

Lung Cancer: Provoking New Concepts, Generating Novel Ideas, and Rekindling Enthusiasm

Lung cancer continues to be a disease of epidemic proportion. In this year alone, it is estimated that 171,900 persons in the United States will be newly diagnosed with lung cancer and 157,200 will die of it. Thus, more people will die of lung cancer than of breast cancer, colorectal cancer, and prostate cancer combined. The magnitude of the problem is similar in Europe. Because of an increasing prevalence of cigarette smoking in most parts of the world, it is anticipated that annual deaths from lung cancer may exceed 10,000,000 by 2030. In the United States, approximately one third of all deaths in people between 35 and 69 years of age are attributable to cigarette smoking, and the relative risk for lung cancer in current smokers is 20- to 80-fold higher than in never smokers, depending on the age of onset and extent of smoking. Interestingly, the lung cancer risk of smokers in Japan, after controlling for daily cigarette consumption and number of years of cigarette smoking, is estimated to be 1/10th the risk of smokers in the United States. There are many reasons for this discrepancy in lung cancer risk, including differences in tobacco manufacturing procedures, use of additives, type of filters used, and population differences in carcinogen metabolism and susceptibility.

The 5-year survival rate in lung cancer, although disappointingly low

at 15%, has kept pace with improvements in survival rates of all cancers over the last 40 years. This progress in 5-year survival is a result of heightened awareness, better technology for detection, better selection of patients for various treatment options, and the selective use of palliative interventions. Yet, lung cancer mortality remains high, and it is the benchmark on which future generations will judge our success in treatment combating this disease.

To generate significant improvements in lung cancer cure rates, a substantial increase in our knowledge of lung cancer biology is required. What allows lung cancer cells to survive, proliferate, and spread in an essentially hostile environment? What mechanisms allow these cells to escape otherwise highly toxic therapeutic interventions? How can our present-day knowledge of cell biology be effectively incorporated into current clinical trial designs? Confronting these formidable challenges requires the collaboration of experts from different disciplines of medicine, surgery, epidemiology, and basic research. It also requires vision, dedication, and boldness in the implementation of novel therapeutic concepts with the goal of curing patients with lung cancer.

In this issue of *Cancer Control*, experts offer their opinions and

views on select subjects of lung cancer research. These papers are certainly not meant to comprehensively represent all important aspects of the disease. However, it is my hope that they will provoke thoughts, generate novel ideas, and rekindle enthusiasm for investigations on issues to be answered in our struggle to make lung cancer a disease of the past.

Novel techniques for the planning and delivery of radiation are presented by Dr. Wagner. Conventional radiation of the chest for local control of lung cancer has been inadequate in achieving cures. The addition of chemotherapy to radiation has increased local control rates, particularly if radiation and chemotherapy are given concurrently. Novel image-guided radiation planning that uses both anatomical and functional parameters shows promise for improvements in cure rates for inoperable patients with lung cancer while minimizing unwanted pulmonary and esophageal toxicity.

Drs. Eberhardt and Korfee from Germany re-examine the role of surgery for small-cell lung cancer. Improvements in the management and outcome of this disease have been limited in the past 20 years. Based on their own single-institution experience, the authors question whether the older dogmas on

small-cell lung cancer management are still valid.

A collaborative group of investigators from Spain and Italy summarize their results on platinum resistance in non-small-cell lung cancer as a result of expression of the DNA repair gene *ERCC1*. The data presented suggest a predictive role of this gene in response and resistance to platinum agents. This opens the door for trials that use molecular markers for selection of chemotherapeutic agents.

A systematic review of lung cancer early detection trials follows. The authors explain the underlying hypotheses for these trials and concisely summarize the results from the pertinent randomized trials. They also describe the results from currently available cohort trials using low-dose computed tomography of the chest, and explain why lung cancer mortality and not 5-year survival remains the gold standard for judging efficacy of early detection trials. The concept of stage shifting is also discussed.

Drs. Cohen and Khuri summarize results from chemoprevention trials for lung cancer and discuss the concept of intermediate biomarker usage as a surrogate endpoint for current and future trials. Currently used and potential future agents are discussed.

Finally, Drs. McBride and Ostroff address how smoking cessation interventions may be integrated into comprehensive cancer care at the time of diagnosis, treatment,

and follow-up of patients. Aside from fostering an overall attitude of a healthy lifestyle and clean environment, smoking cessation among lung cancer patients has been shown to prolong survival. Addressing smoking cessation also fosters hope and may generate patient advocacy within the immediate and extended family and community.

Let us work together to make lung cancer a disease of the past.

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