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W. Archie Bleyer

Epidemiologic impact of children with brain tumors

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W.A. Bleyer
University of Texas
M.D. Anderson Cancer Center,
1515 Holcombe Boulevard,
University of Texas Medical School,
Houston, TX 77030, USA
e-mail: ableyer@nccf.org
Fax: +1-713-7451549

Abstract The impact of CNS tumors during childhood and adolescence has been steadily increasing. In many countries, brain and spinal cord tumors are now second in frequency only to leukemia as a cancer affecting children, and the most common cause of cancer mortality in the young. In the United States, brain tumors are now more common than acute lymphoblastic leukemia, and the proportion of cancer deaths due to CNS tumors has nearly doubled during the past 25 years. Worldwide, approximately 30,000–40,000 children develop CNS tumors each year, and the majority do not survive. Compared with most other malignancies that occur during childhood, CNS tumors have not been treated with comparable success in treatment outcome. Also, no specific risk factor, or set of risk factors, has been identified to explain a substantial proportion of CNS tumor occurrence. In many countries, CNS tumors are now the greatest challenge in pediatric oncology.

Key words CNS tumors · Brain tumors · Epidemiology · Etiology

Introduction

As will be explained in this review, CNS tumors have emerged as the greatest challenge in pediatric oncology. In most countries of the world, brain and spinal cord tumors are second in frequency only to leukemia as a cancer affecting children, and are the most common cause of cancer mortality in the young. Moreover, compared with most other malignancies that occur during childhood, for CNS tumors there has not been a comparable success in treatment outcome. In this review, the incidence, mortality, and survival of children and adolescents up to 20 years of age will be reviewed, including trends that predict what the epidemiology and outcome will be for these patients in the year 2000. Most of the data on children in the United States are derived from the National Cancer Institute Surveillance, Epidemiology and End-Results (NCI SEER) program [29], unless otherwise stated. A new monograph from the SEER program puts the data on pediatric cancers into perspective, and this was particularly helpful in the compilation of this review [22]. It became available on the internet in July, 1999 at http://www.[www-SEER.ims.nci.nih.gov/Publications].

Mortality of childhood cancer and CNS tumors

Most people are unaware of the most common fatal disease of childhood. They are surprised to learn that cancer is the number 1 killer disease of children from late infancy through early adulthood [2]. In most economically advantaged nations of the world, cancer kills more children over the age of 6 months than any other disease; more than 10% of all deaths in children under 15 years of age are caused by cancer. In North America, cancer is the leading medical cause of death in both males and females from 1 to 34 years of age, and in females cancer is the leading cause from 1 to 75 years of age; after age 34 (75 in females), heart disease exceeds cancer as the leading cause of mortality. Only accidents exceed cancer in

frequency as a leading cause of mortality in children and adolescents.

Similarly, few are aware that the most common type of cancer that causes death in children is CNS malignancy. In the United States, the annual mortality rate from CNS tumors among children less than 15 years of age decreased from 1.0 per 100,000 in 1973 to 0.8 deaths per 100,000 in 1995 [29]. The overall cancer mortality rate declined from 5.5 per 100,000 in 1973 to 2.7 per 100,000 in 1995. Thus, the proportion of cancer deaths attributable to CNS tumors increased from 18% to 30% over the 22-year interval. In the year 2000, one-third of the cancer deaths in children will be due to primary CNS malignancies.

The corresponding changes for ALL were 2.7 to 3.3 incident cases per 100,000 and 1.3 to 0.4 deaths per 100,000. All of these trends are statistically significant. Thus, at least in the United States, deaths among children with CNS tumors exceed the next most common type of cancer deaths, those from acute lymphoblastic leukemia, by more than 3-fold [3].

Since 1945, approximately 40,000 children in the United States have died of CNS tumors without reaching the age of 15 years. If the average age at diagnosis among these patients was 5 years, and the average life span would otherwise have been 75 years, then this means that about 4,000,000 person-years of life were potentially affected by the diagnosis, in terms of risk of either premature death or compromised quality of life, by the disease or its treatment. Of these 4 million person-years, at least 2.2 million person-years of life were lost to premature death. Currently more than 30,000 person-years of potential life are lost each year among the children in the United States who die of CNS tumors.

The incidence of childhood cancer and CNS tumors

Worldwide, the incidence of cancer has been estimated at 11 new cases annually per 100,000 persons <20 years of age [25]. Since there are approximately 2.1 billion people in this age range, there are probably 260,000 children who are diagnosed with cancer each year in the world, at least 30,000 of whom – and probably closer to 40,000 – develop CNS tumors. For several decades, CNS tumors have been observed to be the second most common type of cancer in children, exceeded only by leukemia, and specifically ALL, the most common type of leukemia in children.

According to projections of trends predicted from data collected by the United States Statistics, Epidemiology and End-Results (SEER) Program of the National Cancer Institute [29], the current incidence of cancer in American <20-year-olds is 16 cases per 100,000/year. Thus, approximately 11,000 United States children and adolescents under 20 years of age are diagnosed each year as having cancer, and 2,200 as having invasive CNS tumors [22]. On an average weekday, 42 children or adolescents are diagnosed with cancer, and 8–9 are found to have a CNS malignancy. Since 1945, about 280,000 children in the United States have been diagnosed with cancer before the age of 20 years [1], and about 50,000 of these children have been affected by a malignant CNS tumor [15].

In the United States, the overall incidence of malignant CNS tumors is inversely proportional to age, with 3.5–4 cases annually per 100,000 children <5 years of age, 3 per 100,000 5- to 10-year-olds, 2.5 per 100,000 10- to 15-year-olds and 2.2 per 100,000 15- to 20-year-olds. Just over half (52%) of the CNS malignancies in patients <20 years of age are astrocytomas, 21% are primitive neuroectodermal tumors (PNET), 21% are other gliomas, and 9% are ependymomas. Astrocytomas remain relatively independent of age, with a constant incidence of 1.5 per 100,000 per year over the first 20 years of life. PNETs, ependymoma and other gliomas each have a inverse relationship to age, which when combined accounts for most of the dependence of the overall CNS tumor incidence on age [15].

With one exception, Afro-American and white children in the United States have the same incidence rates. The difference is in the first 2–3 years of life, when the rate in Afro-Americans is half to three-fourths that among white children. This raises the possibility that there may be a delay, on average, in diagnosing CNS malignancy in Afro-American infants relative to white infants, but as discussed by Gurney et al. [15], there is no other evidence that supports this speculation.

In children less than 10 years of age, the most common site of malignancy within the CNS is the cerebellum. The second and third most common sites are the cerebrum and the brain stem, in which the frequency is relatively equal. Among 10- to 19-year-olds, the incidence of both cerebellar and brain tumors decreases, while cerebral maligancies increase in incidence. In adults, the most common location by far is the cerebrum.

The incidence of malignant CNS tumors is higher in boys than in girls, with a ratio of 55%:45%. Most of this difference is accounted for by a male predominance in PNETs and ependymomas. There is little gender difference among the other basic tumor types [15]. The higher rate in boys is far more prominent in white children than in Afro-Americans. White males <20 years of age clearly have a higher incidence rate of malignant CNS tumors ($3.2/10^5$ per year) than white females ($2.5/10^5$ per year), Afro-American females ($2.3/10^5$ per year), or Afro-American males ($2.5/10^5$ per year) [15].

Compared with the incidence of AIDS in the United States, cancer is 10–20 times as common in children [1]. Since 1980, when the AIDS epidemic began, CNS malignancies have occurred in more than 14,000 United States children, which can be compared with approxi-

mately 2,000 cases of AIDS in the same age group and over the same period of time [1]. AIDS/HIV-related brain tumors in children account for <1% of the malignant CNS tumors of children and adolescents.

Increasing incidence of childhood cancer and CNS tumors

In the United States, as in most socioeconomically advantaged countries, the incidence of cancer is increasing. The greatest increase has been in the oldest age groups, over 65 years of age. This is followed, however, by those in adolescents and young adults, who have had the second highest increase, and in children <5 years of age. For persons <20 years of age, the overall cancer incidence rate in the United States, as estimated from the SEER program, increased from 13.5 cases per 100,000/year in 1973 to 16.0 cases per 100,000/year in 1994, an 18.5% increase in 21 years.

Two cancers account for nearly all of the increase in children and adolescents: malignant CNS tumors and ALL. The increase in CNS tumors has been reported in independent studies [6, 11, 14]. Since the incidences of both CNS tumors and ALL have been noted to be increasing, the impact of this trend on current national cancer incidence and mortality rates in the United States was assessed [3] by analyzing the data available for children <15 years of age from the United States SEER report [29]. Regression analysis was performed on 22 consecutive years (1973–1994) of national mortality data for the entire United States and of incidence rates over the same interval derived from SEER registries. The incidence of CNS tumors increased from an annual rate in 1973 of 2.4 cases per 100,000 children aged <15 years to a corresponding value in 1994 of 3.5. All of these trends are statistically significant. The incidence of CNS tumors appears to be continuing to increase, whereas the ALL increase seems to be leveling off [3].

One of the most provocative observations on the incidence of CNS tumors in children was the observation by Smith et al. that the incidence did not increase steadily from 1973 to 1994 (the SEER program began in 1973), but rather "jumped" from a relatively constant level *prior* to 1984–85 to a steady but higher rate *after* 1985 [32]. They showed that a jump model regression that had an optimal change point from lower to higher incidence at 1985 produced a significantly better fit than a model using a constant linear rate of increase (P=0.0003). The estimated annual percentage change from 1975 to 1984 was –0.1%, and from 1986 to 1995 it was also –0.1%. Smith and his colleagues associated the timing of the jump with the wide-scale availability of magnetic resonance imaging (MRI) in the United States [33]. They postulated that the reported increased incidence was due to improved diagnosis and reporting rather than to an actual increase in incidence. In support of their hypothesis, they noted that the CNS cancer mortality rate did not undergo a similar stepwise increment during the same period, which would have been expected if the step increase in incidence was real and not artifactual.

A contradictory point, however, is the lack of a return of the incidence rate to the pre-MRI era level during the decade after the incremental increase in 1984–1985. Given that CNS malignancies are eventually detected before death and that MRI allows earlier diagnosis, then the increase would be expected to be transient and the rate would be expected to return to the level known before the advent of MRI technology. Since this return to baseline would have been expected to occur within a few years, and 10 years have passed without a decline in the incidence, the MRI hypothesis seems inconsistent with the data.

Survival of children with cancer and CNS tumors

SEER data predict that mortality from cancer in Americans less than 20 years of age will have dropped from 6 deaths per 100,000/year in 1970 to less than 3 deaths per 100,000/year in 2000, a greater than 50% reduction in 30 years despite an increase in incidence of approximately 25% over this time. SEER survival data may be used to predict the height of the survival plateau, as previously published [2]. The plateau on the survival curve has increased from 50% in the mid-1970s to 70% by the mid-1980s. The most recent data [29] can be used to predict that the expected survival plateau for all patients <15 years of age with cancer will increase from 76% for patients diagnosed in 1992 to 82% in 1997.

Children with brain tumors are not so fortunate, however. Not only do they have a significantly lower rate of survival than children with most other cancers of childhood, but their quality of survival is also usually worse. The 5-year relative survival rates for all CNS cancer in patients <20 years of age increased from 59% in 1975–1984 to 67% in 1985–1994 [15]. The survival rates were inversely proportional to age. For 1986–1994, the 5-year relative survival rates for all CNS cancers were 45% for <1-year-olds, 59% for 1- to 4-year-olds, 64% for 5- to 9-year-olds, 70% for 10- to 14-year-olds, and 77% for 15- to 19-year-olds [15]. The CNS tumor annual mortality rate in United States children <15 years of age decreased from 1.0 deaths per 100,000 in 1973 to 0.78 deaths per 100,000 in 1994.

Survival differs dramatically with histology, size, stage, and location of the malignancy within the CNS. For astrocytomas, the 5-year relative survival rates in United States children and adolescents <20 years of age were 70% and 74% for the 1975–1984 and 1985–1994 intervals, respectively. Corresponding values for PNETs were 52% and 55%, for other gliomas 47% and 57%,

Table 1 Current knowledge on etiology of childhood CNS tumors. (Modified from [15])

Exposure or characteristic	Comments	References
Known risk factors		
Sex	Little difference between males and females, except in medulloblastoma (males higher than in females)	[25]
Therapeutic doses of ionizing radiation to head	Children treated for tinea capitis with orthovoltage irradiation experienced 2.5- to 6-fold increase in risk. Currently, those at risk are children treated with radiation to the CNS for leukemia or a previous brain tumor	[30, 31]
Neurofibromatosis; tuberous sclerosis; nevoid basal cell, Turcot and Li-Fraumeni syndromes	Children with these genetic conditions have a greatly increased risk of brain tumors, for example, 50-fold for neurofibromatosis and 70-fold for tuberous sclerosis. Together, these conditions account for less than 5% of all childhood brain tumors	[16, 19, 21, 15]
Factors for which evidence is suggestive but not conclusive		
Maternal diet during pregnancy	Frequent cured meat consumption has been consistently associated with a 1.5- to 2.0-fold increased risk, but it is unclear whether the meats or another dietary factor are responsible. Most aspects of diet have not been studied	[4, 5, 16, 25, 26]
Parent or sibling with brain tumor	Having a sibling or parent with a brain tumor has usually been associated with a 3- to 9-fold increase in risk. It may be that the excess risk is explained completely by the specific genetic conditions listed below	[5, 16, 17, 25]
Family history of bone cancer, leukemia or lymphoma	The increased risk seen in some studies may be explained by the Li-Fraumeni syndrome	[8, 9, 16, 20, 25]
Factors for which evidence is limited or inconsistent		
Electromagnetic fields	A small increase in risk has been observed in some studies but not in others	[10, 16, 25, 27, 28]
Products containing *N*-nitroso compounds[a]	The data are inconsistent; associations seen in one study have generally not been reported in later studies	[16, 25]
Father's occupation and related exposures	Many associations[b] have been reported, but few have been replicated	[16, 18, 25]
Pesticides	Two small studies suggest an association with use of no-pest strips	[7, 16, 24, 25]
History of head injury	The data are confounded by the possibility that mothers of children with brain tumors are more likely than control mothers to recall head injuries	[12, 16, 25]
Family history of epilepsy or seizures	The data are inconsistent. One study suggests that the effect of family history of seizures may differ by type of tumor and/or type and circumstances of seizures	[13, 16, 26]
Family history of mental retardation	Increased risk observed in one study of adults and one of children	[16]

[a] Examples: beer, incense, make-up, antihistamines, diuretics, rubber baby bottle and pacifier nipples
[b] Examples: aircraft industry, agriculture, electronics manufacturing, petroleum industry, painter, paper or pulp mill worker, printer, metal-related occupation, exposure to paint, ionizing radiation, solvents, electromagnetic fields

and for ependymomas 39% and 56%. For brain stem tumors, survival has been dismal. For diffuse pontine gliomas, the most common type of brain stem tumor during childhood, the 5-year survival is <10% and there is little evidence that the outcome has changed over the last 25 years.

Risk factors and prevention of CNS tumors

The SEER Pediatric Monograph described in the introductory paragraph contains a superb summary of current knowledge on causes of CNS tumors in children. Known, potential, and refuted risk factors are summarized in the monograph in the form of a table that is given in this paper in modified form (Table 1).

To date, despite many epidemiological studies, including several performed by the national cooperative groups, no specific risk factor, or set of risk factors, is known that could explain a substantial proportion of CNS tumor occurrence. Only therapeutic doses of ionizing radiation such as are delivered to the CNS in the treatment of leukemia or brain tumors have been unequivocally identified as an external (environmental) risk factor. Maternal diet during pregnancy has been implicated, particularly cured meats, but the data are not conclusive and it is unclear whether another dietary factor or co-variable may be associated with the increased

risk (Table 1). Electromagnetic fields, *N*-nitroso compounds, and pesticides have been implicated in some studies but not in others, and in general subsequent studies performed with more rigorous scientific methods have not been confirmative (Table 1).

Based on current knowledge, it is highly unlikely that a significant proportion of CNS cancers during childhood will ever be prevented. Most evidence favors spontaneous mutation as the predominant cause of childhood cancers, and neither environmental nor inherited etiologies. Attempts to prevent childhood cancers (cancer *during* childhood) are likely to fail. On the other hand, it is known that most of the cancers of adults can be prevented, and that most of these are due to lifestyles. Since lifestyle is primarily determined during childhood, the best opportunity to accomplish prevention of cancer *during* adulthood is to begin the effort in children by teaching them how they can prevent cancer later in their lives.

Role of clinical trials and cooperative group studies in pediatric oncology

The treatment of most children with cancer is managed at pediatric cancer centers located throughout the United States. These centers enroll ~5000 children/year on clinical trials monitored by the National Cancer Institute. Given that the current clinical-trial accrual rate among adults with cancer is ~20,000/year, children account for 20–25% of all patients entered on clinical trials in the United States.

In the United States, more than 90% of children with cancer who are less than 15 years of are seen at institutions of one of two national collaborative groups: the Children's Cancer Group (CCG) and the Pediatric Oncology Group (POG). The groups are truly multidisciplinary, with representation of all the medical and psychosocial specialties necessary for optimum evaluation and care of the children with cancer. As many as 600 pediatric oncologists, pediatric surgeons (including neurosurgeons), radiotherapists, pathologists, radiologists (including neuroradiologists), pediatric oncology nurses, psychologists, basic scientists, statisticians, and other professionals meet twice yearly to review the results of current studies and plan new strategies of diagnosis, staging, treatment and detection and prevention of adverse effects of therapy. Since 1955 the CCG and POG have accrued more than 90,000 patient entries on therapeutic and diagnostic studies.

Between 1 January 1992 and 30 June 1994, the proportion of CCG and POG patient entries onto *treatment* trials sponsored by the United States National Cancer Institute Division of Cancer Treatment, referred to the proportion of all United States patients <20 years of age, was 73.4% vs 75.9% for white children, 10.3% vs 10.7% for Afro-American children, 11.6% vs 9.1% for Hispanic children, and 4.7% vs 4.3% for Asian and other racial groups. There is no statistical difference in the distributions. For children entered on *cancer control* trials sponsored by the United States National Cancer Institute Division of Cancer Prevention and Control, the proportions were 69.6% (CCG+POG) vs 75.9% (United States) for whites, 5.5% vs 10.7% for Afro-Americans, 18.2% vs 9.1% for Hispanics, and 3.6% vs 4.3% for Asian and other ethnic groups. Thus, data from 1992–1994 indicate that minority children access, and are treated on clinical trials by, the national pediatric cooperative groups similarly to the majority ethnic group. The uneven distribution for cancer control patients appears to be primarily due to a higher proportion of Hispanic children on these trials, which may be a direct result of NCI-sponsored minority initiatives.

In the year 2000, the CCG and POG, along with the two disease-specific pediatric national cooperative groups, the Intergroup Rhabdomyosarcoma Study Group (IRSG) and the National Wilms' Tumor Study Group (NWTSG), will merge into a single North American cooperative group, the Children's Oncology Group (COG.). This will provide an unexcelled opportunity to study the epidemiology of CNS (and other) tumors in the United States and Canada, and should facilitate our understanding of the etiologies and pathogenesis of CNS tumor in infants, children, adolescents and young adults.

International challenges

Bearing in mind that for many countries CNS tumors now represent the greatest challenge in pediatric oncology, it is reasonable to recommend that more resources and effort be devoted to the study of pediatric CNS malignancies in order to develop more effective therapies. Challenges to consider as international priorities for the year 2000, in an approximate order of priority, include:

- Improve understanding of the biology of cancer in our young
- Realize the higher cure rates achieved in some countries worldwide
- Improve the survival of all infants, children, adolescents and young adults with CNS tumors
- Improve the survival of infants with brain tumors, particularly those with ependymoma
- Improve the survival of children with brain stem tumors, especially those with diffuse pontine gliomas
- Detect CNS tumors earlier, before they are less treatable
- Improve the quality of life for each child with cancer and his or her family
- Reduce the morbidity and mortality of therapy
- Eliminate the need for hospitalization
- Diminish the discomfort of diagnosis and staging
- Identify and implement less expensive ways of meeting these challenges

References

1. Bleyer WA (1990) The impact of childhood cancer on the United States and the world. CA Cancer J Clin 40:355–367
2. Bleyer WA (1993) What can be learned about childhood cancer from Cancer Statistics Review 1973–1988. Cancer 71:3229–3236
3. Bleyer A, Sposto R, Sather H (1998) In the United States, pediatric brain tumors and other nervous system tumors are now more common than childhood acute lymphoblastic leukemia (ALL) and have a 3-fold greater national mortality rate than ALL (abstract). Proc Am Soc Clin Oncol 17:389a
4. Bunin GR, Kuijten RR, Buckley JD, Rorke LB, Meadows AT (1993) Relation between maternal diet and subsequent primitive neuroectodermal brain tumors in children. N Engl J Med 329:536–541
5. Bunin GR, Kuijten RR, Boesel CP, Buckley JD, Meadows AT (1994) Maternal diet and risk of astrocytic glioma in children: a report from the Children's Cancer Group. Cancer Causes Control 5:177–187
6. Bunin GR, Feuer EJ, Witman PA, Meadows AT (1996) Increasing incidence of childhood cancer: report of 20 years' experience from the greater Delaware Valley Pediatric Tumor Registry. Paediatr Perinat Epidemiol 10:319–338
7. Davis JR, Brownson RC, Garcia R, Bentz BJ, Turner A (1993) Family pesticide use and childhood brain cancer. Arch Environ Contam Toxicol 24:87–92
8. Draper GJ, Heaf MM, Kinnier Wilson LM (1977) Occurrence of childhood cancers among sibs and estimation of familial risks. J Med Genet 14:81–90
9. Farwell J, Flanner JT (1984) Cancer in relatives of children with nervous-system neoplasms. N Engl J Med 311:749–753.
10. Gurney JG, Mueller BA, Davis S, Schwartz SM (1996) Childhood brain tumor occurrence in relation to residential power line configurations, electric heating sources, and electric appliance use. Am J Epidemiol 143:120–128
11. Gurney JG, Davis S, Serverson RK, Fang J-Y, Ross JA, Robison LL (1996) Trends in cancer incidence among children in the United States. Cancer 78:532–541
12. Gurney JG, Preston-Martin S, McDaniel AM, Mueller BA, Holly EA (1996) Head injury as a risk factor for brain tumors in children: results from a multicenter case-control study. Epidemiology 7:485–489
13. Gurney JG, Mueller BA, Preston-Martin S, McDaniel AM, Holly EA, Pogoda JM, Davis RL (1997) A study of pediatric brain tumors and their association with epilepsy and anticonvulsant use. Neuroepidemiology 16:248–255
14. Gurney JG, Ross JA, Wall DA, Bleyer WE, Severson RK, Robison LL (1997) Infant cancer in the United States: histology-specific incidence and trends, 1973–1992. J Pediatr Hematol Oncol 19:428–432
15. Gurney G, Smith MA, Bunin GR (1999) CNS and miscellaneous intracranial and intraspinal neoplasms. (National Cancer Institute SEER Pediatric monograph (to be published before the meeting), pp 51–63
16. Kuijten RR, Bunin GR (1991) Risk factors for childhood brain tumor: a review. Cancer Epidemiol Biomarkers Prev 2:277–288
17. Kuijten RR, Strom SS, Rorke LB, Boesel CP, Buckley JD, Meadows AT, Bunin GR (1993) Family history of cancer and seizures in young children with brain tumors: a report from the Children's Cancer Group (United States and Canada). Cancer Causes Control 4:455–464
18. McKean Cowdin R, Preston-Martin S, Pogoda JM, Holly EA, Mueller BA, Davis RL (1998) Parental occupation and childhood brain tumors – astroglial and primitive neuroectodermal tumors. J Occup Environ Med 40:332–340
19. McLendon RE, Tien RD (1998) Genetic syndromes associated with tumors and/or hamartomas. In: Bigner DD, McLendon RE, Bruner JM (eds) Russell and Rubinstein's pathology of tumors of the nervous system, 6th edn. Arnold, London pp 371–417
20. Miller RW (1968) Deaths from childhood cancer in sibs. N Engl J Med 279:122–126
21. Narod SA, Stiller C, Lenoir GM (1991) An estimate of the heritable fraction of childhood cancer. Br J Cancer 63:993–999
22. National Cancer Institute (1999) SEER pediatric monograph. NCI, Bethesda (to be published before the meeting)
23. Parker DM, et al (eds) (1988) International incidence of childhood cancer. (Scientific publication no 87) World Health Organization/International Agency for Research on Cancer, Lyon
24. Pogoda JM, Preston-Martin S (1997) Household pesticides and risk of pediatric brain tumors. Environ Health Perspect 105:1214–1220
25. Preston-Martin S, Mack WJ (1996) Neoplasms of the nervous system. In: Schottenfeld D, Fraumeni JF (eds) Cancer epidemiology and prevention. Oxford University Press, New York, pp 1231–1281
26. Preston-Martin S, Pogoda JM, Mueller BA, Holly EA, Lijinsky W, Davis RL (1996) Maternal consumption of cured meats and vitamins in relation to pediatric brain tumors. Cancer Epidemiol Biomarkers Prev 5:599–605
27. Preston-Martin S, Navidi W, Thomas D, Lee P, Bowman J, Pogoda J (1996) Los Angeles study of residential magnetic fields and childhood brain tumors. Am J Epidemiol 143:105–119
28. Preston-Martin S, Gurney JG, Pogoda JM, Holly EA, Mueller BA (1996) Brain tumor risk in children in relation to use of electric blankets and water bed heaters. Am J Epidemiol 143:1116–1122
29. Ries LAG, Kosary CL, Hankey BF, Miller BA, Harras A, Edwards BK (eds) (1997) SEER cancer statistics review, 1973–1994. (NIH publication no 97–2789) NCI, Bethesda
30. Ron E, Modan B, Boice JD, Alfandary E, Stoval M, Chetrit A, Katz L (1988) Tumors of the brain and nervous system after radiotherapy in childhood. N Engl J Med 319:1033–1039
31. Shore RE, Albert RE, Pasternack BR (1976) Follow up study of patients treated by X-ray epilation for tinea capitis: resurvey of post-treatment illness and mortality experience. Arch Environ Health 31:21–28
32. Smith MA, Freidlin B, Gloeckler Ries LA, Simon R (1998) Trends in reported incidence of primary malignant brain tumors in children in the United States. J Natl Cancer Inst 90:1269–1277
33. Smith MA, Freidlin B, Ries LAG, Simon R (1998) Trends in the reported incidence of primary malignant brain tumors in children in the United States. J Natl Cancer Inst 90:1269–1277