Infant Cancers in California, 1988 – 2011

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Acknowledgements and Disclaimer

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Summary of Findings

In California, from 1988 through 2011:

- 2,704 new cases of cancer (all types) were diagnosed among infants (i.e., children less than one year of age), for an average annual incidence rate of 215.4 cases per million infants.
- The five most frequently diagnosed cancers among infants were neuroblastoma, retinoblastoma, lymphocytic leukemia, acute myeloid leukemia, and nephroblastoma (Wilms tumor). Leukemias as a group were the most common infant cancers, followed by neuroblastoma and other peripheral nerve cell tumors, and central nervous system (CNS) malignancies.
- Other than neuroblastoma being almost 30 percent more common in infant boys than girls and extracranial/extragonadal germ cell tumors being 66 percent more common in infant girls, no material differences in the incidence of infant cancers by sex were observed.
- Incidence rates for acute myeloid leukemia (AML) increased more than 100 percent.
- Increased incidence rates of between 26 and 32 percent were also observed for lymphocytic leukemia, CNS malignancies, and retinoblastoma, although only the trend for AML was statistically significant.
- Estimates of relative survival for infants diagnosed with neuroblastoma, nephroblastoma (Wilms tumor), hepatoblastoma, and extracranial/extragonadal germ cell tumors between 2000 and 2006 show that more than 75 percent of these infants have life expectancies of at least five years.
- Survival for infants having retinoblastoma has approached that expected for infants not having this cancer.
- Among infants diagnosed with leukemia, and AML in particular, survival appears to have improved over time. Five-year survival for infants with AML was 44.9 percent among those diagnosed between 1988-1994; this increased to 54.8 percent among those diagnosed between 2000-2006.

Introduction

The risk of developing cancer increases steeply with age. Nearly half of all cancers in California are diagnosed in persons between the ages of 60 and 80.[1] Notwithstanding the greater frequency of cancer among older persons, children are not immune to cancer. Of the 27,338 children (from birth through age 14) newly diagnosed with cancer in California from 1988 through 2011, 2,704 (10 percent) were infants (i.e., children less than one year of age). In fact, incidence rates of childhood cancer are highest during the first year of life (Table 1).

The types of cancer that infants and children develop are different than those that occur in adults. In particular, childhood cancers are not as strongly linked to lifestyle or environmental risk factors. Childhood cancers are more likely to result from genetic changes that take place before birth or during infancy.[2]

This report focuses on the incidence and five-year relative survival rates for the most common cancer types in infants and how these rates have changed since 1988 when statewide cancer reporting in California began. This report also highlights how rates of cancer in infants compare to cancer in children ages one to 14. Because the number of infant cancer cases is small, differences or changes in rates are sometimes difficult to interpret. In this report, some findings that are not statistically significant are highlighted.

Information presented in this report was gathered by the California Cancer Registry (CCR), the state mandated population-based cancer surveillance system in California. The CCR routinely collects demographic, diagnostic, and treatment information on cancer cases diagnosed in California, and has provided the foundation for research studies and cancer control initiatives throughout the state. Since 2012, the California Cancer Reporting and Epidemiologic Surveillance (CalCARES) Program within the Institute for Population Health Improvement, University of California Davis Health System, has partnered with the California Department of Public Health to manage day-to-day operations of the CCR.

Table 1. Age-Adjusted Cancer Incidence Rates by Age Group: California, 1988-2011

Age Group (years)	Incidence Rate (Number of cases per 1,000,000 persons)	Actual Number of Cases
<1	215	2,707
1-14	145	24,631
15-34	458	115,829
35-49	2,130	374,564
50-64	7,879	909,214
65-79	20,343	1,298,268
80+	24,347	543,470

Rates are per 1,000,000 and age-adjusted to the 2000 US Standard Population.

Data Source: California Cancer Registry, California Department of Public Health

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1 *California Cancer Facts & Figures 2013:* http://ccrcal.org/pdf/Reports/ACS_2013.pdf

2 *American Cancer Society:* http://www.cancer.org/cancer/cancerinchildren/detailedguide/cancer-in-children-differences-adults-children

Distribution of International Classification of Childhood Cancer (ICCC) Groups among Infants

Childhood cancers are categorized differently than adult cancers. They are categorized into 12 site groups according to the International Classification of Childhood Cancer (ICCC). This classification is based on the form and structure of the tumor (commonly referred to as tumor morphology) and primary site, with an emphasis on morphology. Adult cancers are also based on morphology and primary site but, in contrast to infant cancers, the emphasis is on primary site (e.g., breast, lung, etc.).

Leukemias were the most commonly diagnosed cancer ICCC group reported among infants from 1988 through 2011 (see Table 2), followed closely by neuroblastomas. These two cancers represented 21 percent and 20 percent, respectively, of all cancers diagnosed among infants. Of the 556 cases of infant leukemia, 47 percent (262 cases) were categorized as lymphoid leukemia and 39 percent (218 cases) as acute myeloid leukemia (AML). Central nervous system (CNS) tumors and retinoblastoma (a tumor of the eye) were the next most common types of infant cancer, representing 14 percent and 12 percent, respectively, of all cancers diagnosed among infants.

Among children ages one through 14, the distribution of cancer types was different than among infants. Similar to infants, leukemias were the most commonly diagnosed site group in children, representing 38 percent of the childhood cancers. In contrast to infant leukemia, however, a large majority of leukemias among children (82 percent) were classified as lymphoid leukemia; 14 percent were classified as AML. Malignant CNS tumors were the second most commonly diagnosed type of cancer among children, representing 20 percent of the cancers diagnosed in this age group. Neuroblastoma, the second most commonly diagnosed cancer group in infants, represented about 5 percent of the cancers in children ages one to 14. Lymphomas were the third most commonly reported type of cancer (11 percent) among children older than one year.

Table 2. Distribution and Incidence Rates of ICCC Cancer Groups among Infants: California, 1988-2011

Cancer ICCC Group[a]	No. Cases	%	Rate per Million
All Cancer Types	2,704	100.0	215.4
I. Leukemias, myeloproliferative & myelodysplastic diseases	556	20.6	44.3
Lymphoid leukemia	262	9.7	20.9
Myeloid leukemia	218	8.1	17.4
II. Lymphomas & reticuloendothelial neoplasms	99	3.7	7.9
III. Central nervous system, misc. intracranial & intraspinal tumors	387	14.3	30.8
Ependymomas & choroid complex tumors	60	2.2	4.8
Astrocytoma	145	5.4	11.6
Intracranial & intraspinal embryonal tumors	129	4.8	10.3
Other gliomas	36	1.3	2.9
IV. Neuroblastoma & other peripheral nervous cell tumors	551	20.4	43.9
V. Retinoblastoma	316	11.7	25.2
VI. Renal tumors	172	6.4	13.7
VII. Hepatic tumors	141	5.2	11.2
VIII. Malignant bone tumors	9	0.3	#
IX. Soft tissue & other extraosseous sarcomas	188	6.9	15.0
Rhabdomyosarcoma	66	2.4	5.3
Fibrosarcoma	46	1.7	3.7
X. Germ cell, trophoblastic tumors & neoplasms of gonads	260	9.6	20.7
Extracranial & extragonadal germ cell tumors	168	6.2	13.4
Malignant gonadal germ cell tumors	64	2.4	5.1
XI. Other malignant epithelial neoplasms & melanomas	16	0.6	1.3
XII. Other & unspecified malignant neoplasms	9	0.3	#

= rate not calculated (less than 15 cases)

[a] International Classification of Childhood Cancer (http://seer.cancer.gov/iccc/iccc-who2008.html).

Data Source: California Cancer Registry, California Department of Public Health

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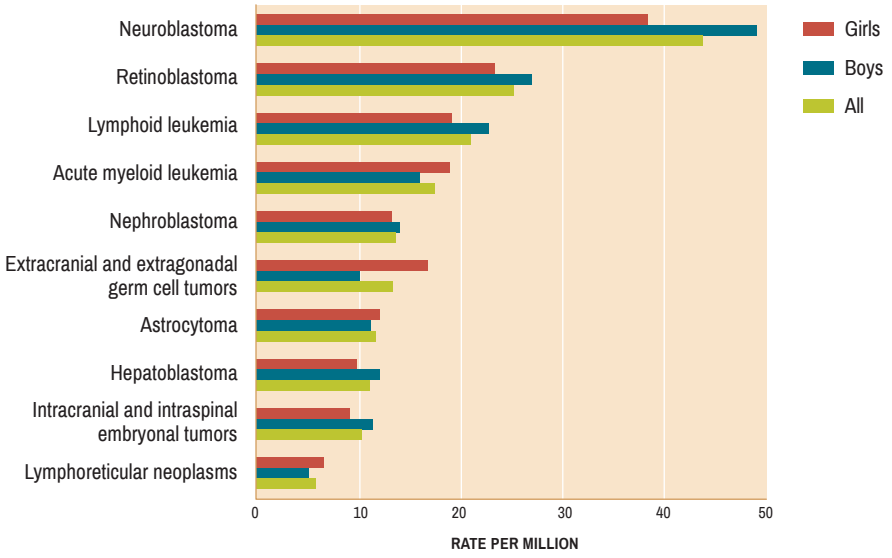
Incidence rates for the most common cancers among infants

Incidence rates for the ten most commonly diagnosed infant cancer types are shown in Figure 1. The incidence of neuroblastoma, the most frequently diagnosed cancer among infants, was almost 30 percent higher among boys (48.9 per million) than among girls (38.4 per million), a statistically significant difference. Retinoblastoma was slightly more common in boys (26.9 per million vs. 23.3 per million among girls). The incidence of lymphoid leukemia was somewhat higher among infant boys, while the incidence of acute myeloid leukemia (AML) was higher among infant girls. The incidence of nephroblastoma (Wilms tumor), the most common type of renal tumor, was similar in boys and girls, with an overall rate of 13.6 per million.

Astrocytoma and intracranial and intraspinal embryonal tumors were the two most common CNS malignant tumors diagnosed among infants, having incidence rates of 11.6 per million and 10.3 per million, respectively.

The incidence of extracranial and extragonadal germ cell tumors (mostly malignant teratomas) among infant girls (16.8 per million) was two thirds higher than among infant boys (10.1 per million).

Figure 1. Incidence Rates for the Ten Most Common Cancers among Infants, by Sex: California, 1988-2011



Data Source: California Cancer Registry, California Department of Public Health

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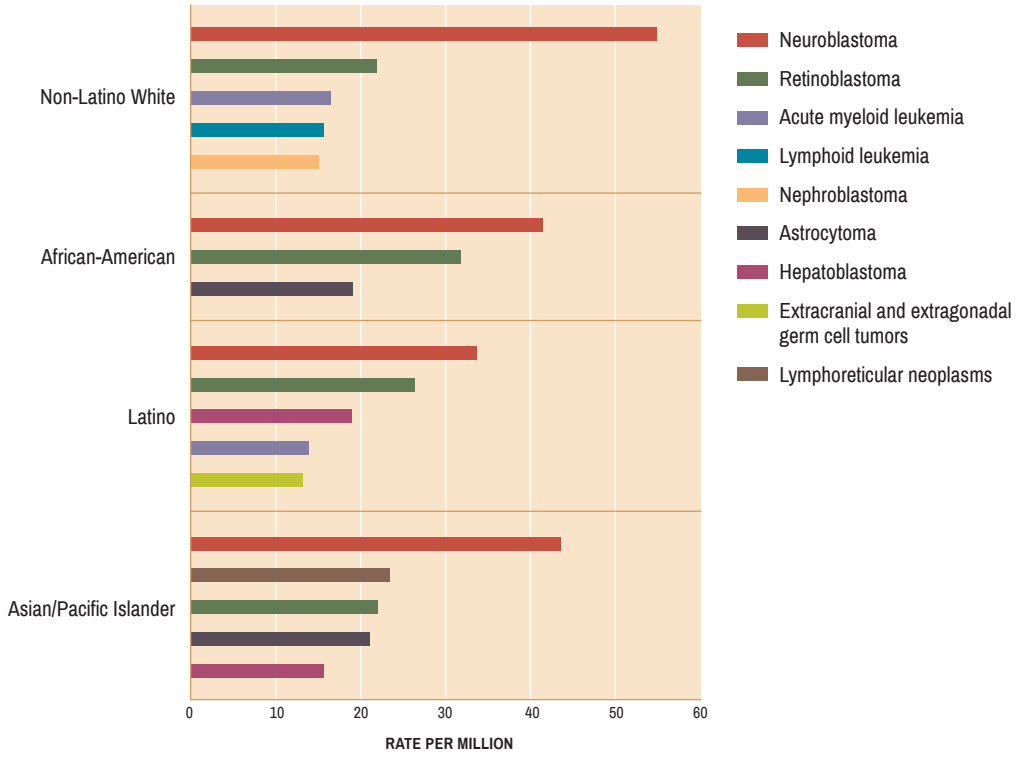
Figure 2 shows incidence rates for the five cancers most frequently diagnosed among infants by race/ethnicity. Rates varied markedly among racial/ethnic groups. Neuroblastoma was the most common cancer in all groups; white infants had the highest incidence rates (54.9 per million) and Latino infants had the lowest (33.6 per million). Retinoblastoma was the second most commonly diagnosed infant cancer, except among Asian/Pacific Islanders among whom lymphoreticular neoplasms, the most common type of lymphoma and reticulendothelial neoplasms, were the second most common cancer. The incidence of retinoblastoma was about 45 percent higher among African American infants than among white infants (the racial/ethnic group of infants with the lowest retinoblastoma incidence). Astrocytoma, a type of CNS tumor, was among the top five infant cancers among African Americans and Asian/Pacific Islanders. Hepatoblastoma, the most common type of hepatic tumor, was one of the top five infant cancers among Asian/Pacific Islanders and Latinos. Among whites, acute myeloid leukemia, lymphoid leukemia, and nephroblastoma (Wilms tumor) were also included in the top five cancers.

Figure 2. Incidence Rates for the Top Five Infant Cancers by Race/Ethnicity: California, 1988-2011



Data Source: California Cancer Registry, California Department of Public Health

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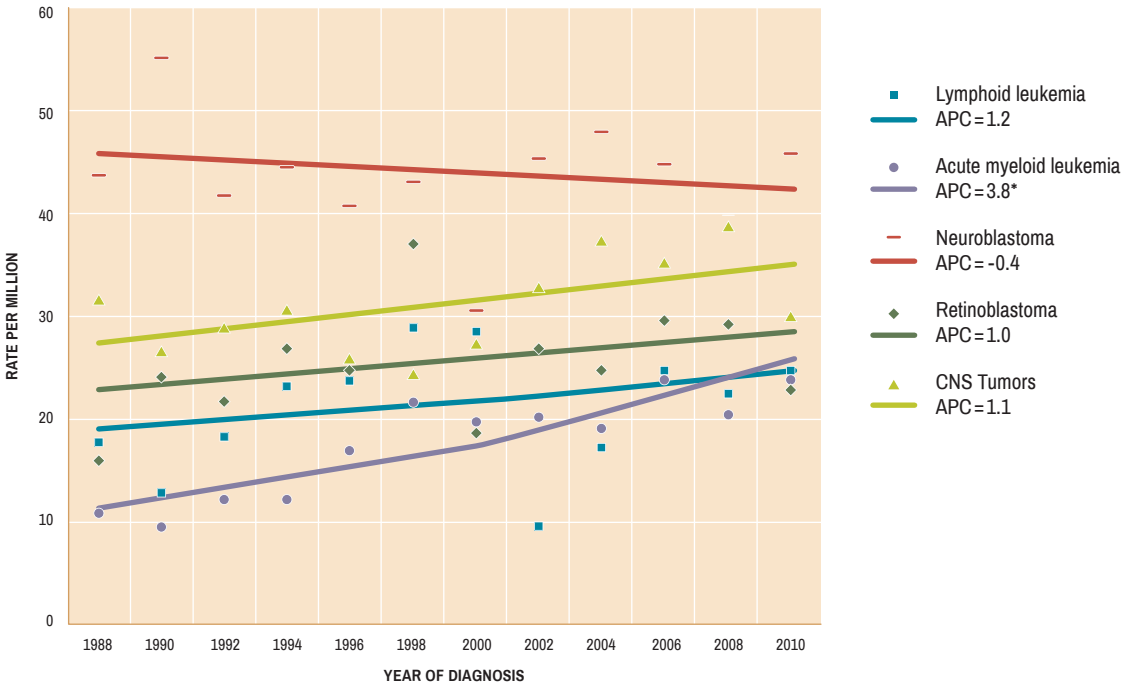
Trends in Incidence Rates for the Top Five Infant Cancers

There was a marked increase in the incidence of AML (3.8 percent increase per year). The incidence rate of AML among infants increased by about 120 percent since 1988 (see Figure 3). The incidence of lymphoid leukemia, CNS tumors, and retinoblastoma increased (estimated annual percent changes of 1.2, 1.1, and 1.0, respectively), but none of these increases were statistically significant. Incidence rates for neuroblastoma were unchanged. Importantly, the number of cancers diagnosed per year among infants was often quite small, so trends were calculated after combining cases diagnosed in two-year periods. Incidence trends for specific types of CNS tumors could not be reliably evaluated due to the small number of cases

Comparatively, cancer incidence trends among children ages one through 14 followed a different pattern. Incidence rates of lymphoid leukemia increased by a significant 0.8 percent per year, while AML rates remained unchanged. The incidence of neuroblastoma and CNS tumors increased significantly after 2002, by 3.7 percent and 3.9 percent per year, respectively. While retinoblastoma incidence rates increased slightly among infants, rates among children were unchanged.

Figure 3. Trends in Incidence Rates for the Top Five Infant Cancers: California, 1988-2011



Note: Marker = actual rates, line = estimated trend. APC: annual percent change in rates.

** = Statistically significant increase*

Data Source: California Cancer Registry, California Department of Public Health

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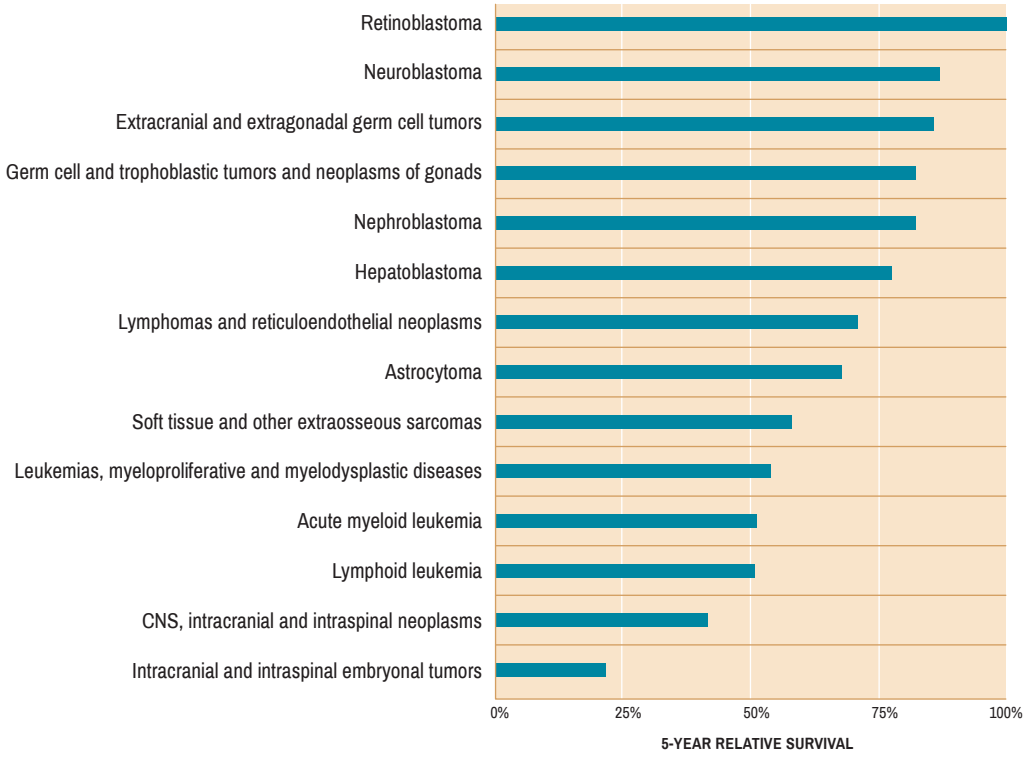
Infant Cancer Relative Survival

Relative survival is a net survival measure that estimates the probability of avoiding death due to a particular cancer. It is defined as the ratio (expressed as a percent) of the observed survival rate divided by the survival rate expected for people of the same sex, race, and age. Therefore, relative survival compares the survival of people who have the disease with those that do not. In this report, the expected survival rate was based on life tables specific for the California population. A relative survival of 100 percent does not mean that everyone will survive the cancer, but instead means that cancer patients in that specific group are as likely to survive during that time period as persons in the general population of the same sex, age, and race.

Five-year relative survival rates for infant cancers diagnosed between 2001 and 2006 are presented in Figure 4. To ensure reliable estimates, cancers with less than 25 cases diagnosed during the period were excluded from the calculations. Based on these estimates, three out of four infants (75%) diagnosed with retinoblastoma, neuroblastoma, nephroblastoma (Wilms tumor), hepatoblastoma, and germ cell/trophoblastic tumors would be expected to be alive five years after the diagnosis.

Figure 4. Five-Year Relative Survival for Cancers Diagnosed among Infants in California, 2001-2006



Note: Follow-up through December 31, 2011

Data Source: California Cancer Registry, California Department of Public Health

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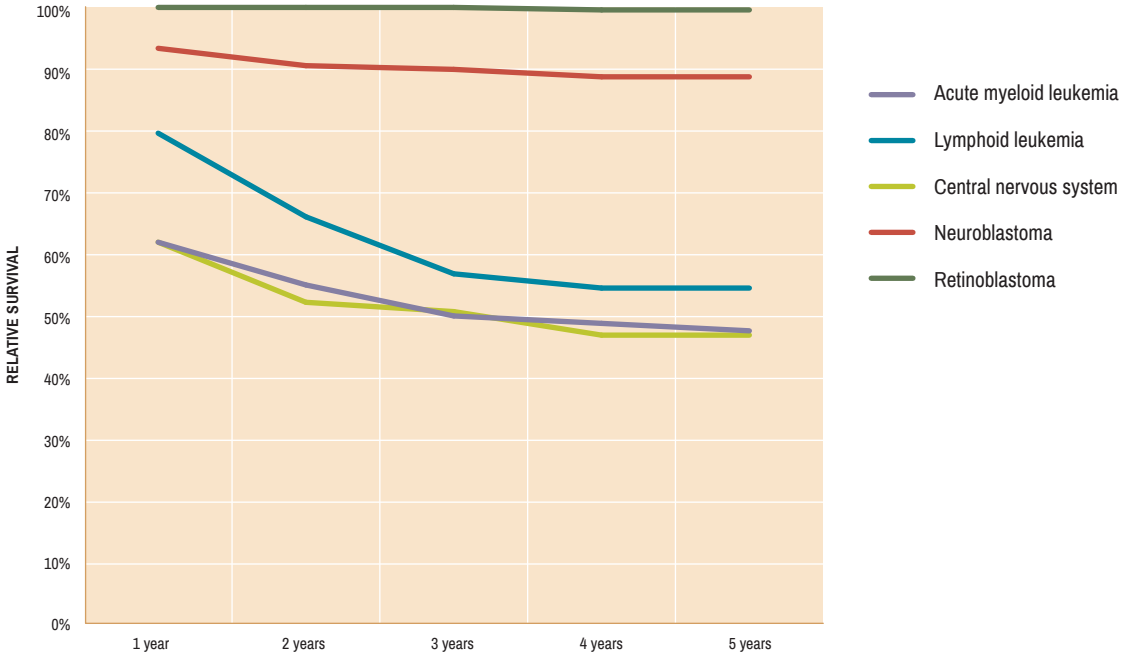
Relative survival percentages for one through five years following diagnosis for the top five most common infant cancers are shown in Figure 5. Survival is also presented for all CNS malignancies combined, which as a group represent the third most common type of cancer among infants (although specific types of CNS tumors were not among the most common cancers). These results show that relative survival

for neuroblastoma and retinoblastoma remained high from one to five years after diagnosis, indicating excellent prognoses for these infants. The one-year relative survival for neuroblastoma among infants was 93.4 percent and decreased to 88.8 percent at five years. One-year relative survival for retinoblastoma was 100.0 percent and at five years was still 99.6 percent. For infants diagnosed with leukemias or CNS malignancies (this latter category excludes neuroblastoma and retinoblastoma) between 2000 and 2011, relative survival percentages were lower, although they appear to stabilize around the three-year time period. The one-, three- and five-year relative survival percentages for lymphocytic leukemia were 79.7 percent, 57.0 percent and 54.7 percent, respectively. Survival for AML and CNS malignancies were similar and much lower than for the other three types of cancer: for AML, the one-, three-, and five-year relative survival percentages were 62.1 percent, 50.2 percent and 47.8 percent, respectively. For CNS malignancies, survival was 62.1, 50.9, and 47.1 percent, respectively, at one, three, and five years following diagnosis.

Among children (ages one through 14) diagnosed with lymphocytic leukemia, AML and malignant CNS tumors between 2000 and 2011, relative survival percentages were consistently higher than for infants. One-year relative survival percentages for children diagnosed with lymphocytic leukemia, AML, or CNS malignancies were 96.8 percent, 82.5 percent, and 86.0 percent respectively; five years after the diagnosis, relative survival was 86.4 percent for lymphocytic leukemia, 62.7 percent for AML, and 71.8 percent for CNS cancers (data not shown). Relative survival percentages for children diagnosed with retinoblastoma were comparable to infants (one-year relative survival for children was 98.6 percent and five-year relative survival was 96.0%). On the other hand, relative survival for neuroblastoma among children was much lower than that among infants: one year after diagnosis relative survival was 91.3 percent, but declined to 67.9 percent after five years

Figure 5. Relative Survival (Percent) for the Top Five Infant Cancers Diagnosed in California, 2000-2010



Note: Follow-up through December 31, 2011

Data Source: California Cancer Registry, California Department of Public Health

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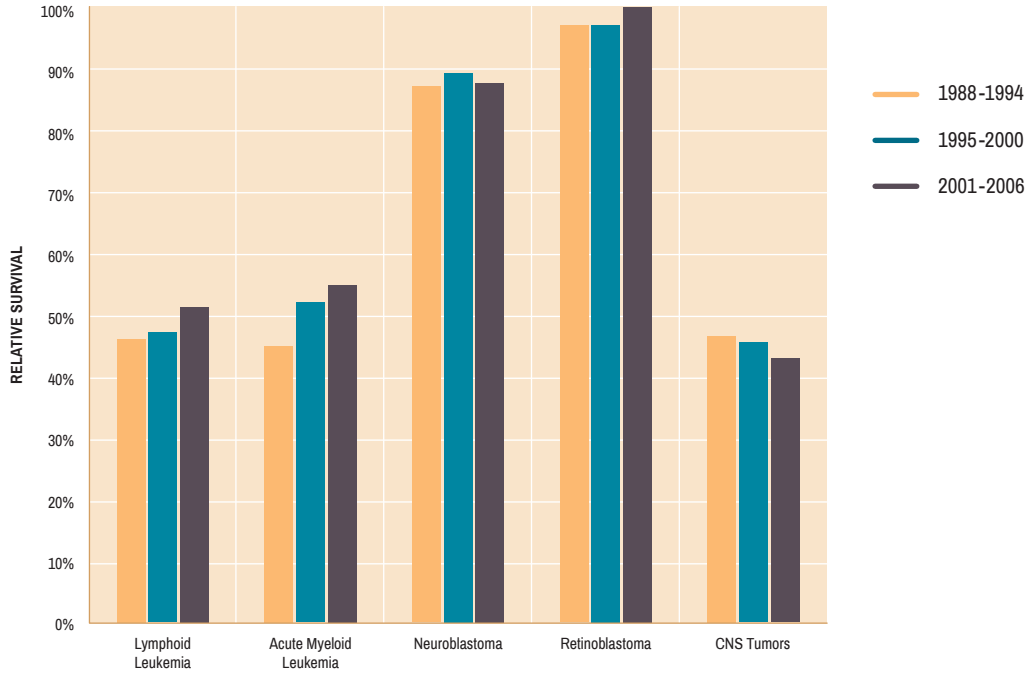
Five-year survival appears to be improving over time for some cancers, and leukemia in particular. When looking at five-year relative survival for infants diagnosed in three different periods: 1988-1994, 1995-2000, and 2001-2006 (Figure 6), survival appears to have increased for AML, from 44.9% among infants diagnosed between 1988-1994 to 54.8% among those diagnosed between 2001-2006. For lymphoid leukemia, 5-year relative survival increased from 46% to 51.3% during the same period. However, because the number of cases diagnosed among infants was small, these apparent improvements did not reach statistical significance. Survival for infants with retinoblastoma is high, and 5-year survival for infants diagnosed with this cancer now approaches the same likelihood of survival as infants without the disease. No survival improvement was noticed among infants diagnosed with neuroblastoma: five-year survival for the most recent period (87.7%) is unchanged from that recorded in 1988-1994. Survival for malignant CNS tumors also did not improve over time.

In contrast with infants, survival among children ages one through 14 diagnosed with lymphocytic leukemia, AML, and CNS malignancies increased significantly over time. Lymphocytic leukemia five-year relative survival increased from 81.1 percent (1988-1994) to 87.2 percent in the most recent period (2001-2006). Similarly, five year survival for AML increased from 40.4 percent to 63.2 percent; for CNS cancers, five-year survival increased from 63.2 percent to 71.2 percent. Survival also appears to have increased for neuroblastoma, although not significantly. Similar to what was described for infants, five-year survival for retinoblastoma was high (96.8 percent) and did not change over time.

Figure 6. Five-Year Relative Survival (Percent) for the Top 5 Infant Cancers Diagnosed in California, by Years of Diagnosis: 1988-2011



Note: Follow-up through December 31, 2011

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Conclusion

This is the first comprehensive analysis of cancer incidence and survival trends among infants in California as far as we know. It revealed significance differences in cancer distribution and survival patterns among infants compared with children older than one year. The population diversity in California also allowed us to detect some differences in incidence rates of infant tumors by racial/ethnic background.

Perhaps the single most significant observation from this review was the more than two-fold increased incidence of AML among infants over a span of 23 years. The cause(s) for this increase is(are) unknown and cannot be determined from the the data available for this review. Clearly, however, this warrants further study. While the cause(s) of AML generally are unknown, some factors are known to increase the risk of being diagnosed with the disease; these factors include certain genetic disorders,[3] having a sibling with leukemia, being exposed to cigarette smoke or alcohol before birth, or being exposed to ionizing radiation or certain chemicals (e.g., benzene) (http://www.cancer.gov/cancertopics/pdq/treatment/childAML).

Data about maternal environmental or medical treatment exposures, lifestyle habits, or other potential risk factors are not available in the California Cancer Registry database, so potential reasons behind the increase in AML incidence could not be specifically evaluated in this review. Nonetheless, the fact that the increased incidence of AML was only seen among infants and that AML is associated with genetic conditions and environmental exposures having genetic effects certainly suggests that the increased incidence is related to some type of genotoxic phenonenon that occurred during the period covered by this review. Regrettably, we do not have data that would allow us to further explore the matter, although it is a disturbing trend that clearly warrants further investigation.

3 AML has been associated with genetic disorders such as Down syndrome, familial monosomy 7, Fanconi anemia, dyskeratosis congenital, neurofibromatosis type 1, and Kostmann syndrome, among others.

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