# TRENDS in CHILDHOOD CANCER

EDITED BY
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# Trends in Childhood Cancer

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# Series Preface

The past five years have produced an explosion in the knowledge, techniques, and clinical application of radiology in all of its specialties. New techniques in diagnostic radiology have contributed to a quality of medical care for the patient unparalleled in the United States. Among these techniques are the development and applications in ultrasound, the development and implementation of computed tomography, and many exploratory studies using holographic techniques. The advances in nuclear medicine have allowed for a wider diversity of application of these techniques in clinical medicine and have involved not only major new developments in instrumentation, but also development of newer radiopharmaceuticals.

Advances in radiation therapy have significantly improved the cure rates for cancer. Radiation techniques in the treatment of cancer are now utilized in more than 50% of the patients with the established diagnosis of cancer.

It is the purpose of this series of monographs to bring together the various aspects of radiology and all its specialties so that the physician by continuance of his education and rigid self-discipline may maintain high standards of professional knowledge.

LUTHER W. BRADY, M.D.

# Preface

Cancer deaths in children under the age of 15 approach 4000 per year in the United States, with leukemia accounting for one-half of these deaths. Although cancer mortality of children comprises approximately 1 percent of all cancer mortality in this country, cancer is the leading cause of death from disease among schoolchildren. Therefore, when the treatment of children with cancer is considered in terms of the expected life span in the general pediatric population, the problem assumes a different perspective.

Furthermore, the relative rarity of cancer in the pediatric age group creates its own problems and compensations. In our heritage, there is a belief that children should be free of the mental encumbrances carried by adults, so that serious illness has a unique impact, not only for the child but also for parents, siblings, friends, teachers, physicians, and other involved medical personnel. It is very easy to feel deep concern for a child with cancer, and the emotional sequelae of diagnosis, treatment, and possible death require particular consideration.

We are fortunate to have been able to bring together in this volume the ideas and findings of a number of eminent leaders in pediatric cancer clinical research and therapy. Advances in the management of malignant disease in children have contributed toward an understanding of the treatment of cancer in other age groups. The unusual circumstances of a pediatric patient with a life-threatening malignancy involve specific obligations and stresses, as well as outstanding rewards, for the physician who participates in the management of pediatric cancer.

For decades, the primary considerations in pediatric oncology have been diagnosis, treatment, and dealing with death. Today we have reached an era of increasingly successful therapy. As a result, we must now turn our concerns to the long-term effects of this success on the children who are cured. The physical and psychosocial impingements of these diseases can be monumental. We now must learn to manage or prevent these effects and to help these patients prepare for a life span which may include higher education, business responsibilities, marriage, and parenthood.

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# Contents

# Introduction: General Aspects of the Diagnosis of Malignancy in Children

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The one word that best describes today's understanding of the general aspects of the diagnosis of malignancy in children is awareness. That word classifies the problems that we see in children, in the family, and in the medical professions. Certainly, as time goes on, an increase level of awareness in each of these groups will make it easier for us to approach increased survival and its concomitant problems with an understanding of the process.

Many children with malignancies now survive for longer and longer periods of time. In the past, a diagnosis of malignancy automatically precluded the planning of a future life, and the role of all health professionals was mainly supportive. That has now changed. The awareness of the physician and of many other people has increased and must continue to increase in order to provide the best possible environment and treatment for the child with malignancy. We must acknowledge and overcome the lack of awareness in many health professionals which often results in inadequate diagnosis and poor management of the child with malignancy. No area today is more important than the education of physicians and families in the problems of pediatric malignancies and the need for adequate evaluations. Proper evaluation of all aspects of the history provides a better understanding of etiologic factors and permits earlier diagnosis.

The awareness of the medical profession of malignancy in childhood is inhibited significantly by the infrequent occurrence. Adults are constantly aware of the dangers to themselves of environment, habits, and symptoms. This is not so for children. To quote Osler, "Familiarity breeds contempt; unfamiliarity breeds misdiagnosis and poor treatment." The average pediatrician, surgeon, or general practitioner sees malignant disease in children so rarely that it is difficult for him to maintain capability for both diagnosis and treatment. In a recent statewide survey in one of our large states, surgeons and pediatricians indicated that they had not read an article *in depth* related to childhood malignancy in the prior 12 months. Some read the summary, some read the title, but none read the article in depth nor read more than one article in 12 months. With the tremendous proliferation of information about adequate diagnosis and treatment of children with malignancy, this level of awareness is not sufficient to assure the best diagnosis and the best treatment. The first axiom of adequate diagnosis is a knowledge of the latest techniques, followed by conceptualization of an appropriate management plan. If this expertise is not available in a community, then it is the responsibility of the physician to refer the child with suspected malignancy to a program that manages such children frequently so the child can receive the best diagnosis and therapy.

In the diagnosis of pediatric malignancy, six major areas require constant awareness: (1) prevention; (2) genetic and familial aspects of malignancy; (3) the problems in the child; (4) the problems in the family; (5) adequate diagnosis; and (6) the best management of the diagnosis.

In reference to prevention, the etiology of malignancy in children as in adults in general, is largely unknown. To define the correlative relationship more completely, a detailed history must be taken on every child with malignancy. Most histories and physical examinations are inadequate. The crucial points of information that allow correlation of the ultimate diagnosis with a wide variety of etiologic factors are not recorded. Factors such as previous exposure to ionizing radiation are obvious positive indications. Less obvious, particularly in children,

are environmental conditions, drug and toxin exposures, genetics, and infection correlations.

A few years ago, there was a maximum interest in the epidemiologic evaluation of "clusters" and also the infection correlation between various types of malignancy and the ultimate outcome of that malignancy. In general, epidemiologic studies of both "clusters" and the infection relationship have not borne out initial premises, and there has been a corresponding waning of interest. Much remains to be done in this area, and an adequate detailed history, as well as development in the family of an awareness of what is being sought, is important to define more specific answers. This will permit better understanding of cause-and-effect possibilities and allow us to ascertain the relationship of specific etiologic agents to certain types of tumors.

A classic example of awareness of relationships was the discovery of vinyl chloride as an etiologic agent in certain malignancies three years before it became a well-known fact. When the first of the malignancies developed in this group of workers, the right questions were asked. However, the information was not properly evaluated, and, over an additional three-year period, many more people, not only in this country but throughout the world, were exposed to this toxin; therefore, the continuing development of the associated malignancies is to be expected. Had an adequate history and an adequate understanding of what was occurring in this group of people been appreciated, many lives would have been saved.

With the varied activities and exposures of a child, a less-than-adequate history provides no information for future prevention. Those who work with pediatric malignancy, in spite of their professional effort, often become too complacent with the ability to diagnose and to treat and too accustomed to saying "the cause of this particular malignancy is unknown." Therefore, the necessary information that could possibly define the cause-effect relationship adequately is not obtained.

In taking an adequate history, there are some significant changes in the child that can lead to an understanding of the start of the malignancy. The first of these is a change in activity pattern, as has been documented by studies in this country and abroad. Examples include the child who has been very introspective, who read for hours, and who now has a short attention span; or the previously active child who is now quiet; these are indications of behavior pattern changes. This becomes important as families are made aware of how to detect early signs of malignancy in their children.

Obviously another aspect is alteration in physical characteristics. This could be a limp, a lump, or a tendency to bruise easily; it could be anything.

These, then, are early signs that often occur before a positive diagnosis of malignancy can be made. The weakness in studying these areas is that much must be done retrospectively, and retrospective analysis is often misleading.

The degree of awarness in the family is another problem that must be explored. One aspect that bothers many who have worked in pediatric oncology is drawing the line between scaring a family, keeping them communicative, and having them understanding the diagnosis and the problem. Most physicians have had an anxious mother come to them and say, "I'm worried that my child has leukemia" because the child is either pale or bruising. This is not awareness, this is fear, but there is a degree of awareness in fear. How does one acquaint the parents with

an understanding of the occurrence of malignancy in children and what it means to the child and to the family? This is one of the challenges in the early diagnosis of malignancies—how to make the family more aware without inducing fear; what comparison can be drawn between adults and the specific problems in children. The so-called seven signs developed through the years are classic for adults; however, they do not pertain to pediatric malignancy except in a very small percentage of the cases, and yet education for all as to the occurrence of malignancy in children concerns everyone. It is obvious that as better approaches to treatment as well as to diagnosis are developed, the early diagnosis of pediatric malignancy becomes an essential point in reference to ultimate survival.

In obtaining an adequate history, it is necessary to ask the right questions of the family at the right time. For most families, the right time is not at the time of diagnosis. At that point, they are experiencing severe emotional strain, and they probably will not be able to recall information that would be significantly helpful. Therefore, it is essential that, as rapport builds between the physician and the family in the management of the child, every opportunity should be taken to pick up fragments and pieces of history that can help the next child in reference to prevention. This brings an awareness in families of what the outcome will be and provides strong support from families for what they believe they can do to help. The continuation of physician interest in the family, even after the death of the child, has provided another source of information that makes it possible to evaluate etiologic relationships.

Unfortunately, there is insufficient manpower to perform preventative physical examinations on enough children to increase the detection rate significantly. A study on pediatric malignancy by the American Cancer Society in 1967 showed that most of the cases would have been detected two or three months earlier by adequate physical examination. Transposing that figure to this country's entire pediatric population and realizing that if every child were examined every six months in order to detect those cases of malignancy two to three months earlier to possibly alter the survival pattern, five times the number of pediatricians and twice the number of general practitioners presently practicing in this country would be needed. These examinations would increase survival rate if nothing else in the environment changed. Since most physicians are already overworked, it is not realistic to hope for earlier diagnosis by more frequent physical examinations. Therefore, the family becomes a critical point, and much of the activity in the future will have to be related to education of the family.

In reference to diagnosis, much remains to be learned; the inability to make a diagnosis is, at times, depressing. Most parents believe that a definite diagnosis can be made if a bone marrow is obtained; the same is true with biopsies. When one obtains permission for the bone marrow or biopsy from an already apprehensive family, the family expects an absolute answer. Often, it cannot be provided.

For pediatric malignancy to be adequately diagnosed, good pathology and good radiology are imperative. Also essential are criteria that will satisfy everyone and a degree of familiarity with the problem as seen in this country today. As one looks at the infrequency of the disease, as one looks at the level of competence needed to treat the disease early, it is apparent that adequate referral to sources where good pathology and good radiology will contribute to an early diagnosis and treatment is essential.

Diagnosis can often be adequately managed in many hospitals, but more than diagnosis must be considered in pediatric malignancy. Diagnosis and treatment must be considered together. The opportunity to move aggressively and progressively to a form of therapy that is often better for a particular child requires this teamwork. An array of tests available immediately for diagnosis and proper interpretation is not possible in every hospital or every doctor's office. Diagnosis is related to the capability of the physicians involved, with the support of such services as pathology and radiology. To improve the entire structure of the management of pediatric malignancy for adequate survival requires such commitment; to do less is a disservice to the patient and the family.

# The Multidisciplinary Team Approach to the Care of Children with Cancer

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