

Care of the Adult Patient with a Brain Tumor

AANN Clinical Practice Guideline Series

This publication was made possible by an educational grant from the American Brain Tumor Association



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Preface

In 1997, the American Association of Neuroscience Nurses (AANN) created a series of patient care guidelines, the *AANN Reference Series for Clinical Practice*, to meet its members' needs for educational tools. To better reflect the nature of the guidelines and the organization's commitment to developing each guideline based on current literature and evidence-based practice, the name of the series was changed in 2007 to the *AANN Clinical Practice Guideline Series*.

The goal of this guideline is to offer evidence-based recommendations on nursing activities that have the potential to maximize outcomes for adult patients with brain tumors. Not all recommendations concern activities independently performed by registered nurses (RNs), but nurses are responsible for implementing and monitoring the outcomes of these activities. The evidence presented here may help nurses make appropriate choices when caring for patients with brain tumors. Depending on the scope of practice regulations, advanced practice nurses

may have independent or collaborative responsibilities for activity performance. Thus, this guideline may assist them in the management of patients with brain tumors as well. Resources and recommendations must describe the best practices that can enable RNs to provide optimal care for patients with brain tumors. Accordingly, adherence to these guidelines is voluntary, and the ultimate determination regarding guideline application must be made by practitioners in light of each patient's individual circumstances. This reference is an essential resource for nurses providing care to the adult patient with a brain tumor. It is not intended to replace formal learning, but rather to augment the clinician's knowledge base and provide a readily accessible reference tool. The nursing profession and AANN are indebted to the volunteers who have devoted their time and expertise to this valuable resource, which was created for those who are committed to excellence in the care of adult patients with brain tumors.

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I. Introduction

A. Purpose

1. The purpose of this guide is to review and evaluate literature about brain tumors, with a focus on the adult patient, and to create a reference for neuroscience nurses who care for patients with brain tumors throughout their lifespan across the continuum of care.

B. Guideline goal

1. The goal of this guideline is to help nurses provide consistent, current, and evidence-based care to patients with brain tumors and their families. Topics include epidemiology; anatomy and physiology; emergent care; diagnosis; treatment including surgery, radiation, and chemotherapy; symptom management; and care at the end of life.

C. Assessment of scientific evidence

1. A review of literature published between January 2000 and January 2013 was conducted using the PubMed/MEDLINE, CINAHL, Cochrane Review, Embase, and Ovid databases with the following search terms: brain tumor, brain neoplasm, glioma, astrocytoma, glioblastoma, oligodendrogliomas, brain metastases, emergent care, diagnostic tests, acute care, magnetic resonance imaging (MRI), diffusion-weighted imaging, vasogenic edema, glucocorticoids, corticosteroids, Idh1 mutation, molecular pathogenesis, nephrogenic systemic fibrosis, cisplatin, carboplatin, procarbazine, vincristine, methotrexate, O⁶-methylguanine-DNA methyltransferase (MGMT) promoter, 1p19q (chromosome) codeletion, carmustine wafer, embolization, cortical mapping, hemorrhage, hypertension, cerebrospinal fluid (CSF) leaks, seizures, infection, perilesional edema, brain metastasis, brain tumor radiation therapy, brain tumor chemotherapy, epilepsy, seizure, depression, anxiety, dysphoria, cognitive, fatigue, venous thromboembolism, anti-coagulation, support, quality of life, body image, sexuality, intimacy, nausea and vomiting, steroids, edema, rehabilitation, support, temozolomide, bevacizumab, brain tumor pathology, brain tumor classification, brain tumor incidence, brain tumor metastasis incidence, brain tumor etiology, brain tumor risk factors, brain tumor symptoms and brain tumor molecular biology, malignant brain tumor, survivor, end of life, symptom management, palliative care, and caregivers. Several publications dated earlier than 2000 are included because of their historical clinical significance.
2. The National Comprehensive Cancer Network's (NCCN) NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) were accessed

and incorporated into this document as appropriate and needed.

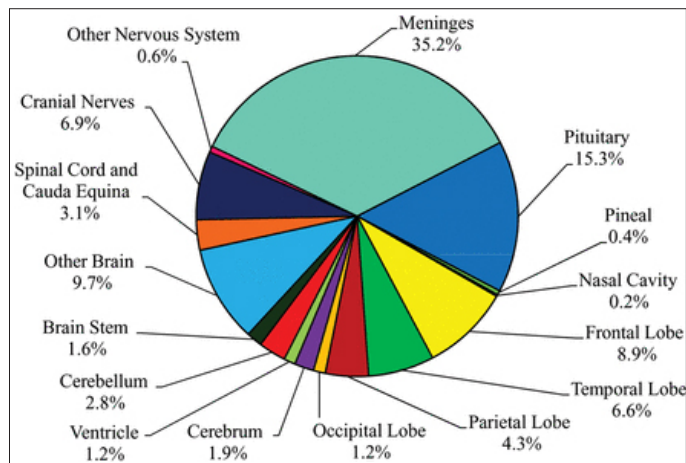
3. For the *AANN Clinical Practice Guideline Series*, data quality is classified as follows:
 - a. Class I: Randomized controlled trials without significant limitations or meta-analysis
 - b. Class II: Randomized controlled trials without important limitations (e.g., methodologic flaws or inconsistent results) and observational studies (e.g., cohort or case-control)
 - c. Class III: Qualitative study, case study, or series
 - d. Class IV: Evidence from expert committee reports and expert opinion of the AANN guideline panel; standards of care and clinical protocols that have been identified.
4. The *Clinical Practice Guidelines* and recommendations for practice are established based upon the evaluation of the available evidence (AANN, 2005; Guyatt & Rennie, 2002; Melnyk, 2004).
 - a. Level 1 recommendations are supported by Class 1 evidence.
 - b. Level 2 recommendations are supported by Class II evidence.
 - c. Level 3 recommendations are supported by Class III and IV evidence.

II. Overview

A. Epidemiology

1. Incidence of primary brain tumors in adults (Central Brain Tumor Registry of the United States [CBTRUS], 2012)
 - a. Overall incidence is 19.89 per 100,000 person-years.
 - b. Incidence does not differ across geographic regions in the United States.
 - c. Overall incidence, both malignant and nonmalignant, increases with age.
 - i. Median age at diagnosis among all patients with brain tumors is 57 years (Fisher, Schwartzbaum, Wrensch, & Wiemels, 2007).
 - ii. Tumors may be located throughout the central nervous system (CNS; **Figure 1**; CBTRUS, 2012). The meninges is the most common location for a CNS tumor.
 - d. Incidence varies based on tumor histopathology (CBTRUS, 2012).
 - i. Malignant tumors: Tumors of epithelial tissue (gliomas) are the most common, followed by lymphoma.
 - ii. Nonmalignant tumors: Meningiomas are most common, followed by sellar region tumors and nerve sheath tumors.
 - e. Age-related incidence of specific tumor types varies by histopathology (CBTRUS, 2012).
 - i. For example, pilocytic astrocytoma and medulloblastoma incidence decreases

Figure 1. Distribution of Tumors in the Central Nervous System



From "CBTRUS Statistical Report: Primary Brain and Central Nervous System Tumors Diagnosed in the United States in 2005–2009" by T.A. Dolecek, J.M. Propp, N.E. Stroup, & C. Kruchko, 2012, *Neuro-Oncology*, 14 (suppl 5): v1–v49. doi: 10.1093/neuonc/nos218. Reproduced with permission from Oxford University Press.

- with age, and glioblastoma incidence increases with age.
- ii. 93% of individuals with brain tumors are 20 years of age or older at time of diagnosis.
- f. Gender characteristics
 - i. Overall incidence: men (43%), women (57%)
 - a) Incidence is higher in women for meningioma and pituitary tumors.
 - b) Glioblastoma is 1.6 times more common in men than women.
 - ii. Incidence is higher in men based on anatomic location, particularly for the cerebral hemispheres.
- g. Overall incidence of brain tumors is higher in nonHispanic whites than blacks.
 - i. The exceptions are craniopharyngioma, pituitary, and meningioma, for which incidence rates are higher in blacks than whites.
 - ii. Glioblastoma is more than two times more common in whites than blacks.

Nursing recommendation: Nurses should be aware that knowledge about epidemiology of primary brain tumors is evolving (Level 3). Nurses should gather epidemiologic information when conducting an assessment (Level 3).

2. Incidence of metastatic brain tumors that originate outside of the CNS and spread secondarily to the CNS (Gavrolicic & Posner, 2005)
 - a. The overall incidence of secondary brain tumors (metastases) is unknown but appears to be increasing (Davis, Dolecek, McCarthy, & Villano, 2012).

- b. Brain metastases are twice as common as gliomas.
- c. Among patients, 47% have single-brain metastases, and 53% have multiple-brain metastases.
 - i. Among patients, 70% have three or fewer brain metastases, making them amenable to focal therapy.
- d. Among brain metastases, 72% occur within 1 year of initial cancer diagnosis, but metastases can occur at any time during a cancer illness. With the exception of lung cancer, it is rare to see symptomatic brain metastases at initial diagnosis.
- e. Routine brain imaging is not recommended for people with cancer unless they have small-cell lung cancer or melanoma.
- f. The most common sources for brain metastases are (in descending order): lung, breast, melanoma, renal, and colon cancers (Louis, Ohgaki, Wiestler, & Cavenee, 2007).
- g. Appearance of a brain metastasis after systemic chemotherapy does not imply tumor resistance to the chemotherapy. Metastasis may be attributable to the inability of the chemotherapy to cross the blood-brain barrier (BBB).

Nursing recommendation: Nurses should be aware that as survival from primary cancers improves, the incidence of brain metastases increases (Level 2). Routine screening for brain metastases is not recommended unless a patient has small-cell cancer or melanoma (Level 1). Nurses should gather epidemiologic information when conducting an assessment (Level 3).

3. Survival rates (CBTRUS, 2012)
 - a. The overall 5-year survival rate for patients with brain tumors is 33.72%; The 10-year survival rate is 27.92%.
 - b. Survival rates vary by tumor histopathology. Glioblastoma is associated with a 4.7% 5-year survival rate and a 2.32% 10-year survival rate, and pilocytic astrocytoma is associated with a 94% 5-year survival rate and 91.32% 10-year survival rate.
 - c. Women have slightly higher overall survival rates for brain tumors; pineal and brain stem locations are associated with slightly higher 5-year survival rates among men.
 - d. Factors contributing to overall prognosis include age, Karnofsky Performance Status (KPS) Scale, extent of resection, volume of residual disease, presence of necrosis, preoperative MRI findings, enhancement, therapy used, tumor size, noncentral tumor location, and albumin level (Fisher et al., 2007; Lacroix et al., 2001).

- e. Influence of genetic factors
 - i. Codeletion of 1P/19q chromosome: The hallmark molecular signature of oligodendrogliomas may indicate a favorable response to chemotherapy in addition to improved survival times (Cairncross et al., 1998).
 - ii. Isocitrate dehydrogenase (IDH1) and IDH2 mutations have been implicated in the tumor biology of gliomas and may be associated with a favorable prognosis and overall prolonged survival (Ichimura, 2012; Qi et al., 2012).
 - iii. MGMT promoter Status: MGMT is a suicide DNA repair enzyme that protects cells against damage from ionizing radiation and alkylating agents. Glial cells with hypermethylation (MGMT promoter) respond better because they lack the ability to efficiently repair the damage introduced by alkylation (Bondy et al., 2008; Esteller et al., 2000; Stupp et al., 2009).
 - iv. Epidermal growth factor receptor (EGFR) gene aberrations: EGFR is the most frequently amplified and overexpressed gene and has been associated with shorter survival times and poorer prognosis (Shinojima et al., 2003).
 - v. Loss of heterozygosity of 10q is associated with a poorer prognosis.
 - vi. People with p53 mutation are more likely to have a secondary glioblastoma, a tumor that would initially be diagnosed as a lower-grade tumor that develops into Grade 4 cells, and people with EGFR amplification are more likely to have a primary glioblastoma, a tumor that has Grade 4 cells from the time of diagnosis (Fisher et al., 2007).
- d. Allergies and other immune disorders may protect against brain tumors.
- e. Familial patterns of brain tumors have been identified, but genetic transmission cannot be distinguished from environmental factors.
 - i. Genetic syndromes such as neurofibromatosis I and II and tuberous sclerosis have been associated with brain tumor risk in families.
 - ii. Fewer than 1% of people with glioblastoma have a genetic syndrome.

Nursing recommendation: Nurses should be aware that the only known risk factor for development of a brain tumor is previous exposure to ionizing radiation (and they should educate patients to avoid ionizing radiation when possible [Level 1]). Nurses should perform a comprehensive and thorough assessment to identify potential risk factors in patients with a brain tumor (Level 3).

B. Classification

Brain tumors are classified on the basis of histopathology (Louis et al., 2007).

1. Cell of origin
 - a. Gliomas are tumors originating from glial cells. Glial cells include astrocytes (which develop into astrocytomas), ependymal cells (which develop into ependymomas), and oligodendrocytes (which develop into oligodendrogliomas).
 - b. Meningiomas arise from meningeal cells.
 - c. Neuromas arise from Schwann cells.
 - d. Germinomas arise from germ cells.
 - e. Pituitary adenomas arise from the adenohypophysis of the pituitary.
 - f. Craniopharyngiomas, dermoids, and epidermoids arise from embryonic remnants.
 - g. Metastatic tumors arise outside of the CNS and move into the CNS via direct or hematologic spread.
2. Histological grading is a means of predicting biological behavior. Such grading also is known as the World Health Organization (WHO) Classification System (Louis et al., 2007).
 - a. Grade I: relatively circumscribed, noninfiltrating, low proliferative potential
 - b. Grade II: atypical cells, well differentiated, infiltrating, low proliferative potential
 - c. Grade III: (anaplastic) diffusely infiltrating, nuclear atypia, significant proliferative activity
 - d. Grade IV: (glioblastoma) poorly differentiated, presence of necrosis and/or microvascular proliferation
 - e. Other factors such as mitotic activity influence overall histopathologic status and prognosis.

- Nursing recommendation:** Survival varies widely and nurses should educate patients regarding the meaning of published survival rates and the implications for individual care (Level 1). The nurse's role also focuses on facilitating a positive yet realistic outlook for individual patients (Level 3).
4. Risk factors (Fisher et al., 2007)

The cause of brain tumors is unknown.

 - a. Exposure to ionized radiation is the only known risk factor that can be modified.
 - b. Very low magnetic radiation from cell phone use has not been shown to increase risk for brain tumors but warrants further investigation (Little et al., 2012; Myung et al., 2009).
 - c. Evidence about environmental and behavioral risk factors contributing to brain tumors has been inconclusive.

- i. MIB-1, a monoclonal antibody, is used as a labeling index to identify cell proliferation. It augments prognostic information based on morphologic tumor characteristics (Ambrose, Khosla, Ghosh, Mallikarjuna, & Annapurneswari, 2011).
 - ii. MIB-1 represents a measure of mitotic activity that is more sensitive than measuring numbers of mitotic figures; the higher the value, the higher the mitotic activity.
3. The terms *malignant* and *benign* are less meaningful when discussing brain tumor pathology. *Malignant* or *benign* refer to histological characteristics, but location, tumor behavior, and patient factors (e.g., age and general health) also play an important role in patient outcomes (Stark, van de Bergh, Hedderich, Mehdorn, & Nabavi, 2012).
4. Location also is important in classifying tumors. A tumor may be histologically nonmalignant but located in an eloquent location that prevents resection or aggressive treatment, or it may be located where minimal change can cause maximum neurologic damage (CBTRUS, 2012).
- a. 61% of all primary brain and CNS gliomas occur in the four lobes of the brain.
 - i. Frontal (25.3%)
 - ii. Temporal (19.6%)
 - iii. Parietal (12.7%)
 - iv. Occipital (3.3%)

Nursing recommendation: Nurses should be aware of the nomenclature of tumors as well as their histopathologic classification so they can educate patients and families accordingly (Level 2). Nurses can use their understanding of tumor location to direct assessment (Level 3).

C. Pathophysiology (McCance & Huether, 2010)

1. Primary brain tumors develop when intracellular changes occur that alter cell differentiation, dysregulate the process of apoptosis, and change cell surface so that immune mechanisms are turned off.
2. Brain tumors cause symptoms by several mechanisms:
 - a. directly infiltrating tissue
 - b. producing adjacent edema
 - c. compressing adjacent structures
 - d. irritating surrounding tissue
 - e. blocking flow of CSF
 - f. creating new blood vessels that hemorrhage.
3. Symptoms can be generalized or localized (Mogensen, Stewart-Amidei, Arzbaecher, & Lupica, 2010).
 - a. General symptoms
 - i. Seizures
 - ii. Cognitive-behavioral deficits
 - iii. Decreased level of responsiveness

- iv. Fatigue
- b. Symptoms associated with increased intracranial pressure (ICP)
 - i. Headache
 - ii. Vomiting
 - iii. Papilledema
- c. Localized symptoms are based on anatomic location (Table 1).

| Tumor Site | Associated Signs and Symptoms |
|----------------|---|
| Frontal | Hemiparesis, difficulties in higher-level functions, personality changes, behavior and mood changes, fluent speech deficits |
| Temporal | Hemiparesis, visual field deficits, memory deficits, speech and language deficits, psychomotor seizures |
| Parietal | Sensory deficits, neglect, difficulties with right-left discrimination |
| Occipital | Visual deficits, homonymous hemianopsia |
| Ventricular | Increased intracranial pressure, obstruction |
| Cerebellum | Ataxia, incoordination, nystagmus, nausea |
| Brain stem | Lower cranial nerve deficits, motor and sensory deficits, ataxia, incoordination, nystagmus, nausea, vomiting |
| Cranial nerves | Deficits related to the specific cranial nerve |

Source. Adapted from "Nervous system tumors" by K. Mogensen, C. Stewart-Amidei, J. Arzbaecher, & K. Lupica, 2010, In M. K. Bader & L. R. Littlejohns (Eds.), *AANN Core Curriculum for Neuroscience Nursing* (5th ed.). Glenview, IL: American Association of Neuroscience Nurses.

- d. Symptom clusters have been identified that are unique to the brain tumor population (Armstrong, Cohen, Eriksen, & Hickey, 2004; Fox, Lyon, & Farace, 2007).
 - i. Focal neurologic symptoms
 - ii. Seizures
 - iii. Headache
- e. Symptoms may worsen during treatment; worsening symptoms do not always indicate worsening disease.

Nursing recommendation: Nurses should be aware that the significance of symptom clusters in people with brain tumors requires further elaboration/delineation. Nurses should be able to distinguish between general and focal symptoms (Level 3). Nurses should perform a focused assessment based upon tumor location and related involved anatomy (Level 3). Nurses should use knowledge of the ways that tumors cause symptoms when educating patients about actual or anticipated symptoms (Level 3).

Emergent and initial care: Specific activities must take place immediately when a patient presents with a neurological injury or illness. This section provides guidelines pertaining to emergent and initial care for patients with neurological symptoms that may lead to a brain tumor diagnosis. Patients who present with a brain tumor exhibit a wide range of signs and symptoms (Table 1).

D. Peritumoral edema

Peritumoral edema is common at presentation and is the cause of most initial symptoms (Lacy, Saadati, & Yu, 2012), and a significant contributor to morbidity and mortality.

1. Vasogenic edema (white matter swelling) occurs because of disruption to the BBB (Gomes, Stevens, Lewin, Mirski, & Bhardwaj, 2005; Lacy et al., 2012).
2. Edema can cause or exacerbate neurologic symptoms, increase ICP, produce obstructive hydrocephalus, and cause pain (Kaal & Vecht, 2004; Lacy et al., 2012).
 - a. Of all headaches reported by patients with brain tumors, between 33% and 71% are related to edema and increased pressure and traction on pain-sensitive structures (Goffaux & Fortin, 2010).
3. Corticosteroids are used to control cerebral edema in symptomatic patients (Galicich, French, & Melby, 1961; Gomes et al., 2005; Lacy et al., 2012; Pace, Metro, & Fabi, 2010).
 - a. Dexamethasone (Decadron) is the preferred drug of choice because of its lack of mineralocorticoid effects and long half-life.
 - b. Most patients respond to initial doses of 4–8 mg/day in divided doses, although higher doses have been used (Gomes et al., 2005).
 - i. A common dosage is 16 mg/day.
 - ii. Intravenous (IV) dosing is not required because oral absorption is excellent.
 - c. Improvement in symptoms often can be seen within 24–72 hours after initiation.
 - d. Multiple side effects are associated with steroids, especially with long-term use.

- e. The dose should be reduced/tapered to the lowest dose that controls symptoms.
- f. Patients should be monitored for adverse effects of corticosteroids (**Table 2**).

4. In patients with severe edema and impending herniation, IV osmotic diuretics (i.e., mannitol [Osmitol]) as well as emergent neurosurgical intervention may be required (Goffaux & Fortin, 2010; Stummer, 2007).

Nursing recommendation: Nurses should recognize and report evidence of cerebral edema and increased ICP promptly (Level 3). Nurses should administer steroids or osmotic diuretics as ordered and monitor for adverse effects (Level 2). Nurses should assess the patient's pain and administer analgesia as needed (Level 3).

III. Diagnosis

After neurological examination, the initial diagnosis is most reliably and efficiently made by radiological imaging (Keogh & Henson, 2012).

A. Imaging techniques

1. Head computed tomography (CT) scan with contrast
 - a. Often ordered initially in the acute care setting
 - b. The sensitivity and specificity of CT compared with MRI varies with the specific disease process and the location of the lesion.
 - c. CT provides information related to edema and hemorrhage.
 - i. Often is required in patients who cannot be safely placed in an MRI scanner
 - ii. Ferrous-containing implantable devices (automatic implantable cardioverter/defibrillators, pacemakers, etc.) are contraindications to MRI.

Table 2. Potential Side Effects of Corticosteroids and Management Recommendations

| Side Effect | Recommendation |
|--|--|
| Hyperglycemia and steroid-induced diabetes | Monitor blood glucose levels; educate patients and families about the diabetic diet, oral hypoglycemic agents, and insulin coverage. |
| Gastrointestinal (GI) distress | Take steroids with food. Give proton pump inhibitors if ordered for GI protection during the perioperative period or for patients with a history of gastritis or ulcers or who are taking nonsteroidal anti-inflammatory drugs or anticoagulation drugs. |
| Immunosuppression | Increased risk of opportunistic infection, including candida and pneumocystis. Assess for thrush, poor wound healing, fever, cough, dyspnea, oxygen desaturation. |
| Fluid retention and weight gain | Monitor edema, weight, and electrolyte values. Encourage the use of support stockings, elevate the lower extremities, promote exercise, and administer diuretics as ordered. |
| Weight gain | Patients may crave sweets and carbohydrates. Encourage a low carbohydrate diet and exercise as tolerated. |
| Proximal myopathy | Assess for muscle weakness seen in the proximal muscles, particularly the quadriceps. This is most noticeable with attempting to stand up or climbing stairs. Recommend physical therapy. |
| Insomnia | Keep steroid dosing schedules to twice a day or three times a day, with the last dose at dinner. |
| Behavioral changes | Monitor for mood swings, anger outbursts, and, in some cases, acute psychosis related to steroids. Educate the patient and caregiver about the cause of the behavior. Consider medication, counseling, or a psychiatric referral. |

Sources: "Glioblastoma multiforme: Enhancing survival and quality of life" by M. E. Davis & A. M. Stoiber, 2011, *Clinical Journal of Oncology Nursing*, 15(3), 291–297. "Complications of brain tumors and their treatment" by J. Lacy, H. Saadati, & J. B. Yu, 2012, *Hematology Oncology Clinics of North America*, 26(4), 779–796. "Steroids in neurooncology: Actions, indications, side-effects" by P. Roth, W. Wick, & M. Weller, 2010, *Current Opinion in Neurology*, 23(6), 597–602. "Medical management of patients with brain tumors" by P. Y. Wen, D. Schiff, S. Kesari, J. Drappatz, D. C. Gigas, & L. Doherty, 2006, *Journal of Neuro-Oncology*, 80(3), 313–332.

- d. An abnormality identified on CT scan is followed by MRI, unless contraindicated (Keogh & Henson, 2012).
2. MRI with and without contrast (Keogh & Henson, 2012; NCCN, 2014c; Rees, 2011)
 - a. The gold-standard noninvasive technique with which to identify tumor location and characteristics, presence of mass effect, and response to surgery or treatment (Rees, 2011)
 - b. Provides precise anatomic localization for operative planning
 - c. MRI sequencing should include T1-weighted spin-echo—a sequence that refocuses the spin magnetism through electromagnetic radiation—and T2 fluid-attenuated inversion recovery (FLAIR)—a sequence that removes fluid, such as CSF, and gadolinium (gadolinium chelate) infusion (Ricard et al., 2012). Contrast enhancement is frequently seen in high-grade gliomas.
 - d. Multimodality MRI imaging is used to describe cellularity, metabolism, and angiogenesis. These data provide information about tissue perfusion, preoperative classification, and grading of gliomas. Imaging types may include diffusion-weighted and diffusion tensor imaging, dynamic susceptibility contrast, or perfusion imaging.
 - e. Functional MRI (fMRI) may be used preoperatively to identify eloquent areas of brain function associated with specific tasks (motor and language). The images can be imported into the surgical navigation systems for intraoperative mapping to reduce postoperative morbidity (Rees, 2011).
 - f. Intraoperative MRI (iMRI) may be used in the operating room to permit real-time imaging to improve tumor resection.
 - g. Gadolinium, an MRI contrast agent, is related to nephrogenic systemic fibrosis.
 - i. Has been reported in patients with renal insufficiency exposed to gadolinium-contrast agents. Usual elimination of gadolinium-containing products is about 2 hours; however, in patients with renal dysfunction, the elimination half-life is prolonged to between 30 and 120 hours (Peak & Sheller, 2007).
 - ii. The U.S. Food and Drug Administration (FDA) recommends using alternate (nongadolinium) imaging methods whenever possible in patients with a glomerular filtration rate (GFR) lower than 60 ml/min/1.73 m². If gadolinium products must be used, hemodialysis should be immediately accessible.

Nursing recommendation: Nurses should monitor serum blood urea nitrogen and creatinine prior to contrast-enhanced CT and MRI procedures and report abnormalities (Level 1).

3. Magnetic resonance spectroscopy
 - a. Noninvasive measurement of the concentrations of metabolites in brain tumors to estimate the proliferation rate of tumor cells may be helpful in distinguishing necrosis from metabolically active areas indicating tumor (Faedhdrich et al., 2011; Rees, 2011; Ricard et al., 2012).
 - b. The metabolites of interest include choline, creatine, N-acetyl-aspartate, myoinositol, lipids, and lactate.
 - c. Can be used as a guide for surgical planning/biopsy
 - d. It is unreliable for small lesions (< 2 cm) or lesions close to bone that are composed primarily of fat or CSF.
4. Positive emission tomography (PET; Dhermain, Hau, Lanfermann, Jacobs, & van de Bent, 2010; Lau et al., 2010)
 - a. Uses radiolabeled tracers to provide quantitative information on the metabolic uptake of glucose in gliomas compared with normal brain tissue
 - b. Hypermetabolic or increased glucose use is suggestive of high malignancy and correlates with tumor grade, cell density, and biological aggressiveness.
 - c. Intensity of tracer uptake is measured and compared to standardized uptake values.
 - d. May be used to detect tumor recurrence or residual disease; rarely used for diagnosis

B. Systemic studies

1. CT scans of the chest, abdomen, and pelvis may be used to identify primary lesions that may have metastasized to the brain (Keogh & Henson, 2012; Ricard et al., 2012).

C. Cerebral angiography

1. Can identify the vascularity of the tumor to assist with surgical planning
2. Preoperative embolization may be useful for vascular lesions.

D. Endocrine battery/diagnostic workup

1. Indicated for tumors located in and around the sellar region to evaluate function of the hypothalamic pituitary axis.
2. Common laboratory studies include adrenocorticotrophic hormone (ACTH) and cortisol, prolactin, growth hormone, insulin-like growth factor-1, thyroid studies (T3, T4, thyroid stimulating hormone [TSH]), testosterone, follicular stimulating hormone, and luteinizing hormone.

E. Visual tests

1. Visual field: Visual pathways encompass multiple pathways in the brain; therefore, visual field defects can help to localize tumors.
2. Fundoscopic examination can document evidence of papilledema (swelling of the optic disk), which is indicative of increased ICP.

F. Audiometric studies

1. Audiometric studies are indicated in patients with hearing loss to document baseline hearing deficits or in patients with lesions in and around the acoustic nerve.

Nursing recommendation: Nurses should anticipate necessary diagnostic tests and educate patients and families (Level 3). Nurses should assess patients prior to MRI for any metal objects or implants and evaluate kidney function when contrast-enhanced CT or MRI is anticipated (Level 3). Nurses should administer pre-medications as needed in a timely fashion (Level 3).

IV. Surgery

Surgery is an essential tool in brain tumor management. Neurosurgeons perform surgery to establish diagnosis, decrease tumor burden, relieve increased ICP, and provide access for treatment. This section will provide detailed guidelines about biopsy, surgery, and complications.

A. Biopsy

1. Imaging is highly sensitive for brain tumors but not particularly specific; surgical biopsy or resection is recommended (Waldman et al., 2009).
 - a. NCCN Guidelines® recommend gross total resection when feasible or stereotactic biopsy to provide sufficient tissue to pathology for evaluation and molecular correlates (Faehndrich et al., 2011; NCCN, 2014c; Rees, 2011).
 - b. Tissue diagnosis is indicated when further treatment is contemplated to rule out nonneoplastic lesions and to provide histologic identification and genotyping.
 - c. Indications for performing biopsy only (and not tumor removal)
 - i. Anatomic location (intra-axial brainstem, deep structures [e.g., basal ganglia]) near eloquent centers or vascular tumors prohibits resection (Rachinger et al., 2009).
 - ii. MRI imaging suggestive of CNS lymphoma (NCCN, 2014c)
 - d. Glial tumors are often heterogeneous with differing areas of malignancy; therefore, biopsy sampling should be taken from the region that appears most malignant on imaging to avoid sampling errors (Faehndrich et al., 2011; Waldman et al., 2009).

e. Pathology

- i. The WHO classification of CNS tumors is the primary means to determine tumor malignancy and prognosis based on histopathologic confirmation (Huttner, 2012).
 - ii. Histologic confirmation is supplemented by molecular diagnostic tests.
 - iii. Several molecular tests have become available and may aid in the prediction of prognosis and development of treatment plans (Huttner, 2012; Ricard et al., 2012).
(See Section II.A.3.e., Influence of genetic factors.)
- f. Reassessment and evaluation should continue throughout the continuum of care.

Nursing recommendation: Nurses should monitor patients after biopsy for neurological deterioration and report neurological changes promptly (Level 3). Nurses should educate patients and families about when the final pathology will be available and dates of postoperative follow-up appointments to discuss the plan of care (Level 3).

B. Extent of resection

Extent of resection depends on tumor size and location, patient age, and comorbidities (Ryken, Frankel, Julien, & Olson, 2008).

1. Location: Patients with a reasonable life expectancy who have a single lesion in the noneloquent brain should have the tumor removed (Barker, 2011).
 - a. Data support maximal resection to improve survival (Ryken et al., 2008).
 - b. Deep and unresectable tumors are diagnosed with stereotactic biopsy.

C. Preoperative management

1. Embolization
 - a. During embolization, a clotting agent is used to selectively block vessels supplying the tumor. Neurosurgeons consider embolization for highly vascular tumors to reduce the vascular supply to the tumor. Embolization is guided by cerebral angiogram. Interventional radiologists perform this procedure several days before surgery.
 - b. The goal of embolization is to reduce intraoperative blood loss, decrease surgical morbidity, shorten operative time, facilitate total resection, and decrease damage to the adjacent tissue by making the tumor smaller, softer, less bloody, and easier to resect (Hirschl & Caragine, 2011).

Nursing recommendation: After a tumor is embolized, nurses should monitor the patient's neurologic status. In addition, nurses should assess the neurovascular status of extremities

(groin site, vital signs, distal pulses) and watch for development of a hematoma (Level 3).

D. Intraoperative management

1. Positioning: Brain tumor can affect any part of the brain, so various positions are used to facilitate tumor access.
 - a. Supine positioning is used for anterior and temporal craniotomies. The head is positioned above the heart to facilitate venous return. Avoiding compression to the vertebral and internal jugular veins is a priority.
 - b. Lateral positioning is used for occipital and suboccipital craniotomies.
 - c. Prone positioning is used for approaches involving the posterior fossa and craniocervical junction.
2. An operating microscope is used for best visualization (Crowley, Dumont, McKisic, & Jane, 2011).

Nursing recommendation: Perioperative nurses should keep the location of the tumor and the surgical approach in mind when positioning patients (Level 3).

E. Special procedures

1. Cortical brain mapping is used to identify eloquent areas that require an awake craniotomy. Eloquent areas of the brain include the sensorimotor cortex, language cortex, basal ganglia, and internal capsule (Chang et al., 2011). The goal is to resect tumor to the greatest extent possible with the lowest morbidity to provide patients with the best possible quality of life.
 - a. Patient selection risk factors or contraindications for awake craniotomy include reduced respiratory function, decreased cardiac output, sleep apnea, emotional instability, or decreased level of consciousness (Carrabba, Venkatraghavan, & Bernstein, 2008; Hoosein, 2006).
 - i. Cortical mapping procedure: The patient is administered general anesthesia or scalp block and sedation for the craniotomy. Once the craniotomy is completed and the brain is exposed, a cortical grid map is placed on the surface of the brain. The patient is awakened and the cortex of the brain is stimulated with a cortical stimulator to map the exposed brain and identify eloquent areas (Chang et al., 2011).
 - ii. Language mapping is performed under local anesthesia with the patient awake. The patient is observed for errors in naming objects during stimulation. If errors occur, those areas are defined as the areas responsible for eloquent speech

and are avoided during resection of the tumor (Ilmberger et al., 2008).

- iii. Motor mapping may be performed with the patient asleep or awake. The brain is stimulated and the patient is observed for visual or electromyographic movements of the face or limbs. These areas are identified as eloquent motor areas, which are then avoided during tumor resection (Chang et al., 2011). Awake craniotomy can produce good outcomes with continuous motor testing (Shinoura, Yoshida, & Yamada, 2009).
- iv. Closure of the craniotomy: Once the tumor resection is complete, the patient is administered general anesthesia for closure of the dura, bone, and scalp.

Nursing recommendation: Circulating nurses on the neurosurgical team should establish a comfortable rapport with patients before the procedure to help them when they are awake by answering questions and calming fears (Level 3).

F. Postoperative complications of craniotomy (Table 3)

1. Hemorrhage may result in decreased neurologic status.
 - a. Signs and symptoms include deteriorating neurologic status, nausea, vomiting, or changes in cranial nerve function or extremity weakness.
 - b. Diagnostic testing includes a noncontrast CT scan, which is necessary to rule out hemorrhage in the tumor bed.
 - c. Postoperative hematoma may require reoperation for evacuation.
 - d. Significant postoperative hemorrhage occurs in 1%–2% of intracranial procedures (Weingart & Brem, 2011).
2. Perilesional edema causes decreased neurologic status and is treated with corticosteroids (Weingart & Brem, 2011).

Nursing recommendation: Nurses should anticipate signs of deteriorating neurologic status (Level 3). Nurses should report any deterioration of the patient to the neurosurgeon (Level 3).

3. Hypertension may lead to hemorrhage in the tumor bed (Parida & Badhe, 2009). Elevated blood pressure is treated with labetalol (Trandate) or hydralazine (Apresoline). If blood pressure cannot be controlled with a single dose of medication, then a titratable infusion such as nicardipine (Cardene) should be started to keep systolic blood pressure in the goal range (Parida & Badhe, 2009).

Nursing recommendation: Nurses should maintain blood pressure parameters as ordered and administer antihypertensives as prescribed (Level 3).

4. Neurologic deficits may be related to tumor location (**Table 1**).
 - a. Alteration in neurologic condition may occur following resection of brain tumors adjacent to the eloquent motor cortex and result in weakness of an arm, leg, or both.
 - b. Personality and memory may be affected if a tumor is located in the frontal lobe.
 - c. Language may be affected if the tumor is situated close to Broca's or Wernicke's areas.
 - d. Sensation and position may be affected with parietal lobe tumors.
 - e. Balance issues may be associated with cerebellar lesions (Warnick, 2011).
 - f. Occupational, physical, and speech therapies may be ordered in the hospital to assess motor skills, activities of daily living (ADLs), speech, and cognition. Evaluation by a rehabilitation medicine physician (a physiatrist) is recommended (Bohan & Glass-Marcenka, 2004).
 - g. Postoperative deficits are expected to improve following tumor resection, but intraoperative manipulation with resulting transient postoperative edema may cause symptoms to persist or worsen immediately after surgery (Weingart & Brem, 2011).

Nursing recommendation: Nurses should assess deficits by correlating them with the anatomic location of the tumor (Level 3). Nurses need to ensure that patients are evaluated by the physiatrist and therapists to establish their baseline and set realistic goals. They need to involve families so everyone can work toward the same discharge goals (Level 3).

5. CSF leaks

- a. Postoperative pseudomeningoceles or CSF leaks may occur following surgical procedures involving the posterior fossa. A water-tight dural closure is often more difficult to achieve in this location (Origitano, Petruzzelli, Leonetti, & Vandevender, 2006). CSF leaks occur in approximately 8% of patients undergoing skull base surgery (Fatemi, Dusick, de Paiva Neto, & Kelly, 2008).
- b. Assessment: Presents as otorrhea or rhinorrhea. Watery drainage from the nose, ear, or incision may be observed. CSF leaks may be confirmed by radioisotope cisternography with cotton pledgets in the nasal cavity.
- c. CSF leak treatment: A lumbar drain may be used to treat CSF leaks (Slazinski, Anderson, Cattell, Eigsti, & Heimsoth, 2011). If the leak continues after the lumbar drain is removed, then reexploration of the surgical site and

closure of the leak is necessary. The risk of meningitis increases the longer the CSF leak is present (Lemole, Henn, Zambranski, & Sonntag, 2001).

- d. Postoperatively, CSF leaks are seen in fewer than 5% of transsphenoidal procedures (Esposito, Dusick, Fatemi, & Kelly, 2007; Lemole et al., 2001; National Institutes of Health [NIH], 2008). The anesthesiologist performs an intraoperative Valsalva maneuver to increase ICP to check for CSF leaks. If a leak is discovered during surgery, it is closed with collagen mesh, muscle, or fat, or a combination of the above (Fatemi et al., 2008).
- e. Prevention of subsequent CSF leaks: Patients with a CSF leak should be instructed to avoid coughing, sneezing, nose blowing, or Valsalva maneuvers so they do not increase their ICP. Open-mouth coughing and sneezing is advised (NIH, 2008).

Nursing recommendation: Nurses should monitor patients who have had skull base surgery or transsphenoidal surgery for CSF leaks (Level 3).

6. Seizures

- a. If a patient has had a preoperative seizure, he or she is placed on antiepileptic drugs (AEDs) prior to surgery and remains on AEDs after surgery. If a patient has never had a preoperative seizure, he or she may still be vulnerable to a seizure resulting from cortical irritation during the postoperative period. Seizure risk is based on tumor type, grade, and location (Tremont-Lukats, Ratilal, Armstrong, & Gilbert, 2008).
- b. Occurrence: Seizures are more common in Grade I and Grade II gliomas and meningiomas. Seizures usually result from tumor progression, causing irritation of brain tissue. Patients with tumors in the cortical grey matter will present with seizures more often than deeper tumors of the white matter (Bromfield, 2004).
- c. Seizure types: Postoperative seizures may be focal or generalized.
- d. Seizure treatment: Treatment includes a loading dose of an AED followed by daily dosing of an AED (Klimek & Dammers, 2010). Any seizure activity should be treated immediately to prevent status epilepticus. Status epilepticus has traditionally been defined as more than 30 minutes of seizure activity or two or more sequential seizures without full recovery of consciousness between seizures (Dodson et al., 1993; Roth, 2011). The 30-minute duration has been challenged. According to

current recommendations, an unrelenting seizure lasting more than 5 minutes can be considered status epilepticus and may necessitate treatment soon after the first 5 minutes (Claassen, Silbergleit, Weingart, & Smith, 2012).

- e. Rule out other complications: A patient who sustains a postoperative seizure should have a CT scan to rule out structural causes such as edema, hemorrhage, or stroke.
- f. Use of AEDs: Prescribing AEDs postoperatively for patients who have never had a seizure is not recommended by the American Academy of Neurology (Das et al., 2012; Thompson, Takeshita, Thompson, & Mulligan, 2006).
- g. AED adverse effects: Adverse effects include, but are not limited to, headache, rash, nausea, somnolence, confusion, diplopia, and dizziness (Thompson et al., 2006). AEDs also may interact with corticosteroids and chemotherapeutic agents (Glantz et al., 2000; Smith, 2010).

Nursing recommendation: Nurses should monitor for seizure activity and adverse AED effects in patients who undergo postoperative craniotomy. If seizure activity occurs, they should notify the appropriate provider and begin prescribed management (Level 3).

- 7. Infection: Infection is a possible complication after craniotomy surgery. Predisposing risk factors can be increased by the procedure's proximity to the paranasal sinuses, long surgical time, and corticosteroid use (Warnick, 2011). Signs and symptoms of infection include fever of 101.5° F (38.6° C) or higher or drainage from the incision (Warnick, 2011).
 - a. Rate of infection: Supratentorial infection rates are 1%–2% (Warnick, 2011).
 - b. Prevention of infection: Preoperative antibiotics are started within 1 hour before incision. Surgical Care Improvement Project guidelines identify measures to prevent infection that include skin asepsis, barrier devices, surgical hand hygiene, surgical technique, and preoperative antibiotics (Anderson, Harris, Baron, & Sexton, 2012). Antibiotics are administered during induction of anesthesia (Warnick, 2011).
 - c. Antibiotic coverage: The antibiotics of choice are cefazolin (Ancef) or vancomycin (Vancocin) for patients who are penicillin allergic (Anderson et al., 2012).
 - d. Incision management: Postoperatively, incisions are covered with a turban or occlusive dressing. There is no consensus

in the literature supporting management of surgical dressings. There is no difference in postoperative infection in patients who wash their hair at 72 hours versus patients who wait 5–10 days to shampoo or until staples or sutures are removed (Ireland et al., 2007). Patients are advised to avoid sun exposure until the incision is completely healed. Sutures or staples are generally removed after 7–14 days (Bohan & Glass-Marcenka, 2004).

Nursing recommendation: Nurses should monitor patients for infection. Patients may be discharged from the hospital before infection develops, so they must be instructed to call their physician to report any drainage from the incision or fever higher than 101.5° F (38.6° C; Level 3).

- 8. Meningitis: Patients who undergo craniotomy are at risk for meningitis. Meningitis is an inflammation of the meninges, the protective covering of the brain and spinal cord. The infection may be caused by bacteria, viruses, or other microorganisms.
 - a. Symptoms include fever, headache, nuchal rigidity, and altered level of consciousness. Ninety-five percent of patients with meningitis exhibit fever at the time of presentation (Tunkel, Calderwood, & Thorner, 2009). When meningitis is suspected, a lumbar puncture is performed in the absence of significant increased ICP to obtain CSF for analysis.
 - b. CSF findings in cases of bacterial meningitis include white cell count value of 500–100,000 (cells/mm³) elevated protein, glucose lower than two-thirds of the serum glucose, and a positive culture (McCutcheon, 2011).
 - c. Treatment: Antibiotics are used to treat meningitis. The antibiotic regimen will be specific to the microorganism found in the CSF (Siegel, Rhinehart, Jackson, Chiarello, & Health Care Infection Control Practices Advisory Committee, 2007).
 - d. For aseptic, fungal, listeria, and some bacterial meningitis, standard precautions are used. For *Haemophilus influenzae* or *Neisseria meningitidis*, droplet precautions are used (Siegel et al., 2007).

Nursing recommendation: Nurses should monitor for decreased neurological status and symptoms of meningitis. Nurses caring for a patient with possible meningitis should always use isolation procedures until communicable bacterial meningitis is ruled out (Level 1).

- 9. Hydrocephalus is associated with enlargement of the ventricular system.
 - a. Causes of hydrocephalus include

- i. Tumor in the posterior fossa that is obstructing the flow of CSF
 - ii. Tumor within the ventricular system
 - iii. Leptomeningeal infiltration by tumor cells, which prevents reabsorption of CSF by the arachnoid villi
 - iv. Postoperative blood in the CSF causing obstructive hydrocephalus (Litofsky & Musinich, 2011).
- b. Signs and symptoms include headache, decreased level of consciousness, nausea and vomiting, and pupillary abnormalities.
 - c. Treatment: Acute hydrocephalus may be treated with an external ventricular drain (Litofsky & Musinich, 2011). An external ventricular drain will allow for monitoring of ICP; drainage of CSF; and laboratory monitoring of CSF, including culture, gram stain, cell count, protein, and glucose. If the hydrocephalus does not resolve, the patient may require permanent shunting of CSF and a ventriculoperitoneal shunt will be inserted (Litofsky & Musinich, 2011; Slazinski et al., 2011).

Nursing recommendation: Nurses should observe for hydrocephalus and monitor ICP and CSF laboratory results as ordered by the neurosurgeon (Level 3).

10. Venous thromboembolism (VTE) is a cause of morbidity and mortality in all patients with cancer, including those with brain tumors. Patients with primary or metastatic brain tumors have hypercoagulable states that predispose them to thromboembolism during the postoperative period. Tumor cells express a procoagulant that induces thrombin generation (Bauer, Leung, & Landaw, 2012).
 - a. Risk is associated with tumor type, stage of disease, surgical interventions, anesthesia duration, patient age, immobility, and previous history of VTE (Mandala, Falanga, & Roila, 2011).
 - b. Signs and symptoms of VTE include leg pain, calf tenderness, edema, fever, and elevated white blood cell (WBC) count (Bates et al., 2012).
 - c. VTE is diagnosed with venous duplex ultrasonography.
 - d. VTE prevention involves administration of unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH). A recent trial comparing UFH with LMWH demonstrated no significant difference between the two for mortality or major bleeding events (Qaseem et al., 2011).
 - e. Prophylaxis can begin on the second postoperative day without an increase in

hemorrhagic complications provided the postoperative CT and MRI findings do not demonstrate hemorrhage (Warnick, 2011).

- f. Mechanical devices such as pneumatic compression sleeves for the lower extremities should be used the operative day and postoperative day 1 (Guyatt et al., 2012).

Nursing recommendation: Nurses should be aware of the high risk for deep venous thrombosis (DVT) in patients with brain tumors. Nurses should begin a DVT prevention program on postoperative day 1 (Level 3).

11. Pain management for patients who undergo craniotomy is dependent upon the location of the craniotomy. Pain assessment encompasses location, intensity, quality, onset, and duration. A 1–10 pain scale, with 1 indicating no pain and 10 indicating the worst pain may be used. For approaches in the frontal, temporal, or parietal areas, IV opioids are used until oral intake is accomplished. Once the patient can take medication by mouth, the medication may be changed to oral analgesics if swallowing is not impaired. If swallowing is impaired, a feeding tube may be needed, at least temporarily.
 - a. If the temporal muscle has been cut, the patient will have pain with facial movement and chewing.
 - b. Patients who undergo posterior fossa approaches generally require more intense pain and nausea management because of more invasive and traumatic muscle dissection. This may be attributable to surgical stress in major muscles (Gray & Matta, 2005; McCaffery & Pasero, 1999).

Nursing recommendation: Nurses should assess for postoperative pain. Pain medication should be given often enough to keep pain at a reasonable level for the patient (Level 3).

12. Dizziness: Posterior fossa approaches are frequently associated with postoperative postural dizziness that usually subsides with time. Patients treated with this approach might require a few more days in the intensive care unit and are fall risks (Muraszko & Hervey-Jumper, 2011).

Nursing recommendation: Nurses should offer pain medication and antiemetics for patients who undergo a posterior fossa operative approach (Level 3). Nurses or physical therapists should ambulate patients with assistance (Level 3).
13. Periorbital edema occurs in frontal craniotomies because of manipulation of the scalp. Swelling around the eye may be accompanied by ecchymosis, which continues for 48–72 hours postoperatively. Elevation of the head of the bed

decreases gravity-dependent swelling. Ice packs also can be used to decrease swelling (Shin, Lim, Yun, & Park, 2009). Use of lubricating eye drops makes the patient more comfortable and protects the cornea.

Nursing recommendation: Nurses should keep the head of the bed elevated to decrease periorbital edema unless contraindicated (Level 3).

14. Intracranial hypotension may occur following skull base surgery. This condition results from excessive CSF drainage.
 - a. Symptoms include headache, cranial nerve palsies, decreased neurologic status, and coma.
 - b. To confirm the problem, an ICP monitoring device may be inserted. With intracranial hypotension, the ICP will have negative values that worsen when the head of the bed is raised. If a lumbar drain is in place, the drain is clamped and the patient is positioned flat for 24 hours (Origitano et al., 2006). Positioning the patient flat should improve neurologic status. The head of the bed may be slowly raised after 24 hours, but the lumbar drain should remain closed or removed (Origitano et al., 2006).

Nursing recommendation: Nurses should lay the patient flat if intracranial hypotension is suspected. If a lumbar drain is present, close or remove the drain (Level 3).

G. Support

1. Patients with brain tumor and their families require support during and after surgery. They have numerous questions regarding pathology. The effects of a brain tumor may cause fear and uncertainty about the patient's future. Oncologists and radiation oncologists are consulted to provide some answers. A hospital chaplain or social worker may be called to help families cope. Patients are interested in care that will improve and extend their lives. It is important to provide appropriate contact information, and access to local or online support groups may be helpful (Remer & Murphy, 2004).

Nursing recommendation: Nurses need to provide support, answers, comfort, and appropriate resources for patients with brain tumors and their families (Level 3).

V. Radiation therapy

A. Single modality therapy

1. Radiation therapy (RT) may be used as the only therapy in the management of brain tumors or in conjunction with chemotherapy.
 - a. For high-grade gliomas, radiation with chemotherapy is the standard of care (Stupp et al., 2002).

B. Biologic effects of radiation

1. Three mechanisms of cell destruction are caused by exposure to gamma radiation (Sharma, Vallis, & McKenna, 2008).
 - a. Induction of apoptosis (programmed cell death)
 - b. Permanent cell cycle arrest (stopping cell cycle activity)
 - c. Induction of catastrophic aberrant mitosis (cells dividing improperly)
2. Affects normal cells as well as tumor cells
 - a. Each tissue type has a known tolerance for radiation before the cell will be destroyed.
 - b. Brain tolerance for radiation is approximately 60 Gy. Gy is a standard measure of joule of energy absorbed/kg mass (Sharma et al., 2008).
 - i. The mechanism by which radiation toxicity affects the brain is necrosis; radiation toxicity is variable and irreversible (Shaw & Robbins, 2005).
 - ii. Effects occur in astrocytes and myelin-producing cells (resulting in impaired cellular repair and myelin synthesis).
3. These mechanisms are considered when planning radiation dose so brain cells can survive while the radiation destroys tumor cells (Sharma et al., 2008).
 - a. Dose: amount of radiation delivered to the target tissue
 - i. Measured in Gy
 - ii. Total dose is the amount of Gy delivered over time. A total dose of radiation is broken into a number of even parts called fractions.
 - iii. A fraction is the amount of Gy in one dose. The aim of fractionation is to find the delicate balance between delivering enough dose to destroy the tumor and allowing enough time for normal cells to heal between treatments.
 - a) The usual dose is 1.8–2 Gy per fraction (NCCN, 2014c).
 - b) Hyperfractionated: Delivering a total dose, but in more fractions than the usual dose
 - c) Hypofractionated: Fewer fractions of the total Gy; used most commonly for reirradiation or poor functional status
 - iv. Radiation doses are calculated based on specific histologic characteristics as well as tissue volumes and tumor type.
 - v. Certain structures are more radiosensitive than others. The brain stem and optic nerve tissues are more sensitive to the effects of radiation.

Nursing recommendation: Nurses should use information on biologic effects of radiation as a

Table 3. Postoperative Complications After Brain Tumor Surgery: Signs and Symptoms and Related Nursing Actions

| Complication | Signs and Symptoms | Nursing Action |
|--------------------------------|---|--|
| Hemorrhage | Deterioration in neurologic status; nausea/vomiting; change in cranial nerve function; extremity weakness | Report findings to the neurosurgeon; patient is taken for STAT computed tomography scan |
| Hypertension | Systolic blood pressure higher than 140 mmHg (Morgenstern et al., 2010) | Treat with labetalol (Trandate) hydralazine (Apresoline), or nicardipine (Cardene), a titratable intravenous infusion, if continuous blood pressure control is needed |
| Cerebrospinal fluid (CSF) leak | CSF-related otorrhea, rhinorrhea; salty taste in posterior pharynx; CSF drainage from incision | Report findings to the neurosurgeon; instruct the patient to use an open mouth for coughing and sneezing; no nose blowing allowed. |
| Seizures | Abnormal movements of the body; changes in sensation, awareness, behavior; tonic clonic movements; staring spells | Observe seizure and related documentation: Document presence of aura, where seizure began, how seizure progressed, deviation of the head or eyes, movement of specific body parts, duration of seizure, level of consciousness (LOC), behavior after seizure, postictal weakness, or paralysis (notify neurosurgeon) |
| Infection | Drainage from the incision; fever of 101.5° F (38.6° C) or higher. | Notify neurosurgeon |
| Meningitis | Fever, headache, nuchal rigidity, altered LOC | Assist with lumbar puncture; use isolation procedures until communicable bacterial meningitis is ruled out |
| Hydrocephalus | Headache, decreased level of consciousness, pupillary abnormalities, nausea, vomiting | Notify neurosurgeon. Usually a CT scan is done to check the size of the ventricles. |
| Venous thromboembolism | Pain, redness, or swelling in the calf or, rarely, arm | Obtain ultrasound of affected extremities as ordered; notify neurosurgeon of ultrasound result |
| Pain | Patient may state he or she has pain; if in a coma, observe for facial grimace or other nonverbal behaviors | Treat with oral or intravenous medication; the goal of many institutions is to reduce pain to a tolerable level on the pain scale. |
| Periorbital edema | Swelling around the eye or incision; may be accompanied by ecchymosis | Elevate head of bed; ice packs on eye |
| Intracranial hypotension | Headache, cranial nerve palsy, decreased neurologic status, coma | Position patient flat, close lumbar drain if present; notify neurosurgeon |

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framework with which to conduct assessments and provide patient education (Level 3).

C. RT techniques (Sharma et al., 2008)

1. External beam
 - a. External beam directs a beam of radiation from an external source to a defined penetration and trajectory.
 - i. Uses a cobalt source of gamma radiation
 - ii. Fields and portals are adjusted along with total dose to achieve desired goals of control or palliation.
2. Intensity-modulated RT uses multiple overlapping fields to adjust target dose while protecting surrounding tissue.
3. Whole-brain RT (WBRT) is administered through parallel portals, usually from the right and left side of the head to avoid sensitive eye and ear structures.
 - a. WBRT usually is used for multiple metastatic lesions rather than primary disease.
 - b. Several dose regimens: May be administered as 30 Gy in 10 fractions or 40 Gy in 20 fractions. It may be given in conjunction with a radiosurgery boost, which provides better brain control but does not increase survival (Tsao et al., 2012).
4. Stereotactic radiosurgery delivers high-dose external beam radiation in a single fraction to tightly defined margins. Many systems are available for delivery.
 - a. Gamma knife: Up to 200 multidirectional beams converge on one predefined target with only a small dose of radiation delivered to surrounding structures.
 - b. Accuracy is determined by three-dimensional (3D) stereotactic reference points using a frame-based or frameless approach.
5. Proton therapy (DeLaney, 2011)
 - a. May be beneficial for some adult tumors because of normal-tissue sparing distal to the tumor
 - b. Uses 3D conformal approaches in treatment planning
 - c. Used ideally for anatomic sites and tumors not well treated with photons
 - d. Beneficial in skull-base and sellar tumors (Fuji et al., 2011)

6. Interstitial brachytherapy involves a temporarily implanted radiation source that delivers radiation in a concentric manner to a 1-cm depth within target tissue (Kreth, Thon, Siefert, & Tonn, 2010).
 - a. Iodine-125 or iridium-192 are radiation sources.
 - b. A balloon catheter is placed in the target to deliver a 40–60-Gy total dose for temporary seeds, or 60–100 Gy for permanent seeds.
 - c. Used in only a few centers because of its complexity and the advance of techniques such as stereotactic radiotherapy

Nursing recommendation: Nurses should use information about RT techniques to develop a plan of care for patients undergoing brain irradiation (Level 3). They also should use information on brain RT techniques to provide patient-specific education (Level 3). Nurses should explore patient and family understanding of brain RT options in conjunction with providers to ensure informed decision making (Level 3).

D. Decisions about radiotherapy

When choosing the radiation approach and delivering the radiation dose, tumor histopathology, margins, and MRI characteristics are considered.

1. Meningioma treatment: Conventional RT may be considered for patients with incomplete resection, unresectable meningioma, recurrent meningioma, or higher-grade meningioma (Ghondi, Tome, & Mehta, 2010).
 - a. Radiation is delivered to the gross total volume with minor expansion of the radiation field to include the dural tail with conformal therapy to accommodate bony invasion (Flickinger & Naranjan, 2008). Conformal therapy is imaging technology used by radiation oncologists that shapes the radiation treatment beam to the shape of the tumor.
 - b. A firm dose has not been established. Doses of 50–55 Gy in fraction sizes of 1.8–2.0 Gy commonly are used. Doses depend on grade and size (Ghondi et al., 2010).
2. High-grade glioma: Conventional RT is the standard of care for patients with high-grade gliomas (Flickinger & Naranjan, 2008; Stupp et al., 2002).
 - a. The total target volume is seen on MRI as FLAIR or T-2 abnormality plus 2-cm margin (NCCN, 2014c). The usual dose is 60 Gy in 1.8–2.0 Gy fractions; for larger tumor volumes (gliomatosis) or Grade 3, the total dose may be reduced (NCCN, 2014c).
 - b. In poorly performing patients or the elderly, a hypofractionated accelerated course was found to be effective with the goal of completing the treatment in 3–4 weeks (NCCN, 2014c).
3. Low-grade glioma: RT may be considered for patients with lower-grade gliomas when resection is incomplete.
 - a. Because these tumors tend not to enhance, the MRI FLAIR volume plus a 1- to 2-cm margin is used as the target area (NCCN, 2014c).
 - b. The usual dose is 45–54 Gy in 1.8–2 Gy fractions (NCCN, 2014c).
4. Metastases: RT is considered as a palliative measure.
 - a. The number, location, and size of lesions and stable systematic disease dictates the radiation approach used (Tsao et al., 2012).
 - b. There is a lack of consensus on optimum doses and fractions; usual doses range from 20–40 Gy in 5–20 fractions (Tsao et al., 2012).
5. Stereotactic radiosurgery (SRS) is an acceptable option for patients with a limited number of lesions. SRS may be used in combination with WBRT or separately (Schag, Heinrich, & Ganz, 1984) in patients with 1–4 brain lesions and a good KPS Scale value (> 70) (Table 4).
 - a. SRS is associated with comparable local control and lesser cognitive effects (Elaimy et al., 2011; Khalsa, Chinn, Kurucoff, & Sherman, 2013).
 - b. Dose is determined by tumor volume and ranges from 15–24 Gy in a single fraction.

Nursing recommendation: Nurses should function within a team to ensure safety and integrity of the RT plan for patients with brain tumor (Level 3). Nurses should be aware of radiation dose and fractions based upon tumor type (Level 1).
6. Radiosensitizing agents sensitize tumor cells, but not normal brain cells, to the effects of radiation so a small dose causes large effects.
 - a. No FDA-approved drug is available as a radiosensitizing agent (Tsao et al., 2012).
 - b. Some radiosensitizing agents are undergoing investigation.
7. Radioprotective agents are designed to increase brain cell tolerance of RT. No FDA-approved drug is available as a radioprotective agent (Tsao et al., 2012)

Nursing recommendation: Nurses should be knowledgeable about the role of radioprotective and radiosensitizing agents in patients undergoing brain radiation because they are under current research protocols (Level 3).

E. Adverse effects of brain radiation (Greene-Schloesser et al., 2012)

1. Adverse effects are divided into acute (onset of treatment up to 6 weeks after treatment), early

Table 4. Karnofsky Performance Status Scale

| Value | Level of Functional Capacity | Definition |
|-------|---|--|
| 100 | Normal, no complaints, no evidence of disease | Able to carry on normal activity and to work; no special care needed |
| 90 | Able to carry on normal activity, minor signs or symptoms of disease | |
| 80 | Normal activity with effort, some signs or symptoms of disease | |
| 70 | Cares for self, unable to carry on normal activity or to do active work | Unable to work; able to live at home and care for most personal needs; various degrees of assistance needed |
| 60 | Requires occasional assistance but is able to care for most needs | |
| 50 | Requires considerable assistance and frequent medical care | |
| 40 | Disabled, requires special care and assistance | Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly |
| 30 | Severely disabled, hospitalization is indicated, although death is not imminent | |
| 20 | Hospitalization is necessary, very sick, active supportive treatment necessary | |
| 10 | Moribund, fatal processes progressing rapidly | |
| 0 | Dead | |

Source. Adapted from "The clinical evaluation of chemotherapeutic agents in cancer" by D. A. Karnofsky & J. H. Burchenal, 1949. In C. M. Macleod (Ed.), *Evaluation of chemotherapeutic agents* (p. 196). Columbia University Press.

- delayed (6 weeks to 6 months after treatment), and late effects (6 months to years after treatment).
2. Acute effects (onset of treatment up to 6 weeks after treatment)
 - a. Toxicities are attributable to transient peritumoral edema and include fatigue, headache, nausea and vomiting, anorexia, and focal neurologic deficits.
 - b. Rapidly dividing cells also can be affected, causing alopecia, otitis externa, dry eye, and radiation dermatitis.
 - c. Adverse effects are more severe when RT is accompanied by cytotoxic therapy (Butler, Rapp, & Shaw, 2006).
 3. Early delayed effects (6 weeks to 6 months later)
 - a. Occur because of alterations in capillary permeability and transient demyelination
 - b. Toxicities include headache, somnolence syndrome, fatigue, cranial neuropathies, exacerbation of existing neurologic deficits, persistent alopecia, otitis externa, dry eye, radiation dermatitis, attention deficits, and short-term memory loss (Costello, Shallice, Gullan, & Beaney, 2004; Prados & Levin, 2000).
 4. Late (6 months to years later)
 - a. Thought to be attributable to white-matter demyelination and necrosis as well as vascular changes
 - b. Toxicities include neurocognitive deficits, radiation necrosis (which can mimic recurrent tumor), and diffuse leukoencephalopathy, a disease that causes deterioration of the white matter.
 - c. Hippocampal structures involved in memory, learning, and spatial functions may

be most affected (Armstrong, Shera, Lustig, & Phillips, 2012; Monje et al., 2007).

- d. Nonhippocampal-dependent reductions in cognitive functions also occur. Neurologic inflammation may play a significant role in radiation-induced cognitive impairment (Greene-Schlosser et al., 2012; Moravan, Olschowka, Williams, & O'Banion, 2011).

F. Prevention and treatment of adverse effects of radiation

1. There are no known effective preventive interventions for long-term effects of radiation.
 - a. Prophylactic use of methylphenidate (Ritalin) in patients with brain tumor undergoing RT did not result in improved quality of life (Butler et al., 2007).
 - b. Hippocampal-sparing radiation techniques decrease hippocampal damage (Pinkham et al., 2014).
2. Radiation-induced edema may respond to low-dose corticosteroids.
3. Radiation necrosis: necrosis of tumor as well as normal brain tissue
 - a. Few interventions effectively prevent radiation necrosis. Bevacizumab (Avastin) decreased effects of radiation necrosis in patients receiving stereotactic radiosurgery for metastasis (Boothe et al., 2013).
 - b. Radiation necrosis may be difficult to differentiate from tumor progression, and biopsy may be required.
 - c. Managed with steroids; evidence suggests potential for symptom improvement or reversal with hyperbaric oxygenation, warfarin (Coumadin), or vitamin E (Butler et al., 2006; Williamson, 2007).

4. Cognitive dysfunction can range from subtle changes such as memory loss to global changes such as loss of executive function and decreased IQ (Hahn et al., 2009). RT-related cognitive dysfunction may be difficult to distinguish from effects of tumor.
 - a. May affect ability to make decisions about and adhere to treatment
 - b. May respond to pharmacologic, behavioral, or rehabilitative therapies
 - i. Early evidence suggests improvement in cognitive function after using donepezil (Aricept) and ginkgo biloba for a duration of at least 6 months, beginning 6 or more months after completion of RT (Butler et al., 2006; Shaw et al., 2006).
 - c. Memantine (Namenda) given with WBRT showed a reduced decline in cognitive status compared with a placebo group (Brown et al., 2013)
5. Fatigue (see section VII. Symptom Management)
 - a. Rest
 - b. Methylphenidate may improve fatigue as well as cognitive function as a therapeutic (but not prophylactic) intervention (Butler et al., 2007).
 - c. Exercise may improve fatigue.
6. Hair loss: There are no known effective interventions to prevent hair loss.
7. Skin erythema: no known prophylactic measures
8. Somnolence syndrome: usually transient; consider reimaging if symptoms persist (Butler et al., 2007)

G. Nursing interventions

1. Assessment is focused on neurologic and cognitive function, skin integrity, presence of fatigue, potential toxicities, and anxiety level (Haas, 2011).
2. Patient education should include
 - a. A review of the treatment plan, expected outcomes, specific anticipated adverse effects and how to manage them, and correction of any misunderstanding.
 - b. Educational materials about different types of radiotherapy.
3. Nurses play a unique role in management during RT by providing evidence-based symptom management and monitoring for late adverse effects.

Nursing recommendation: Nurses should assess patients undergoing brain RT for specific adverse effects at acute, subacute, and delayed time frames (Level 1). Nurses should develop problem-focused interventions to address specific adverse effects experienced by patients undergoing brain RT (Level 2). Nurses should educate patients undergoing brain RT (and their families) about potential

adverse effects and how to manage those problems (Level 2).

VI. Chemotherapy

A. Basic considerations

1. Chemotherapy may be used in addition to surgery and radiation for treatment of a wide variety of brain tumors. It may be given before, during, and/or after RT. In addition, it often is used at the time of tumor recurrence.
2. Administration of systemic chemotherapy requires consideration of the BBB. The BBB is a complex network of blood vessels and cells that protects the brain and may limit the effectiveness of certain chemotherapeutic agents.
3. Most chemotherapeutic drugs are administered via the IV or oral route. Other potential chemotherapy delivery options include intra-arterial, intrathecal, or intracavitary (directly into tumor bed).

B. Chemotherapy and tumor biology

1. MGMT promoter methylation benefit in glioblastoma
 - a. MGMT is a DNA repair protein that transfers a methyl group from guanine to itself (Hegi et al., 2005).
 - b. Methylation of the MGMT promoter present in tumor cells prevents expression of MGMT, limiting DNA repair ability of the cell.
 - c. Methylation of MGMT promoter makes tumor cells more responsive to alkylating agents such as temozolomide and carmustine (BCNU; Hegi et al., 2005).
2. 1p/19q codeletion in oligodendroglial tumors
 - a. Anaplastic oligodendrogliomas with losses of chromosome 1p and 19q are associated with an enhanced response to chemotherapy and prolonged survival (Cairncross et al., 1998).

C. Chemotherapy for newly diagnosed high-grade glioma (anaplastic gliomas/glioblastoma)

1. Temozolomide (Temodar): Oral administration
 - a. Standard of care for newly diagnosed high-grade gliomas (Stupp et al., 2005)
 - b. Usually initiated postoperatively in patients with good performance status (KPS \geq 70), and administered concurrently with fractionated external beam RT. Temozolomide is continued as adjuvant therapy after RT is completed (Stupp et al., 2005)
 - c. Mechanism of action: a DNA-damaging alkylating agent that crosses the BBB
 - d. Side effects: Nausea, vomiting, myelosuppression, constipation, headache, and fatigue (Stupp et al., 2005)

Nursing recommendation: Nurses should know that temozolomide is a first-line chemotherapeutic agent for newly diagnosed high-grade gliomas (Level 1). Nurses should be aware that patients with high-grade glioma containing a methylated MGMT promoter may respond better to treatment with temozolomide, whereas patients who do not have a methylated MGMT promoter may not experience such benefit (Level 1).

Nursing recommendation: Nurses should practice prevention strategies for nausea and vomiting and engage patients in behavioral therapies such as relaxation, hypnosis, and guided imagery. Nurses should also monitor WBC and platelet counts, address constipation, monitor and treat headache, and assist the patient with developing strategies to combat fatigue (Level 3).

D. Chemotherapy in recurrence of high-grade glioma

1. Bevacizumab (Avastin): IV or intra-arterial administration
 - a. Approved by the FDA for treatment of recurrent glioblastoma (Cohen, Shen, Keegan, & Pazdur, 2009)
 - b. Bevacizumab, which is used as a single agent for recurrent glioblastoma, is supported by two studies assessing progression-free survival and overall survival.
 - i. Treatment with bevacizumab plus irinotecan (CPT-11 or Camptosar; Vredenburgh et al., 2007)
 - ii. Treatment with bevacizumab alone and in combination with irinotecan (Friedman et al., 2009)
 - c. Mechanism of action: No need to cross the BBB; a monoclonal antibody that binds directly to vascular endothelial growth factor (VEGF), a factor released by endothelial cells and other tumor cells (Cohen et al., 2009)
 - d. Usually administered over 30–90 minutes every 14 days. Should not be started for at least 28 days following surgery, and should be discontinued 28 days before elective surgery to prevent risk of infection and delayed wound healing (Cohen et al., 2009).
 - e. Side effects: Hemorrhage, hypertension, proteinuria, delayed wound healing, thromboembolism, gastrointestinal perforation, local phlebitis (Cohen et al., 2009)
 - f. Bevacizumab has been associated with a significant dose-dependent increase in risk of proteinuria and hypertension (Zhu, Wu, Dahut, & Parikh, 2007). With bevacizumab therapy, proteinuria usually precedes hypertension, supporting the possibility that this toxicity is related to endothelial wall inflammation (Patel et al., 2008).

- g. Eleven to 16 percent of patients receiving bevacizumab have significant enough hypertension to require addition or adjustment of antihypertensive medications (Yusuf, Razeghi, & Yeh, 2008).

Nursing recommendation: Nurses should be aware that bevacizumab can be administered to treat recurrence of high-grade gliomas (Level 2). With the administration of bevacizumab, nurses should monitor urinalysis for suspected proteinuria and monitor blood pressure by checking vital signs at baseline and with each clinic visit. Nurses may need to establish home blood pressure routines while antihypertensive medications are adjusted (Level 3). Nurses should assess for proper wound healing following surgery, signs and symptoms of DVT and pulmonary embolism (PE), and apply ice to the puncture site after infusion (Level 3).

2. Nitrosureas

- a. Mechanism of action: DNA-damaging methylating agents that cross the BBB (Schallreuter, Gleason, & Wood, 1990)
- b. BCNU: IV administration over 60 minutes; side effects include nausea, vomiting, local phlebitis, myelosuppression, fatigue, pulmonary fibrosis, pulmonary or hepatic veno-occlusive disease, renal and liver damage, and hair loss (Wilkes & Barton-Burke, 2014)

Nursing recommendation: Nurses should administer antiemetics before and during drug administration when patients are taking nitrosurea drugs; apply ice to the puncture site; monitor weekly laboratory analysis, especially WBC and platelet counts; obtain periodic chest X rays; and monitor for respiratory, liver, and kidney dysfunction (Level 3).

- c. Carmustine polymer wafer (Gliadel wafer): intracavitary administration
 - i. Implanted into the surgical cavity after tumor is removed at the time of surgery
 - ii. Provides slow, direct drug to the tumor site with the benefit of minimal systemic toxicity and no limitation posed by the BBB (Nagpal, 2012)
 - iii. Improves survival in patients with newly diagnosed high-grade gliomas: 13.9-month survival with the carmustine polymer wafer at time of initial resection vs. 11.6-month survival for patients without the carmustine polymer wafer at time of initial resection (Westphal et al., 2003)
 - iv. Definitive guidelines for the optimal use in combination with systemic

- chemotherapy have not yet been established (Westphal et al., 2003).
- d. Side effects: Seizures, intracranial infection, delayed wound healing, brain edema. (Wilkes & Barton-Burke, 2014).
Nursing recommendation: Carmustine polymer wafers may prolong survival when implanted into the resection cavity at the time of surgery for high-grade gliomas (Level 2). Nurses should monitor patients for seizures and signs of infection and assess for adequate wound healing (Level 3).
 - e. Lomustine (CCNU): Oral administration
 - i. Side effects: Nausea, vomiting, myelosuppression, elevated aspartate aminotransferase (AST) level, pulmonary fibrosis, renal damage (Wilkes & Barton-Burke, 2014)
Nursing recommendation: Nurses should administer antiemetics as needed; monitor weekly laboratory analysis, especially WBCs and platelets; obtain periodic chest X rays; and monitor for respiratory, liver, and kidney dysfunction (Level 3).
3. Platinum compounds
 - a. Mechanism of action: Alkylating agents, which interfere with DNA replication by producing DNA crosslinks (Heiger-Bernays, Essigmann, & Lippard, 1990)
 - b. Cisplatin (Platinol): IV administration; side effects include nausea, vomiting, neuropathy, hearing loss, tinnitus, peripheral neuropathy, fatigue, electrolyte imbalance, renal failure, thrombocytopenia, and hair loss (Wilkes & Barton-Burke, 2014)
 - c. Carboplatin (Paraplatin): IV administration
 - i. Side effects: Delayed nausea and vomiting, hair loss, fatigue, loss of appetite, peripheral neuropathy, neutropenia, thrombocytopenia (Winkeljohn & Polovich, 2006)
 - ii. The incidence of carboplatin hypersensitivity may increase with multiple doses; an intradermal skin test is suggested for patients after the seventh dose (Winkeljohn & Polovich, 2006). A positive skin test results in a wheal of at least 5 mm in diameter with a surrounding flare (Winkeljohn & Polovich, 2006).
Nursing recommendation: Nurses should administer antiemetics as necessary if a patient is taking a platinum-based chemotherapeutic agent. They should assess for numbness or tingling of fingers and toes and hearing loss, monitor for electrolyte imbalance including intake and output, and encourage fluid intake. With carboplatin administration, nurses should monitor complete blood count (CBC). Nurses should consider an intradermal skin test after multiple doses of carboplatin to assess for hypersensitivity (Level 3).
 4. Procarbazine (Matulane): Oral administration
 - a. Mechanism of action: An alkylating agent that inhibits DNA, RNA, and protein synthesis; crosses the BBB
 - b. Side effects: Nausea, vomiting, myelosuppression, rash, stomatitis, constipation, pneumonia, peripheral neuropathy, and abdominal pain; hypertensive crisis or intracranial hemorrhage from interaction with tyramine in food (Wilkes & Barton-Burke, 2014)
Nursing recommendation: Nurses should administer antiemetics as needed; monitor weekly CBC; maintain good oral hygiene; monitor periodic chest X rays; assess for respiratory problems; assess peripheral nerve function; and teach avoidance of foods high in tyramine that can contribute to hypertension such as beer, red wine, cheese, bananas, eggplant, and avocados (Level 3).
 5. Vincristine (Oncovin or Vincasar PFS): IV administration
 - a. Mechanism of action: A plant alkaloid that inhibits mitosis; does not cross the BBB
 - b. Vincristine can cause neurotoxicity that affects the smooth muscles of the gastrointestinal (GI) tract, leading to decreased peristalsis.
 - c. Vincristine is used in combination with procarbazine and CCNU (referred to as procarbazine, CCNU, and vincristine treatment).
 - d. Side effects: neurotoxicity that affects the smooth muscles of the GI tract leading to constipation, abdominal pain, and paralytic ileus (Wilkes & Barton-Burke, 2014). Peripheral neuropathy can occur with the first dose, and symptoms may appear after vincristine has been stopped (Verstappen et al., 2005).
Nursing recommendation: Nurses should assess for abdominal pain or cramping and instruct patients to report constipation if it occurs. Patients and nurses should be alert to constipation complications such as fecal impaction. Nurses should encourage high fluid intake and a high-fiber diet. In addition, nurses should assess for numbness and tingling of fingers and toes (Level 3).
 6. Topoisomerase inhibitors
 - a. Mechanism of action: Topoisomerases are enzymes critical for regulation of cellular

growth; inhibition of these enzymes can lead to DNA damage (Hsiang, Lihou, & Liu, 1989).

- b. Irinotecan (CPT-11 or Camptosar): IV administration
 - i. Side effects: Nausea, vomiting, fatigue, neutropenia, thrombocytopenia, and hair loss. Severe diarrhea can be a potentially fatal complication (Sharma, Tobin, & Clarke, 2005).
 - ii. Irinotecan is associated with both acute and delayed diarrhea, and each requires a different treatment strategy. Atropine can be used for early-onset cholinergic diarrhea; loperimide (Imodium) can be used for late-onset diarrhea (Benson et al., 2004).

Nursing recommendation: When topoisomerase inhibitors are given, nurses should consider administering an antiemetic and CBC monitoring. They should discuss with the patient possible hair loss and coping strategies with support of body image. Replacement of fluid and electrolytes, including potassium, may be necessary because of possible diarrhea. Nurses should administer medication as appropriate for both acute and delayed diarrhea (Level 3).

- c. Etoposide (VePesid or VP-16): Oral or IV administration
 - i. Side effects: Nausea, vomiting, diarrhea, fever, hypotension, myelosuppression, leukopenia, neutropenia, thrombocytopenia, hair loss, peripheral neuropathy, mucositis, and hepatotoxicity (Wilkes & Barton-Burke, 2014)

Nursing recommendation: Nurses should premedicate patients with antiemetics and continue prophylactically after drug administration. Nurses should also monitor WBCs and platelets and assess for signs of bleeding secondary to low platelets, blood in urine or stools or black tarry stools, bleeding gums, and easy bruising. Nurses should discuss with patients possible hair-loss and coping strategies, assess for numbness and tingling of fingers and toes, observe the patient's mouth for signs of ulceration, monitor AST/alanine aminotransferase for hepatotoxicity, obtain baseline blood pressure before IV administration, and check blood pressure every 15 minutes during infusion to monitor for hypotension (Level 3).

- 7. Clinical trials in chemotherapy
 - a. No standard therapy has demonstrated benefit over any other, which necessitates a reanalysis of currently accepted treatment strategies and newly designed approaches

(Wainwright, Nigam, Thaci, Dey, & Lesniak, 2012).

- b. New trials assess the efficacy of chemotherapy, vaccination for immunotherapy, and drug delivery modalities. Specifically, trials assess convection-enhanced delivery via catheters that will provide more reliable drug delivery to the tumor site and viruses for gene delivery (Vogelbaum & Iannotti, 2012).
- c. Clinical trial resources include
 - i. NIH's Clinical Trials website (www.clinicaltrials.gov)
 - ii. National Cancer Institute's Cancer Trials Support Unit (www.ctsu.org)
 - iii. American Brain Tumor Association TrialConnect (www.emergingmed.com/networks/abta/)

Nursing recommendation: Nurses should provide educational materials as appropriate and ensure informed consent is obtained if a patient decides to participate in a clinical trial. Nurses should also be aware that treatment with carmustine wafer, reradiation, or multiple systemic therapies may influence eligibility in some clinical trials (Level 3).

E. Chemotherapy for low-grade gliomas

1. The role of chemotherapeutic agents in the treatment of low-grade gliomas is evolving and no consensus exists for a standard treatment regimen (Neyns et al., 2005).
2. Some patients with low-grade gliomas who undergo gross total resection of their tumor can be followed with serial imaging alone (Neyns et al., 2005).
3. Upon tumor recurrence and progression, the chemotherapeutic agents listed in **Table 5** may be used along with consideration for tumor biology (Neyns et al., 2005).

F. Chemotherapy for CNS lymphoma

1. Primary CNS lymphoma is a rare, yet aggressive, lymphoma.
2. Methotrexate-based chemotherapy, possibly combined with RT, is standard (Thiel et al., 2010).
3. Methotrexate (Rheumatrex or Trexall): Oral, IV, or intrathecal
 - a. Side effects: Nausea, vomiting, loss of appetite, mucositis, oral or GI ulceration, fatigue, pulmonary fibrosis (Thiel et al., 2010)

Nursing recommendation: For patients receiving methotrexate for CNS lymphoma, nurses should administer an antiemetic as needed, promote good oral hygiene by encouraging patients to follow oral care protocols, and obtain periodic chest X rays (Level 3).

Table 5. Chemotherapeutic Agents: Route and Common Side Effects in the Management of Brain Tumors

| Drug | Route | Side Effects |
|--|-----------------------------------|--|
| Temozolomide (Temodar) | Oral or Intravenous | Nausea and vomiting Myelosuppression Constipation Headache Fatigue |
| Bevacizumab (Avastin) | Intravenous | Hemorrhage Delayed wound healing Hypertension Thromboembolism Gastrointestinal perforation Proteinuria Local phlebitis |
| Carmustine (BCNU) | Intravenous | Nausea and vomiting Myelosuppression Pulmonary or hepatic veno-occlusive disease Pulmonary fibrosis Renal and liver damage Fatigue Local phlebitis |
| Carmustine Polymer Wafer (Gliadel wafer) | Intracavitary | Intracranial infection Delayed wound healing Brain edema Seizures |
| Lomustine (CCNU) | Oral | Nausea and vomiting Myelosuppression Elevated aspartate aminotransferase Renal damage Pulmonary fibrosis |
| Cisplatin (Platinol) | Intravenous | Nausea and vomiting Neuropathy Electrolyte imbalance Eripheral neuropathy Renal failure Thrombocytopenia Fatigue Hearing loss Tinnitus |
| Carboplatin (Paraplatin) | Intravenous | Nausea and vomiting (delayed) Thrombocytopenia Loss of appetite Peripheral neuropathy Hair loss Neutropenia Hypersensitivity |
| Procarbazine (Matulane) | Oral | Nausea and vomiting Myelosuppression Peripheral neuropathy Constipation Abdominal pain Pneumonia Stomatitis Hypertensive crisis or intracranial hemorrhage from interaction with tyramine in food |
| Vincristine (Oncovin or Vincasar PFS) | Intravenous | Peripheral neuropathy Constipation Abdominal pain Paralytic ileus |
| Irinotecan (CPT-11 or Camptosar) | Intravenous | Nausea and vomiting Neutropenia Thrombocytopenia Acute and delayed diarrhea Fatigue Hair loss |
| Etoposide (VePesid or VP-16) | Oral or Intravenous | Nausea and vomiting Myelosuppression Diarrhea Leukopenia Peripheral neuropathy Fever Thrombocytopenia Hypotension Hair loss Hepatic damage Neutropenia |
| Methotrexate (Rheumatrex or Trexall) | Oral, Intravenous, or Intrathecal | Nausea and vomiting Loss of appetite Mucositis Oral or gastrointestinal ulceration Fatigue Pulmonary fibrosis |

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G. Chemotherapy for brain metastases

1. Metastasis lesions are the most common brain tumors. Surgical resection and RT are the primary treatments. Systemic chemotherapy plays a limited role (Armstrong & Gilbert, 2001; Davies, 2012).
2. In a dose escalation trial for patients with multiple brain metastases, outcomes did improve in those treated with concurrent temozolomide and WBRT (Mikkelsen, Anderson, et al., 2010).

H. Patient and family education

1. Nurses are uniquely positioned to guide and educate patients and their families during brain tumor chemotherapeutic treatment. Patient and family education is crucial to promoting medication regimen adherence for optimal response to therapy.
2. Anxiety should be addressed.
 - a. Emotional support and introduction of new information should be provided as appropriate.

- b. Patients or family members should be encouraged to keep a notebook to record information such as appointments, medication changes, treatment dates, new symptoms, and questions as they arise.
 - c. Patients and family members should be screened for psychological distress and referred to social work services, pastoral services, or mental health services as appropriate (Klimaszewski, 2008).
3. Chemotherapy-induced nausea and vomiting (CINV) is a common side effect of chemotherapy regimens, and uncontrolled CINV can become a significant quality-of-life issue if not properly managed.
- a. Patients should be encouraged to eat small, frequent meals (Tipton et al., 2007).
 - b. Antiemetic administration instructions specific to the chemotherapeutic agent should be provided. 5-HT₃ receptor agonists such as ondansetron (Zofran) have proven effective in the management of nausea and vomiting when administered prior to chemotherapy (Vrabel, 2007).
 - c. Effective oral care protocols such as using a soothing oral rinse or topical solution should be established (Rubenstein et al., 2004).
4. Management of oral mucositis
- a. Adherence to an oral care protocol can reduce the duration and severity of mucositis (McGuire, Correa, Johnson, & Wienandts, 2006; Rubenstein et al., 2004).
 - b. Randomized study results support the benefits of a systemic oral care protocol and the use of an inexpensive salt and sodium bicarbonate rinse (Dodd et al., 2003).
 - c. Basic components include assessment, patient education, tooth brushing, flossing, and oral rinses.
 - d. Tobacco, alcohol, or irritating foods (acidic, hot, spicy) should be avoided and adequate hydration maintained (Dodd et al., 2003)
5. Chemotherapy-related cognitive impairment
- a. The prevalence of cognitive impairment among patients with brain tumors is reported as 50%–80% (Tucha, Smely, Preier, & Lange, 2000). Initiation of chemotherapy may compound cognitive impairment.
 - b. Research is limited regarding pharmacologic and nonpharmacologic interventions for the prevention, treatment, and management of cognitive impairment (Von Ah, Jansen, Allen, Schiavone, & Wulff, 2011).
 - c. Nonpharmacologic interventions for improving cognitive impairment in patients with brain tumors include exercise (Locke et al., 2008) and cognitive training (Gehring, Aaronson, Taphoorn, & Sitskoorn, 2010).
- d. Psychostimulants such as donepezil may improve cognitive functioning and mood in patients with brain tumors (Shaw et al., 2006).
 - e. The need to monitor neurological changes should be addressed (Von Ah et al., 2011).
 - f. Patients and families should be educated on symptoms that may indicate tumor growth and/or chemotherapeutic drug toxicity.
 - i. Seizure
 - ii. Headache
 - iii. Drowsiness
 - iv. Progressive weakness or numbness
 - v. Visual changes
- Nursing recommendation:** Nurses should assess for adverse effects related to chemotherapeutic management of brain tumors and provide the appropriate interventions discussed above. Nurses should provide patients and families with education and guidance throughout the brain tumor treatment process and anticipate that psychosocial and emotional needs may evolve during the course of treatment (Level 3).
- Nursing recommendation:** Nurses should provide written and verbal instructions and educate patients regarding oral care. They should emphasize core elements of an oral care protocol and verify understanding with return explanation and demonstration (Level 2).
- Nursing recommendation:** Nurses should address the potentially debilitating problem of chemotherapy-related cognitive impairment. If a patient exhibits signs of cognitive impairment, initiate nonpharmacologic and/or pharmacologic interventions as described above (Level 3).
- Nursing recommendation:** Nurses need to focus on patient education by ensuring patient and caregiver understanding of the importance of adhering to the chemotherapeutic agent regimen for optimal treatment. Nurses can promote the use of medication reminders and self-management of symptoms from adverse effects to support adherence to the regimen. Nurses should provide verbal and written instructions including the name of each medication, dose, and schedule; a calendar to show which days the medication is taken and breaks; and how the drug is taken (Level 3).
- I. Novel therapies for primary malignant brain tumor**
- 1. NovoTTFTM-100A
 - a. Approved for use by the FDA in 2012
 - b. Continuously worn electrodes are placed on the surface of the head that deliver low-intensity, intermediate-frequency alternating electrical fields.

- i. Postulated mechanism of action is mitotic spindle disruption, which prevents cells from transitioning from metaphase to anaphase, leading to cell death (Salzberg, Kirson, Palti, & Rochlitz, 2008).
- ii. Low-intensity, intermediate-frequency electrical stimulation has a selective effect on dividing cells (Mrugala, Adair, & Kiem, 2012).
- b. In a study of patients with recurrent malignant glioma that compared NovoTTF-100A with chemotherapy of physician choice, participants were randomized to either the device (worn a mean of 20.6 hours/day or 86% median compliance) or received oral or IV chemotherapy (Stupp, et al., 2012).
 - i. NovoTTF-100A was found to be at least as effective as chemotherapy without the hematologic, infectious, or GI effects associated with chemotherapy (Stupp et al., 2012).
 - ii Contact dermatitis was the primary adverse event, and it resolved completely with topical steroids and did not require treatment to be held or discontinued (Stupp et al., 2012).
 - iii. No significant differences in quality of life were found between groups, although cognitive, emotional, and role functions were slightly better in the Novo-TTF-100A-treated group (Stupp et al., 2012).
 - a) Physical function was slightly worse in this group, but thought to be related to the need to transport the device.
 - c. Compliance with therapy is a key issue that improves with experience and education (Fonkem & Wong, 2012).
 - d. Ongoing studies are being conducted in patients with newly diagnosed glioblastoma and brain metastases (Mrugala et al., 2012).
- 2. Laser interstitial thermal therapy (LITT) applies transcranial laser energy to a tumor (Butowski & Berger, 2012).
 - a. As laser energy is absorbed into tissue, it denatures the tissue.
 - b. LITT currently is under study for patients with inaccessible tumors or tumors that have failed RT or radiotherapy and for those who cannot undergo surgical resection

Nursing recommendation: Nurses should be aware that use of electrical tumor treatment fields may be considered a comparable treatment option to chemotherapy for patients with recurrent malignant glioma, particularly when hematologic, infectious, or GI toxicities limit treatment options (Level 1). When tumor treatment fields are used, nurses should assess the skin for topical dermatitis (Level 1). Nurses should educate patients about measures to improve comfort and compliance with the system (Level 3).

J. Vaccine immunotherapy for brain tumors

1. Application
 - a. Has been studied primarily in glioblastoma (Finnocchiaro & Pellegatta, 2011)
 - b. May be of benefit in certain types of metastases, such as melanoma (Allen & Gundrajakuppam, 2012)
 - c. Vaccines induce an immune activation (response) either peripherally (a generalized response), within the tumor itself (specific response), or both (Polivka, Polivka, Rohan, Topolcan, & Ferda, 2012).
 - d. There currently is no approved vaccine against brain tumor, but many approaches are under study in various clinical trials (Finnocchiaro & Pellegatta, 2011)
2. Strategies
 - a. Adoptive immunotherapy involves administering sensitized immune cells.
 - i. A patient's immune cells are activated outside the body and then delivered into the tumor cavity.
 - ii. Current studies are limited because of lack of tumor specificity and clinical efficacy (Finnocchiaro & Pellegatta, 2011).
 - b. Active immunotherapy boosts antitumor activity of T cells, specifically, the antigen-presenting cells tumor (Xu, Stockhammer, & Schmitt, 2012)
 - i. Autologous vaccine: Antigens or parts of cells removed during tumor resection are used to develop a vaccine against that specific antigen.
 - ii. Dendritic cell (DC) vaccine: Activates the DCs, which are responsible for regulating antitumor T-cell response
 - iii. Glioblastoma-associated antigen vaccine: Targets a specific antigen expressed by glioblastoma; the vaccine furthest in development targets EGFRvIII
 - iv. Viral antigen vaccine targets specific viral antigens present in tumor tissue (cytomegalovirus, Epstein-Barr, Hepatitis, and Human T-lymphotropic virus).
3. Limitations of vaccine therapy
 - a. Clinical studies have produced variable responses (Finnocchiaro & Pellegatta, 2011).
 - b. Timing and need for repeat injections varies among studies and is difficult to standardize.
 - c. An "immunoprivileged" site presents challenges for inducing vaccine response in the brain (Marsh, Goldfarb, Shafman, & Diaz, 2013).
 - d. Applications are likely to evolve as understanding of neuro-immunology and potential molecular targets expands (Polivka et al., 2012).

- e. Interactions of immune-based therapies with chemotherapy and RT are not known (Marsh et al., 2013).

Nursing recommendation: Nurses should be knowledgeable about immune-based brain tumor therapies currently in clinical trials (Level 3).

VII. Symptom Management

Patients with CNS malignancy experience a range of neurologic and systemic conditions adding to overall morbidity (Lacy et al., 2012). Symptoms may be caused by the tumor or peritumoral edema—specifically, seizures, cognitive dysfunction, fatigue, or focal deficits—and/or as a result from treatment-related toxicities from chemotherapy or radiation. Corticosteroids and antiepileptic drugs may cause additional symptoms. Nurses are challenged with identification and successful management of these symptoms to optimize quality of life for their patients.

A. Vasogenic edema

1. Etiology: Disruption of the BBB by the tumor, resulting in increased capillary permeability. Plasma proteins and water-soluble substances are transported into the brain surrounding the tumor, resulting in edema. The edema tends to extend around white matter tracts in preference to the more cellular grey matter (Batchelor & Byrne, 2006).
 2. Symptoms: Focal symptoms reflect tumor location. Increasing headache, projectile emesis, rapid cognitive changes, or somnolence may be signs of increased ICP (Lacy et al., 2012).
 3. Treatment: Corticosteroids are believed to decrease edema by decreasing the permeability of tumor capillaries and improving integrity of the BBB. In the absence of randomized controlled trials (RCTs), clinical experience has established practice guidelines (Lacy et al., 2012).
 4. Dexamethasone is the drug of choice for the treatment of vasogenic edema in symptomatic patients because of its low mineralocorticoid effects and long half-life (Roth, Wick, & Weller, 2010). Initially, the dose may be 4–6 mg IV or by mouth every 6 hours and adjusted based on clinical response.
 - a. Although dexamethasone often is given every 6 hours in the hospital, it has a long half-life and can safely be dosed twice a day (Lacy et al., 2012).
 - b. Steroid dose commonly is adjusted over the course of treatment. In an effort to decrease side effects, the lowest effective dose that maximizes neurologic function is recommended (Batchelor & Byrne, 2006).
 - c. When discontinuing steroids, the dose should be tapered gradually based on dose, length of treatment, and patient response (Batchelor & Byrne, 2006; Lacy et al., 2012).
5. Prolonged use of corticosteroids can cause suppression of the hypothalamic-pituitary-adrenal axis and secondary adrenal insufficiency. A too rapid taper schedule can lead to nonspecific symptoms including nausea, myalgias, headache, and hypotension (Roth et al., 2010; Wen et al., 2006).
 6. Ongoing assessment and management of potential side effects of steroids (**Table 2**).
 - a. Steroids can cause an extensive array of side effects as listed in **Table 2**. Additional side effects can include, but are not limited to, acne, blurred vision, cataracts, hirsutism, hypokalemia, thinning of the skin, and striae (Lacy et al., 2012; Roth et al., 2010; Wen et al., 2006).
 - b. For osteoporosis and increased risk for fracture, daily calcium of 1,500 mg and vitamin D 800 IU are recommended by the American College of Rheumatology (American College of Rheumatology Ad Hoc Committee on Glucocorticoid-Induced Osteoporosis, 2011).
 7. Education: *Steroids: Focusing on Treatment* (2011) is an educational pamphlet supplied by the American Brain Tumor Association (ABTA; 800.886.2282, www.abta.org).

Nursing recommendation: Nurses should be aware of the potential side effects of steroids and provide ongoing assessment of symptoms. Nurses should work with the healthcare team and caregivers to manage these symptoms (Level 2).

B. Seizures

1. Among patients with a brain tumor, 20%–40% experience a seizure prior to diagnosis, and an additional 20%–45% will eventually have a seizure (Glantz et al., 2000).
2. Seizures can increase morbidity, provoke anxiety, decrease independence, interfere with the ability to work, require additional medications, and decrease a patient's overall quality of life (Stevens, 2006).
3. The etiology of epilepsy in patients with brain tumors is multifactorial and involves tumor, vascular changes, altered BBB, edema, necrosis, scar tissue, hemosiderin deposits, treatment, medication interactions, and metabolic disturbances (Englot, Berger, Chang, & Garcia, 2012).
4. Lower-grade tumors; cortical-based lesions; tumors in the grey matter, frontal or temporal location; multifocal disease; and proximity to the Rolandic fissure or central sulcus may increase seizure risk (Rudá, Trevisan, & Soffietti, 2010).
5. Gross total resection of the tumor may resolve seizures (Chang et al., 2008).

6. Clinical picture: Patients with brain tumors most often will have simple or complex-partial seizures. They may have secondary generalization (Hildebrand, Lecaille, Perennes, & Delattre, 2005). Symptoms of the seizure reflect the location of the lesion, although some patients also may have a seizure focus distant from the lesion (Sperling & Ko, 2006; Vecht & van Breeman, 2006).
 - a. Frontal lobe: Motor symptoms on the contralateral side; left frontal/temporal speech center involvement; may exhibit speech arrest
 - b. Temporal: May be complex partial; déjà vu, a strong feeling that an event has already occurred; may present with auras (e.g., olfactory)
 - c. Parietal lobe seizures often are sensory.
 - d. Occipital lobe seizures may present as visual hallucinations.
 7. Indications for an AED
 - a. The American Academy Neurology (AAN) Practice Parameter does not recommend the routine use of AEDs in patients with brain tumors who have never had a seizure (Glantz et al., 2000).
 - b. Despite a lack of RCTs, similar guidelines should apply to patients with brain metastases; routine prophylactic use of AEDs is not recommended (Mikkelsen, Paleologos et al., 2010).
 - c. In patients who have never had a seizure, are medically stable, or are experiencing side effects of an AED, the AAN Practice Parameter supports tapering and stopping the AED after the first postoperative week (Glantz et al., 2000).
 8. Choice of AED medication
 - a. Selections based on patient response, potential for interaction with other drugs, and side effect profile (Kerrigan & Grant, 2011; Rossetti & Stupp, 2010)
 - b. Patients may experience fatigue, dizziness, rash, or neurocognitive deficits (Thompson et al., 2006).
 - c. Enzyme-inducing AEDs such as carbamazepine (Tegretol), phenobarbital, and phenytoin (Dilantin) affect the metabolism of other drugs, including several chemotherapy agents. These drugs should be avoided if possible (NCCN, 2014c).
 - d. Nonenzyme-inducing AEDs are generally preferred (Rossetti & Stupp, 2010). These drugs include gabapentin (Neurontin), lacosamide (Vimpat), lamotrigine (Lamictal [generic available]), levitericetam (Keppra [generic and IV available]), pregabalin (Lyrica), topiramate (Topamax [generic available]), and zonisemide (Zonegran).
 - e. Patient comorbidities may influence medication choice. Newer AEDs also may be used to treat pain and psychiatric disorders (Thompson et al., 2006).
 9. Nursing care: Patient and family education
 - a. The seizure threshold is lowered by physical or emotional stress, fatigue, sleep deprivation, and alcohol (Nakken et al., 2005).
 - b. The patient should take AEDs as prescribed. Because patients may have cognitive issues, use of a pill box or having the caregiver or family member supervise dosing may improve compliance. Enough time should be allowed for refills, especially if using a mail order pharmacy.
 - c. The patient and caregiver or family member should have an accurate list of medications available.
 - d. For partial or complex partial seizures, advise the caregiver or family member to document the clinical presentation, duration, and possible provoking factor. When a generalized seizure or recurrent seizures occur, call 911. See www.abta.org/brain-tumor-treatment/caregivers/seizure-first-aid.html.
 - e. A seizure education resource is available at www.epilepsyfoundation.org.

Nursing recommendation: Nurses should be familiar with the dosing and potential side effects of AEDs used for patients with tumors. Patient and caregiver/family education should include correct use, potential side effects, and what to do in the event of a seizure (Level 3).
- ### C. VTE (DVT and PE)
1. Thrombus formation is the result of a hypercoagulable state, endothelial injury, and venous stasis (Winters & Garcia, 2010).
 2. Risk factors include immobility, poor performance status, older age, prior history of VTE, smoking, obesity, and a hypercoagulable state related to cancer (Winters & Garcia, 2010). Malignant gliomas in particular confer a high risk. Gliomas overexpress VEGF. This is associated with upregulation of tissue factor, a principal initiator of the coagulation cascade. The reported 6- to 12-month risk of DVT in high-grade glioma is 20%–30% (Gerber, Grossman, & Streiff, 2006).
 3. VTE is associated with increased morbidity, mortality, the need for additional medication, and consequent risk of hemorrhage.
 4. Symptoms of DVT can include pain, swelling, and heaviness or cramping of a limb; most often occur in a lower extremity; often are unilateral; edema of the face, neck, or supraclavicular space may occur (NCCN, 2013b).
 5. Assessment for a DVT involves duplex venous ultrasound (NCCN, 2013b).

6. Symptoms of PE include dyspnea, chest pain, and/or tachypnea.
7. PE assessment: Chest X ray and electrocardiogram are helpful to rule out other etiology of symptoms. CT angiogram is the preferred evaluation for initial diagnosis (NCCN, 2013c).
8. Prophylaxis of VTE
 - a. Anticoagulation prophylaxis is recommended for inpatients with active cancer without contraindication to therapy including LMWH, fondaparinux (Arixtra), or subcutaneous UFH (NCCN, 2013c).
 - b. Intermittent pneumatic compression device use and graduated compression stockings are recommended if anticoagulation is contraindicated (NCCN, 2013c).
 - c. Inferior vena cava (IVC) filters are indicated for prevention of PE in patients who cannot be treated with anticoagulation. There are no appropriate clinical trials in this setting. IVC filters do not prevent DVT and may be associated with increased risk of recurrent DVT. An IVC filter is recommended only for patients when the benefit outweighs the risk (NCCN, 2013c).
9. Acute treatment of VTE: Begin immediate treatment (for 5–7 days) with UFH, LMWH, or fondaparinux in patients without contraindication to anticoagulation. Minimum duration of treatment of DVT is 3–6 months; for PE, the minimum duration of treatment is 6–12 months. LMWH without warfarin is recommended for the first 6 months of chronic treatment (NCCN, 2013c).
10. Chronic therapy: Medication choice is based on the clinical situation, cost, ease of administration, and need. A summary of the National Comprehensive Cancer Network® (NCCN®) recommendations (2013c) is provided in this guideline; access the full guideline for complete recommendations.
 - a. LMWH is preferred in patients with uncomplicated DVT because this allows for outpatient treatment and does not require laboratory monitoring. Drugs include enoxaparin (Lovenox), tinzaparin (Innohep), and dalteparin (Fragmin).
 - b. Warfarin may be used for long-term therapy of VTE. This should be started with UFH, LMWH, or fondaparinux until an international normalization ratio (INR) of 2 or higher is achieved. Dose requirements are highly variable. Ongoing monitoring of INR is needed; an INR of 2–3 is typically the goal (NCCN, 2013c). A list of foods and medications that interact with warfarin and alter efficacy should be considered. Vitamin K reverses the anticoagulant effects of warfarin (Eisenson, 2007).
 - c. Fondaparinux is given subcutaneously and dosing is based on body weight. The dose should be adjusted or avoided with renal insufficiency.
 - d. UFH: Subcutaneous for VTE prophylaxis, IV infusion for treatment. During heparin infusion, an activated partial thromboplastin time therapeutic range of 2–2.5 times the control value is recommended, or follow institutional guidelines. Anticoagulant effects of heparin are reversible with protamine sulfate.
11. Anticoagulation in patients on bevacizumab (Avastin).
 - a. In a review of 1,024 patients with intracranial hemorrhage, the overall rate of intracranial hemorrhage in patients on bevacizumab was 3.7%, similar to the 3.6% rate of patients not on bevacizumab (Khasraw, Holodny, Goldlust, & DeAngelis, 2012).
 - b. Norden and associates (2012) reviewed 282 patients treated with bevacizumab, 64 of whom were on anticoagulant therapy. There was a higher rate of overall hemorrhage (20%), serious hemorrhage (6%), and intracranial hemorrhage (11%) in patients on anticoagulation as compared with 1% serious hemorrhage in patients not on anticoagulation.
12. Nursing care and patient education (Eisenson, 2007)
 - a. Prevention: Avoid prolonged bed rest or immobility by encouraging ambulation, alternative exercises for nonambulatory patients, correct use of graduated compression stockings, and adequate hydration.
 - b. Assess with a high level of suspicion for swelling, redness, and pain in the lower extremities; monitor for chest pain, tachypnea, and hypoxia; review these symptoms with the patient and caregiver or family member, advising them when and who to call with concerns.
 - c. Educate regarding the correct injection technique for LMWH or heparin.
 - d. Review foods and medications that affect warfarin and the importance of keeping laboratory appointments for coagulation studies.
 - e. Monitor INR results per institutional protocol.
 - f. Discuss fall prevention and risk, avoidance of head injury, and what to do in case of bleeding.

Nursing recommendation: Nurses should work to decrease VTE risk, monitor patient symptoms, report any concerns to a provider, and administer medication as ordered (Level 2). Patients and caregivers/family members should be taught signs and symptoms and when to call the healthcare provider (Level 3).

D. Nausea and vomiting

Nausea and vomiting in patients with brain tumors may be secondary to chemotherapy, other medications, or, occasionally, a function of tumor location.

1. Among pharmacologic interventions for CINV, prevention is the most successful treatment (NCCN, 2014a).
2. Temozolomide is considered moderately to highly emetogenic; there is a 30%–90% incidence of emesis in the absence of effective antiemetic prophylaxis (NCCN, 2014a).
 - a. Medications recommended as effective include 5HT₃ antagonists: Granisetron (Kytril) and ondansetron (Zofran) are equally effective orally or IV. Dolasetron (Anzamet) is recommended orally; IV use is associated with cardiac arrhythmias.
3. Bevacizumab is listed as minimally emetogenic (NCCN, 2014a).
4. Other chemotherapeutic agents may require more aggressive prophylaxis (refer to the 2014 NCCN Guidelines [NCCN, 2014a] and **Table 5**).
5. Pretreatment for anticipated nausea and vomiting
 - a. Alprazolam (Xanax) or lorazepam (Ativan) are recommended beginning the evening before and the morning of treatment (NCCN, 2014a).
 - b. Progressive muscle relaxation may be effective (Tipton et al., 2007).
6. Nonpharmacologic interventions
 - a. Acupuncture, acupressure, guided imagery, music therapy, progressive muscle relaxation, and psychosocial support and education likely may be effective (Tipton et al., 2007).
 - b. Smaller, more frequent meals; avoidance of spicy, fatty, or highly salty foods; the use of comfort foods; and taking antiemetics prior to meals for maximum effect (Tipton et al., 2007).
7. Nausea, vomiting, or anorexia unrelated to chemotherapy for patients with brain tumors
 - a. Nausea and vomiting may be treated with antiemetics.
 - b. Dexamethasone and megestrol acetate (Megace) may be effective (Adams et al., 2009).

Nursing recommendation: Nurses should provide an appropriate antiemetic regimen as prescribed (Level 1). Nurses should monitor the effectiveness of the pharmacologic and nonpharmacologic regimen (Level 2).

E. Cognitive dysfunction

1. Cognitive dysfunction is estimated to occur in 50%–90% of people with brain tumor (Tucha et al., 2000).
 - a. Deficits are classified in areas of attention, memory, executive function, and language. Symptoms commonly reported by patients include short-term memory loss, decreased concentration, trouble multitasking, problems with new learning, and trouble with word finding (Gehring et al., 2010).
2. Cognitive dysfunction affects performance of ADLs, interpersonal relationships, levels of independence, ability to work, adherence to treatment regimens, and the ability to make treatment decisions or give informed consent (Fox, Mitchell, & Booth-Jones, 2006). Cognitive dysfunction has been identified by patients, caregivers, and family members in long-term survivors (Lovely et al., 2013)
3. The cause of cognitive dysfunction is multifactorial (Correa, 2006; Gehring et al., 2010). Possible causes include
 - a. The location, size, and growth rate of the tumor
 - b. Edema, seizures
 - c. Side effects of RT, chemotherapy, and AEDs
 - d. Polypharmacy
 - e. Comorbid medical conditions
 - f. Sleep disturbance, anxiety, or depression.
4. Patients with suspected cognitive dysfunction may be referred for neuropsychologic testing. This includes a battery of validated tests to assess a wide range of cognitive abilities.
 - a. Testing may be used as a baseline for comparison over time, is valuable in documenting disability in patients who appear physically well, and helps to identify depression or anxiety as a contributing dysfunction factor.
 - b. Once deficits are identified, a treatment plan can be implemented.
5. Pharmacologic treatment: Methylphenidate (Ritalin), modafinil (Provigil), and donepezil were found to be inconsistent in regard to cognitive improvement, and further studies are recommended (Gehring et al., 2010).
6. Nonpharmacologic treatment
 - a. An RCT of a cognitive rehabilitation program demonstrated a positive effect on attention, verbal memory, and decreased mental fatigue at 6 months compared to a control group (Gehring et al., 2009).

- b. Five areas of intervention yield the most benefit (Gehring et al., 2010):
 - i. Modification of the environment to simplify the demands of daily living
 - ii. Use of a planner or electronic diary
 - iii. Coping strategies: minimize distractions, organization, memory aids
 - iv. Retraining of specific skills by repetition
 - v. Patient and family education regarding brain function, cognitive deficits, and impact on daily activities
- 7. Nursing interventions
 - a. Encourage referrals and participation in occupational therapy, speech therapy, and cognitive rehabilitation programs (Fox et al., 2006).
 - b. Encourage cognitive exercises that are fun, relevant, and appropriate to the individual, such as word search or crossword puzzles, Sudoku, computer games, hobbies, BINGO or card games with friends, or helping children with homework. Recognize that these activities may be very taxing to the patient. Taper to their personal needs.
 - c. Review the medication list for polypharmacy; avoid evening dosing of steroids and diuretics. If possible, patients should not wake to take their medication.
 - d. Discuss appropriate sleep patterns, nutrition (Fox et al., 2006), and safety.

Nursing recommendation: Nurses should assess for cognitive dysfunction as a symptom of the overall disease state (Level 2). Nurses should recommend neuropsychological testing in specific cases (Level 3). Nurses need to be aware of interventions that will help patients cope with cognitive changes (Level 3).

F. Fatigue

1. Fatigue is experienced by a majority of patients with cancer, including those with brain tumors. The fatigue may persist for months or years after completion of active treatment (Armstrong & Gilbert, 2012).
2. Cancer-related fatigue is defined as “a distressing persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning” (NCCN, 2014b, p. FT-1).
3. Cancer-related fatigue is multifactorial, including effects of the tumor, surgery, chemotherapy, radiation, and medication. Fatigue may be part of a symptom cluster including emotional and cognitive factors (NCCN, 2014b).
4. Assessment
 - a. The NCCN (2014b) recommends a 10-point

numeric scale similar to a pain scale (0 = *no fatigue*, 10 = *the worst fatigue imaginable*).

- b. Piper and associates (2008) have published a list of fatigue assessment scales.
5. Screen for potentially treatable causes of fatigue including side effects of prescription and over-the-counter medication, sleep disturbance, anemia, pain, deconditioning, depression, adrenal insufficiency, electrolyte imbalance, poor nutritional status, and medical comorbidities. Laboratory work should include CBC/differential, chemistry metabolic profile, thyroid panel, TSH, and vitamin B-12 and vitamin D levels (Wen et al., 2006).
 6. Nonpharmacologic management
 - a. A moderate exercise program within limits of disease is the only intervention with a sufficient body of evidence to be “recommended for practice” (Mitchell et al., 2007).
 - b. Energy conservation techniques have been shown to be beneficial (Barsevick et al., 2004).
 - c. Cognitive behavioral therapy for sleep (Armstrong & Gilbert, 2012)
 - d. Avoid overdoing things; patients cannot “push through” cancer-related fatigue.
 7. Pharmacologic management
 - a. Methyphenidate and modafinil are psychostimulants used to decrease fatigue, although the results of trials are mixed (Kirshbaum, 2011; NCCN, 2014b).
 - b. Encourage appropriate therapy for insomnia, emotional distress, (Armstrong & Gilbert, 2012), and pain.

Nursing recommendation: Nurses should assess for fatigue throughout the trajectory of care (Level 1). Nurses should provide education for self-management and encourage psychosocial support (Level 3).

G. Distress

1. Distress is the term used by the NCCN to describe psychosocial, emotional, and psychiatric concerns in an effort to decrease the stigma associated with these terms, open up discussions, and move toward appropriate treatment (NCCN, 2013a).
2. The Glioma Outcomes Project studied 600 patients with glioma. Although more than 90% of patients reported symptoms consistent with depression, providers believed that only 15% of patients were depressed (Litofsky et al., 2004).
3. Identification and management of distress should be an integral part of the overall treatment plan for people with cancer (NCCN, 2013a).
4. Distress is “a multifactorial unpleasant emotional experience of a psychological, (cognitive, behavioral, emotional) social, and/

or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms, and its treatment" (NCCN 2013a, p. DIS-2).

5. Factors that cause distress in patients with brain tumor were dissatisfaction with communication with providers, uncertainty about the future, incomplete understanding of the disease course and treatment, and lack of direct access to a specific provider (Ford, Catt, Chalmers, & Fallowfield, 2012).
6. Risk for distress increases with (NCCN, 2013a)
 - a. History of psychiatric illness, depression, or substance abuse
 - b. Cognitive impairment
 - c. Difficulty with communication (receptive or expressive dysphasia, language barrier)
 - d. Inadequate support systems, psychosocial conflict, or family discord
 - e. Financial problems and/or limited access to care.
 - f. Severe comorbid illnesses or uncontrolled symptoms
 - g. Spiritual/religious concerns
7. Assessment
 - a. Patients should be screened for distress at the initial visit, with changes in disease status, and at appropriate intervals (NCCN, 2013a).
 - b. The Distress Thermometer (DT) is a single-question self-report scale. Patients are asked to rate their distress over the past week on a scale of 0 to 10. A score of four or more suggests a clinically relevant level of distress. The DT has demonstrated sensitivity and specificity. This is accompanied with a 39-item problem list to elicit more specific information, the NCCN Guidelines for Distress Management Version 2.2013 (**Figure 2**; NCCN, 2013a).
8. Patients also should be engaged in nonjudgmental guided discussions about possible symptoms of depression such as mood, energy level, enjoyment of usual activities, sleep, and appetite (Van Fleet, 2006).
9. Treatment should address symptoms including fatigue, cognitive changes, sleep disturbance, anxiety, or depression (Van Fleet, 2006).
10. Pharmacologic treatment may include antidepressants, anxiolytics, or hypnotics (Van Fleet, 2006).
11. Nonpharmacologic treatment
 - a. Referral to social work, counseling, chaplain services, or psychology (NCCN, 2013a)
 - b. Support groups, relaxation techniques, or exercise (NCCN, 2013a)
 - c. Ongoing access to a member of the healthcare team, preferably a nurse, with the

ability to establish a relationship to discuss treatment and psychosocial issues (Janda, Eakin, Bailey, Walker, & Troy, 2006)

- d. Many centers have developed programs to meet the needs of adolescents and young adults with cancer.

Nursing recommendation: Nurses should recognize and assist with the management of patient distress, which should be part of the overall treatment plan for people with cancer (Level 2).

H. Body image

1. Patients with brain tumors may experience a range of physical changes including skull defects, hair loss, cushinoid facies, weight gain, weakness, and impaired mobility.
2. Less visible changes such as difficulty with speech or cognitive slowing also may negatively impact identity.
3. Changes in body image may influence personal and social interactions (Freitas, 2005).
4. Interventions to decrease the impact
 - a. Allow the opportunity to discuss concerns and coping with loss (Freitas, 2005).
 - b. Use scarves or hats to cover scars, skull defects, or hair loss.
 - c. Stress that many changes will improve with time, especially the effects of steroids or RT.

Nursing recommendation: Nurses should be aware of the effect of physical changes and offer strategies to decrease the impact of changes on the patient (Level 3).

I. Rehabilitation

1. People with brain tumors may experience a range of physical, cognitive, and language deficits.
2. In the past, possibly because of concerns surrounding the short life expectancy associated with high-grade glioma, rehabilitation for neuro-oncology patients was not as well established as rehabilitation for patients with other neurologic diagnoses (Formica et al., 2011).
3. A recent meta-analysis of patients with cancer with CNS involvement undergoing inpatient physical rehabilitation showed 36% improvement in functional status (Formica et al., 2011). Patients with brain tumors receiving acute rehabilitation showed improvement comparable to patients with stroke or traumatic brain injury (Vargo, 2011). They also recognized a need for programs specific to an individuals' brain tumor deficits.
4. The goal of rehabilitation is to improve or maintain functional status. A range of rehabilitation services should be offered throughout the trajectory of the illness on an inpatient or outpatient basis (Bartolo et al., 2012).

- Cognitive rehabilitation (Section VII.E.6)
Nursing recommendation: Rehabilitation has been shown to be effective for patients with brain tumors (Level 2). Nurses should facilitate referrals and encourage patient participation (Level 2).

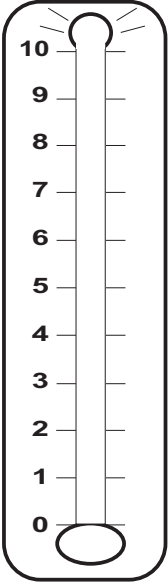
J. Caregivers and family members

- Caregivers and family members of people with brain tumors must deal with changes in cognitive function and neurobehavioral changes in addition to physical issues caused by the tumor and treatment (Sherwood et al., 2004).
- Caregivers and family members report a need for information on diagnosis, treatment options, symptom management, dealing with uncertainty and decreased cognitive function, neuropsychiatric issues, financial matters, and terminal care (Janda et al., 2006).
- Caregivers and family members report a high burden in the realm of emotional needs (Parvataneni et al., 2011).
- Although caregivers and family members need information and support, they may not have

the time or energy to attend formal caregiving programs or support groups (Schmer, Ward-Smith, Latham, & Salacz, 2008).

- Caregivers and family members have reported that interacting with others who have been in a similar situation was a significant form of support (Hricik et al., 2011). Such interactions may be facilitated by connecting a new caregiver with an experienced caregiver within one's facility, virtual support groups, or online blogs. ABTA Connections is an online community of the ABTA at www.abta.org or www.braintrust.org.
 - Refer to caregiver programs sponsored by your facility, ABTA, or other organizations such as the National Family Caregivers Association: www.nfca.org and www.familycaregiving101.org/help/financial/cfm.
- Nursing care: At the bedside, clinic, or over the phone, nurses are uniquely positioned to assess

Figure 2. The NCCN Guidelines Distress Thermometer 2013

| SCREENING TOOLS FOR MEASURING DISTRESS | | | |
|--|---|--|---|
| <p>Instructions: First please circle the number (0-10) that best describes how much distress you have been experiencing in the past week including today.</p> | <p>Second, please indicate if any of the following has been a problem for you in the past week including today. Be sure to check YES or NO for each.</p> | | |
| <p>Extreme distress</p>  <p>No distress</p> | <table border="0"> <tr> <td style="vertical-align: top;"> <p>YES NO Practical Problems</p> <p><input type="checkbox"/> <input type="checkbox"/> Child care</p> <p><input type="checkbox"/> <input type="checkbox"/> Housing</p> <p><input type="checkbox"/> <input type="checkbox"/> Insurance/financial</p> <p><input type="checkbox"/> <input type="checkbox"/> Transportation</p> <p><input type="checkbox"/> <input type="checkbox"/> Work/school</p> <p><input type="checkbox"/> <input type="checkbox"/> Treatment decisions</p> <p>Family Problems</p> <p><input type="checkbox"/> <input type="checkbox"/> Dealing with children</p> <p><input type="checkbox"/> <input type="checkbox"/> Dealing with partner</p> <p><input type="checkbox"/> <input type="checkbox"/> Ability to have children</p> <p><input type="checkbox"/> <input type="checkbox"/> Family health issues</p> <p>Emotional Problems</p> <p><input type="checkbox"/> <input type="checkbox"/> Depression</p> 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type="checkbox"/> Tingling in hands/feet</p> </td> </tr> </table> <p>Other Problems: _____</p> | <p>YES NO Practical Problems</p> <p><input type="checkbox"/> <input type="checkbox"/> Child care</p> <p><input type="checkbox"/> <input type="checkbox"/> Housing</p> <p><input type="checkbox"/> <input type="checkbox"/> Insurance/financial</p> <p><input type="checkbox"/> <input type="checkbox"/> Transportation</p> <p><input type="checkbox"/> <input type="checkbox"/> Work/school</p> <p><input type="checkbox"/> <input type="checkbox"/> Treatment decisions</p> <p>Family Problems</p> <p><input type="checkbox"/> <input type="checkbox"/> Dealing with children</p> <p><input type="checkbox"/> <input type="checkbox"/> Dealing with partner</p> <p><input type="checkbox"/> <input type="checkbox"/> Ability to have children</p> <p><input type="checkbox"/> <input type="checkbox"/> Family health issues</p> <p>Emotional Problems</p> <p><input type="checkbox"/> <input type="checkbox"/> Depression</p> 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and address the needs of caregivers (Honea et al., 2008).

- a. This may include teaching physical care tasks and symptom management tasks involving medication schedules, injections, and patient safety.
 - b. Nurses may listen to caregiver frustrations and validate their efforts (Whisenant, 2011).
 - c. Caregivers and family members may need direction to identify their needs and potential sources of support and communicate these needs to persons offering help (Hricik et al., 2011).
 - d. A specific contact person, proactive education and psychosocial support, and facilitating communication about difficult illness-related topics are recommended for caregivers (Janda et al., 2006).
6. Caregivers and family members of people with brain tumors may experience fatigue, health problems, and depression (Sherwood et al., 2004). Perception of adequate social support has been reported to lessen their distress (Ownsworth, Henderson, & Chambers, 2010; Thielemann & Conner, 2010).

Nursing recommendation: Nurses are a primary source of support for caregivers. They should provide information regarding the diagnosis, side effects of treatment, and medication schedules. Nurses should assess caregiver strain and burden and make appropriate referrals. Active listening to the concerns of the caregiver in itself may be therapeutic. Nurses can direct caregivers to other sources of support such as professional and community resources (Level 3).

VIII. Survivorship and end of life

A. Defining survivorship

1. The survival period begins at the time of diagnosis and ends at the time of death (NCI, 2012a). Some consider end of treatment as the beginning of the survival period.
2. Progression-free survival (PFS) is the period of time from diagnosis to progression (NCI, 2012b).
 - a. PFS is a common end-point measure in research studies.
 - b. For malignant brain tumors, the usual outcome measure is 6 month PFS.

B. Persisting symptoms

Upon completion of treatment, care and assessment often is limited to disease assessment, yet research indicates that symptoms can persist for survivors, even in the absence of disease (Remer & Murphy, 2004).

1. Symptoms may be due to local damage from the tumor or to adverse effects of treatment (Byrne,

2005; Remer & Murphy, 2004). Treatment consequences may not develop for years (Armstrong et al., 2002; Brown, Buckner, Uhm, & Shaw, 2003).

2. Survivors may experience persistent neurologic deficits, cognitive deficits, fatigue, depression, anxiety, and sleep disorders (Feuerstein, Hansen, Calvio, Johnson, & Ronquillo, 2007; Lovely et al., 2013; Peterson, 2001; Remer & Murphy, 2004).
3. Assessment of persistent symptoms in survivors entails (Lovely et al., 2013)
 - a. Evaluation of all areas of performance (functional, cognitive-behavioral, social)
 - b. Ongoing assessment of neurologic deficits for worsening: The presence of neurologic deficits may indicate disease progression, long-term consequences of treatment (e.g., radiation necrosis), or other unknown etiology.
 - c. Ongoing assessment of cognitive function with a standardized instrument (e.g., Cognitive Functioning Scale [Remer & Murphy, 2004]; Cognitive Symptom Checklist [Feuerstein et al., 2007]; or Cognistat [Mueller, Kiernan, & Langston, 2007]). Age may have an influence; deficits should be compared with an age-expected norm (Remer & Murphy, 2004).
 - d. Ongoing assessment of fatigue with a standardized instrument (e.g., the Multidimensional Fatigue Symptom Inventory-Short Form [Feuerstein et al., 2007]).
 - e. Ongoing assessment and monitoring for depressive symptoms with standardized instruments (e.g., Hospital Anxiety and Depression Scale [Feuerstein et al., 2007]); Beck Depression Inventory II [BDI-II; Beck, 2012], or Center for Epidemiologic Studies Depression Scale [Radloff, 1977]). An evaluation of the medication profile for drugs that may influence mood should be conducted.
 - f. Ongoing assessment of subjective reports of sleep disturbance with a standardized instrument such as the Brief Sleep Disturbance Scale (Carney et al., 2011)
4. Management of persistent symptoms
 - a. Consider referral for rehabilitation
 - i. Rehabilitation options for patients with malignant brain tumors are limited and need to be tailored to the individual, not just a brain injury regimen.
 - ii. Rehabilitation for a person with a brain tumor costs less than rehabilitation for patients with traumatic brain injury.

- iii. Rehabilitation maintains independence and improves quality of life, employment ability, and financial situation (Greenberg, Treger, & Ring, 2006; Pace et al., 2010).
- iv. Refer to a physical therapist, occupational therapist, or speech-language pathologist to address specific functional deficits.
- v. Rehabilitation may be taxing and frustrating for the patient and family.
- vi. Cognitive rehabilitation improves cognitive issues and cognitive performance (Pace et al., 2010).
- b. Encourage activity and exercise.
- c. Refer patients with a positive depression screen to a psychologist or social worker for further assessment.
- d. Consult with the provider about the need for antidepressant medications.
- e. Refer to a support group for social support (Pace et al., 2010)

Nursing recommendation: Nurses should be aware that patients may experience ongoing problems (Level 2). Survivors should be assessed for persistent symptoms even if not in active treatment (Level 2). Nurses should work with health-care team members to manage persistent symptoms (Level 2). The etiology of progressive neurologic decline in the absence of disease or treatment effects requires further study (Level 3). Referral should be made for rehabilitation for functional and cognitive deficits (Level 2). Nurses need to be aware that rehabilitation may be tiring and frustrating to survivors. Nurses should refer patients and their families to support groups (Level 3).

C. Returning to work

1. Two years after treatment, 58%–75% of people with malignant brain tumors were still working but had more work limitations and had taken more time off work than those in a comparable noncancer group (Feuerstein et al., 2007).
2. Modifiable factors contributing to change in employment status were fatigue, depression, anxiety, cognitive deficits, and sleep disorders.

Nursing recommendation: Nurses should work with brain tumor survivors and their employers to modify factors that affect ability to work and develop work setting innovations that accommodate their limitations (Level 1).

D. Family dynamics after a brain tumor diagnosis

1. Changes experienced include role and relationship changes, loss of intimacy, and divorce (Hawkins et al., 2009; Lovely et al., 2013).
2. Cognitive deficits and lack of insight experienced by survivors limits their grieving process (Remer & Murphy, 2004) and renders survivors unable to share anxieties and concerns

and address loss with their caregivers (Salander & Spetz, 2002).

3. Family members create a protective environment for survivors (Lovely et al., 2013).
4. Families are concerned that they are not prepared and have too little information to care for a family member with a brain tumor (Wideheim, Edvardsson, Pålsson, & Ahlström, 2002). Referral to a support group may enhance family dynamics (Pace et al., 2010).

Nursing recommendation: Nurses should educate families of patients with brain tumors about anticipated deficits and approaches to managing those deficits (Level 2). Nurses should refer patients with brain tumors and their families to support groups (Level 3).

E. Palliative and end-of-life care considerations

1. Physician estimates of death are unreliable (Gripp et al., 2007).
2. Objective prognostic factors may be useful in estimating survival (Gripp et al., 2007).
3. Palliative and end-of-life management require a multidisciplinary approach (Taillibert & Delattre, 2005).
 - a. Healthcare providers may not be trained to address palliative care needs and may avoid discussions about palliation (Pace et al., 2010).
 - b. Patients with malignant brain tumors may receive too little palliative care or receive it too late, with the burden of care then falling to the family (Pace et al., 2010).

Nursing recommendation: Nurses should encourage a multidisciplinary approach to palliative care early in the disease course for patients with malignant brain tumors (Level 2).

F. End-of-life needs and preferences

1. Patients with brain tumors have compromised medical decision-making capacity at end of life (Triebel, Martin, Nabors, & Marson, 2009).
 - a. Coma often occurs, necessitating decisions about nutrition and hydration.
 - b. Patients are infrequently involved in decisions about their end-of-life care (Pace et al., 2010).
2. Patient preferences for end-of-life care may differ from family and provider preferences (Steinhauser et al., 2001).
 - a. Preferences for pain management, avoidance of unnecessary care, and maintenance of dignity were congruent among patients, caregivers, and providers (Gardner & Kramer, 2009).
 - b. Concerns about accepting dependence, fear of being a burden, and preparation for death were incongruent among patients, caregivers, and providers (Gardner & Kramer, 2009).

- c. Communication and education and early planning may alleviate incongruencies (Gardner & Kramer, 2009).
- 3. Patients and families want to know what to expect of the dying process and the role of palliation and hospice (Holdsworth & King, 2011).
- 4. Patients have spiritual needs for supportive relationships, reassurance, solitude, and talk about end-of-life decisions (Nixon & Narayanasamy, 2010).
- 5. Health literacy is predictive of end-of-life preferences (Vollandes et al., 2008).
- 6. End-of-life preferences may be assessed using the Quality of Death and Dying Questionnaire (Downey, Curtis, Lafferty, Herting, & Engelberg, 2010).

Nursing recommendation: Nurses should encourage patients with malignant brain tumors to appoint a surrogate decision maker (Level 1). Nurses should encourage patients with malignant brain tumors to express end-of-life wishes in advance (Level 2). Nurses should consider patients' end-of-life preferences and spiritual needs in planning care (Level 1). Nurses should educate patients and families about the process of dying and the role of palliative and hospice care (Level 2).

G. End-of-life symptom management

1. Patients with brain tumors may experience symptoms at the end of life.
 - a. Delirium, a hyperarousal state with altered perception, awareness, and cognitive status with psychomotor behaviors, is common in all people with cancer, especially those with brain tumors (Cobb et al., 2000).
 - i. May wax and wane
 - ii. More common in men
 - iii. Common reason for inpatient hospice admission (Cobb et al., 2000)
 - iv. Increases cost of care and complicated management of other problems such as pain and anxiety (Cobb et al., 2000)
 - v. May be managed with mild sedation or antipsychotic medications
 - b. Seizures may be more frequent and difficult to control at the end of life (Krouwer, Pallagi, & Graves, 2000).
 - i. Patients and families are fearful of seizures (Krouwer et al., 2000).
 - ii. Patients at end of life may not be able to swallow AEDs (Krouwer et al., 2000).
 - a) Use the rectal route for carbamazepine (suppository or suspension), diazepam gel (Diastat), lorazepam (suspension), or valproic acid (suppository); may need to be compounded.
 - b) Use the intramuscular route for phenytoin or fosphenytoin (Cerebyx).
 - c) Increase steroid dose if the AED level is adequate (Krouwer et al., 2000)
- iii. Hospice programs often include sublingual and rectal seizure medications for emergency use in home care settings, although the exact content of hospice kits may vary widely (Bishop, Stephens, Goodrich, & Byock, 2009).
 - a) Hospice kits are inexpensive (Bishop et al., 2009).
 - b) Use may eliminate the need for emergency department visits or hospitalization (Bishop et al., 2009).
- c. Pain may occur; the most common type of pain related to brain tumor is headache (Morita, Tsunoda, Inoue, Chihara, 1999).
 - i. Pain is less problematic and opioid requirements are reduced in patients with primary versus secondary brain tumors (Morita et al., 1999).
 - ii. Steroids may assist in controlling pain, and, for some patients, may replace the need for opioids (Morita et al., 1999; Stewart-Amidei, 2005).
 - iii. RT may provide palliative relief of headache in brain metastases (Fine, 2002).
 - iv. End-of-life guidelines for pain management in people with cancer include (NCCN, 2014d)
 - a) Titration of analgesia to comfort level with ongoing assessment of pain and physiologic stability
 - b) Management of opioid toxicities including sedation, constipation, and respiratory depression
 - c) Modification of route of administration to sublingual, rectal, subcutaneous, transdermal, or IV based on patient condition.
 - d. Multiple other symptoms may occur because of local and systemic factors: anorexia, nausea, vomiting, malaise, dyspnea, edema, fever, cough, and increased oral secretions (Morita et al., 1999).
 - e. People with brain tumors are at increased risk for drug interactions that may adversely affect quality of life during the terminal stage of illness (Riechelmann et al., 2008).
 - f. Symptom assessment often is inadequate and focuses on prevalence and severity (Cheng, Thompson, Ling, & Chan, 2005).
 - g. Questionnaires elicit more symptoms than are mentioned during physician interview (Teunissen et al., 2007).

Nursing recommendation: Nurses should identify signs and symptoms of end of life early and maintain a therapeutic environment to minimize

delirium and pain and keep patients in their homes as long as possible (Level 3). Nurses should use questionnaires to assess each symptom separately and describe the meaning of each symptom for the individual patient (Level 1). Nurses should observe for seizures and consider alternative routes for AED administration (Level 2). Hospice kits that include emergency seizure management drugs may decrease the need for emergency care or hospitalization (Level 2). Assessment tools to identify end-of-life symptoms are lacking. Nurses should screen for drug interactions that may adversely affect life quality at end of life (Level 2).

H. Caregiver and family support at end of life

1. Caregivers and families experience stress and are burdened by the end-of-life process.
 - a. Issues can occur because of personal, spiritual, or cultural perspectives of the meaning of the illness and impending death.
 - b. Ongoing assessment and management of stressors and burdens is recommended (NCCN, 2014d).
 - c. Consider caregiver referrals to support services and counseling as needed (NCCN, 2014d).
2. Educating caregivers and families about caregiving aspects and what to expect at end of life may limit burden and alleviate stress (NCCN, 2014d).
 - a. Resources to support caregivers may need to be identified and mobilized, including social and spiritual support (NCCN, 2014d).

- b. Family members may benefit from respite care during the end-of-life period (NCCN, 2014d).
3. Caregivers and families may be at risk for complicated bereavement and bereavement risk should be assessed (NCCN, 2014d).
 - a. Refer to specialists in bereavement counseling if appropriate.

Nursing recommendation: Nurses should recognize that caregivers experience stress and are burdened by the end-of-life process (Level 1). Nurses should assess caregiver perception of the meaning of the illness and impending death (Level 1). Nurses should identify sources of support for the caregiver and facilitate mobilization of those supports at end of life (Level 1). Nurses should assess caregiver risk for bereavement problems (Level 1).

I. Additional end-of-life interventions

1. Active discussion with patients about life completion and preparation improves functional status and quality of life for terminally ill patients (Steinhauser et al., 2008; Steinhauser et al., 2009)
2. A palliative care team consult improves symptom control at end of life (Yennurajalingam et al., 2010).

Nursing recommendation: Nurses should consider use of a palliative care team for symptom management (Level 1). Nurses should facilitate end-of-life completion and preparation discussions with patients (Level 2).

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