Brain Tumors:
Where do they come from?

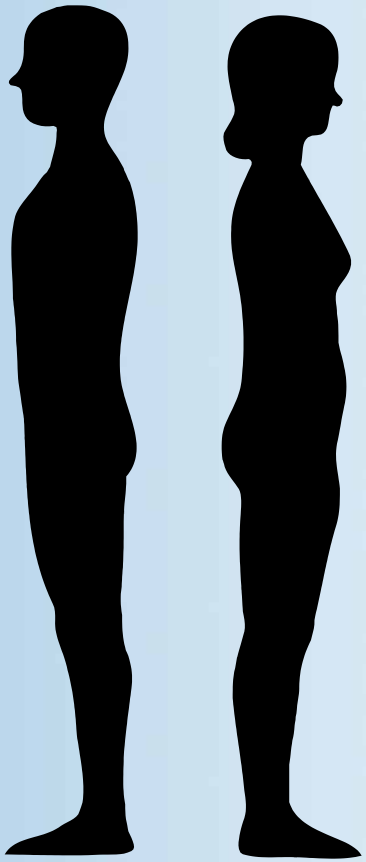
Tania Carreón-Valencia, MS, PhD
Assistant Professor of Epidemiology
Department of Environmental Health

Topics

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

Estimated new cases of cancer in US, 2011

Men 822,300		Women 774,370	
Prostate	29%	30%	Breast
Lung and bronchus	14%	14%	Lung and bronchus
Colon and rectum	9%	9%	Colon and rectum
Urinary bladder	6%	6%	Uterine corpus
Melanoma of the skin	5%	5%	Thyroid
Kidney and renal pelvis	5%	4%	Non-Hodgkin lymphoma
Non-Hodgkin lymphoma	4%	4%	Melanoma of the skin
Oral cavity and pharynx	3%	3%	Kidney and renal pelvis
Leukemia	3%	3%	Ovary
Pancreas	3%	3%	Pancreas
All other sites	19%	19%	All other sites

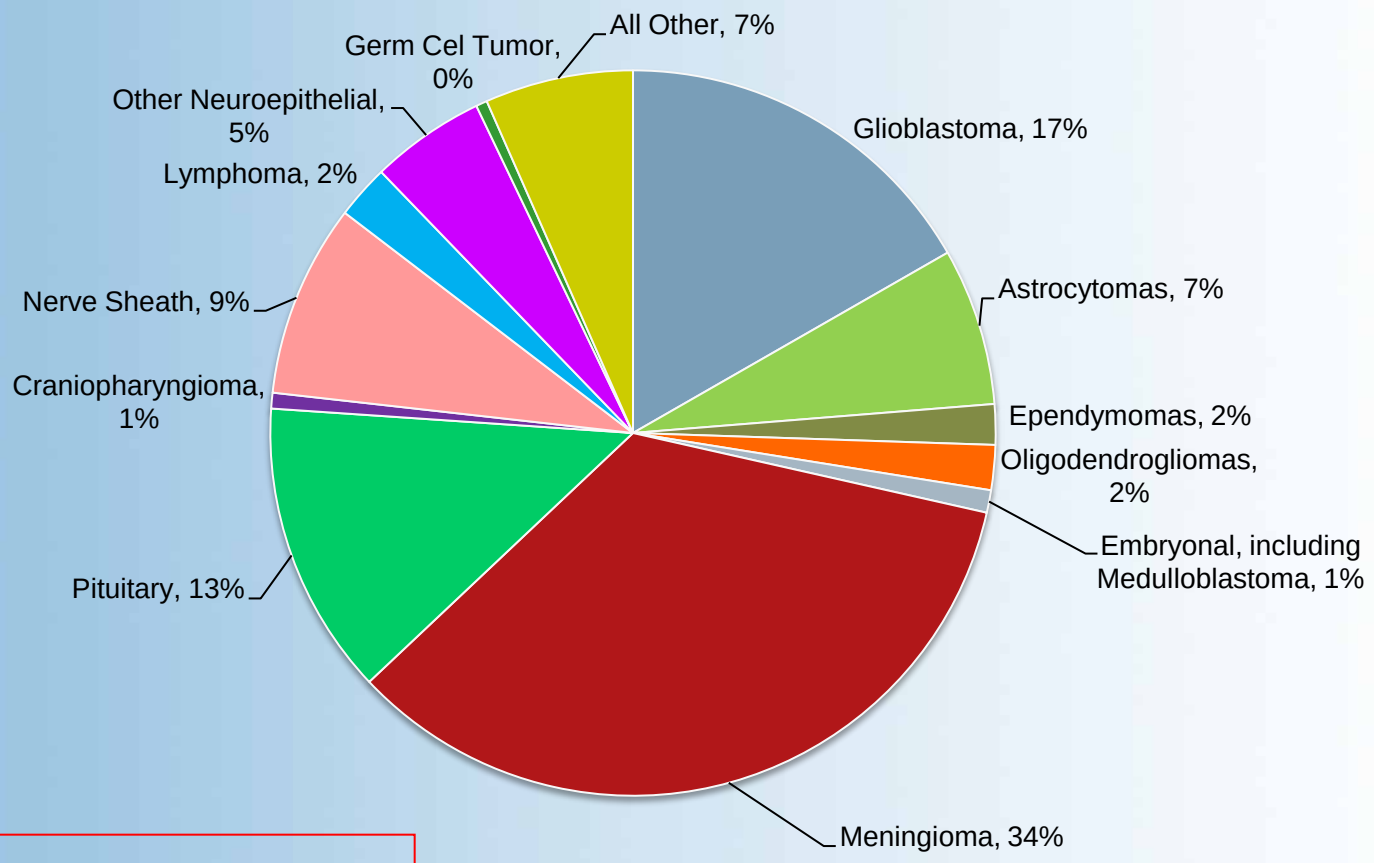


Source: American Cancer Society, 2011

Brain tumors

- In 2011, the estimated number of new cases of brain tumors will be 22,340 (12,260 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



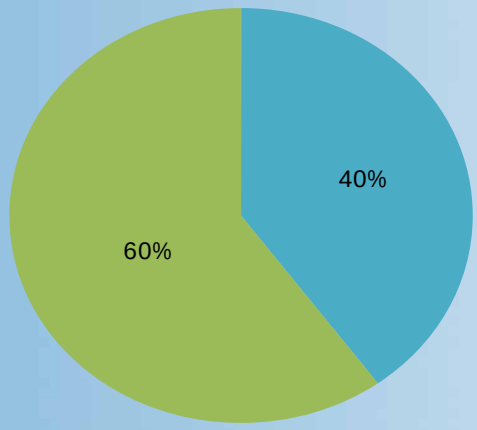
Gliomas account for 31% of all brain tumors and 80% of malignant brain tumors

Source: CBTRUS, 2011

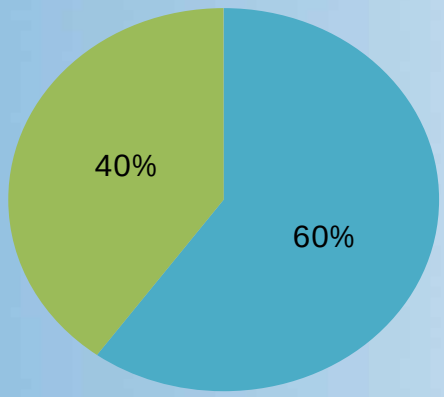
UC Neuroscience Institute

Distribution of brain tumors by age & grade

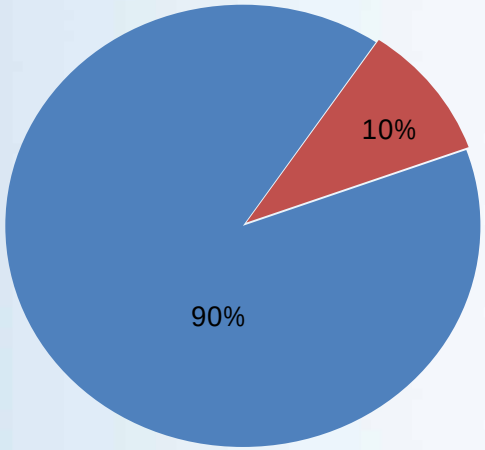
40-49 years old



more than 60 years old



High grade tumors

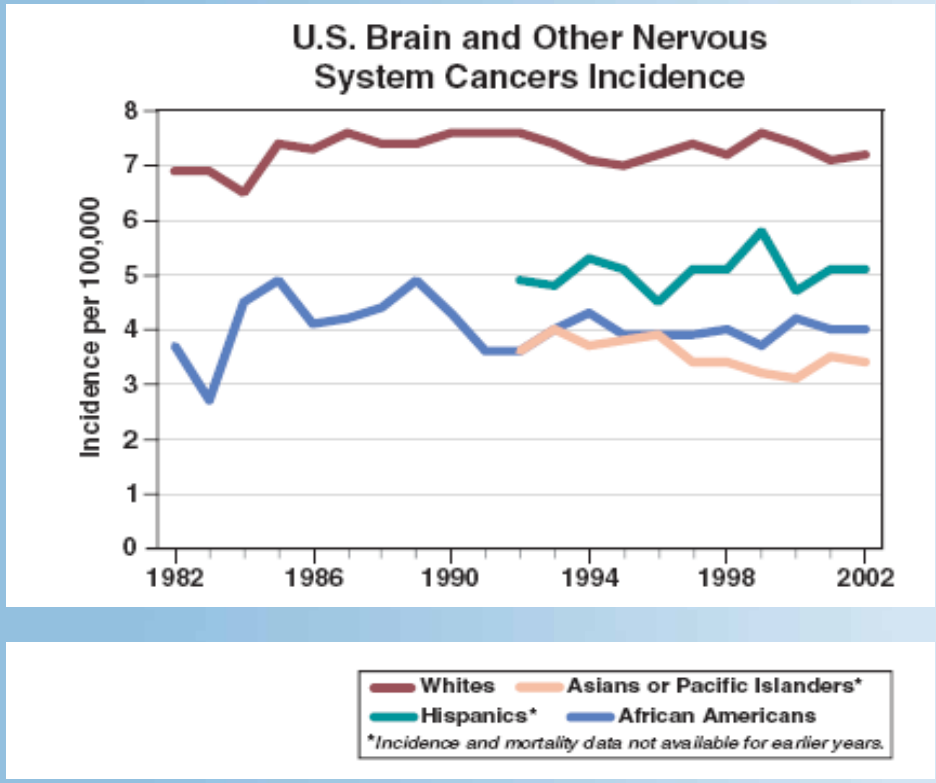


Grade III and IV gliomas

Grade III gliomas

Grade IV gliomas

Distribution of brain tumors by ethnic group

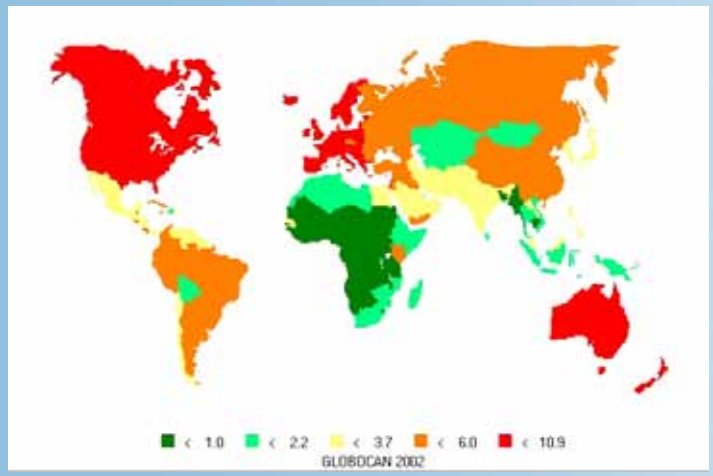


Source: American Cancer Society, 2005

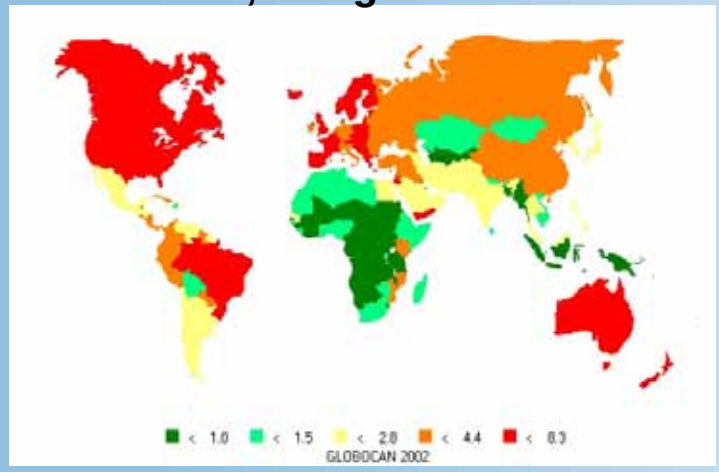
- Incidence rates are higher in Caucasian populations than in other ethnic groups
- These differences have also been observed in children

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)**

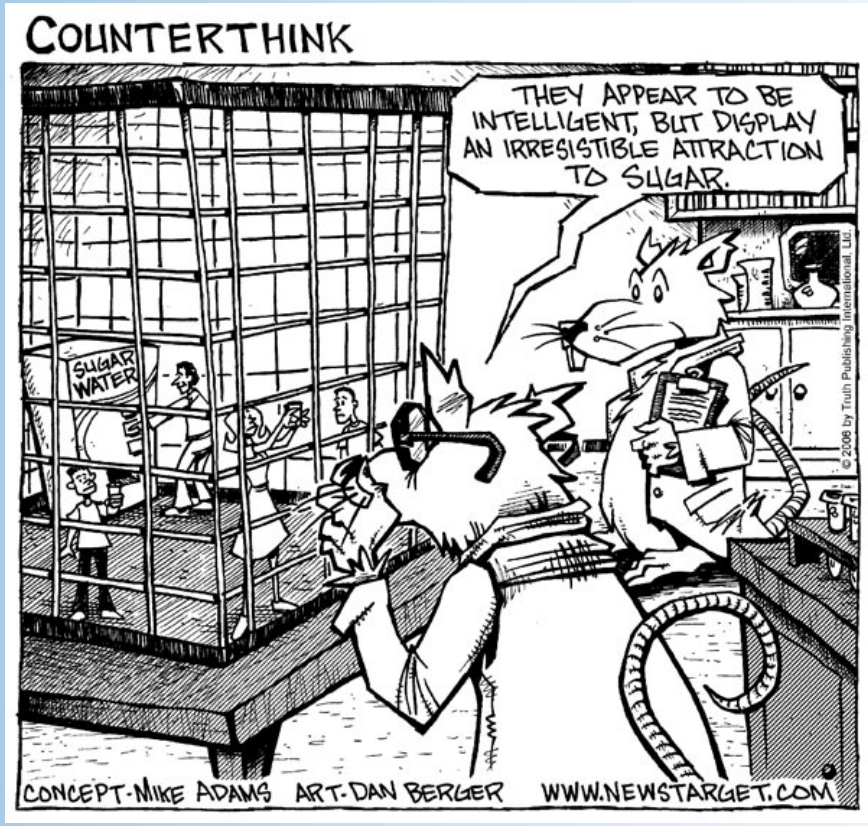
Source: GLOBOCAN 2002 database

Risk factors of brain cancer

Epidemiologic studies of the effect of:

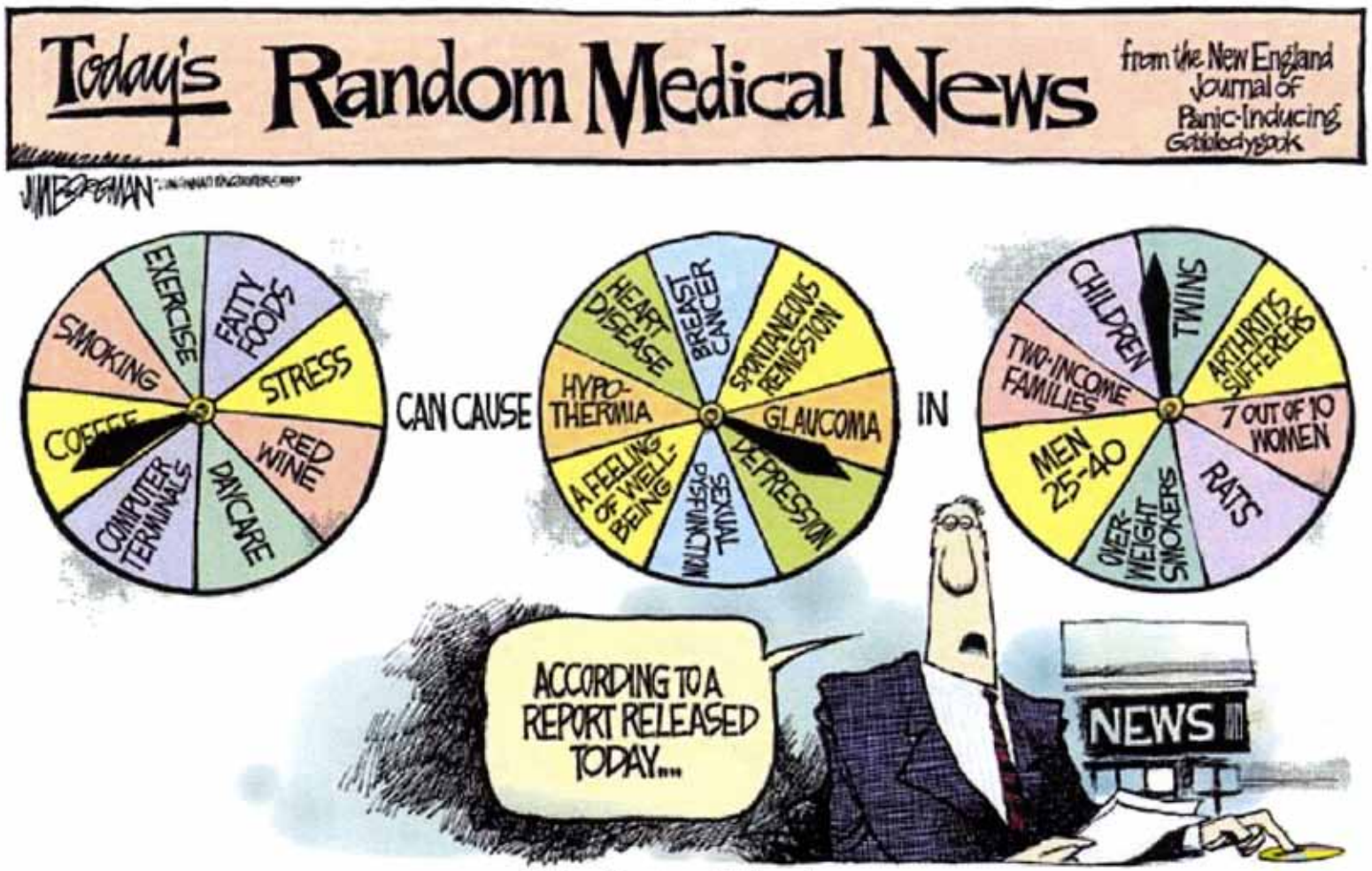
- **Radiation**
- **Lifestyle**
- **Occupational and environmental exposures**
- **Genetic factors**

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



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**

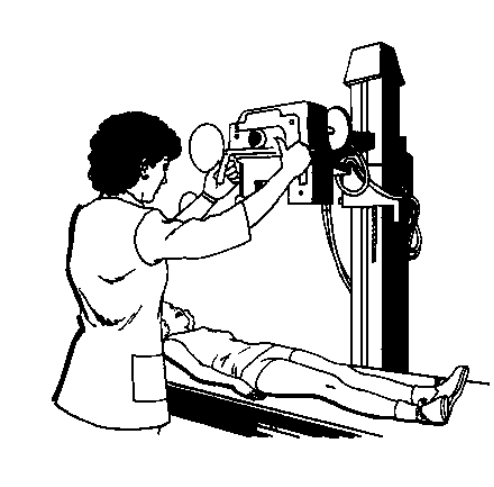
Established risk factors

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

- **Increased risk in children who received radiation for leukemia**
- **Increased risk in children who received low-dose radiation therapy to treat ringworm of the scalp**
- **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

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- 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
- The International Agency for Research on Cancer recently classified cell phone radiation as “possibly carcinogenic to humans”

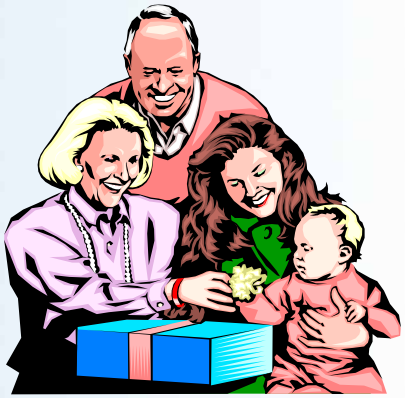
INTERPHONE study

- A study in 13 European countries, evaluated cell phone use among more than 5,000 people who developed gliomas or meningiomas and a similar group of people without tumors
- No link between brain tumor risk and the frequency of calls, longer call time, or cell phone use for 10 or more years
- Possible increased risk of glioma, and smaller suggestion of increased risk of meningioma, in the 10% of people who used their cell phones the most
- Increased risk for ipsilateral exposure (on the same side of the head as tumor) and for tumors in the temporal lobe, where RF exposure is highest

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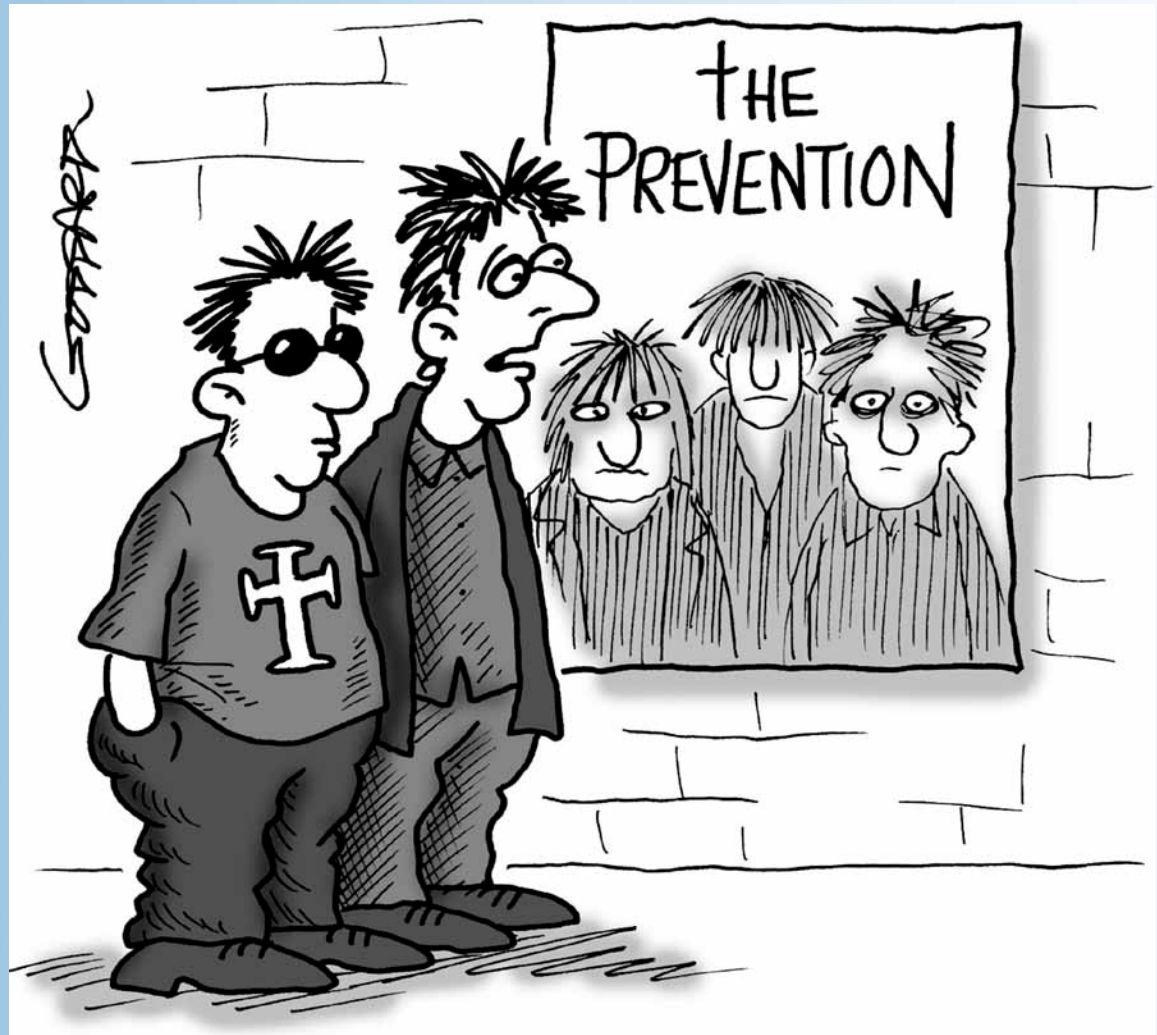
- Role of immune function
- Genetic components in families
- Metabolic and DNA-repair pathways
- Neurocarcinogen exposures
- Genes responsible for etiology and progression of brain tumors

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



"Apparently they're better than The Cure."