

Brain and Other Central Nervous System Cancers



Yesterday

- In 1975, the annual incidence of brain and other central nervous system (CNS) cancers, including cancers of the spinal cord, among adults in the United States was 5.9 new cases diagnosed for every 100,000 persons. The incidence of these cancers among children 19 years of age or younger was 2.1 new cases per 100,000 persons.
- In the same year, the annual mortality from brain and other CNS cancers among adults was 4.1 deaths per 100,000 persons; among children 19 years of age or younger it was 0.9 deaths per 100,000 persons.
- Magnetic resonance imaging (MRI), which facilitates diagnosis as well as treatment of brain and other CNS tumors with surgery and radiation therapy, first became widely available in the 1980s.
- Clinical trials in the 1970s and 1980s showed that adding radiation therapy to surgery prolonged the survival of patients with glioma, a type of brain tumor that accounts for approximately 70% of the malignant primary brain tumors diagnosed in adults in the United States each year.
- Chemotherapy was not a standard treatment for brain tumors because most early chemotherapy drugs could not cross the blood–brain barrier. One class of drugs, the nitrosoureas, was found to cross the blood–brain barrier and was shown in clinical trials to produce a small but clear improvement in the length of patient survival when combined with surgery and radiation therapy.

Today

- In 2007, the latest year for which we have updated statistics, the U.S. incidence rate of brain and other CNS cancers among adults was 6.4 new cases per 100,000 persons; among children 19 years of age or younger it was 2.9 new cases per 100,000 persons. The higher incidence rates observed today are likely due, in part, to an improved ability to diagnose brain and other CNS tumors with advanced imaging technologies.
- MRI is now an accepted standard technology for imaging brain and other CNS tumors. A newer technology called functional MRI, which measures changes in blood flow that accompany brain activity, can be helpful in determining how well brain regions are working, in assessing potential risk from surgery, and in planning treatment. New intraoperative MRI machines can be used to monitor the extent of tumor removal during surgery.
- The orally administered drug temozolomide, which first became available in the United States in 1999, can prolong the survival of patients with glioma when combined with radiation therapy. High-dose chemotherapy regimens for the treatment of some types of childhood brain tumor can delay the need for radiation therapy, possibly reducing harm to the developing brain.
- Antiangiogenesis agents – drugs that block the growth of new blood vessels to tumors – have shown some promise in the treatment of gliomas. Gliomas are highly vascularized tumors, meaning they have a large number of blood vessels. Drugs that block the development of these blood vessels are being tested in clinical trials of patients with brain tumors. Based on the promising results of two clinical trials, one of which was conducted at the NIH, the Food and Drug Administration gave accelerated approval in May 2009 to the antiangiogenesis agent bevacizumab (Avastin®) for the treatment of recurrent glioblastoma, which is the most common form of glioma. Two phase III clinical trials, including one supported by NIH, are testing the drug in newly diagnosed patients.
- Advanced radiation therapy techniques that target tumor tissue more precisely and reduce radiation damage to surrounding normal tissue (such as 3-dimensional conformal therapy, stereotactic radiation therapy, and intensity-modulated radiation therapy) are being refined.
- Researchers are exploring the use of other novel approaches, such as targeted therapy, gene therapy, immunotherapy, and vaccine therapy for the treatment of brain and other CNS cancers.

- A new scale developed by NIH, which is based on tumor size, tumor location, and a patient's ability to perform everyday tasks, can help surgeons identify which patients with glioblastoma will benefit from additional surgery when their tumor recurs.
- Scientists are beginning to understand the genetic complexity of brain tumors, which facilitates the design of more effective treatments. An understanding of the genetic changes that drive the growth of brain tumors will allow researchers to choose the best candidate targeted drugs for testing in clinical trials.
- In 2008, The Cancer Genome Atlas (TCGA) (<http://tcga.cancer.gov/>) project reported the first results of its large-scale, comprehensive study of gene changes in glioblastoma (a type of glioma). These results identified three previously unrecognized mutations that occur frequently in glioblastoma and three cell-signaling pathways that may help drive tumor growth. The results also shed new light on molecular mechanisms that may make tumors resistant to some chemotherapy drugs. In 2010, additional results from TCGA showed that glioblastoma comprises four different molecular subtypes that have different responses to chemotherapy and radiation therapy.
- The Glioma Molecular Diagnostic Initiative (<http://home.ccr.cancer.gov/nob/mds/research.asp#1>) has already made extensive genetic and related clinical data from more than 800 glioma patients available to researchers worldwide in a public data repository and bioinformatics work space known as REMBRANDT (<http://caintegrator-info.nci.nih.gov/rembrandt>).

Despite tremendous advances in our understanding of brain cancer biology, substantial progress in brain tumor diagnosis and treatment, and marked improvements in the quality of life of brain tumor patients, the mortality rate for brain and other CNS cancers has remained largely unchanged over the past 30 to 40 years.

Tomorrow

- We will continue to explore the use of new imaging technologies in the diagnosis, treatment, and follow-up care of brain and other CNS cancers. For example, magnetic resonance perfusion imaging is a technology that enables measurement of the volume of blood flowing through the brain. This information will allow better estimates of tumor grade, size, and location

before surgery and permit recurrent tumor tissue to be distinguished from damage to brain tissue caused by radiation therapy, thereby reducing the need for follow-up surgical biopsies. In addition, imaging technologies such as positron emission tomography (PET), *single photon emission computed tomography* (SPECT), and diffusion-weighted MRI can help measure tumor metabolic activity, tumor cell proliferation, and the amount of oxygen that reaches tumor cells.

- We will refine methods of delivering chemotherapy drugs and other agents to the brain and CNS, including the development of drugs that have the ability to penetrate the blood-brain barrier. Other delivery techniques, such as convection-enhanced delivery, in which drugs or other anticancer agents are delivered under pressure (convection) through a catheter that is inserted directly into or near a tumor, may prove valuable.
- We will continue to explore the potential of new antiangiogenesis agents in controlling tumor growth.
- Intensive research into the genetic changes that lead to the formation of brain and other CNS cancers, through TCGA and other collaborative projects, will yield new opportunities for developing therapies that target these changes.
- We will expand our understanding of the role that tumor stem cells play in the formation of brain and other CNS tumors and their resistance to treatment and will use that knowledge to develop new therapies that target tumor stem cell signaling pathways. First discovered in 2003, brain tumor stem cells make up only a small proportion of the cells in human brain tumors, but they may drive tumor growth and metastasis and contribute to resistance to treatment.

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