a mammogram, huge regional, age, and racial differences exist. At the national level, race differences in mammography use largely disappeared as of the 1990 survey and differences were almost totally driven by class, income, and education..
- Data (1995-6) from a Los Angeles study of the efficacy of churches as mammography- promoting agents found significant racial differences in mammography use. Approximately two thirds of white and black women over age 50 were being screened, but only 24 percent of Hispanic women reported recent screening. The most recent data, however, show a jump to 60 percent in screening rates for Hispanic women.
- Many factors predict screening rates; some of these are modifiable, others are non-mutable demographic factors. We know little about gender differences in screening behavior because almost all of the studies have been done in female-only cancers. Colorectal cancer screening studies now being initiated will provide more data on gender differences in adoption or rejection of screening. Except as seen in Los Angeles, screening rates tend to drop with age. Race/ethnicity issues

tend to vary regionally (for example, underscreening is common among black women in the South and among Hispanic and non-English speaking immigrant populations in Los Angeles), although screening rates of minorities overall tend to lag behind those of white women. Higher socioeconomic status (SES), particularly income and education, is a strong predictor of screening. Urban areas tend to have higher screening rates than do rural areas. Access, which includes health insurance, regular source of care, and continuity of care, is also a strong predictor of screening. Continuity of care is particularly important, since physicians are more likely to recommend screening to patients in an ongoing care relationship compared with new or intermittent patients.

- Group predictors at the community level, which represent intervention opportunities for enhancing screening rates among older populations, include physician offices and health maintenance organizations, churches, and retirement homes.
- Attitudes also represent modifiable predictors of screening. Older patients, despite their high cancer risk, feel less vulnerable. They feel more fatalistic about cancer should they develop it, however, not recognizing the distinction between early and late stage disease. Older people have more worries in general as they age, which can have a negative effect on screening, but they also find social support effective and respond quite well to physician recommendations. Physician attitudes can also make a difference in screening behavior. Doctors often underestimate life expectancy (e.g., a 65 year old woman has a life expectancy of 18 years and should be screened); they also misunderstand patient expectations, and believe these patients do not want screening or cannot afford it. This is not true for the majority of older people. On the other hand, physicians are highly supportive of guidelines (especially the American Cancer Society guidelines) and are open to education interventions that address their misunderstandings.
- Aspects of communication comprise another modifiable predictor of screening. Doctor/patient gender matching can be important, particularly for older women patients, who may strongly prefer women physicians when potentially embarrassing tests (e.g., digital rectal exam, sigmoidoscopy) must be performed. Physician communication decreases with patient age, and physician recommendation for screening decreases for patients with comorbidities. Physician support is important to motivating screening behavior in older adults, and physicians respond well to requests for a referral. Older patients, however, are less likely to ask for referrals or information.
- Knowledge levels affect screening rates; compared with younger patients, older patients tend to be more confused about screening guidelines, and are less knowledgeable about risk factors. Hispanic and immigrant populations also have misperceptions, anxieties, and worries about cancer that need to be corrected. It is known that greater levels of knowledge lead to higher screening rates.

## Additional Research Needs and Other Recommendations

- There is a need for more community-based programs to increase cancer screening rates among older populations. Such programs have distinct advantages: they are geographically based and therefore exportable, can achieve economies of scale in terms of modifying knowledge levels and attitudes, can include all income and race groups, and can establish networks that are reusable. It must be recognized, however, that launching a community intervention requires a great deal of money, particularly at the beginning stages of the project (e.g., to develop networks, an activity that may be unfunded or underfunded) and are difficult to complete within the typical four year grant period. In addition, it is challenging to assemble and maintain the interdisciplinary teams such efforts require.
- The power of the physician relationship can be better exploited to increase cancer and other disease screening rates among older individuals. Physicians can learn different communication techniques, particularly if they are simple, clear, and help alleviate patient adherence problems. Communication interventions are also adaptable to a variety of practice settings. Challenges to research in this area, however, include physician resistance to recruitment for studies and to being taped or observed, and costs associated with physician recruitment and their time. Despite these drawbacks, physician-oriented research is worthwhile, because of the economies of scale that can be achieved (i.e., a single primary care physician, convinced of the value of screening and trained to do it effectively, will influence the care of thousands of patients over his or her practice lifetime).
- The cost effectiveness of screening programs should be established prior to implementation.
- Better screening tests for prostate, ovarian, and pancreatic cancers are needed.
- Timely, targeted screening programs should be encouraged; some of the populations we need to reach with tailored messages are older persons, older minorities, the poor, and physicians and their patients.
- Greater funding is needed for community-based interventions.
- Interventions should focus on influencing modifiable characteristics, such as communication, knowledge, and attitudes.
- At the NIH level, funding should be increased for behavioral sciences, for community-based studies, and for the NIA. In addition, collaboration between Institutes (e.g., NCI/NIA; NCI/National Heart, Lung, and Blood Institute) should be encouraged.

## Discussion

### Key Points

- High yield (i.e., number of positive screens) in screening older people has been demonstrated; this is in part related to the prevalence of the target disease in the population. It is important to remember that the size of the target population

shrinks in the older age groups, affecting calculation of the screening yield. In addition, the subset of the older population that gets screened is also related in part to the measures needed to reach them and the cost associated with getting these individuals in for testing.

- The older population should be considered targets for chemoprevention. The Breast Cancer Prevention Trial and the Prostate Cancer Prevention Trial both included older individuals. Chemoprevention in older women may deal with preventing both cancer initiation and promotion. A healthy older person who is at high risk for a condition (e.g., epithelial breast, bladder, pancreatic cancers) would still be a candidate for interventions that addressed the promotion aspects of the cancer process. We currently do not have a useful multi-organ preventive strategy.

## Treatment

### Key Points

- In terms of physiologic robustness, population diversity generally begins to increase after age 50, peaking at around age 70; by age 90, most of the population belongs to the group defined by geriatricians as the "frail elderly." The diversity of the older population complicates efforts to draw meaningful conclusions from clinical trials of cancer treatment in this group (those aged 65-90). It impacts the two major outcomes of treatment--life expectancy and quality of life--which are a function of an array of variables including physical function, comorbidity, cognition, emotion, social support, and resources.
- Certain studies of surgical outcome indicate that mortality increases with age; closer inspection of the data suggests that the increase is almost completely due to increasing mortality in emergency surgery. For elective surgery, the mortality difference between older and younger individuals is not statistically significant. This finding argues strongly for early detection in this population (e.g., identifying colorectal masses early and scheduling elective surgery before emergency bowel obstructions occur).
- Similarly, studies from Belgium and Italy of radiation therapy in several thousand older adults show that the incidence of grade 3 and 4 toxicity was minimal; similar smaller studies in the United States show similar results. It does not appear, therefore, that age is a contraindication to most, if not all, forms of radiotherapy.
- About 77 percent of patients aged 55 years and older with acute leukemia overexpress the MDR-1 gene (which indicates resistance to most chemotherapy agents) compared with 17 percent of patients younger than 50 years. This difference largely accounts for the poorer prognosis of older people with leukemia.
- Older patients (over age 70) are at increased risk of cardiotoxicity from the anthracyclines; chemotherapy-associated cerebellar toxicity is also increased in the elderly, as is myelosuppression and both peripheral and central marrow toxicity. It is possible that greater toxicities in older leukemia patients may be

related to the loss of the normal reserve of bone marrow stem cells. Some strategies exist to minimize or avoid certain treatment toxicities (e.g., digoxin for anthracycline-associated cardiotoxicity, amifostin for cisplatin-caused kidney toxicity).

- Drug clearance can be affected by reduced liver volume and kidney function in the older patient. Many chemotherapy drugs (and their active and toxic metabolites) are excreted through the kidney. Compromised kidney function, therefore, may in part explain increased chemotherapy toxicity in older patients. It is possible, however, to adjust chemotherapy dose to renal function.
- In addition to MDR-1-mediated drug resistance, apoptotic abnormalities are associated with multi-drug resistance. These abnormalities increase bcl-2 and p53 expression, which are associated with poor prognosis in many cancers, especially in older people. Other mechanisms of drug resistance include increased concentration of drug target enzymes and DNA repair abnormalities. It is also believed that tumors in older people may grow more slowly than in younger people; the lower growth fraction may offer a reduced target for the activity of cytotoxic and other agents.
- In acute myelogenous leukemia, Hodgkin's lymphoma, and some ovarian cancers, age is a predictor of poor outcome independent of stage of disease or chemotherapy dose. For a number of cancers, it is not clear why chemotherapy outcome is poorer in older patients.

#### Additional Research Needs and Other Recommendations

- Cancer patients less than 70 years of age should be treated in accordance with their performance status and organ function. Chemotherapy technique should be tailored to the individual situation and should err on the side of conservative treatment (i.e., using safer drugs when alternatives are available) unless individual circumstances require aggressive treatment. For example, unless necessary, older individuals should not be involved in high dose chemotherapy trials. At the same time, being conservative does not mean compromising therapeutic effects for fear of complications or excluding older individuals from the majority of clinical trials.
- Creatinine clearance should be used to adjust chemotherapy dosage for older patients.
- Immunopoeitic growth factors and cardio-protectors should be used routinely.

#### **Management**

#### Key Points

- Physiological age is more important than chronological age in treating older cancer patients. Physicians must consider the whole patient and base treatment on the individual's physiologic and other characteristics.
- Wisconsin data indicate that 78 percent of persons 65 years of age and older have at least one chronic condition (cancer, diabetes, hypertension, coronary heart

disease, emphysema/bronchitis, arthritis). It is unclear how many of these conditions are important enough to affect primary cancer therapy. Older patients in good health should be considered differently for treatment compared with patients with multiple diseases and medications. Yet physicians are less likely to offer all older patients adjunctive treatment.

- If cancers in older individuals grow more slowly than those in younger people, preventive interventions need to be initiated early. If, as Dr. Carbone believes, tumors in older people do not grow more slowly, the preventive window of opportunity probably remains open up to age 50 or 60 years.
- Data from Holland and the United States (Wisconsin) indicate that while surgeons do not hesitate to operate on older breast cancer patients (though the surgery performed may be less than optimal), these patients are not receiving adjunctive radiotherapy or other potentially curative treatment.
- Wisconsin data also suggest that with increasing age, cancer patients are more likely to be diagnosed and treated at a small community hospital, and less likely to be referred to another hospital or cancer center for second opinions or other treatment. Similarly, data from the Eastern Cooperative Oncology Group (ECOG) show that accrual of patients aged 65 and older to clinical studies, which should average about 50 percent, is only 27 percent.
- In a 1989 study by Begg and Carbone of drug toxicity (19 drugs) among almost 5,500 elderly ECOG cancer patients with tumors at any of 18 sites, factors such as performance status, prior treatment, and weight loss were not age-related. Response and survival were not age-related, nor was specific organ toxicity (gastrointestinal, renal, cardiac, skin, infections, and neurologic toxicities). Most drugs were not associated with increased toxicity in the elderly; one exception was methotrexate, which was associated with greater hematologic toxicity, particularly in ovarian cancer patients. Methotrexate is excreted by the kidney; reduced renal clearance results in prolonged serum concentration and a greater likelihood of toxicity. Subsequent to this study, methotrexate dose has been based on the patient's renal clearance rate. In addition, the study concluded that chronologic age is not as important as physiologic age, and that chemotherapy for older patients needs to be individualized.
- Another study of hematologic toxicity of 20 chemotherapy drug in 16,000 patients found that certain drugs did have increased toxicity in patients older than 70 years. Chief among these were vinblastine (three-fold increase compared with younger patients), methotrexate, and VP-16. Drugs with smaller increases in toxicity in older patients included melphalan, adriamycin, cisplatin, dacarbazine, procarbazine, and cytoxan. The study concluded that while most drugs did not cause excess age-related toxicities, risk of toxic effects was greater for drugs that require biliary excretion and kidney clearance.
- A case control study of 645 Wisconsin breast cancer patients found that older women were less likely to see a radiotherapist or a medical oncologist. Surgery and hormone therapy were reported essentially equally in all age groups, but chemotherapy and radiotherapy were less often used in older patients. Younger patients were somewhat more likely than older patients to receive lumpectomy rather than mastectomy. This study did not identify geographic or insurance

factors that might have influenced these differences in therapy. Older women were more likely to be diagnosed in the smaller hospitals lacking American College of Surgeons- approved hospital programs and were less likely to be referred.

- Analysis of the Wisconsin data on breast cancer patients by age and extent of disease at diagnosis did not find significant differences in stage of disease by age that would account for the observed differences in treatment.
- The World Health Organization defines palliative care as active and total care to maintain the best quality of life. Palliative care affirms life, and neither hastens nor postpones death. It provides relief from pain and other symptoms, provides psychological and spiritual support and helps the family cope with the patient's illness and death.
- Presently, palliative care is usually initiated only when anti-cancer treatment ceases. Since some of the goals of cancer treatment are relief of symptoms, pain, and chemotherapy side effects, it is appropriate to integrate palliative measures into anti-cancer treatment. Pain control is a particular issue in the older population; pain may result from non-cancer causes (e.g., arthritis, osteoporosis), and many older patients resist taking opioid pain control medications for fear of their side effects and addiction potential.
- Barriers to effective palliative care include a lack of integration of these services in most health care systems, lack of knowledge of palliation principles and methods, limited knowledge of pain control options, cultural or religious barriers, insufficient numbers of minority health professionals, and inaccessibility of hospice care.

#### Additional Research Needs and Other Recommendations

- To overcome barriers to effective palliative care of older cancer patients, we need to: improve the education of students, residents, and physicians in this area; integrate palliative and hospice care into practice; revise reimbursement mechanisms for terminal care; ensure knowledge of and access to opioids; respect cultural and religious differences; and recruit minority physicians to this field.
- Management of symptoms should not be limited to terminal care. The spectrum of palliation extends from the initial care for cure until the terminal phase.
- Continuity of care from care for cure to palliation to hospice must be stressed.
- Oncology training must include adequate exposure to palliative and hospice care.
- Economical and humane care are important features of cancer care in the elderly.
- Oncologic management and geriatrics should be integrated.
- More studies are needed to learn how to treat older people more effectively and safely.
- Physicians must understand that most older cancer patients want the best possible treatment. It is essential to maintain communication with patients throughout the disease process to help maintain quality of life and hope; this is as important as curing the cancer.

## Access and Outreach

### Background

Like the other major Cooperative Groups, the Southwest Oncology Group (SWOG) began with a number of member institutions and expanded to involve physicians throughout the community and throughout the country. These community oncology programs (focusing on high priority trials, minority recruitment, urologic cancer, and gynecologic cancers) have brought clinical trials to the communities where patients live.

### Key Points

- Of nearly 700 cancer patients entered onto primarily Phase I and II clinical trials in 1996 at the University of Michigan, only 11 percent were aged 65 years or older.
- Currently, the principal participation of SWOG member institutions is in generating new ideas for trials; the community institutions enroll the vast majority of the patients.
- Of nearly 3,500 breast cancer patients treated in SWOG trials in 1995, only seven percent were older than age 65. This is explained largely by age caps on participation (typically up to age 65) and by age limitations specifically on intensive chemotherapy trials in breast cancer. For all sites combined, only 24 percent of more than 10,000 patients in SWOG trials were over age 65. Participation of older patients varied considerably by cancer site, however, ranging from seven to 50 percent for the most current year measured. Although participation in trials by older patients has increased for some cancers (leukemia, lung, and melanoma), it has decreased in others (breast, gynecologic, lymphoma, and myeloma) as the Group's interest has focused on transplantation treatment strategies.
- A study of patients presenting for inclusion in clinical trials found that more than 50 percent were not entered onto a protocol because there was no ongoing study on their clinical problem, not because there was an age or other exclusion that prevented their participation.
- Major barriers to participation of the older patient in clinical trials include transportation (which may explain why so many older patients are treated in small community hospitals), cost (such as Medicare prohibition on reimbursing for antiemetics if given orally rather than intravenously), loss of mobility, physician prejudice against treating the older patient, and patient prejudices such as fear of cancer, cancer care, and its costs.

### Additional Research Needs and Other Recommendations

- Older patients= access to clinical trials can be improved by raising awareness of issues related to aging and cancer treatment, supporting joint oncology-geriatrics training opportunities, and tailoring protocols to the needs of older patients.

## Discussion

### Key Points

- Some of the complex issues of increasing older patients' participation in trials were revisited: lack of a trial addressing the patient's particular problem, perhaps excessive focus on treatment strategies that may not be appropriate to the majority of patients (e.g., bone marrow transplant for breast cancer), physician reluctance to treat eligible older patients, and patient reluctance to enter a trial.
- Another barrier is the manner in which clinical trials are presented to older patients. The NIA and AARP could have a significant role in improving the informed consent process for older people and helping older patients (particularly those in good health) understand that clinical trials are the principal avenue for finding ways to remove one of the major threats to their health and welfare.
- To the extent the question has been investigated, it appears that outcomes for patients who do enter trials are not markedly better or worse than those who do not participate in clinical studies. This question has not, however, been studied specifically concerning the older population.
- The importance of carefully selecting older patients for clinical studies was reemphasized. Many can do well, even in autologous bone marrow transplant and myeloma treatment trials, but there are instances in which older patients are at risk for serious toxicities (e.g., ifosfamide treatment for sarcoma).
- To adequately tailor trials to the older patient, more data are needed on age-related functional changes that may need to be accommodated.
- Questions needing further study regarding older patients' appropriateness for bone marrow transplant include whether older patients do less well because their own bone marrow has limited reproductive potential (i.e., too many senescent cells) and whether their bone marrow has a greater potential to develop malignancies. It was suggested that in addition to physicians' reluctance to place older patients at risk for serious toxicity in transplant settings, there are clear indications that graft versus host disease (GVHD) can be very severe in some of the oldest patients enrolled in transplant studies.
- Chemotherapy does reduce mortality among cancer patients; considerable advances have been made in certain cancers (e.g., breast cancer, Hodgkin's disease). Conversely, chemotherapy has shown little efficacy for certain other malignancies, such as lung and pancreatic cancers.

## Health Advocacy

### Opening Remarks

### Key Points

- In health care, advocacy is the active informing and supporting of persons so that they can make the best decisions possible for themselves. In cancer survivorship,

advocacy is a continuum. It begins at the personal level, but it may encompass organizational and political advocacy.

- Survivorship is not only about long-term survival or cure. Rather, cancer survivorship is a term used to represent the state of living with the challenges of the cancer experience. It is a dynamic concept that avoids creating unnecessary and inaccurate boundaries in the lives of people with cancer. Equating survivorship only with cure fails to take into account those persons who live for many years with cancer as a chronic disease, those who indefinitely require maintenance therapy, and those who experience recurrences, or second or tertiary malignancies.
- There is little consensus as to what underlying processes explain different levels of long-term functioning after cancer diagnosis, but many researchers believe empowerment plays an important role. Empowerment assumes that individuals typically understand their own needs better than do others, and that it is optimal for individuals to have the greatest possible control in determining various aspects of their lives and in making informed decisions about actions that will shape the quality of their lives. Patients' need for empowerment emphasizes the importance of education as a part of health advocacy.
- Nationally, interest in end-of-life issues has centered on issues of physician assisted suicide, but many cancer advocates feel that policymakers and the cancer community should concentrate first on improving the quality of life of terminally ill individuals, in part by ensuring that they receive adequate pain treatment and psychosocial care.

#### Additional Research Needs and Other Recommendations

- We need to ensure that elderly people with cancer have Medicare coverage for the full range of quality cancer care--from screening and access to specialists' care, to pain management and psychosocial care, to long-term and hospice care. As increasing numbers of Medicare beneficiaries are covered under managed care plans, it is increasingly critical that these plans provide access to all necessary cancer care.
- Older cancer patients must have access to clinical trials when such care offers the opportunity for the best possible outcome.
- Cancer care includes not only therapies designed to extend an individual's life but also care focusing on improving the cancer patient's quality of life. Therefore, people with cancer, including the elderly, must have access to the full spectrum of cancer care, including palliative treatments like pain medications and antiemetics.
- The phrase "quality of life" must be used with some caution. It has been discussed as a tool for assessing which older patients (i.e., those with the expectation of a good quality of life for the next five years) should receive cancer screening. But questions remain as to how quality of life is being measured and who should make the determination as to whether an individual's quality of life is good, or good enough, to merit screening or treatment. Quality of life research is still largely uncharted territory concerning elderly populations, and we are only just beginning to conduct research in long-term cancer survivorship.

- Elderly persons with chronic conditions such as cancer require access to long-term care. Public policies must ensure quality nursing home care, home health care, and hospice care.
- As the number of our elderly citizens who are survivors of early cancer diagnoses continues to rise, advocates and policymakers must consider the special needs of these long-term survivors. Medicare must cover long-term follow-up care, including appropriate screening and treatment for secondary diagnoses for these survivors. Research on the late and long-term effects of cancer and cancer treatment on long-term survivors is becoming increasingly important.
- Health care professionals need to be more creative and assertive in fostering consumer empowerment. This is especially critical for the elderly person with cancer who may already be disempowered due to other psychosocial factors.
- Practitioners also must become more informed advocacy partners with their patients in the public debate about health care and health care delivery.

### Survivorship for Aging Patients with Cancer

#### Key Points

- Much of cancer care is now provided in ambulatory or short-stay acute care settings; elderly patients are discharged with the expectation that they will rely on their own resources and family members for the care they need. Improvements in diagnosis and treatment have extended the survival period of many older patients with cancer. Therefore, there are many survivorship transition points at which the family and patient must work in partnership with health professionals.
- Health care professionals need to have a better understanding of the antecedents to positive long-term survivorship so that they can work effectively with the patient and caregiver.
- Unmet needs of the older cancer patient include symptom control; assistance with regaining mobility and function; emotional support and mental health needs; caregivers' need for knowledge and skills related to care, surveillance, and monitoring; coordination of care, and more effective family assistance.
- Desired outcomes for positive survival include continuity of care, return to physical and role function, mental health, symptom management and control, early detection of problems and complications, and continued and supportive care.
- In a community study of newly diagnosed lung, prostate, colorectal, and breast cancer patients over age 65 years, the average age of the patient's caregiver was 65 years and 48 percent of patients had three or more comorbid conditions. Of patients eligible for the study, 37 percent had no caregiver; these patients in particular represent a population at risk for less than optimal recovery and rehabilitation.
- In this study, patients were interviewed (after four to six weeks of treatment and again after 14-16 weeks of treatment) about the number and type of cancer- and cancer treatment-related symptoms they experienced. After 14-16 weeks, more than 50 percent of those interviewed still reported a high number of symptoms or had even deteriorated (i.e., reported more symptoms than at the earlier interview).

Chief among the symptoms reported were pain, fatigue, and insomnia; there were no significant differences by cancer site. Further, measures of physical functioning and depression showed that physical functioning was still reduced, and depression still greater, at the second interview.

- This study suggests that cancer patients with continued unmanaged symptoms, particularly pain and fatigue, are at risk for negative survivorship. Symptom experience is related to depression and functional status. Mental health needs of these patients continue into their survivorship experience; situational depression may be a particular issue. Patients in the study were provided few formal skilled care services and none focused on mobility, mental health, recovery, or physical function. Services that were provided were short-term and related to discharge from an acute care setting (e.g., catheters, wound dressing) rather than an overall rehabilitation or recovery plan.
- In this study, some caregivers were more ill than the cancer patient; in other cases, a cancer patient in the study was called upon to be a caregiver for someone sicker than they were. This reality highlights a major issue in chronic illness management.

#### Additional Research Needs and Other Recommendations

- Prevention of disability in the highly heterogeneous older cancer survivor population is critical to avoid major long-term care needs. We need to focus on maximal recovery and return to function in this population. Families need guidelines on how to help with recovery and manage symptoms.
- We need to develop risk profiles for all phases of survivorship to examine how age, stage, treatment, disease site, and comorbidity influence completion of treatment, symptom control, functional status, and mental health.
- Evidence-based guidelines for survivorship that include the patient and family are needed to address issues related to completion of treatment, symptom control, functional status, and mental health.
- These risk profiles and guidelines should be tested in randomized clinical trials to determine their impact on families, resource usage, health costs, and the clinical outcomes and recovery of patients.

#### Supportive Care Models

##### Key Points

- The transition that occurs when a patient is transferred from active treatment (with curative intent) to symptom palliation only is jarring to the patient, the family, and the health care provider. In the case of advanced prostate cancer patients whose disease has not responded to hormonal therapies, a choice must usually be made between trying chemotherapy to extend life beyond the typical six-month average remaining life span of these patients, or supportive care through a hospice program. This choice is a difficult one, since chemotherapy is hard on these

- patients, but choosing hospice may be perceived as surrender. Traditionally, hospice programs do not accept patients who are being actively treated.
- The goals of the oncologist and the hospice team in treating these patients are essentially the same--control of pain and other disease-related symptoms, helping patients and family cope with psychological issues of terminal disease and death, emphasis on palliative care and quality of life. The major difference is that the oncologist is also trying to help patients live longer and typically has less time to attend to the patient's supportive and psychosocial care needs.
  - To address all of these needs, Dr. Pienta and colleagues developed a supportive care program that enables patients to choose both to actively fight the disease and at the same time get the best possible supportive care. Combining the medical care model (disease oriented, with an emphasis on recovery, disease eradication, and prolongation of life) and the hospice model (which is symptom oriented and emphasizes quality of life), the goals of the program included elimination of abandonment, improved patient care, improved quality of life, and cost effective health care delivery.
  - The supportive care program involves a patient care team that includes the oncology team (the primary care providers, consisting of the oncologist and nurse practitioner or physician assistant), hospice social worker, hospice nurse, and a program coordinator who oversees the patient's inpatient and outpatient care and serves as a liaison between the oncology team, hospice team, and patient.
  - Patients are offered enrollment in the program when they enter chemotherapy; those who enroll are visited by the program coordinator and hospice team in their home. They are seen routinely in the clinic by the oncology team and as needed (even daily at the end of life) by the hospice team. All team members meet monthly to discuss each patient.
  - Outcomes being tracked through the program included quality of life, cost, symptom management, and patient and provider satisfaction with care. In one (non-randomized) study of enrolled patients and a control group, all of whom had advanced metastatic prostate cancer, surveys and anecdotal feedback demonstrated high levels of patient and family satisfaction in level of support, timely assessment of potential side effects and toxicity, and decreased emergency room and clinic visits (made possible by the 24-hour availability of team members for home visits to assess symptoms). Providing patients with access to the hospice supportive care network through which they could deal with the issues of terminal disease and dying also proved to be an important benefit for the patients= care givers and family. Importantly, the supportive care program provides patients and family with six months of such support in the home environment, instead of the average of two weeks most patients receive hospice care in southeastern Michigan. Ongoing bereavement support was also important to family members.
  - Patients enrolled in the program and others not enrolled also were assessed using a Functional Assessment of Cancer Treatment--Prostate (FACT-P) quality of life assessment instrument. The FACT-P indicated that patients in the program had a better quality of life than those not enrolled.
  - It was also demonstrated that by enrolling patients for the Medicare (???) hospice benefit, through which noninvestigational chemotherapy drugs used for symptom

relief, CT scans, and palliative radiotherapy could also be provided, it was possible to provide a more comprehensive level of total care at a cost commensurate with (three dollars per patient day more than) the cost of care provided to the control group patients.

- Based on these results, Dr. Pienta and colleagues have partnered with the Robert Wood Johnson Foundation and several community hospitals in Michigan to conduct a randomized study of the supportive care model versus standard care, and track quality of life, health outcomes, and cost in both the community and academic setting. Approximately 600 advanced prostate, breast, and lung cancer patients, and patients with congestive heart failure, will be included in the study, which is expected to begin in the spring of 1998.

## Education

### Background

The American Cancer Society (ACS), the largest voluntary health agency in the Nation, was established more than 80 years ago. Its current budget is \$400 million. Its staff number 4,000, plus two million volunteers working in 3,400 communities in the United States. The ACS estimates that this combination of paid and volunteer effort brings to bear the equivalent of \$3-4 billion on the Nation's cancer problem. The ACS is currently reorganizing to maximize its efficiency and effectiveness. Approximately 50 percent of the budget supports programs and services delivered in the community. The ACS enjoys exceptional public recognition and trust--95 percent of Americans surveyed recognize its name, and 50 percent cite the ACS when asked to name a voluntary health agency. The principal mission of the ACS is to educate the public and health care professionals. The agency also funds approximately \$100 million of research and maintains an active program in cancer epidemiology and surveillance. Its Cancer Information Program receives an estimated one million calls per year; approximately 60 percent of callers are patients or family members, and information on breast cancer is most frequently requested.

### Key Points

- ACS's Cancer Prevention Study No. 2 (CPS-2), a cohort study of 1.2 million Americans with an average age of 60 years at enrollment in 1982, continues to generate data. Among its findings were that individuals aged 60 and older between 1982 and 1995 who smoked, ate a diet low in fruits and vegetables, had a low activity level, and were overweight had a four-fold increased risk of death from all causes and a three-fold increased risk of cancer death. Follow-up surveys of this population demonstrate that changing these lifestyle parameters and body weight can modify these negative outcomes. ACS is currently following up on the diet studies in this cohort to accumulate more data in this area.
- CPS-2 data suggest that preventive behaviors may be of benefit throughout life, not only up to age 50 or 60, as has been suggested. Data are needed to help older individuals make healthful lifestyle choices.

- The ACS Behavioral Center is planning a 50,000-100,000 person cohort longitudinal study of cancer survivors that will sample age groups including the elderly population; further, the study will over-sample certain minority populations to generate more accurate data about these groups, and will also include cross-sectional studies.
- The average age of callers to the ACS Cancer Information Program 800 number is around 48 years. Less than 10 percent of callers are over age 65. To help callers become more effective self-advocates, the ACS is striving to individualize the pamphlets, printouts and other information sent to those requesting such information. This will include listings of American College of Surgeons and NCI-designated cancer centers to address the issue of older individuals with cancer receiving treatment in small community hospitals that lack systematic processes for ensuring quality cancer care.
- The evolving health care system poses one of the biggest threats to the quality of health care across the country. The ACS is concerned that the SEER program inadequately captures data on health system effects on cancer care, particularly in the southern region of the Nation. The ACS is exploring the possibility of establishing a population-based national cancer care surveillance program to help gather these data so they can be provided to the public.
- ACS is also increasing its advocacy program; recent efforts have included advocacy for colorectal cancer screening reimbursement, currently being considered by the Congress.
- Cancer control activities of the ACS are ongoing across the country; in smaller communities these are run by volunteers only, while larger communities also have paid staff with diverse expertise. ACS provides support programs, transportation, and targeted programs such as Look Good, Feel Better for women cancer patients. Though resource-intensive, these programs are important in a health care delivery environment in which resources for ancillary support services are diminishing.

#### Additional Research Needs and Other Recommendations

- In the area of prevention, several areas warrant further investigation: What preventive interventions are possible in the elderly population, specifically concerning smoking control, diet and exercise, and clinical trials participation?
- In screening and early detection, we need to determine the best use of resources to effect behavioral change in older populations.
- Ongoing national monitoring of quality of care is needed to ensure that the elderly are receiving appropriate cancer treatment; monitoring care provided in small community hospitals will be particularly difficult.
- There is a need to better catalog available patient support services and other community resources so that unmet needs can be identified and the most appropriate mechanisms for delivering needed services can be determined.

## Discussion

### Key Points

- Physicians should avoid referring to cancer patients as terminal, since this term has a negative impact on patient attitude. It is important for patients to have a realistic understanding of their disease, but avoiding this term better enables them to address issues that occur any phase of disease in a more positive way.
- It was clarified that cancer itself does not cause depression, however, cancer patients are vulnerable to situational depression and should be evaluated periodically for clinical depression.
- Treatment cost is a major issue for older cancer patients, who may have to choose between buying food or medications.
- Physicians' choice of medication may be constrained by health plan and Medicare requirements to select the least costly alternative that may not always represent the best choice for the patient.
- Physicians do not always provide complete information about treatment options, including clinical trials; this deprives the patient and family of the opportunity to make an informed choice.
- Concern was expressed about the effect of managed care on the doctor-patient relationship. Dr. Kennedy suggested that it will be up to patients, not doctors, to insist that current restrictions on the duration of office appointments be modified. Dr. Clark indicated that while patient advocates are becoming more sophisticated and activist in their approach, a partnership between patients and health care professionals will be needed to ensure quality cancer care.
- The ACS's I Can Cope program for cancer patients and their families has been incorporated into the hospice system in some areas; this application of the program should be more widely considered.
- Joint funding and joint treatment and training programs in geriatrics and oncology should be pursued. For example, the ACS has a new clinical research training grant that would be highly appropriate for such dual focus studies. In addition, ACS targeted research in prostate cancer is focusing on quality of life and age-related issues; part of the goal of this targeted research is to attract behavioral and other investigators who have not necessarily been working on aging or cancer issues.

### Closing Remarks

In closing, Dr. Calabresi noted that:

- The magnitude of the problem of cancer in aging is great and will be increasing in the future. Accordingly, in its charge to report to the President blockages or delays in the execution of the National Cancer Program, these issues will be given high priority.

- He shares the view of the presenters on basic science issues that fundamental research in cancer and aging are intrinsically related; molecular and genetic insights can be expected to come from either field of research.
- Pharmacologic studies of drugs and the elderly are essential; such studies will probably be best conducted in specialized centers rather than in large Phase III Cooperative Group clinical trials.
- As the older population is at high risk for cancer, prevention and early detection interventions should have rewarding benefits.
- Choice of therapy, including bone marrow transplant and other aggressive therapies, should be based on physiological rather than chronological age. New and better growth factors and other agents are needed to mitigate treatment toxicity in the older population.
- It should be remembered that cure (eradication of the disease) may not be necessary in the older patient in whom effective palliation and control of the cancer may be just as desirable. There are many diseases (e.g., hypertension, diabetes, pernicious anemia) that cannot be eliminated but can be controlled effectively.
- Survivorship will be a major topic of a planned future meeting of the President's Cancer Panel. These issues are important because the survivor population is growing (more cancer patients are now surviving than are dying) but is at high risk for second and third cancers.
- Joint programs and funding for professional and public education in geriatric oncology are much needed. Dr. Calabresi congratulated Drs. Halter and Wicha for their vision and collaboration in establishing a center for geriatric oncology at the University of Michigan.

In his closing remarks, Dr. Freeman highlighted aspects of the day's presentations and indicated that:

- The geriatric oncology center at the University of Michigan will serve as an organizational model for the rest of the country in addressing the questions of cancer and aging.
- We should not automatically accept that cancer comes with aging. The scientific and biological reasons that older people get more cancer must be elucidated; finding these answers will have a major impact on the total cancer problem.
- It is natural that as people age, they have more medical conditions, but these comorbidities should not necessarily be a barrier to participation in clinical trials.
- The issues of cancer and aging raised by the presenters have received relatively little attention. The Panel will carry these issues to the President with vigor, and its report will be made available to the public.

I certify that this summary of the President's Cancer Panel meeting on Concerns of Special Populations in The National Cancer Program, Cancer and the Aging Population, held on July 31, 1997, is accurate and complete.