Prognosis for adolescents with Hodgkin's disease[1]

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From 1972 to 1983, 68 adolescents, aged 12 to 20 years (median 17.6 years), with Hodgkin's disease received treatment at the Cleveland Clinic. Although the overall male:female ratio was 1.2:1.0, male predominance was greater in younger adolescents. The histopathologic distribution was overwhelmingly nodular sclerosing (69%), but 24% were mixed cellularity, and 7% were lymphocyte-predominant. There was no statistical relationship between histopathology and survival. All patients were pathologically staged (PS): PS-I = 11 patients, PS-II = 26 patients, PS-III = 17 patients, and PS-IV = 14 patients. The overall five-year survival rate was 83%, and there was no significant difference between pathological stage and chance of survival. Treatment programs had been based on pathological staging, usually irradiation therapy for stages I and II, combination chemotherapy for stage IV, and both modalities combined for stage III. This therapy has resulted in an excellent five-year survival rate for these adolescents.

Index term: Hodgkin's disease

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In the 150 years since Thomas Hodgkin first described the syndrome that now bears his name,[1] much has been learned about its clinical spectrum,[2] epidemiology,[3] and treatment with chemotherapy[4] and radiation therapy.[2] Few developments in oncology have been as striking as the changing prognosis for patients with this disease. During the last 20 years it has become apparent that multiple-drug chemotherapy can cure many patients with widespread disease. In 1964 the mean survival time for afflicted children was only 2.7 years.[5] Although the clinical course of children with Hodgkin's disease has recently been reviewed

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Table 1. Ann Arbor staging for Hodgkin's disease

Stage	Definition
I	Single lymph node region or a single extralymphatic site by direct extension.
II	Limited to one side of the diaphragm, either of two or more lymph node regions, or of localized involvement of an extralymphatic site and one or more lymph node regions.
III	Lymph node regions on both sides of the diaphragm, which may include the spleen or a single localized extralymphatic site.
IV	Diffuse or disseminated involvement of one or more extralymphatic organs.

"A" is used if there are no systemic symptoms, and "B" if there are: (1) unexplained fever, (2) weight loss over 10%, (3) night sweats.

by the Mayo Clinic[6] and others,[7–10] little has been said about adolescents as a distinct group. The purpose of this study is to review the histopathologic classification, pathological stage, and survival statistics of a large group of adolescents with Hodgkin's disease who began treatment during the last decade at this institution.

Method

From 1972 to 1983 inclusive, 68 patients with newly diagnosed Hodgkin's disease between 12 and 20 years of age received treatment at the Cleveland Clinic. Their records were reviewed and form the basis of this study. All underwent a staging laparotomy unless there was pathologically proved evidence of advanced disease, and the usual Ann Arbor staging system (*Table 1*) was used.[11] Different therapeutic techniques were used depending upon stage, physician preference, and clinical research protocols available, but they were not separately reviewed for degree of effectiveness.

Results

Age and sex: The mean age of the 68 patients was 17.6 years, with a range of 12 to 20 years. There were 37 males and 31 females (overall sex ratio 1.2:1.0). The mean age for the boys was 17 years 4 months and 17 years 11 months for the girls. Details of age and sex distribution are indicated in *Table 2* and *Figure 1.*

Table 2. Age and sex distribution

Age group (yr)	No. of patients Male	Female	Percent of total	Ratio Male:Female
12–14	10	6	23%	1.7:1.0
15–17	10	6	24%	1.7:1.0
18–20	17	19	53%	1.0:1.1
Total	37	31	100%	1.2:1.0

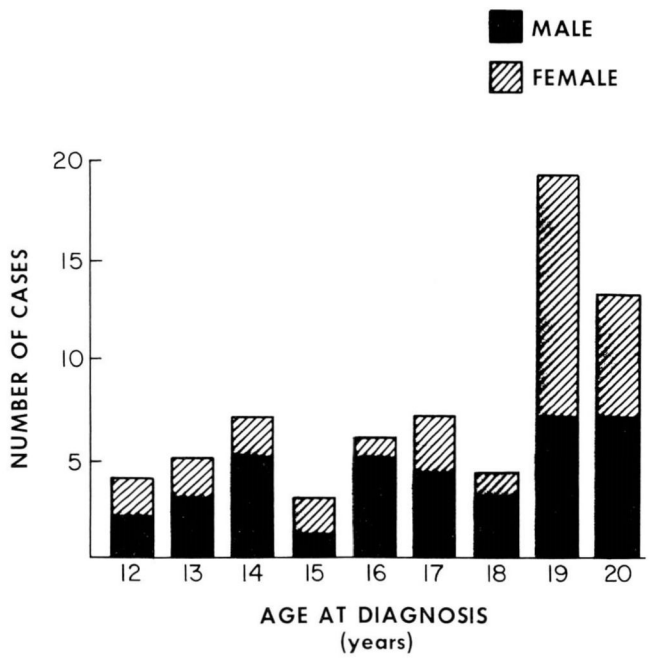

Fig. 1. Distribution of patients by age and sex.

Histopathologic distribution: Forty-seven of the cases were nodular sclerosing (69%), 16 had the mixed cellularity type (24%), and only five were lymphocyte predominant (7%). There were no examples of the lymphocyte depletion type.

Pathological staging: The patients were fairly evenly divided between early stages I and II (37 patients) and later stages III and IV (31 patients). A detailed breakdown by pathological state and absence or presence of systemic symptoms ("A" or "B") is presented in *Table 3.*

Survival: Because of the small numbers in each of the pathological substages, both A and B groups of patients are combined in the survival curves for each of the pathological stages (*Fig.*

Table 3. Pathological stages

Stage	Frequency	Percent
I	11	16.2
A	10	14.7
B	1	1.5
II	26	38.3
A	18	26.5
B	8	11.8
III	17	25.0
A	10	14.7
B	7	10.3
IV	14	20.6
A	5	7.4
B	9	13.2

2).There is no statistical difference between survival in any of these curves (P = 0.20). Of the 14 deaths, all were due to Hodgkin's disease except one that was the result of an automobile accident of a boy in apparent clinical remission. Two patients never achieved remission, and 21 suffered a relapse at some time after achieving remission.

The chance of surviving five years was 100% for stage I, 80% for Stage II, 93% for stage III, and 73% for stage IV (overall 83%). Because of the small number of patients in each group and their high survival rate, a significant difference could not be demonstrated between these five-year survival rates (P = 0.30). There was no difference in five-year survival (P = 0.17) between the two principal histopathologic groups, nodular sclerosis (86%), and mixed cellularity (77%). The overall survival curve is presented in *Figure 3.*

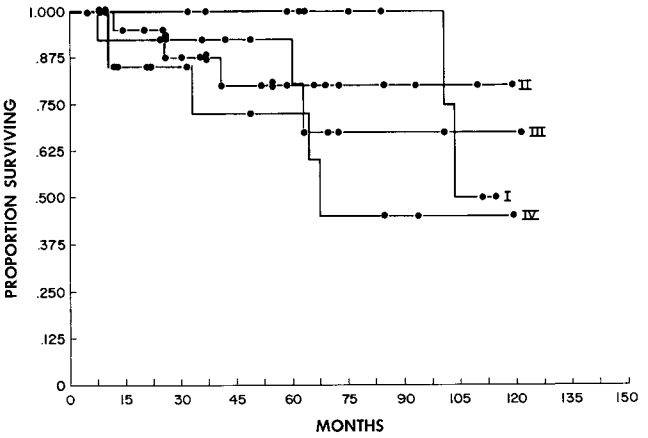

Fig. 2. Survival data by stage.

Discussion

Although there is no "optimal therapeutic regimen" for Hodgkin's disease, current treatment programs based on pathological staging are so effective that most adolescents can now look forward to a normal life expectancy. In general the patients in this study with stage I and II disease were treated with either involved-field or extended-field radiotherapy; those with stage IV were treated with combination chemotherapy; and those with stage III, with a combination of both modalities.

The 83% overall five-year survival rate for these young patients is encouraging. Even if a patient experiences a relapse he can usually be successfully reinduced into long-term remission with another treatment regimen that includes chemotherapy. Even patients who have suffered a relapse during or shortly after treatment with the classical MOPP group of chemotherapeutic agents (mechlorethamine, vincristine (Oncovin), prednisone, and procarbazine) usually can be successfully treated with another noncross-resistant group of drugs such as the ABVD regimen (doxorubicin [Adriamycin], bleomycin, vinblastine, and dacarbazine).[12] Our overall survival statistics for these adolescents is practically identical to the 84% recently reported for all pediatric patients (ages 4 to 20 years with a median age of 11 years) with Hodgkin's disease at the Memorial Sloan-Kettering Cancer Center.[9]

Our series shows a marked increase in the number of patients in late adolescence, which is typical of the disease in this country. Hodgkin's disease classically has a bimodal age distribution with peaks at ages 20 and 50. The earlier of the two peaks occurs in late childhood in developing countries. In the United States this early peak incidence shifted to adolescence between 1921 and 1951.

The distribution of histopathological types is consistent with the ratios reported from predominantly adult series, with most patients having the nodular sclerosing variant generally associated with mediastinal involvement. A marked male preponderance in children under the age of 11 (3:1) has been reported decreasing to the overall 2:1 male predominance reported when large groups of patients are studied.[13] Our data also show a changing ratio with age with the younger adolescents having a greater male predominance.

Complications of these treatment programs are not addressed here. A list of the long-term com-

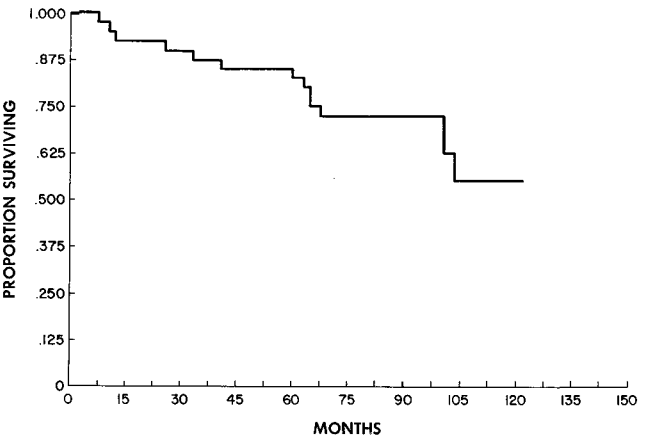

Fig. 3. Overall survival.

plications would include closure of skeletal growth centers and thyroid failure secondary to radiation therapy, ovarian dysfunction and azoospermia secondary to chemotherapy, and a second malignancy occurring primarily when both therapeutic modalities have been used. Only after long-term follow-up can the real cost of their cure be calculated.

Acknowledgment

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