

RISK FACTOR INFORMATION FOR SELECTED CANCER TYPES

Brain and CNS Cancer

Brain and central nervous system (CNS) tumors can be either malignant (cancerous) or benign (non-cancerous). Primary brain tumors (i.e., brain cancer) comprise two main types: gliomas and malignant meningiomas. Gliomas are a general classification of malignant tumors that include a variety of types, named for the cells from which they arise: astrocytomas, oligodendrogliomas, and ependymomas. Meningiomas arise from the meninges, which are tissues that surround the outer part of the spinal cord and brain. Although meningiomas are not technically brain tumors, as they occur outside of the brain, they account for about 50% of all reported primary brain and spinal cord tumors. The majority of meningiomas (about 85%) are benign and can be cured by surgery. Therefore, approximately 7.5% of brain and CNS tumors are malignant meningiomas. In addition to these main types, there are a number of rare brain tumors, including medulloblastomas, which develop from the primitive stem cells of the cerebellum and are most often seen in children. Also, the brain is a site where both primary and secondary malignant tumors can arise; secondary brain tumors generally originate elsewhere in the body and then metastasize, or spread, to the brain (ACS, 1999a). The American Cancer Society estimates that 17,000 Americans (9,600 men and 7,400 women) will be diagnosed with primary brain cancer (including cancers of the central nervous system, or spinal cord) and approximately 13,100 people (7,200 men and 5,900 women) will die from this disease in 2002 (ACS, 2002).

Brain and spinal cord cancers account for over 20% of all cancer types diagnosed among children aged 0-14 (ACS, 2002). About half of all childhood brain tumors are astrocytomas and 25% are medulloblastomas (ACS, 1999b). After a peak in childhood (generally under 10 years of age), the risk of brain cancer increases with age from age 25 to age 75. In adults, the most frequent types of brain tumors are astrocytic tumors (mainly astrocytomas and glioblastoma multiforme). Incidence rates are higher in males than in females for all types. In general, the highest rates of brain and nervous system cancer tend to occur in whites. However, this varies somewhat by type; the incidence of gliomas is lower among black men and women than whites, but for meningiomas, the reverse is true (Preston-Martin and Mack, 1996).

Despite numerous scientific and medical investigations, and analyses, the causes of brain cancer are still largely unknown. Among the possible risk factors investigated in relation to this type of cancer are ionizing radiation, electromagnetic fields, occupational exposures, exposure to N-nitroso compounds, head trauma, and genetic disorders.

The most established risk factor (and only established environmental risk factor) for brain tumors (either cancerous or non-cancerous) is high-dose exposure to ionizing radiation (i.e., x-rays and gamma rays). Most radiation-induced brain tumors are caused by radiation to the head from the treatment of other cancers (ACS, 1999a). Meningiomas are the most common type of tumors that occur from this type of exposure, but gliomas may also occur (Preston-Martin and Mack, 1996). Among adults, the risk of developing meningiomas has been associated with full-mouth dental x-rays taken decades ago when radiation doses were higher than today. Although the relationship between low-dose radiation exposure and increased risk of brain tumors has been debated in several studies, prenatal exposure from diagnostic x-rays has been related to an increase in childhood brain tumors (Preston-Martin and Mack, 1996).

In recent years, there has been increasing public concern and scientific interest regarding the relationship of electromagnetic fields (EMF) to brain cancer. However, results from recent epidemiological investigations provide little or no evidence of an association between residential EMF exposure (e.g., from power lines and home appliances) and brain tumors (Kheifets, 2001).

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Studies also suggest that the use of handheld cellular telephones is not associated with an increased risk of primary brain cancer (Muscat et al., 2000). However, given the relatively recent use of cellular phones, evidence is preliminary and few studies have been conducted.

Other environmental factors such as exposure to vinyl chloride (used in the manufacturing of some plastics) and aspartame (a sugar substitute) have been suggested as possible risk factors for brain cancer but no conclusive evidence exists implicating these factors (ACS, 1999a). Although some occupational studies have suggested that electrical and electric utility workers may be at a slightly increased risk of brain cancer, these studies have important limitations, such as exposure misclassifications and a lack of dose-response relationships (Kheifets, 2001). Some researchers have also reported an increased risk of brain tumors in adults among veterinarians and farmers. Exposure to farm animals and pets have been considered as possible risk factors because of their association with bacteria, pesticides, solvents, and certain animal oncogenic (cancer-related) viruses (Yeni-Komshian and Holly, 2000). However, the relationship between farm life and brain cancer remains controversial.

Recent reports have proposed a link between occupational exposure to lead and brain cancer risk, but further analytic studies are warranted to test this hypothesis (Cocco et al., 1998). In a recent case-control study, the concentrations of metal and non-metal compounds in brain biopsies from patients with primary brain tumors were compared to results from an analysis of tumor-free brain tissue. Statistically significant associations were observed between the presence of brain tumors and the concentrations of silicon, magnesium, and calcium (Hadfield et al., 1998). However, further research using a larger sample size is needed to determine whether exposure to these elements plays a role in the development of brain cancer. Other occupations that may be associated with elevated risks include workers in certain health professions (e.g., pathologists and physicians), agricultural workers, workers in the nuclear industry, and workers in the rubber industry, although specific exposures have not been established (Preston-Martin and Mack, 1996). Studies investigating the possible association between occupational exposure of parents (in particular, paper or pulp-mill, aircraft, rubber, metal, construction, and electric workers) and the onset of brain tumors in their children have provided inconsistent results (Preston-Martin and Mack, 1996).

The association between the development of brain cancer and nitrites and other N-nitroso compounds, among the most potent of carcinogens, has been heavily researched. N-nitroso compounds have been found in tobacco smoke, cosmetics, automobile interiors, and cured meats. A recent study concluded that an increased risk of pediatric brain tumor may be associated with high levels of nitrite intake from maternal cured meat consumption during pregnancy (Pogoda and Preston-Martin, 2001). However, the role of nitrites and cured meats in the development of brain cancer remains controversial (Blot et al., 1999; Bunin, 2000). Because most people have continuous, low level exposure to N-nitroso compounds throughout their lives, further studies, especially cohort studies, are needed to determine if this exposure leads to an increased risk of brain tumors (Preston-Martin, 1996).

Injury to the head has been suggested as a possible risk factor for later development of brain tumors but most researchers agree that there is no conclusive evidence for an association (ACS, 1999b). Head trauma is most strongly associated with the development of meningiomas compared with other types of brain tumor. Several studies have found an increased risk in women with histories of head trauma; in men who boxed; and in men with a previous history of head injuries. Gliomas are the most common type of childhood brain tumor and have been

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positively associated with trauma at birth (e.g., Cesarean section, prolonged labor, and forceps delivery). However, other studies have found no association (Preston-Martin and Mack, 1996).

In addition, rare cases of brain and spinal cord cancer run in some families. Brain tumors in some persons are associated with genetic disorders such as neurofibromatosis types I and II, Li-Fraumeni syndrome, and tuberous sclerosis. Neurofibromatosis type I (von Recklinghausen's disease) is the most common inherited cause of brain or spinal cord tumors and occurs in about one out of every 3,000 people (Preston-Martin and Mack, 1996). The disease may be associated with optic gliomas or other gliomas of the brain or spinal cord (ACS, 1999b). Of those afflicted with the disease, about 5-10% will develop a central nervous system tumor (Preston-Martin and Mack, 1996). In addition, von Hippell-Lindau disease is associated with an inherited tendency to develop blood vessel tumors of the cerebellum (ACS, 1999a). However, malignant (or cancerous) brain tumors are rare in these disorders; inherited syndromes that predispose individuals to brain tumors appear to be present in fewer than 5% of brain tumor patients (Preston-Martin and Mack, 1996).

Other possible risk factors investigated for brain cancer have included alcohol consumption, use of barbiturates, smoking and exposure to second-hand smoke, pesticides, and infectious diseases (i.e., tuberculosis and chicken pox). To date, studies on these risk factors have yielded inconclusive results. Further, the majority of individuals diagnosed with brain cancer have no known risk factors (ACS, 1999a).

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