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Pain in Children With Central Nervous System Cancer: A Review of the Literature

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Each year, more than 800 Canadian children aged 0–14 years old are diagnosed with cancer and approximately 135 children die as a result of cancer (Canadian Cancer Society & National Cancer Institute of Canada, 2008). In the United States, current statistics estimate that 10,700 children will be diagnosed with cancer this year (American Cancer Society, 2010). Cancer of the central nervous system (CNS) accounts for about 20% of new cases and 30% of cancer-related deaths in Canadian children (Canadian Cancer Society & National Cancer Institute of Canada, 2008). Throughout North America, brain and spinal cord tumors are the most frequent type of solid tumors in children younger than 15 (Stiller & Bleyer, 2004). The tumors are heterogeneous in nature based on numerous histologies, patterns of incidence, and etiologies. CNS tumors require a wide range of treatments, including surgery, radiation therapy, and chemotherapy, which lead to a variety of outcomes, ranging from cure to certain death (Ryan-Murray & Petriccione, 2002).

The intense treatment that children with CNS tumors undergo and the cancer itself are associated with distressing symptoms related to the various treatment modalities. Therefore, the focus of care for such children must be on managing their symptoms and improving their quality of life. One symptom that is burdensome for children with CNS cancer is pain. The Human Response to Illness (HRTI) model provides a suitable organizing framework to review the literature related to the symptom of pain in childhood CNS cancers because it addresses the multidimensional aspects of the pain experience. This article provides a comprehensive description of current literature about pain in children with CNS cancer.

Pain in Children With Cancer

The International Association for the Study of Pain ([IASP], 2008) defines pain as “an unpleasant sensory

Purpose/Objectives: To explore the current state of the science regarding pain in children with cancer, with special attention to literature related to central nervous system (CNS) tumors. This review used the Human Response to Illness (HRTI) model as an organizing framework.

Data Sources: PubMed, CINAHL®, and Scopus™ databases.

Data Synthesis: The literature review is presented with the four components of the HRTI model, including the physiologic, pathophysiologic, experiential, and behavioral perspectives of the pain response related to childhood cancer and childhood CNS cancer. The person and environmental factors that may influence a child's pain response are described.

Conclusions: Children with cancer, including CNS cancer, continue to experience pain despite the improvements in knowledge related to pain. Pain assessment and management strategies must continue to evolve and improve for nursing professionals to provide a high level of care to this patient population. The HRTI model provides an appropriate framework to gain insight into the pediatric oncology nursing role in the assessment, management, and evaluation of pain from childhood cancers.

Implications for Nursing: Nurses play a vital role in pain assessment and management for children with cancer. The HRTI model can be used to identify areas of clinical practice, education, and research that require further improvements in relation to pain in children with CNS cancer.

and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. The inability to communicate verbally does not negate the possibility that an individual is experiencing pain and is in need of appropriate pain-relieving treatment. Pain is always subjective” (IASP, 2008, section 19). This definition is critically important for infants, preverbal children, and anyone else who cannot communicate because it recognizes behavioral and physiologic indicators as essential aspects of pain assessment (Stevens, 2007).

For children with cancer, pain is a frequent experience (Campbell-Fleming & Williams, 2008; Sentivany-Collins, 2002), and children with CNS tumors are no exception. Pain may occur prior to diagnosis, during treatment, and beyond treatment into remission or palliative care. Pain in patients with cancer has one of four etiologies: the cancer itself, treatment, procedures, or unrelated causes (Jacob, Hesselgrave, Sambuco, & Hockenberry, 2007; Ljungman, Gordh, Sorensen, & Kreuger, 1999; Sentivany-Collins, 2002). Major causes of pain for children with cancer include bone and CNS metastases; postoperative pain; mucositis; procedures such as venipunctures, bone marrow aspirations, and lumbar punctures (Jacob et al., 2007); phantom limb pain; infections; and chemotherapy side effects (Hockenberry & Hooke, 2007). Pain can impede children's recovery and quality of life, thus affecting many facets of their lives and the lives of their families (Campbell-Fleming & Williams, 2008; Hooke et al., 2007; Woodgate & Degner, 2004). Assessment and management of pain related to CNS tumors in children are important components of pediatric oncology nurses' role.

Human Response to Illness Model

Using the HRTI model (see Figure 1) developed by Mitchell, Gallucci, and Fought (1991) as an organizing framework, this article explores pain from CNS tumors in children from a nursing perspective. The HRTI model encompasses four components: physiologic, pathophysiologic, experiential, and behavioral perspectives of a specific illness, within the internal and external environments (Mitchell et al., 1991). This model was chosen because it provides a comprehensive method of examining the response of pain using a nursing perspective in the context of childhood CNS tumors and recognizes the multidimensional aspects of the pain experience. In addition, the HRTI model is relevant to nursing because it establishes the foundation for a holistic approach to care and highlights key areas for nursing practice, education, and research.

Physiology of Pain

The initial component in the HRTI model is the physiologic perspective that identifies the body's normal way of functioning. Pain can be viewed as a physiologic or pathophysiologic process. For this review, the physiology of pain is interpreted as the body's normal way of perceiving pain as a protective mechanism, as in acute nociceptive pain, whereas pathophysiology of pain is an alteration of the norm, as in chronic nociceptive and neuropathic pain.

The acute pain response is initiated by stimulation of nociceptors, peripheral sensory receptors that relay the intensity, location, and duration of a painful stimulus.

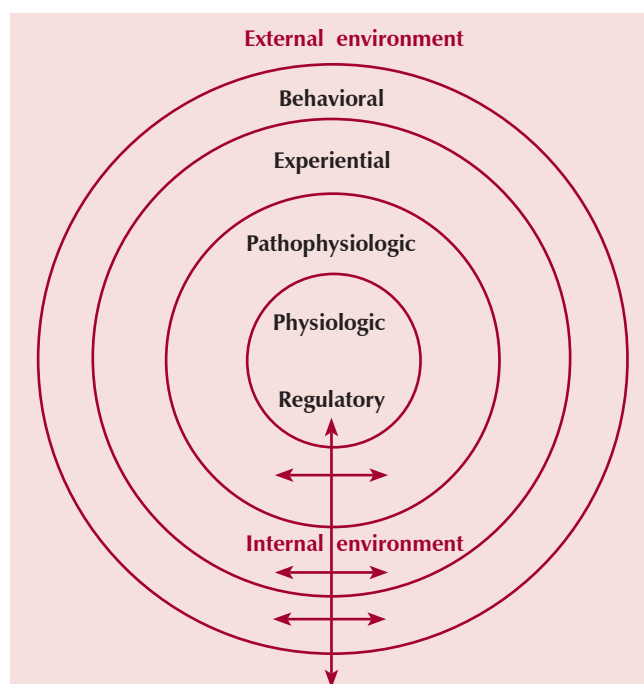


Figure 1. The Human Response to Illness Model

Note. From "Perspectives on Human Response to Health and Illness," by P.H. Mitchell, B. Gallucci, and S.G. Fought, 1991, *Nursing Outlook*, 39, p. 155. Copyright 1991 by Elsevier. Reprinted with permission.

Impulses are conducted along first-, second-, and third-order neurons from the nociceptors to the brain stem or spinal cord, the thalamus, and then to the primary somatosensory area of the cortex via the spinothalamic pathway (Collins & Walker, 2006; Tortora & Grabowski, 2000). The thalamus relays information to the hypothalamus, which activates the parasympathetic nervous system, leading to physiologic signs of acute pain such as hypertension, tachycardia, dilated pupils, and palmar sweating (Sentivany-Collins, 2002). Acute pain in childhood CNS cancer may be caused by the tumor itself or diagnostic, surgical, or therapeutic procedures causing damage to the child's body or pressing on components of the pain pathway.

The pain pathway involves four steps: transduction, transmission, modulation, and perception. Transduction is the process executed by the nociceptors when they convert painful stimuli to electrical signals releasing prostaglandins, serotonin, and histamine (Vanderah, 2007). Transmission occurs as the electrical signals travel along the C-fibers and A-δ-fibers from the transduction site to the cortex via the spinal cord and the thalamus (Vanderah, 2007). Modulation is the activation of the descending pathways that inhibit the painful stimuli, such as neurons located in the dorso-lateral portion of the spinal cord that release norepinephrine, serotonin, and endogenous opioids (Vanderah, 2007). Perception of pain is the final step of the pain

pathway. It occurs in the primary somatosensory area of the cerebral cortex and is influenced by many factors, including previous pain experiences, emotions, and memories.

Pathophysiology of Pain

The second component of the HRTI model is the pathophysiologic perspective, which results “from disordered biologic functioning” (Mitchell et al., 1991, p. 155). The pathophysiologic perspective of pain involves actual or potential damage and inappropriate sensations that do not have a regulatory purpose such as chronic nociceptive and neuropathic pain.

Chronic pain in children with CNS cancer often is a result of tumor infiltration into the tissue and nerves (Gallagher, 2005). This type of pain does not have a protective purpose, lasts for several months or years, and may involve changes in the nervous system. Chronic pain often involves physiologic, psychological, social, and environmental components (Kaczynski, Claar, & Logan, 2009). The body of a child with chronic pain adapts to the stress of the pain to maintain homeostasis and may not exhibit any physiologic signs (Sentivany-Collins, 2002).

Neuropathic pain, resulting from neural tissue damage (Gilron Watson, Cahill, & Moulin, 2006; Jacob, 2004; Vargas-Schaffer & Pichard-Léandri, 1996), is common in children with CNS tumors (Jacob, 2004). The damage may be caused by tumor compression or infiltration of the nerves, nerve trauma as a result of diagnostic or surgical procedures, or CNS injury related to chemotherapy or radiation therapy (Jacob, 2004). Children and adolescents experiencing neuropathic pain describe it as “burning, tingling, electrical, pins and needles, cold, numb, pricking, shooting, and electric shock-like” (Jacob, 2004, p. 350). Children who cannot talk or describe aspects of their neuropathic pain may not receive adequate pain relief because of the inability to articulate what and how they feel (Vargas-Schaffer & Pichard-Léandri, 1996).

Experiential Perspective

A third component of the HRTI model is the subjective experiential perspective that can be assessed “through patient reports . . . divided into symptoms, cognitions/emotions, and drives/sensations” (Heitkemper & Shaver, 1989, p. 416). Pain is a subjective experience that occurs within a child’s physiologic, psychological, social, and environmental contexts. Coping mechanisms, pain tolerance levels, and responses to the pain and pain treatment are unique to each child (Enskar et al., 2007). In addition, previous painful experiences (Collins & Walker, 2006; Stevens, 2007) and a child’s understanding of pain and pain relief may contribute to current experiences of pain. Some children have reported that

they dreaded pain more than any other cancer symptom (Ljungman et al., 1999), and some children may believe that to survive cancer, they must endure pain and suffering (Ljungman et al., 1999; Woodgate, 2008). This may influence how a child experiences and responds to pain, whether pain management strategies succeed, and additional related symptoms.

Common emotional responses to pain in childhood include fear, anxiety, anger, and sadness (Woodgate & Kristjanson, 1996). A child may or may not realize the connection between such emotions and pain. Relieving pain may reduce such emotions. Quality of life may decrease as the pain affects “the physical, psychological, social, and spiritual well-being of the patient” (Hooke et al., 2007, p. 29).

A child’s quality of life can be impacted by other symptoms that may manifest as a result of, or along with, pain (e.g., weakness, weight gain, anorexia, constipation, headache, mobility, skin pressure areas, edema, fever, bleeding, anxiety, depression) (Goldman, Hewitt, Collins, Childs, & Hain, 2006). Living with any of these symptoms is difficult, but they may be exacerbated in the presence of cancer pain. Cancer pain can interfere with activities of daily living, such as eating and sleeping, which may lead to depression and fatigue (Campbell-Fleming & Williams, 2008). Assessing for symptoms of depression, fatigue, and anxiety, as well as the underlying cause of the pain itself, is important (Kaczynski et al., 2009). When children are in pain, they often feel sick and are perceived by others to be sick (Woodgate, Degner, & Yanofsky, 2003). The longer the pain remains, the more disruptions it causes in a child’s and his or her family’s daily life (Woodgate et al., 2003).

Behavioral Perspective

A fourth component of the HRTI model is the behavioral perspective, which identifies the objective, observable behavior that communicates the experience of the response with the individual’s local environment (Mitchell et al., 1991). Assessing pain with behavioral indicators is challenging for nurses because pain is a subjective experience that is displayed in different ways by each individual. Adding complexity to the issue is the objectivity of pain assessment tools for children in pain. Nonetheless, behavioral indicators of pain in children with CNS cancer are a valuable component of comprehensive pain assessments.

Infants, children, and adolescents with cancer exhibit a variety of behaviors as a result of pain, such as crying, being irritable, withdrawing from social interaction, having sleep disturbances, facial grimacing, guarding, being inconsolable, or acting uncooperatively (Hockenberry-Eaton, Barrera, Brown, Bottomley, & O’Neill, 1999). Such behaviors are dependent on the child’s age and developmental level. A number of tools have been developed to measure pain in children based

on observable behavior. The FLACC pain tool includes evaluation of Facial expression, Legs, Activity, Crying, and Consolability (Merkel, Voepel-Lewis, Shayevitz, & Malviya, 1997). The Premature Infant Pain Profile (PIPP) includes observations of an infant's behavioral state prior to and during painful stimulus (Stevens, Johnston, Petryshen, & Taddio, 1996). One method of pain assessment that addresses the challenge of measuring a subjective occurrence with an objective tool is the QUESTT method (Question the child, Use pain rating scale, Evaluate behavior, Secure parents' involvement, Take cause of pain into account, and Take action and evaluate results) (Hockenberry, Wilson, Winklestein, & Kline, 2003). This method complements the HRTI model because it covers all four perspectives and person and environmental factors.

Symptoms of childhood CNS cancer depend on the size and location of the tumor. Children who present with brain tumors often exhibit headaches, which range from vague to severe and may awaken children at night (Sentivany-Collins, 2002). The pain may be displayed as irritability or refusal to ambulate in infants and young children (Sciubba, Hsieh, McLoughlin, & Jallo, 2008). Pain from a spinal tumor often occurs overnight and causes children to wake from sleep and feel pain at the location of the tumor; the pain tends to increase over time and is not related to the children's level of activity (Sciubba et al., 2008). They may have reduced mobility "as a result of a muscular response to pain or asymmetric vertebral destruction" (Sciubba et al., 2008, p. 82) that develops in as many as 40% of such cases.

Person Factors

Two types of person factors are identified within the HRTI model: nonmodifiable and modifiable (Mitchell et al., 1991). Nonmodifiable factors cannot be changed but they affect an individual's response and compliance to treatment (Heitkemper, Levy, Jarrett, & Bond, 1995). Modifiable factors can be altered and influence an individual's response to the illness.

Nonmodifiable person factors: For children with CNS tumors, nonmodifiable person factors include age, developmental stage, gender, culture and ethnicity, biology, and previous pain experiences. To date, limited work has examined the role of these factors in the context of pain associated with CNS tumors (Ruland, Hamilton, & Schjødt-Osmo, 2009).

A child's age and developmental stage influence how pain is perceived, demonstrated, described, and treated. Thus, the experience of pain can be very different for infants, children, and adolescents based on prior experiences of pain (Stevens, 2007), their abilities to describe pain and the descriptors used (Woodgate & Kristjanson, 1996), and the choice of treatments such as type and route of medications. Parents often are asked to report on their children's pain because of age, developmental stage, and

cooperation. Variations of the pain experience based on a child's developmental stage have, to date, received limited attention in symptom research concerning children with cancer; particularly lacking is information about children younger than five years of age (Linder, 2008). The prevalence of chronic pain has been found to increase with age for boys and girls (Huguet & Miro, 2008).

Gender also may affect children's pain experiences. Two recent studies involving children with chronic pain found that girls and boys indicated similar levels of pain intensity, although girls were more likely to experience chronic pain and exhibit greater functional disability (Huguet & Miro, 2008; Kaczynski et al., 2009). Girls were more likely to have taken medication to alleviate pain than boys (Huguet & Miro, 2008) and were more likely to report at-risk or clinically significant symptoms of depression (Kaczynski et al., 2009). This reinforces the need to assess for psychological issues related to chronic pain. Kaczynski et al. (2009) concluded that "girls were more likely to attribute their pain to emotional distress, whereas boys are more likely to attribute their pain to physical problems" (p. 2).

Culture and ethnicity may play a role in children's experiences of pain and pain management. Language acquisition and socialization processes are the ways that children learn their own culture (Gharaibeh & Abu-Saad, 2002). Language may prove to be a barrier to pain relief (Jacob, McCarthy, Sambuco, & Hockenberry, 2008) if a child or family cannot describe the pain or a healthcare provider cannot understand the child or family. Children's responses to pain and pain management strategies are influenced by their parents' beliefs, values, and norms (Gharaibeh & Abu-Saad, 2002). Certain cultures may underreport or underrate pain in an effort to be stoic. Culture and ethnicity also influence gender roles, which may influence children's experiences of pain and pain management.

A child's biology, specifically the CNS tumor, is a non-modifiable factor that can influence the pain response. The type, location, and size of the tumor are aspects that may influence the amount of pain. Although the causes of childhood CNS cancer generally are unknown, correlations have been found with hereditary factors and family history of cancer (Fitzmaurice & Beardsmore, 2005).

Pain that occurs early in life may have long-term consequences (Collins & Walker, 2006; Stevens, 2007). It may change baseline nociceptive processing, affect pharmacodynamic responses to analgesic agents, alter normal development, and produce behavioral and structural changes (Collins & Walker, 2006).

Modifiable person factors: Modifiable factors for children with CNS cancer experiencing pain include coping strategies and knowledge about cancer, pain, and pain management. Children with CNS cancer may want to talk about their pain, try to deny their pain, or

try to protect their families from worrying by keeping symptoms to themselves. This has important ramifications when parents are assumed to be the best proxy for their children's symptom experiences (Ruland et al., 2009). Parental insights into their children's pain should be considered along with the children's to ensure accurate assessment. Children's knowledge about cancer and pain affects coping mechanisms and pain experiences. Education related to pain and pain management strategies is integral to ensuring optimal treatment.

Environmental Factors

Environmental factors are physical and social factors that influence an individual's illness response (Heitkemper et al., 1995). For children with pain from a CNS tumor, environmental factors may include hospitalization, procedures, interactions with healthcare providers, and family interactions.

Children with CNS tumors are hospitalized at some point in the illness trajectory. During hospitalizations, children may incur treatments that result in pain, such as central line insertions, lumbar punctures, bone marrow aspirates, and chemotherapy. Hospital and unit-specific policies direct the type of pain management and dictate what medications can be given by what routes. This influences the effectiveness of pain management strategies. While in the hospital, children with CNS tumors may receive chemotherapy that causes side effects (e.g., mucositis) that can be painful and may influence other aspects of care, such as delaying treatment and altering nutritional status.

Healthcare providers, nurses in particular, can impact children's pain experiences. Each nurse's knowledge, experience, and attitude (Enskar et al., 2007) influence how children's pain is assessed and managed. Nurses may have misconceptions about pain in children or a lack of knowledge about pain interventions in children (Enskar et al., 2007). Nurses caring for children with cancer pain may not realize the extent to which environmental, personal, and treatment-related factors can contribute to the symptom experience (Woodgate et al., 2003). Collaboration among nurses, children, families, and other healthcare providers can impact the way pain is managed in children with cancer (Enskar et al., 2007).

Families have a tremendous influence on children's pain. Because the entire family is affected when a child is diagnosed with cancer, the symptoms, such as pain, also have an enormous effect on the entire family. A family's knowledge and familiarity with pain and its management will impact the child's experience and willingness to accept interventions for pain. Families often are unable to separate symptoms from the cancer experience (Ruland et al., 2009; Woodgate & Degner, 2004), and many siblings and parents report mental distress as a result of patients' physical pain (Woodgate et al., 2003).

Children with cancer also may experience additional feelings, such as guilt, because of families' responses to their symptom experiences (Woodgate, 2008).

Implications for Nursing

The HRTI model has provided a framework to explore a nursing perspective of pain in children with CNS cancer (see Table 1). Information obtained from the examination of the four components of the model provides insight for the three domains of nursing: clinical practice, education, and research.

Clinical Practice

Nurses are a vital component of the multidisciplinary team that provides care to children with cancer. Collaboration among healthcare providers is necessary to ensure a high level of care to children with cancer, especially in relation to pain management. Nursing care encompasses a comprehensive assessment of a child's pain within the context of the family. Nurses must discuss pain interventions with the family, then implement and evaluate the interventions. Children with cancer and their families must be treated as equal partners with healthcare providers in the management of pain (Hooke, Hellsten, Stutzer, & Forte, 2002).

Pain assessment: Responsibility for assessment of pain in children with CNS cancer should be shared by healthcare providers, the child, and the child's family (Hooke et al., 2002; World Health Organization [WHO], 1998). Nurses must assess symptoms routinely by using child-friendly, age-appropriate, and developmentally appropriate methods (Ruland et al., 2009). Physiologic symptoms should be included in children's pain assessments, but nurses must be aware that in chronic pain, such signs may not be present. Observing the behaviors of children with cancer, especially infants and younger children, is a key component of comprehensive pain assessment. Tools should elicit quantitative and qualitative data, such as the QUESTT method (Hockenberry et al., 2003). Person and environmental factors also should be considered. Including experiential and behavioral perspectives ensures comprehensive assessment and individualized plans for pain management. A multidimensional and contextual approach is necessary to include the complex and multifaceted nature of pain (Stevens, 2007).

Nurses should allow children with CNS cancer an opportunity to talk about their pain and related emotions. To acknowledge that symptoms of children with cancer represent dynamic multidimensional experiences that occur within a particular context (Woodgate et al., 2003), Woodgate (2008) advocated use of a new "feeling states" approach to help understand how children with cancer experience symptoms. Woodgate (2008) revealed that children with cancer "experienced and described

Table 1. Articles About Pain and the Human Response to Illness Model

Study	Purpose	Application to Model	Limitations
Kaczynski et al., 2009	To evaluate gender as a moderator of associations between psychosocial variables and functional disability in children and adolescents with chronic pain	Physiologic, experiential, and behavioral: Results of this study found differences in patients with chronic pain based on gender that influenced the patients' experiences of pain and behavior as well as their families' reaction to the children's pain.	Age range = 8-17 years; participants: 89% Caucasian; 66.5% female
Ruland et al., 2009	Literature review describing symptoms and problems in children with cancer	Physiologic, experiential, and behavioral: Children reported many distinct symptoms or problems related to their cancer (psychological, physiologic, both physical and psychological, and school-related and behavioral).	Little discussion in the literature about change in symptoms over time, age and gender differences in symptom experiences over the course of illness, and racial differences and symptoms
Campbell-Fleming & Williams, 2008	Description of how and when ketamine may be effective for patients with cancer in pain. Nursing considerations are discussed.	Physiologic: Ketamine is the most potent N-methyl-D-aspartate (NMDA) receptor antagonist. It is an anesthetic with analgesic properties. In combination with opioids, ketamine can improve pain control and may allow a decrease in dose of each agent.	Children must be monitored carefully for side effects such as altered mental status, opioid toxicity, nausea, fatigue, and dizziness.
Hughes et al., 2008	Review of literature about massage therapy in children with cancer	Experiential: Massage has been used in patients with cancer and is reported to have significantly decreased pain and pain intensity. Physiologic: Reported benefits of massage include alleviation of psychosocial symptoms during cancer therapy, as well as reductions in anxiety and depressed mood; long-term massage effects include increases in natural killer cells, lymphocyte cell numbers, dopamine and serotonin levels, mean white blood cell counts, and mean neutrophil counts.	Massage therapy should be provided by a licensed massage therapist.
Huguet & Miro, 2008	Provides information about incidence of pain in school children and suggests a new pain grading system of chronic pediatric problems	Physiologic, experiential, and behavioral: Pain and related characteristics were examined, such as age, gender, socioeconomic status, and parental marital status.	Study was done in Spain. Cultural variations may limit generalizability.
Jacob et al., 2008	Exploration of pain in previous week of Spanish-speaking children with cancer	Physiologic and experiential: Children completed the Spanish version of the Adolescent Pediatric Pain Tool (location, intensity, and quality of pain). Children were underreporting their pain and therefore not receiving medication to relieve the pain.	Small sample size. Children were aged 8-12. Cannot generalize to younger children
Linder, 2008	Review of the literature of developmental diversity in studies describing physical symptoms in children and adolescents with cancer	Experiential and behavioral: Children's reports of pain and behaviors exhibited while they were experiencing pain were influenced by developmental stage.	Research has not addressed how the symptom experience varies across developmental stages. Children younger than 5 years were the least represented in the literature.
Sciubba et al., 2008	Review of tumors that occur in the spinal column of pediatric patients	Physiologic, experiential, and behavioral: Spinal tumor pain characteristics were provided. Pain may manifest as irritability or refusal to ambulate, especially in pre-verbal children unable to communicate their discomfort.	—
Wood & Bioy, 2008	Development of latest knowledge about hypnosis as applied to pain management in children	Physiologic and experiential: "Over time, hypnosis produces analgesia resulting from neural reorganization so that pain responses are replaced by new, non-painful responses that are developed in response to painful stimuli that no longer produce suffering" (p. 440).	Hypnotic responsiveness changes with age and peaks during middle childhood (7-14 years). Two requirements for hypnosis in children: establishing a good rapport and adapting the technique to the child's cognitive development and preferences

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Table 1. Articles About Pain and the Human Response to Illness Model (Continued)

Study	Purpose	Application to Model	Limitations
Woodgate, 2008	Provide an interpretive description of children's and adolescents' perspectives about their cancer symptoms, with a focus on what they think and feel about their symptoms	Experiential and behavioral: Children with cancer conceptualize their symptom experiences as a multidimensional phenomenon. They may find communicating how they feel difficult. Having to quantify their symptom experiences is viewed by some children as restrictive.	Participants were 9–17 years old.
Enskar et al., 2007	Identify and describe knowledge and attitudes about pain and pain management in nurses working with children with cancer; compare these perspectives among three countries	Experiential: Nurses' knowledge and attitudes about pain and pain management may affect pain experienced by children. A high level of knowledge was correlated with a positive attitude about pain management.	The instrument used had to be translated several times.
Finkel et al., 2007	Examine the use of ketamine in children with uncontrolled cancer pain despite high doses of opioids	Pathophysiologic: NMDA receptor antagonists may prove valuable as an adjuvant pain management strategy because opioid-induced tolerance and hyperalgesia are associated with NMDA activation. Opioid-related side effects are reduced with the use of ketamine in conjunction with opioids. Behavioral: According to subjective reports from parents, children on ketamine and opioids were more interactive and appeared to be more comfortable than those on opioids alone.	Retrospective case series, lack of standardized protocol for administration of ketamine, lack of controls
Hockenberry & Hooke, 2007	Offer framework for clustering fatigue, sleep disturbance, and pain in children with cancer	Experiential and behavioral: Children are aware of physical and emotional changes in themselves during treatment, which result from the disease, the treatment, or side effects of the treatment. Pain, sleep, and fatigue often occur in tandem and are referred to as a symptom cluster.	Provides a framework that requires further research to explore relationships among related symptoms
Hooke et al., 2007	Chart audit describing the use and effectiveness of adjuvant propofol for pain control for children with cancer at the end of life	Experiential and behavioral: Pain assessments (patient self-report tools, behavioral assessments, and patient reports) were documented regularly.	Used in end-of-life situations only. Used only in combination with opioids as it is unknown what the pain relief of only propofol is.
Jacob et al., 2007	Examine the pain experiences of children with cancer during hospitalization: a) characterize the intensity, location, and quality of pain; b) evaluate pain management; c) examine relationships among pain, perception of sleep, and activity during hospitalization	Experiential: Researcher asked the children (aged 8–17) to complete the Adolescent Pediatric Pain Tool (AAPT), to answer the following questions related to their experience of pain: "How well do the medicines help with your hurt?" "How much sleep did you have during the night?" "How much activity did you have today?"	Small sample size with English speakers only (APPT validated only in English)
Stevens, 2007	Overview of assessing and managing pain in infants with cancer	Physiologic, experiential, and behavioral: Article described the capability of infants to experience pain and stressed the importance of interaction between the infant and the caregiver in assessing and managing the infant's pain. Pharmacologic and nonpharmacologic methods of pain relief were provided.	Know about infants' personal experiences of pain is difficult without observing their behavior and their interaction with their caregivers. This does not imply that the infants do not feel pain.
Vanderah, 2007	Overview of the pathophysiology of pain	Physiologic and pathophysiologic: Article described the steps in the pain pathway, chronic pain, and the role of opioids as a form of analgesia.	—
Zernikow et al., 2007	Review of literature about transdermal fentanyl in pediatric pain management	Physiologic: Children may require different dosing (higher amounts with respect to body weight) because of drug clearance time.	—

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Table 1. Articles About Pain and the Human Response to Illness Model (Continued)

Study	Purpose	Application to Model	Limitations
Gilron et al., 2006	Overview of neuropathic pain	Pathophysiologic: not a protective type of pain. Physiologic, experiential, and behavioral: neuropathic pain requires multidimensional assessment in order to obtain qualitative and quantitative information about the pain.	Fentanyl should not be first analgesic chosen, is not as effective for acute pain control, and is not recommended for opioid-naïve children. More research is required.
Goldman et al., 2006	Report of survey of symptoms of children with cancer	Experiential: Pain was considered a “major” symptom in all children with progressive cancer but was less common in children with brain tumors. Pain was usually resolved with appropriate intervention for children in this study.	Neuropathic pain requires further research and complex therapeutic approaches including a variety of pharmacologic and nonpharmacologic therapies.
Ladas et al., 2006	Summary of research evidence on use of complementary and alternative medicine (CAM) in children with cancer	Physiologic and experiential: Several randomized controlled trials support the efficacy of relaxation, imagery, and hypnosis as pain relieving measures in cancer pain. Acupuncture and massages are shown to relieve symptoms and improve physical and emotional well-being.	Because of the children's health status, attrition from time point one to six was significant.
Post-White, 2006	Summary of research on CAM in children with cancer	Experiential: CAM therapies may be best used by children with cancer as adjuncts to reduce treatment- and illness-related symptoms and distress. Physiologic: CAM therapies may help reduce or prevent late effects and promote long-term health in childhood cancer survivors.	Further research is required in evaluating safety and efficacy of CAM therapies. Further research is needed in childhood cancer survivors related to their use of CAM therapies.
Myers et al., 2005	Review of literature of use of CAM for children with cancer	Parents of children with cancer report using CAM therapies for the following reasons. Physiologic: to improve immune system Experiential: to help manage symptoms and to feel that they were doing everything possible for their child.	Further research required to provide evidence of effectiveness, mechanisms of action, safety, interactions, and cost-effectiveness of CAM therapies.
Jacob, 2004	Explain the nature of neuropathic pain; review the literature about children with neuropathic pain, assessment strategies, and management challenges	Pathophysiologic: not a protective type of pain Physiologic, experiential, and behavioral: neuropathic pain requires multidimensional assessment for qualitative and quantitative information about the pain.	—
Woodgate & Degner, 2004	Explore and describe the symptom course in childhood cancer as experienced by children and their families	Experiential: Children's and families' thoughts and feelings about cancer often paralleled the changing symptom course. In responding to symptoms, families strove to protect not only their ill children, but also the family unit.	Neuropathic pain often is not well controlled and requires complex therapeutic approaches (pharmacologic and nonpharmacologic).
Dougherty & DeBaun, 2003	Examine increasing doses of morphine and benzodiazepine in children at the end of life in relation to neuropathic pain	Physiologic: Children without neuropathic pain at the end of life received escalating doses of morphine but no significant increase in benzodiazepines. Pathophysiologic: Children with neuropathic pain at end of life received escalating doses of morphine and benzodiazepines. Methadone proved effective in controlling pain as an adjuvant to morphine and benzodiazepines.	Retrospective case analysis of drug dosage, not pain relief. Small sample size limits generalizability.
Woodgate et al., 2003	Explore and describe the childhood cancer symptom course from the perspectives of children and their families	Experiential and behavioral: Interviews and participant observation were used in data collection. Symptoms were more than objective side effects or singular physical and psychological states; they represented dynamic multidimensional experiences that occurred within a particular context. Understanding meanings that children and families assigned to the symptoms was important.	Most participants were Caucasian. The sample included few preschool-aged children.

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Table 1. Articles About Pain and the Human Response to Illness Model (Continued)

Study	Purpose	Application to Model	Limitations
Gharaibeh & Abu-Saad, 2002	Examine the cultural validity, reliability, and preference of three pain assessment tools among Jordanian children	Experiential: The pain assessment tools were found to be valid and culturally appropriate.	Participants included children aged 3–14 years. The study used self-report only.
Hooke et al., 2002	Provide best practice advice from the Association of Pediatric Oncology Nurses to all nurses caring for children with cancer	Physiologic, pathophysiologic, experiential, and behavioral: Complete assessment, treatment planning, and evaluation of the child and the pain relief strategies are the responsibility of the nurse. The child and his or her family are important partners in pain management.	—
Ljungman et al., 1999	Evaluate the extent and causes of pain in children with cancer, methods for monitoring pain intensity, principles of pain management, and adverse effects of pain treatment.	Experiential: Children and parents were asked about extent, causes, side effects, evaluation, and information about pain. Behavioral: Observation of children's behavior as a means to evaluate pain (especially younger children) is important.	Children with central nervous system tumors were under-represented in the sample.
Merkel et al., 1997	Evaluate the validity and reliability of the FLACC (Facial expression, Legs, Activity, Crying, and Consolability) pain assessment tool	Behavioral: Tool uses five categories of behaviour: facial expression, leg movement, activity, crying, and consolability. Scale of 0–2 for each of the five categories provides a maximum score of 10. Tool quantifies pain behavior in children unable to verbalize pain experience.	Tool originally was tested only in young postoperative children.
Stevens et al., 1996	Develop and validate a measure for assessing pain in premature infants that is useful to clinicians and researchers	Physiologic and behavioral: Pain is a complex, multidimensional phenomenon. For infants, pain must be inferred through observation of physiologic and behavioural indicators. The Premature Infant Pain Profile (PIPP) is a seven-item, four-point scale for assessment of pain in premature infants.	Further research is required to establish normal ranges of PIPP scores for different groups of infants.
Vargas-Schaffer & Pichard-Léandri, 1996	Describe how to diagnose neuropathic pain and treatment options	Physiologic, pathophysiologic, experiential, and behavioral: Diagnosis of neuropathic pain requires a thorough clinical examination of the child. This includes how the child behaves, reacts, responds, moves, talks, and interacts with the clinician.	Time consuming
Woodgate & Kristjanson, 1996	Explore younger hospitalized children's experiences of pain	Experiential and behavioral: Data collection occurred through participant observation and interviews with the children and their parents. Young children responded to pain in loud, expressive ways as well as quiet, subtle ways. The children's pain experiences had a strong emotional component.	Small sample of young children with procedural pain in hospital. Requires further research to verify model in other ages and developmental stages with different types of pain in different settings

their symptoms as overall feeling states with assigned meanings that when approached solely as side effects or singular physical and psychological states, limited their ability to convey the impact that the symptoms had on them" (p. 230). To understand children's feeling states, healthcare professionals must learn the meanings that the children and their families have assigned to symptoms (Woodgate et al., 2003).

Pain interventions: Nurses' knowledge about pain interventions influences the care they provide. To implement appropriate pain interventions, nurses must have sufficient knowledge of the physiology and

pathophysiology of pain, as well as the mechanisms of action of pain interventions (Sentivany-Collins, 2002). For children with CNS cancer, knowledge about the disease and treatment protocol also is required. A variety of pharmacologic and nonpharmacologic pain management strategies are used to treat children with cancer in pain.

Pharmacologic interventions: Analgesia for children with CNS cancer pain should be initiated with the WHO ladder of pain analgesia (WHO, 1998) (see Figure 2). In the presence of pain, analgesia with or without adjuvant therapy is provided. If pain persists

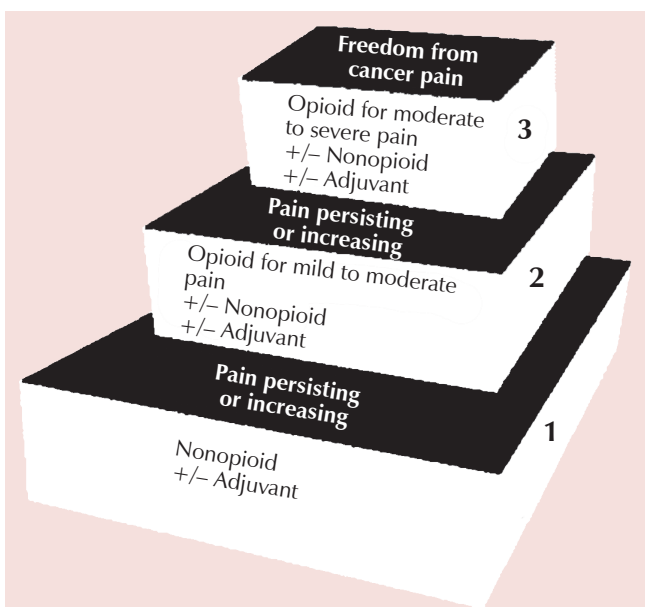


Figure 2. World Health Organization Ladder of Pain Analgesia

Note. From "WHO's Pain Ladder," by World Health Organization, 1998. Retrieved from <http://www.who.int/cancer/palliative/painladder/en>. Used with permission.

or increases, analgesia is increased accordingly. In cases of severe pain, such as at the end of life, more intense therapy such as IV boluses and continual infusions may be required (Dougherty & DeBaun, 2003). In such situations, waiting for oral medication to take effect would be inappropriate (Susman, 2005).

Analgesic choices also should be based on the physiology and pathophysiology of the pain. For example, aspirin and nonsteroidal anti-inflammatory drugs block prostaglandin formation, inhibiting nociceptor stimulation (Tortora & Grabowski, 2000), and are effective for bone and soft tissue pain (Jacob, 2004). Morphine and other opiate drugs inhibit the release of pain neurotransmitters, altering pain perception (Vanderah, 2007), so pain is sensed but perceived as less painful (Tortora & Grabowski, 2000). Opioids activate the opioid receptors to relieve pain in four different sites: the midbrain, the second-order pain transmission cells, the C-fibers in the spinal cord, and peripherally to inhibit nociceptor activation and cells that release inflammatory mediators (Vanderah, 2007). In children with CNS cancer, opioids such as morphine and methadone are effective for cancer pain and neuropathic pain (Dougherty & DeBaun, 2003). Transdermal fentanyl also is reported to be a successful opiate analgesic for controlling pain in children (Zernikow, Michel, & Anderson, 2007). At the end of life, children may require escalating doses of opioids to achieve relief from cancer pain (Dougherty & DeBaun, 2003; Finkel Pestieau, & Quezado, 2007; Hooke et al., 2002).

Ketamine is a potent N-methyl-D-aspartate (NMDA) receptor antagonist that produces an agonist effect at opioid receptor sites and blocks NMDA and non-NMDA glutamate receptors in the dorsal horn of the spinal cord (Campbell-Fleming & Williams, 2008). Ketamine is used for neuropathic, inflammatory, and ischemic pain etiologies (Campbell-Fleming & Williams, 2008) and has been used with success in children with cancer pain (Finkel et al., 2007; Vargas-Schaffer & Pichard-Léandri, 1996). When used with opioids, ketamine has had an opioid-sparing effect that may reverse opioid tolerance and hyperalgesia (Finkel et al., 2007). The result of the opioid-sparing effect was an increase in opioid efficacy and a reduction in opioid-related side effects such as constipation and respiratory depression; children were more interactive and appeared to be more comfortable (Finkel et al., 2007).

Neuropathic pain, common in children with CNS cancer, is treated with several classes of drugs, including opioids, corticosteroids, anticonvulsants, and antidepressants (Gilron et al., 2006; Jacob, 2004). Corticosteroids are used in conjunction with analgesics because of their anti-inflammatory effects. Anticonvulsants act on the electrical impulses and shooting pain, and antidepressants work on the allodynia (Vargas-Schaffer & Pichard-Léandri, 1996).

Nonpharmacologic interventions: A variety of nonpharmacologic interventions can be used to treat children with CNS cancer pain, including complementary and alternative medicine (CAM) treatments, distraction techniques, nerve stimulation, and psychotherapy.

Children with cancer and their parents report using CAM "to reduce symptoms, cope with life-threatening illness, and improve overall well-being" (Post-White, 2006, p. 244). Surveys report that as many as 84% of children with cancer use at least one type of CAM therapy in addition to conventional therapies, often without informing healthcare providers (Ladas, Post-White, Hawks, & Taromina, 2006; Myers, Stuber, Bonamer-Rheingans, & Zeltzer, 2005). Many different types of CAM therapies are used in children with cancer, including imagery, hypnotherapy, relaxation, diets, megavitamins, spiritualism, faith healing, meditation, chiropractics, homeopathy (Myers et al., 2005), acupuncture, and massage (Post-White, 2006).

The most commonly reported CAM therapy for pain reduction in children with cancer is massage (Hughes, Ladas, Rooney, & Kelly, 2008). It is used to "alleviate stress and muscle cramping, induce relaxation, improve circulation and lymph flow, promote muscle tone, increase range of motion, and encourage recovery from injuries and medical procedures" (Hughes et al., 2008, p. 431). It also may help children with CNS cancer to cope with the psychological issues associated with treatment, thus enhancing quality of life (Hughes et al., 2008; Ladas et al., 2006).

Randomized, controlled trials in adults with cancer have supported the use of relaxation, imagery, and hypnosis to decrease cancer pain (Ladas et al., 2006). Relaxation, meditation, and other forms of distraction techniques reduce pain by the release of natural endorphins in the descending pain modulation pathways (Gallagher, 2005). Research evidence supports hypnosis as a treatment for pediatric pain, anxiety, nausea, and vomiting (Post-White, 2006). Children reportedly are more responsive to hypnosis than adults (Wood & Bioy, 2008). The analgesia effect of hypnosis is reported to be a result of neural reorganization in which new, nonpainful responses replace previous pain responses to painful stimuli (Wood & Bioy, 2008).

For infants with CNS cancer, several distraction techniques are recommended for pain management: sucrose water, swaddling and positioning, non-nutritive sucking, breast-feeding, and Kangaroo Mother Care (Stevens, 2007). In addition to providing distraction from procedures, these approaches afford reassurance of the mother's presence with the child and can be used alone or in combination with pharmacologic approaches to pain management.

Management of neuropathic pain is complex and requires multiple approaches. Noninvasive management strategies for neuropathic pain include exercise, graded motor imagery, transcutaneous or percutaneous electrical nerve stimulation, and cognitive behavioral therapy or supportive psychotherapy (Gilron et al., 2006). Further research is needed to examine the safety and efficacy of nonpharmacologic treatments on children with neuropathic pain.

Education

Pediatric oncology nurses play a key role in providing education to children with CNS cancer and their families, as well as all members of the multidisciplinary healthcare team.

Coping strategies and knowledge about cancer, pain, and pain management are modifiable person and environmental factors identified by the HRTI model. Nurses can suggest positive coping mechanisms for children and their families that are appropriate to their unique situations. Nurses must talk with children and their families to determine their levels of pain and pain relief knowledge. Written information is helpful because they can refer back to it at a later date. Families must be taught the importance of telling a member of the healthcare team when children are in pain, being able to describe the pain, evaluating whether a pain management strategy worked, and being able to explain whether side effects are associated with a pain medication (Hooke et al., 2002; Susman, 2005).

Nurses should provide parents with information about CAM therapies and their potential interactions

with traditional therapy. Although many parents think such therapies are harmless (Myers et al., 2005), they can be hazardous. Parents must be informed of the importance of sharing information with healthcare providers about any CAM therapies that are being used by children with cancer. The information should be elicited with nonjudgmental language, in a supportive dialogue between the family and the healthcare provider.

Nurses must share their knowledge of the physiology and pathophysiology of pain with other nurses and members of the multidisciplinary team—formally in education sessions or informally during rounds and patient care conferences. Keeping the healthcare team abreast of advances in pain assessment and management strategies is another role of the pediatric oncology nurse. Nurses who develop new and innovative interventions that aim to improve pain assessment and management in children with CNS cancer should share the insights with others. Such teaching and learning strategies ensure that patients will receive optimal, evidence-informed care.

Research Directions

A dearth of evidence exists related to pain in children with CNS cancer, which highlights the importance of future nursing research in this area. The information elicited from this review applying the HRTI model to pain in children with CNS cancer highlights several important areas for nursing research. Further exploration of the etiologies of pain, pain assessment, and management strategies for children with CNS cancer is needed.

Pain measurement tools for children with CNS cancer that are clinically efficient and provide quantitative and qualitative data must be developed, tested, and refined. Longitudinal studies on children with pain from cancer would be beneficial to elucidate how symptoms change over time (Ruland et al., 2009). Research related to pain in children with cancer also should explore the influence of cultural, ethnic, and socioeconomic factors (Ruland et al., 2009), as well as potential gender and age differences. Stevens (2007) suggested that research is required to determine whether pain in the neonatal period affects future cognition, behavior, and neurodevelopment. Further research is required regarding the efficacy and mechanisms of action of CAM therapies to manage pain in children with CNS cancer (Post-White, 2006).

Conclusion

Children with CNS tumors experience pain related to many facets of their malignancy and its treatment. Assessment, management, and evaluation of interventions related to childhood cancer pain are major functions of the nursing role. Advanced knowledge related to the

physiology and pathophysiology of pain, as well as the experiential and behavioral perspectives and the person and environmental factors, enables pediatric oncology nurses to provide an optimal level of care to this patient population. Thus, the HRTI model serves as an appropriate nursing framework to investigate the response of pain in childhood CNS cancer.

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