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Great care has been taken to maintain the accuracy of the information contained in the volume. However, the Editorial Staff and The University of Texas System Cancer Center cannot be held responsible for errors or for any consequences arising from the use of the information contained herein.

Introduction

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The concepts that human tumors are antigenically distinct from the host and might be subject to attack by host defense mechanisms, and that therapeutic manipulations might alter or augment these host defense mechanisms go back to the turn of the century and to the writings of Paul Ehrlich. These concepts remained highly controversial until the 1950s, when Ludwik Gross unequivocally demonstrated the presence of tumor antigens and tumor immunity in mouse tumor systems. During the last two decades, many studies have demonstrated that tumor-associated antigens and tumor-associated immune responses are present in many, if not all, experimental animal and human tumors. These responses include classic cell-mediated and humoral immunity as well as nonspecific host defense mechanisms involving the reticuloendothelial system and macrophages.

Slightly less than 20 years ago, it was demonstrated in mice that immunologic manipulation of the host, namely, administration of bacillus Calmette-Guérin (BCG), protects animals from the subsequent development of tumors induced by chemical carcinogens or oncogenic viruses. During the last decade, expansion of this experimental basis has laid the foundation for the gradually emerging clinical discipline of immunotherapy. Also during the last decade, development of techniques through which the human immune response can be critically evaluated, demonstration of the immunosuppressive effects of the tumor-bearing state, characterization of the immunosuppressive effects of conventional cancer treatment, and documentation of the relationship between immunocompetence and prognosis in cancer have added a strong, rational, scientific basis to this field.

During the first half of the 20th century, a number of empirical clinical trials of immunotherapy appeared positive. However, several subsequent clinical experiments, which now can be considered classic, have established the clinical foundations of immunotherapy. These include the demonstration by Professor Georges Mathé that remission duration in childhood acute leukemia can be

prolonged by the administration of BCG, irradiated allogeneic tumor cells, or both. Also important were the demonstration by Dr. Donald Morton that cutaneous, metastatic melanoma nodules can be induced to regress in immunocompetent patients through the intralesional injection of BCG, and the demonstration by Edmund Klein that a variety of primary cutaneous tumors can be caused to regress by the topical application of DNCB after sensitization of the subject to that hapten. In the latter study, it was most important that in patients with multiple, recurrent, primary skin tumors, the rate of new tumor formation was retarded after intralesional or topical therapy for a few primary tumors.

Tumor immunobiology and experimental and clinical immunotherapy have been prominent in the program at M. D. Anderson Hospital and Tumor Institute of The University of Texas System Cancer Center for some time. This is evidenced by the prominence of these topics in several of our annual basic science symposia and the presentation of the annual Ernst W. Bertner Memorial Award to Dr. Ludwik Gross in 1963 and to Dr. George Klein in 1973 for their preeminent work in tumor immunobiology and virology. Furthermore, our staff has developed a major program for both animal model work and clinical immunotherapy trials during the last seven years. Currently, there are more than 20 active clinical immunotherapy protocols at M. D. Anderson Hospital, and several thousand patients are receiving immunotherapy as an adjunct to conventional therapy.

As the science of modern immunobiology has developed, the various approaches to immunotherapy have become well defined; these include active-nonspecific immunotherapy with adjuvants such as BCG, active-specific immunotherapy by immunization with tumor cells or tumor antigen, adoptive immunotherapy with host defense cells or subcellular components such as transfer factor, immunorestorative immunotherapy with such agents as thymic hormones and levamisole, and possibly, passive immunotherapy with specific antitumor antibody.

Immunotherapy, now in its earliest stages of development, should be considered the fourth major modality of cancer treatment. The immunotherapeutic agents and approaches currently available for clinical application are, in general, crude and poorly defined. The mechanism of action of many of the immunotherapeutic agents is poorly or incompletely understood. The optimal timing of immunotherapy in relationship to conventional therapy has not been worked out. Highly purified and specific immunotherapeutic agents are yet to be developed. Despite these obstacles, there is evidence that immunotherapy of various types has activity in terms of increasing the remission rate or prolonging remission duration and survival for patients with such diverse malignancies as acute leukemia, soft tissue and osteogenic sarcoma, and malignant melanoma, as well as the more common malignancies, such as gynecologic and genitourinary cancer, and carcinoma of the breast, colon, and lung. In addition, several newer and unique approaches, such as the use of thymic hormones or the immunorestorative agent levamisole, and specific immunologic maneuvers, such as plasmapheresis

to remove blocking factors, offer considerable promise for the future. It is our feeling that the proceedings of this conference adequately summarize the past development, current status, and future prospects for immunotherapy and will represent a landmark in its development.

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