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**Preface**

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Lodovico Balducci and Martine Extermann

**Cancer and Aging: An Evolving Panorama**

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Lodovico Balducci and Martine Extermann

The association of cancer and aging is becoming more common with the aging of the general population. This association brings about questions related to the pathogenesis, biology, management, and prevention of cancer. Aging may predispose people to cancer because many of the molecular changes of aging parallel early carcinogenic changes. Aging may influence cancer growth by two different mechanisms: different cancers (acute myelogenous leukemia), different tumor host (large cell non-Hodgkin's lymphoma), or a combination of both (breast cancer). Prevention of cancer in older persons may include both chemoprevention and screening. The management of cancer in the older person is based on an assessment of risks and benefits provided by comprehensive geriatric assessment.

**Aging and Cancer in America: Demographic and Epidemiologic Perspectives**

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Rosemary Yancik and Lynn A.G. Ries

Data on cancer that emphasize the impact of this disease on older persons in the context of an expanding aging population in the United States is described using population-based statistics on incidence and mortality. Sixty percent of all incident cancers and 70% of all cancer mortality occur in people 65 years and older. A combined cancer and aging epidemiologic perspective of the cancer burden for the elderly is given, providing a backdrop for the articles in this issue. There is an urgent need for special attention

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**HEMATOLOGY/ONCOLOGY CLINICS OF NORTH AMERICA**


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to older persons as a target group for the integration of aging and cancer research. A discussion on pertinent clinical issues and questions that should be considered in treatment of cancer in the elderly is also provided.

## **Molecular Interactions of Cancer and Age**

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J. Albert Fernandez-Pol and Michael G. Douglas

Endogenous and exogenous factors and intrinsic chemical instability of biological systems continuously challenge DNA integrity. To ensure genetic stability, cellular systems have acquired an intricate network of complementary DNA repair systems. DNA damage and defects in repair and transcription result in cancer and aging. Accumulation of somatic mitochondrial DNA (mtDNA) mutations is a major causal factor in the aging process. The role of mtDNA in cancer seems to be secondary. The aging process—the loss of youthful resilience—likely is caused by the decline of numerous hormones and growth factors. By restoring these hormones and growth factor levels, the decay associated with old age may be eliminated and, in some cases, perhaps reversed.

## **Hematopoiesis and Cytokines: Relevance to Cancer and Aging**

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Carole A. Baraldi-Junkins, Anna C. Beck, and  
Gerald Rothstein

Impaired hematopoiesis and dysregulated cytokine expression have important implications for cancer in the elderly. In aged people, hematopoiesis is dysregulated and becomes paradoxically down-modulated under periods of increased hematopoietic demand. This down-modulation may explain, at least in part, the increased incidence of anemia in the elderly, although the cause of anemia can usually be identified in these patients and frequently reversed with targeted therapy. An age-associated decrease in the expression of interleukin-2 may contribute to impaired cellular immunity. Additionally, the increased interleukin-6 production frequently found in the elderly may participate in promoting the survival and proliferation of malignant myeloma and in inducing resistance by myeloma cells to therapies that act through apoptosis. Dysregulation of the expression of these and other cytokines may be a mechanism contributing to age-related impairment of the hematopoietic response, the genesis and therapeutic resistance of specific malignancies, and cancer cachexia.

## **Assessment of the Older Cancer Patient**

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Martine Extermann and Matti Aapro

The correct assessment of a cancer patient is a key step in the treatment process. In older people, this assessment entails not

only the patient's basic medical history and the standard cancer staging, but also much more comprehensive evaluation of the various facets of the patient's health and environment that may interfere with his or her therapy. Patient fitness for elective surgery, radiation therapy, and chemotherapy must be considered. Geriatricians have defined the relevant aspects of the general evaluation of the older person, and now this work is being adapted to cancer patients. This article reviews the various aspects of a comprehensive assessment applicable to the cancer patient in settings such as academic oncology programs, cooperative group studies, and private oncology practice.

## **Qualitative Research for the Study of Cancer and Age**

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Rose C. Maly

Qualitative research emphasizes identification, illumination, and understanding of phenomena, the meaning and theory behind which are unpresumed by the investigator. Although quantitative techniques are used to test predetermined hypotheses, qualitative techniques are used to generate hypotheses. Qualitative techniques have only begun to be used in medical research in the past decade but are especially useful in exploring content areas about which little is known and in eliciting and understanding the patient's perspective. Despite the aging of the United States population, the cancer illness experience has not been well studied in older patients. Because communication preferences, treatment decision-making styles, psychosocial issues, and the illness experience itself may be significantly different for older persons diagnosed with cancer than for younger persons, qualitative research techniques can be used to identify those differences critical to the effective health care of this burgeoning population.

## **Cancer Screening in the Elderly Population**

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Michael A. Silverman, Uzma Zaidi, Scott Barnett,  
Carlos Robles, Vikas Khurana, Howard Manten,  
David Barnes, Lucy Chua, and Bernard A. Roos

This article reviews the current state of knowledge regarding cancer screening in the geriatric population. Care of the elderly requires knowledge of underlying physiologic changes, comorbidities, quality-of-life factors, and life expectancies. There is always the danger that ageism may prevent elderly cancer patients from receiving the proper treatment. On the other hand, overzealous treatment can lead to adverse results if elderly patients are not properly targeted based on current evidence of the benefits and risks of specific screening practices.

## **Chemoprevention of Breast Cancer in the Older Patient**

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Susan E. Minton

Breast cancer is the most common cancer in women and is the second leading cause of death from cancer in women. Age is an

important risk factor for breast cancer: 1 in 15 American women between the ages of 60 and 79 years will develop breast cancer. This article discusses the attempts at developing a model, such as the Gail model, that adequately estimates the risk of developing breast cancer for those who are not thought to be genetic carriers. The use of the antiestrogen Tamoxifen in treatment and prevention of breast cancer is examined, as are other treatments, such as raloxifene and retinoids.

## **Radiation Therapy of the Older Patient**

Babu Zachariah and Lodovico Balducci

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Radiotherapy is widely used for both curative and palliative treatment of cancer. It is of particular benefit to older and frail patients as an alternative to surgery and systemic therapy. Very little information is available regarding the tolerance and effectiveness of radiotherapy in older patients. Review of the literature shows that selected patients who have good performance status and fewer comorbid illnesses tolerate radiotherapy as well as younger patients. Older patients with early stage cancer should be treated aggressively, including treatment with combined chemoradiation, if indicated. Innovative methods of treatment delivery, namely brachytherapy, stereotactic radiosurgery, hyperfractionated radiotherapy, three-dimensional conformal radiotherapy, and others, were tried successfully in selected older patients with no added morbidity. Older patients with good performance status after comprehensive geriatric assessment should be considered for prospective studies. Aggressive treatment should not be denied to older patients based on age alone.

## **Cancer Surgery in the Elderly**

M. Margaret Kemeny, Erna Busch-Devereaux,  
Louis T. Merriam, and Brian J. O'Hea

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Surgery is still the most important treatment for solid tumors, regardless of the age of the patient. For lymphomas and leukemias, surgery is needed for diagnosis and sometimes for resection. Because the American population is both growing and aging, and because the incidence of tumors increases with age, the number of elderly patients with cancers requiring surgical intervention can be expected to rise in the next decade. This article reviews the current knowledge regarding risk assessment, laparoscopic surgery, and the appropriate use of surgical therapy in breast cancer, gastrointestinal cancers, and melanoma, as they pertain to the elderly population.

## **Antineoplastic Chemotherapy of the Older Cancer Patient**

Lodovico Balducci and Mary Beth Corcoran

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Cancer chemotherapy may be effective and safe in older patients if some proper provisions are made. Doses of chemotherapy

should be adjusted to the patient's glomerular filtration rate, and his or her hemoglobin should be maintained for the duration of the therapy. For patients who are 70 years of age or older and who are receiving moderately toxic chemotherapy, growth factors should be used. The risk of mucositis increases with the age of the patient, so it is important to treat it aggressively at the first signs of the complication.

## **Breast Cancer and Aging: Clinical Interactions**

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Gretchen G. Kimmick and Lodovico Balducci

Breast cancer is more common in older women, and the geriatric population is growing dramatically. The presence and severity of comorbid conditions must be considered when making management decisions for treatment of breast cancer. Women whose life expectancy exceeds 5 years should continue annual screening mammography. Choices for local definitive therapy, systemic adjuvant therapy, and treatment of metastatic disease should be based on patient preference and ability to tolerate the planned procedure.

## **Cancer in the Frail Patient: A Coming Epidemic**

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Lodovico Balducci and Giorgio Stanta

With the aging of the population, frailty has emerged as a new clinical entity. The frail person has exhausted any functional reserve. Current criteria for the recognition of frailty include age of over 85 years, dependence in one or more activities of daily living, three or more comorbid conditions, and the presence of one or more geriatric syndromes. It is calculated that there are approximately 6 million frail patients in the United States and approximately 400,000 of them have cancer. Management of cancer in the frail person is mainly comprised of palliation, which may include some forms of chemotherapy, such as navelbine, gemcitabine, or low-dose taxanes.

## **Acute Myelogenous Leukemia and Aging: Clinical Interactions**

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Jeffrey E. Lancet, Cheryl L. Willman, John M. Bennett

Acute myelogenous leukemia (AML) is a devastating disease that afflicts the elderly much more frequently than the young, yet therapeutic advances over the past several years are often deemed unsuitable for the very population of patients most commonly affected by the disease. Although outcomes for elderly patients with AML remain poor, much insight into the biologic and clinical characteristics of the disease has been gained in recent years, lending important prognostic information to physicians treating this high-risk patient group. Accordingly, benefits and risks of treatment now can be more accurately assessed. It is clear that

aspects of AML in the elderly, specifically multidrug resistance gene expression and well-described karyotypic abnormalities, will lay the groundwork for novel therapeutic strategies to complement traditional chemotherapeutic approaches.

### **The Family Caregiver of the Older Cancer Patient**

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Michael A. Weitzner, William E. Haley, and  
Hongbin Chen

Cancer is a family affair. Family members are increasingly being required to participate in and coordinate home care for their loved one with cancer. This active care can have untoward effects on the older caregiver, who most likely has medical problems of his or her own. The effects of caregiving on caregiver mental and physical health are reviewed. A theoretical model of caregiving is outlined, which can help to direct future research in this area.

### **Clinical Research in the Older Cancer Patient**

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Hyman B. Muss, Harvey J. Cohen, and  
Stuart M. Lichtman

Despite the well-recognized increase in cancer incidence with age, and the increasing proportion of elderly in our population, little research has been specifically targeted to elderly subjects. Three areas that represent current efforts to increase clinical research on the elderly cancer patient are addressed in this article. The first is a series of research initiatives proposed by the National Institutes of Health through a collaboration of the National Institute of Aging and the National Cancer Institute. The second area is comprised of studies conducted by Cancer and Acute Leukemia Group B (CALGB), one of the major clinical cancer trials cooperative groups in the United States, and the third is comprised of specific approaches aimed at better defining cancer drug pharmacology in the elderly, using specific examples from CALGB studies.

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