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*Principles
and
Practice of*

Pediatric Oncology

NOT FOR RESALE

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and
Practice of

Pediatric Oncology

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Being up-to-date on the clinical and scientific base of pediatric oncology is invaluable for all of us who practice cancer medicine. Pediatric malignancies have been a wellspring of information regarding all cancers. *Principles and Practice of Pediatric Oncology* promises to continue that tradition. Most of the current generation of medical oncologists, for example, began their education with the study of pediatric tumors. It was there that they learned the lessons of the need for, and the value of, systemic therapy, and the relation between tumor volume and outcome. The most important lesson of all, as it turned out, was applicable to all cancer specialists: the need for a combined-modality approach, to integrate regional and systemic treatments. This approach has now evolved in both pediatric and adult cancer medicine to more than

just adding one therapy to another; it involves a carefully crafted matching of the right amounts of the different modalities to effect maximum benefit and minimize side-effects. In adults, this approach in breast cancer, sarcomas, and lymphomas—to name just a few tumors for which the benefits of combined modality treatment are apparent—came from lessons learned in childhood leukemia, Wilms' tumor, and rhabdomyosarcomas. We have also learned from pediatric oncologists that advances can be rapidly translated into practice. To the credit of pediatricians, it is an unusual child with cancer who is not part of a program that both standardizes the delivery of optimum treatment and collects information vital to the next generation of protocols, all the while preserving the practice of pediatric cancer medicine. Sadly, medical, surgical, and radiation oncologists have yet to learn this valuable lesson of constancy from our pediatric colleagues.

As we close in on cancer at the molecular level, we can continue to learn by focusing on the clinical differences and similarities between pediatric and adult tumors. In the flurry of new information available to us concomitant with the biologic revolution, for example, the puzzle of the histologic differences between pediatric and adult malignancies is yielding to our curiosity. In experimental animals, carcinogens that induce, say, breast cancer in an exposed adult can produce neuroblastoma and other types of tumors characteristic of the pediatric population, if exposure takes place during embryogenesis when more genetic programs are apparently vulnerable to damage. We now have, I believe, an understanding of what the cancer cell is trying to do: it is trying to create a whole human being. In this somewhat animated view of the cancer process, exposure to carcinogenic influences very likely triggers highly conserved genetic programs, under the influence of what we now know as oncogenes, that are essential to embryologic growth and development—hence the different phenotypes in pediatric and adult malignancies, vis-à-vis time of exposure. Most of the programs required to create a whole human being are, of course, not available in adults, although teratomas with hair and teeth tell us how frighteningly close the cancer cell can come to its goals. The most lethal of these developmental programs is the capacity for rapid cellular expansion and the ability to migrate, the malignant counterparts being unrestricted growth and lethal metastases.

All these lessons, learned and unlearned, are in *Principles and Practice of Pediatric Oncology* in their modern-day version. This is the most comprehensive textbook of pediatric oncology yet assembled. The first section is sufficiently broad on the basics of the new biology and genetics to bring the physician up-to-date in the science behind the management of pediatric cancers. The remainder of the book covers every aspect of childhood cancers, including the most important aspects of managing the fruits of the success in this field, the complications of long survival.

Those of us concerned with cancer medicine in adults can, I suppose, never really catch up with the pediatric oncologists. Long survivors of combined modality treatment from the pediatric population will always be the benchmark for observing the consequences of successful treatment. The need to continue to share our experiences is even greater today. These

long survivors of combined modality therapy are now becoming adults, and, in addition to giving us the vital information we need on the consequences of successful treatment in the patients themselves, the normal children of these patients are now just beginning to provide us some assurance that the genetic consequences of our treatments in offspring appear to be minimal.

Given the fluid nature of the practice of cancer medicine these days and the maturity of pediatric oncology as a specialty, it is an unusual oncologist or general physician who does not or will not have the occasion to deal with problems related to pediatric oncology in his or her practice. *Principles and Practice of Pediatric Oncology*, at long last, gives the physician the long-needed single, up-to-date reference source missing for so many years.

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p r e f a c e

The education of the pediatric oncologist and all who engage in the care of children with cancer must be comprehensive and complete. The range of knowledge that must be acquired needs to include the principles of epidemiology, cell biology, molecular genetics, and immunology as well as the fundamentals of pharmacology, surgery, and radiation therapy. Moreover, because cancer impacts on the *total child and family*, every caregiver must also be knowledgeable about the physical and psychosocial care and rehabilitation of the patient and his or her family. The scope of the pediatric oncologist also includes an in-depth understanding of the long-term sequelae of cancer and its treatment, including its impact on the education and occupation of cancer survivors. *Principles and Practice of Pediatric Oncology* has been structured to

provide a comprehensive review of the multiple disciplines that make up the care and research agendas for children with cancer.

Pediatric oncology serves as a unique model for the study, treatment, and, possibly, prevention of cancer. The successful use of combination chemotherapy and multimodal regimens for acute lymphoblastic leukemia (Chapter 16) and a variety of solid tumors (Chapters 24–34) represents a cornerstone of modern oncology. With effective therapies, however, the complexity and the heterogeneity of cancer in children have become more apparent (Chapter 6), and it is increasingly common for clinical and biological prognostic factors to be included in the design of treatment regimens. Accordingly, just as immunophenotyping and cytogenetics provided evidence of tumor diversity (Chapter 2 and 4) in the 1970s, gene rearrangements, oncogene profiles, and other techniques of modern molecular biology are being employed in the 1980s to evaluate tumor tissue (Chapter 3), provide biological markers (Chapter 8), and guide management. Indeed, the boundaries between pathology, immunology, cell biology, and molecular biology are becoming increasingly blurred and coalesced in pediatric oncology.

Because cancer is a rare entity in children, the pediatrician must be able to differentiate its signs and symptoms from other more common clinical entities. Knowing when a child requires more intensive and invasive investigation is a critical component of the diagnostic process (Chapters 1 and 5). Understanding which tests to perform, in what sequence, and what their advantages and limitations are requires special expertise in relation to the pediatric patient (Chapter 7).

Because cancer in children interrupts normal growth and development, unique care must be taken in defining the dose, route, and schedule of chemotherapy and radiation therapy (Chapters 9 and 11) as well as in the choice of the surgical procedures that may be required for diagnosis or for achieving local tumor control (Chapter 10). These issues are particularly critical in the management of the infant with cancer (Chapter 12), further emphasizing that any physician involved in the care of children with cancer must be cognizant of the principles that ensure the optimal safety and quality of treatment.

Skill in the supportive care of the child or adolescent undergoing cancer treatment is also an essential element of successful treatment. This must include a detailed knowledge of the metabolic and mechanical emergencies that may ensue from cancer or its treatment (Chapter 37), including the diagnosis, management, and prevention of infectious complications (Chapter 39) as well as the management of nausea and vomiting (Chapter 45), pain (Chapter 44), and hematologic (Chapter 38) and nutritional supportive care (Chapter 40). An awareness and understanding of the impact of cancer and its treatment on the psychological health of the patient and family are also necessary prerequisites for appropriate intervention (Chapters 41, 42, and 46).

The impact of cancer in the child reaches beyond medical and emotional health issues. The financial cost of care can be considerable, and awareness of the direct and out-of-pocket expenses and resources for reimbursement is critical (Chapter 43). A number of important ethical, legal, and advocacy issues may also arise in the treatment of the child or adolescent with cancer, revolving about such issues as compliance, consequences of therapy, and experimental regimens (Chapters 15 and 53).

The pediatric oncologist must also be knowledgeable in the design, execution, analysis, and interpretation of clinical trials (Chapter 13). This is underscored by the relative rarity of childhood tumors, which makes it important that clinical studies be designed to address critical questions and provide meaningful answers in an efficient manner. Limited numbers of patients also requires close cooperation among investigators. The development of cooperative trials in pediatric oncology thus serves as a highly successful model for medical oncology.

Today, more than 50% of children with cancer will survive. Attention to the long-term rehabilitation (Chapter 47), educational needs (Chapter 51), and vocational and occupational needs (Chapter 52) of cancer survivors has therefore become increasingly important. The long-term complications of cancer (Chapter 50) and its treatment require close monitoring. New

and unanticipated diseases, such as AIDS (Chapter 36), can also impact on the child with cancer and the practice of the pediatric oncologist.

Despite the available therapy and current advances, many children who are diagnosed with cancer will not survive. Helping these children and their families to face terminal illness and death, whether it occurs in the hospital, at home, or in a hospice, becomes an important consideration for all caregivers (Chapters 46 and 49).

The success of pediatric oncology in the western world is unprecedented. Although malnutrition and infectious diseases are numerically more important, children in developing countries still develop cancer. Understanding the epidemiologic and biological aspects of childhood cancer around the world and developing and modifying methods for intervention are important considerations (Chapters 1 and 54).

In *Principles and Practice of Pediatric Oncology* we have attempted to deal with a broad range of important topics in conceptual and practical detail. We acknowledge the efforts, care, and patience of the contributors to *Principles and Practice of Pediatric Oncology*. To develop a textbook that presents a current and unified approach required considerable integration and organization. The process, although demanding, was a stimulating and exciting venture, and it is our hope that the final product reflects well on the cooperation and enthusiasm of all who have been involved.

Finally, we acknowledge the help and assistance of the J. B. Lippincott Company, especially Stuart Freeman, Sanford Robinson, Delois Patterson, and Leslie Hoeltzel. We particularly appreciate the wisdom of our co-workers and fellows at the National Cancer Institute and the continued motivation to advance our knowledge that we receive from caring for children with cancer. We especially hope that the words contained in these pages will help to improve the care and treatment of children with cancer everywhere.

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