HODGKIN'S DISEASE

Edited by

MORTIMER J. LACHER, M.D.

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New York, New York

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It must be stated that my contributions represent only my ideas and in no way are representative or imply approval by the Memorial Sloan-Kettering Cancer Center.

My own support was uniquely dependent on a fee for service patient care system and credit therefore must be given to all of the patients of Mortimer J. Lacher, M.D., P.C., for giving me the wherewithal to support and survive this enterprise.

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MORTIMER J. LACHER

New York, New York
January 1976

Contents

CHAPTER ONE

Introduction

MORTIMER J. LACHER, M.D.,

"Let us be critical of ourselves, of our present methods of treatment and of our instructions to our colleagues and students and impart a dynamic philosophy in treatment. Let us continue to search out the past experiences, the natural history, and the vagaries of the biological activity of Hodgkin's disease while we press forward in our search for better radiotherapeutic and chemotherapeutic measures for this disease." [Henry D. Diamond, *Ann. N.Y. Acad. Sci.* **73,** Art. I, pp. 357–362 (Sept. 5, 1958)].

If Henry Diamond had survived into this recently past decade, he might have benefited from the remarkable advances in the modern application of radiation therapy, and from the extraordinary discoveries and utilization of modern chemotherapy. He lived with Hodgkin's disease for 17 years and during that time worked as a physician and teacher[2] only to prove that long survival was not a guarantee of cure.[6] Except for a single agonal injection of thio-TEPA, he survived that long productive period of time with only the benefit of repeated orthovoltage radiation therapy.

When the promise was advanced, more than a decade ago, that it might be possible to cure large groups of patients with Hodgkin's disease utilizing initial extended-field, high/dose radiotherapy,[5] we joined enthusiastically in this therapeutic approach. Despite the anticipation that the application of a single high dose of radiation therapy would lead to a cure for all, the majority of patients still require repeated therapy and especially chemotherapy to achieve long survival.

There is no doubt, however, that in the past 20 years we have improved the 5-year survival rate with the use of radiation therapy and chemotherapy from approximately 24% to 64%.[4,6,8] But both before and after the 5-year survival mark, the death rate from relapsing Hodgkin's disease remains unacceptably high.

Hodgkin's disease is a chronic recurring disorder, and radiation therapy alone, no matter how intense or extensive, is not the panacea for the majority of patients. In addition, after initial intense radiation therapy, only very limited doses and carefully selected radiation fields can be used again when the patient relapses. After relapsing following initial intense radiation therapy, the patient must depend on chemotherapy to achieve remission for long survival. Efforts are now being made to employ chemotherapy early in the course of the disease, either alone or in combination with radiation therapy or in sequential treatment.[7,10]

Eventually the discovery of new effective chemotherapeutic agents and techniques of application (including the use of immunotherapy) will lead to the cure of Hodgkin's disease in all patients. I believe that the cure will eventually be achieved without the use of radiation therapy and that it will probably antedate the discovery of any specific etiology for Hodgkin's disease. It may turn out that there is no specific single cure, but that repeated treatment of an intermittent nature will be required for almost all patients to achieve long survival.

Until recently we had very little basic science to apply to our clinical problems, and we were stumbling along with only cookbook concepts of chemotherapy. Fortunately, that situation is changing. The more recent mathematical approaches of Skipper et al.[9] regarding "cell kill," and the relatively new attempt to categorize antitumor agents according to their cell cycle activity, are the building blocks of basic science that will be applied in the future.[1]

We already have the mechanism and organization to apply new basic knowledge. The chapter on multiple-drug chemotherapy is an extraordinary testimony to the achievements of multiple centralized authorities. Cancer chemotherapists have created a national and worldwide network of physicians to conduct applied research at a clinical level. It is a technique that will eventually be borrowed by all clinical disciplines. The chapter on cooperative chemotherapy groups presents the inside workings of one such regional chemotherapy group.

For the first time physicians in small or large institutions with only a few patients or a large number of patients may all contribute to an orderly application and analysis of treatment and, by so doing, physicians may educate themselves and generally raise the level of care throughout the nation and the world.[3]

The complexity of the therapy of Hodgkin's disease and the problems and complications that may be encountered challenges all disciplines. This book is presented therefore by multiple authors to explore our current positions with regard to the incredibly complex nature and treatment of Hodgkin's disease. An attempt will be made to survey the epidemiological and etiological quandaries, the practical application of drugs and radiation therapy, the side effects and complications of treatment, and even the socioeconomic dilemmas faced by this extraordinary population of patients.

It is impossible to be complete, but the hope is that enough information will be presented to help those who might seek some knowledge about the treatment of the Hodgkin's disease patient, as well as act as a springboard for controversy regarding theoretical problems (e.g., is Hodgkin's disease an infectious disease?), as well as the more "humdrum" problems involved in day-by-day therapeutic decisions (e.g., Should I recommend splenectomy or shouldn't I? If I do recommend it, how should it be done? What problems may I anticipate during the course of life for my patients with Hodgkin's disease?)

And when everything fails and death from recurrent disease, drug toxicity, or

combinations of these factors occurs, let everyone know that he is not alone in this frustration of repeated failure. And let everyone know that real progress has been made in the past and that the next decade will undoubtedly surpass all previous efforts with regard to success in the management of patients with Hodgkin's disease.

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CHAPTER TWO

Epidemiology of Hodgkin's Disease

DAVID SCHOTTENFELD, M.D..

The American Cancer Society estimated that in 1973 there would be 3700 deaths and 4800 new cases of Hodgkin's disease. During 1950–1968, in the United States white population the age-adjusted mortality due to Hodgkin's disease was between 2.1 and 2.3 per 100,000 for males and 1.3 to 1.4 per 100,000 for females (Table 1, Fig. 1). Although Hodgkin's disease accounted for approximately 1% of

TABLE 1 AGE-ADJUSTED AND AGE-SPECIFIC DEATH RATES PER 100,000 FOR HODGKIN'S DISEASE, UNITED STATES WHITE POPULATION, 1950, 1955, 1962, 1968[a]

	1950		1955		1962		1968	
Age	Male	Female	Male	Female	Male	Female	Male	Female
All ages[b]	2.2	1.3	2.3	1.4	2.2	1.3	2.1	1.4
0–4	*c*	*c*	*c*	*c*	*c*	*c*	*c*	*c*
5–14	0.3	*c*	0.3	*c*	0.3	*c*	0.2	*c*
15–24	1.1	0.9	1.4	0.9	1.2	0.9	1.3	1.0
25–34	2.4	1.3	2.2	1.5	2.4	1.4	2.6	1.5
35–44	2.2	1.1	2.6	1.4	2.5	1.6	2.6	1.3
45–54	3.5	1.8	3.3	1.5	3.2	1.5	2.9	2.0
55–64	5.0	2.1	4.8	2.6	4.7	2.1	4.4	2.6
65–74	5.9	4.2	7.1	4.0	5.5	3.5	6.0	3.7

[a]From T. Gordon, M. Crittenden, and W. Haenszel. Cancer mortality trends in the United States, 1930–1955, Part II. In *End Results and Mortality Trends in Cancer*, Washington, D.C., National Cancer Institute Mongraph No. 6, 1961; and *Statistical Bulletin Metropolitan Life Insurance Company* **54:6** (1973).
[b]Adjusted on basis of age distribution of United States 1950 census population.
[c]Less than 20 deaths—rate not computed.

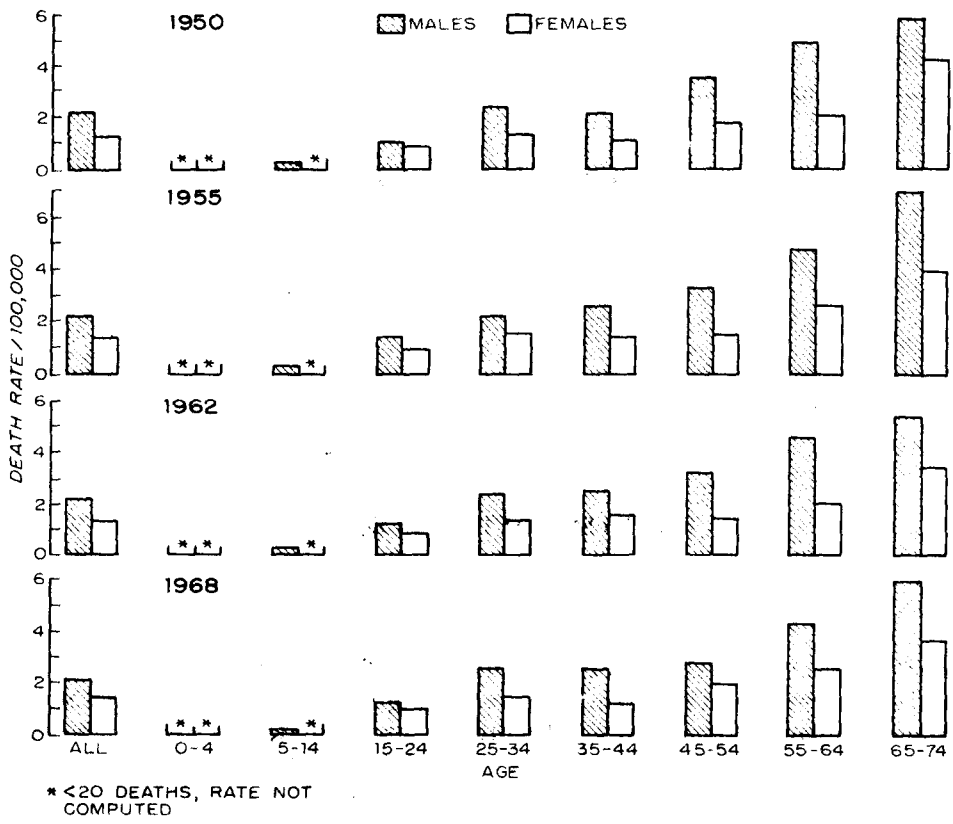

Fig. 1 Age-adjusted and age-specific death rates per 100,000 for Hodgkin's disease, United States white population, 1950, 1955, 1962, 1968.

all incident cancer cases in United States white males at all ages, it was responsible for 7% of all cancer cases under age 14 years, and for 17% in the age interval 15 to 34 years. Of all incident cancer cases in United States white females, Hodgkin's disease accounted for less than 1% at all ages, 3% under age 14 years, 9% between 15 and 24 years, and slightly more than 1% between 25 and 34 years (Table 2, Fig. 2). Hodgkin's disease accounts for 39% of lymphomas in patients of all ages, and for 66% of lymphomas in patients under 35.

DESCRIPTIVE EPIDEMIOLOGY

Deaths in the United States from Hodgkin's disease are rare before 5 years of age and then increase gradually so as to form one peak between 15 and 34 years and a second peak after 50 years. The second mode is more prominent, and its configuration similar to that of other lymphoid neoplasms, that is, lymphosarcoma, reticulum cell sarcoma, chronic lymphatic leukemia, and multiple myeloma. The pattern of mortality for Hodgkin's disease, which is