

Brain Tumors: Where do they come from?

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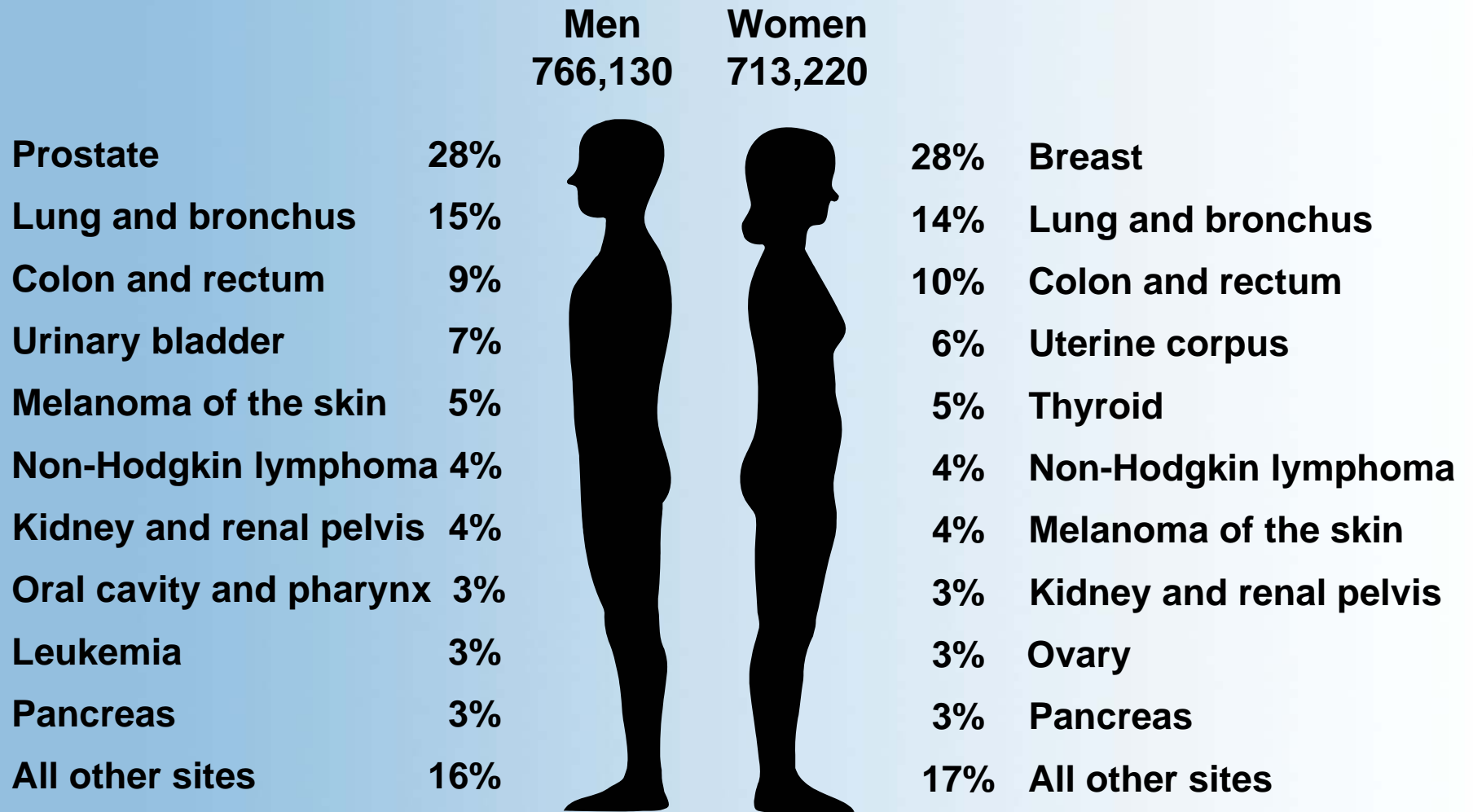
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Topics



- **Characteristics and distribution of brain tumors**
- **Risk factors for brain tumors**
- **Promising avenues of research**

Estimated new cases of cancer in US, 2010

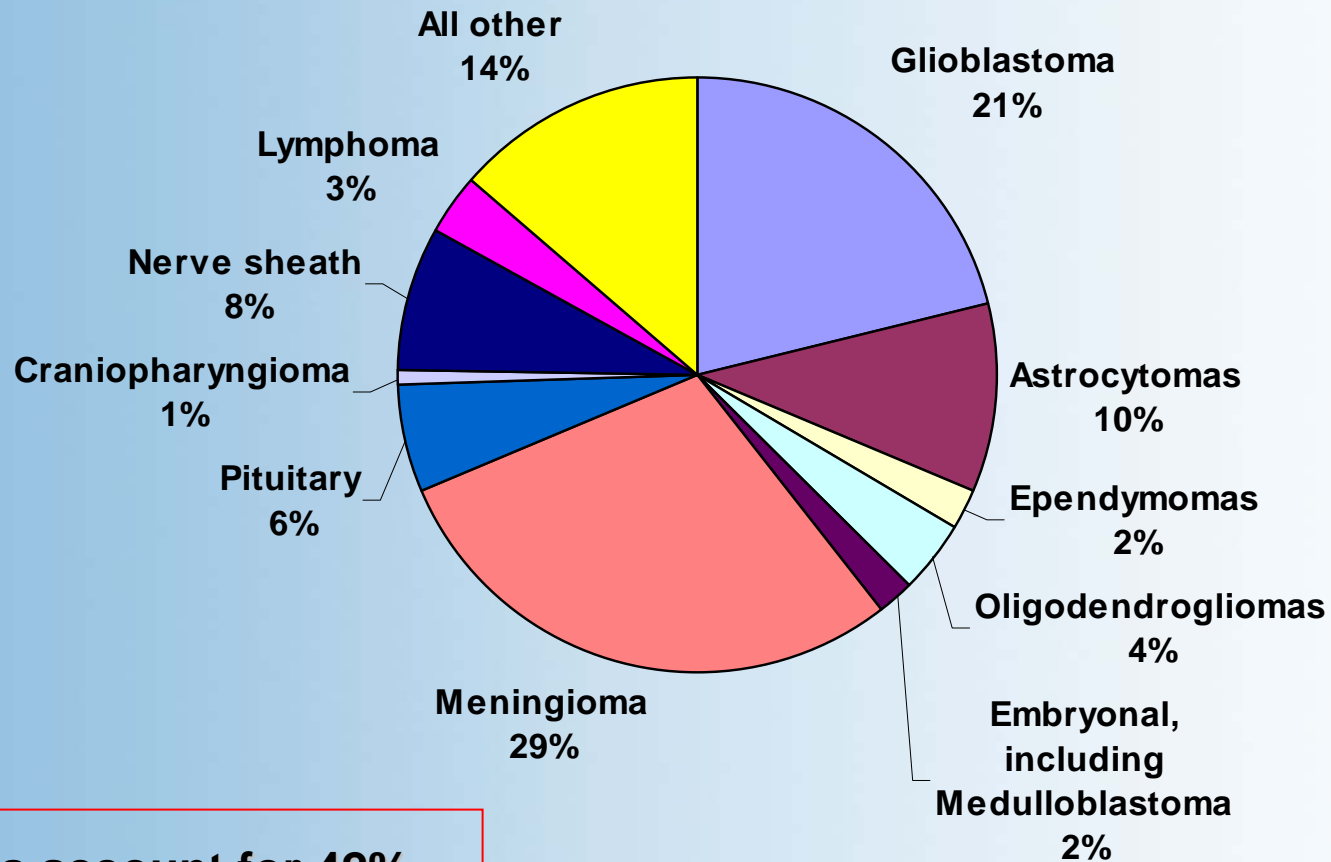


Source: American Cancer Society, 2010

Brain tumors

- In 2010, the estimated number of new cases of brain tumors will be 22,020 (11,980 men and 10,040 women)
- Brain tumors represent ~ 1.3% of all cancers (adults and children)
- Metastatic brain tumors are most common and occur in 10-15% of people with cancer
- Primary brain tumors generally do not metastasize to other parts of the body
- Breast, lung and melanoma are most common cancers to metastasize to the brain
- Brain tumors in children are different from those in adults

Distribution of brain tumors by histology

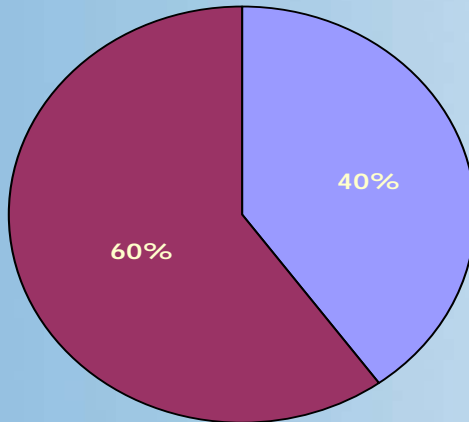


Gliomas account for 42% of all brain tumors and 77% of malignant brain tumors

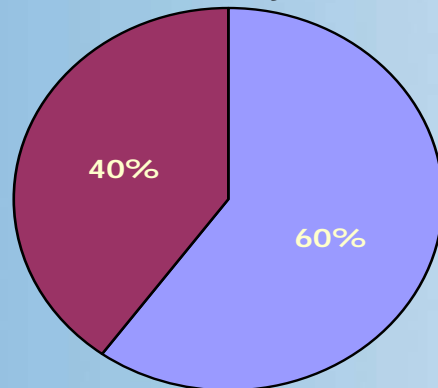
Source: CBTRUS, 2005

Distribution of brain tumors by age & grade

40-49 years old

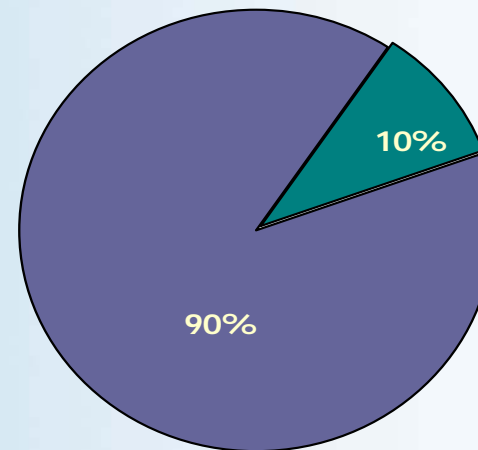


more than 60 years old



□ Grade III and IV gliomas

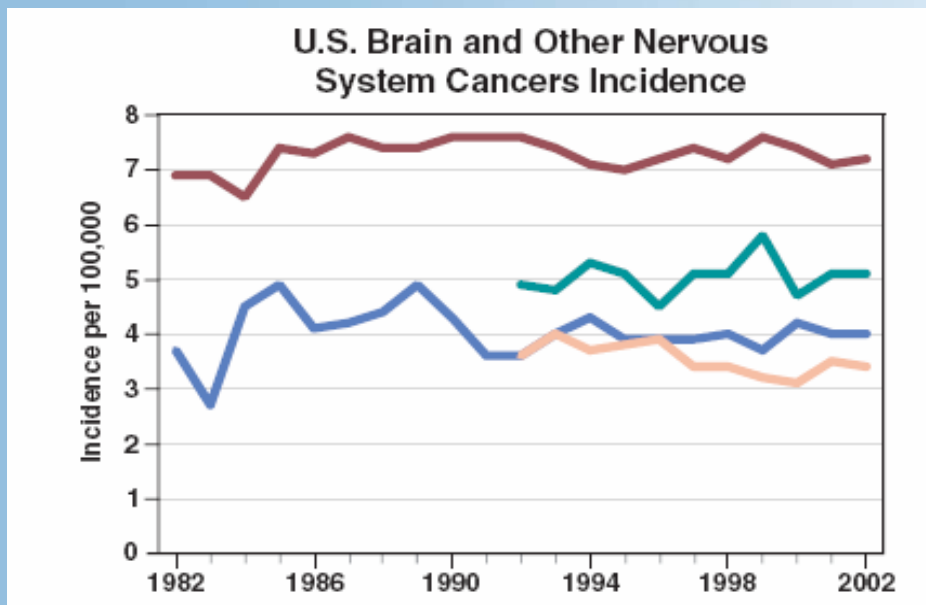
High grade tumors



■ Grade III gliomas

■ Grade IV gliomas

Distribution of brain tumors by ethnic group

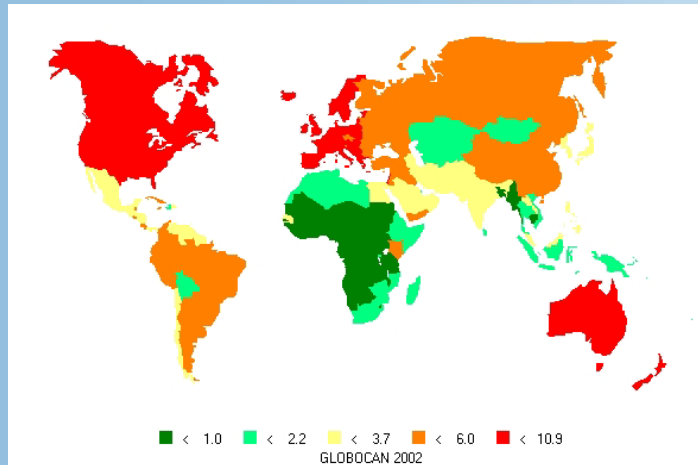


- Incidence rates are higher in Caucasian populations than in other ethnic groups
- These differences have also been observed in children

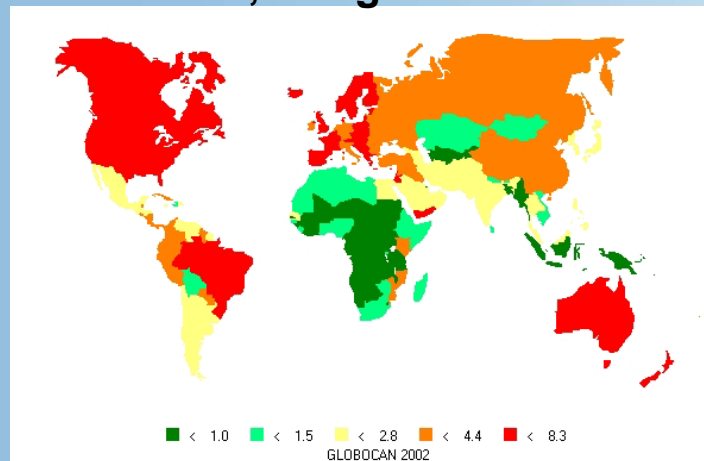
Source: American Cancer Society, 2005

Global distribution of brain cancer

Men, all ages



Women, all ages



- Incidence rates more elevated in industrialized countries (could be due to underreporting or ethnic differences in susceptibility)
- Men have higher incidence rates than women (independently of ethnic group)

Source: GLOBOCAN 2002 database

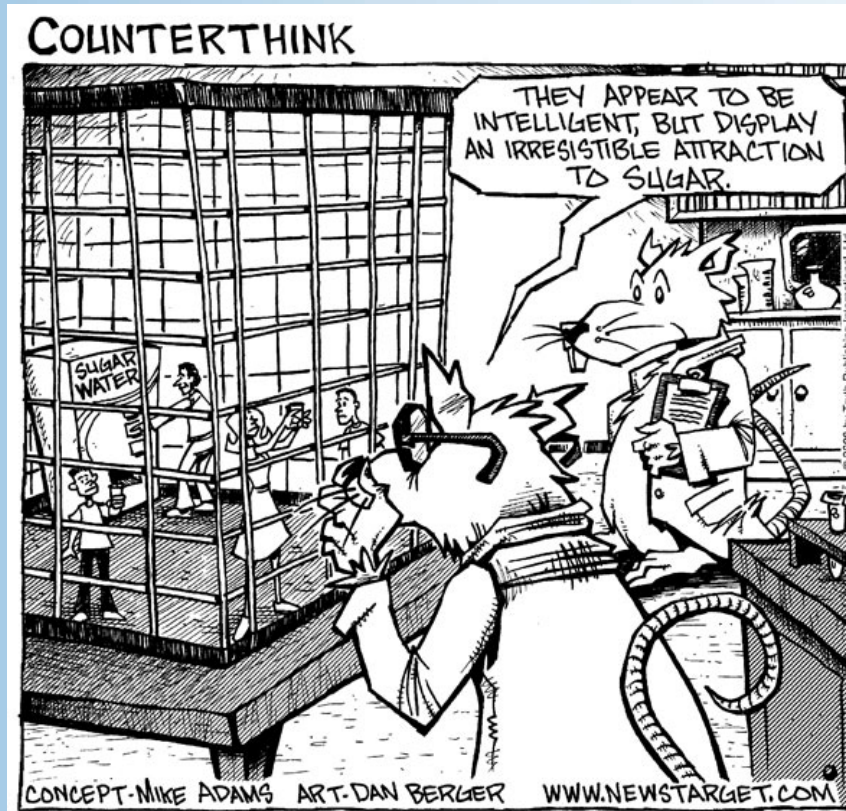
Risk factors of brain cancer

Epidemiologic studies of the effect of:



- Radiation
- Lifestyle
- Occupational and environmental exposures
- Genetic factors

Epidemiology

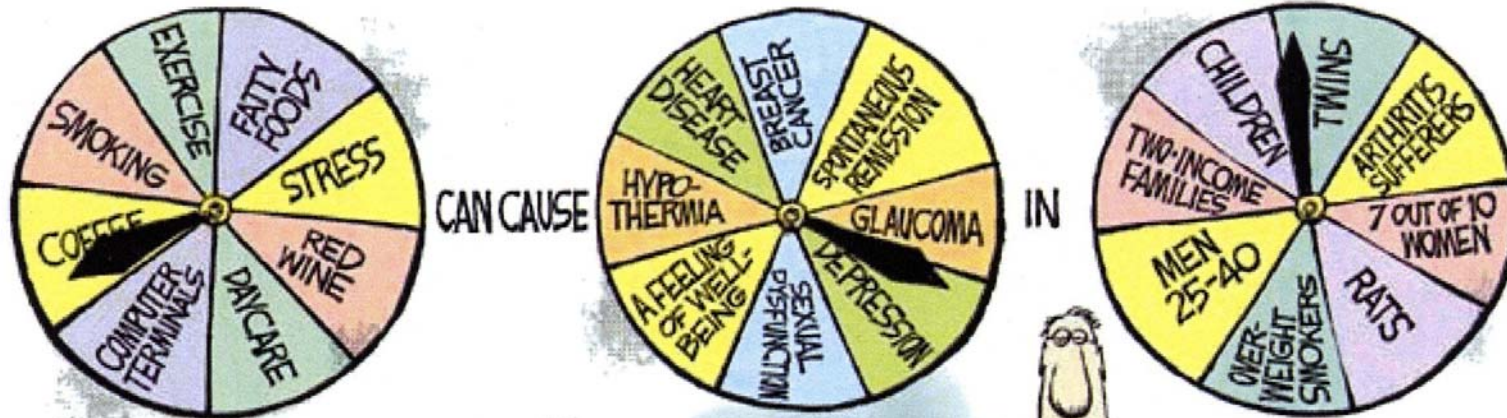


A scientific process that attempts to link the effects of factors such as lifestyle or exposure to toxic chemicals to disease

Limitations of epidemiologic studies

Today's Random Medical News from the New England Journal of Panic-Inducing Gobbledygook

JIM FISHMAN



CAN CAUSE IN

ACCORDING TO A REPORT RELEASED TODAY...

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Epidemiologic studies of brain tumors

Variation in:

- Study designs
- Population characteristics
- Information sources
- Measurement
- Classification

Reliance on proxy and historic information

Environmental exposures:

- Suspect agents can cross blood brain barrier

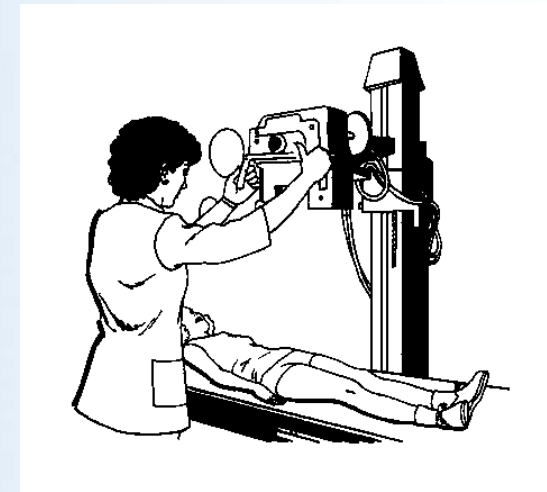
Established risk factors

High dose radiation	+++
Hereditary syndromes	+++
Man vs. woman	+
White vs. African-American	+
Increasing age	+++
Epilepsy, seizures, convulsions (probably an early symptom)	+
Exogenous hormones (for meningioma)	+

Ionizing radiation

Therapeutic X rays are only environmental factor unequivocally associated with an increased risk of brain tumors

- **Several studies: increase risk of brain cancer in children who received radiation for leukemia**
- **Atomic bomb survivors: dose-related excess of nervous system tumors**



Probable risk factors

- **Family history of brain tumors** +
- **Mutagen sensitivity** +
- **Allergies/asthma/elevated IgE** -
- **Chickenpox/
anti-varicella zoster virus IgG** -

Allergy & immunological conditions



- Reduced glioma risk has been attributed to allergy and allergic conditions
- Reduced risk for people who reported a history of infectious disease (colds, influenza)

Suggests an influence of immunological factors on development of gliomas, but molecular basis has not been elucidated

Probably not risk factors

- **Dental x-rays**
- **Head injury**
- **Residential power frequency EMF**
- **Prior cancers**
- **Filtered cigarette smoking**
- **Alcohol consumption**



Head injury

- **Case reports on occurrence of gliomas after a head injury at the same site**
- **Plausible association since trauma induces a strong proliferative astrogliosis**
- **Studies have found a weak but inconsistent association with adult and perinatal traumatic head injury and brain tumors**
- **Brain tumors may be a factor in development of falls and subsequent head injury**



Too few studies

- Cellular telephone use
- Diagnostic radiation (CT)
- Dietary intake
 - Calcium (high vs. low) –
 - Cured foods +
 - Antioxidants –
 - NSAIDs drugs –
- Genetic susceptibility factors

Cell phones



www.funnytimes.com

- Operate at radio frequencies, a form of EM energy
- Widespread use is just two decades old
- Decreasing levels of non-ionizing radiation with time and these levels vary across cell phone types

Cell phone use



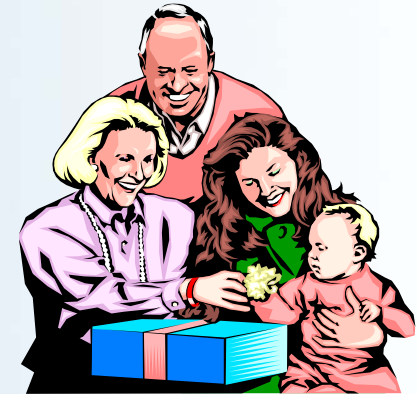
- Most early studies provide no evidence for association
- Positive association with malignant brain tumors in a study in Sweden
- Studies in US, Germany, France, and Japan, did not find associations with glioma, meningioma or acoustic neuroma
- INTERPHONE study in 13 European countries showed no increase in glioma or meningioma with use of cell phones

Genetic factors

- Different forms of genes involved in the metabolism of chemical carcinogens may be associated with higher susceptibility to glioma
- A study found that glioblastoma patients with mutations in either of two genes, IDH1 or IDH2, had a longer survival than patients whose tumors lacked either mutation
- Another study identified up to 31 genes that, when containing certain mutations, set the stage for the development of gliomas
- A third study showed that one particular gene, the ANXA7 gene, may make a good target for future treatments for glioblastomas

Family history

- **Familial cancer syndromes associated with tumors of nervous system:**
 - Li-Fraumeni syndrome
 - Neurofibromatosis 1
 - Turcot syndrome
- **Family members of glioma patients may be more susceptible to glioma development than general population**
- **Recent study found twice the risk of brain tumors in people with immediate relatives who had glioblastomas and four times the risk in those with relatives with astrocytomas**



Occupational exposure

Studies have shown associations with exposure to:



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- Vinyl chloride (glioblastomas)
- Arsenic, mercury, and petroleum products in men (gliomas)
- Polycyclic aromatic hydrocarbons
- Lead (gliomas)

Promising research avenues



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- Role of immune function
- Genetic components in families
- Metabolic and DNA-repair pathways
- Neurocarcinogen exposures
- Genes responsible for etiology and progression of brain tumors

Brain Tumor Epidemiology Consortium - open scientific forum to foster development of multicenter, international and inter-disciplinary collaborations that will lead to better understanding of etiology, outcomes, and prevention of brain tumors

An ounce of prevention is worth a pound of cure



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