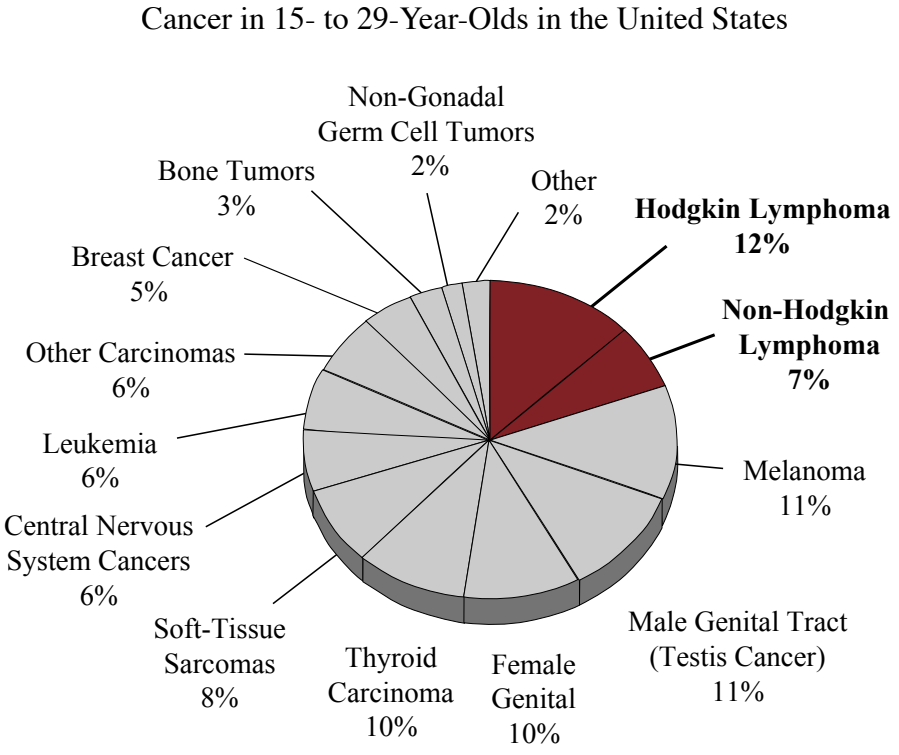
Chapter 3

Lymphomas and Reticuloendothelial Neoplasms



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HIGHLIGHTS

Incidence

- Lymphomas now represent 4-5% of all new malignancies diagnosed in the United States and are the most common hematologic malignancy.
- Lymphomas accounted for 19% of all cancers in 15- to 29-year-olds in the United States during the time period 1975 to 1999.
- In the adolescent and young adult population, the incidence of all lymphomas relative to other cancers decreased with age during this period—from 26% in 15- to 19-year-olds to 15.8% in 25- to 29-year-olds.
- Females had a higher incidence of Hodgkin lymphoma in the 15- to 19-year age group. Males had a higher incidence of all lymphomas in all other age groups.
- Incidence of Hodgkin lymphoma in the adolescent and young adult age group was highest in white non-Hispanics.
- The incidence of Hodgkin lymphoma as a function of age is bimodal, with a peak between 20 and 25 years of age and a second peak between 75 and 80 years of age.
- The incidence of non-Hodgkin lymphoma was highest in white non-Hispanics in the 15- to 19-year age group but highest in African Americans/blacks in the 20- to 29-year age group.

Mortality & Survival

- Males had higher mortality from lymphomas than females at all ages.
- Mortality for all lymphomas was comparable for 15- to 19-year-old whites and African Americans/blacks, but was higher for African Americans/blacks at all ages ≥ 20 years.
- Although little change in lymphoma survival for the 15- to 29-year age group has been observed, there has been marked improvement in survival in the < 15-year age group.
- Five-year survival for lymphomas in the 15- to 29-year age group was similar for all racial/ethnic groups.

Risk Factors

- Factors associated with a high standard of living may contribute to delayed exposure to childhood infections and subsequent delay in maturation of cell immunity. EBV infection acquired in adolescence, with subsequent development of infectious mononucleosis, may increase the risk of Hodgkin lymphoma in adolescents and young adults.
- A history of autoimmune disorder, family history of malignancy/hematopoietic disorder, and Jewish ethnicity are all risk factors for Hodgkin lymphoma.
- HIV infection predisposes to both Hodgkin and non-Hodgkin lymphoma.
- EBV infection has been linked to non-Hodgkin lymphoma.
- Autoimmune disorders, Helicobacter pylori infection, genetic susceptibility, male gender, tobacco use, and chemical exposure have been linked to an increased risk of non-Hodgkin lymphoma.

INTRODUCTION

In the time period 1975 to 1999, lymphomas accounted for 19% of cancers in 15- to 29-year-olds in the United States. In 2004 they represented 4-5% of all new malignancies diagnosed in the United States and were the most common hematologic malignancy.[1,2] Cancer was the second leading cause of death for all ages combined. In males between the ages of 20 and 40, non–Hodgkin lymphoma was the fourth most common malignancy and the fifth leading cause of cancer death. In the adolescent and young adult population, the incidence of all lymphomas relative to

other cancers decreased with age during the time period 1975 to 1999—from 26% in 15- to 19-year-olds to 15.8% in 25- to 29-year-olds (Figure 3.1).

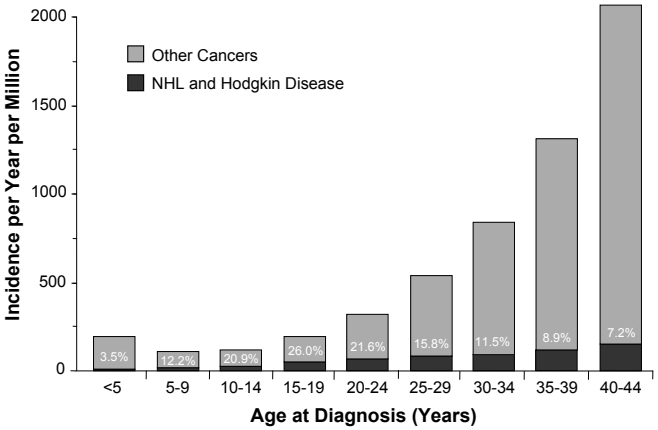

Figure 3.1: Incidence of All Lymphoma Relative to All Cancer, SEER 1975-1999

METHODS, CLASSIFICATION SYSTEM, AND BIOLOGICAL IMPLICATIONS

In the International Classification of Childhood Cancer (ICCC), Lymphomas and Reticuloendothelial Neoplasms are in category II. Since many of the morphology codes used to designate ICCC category II changed between ICD-O-2 and ICD-O-3, the following discussion on specific histologies will only use the ICD-O-2 classification. Not included in ICCC is Letterer-Siwe disease (9722).

In the ICCC, category II is divided into: II(a) *Hodgkin lymphoma*; II(b) *Non-Hodgkin Lymphoma*; II(c) *Burkitt Lymphoma*; II(d) *Miscellaneous Lymphoreticular Neoplasms*; and II(e) *Unspecified Lymphomas*. Hodgkin lymphoma spans codes 9650-9667 and includes specific types of Hodgkin lymphoma [mixed cellularity (9652), lymphocytic depletion (9653-9655), lymphocytic predominance (9657-9659), nodular sclerosis (9663-9664), and mixed types (9665-9667)], Hodgkin lymphoma not otherwise specified (9650), Hodgkin paragranuloma (9660), Hodgkin granuloma (9661), and Hodgkin sarcoma (9662). The ICCC *Non-Hodgkin lymphoma* category II(b) is constituted by specific types of non-Hodgkin lymphoma (9670-9686, 9688, 9690-9717), non-Hodgkin malignant lymphoma (9591), lymphosarcoma (9592), reticulosarcoma (9593), microglioma (9594), true histiocytic lymphoma (9723), and diffuse malignant lymphoma (9595). The ICCC *Burkitt Lymphoma* II(c) category is Burkitt lymphoma (9687). The ICCC *Miscellaneous Lymphoreticular Neoplasm* category—II(d)—includes malignant histiocytosis (9720), plasmacytoma (9731), multiple myeloma (9732), mast cell tumors (9740-9741), immunoproliferative disease NOS (9760), Waldenstrom macroglobulinemia (9761), alpha heavy chain disease (9762), gamma heavy chain disease (9763), and immunoproliferative small intestinal disease (9764). ICCC *Unspecified Lymphoma* category II(e) is limited to malignant lymphoma, NOS (9590) in the ICD-O-2.

As explained in the *Methods* chapter, data are presented for 15- to 29-year-olds with comparisons to the age groups 0 to 15 years and 30 to 44+ years, as appropriate. For some analyses the entire age range from birth to 85+ years is included. The absence of data in any figure or table within this chapter means that too few cases were available for analysis; it does not mean that the rate or change in rate was zero.

Non-Hodgkin lymphoma (NHL) can be defined as only II(b) or as multiple subgroups of II. For example, ICCC categories II(b,c,e) constitute non-Hodgkin lymphoma in the SEER site recode and in the mortality data and II(d) is reported under *Miscellaneous* neoplasms for both. Since medical terminology used to describe the subtypes of NHL has undergone change, the specific subtypes have not been emphasized. When lymphoma occurs among 15- to 29-year-old patients, it represents a transition from pediatric to adult disease.

INCIDENCE

Age-Specific Incidence

Table 3.1 depicts the incidence of all lymphomas in the pediatric and adolescent/young adult age group. Average incidence in the U.S. increased with age for all lymphomas per million people. When observing the incidence trend and the average annual percent increase in incidence, the greatest increase was within the

non-Hodgkin lymphoma group, consistent with the adult experience.[3]

In Figure 3.2, the incidence of lymphoma by ICCC type from 1975 to 2000 is further delineated by age. A progressive increase was seen in non-Hodgkin lymphoma II(b) from birth to age 80. Burkitt lymphoma occurred at all ages, with three peaks in incidence: between the ages of 5 and 10 years, 35 and 45 years, and after 70 years. Over all age groups, the lowest rate of Burkitt lymphoma was in 20- to 24-year-olds. The incidence of Hodgkin lymphoma peaked twice, during the 20- to 24-year age interval and again in late adulthood as described further below.

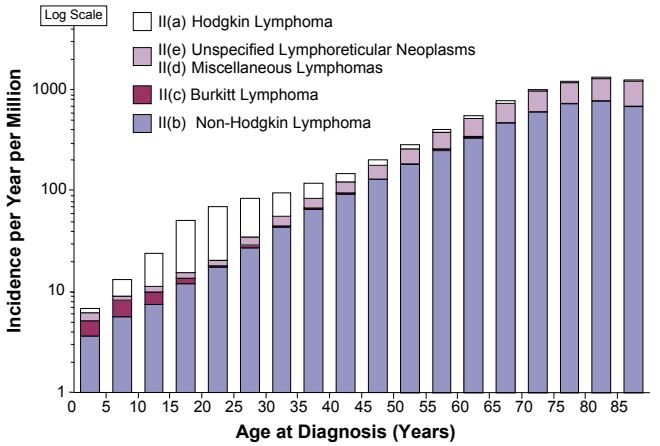

Figure 3.2: Incidence of Lymphoma by ICCC Group, SEER 1975-2000

Gender-Specific Incidence

Figure 3.3 depicts overall incidence per year per million for all lymphomas, by gender. Male incidence was predominant in all age groups, particularly in very young children and those over 30 years of age. If one observes incidence by gender for Hodgkin lymphoma, male predominance was not as striking as in lymphoma overall (Figure 3.4).

Female incidence of Hodgkin lymphoma was higher than the male incidence in the 15- to 19-year age group, but male incidence was slightly higher in 20- to 24- and 25- to 29-year-olds (Figure 3.4). In Non-Hodgkin lymphoma, male incidence was higher for all age groups (Figure 3.5). This held true when the numbers were age-adjusted to the 2000 U.S standard.

McMahon first noted the bimodal incidence of Hodgkin lymphoma in 1957.[4,5] Between 1975 and 2000, the first peak occurred between 20 and 25 years of age (Figure 3.5).

Table 3.1 *Incidence of Lymphoma in Persons Younger Than 30 Years of Age, U.S., 1975-2000*

AGE AT DIAGNOSIS (YEARS)	<5	5-9	10-14	15-19	20-24	25-29
U.S. population, year 2000 census (in millions)	19.176	20.550	20.528	20.220	18.964	19.381
HODGKIN LYMPHOMA*						
Average incidence per million, 1975-2000, SEER	0.5	4.1	13.3	36.6	49.9	49.8
Average annual % change in incidence, 1975-2000, SEER	na	-2.3%	-0.6%	-0.4%	0.2%	1.0%
Estimated incidence per million, year 2000, U.S.	na	2.5	12.2	34.7	51.3	55.3
Estimated number of persons diagnosed, year 2000, U.S.	10	84	273	702	973	1,072
NON-HODGKIN LYMPHOMA**						
Average incidence per million, 1975-2000, SEER	3.4	5.4	7.1	11.7	16.5	27.3
Average annual % change in incidence, 1975-2000, SEER	na	0.2%	2.2%	2.3%	3.6%	6.2%
Estimated incidence per million, year 2000, U.S.	2.8	5.5	8.8	14.3	21.8	39.3
Estimated number of persons diagnosed, year 2000, U.S.	66	110	147	290	413	762
OTHER LYMPHOMA***						
Average incidence per million, 1975-2000, SEER	2.0	3.7	3.9	3.1	3.6	7.5
Average annual % change in incidence, 1975-2000, SEER	na	-1.0%	-0.7%	1.6%	9.8%	18.5%
Estimated incidence per million, year 2000, U.S.	1.9	3.	3.6	3.5	5.6	12.5
Estimated number of persons diagnosed, year 2000, U.S.	54	76	81	72	108	243

*ICCC II(a) **ICCC II(b) ***ICCC II(c,d,e)

The second peak—among older persons—occurred between 75 and 80 years of age, and was not as high as the initial incidence peak. As shown in Figure 3.4, more males than females were diagnosed in older patients.

Non-Hodgkin lymphoma was more common in males than females for all ages up to 45, with the male:female ratio increasing over this age interval to nearly 2-fold greater in males (Figure 3.6).

In Burkitt lymphoma, the male predominance was striking, with male:female ratios approaching 6 for the 5- to 14- and 25- to 44-year age groups (Figure 3.7). Females in the 15- to 24-year age group had a higher incidence of Burkitt lymphoma relative to males than in younger or older age groups, with a male:female ratio at a nadir of 2.6 to 3.2.

When analyzed according to histologic type diagnosed between 1975 and 2000, the greatest change in non-Hodgkin lymphoma over the 15- to 29-year age span was the appearance of follicular (nodular) lymphoma, which was virtually non-existent before age 15 and increased in relative proportion to 11% among 25- to 29-year-olds (Figure 3.8). Diffuse small-cell lymphoma also increased, and mantle cell lymphoma made its appearance in 15- to 29-year olds. Significant decreases as a function of age were noted for lymphoblastic lymphoma and Burkitt lymphoma, with cases decreasing from 12% to 4% and 10% to 4%, respectively, from the 15- to 19-year

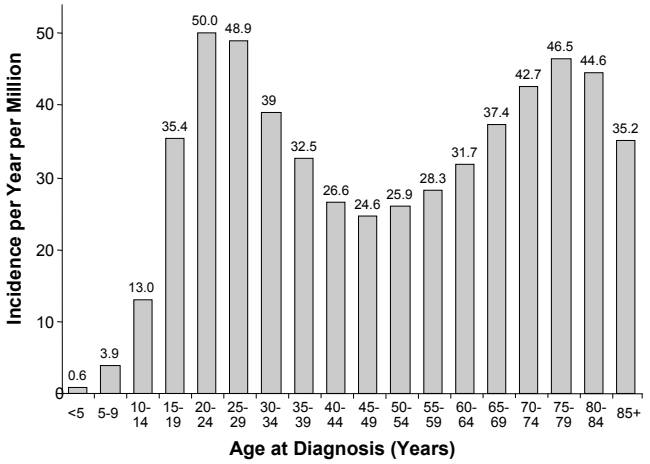

Figure 3.5: Incidence of Hodgkin Lymphoma, SEER 1975-2000

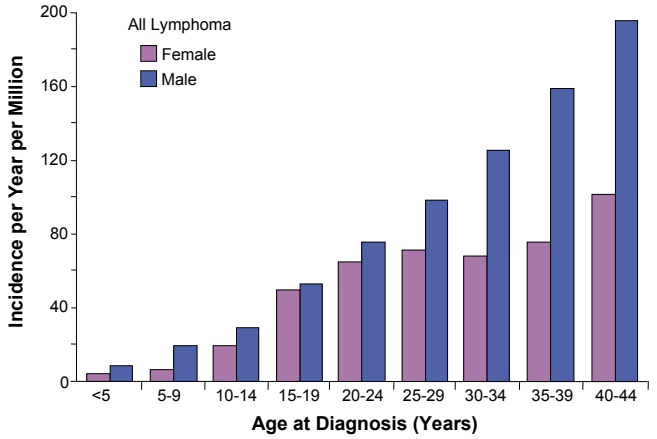

Figure 3.3: Incidence of All Lymphoma (ICCC II) by Gender, SEER 1975-1999

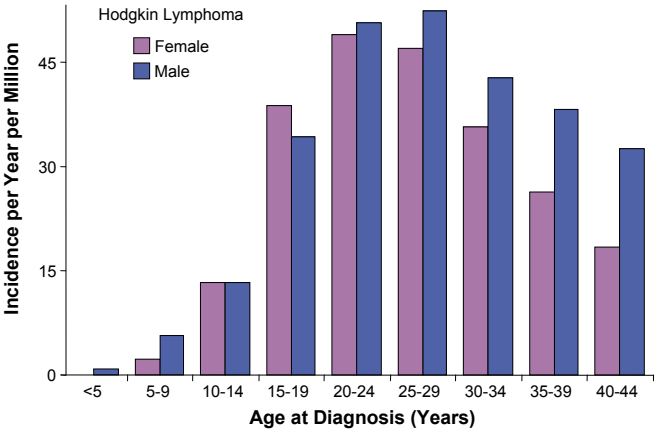

Figure 3.4: Incidence of Hodgkin Lymphoma (ICCC IIa) by Gender, SEER 1975-1999

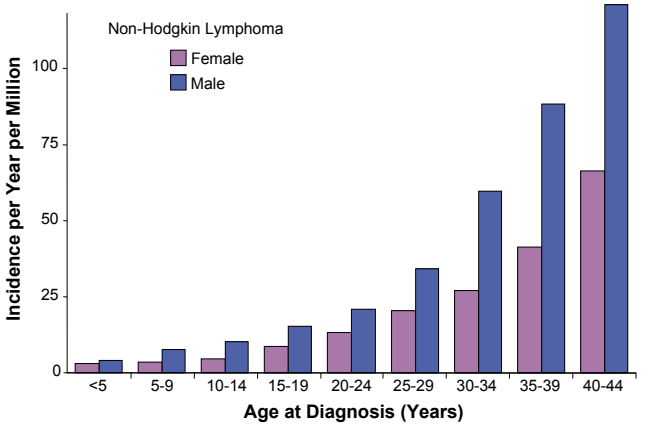

Figure 3.6: Incidence of Non-Hodgkin Lymphoma (ICCC IIb) by Gender, SEER 1975-2000

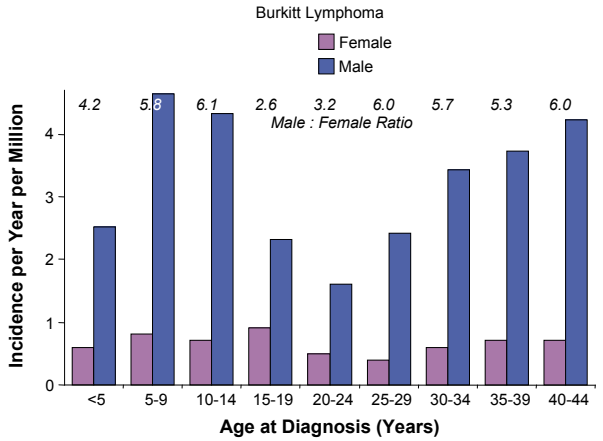

Figure 3.7: Incidence of Burkitt Lymphoma (ICCC IIc) by Gender, SEER 1975-2000

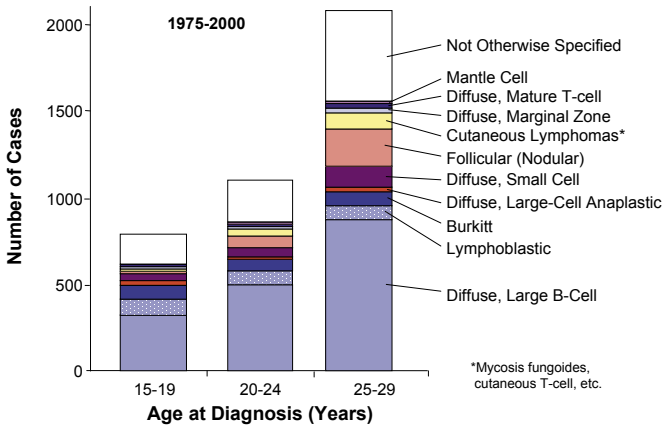

Figure 3.8: Histologic Types of Non-Hodgkin Lymphoma, SEER 1975-2000

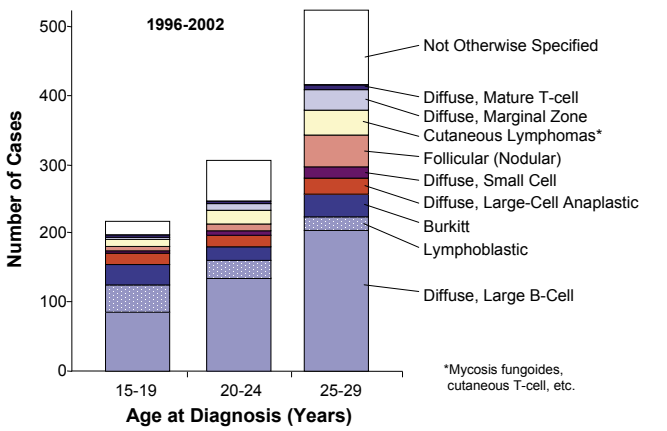

Figure 3.9: Histologic Types of Non-Hodgkin Lymphoma, SEER 1996-2002

age interval to the 25- to 29-year interval. When a more recent interval—1996 to 2002—was assessed according to histologic type, four types were more prominent than in the earlier era, particularly in 25- to 29-year-olds: Burkitt lymphoma, diffuse anaplastic large-cell lymphoma, cutaneous lymphomas, and diffuse marginal zone lymphoma (Figure 3.9 versus. Figure 3.8). There was a commensurate decrease in diffuse, small-cell lymphoma. This was probably due to pathologists being more specific about subtypes during recent years rather than to a real change in the incidence of the subtypes.

Correlative studies on the subtypes of non-Hodgkin lymphoma have shown that the incidence has risen, but that when the pathology of the subtypes were reviewed by a central reference, the subtype assignment varied from 5-100% correlation and 77% of unclassified lymphomas were placed into a subtype classification.[6] The SEER database does not reflect a centrally-reviewed population.

Racial/Ethnic Differences in Incidence

Figure 3.10 displays incidence by race/ethnicity for all lymphomas. In the 15- to 29-year age group, incidence was highest in white non-Hispanics while American Indians/Alaska Natives had the lowest incidence. A shift occurred in the next age group (30 to 44 years), where incidence was highest in the African American/black population.

Figure 3.11 shows the racial/ethnic differences in the incidence of Hodgkin lymphoma among the young. Non-

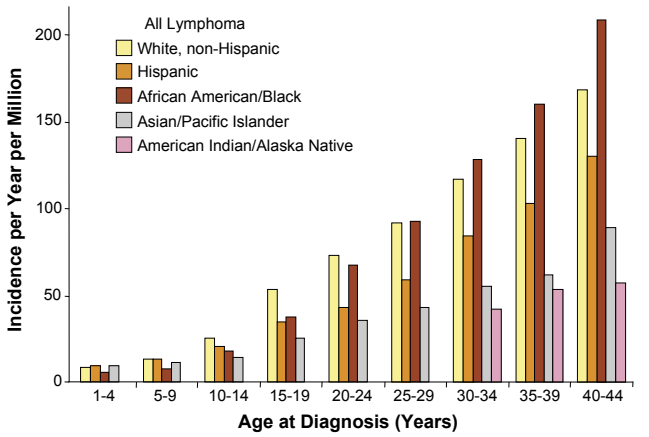

Figure 3.10: Incidence of All Lymphoma by Race/Ethnicity, SEER 1992-2000

Hispanic whites had by far the greatest incidence in 15- to 29-year-olds, followed by African Americans/blacks, Hispanics, Asians/Pacific Islanders, and American Indians/Alaska Natives. The range in incidence of Hodgkin lymphoma according to race/ethnicity varied nearly 10-fold in the 15- to 29-year age group. Above age 30, the incidence of Hodgkin lymphoma among whites and African Americans/blacks converged, but both races/ethnicities remained 2-fold or higher above the others. The higher incidence in white non-Hispanics in the adolescent and young adult group has been attributed to higher socioeconomic status.[7]

Figure 3.12 displays the incidence of all non-Hodgkin lymphoma by race/ethnicity. Incidence increased for all groups as a function of age. Although white non-Hispanics or Asians/Pacific Islanders had the highest incidence in the younger age groups, African Americans/blacks had the highest incidence at 20 years of age and older.

Trends in Incidence

Malignant lymphoma increased in incidence during the past quarter century among all age groups younger than age 45. The change in incidence for all lymphomas in the SEER registry from 1975 to 1999 was statistically significant in all age groups over 19 years (Figure 3.13).

Average annual percent change (AAPC) from 1975 to 1999 is shown in Figure 3.14 for Hodgkin and non-Hodgkin lymphoma. In all age groups, there was a greater increase in the incidence of non-Hodgkin lymphoma than in Hodgkin lymphoma. In non-Hodgkin lymphoma, the increase in incidence for all age groups over 15 years was statistically significant. In Hodgkin lymphoma there was less of an increase for those over 45 years of age.

In Hodgkin lymphoma, only those 30- to 44-years of age demonstrated a statistically significant increase in incidence; in patients over 45 years of age, a statistically significant decrease in incidence was seen (Figure 3.14; yellow bars). As seen in Figures 3.15 and 3.16, the increase in Hodgkin lymphoma occurred in females (Figure 3.15), whereas in non-Hodgkin lymphoma, the increase was in males (Figure 3.16)

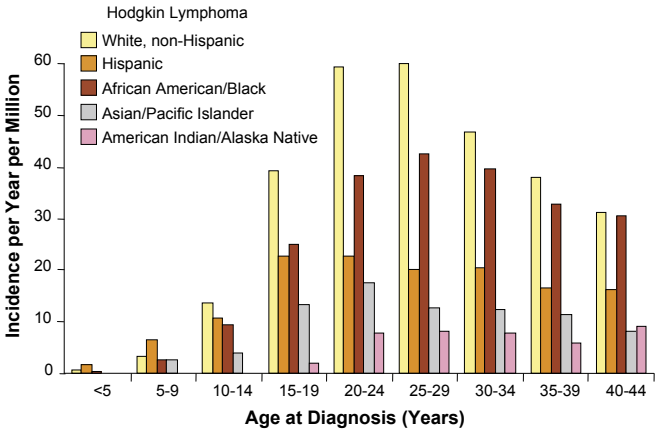

Figure 3.11: Incidence of Hodgkin Lymphoma by Race/Ethnicity, SEER 1992-2000

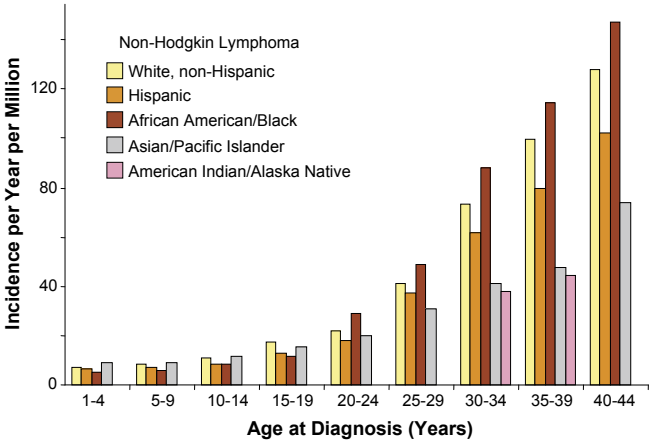

Figure 3.12: Incidence of Non-Hodgkin Lymphoma by Race/Ethnicity, SEER 1992-2000

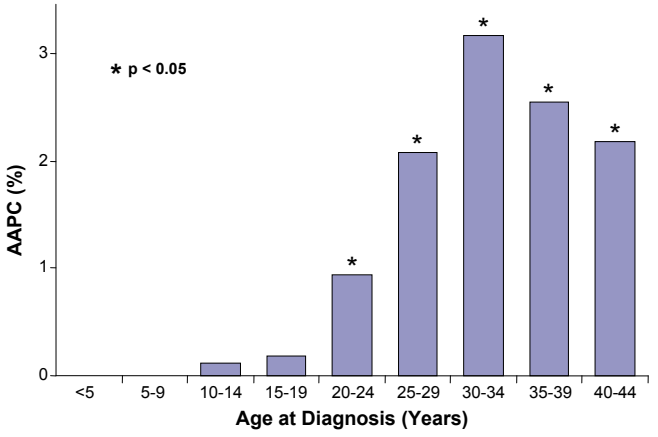

Figure 3.13: Average Annual Percent Change (AAPC) in Incidence for All Lymphoma, SEER 1975-1999

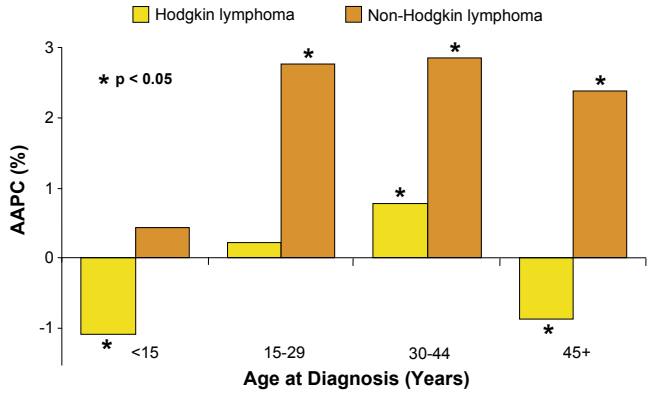

Figure 3.14: Average Annual Percent Change (AAPC) in Incidence for Non-Hodgkin Lymphoma and Hodgkin Lymphoma, SEER 1975-1999

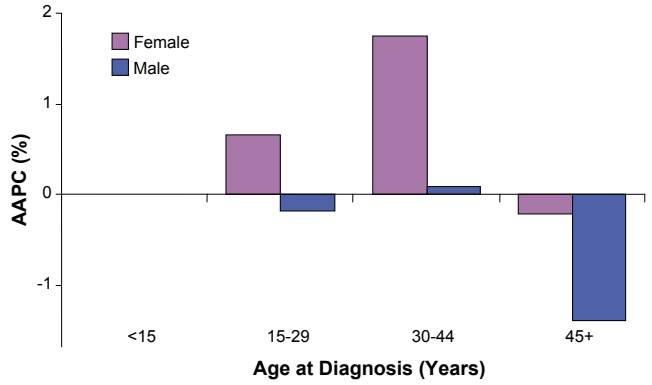

Figure 3.15: Average Annual Percent Change (AAPC) in Incidence for Hodgkin Lymphoma by Gender, SEER 1975-1999

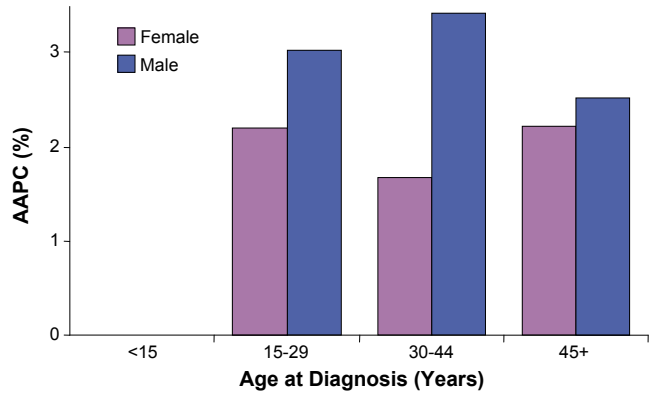

Figure 3.16: Average Annual Percent Change (AAPC) in Incidence for Non-Hodgkin Lymphoma by Gender, SEER 1975-1999

OUTCOME

Mortality

Mortality in 15- to 29-year-olds with Hodgkin lymphoma during the time period 1975 to 1999 was 4.82 deaths per year per million (Figure 3.17; inset). The death rate doubled for 20- to 24 year-olds when compared to 15- to 19-year-olds; rates for 25- to 29-year-olds reached nearly the maximum, as seen in Figure 3.17.

Mortality for adolescents and young adults with non-Hodgkin lymphoma over a similar time period was 59 deaths per year per million (Figure 3.18; inset). Mortality for non-Hodgkin lymphoma increased slowly as a function of age, with the highest rate in the over 45-year age group (Figure 3.18; inset).

Figure 3.19 displays mortality from 1975 to 1999 for those younger than 45 years of age for all lymphomas by gender. In all age groups, males had a higher mortality. This male predominance increased as a function of age, with nearly two times as many deaths among 25- to 44-year-old males as among females. Most of this gender difference was due to the higher incidence in males (Figure 3.3).

For Hodgkin lymphoma, the male excess occurred only over age 10 (Figure 3.20), and the comparison with incidence showed that there were more males than females dying of the disease between 15 and 40 years of age than expected from the incidence pattern (Figure 3.21). This analysis suggests that male gender was an

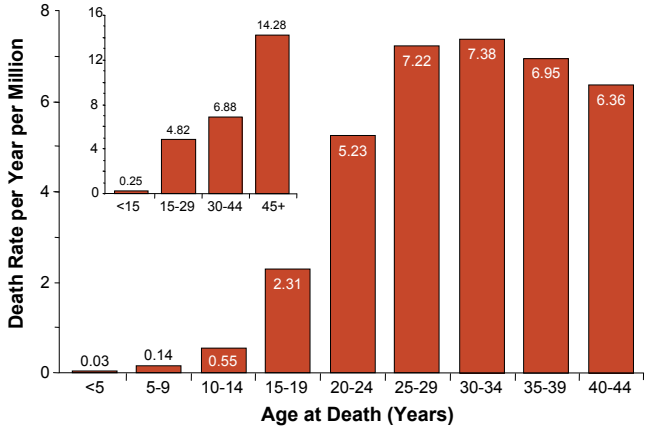

Figure 3.17: National Mortality for Hodgkin Lymphoma, U.S.,1975-1999

adverse prognostic factor in patients between 15 and 40 years of age. Females are known to present with more favorable histology and lesser stage disease.[7]

For non-Hodgkin lymphoma, the male excess in mortality occurred at all ages (Figure 3.22), and the comparison with incidence revealed that under age 30 (Figure 3.6), the excess was not accounted for by differences in incidence. This analysis suggests that male gender was an adverse prognostic factor in patients younger than 30 years of age.

Similar analyses of mortality by race/ethnicity as function of age are shown in Figures 3.23 to 3.25. For all lymphoma, African Americans/blacks had the highest death rate for those over 20 years of age (Figure 3.23). The African American/black excess occurred for both Hodgkin lymphoma (Figure 3.24) and non-Hodgkin lymphoma (Figure 3.25). When compared with incidence patterns (Figures 3.10 and 3.11, the excess death rate among African Americans/blacks was not explained by differences in incidence, either in Hodgkin or non-Hodgkin lymphoma.

Survival

Figure 3.26 depicts the 5-year survival rate for all lymphomas as function of age at diagnosis, by 15-year intervals until age 45, and as a single group in older patients. There was no progress in improving the 5-year survival rate among 15- to 44-year-old patients with lymphoma during the past quarter century, in contrast to steady gains in this outcome measurement among younger and older patients. Hodgkin and non-Hodgkin lymphoma showed little to no significant gain in 5-year survival rates over the years 1975 to 1998.

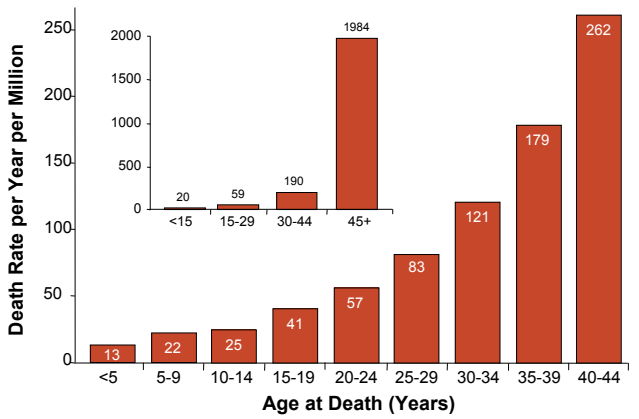

Figure 3.18: National Mortality for Non-Hodgkin Lymphoma, U.S.,1975-2000

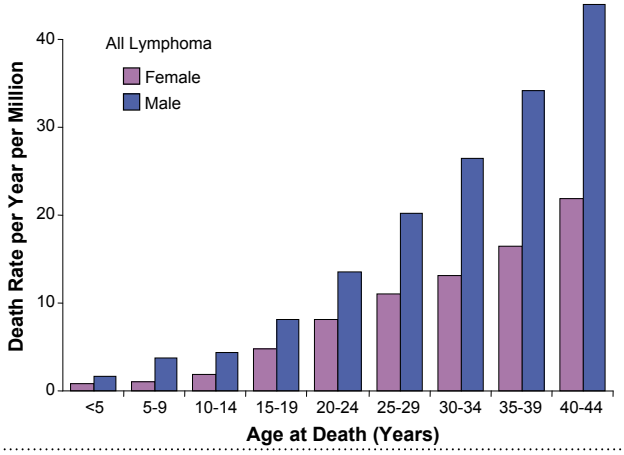

Figure 3.19: National Mortality for All Lymphoma by Gender, U.S.,1975-1999

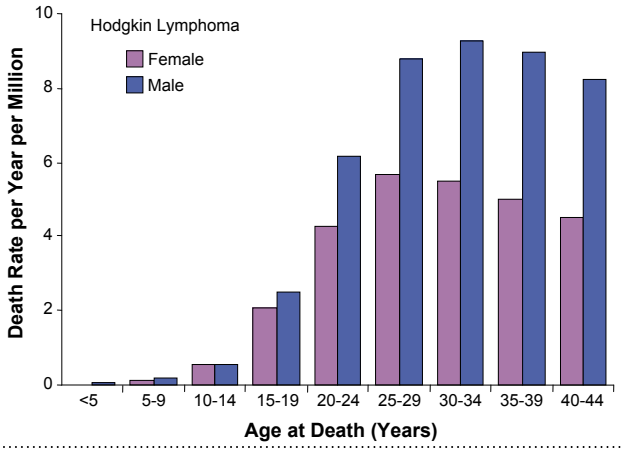

Figure 3.20: National Mortality for Hodgkin Lymphoma by Gender, U.S.,1975-1999

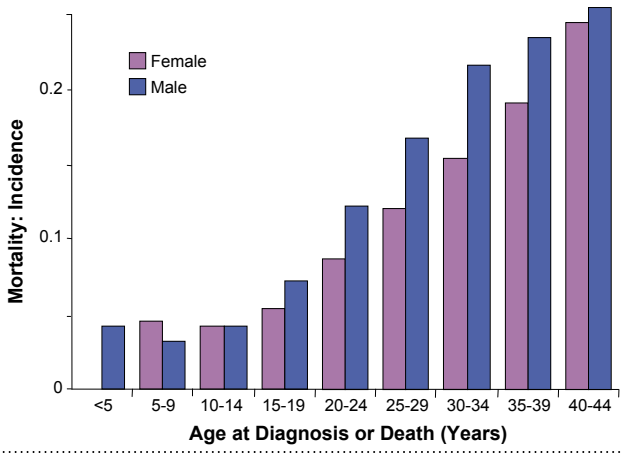

Figure 3.21: Ratio of National Mortality to SEER Incidence for Hodgkin Lymphoma by Gender, U.S.,1975-1999

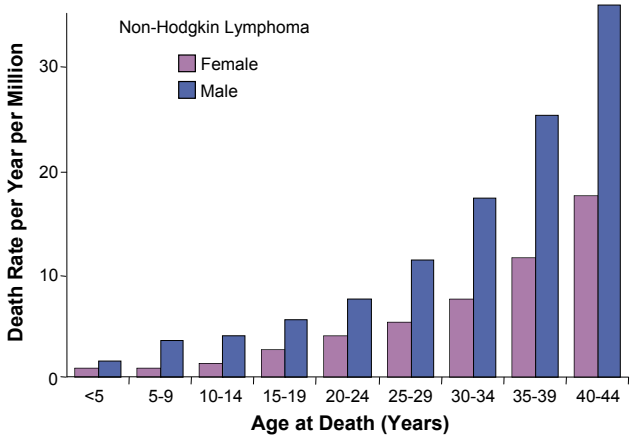

Figure 3.22: National Mortality for Non-Hodgkin Lymphoma by Gender, U.S.,1975-1999

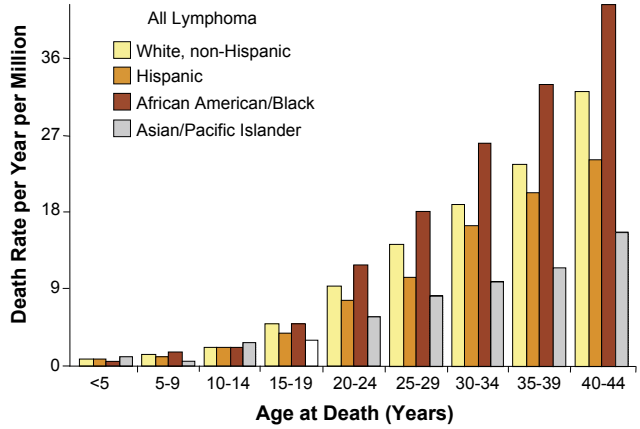

Figure 3.23: National Mortality for All Lymphoma by Race/Ethnicity, U.S.,1990-2000

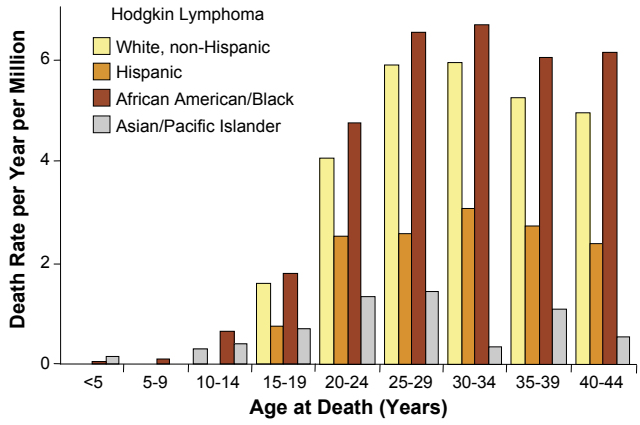

Figure 3.24: National Mortality for Hodgkin Lymphoma by Race/Ethnicity, U.S.,1990-2000

Since 1990, there have been no significant differences in 5-year survival rates among whites of either Hispanic or non-Hispanic ethnicity, African Americans/blacks, or Asians/Pacific Islanders with Hodgkin (Figure 3.27) or non-Hodgkin lymphoma (Figure 3.28). The suggestion from comparisons of death rates to incidence that show a deficit among African Americans/blacks applies to the period 1975 to 1998. It appears that this racial inequity may have been overcome by 1990.

Survival curves as a function of age are shown in Figures 3.29 to 3.31 for patients followed by SEER from 1975 to 1998. For all lymphomas, 15- to-29-year-old patients had an outcome similar to those younger than age 15 when diagnosed, with the exception that there was less evidence for a plateau in the survival curve for 15- to 29-year-old patients (Figure 3.29).

For Hodgkin lymphoma, 15- to-29-year-old patients did not fare as well as younger patients, with a continued fall-off in Hodgkin lymphoma survival and no evidence for a plateau in the survival curve (Figure 3.30). For non-Hodgkin lymphoma, a progressive decline in survival was apparent when observed by 5-year age intervals (Figure 3.31).

The AAPC in 5-year survival rates from 1975 to 1997 for Hodgkin and non-Hodgkin lymphoma are shown in Figures 3.32 and 3.33. As suggested by the mortality versus incidence comparisons above, the least amount of progress occurred in 15- to 50-year-olds with Hodgkin lymphoma (Figure 3.32) and in 25- to 45-year-olds with non-Hodgkin lymphoma (Figure 3.33). The lack of progress was

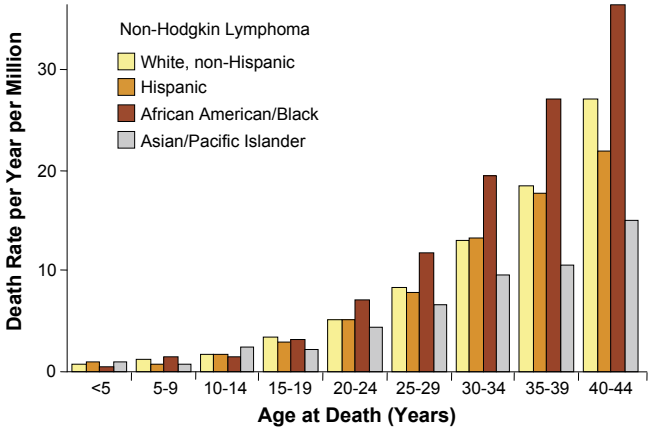

Figure 3.25: National Mortality for Non-Hodgkin Lymphoma by Race/Ethnicity, U.S.,1990-2000

particularly obvious for non-Hodgkin lymphoma. Both non-Burkitt, non-Hodgkin lymphoma and Burkitt lymphoma had little to no evidence for survival improvement when the 5-year survival rates were averaged out over the past quarter century (Figure 3.33). Some of the latter non-Burkitt, non-Hodgkin lymphoma survival improvement deficit may be due to lymphomas with a particularly poor prognosis that occurred during the human immunodeficiency virus (HIV) epidemic of the 1980s.

RISK FACTORS

Hodgkin Lymphoma

Evidence suggests that Hodgkin lymphoma may represent several disease entities over the age spectrum, with different etiological factors for different age groups. In developing countries, children acquire Hodgkin lymphoma at an earlier age than in developed countries, and commonly show Epstein-Barr virus (EBV) genomic sequences in the Reed-Sternberg cells.[8,9] Incidence of Hodgkin lymphoma in developed countries peaks in the adolescent and young adult years, and again in older adults.[10] This reflects the bimodal peak first noted by McMahon.[4] An increased risk of developing Hodgkin lymphoma in the early age group has been linked to a higher socioeconomic status and standard of living during childhood that includes low housing density, high maternal education, and few older siblings. These conditions may contribute to a delay in exposure to common childhood infections and a subsequent delay in

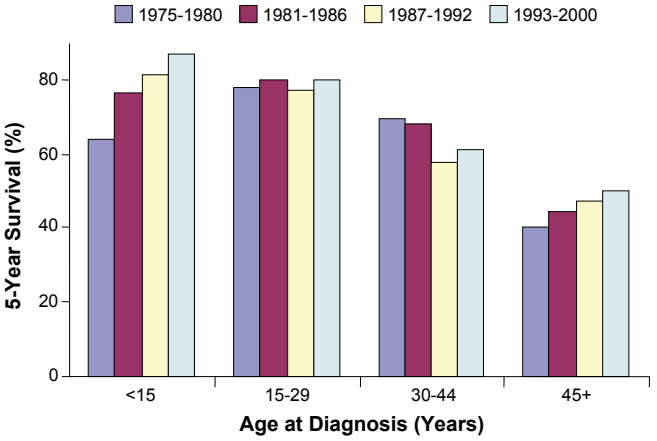

Figure 3.26: 5-Year Survival for All Lymphoma by Era, SEER

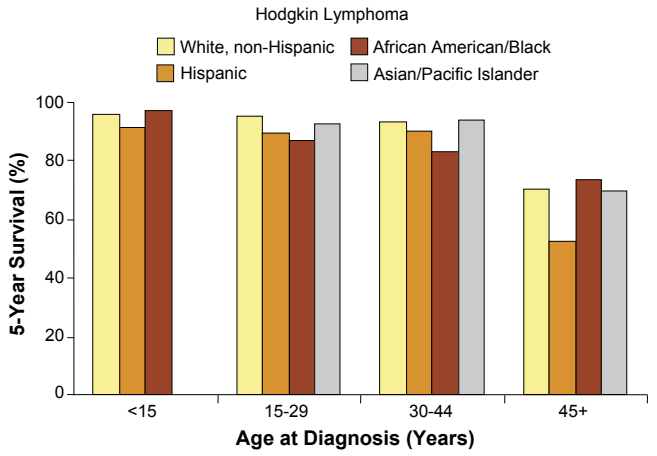

Figure 3.27: 5-Year Survival for Hodgkin Lymphoma by Race/Ethnicity, SEER 1990-1998

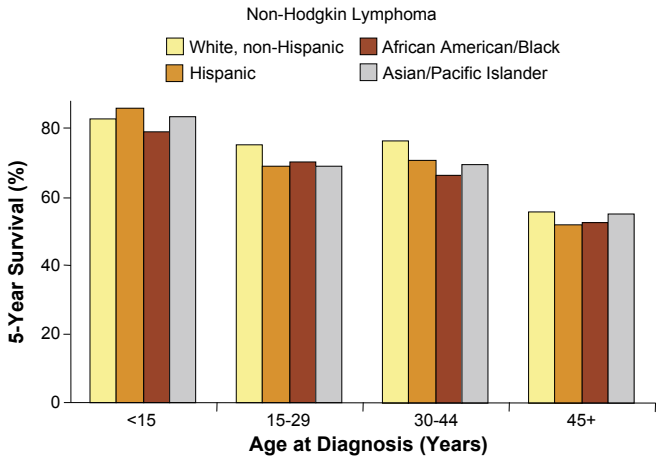

Figure 3.28: 5-Year Survival for Non-Hodgkin Lymphoma by Race/Ethnicity, SEER 1990-1998

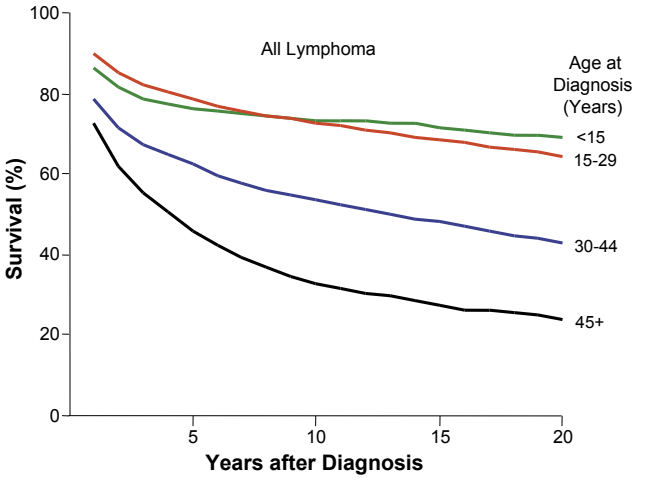

Figure 3.29: Survival Rates for All Lymphoma, SEER 1975-1998

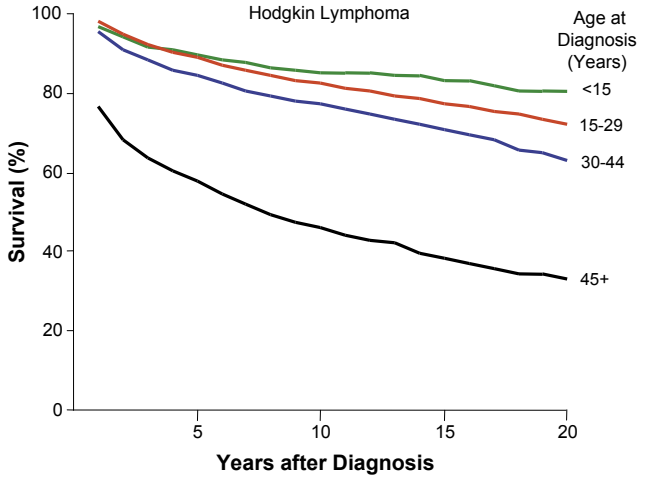

Figure 3.30: Survival Rates for Hodgkin Lymphoma, SEER 1975-1998

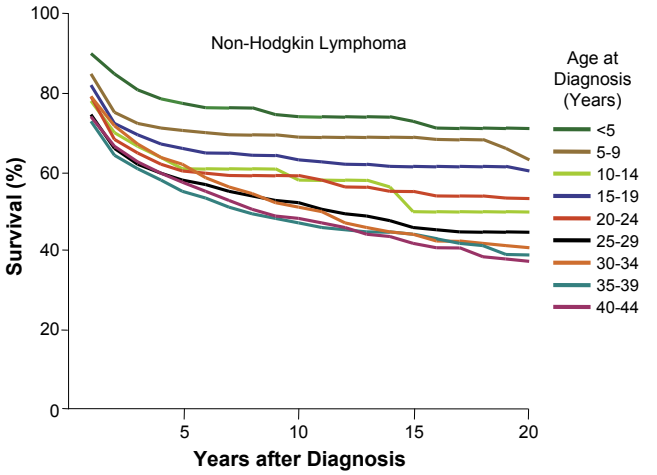

Figure 3.31: Survival Rates for Non-Hodgkin Lymphoma, SEER 1975-1998

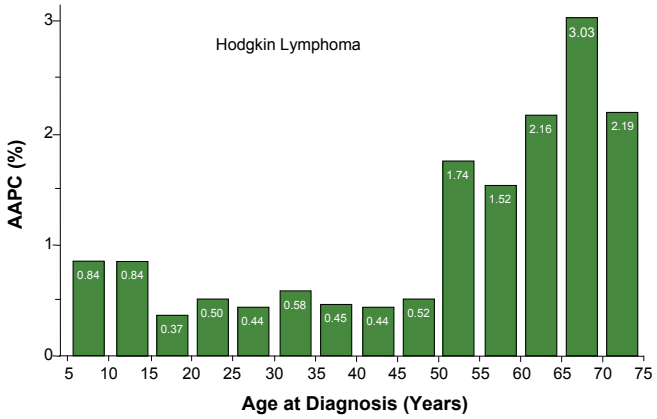

Figure 3.32: Average Annual Percent Change (AAPC) in 5-Year Survival for Hodgkin Lymphoma, SEER, 1975-1997

maturation of cell immunity.[11] Yet in the younger (< 10 years) and older (> 45 years) age groups, the association with higher socioeconomic status is reversed.[12] Among the histologic subtypes of Hodgkin lymphoma, the nodular sclerosing subtype has a more favorable prognosis.[13]

Epstein Barr virus (EBV) is considered a primary etiologic agent for Hodgkin lymphoma.[14] While the evidence points to EBV as a cofactor in the development of Hodgkin lymphoma, the exact relationship of the infection to the subsequent development of tumor is not completely delineated.[12] The presence of the EBV genome in Reed-Sternberg cells is associated with the mixed cellularity sub-type.[7]

Genetic susceptibility is also a factor for adolescents and young adults. The risk of developing Hodgkin lymphoma is significantly higher for those with relatives with the disease; the risk is higher for males than females, and for siblings than for parents or offspring.[15] Adults with Hodgkin lymphoma are more likely to have children who develop the disease at a younger age, that is, in adolescence and young adulthood.[16]

In patients with HIV infection, there is an increase in both Hodgkin and non-Hodkgin lymphoma.[17,18] Other risks associated with the development of Hodgkin lymphoma in this age group are a history of autoimmune disorder, a family history of cancer/hematopoietic disorder, and Jewish ethnicity.[11,15,16]

Non-Hodgkin Lymphoma

The etiology of non-Hodkgin lymphoma in adolescents and young adults is complex. Several risk factors have been identified, including HIV infection, immunodeficiency syndromes, immunosuppressive therapies, EBV or helicobacter pylori infection, genetic susceptibility, tobacco, chemical or other environmental exposure.[2,19-23] Incidence is twice as high in males than females, and is higher in whites than African Americans/blacks.[24]

Recent studies indicate that the incidence of non-Hodkgin lymphoma has increased nearly 80% since the 1970s.[1,24] In underdeveloped countries, there is a documented link between EBV and Burkitt lymphoma,[19] while in the developed world EBV is also associated with other subtypes of non-Hodgkin lymphoma.[12]

Secondary neoplasms are well documented sequelae of HIV infection, and account for an increase in non-Hodgkin lymphoma incidence, particularly in males.[18,25] The increase in non-Hodgkin lymphoma has persisted in the face of a stabilization of the incidence of new cases of HIV and with improved treatments for the infection.

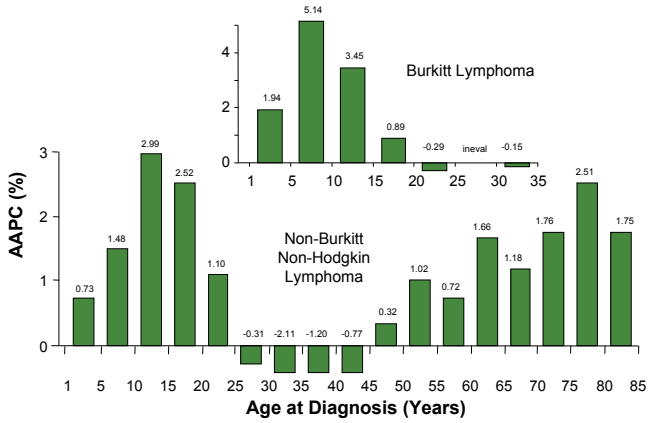

Figure 3.33: Average Annual Percent Change (AAPC) in 5-Year Survival Rate, SEER 1975-1997

SUMMARY

Lymphomas are common cancers in the 15- to 29-year age group. Hodgkin and non-Hodgkin lymphomas, while distinct entities, share some common risk factors such as EBV and HIV infection, overall male predominance and an association with immunodeficiency syndromes. There is no apparent racial/ethnic influence over the entire age spectrum. While there has been an improvement in survival in the pediatric non-Hodgkin lymphoma group under 15 years of age, no such improvement has been noted in the older adolescent and young adult age group. With the advent of monoclonal antibody biologic treatments, an improvement in survival is anticipated for both Hodgkin and non-Hodgkin lymphoma. Follicular lymphoma and mantle cell lymphoma, both subsets of non-Hodgkin lymphoma, have shown durable responses to combination therapy with anti CD20 antibody and aggressive chemotherapy.[26-28]

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