

PEDIATRIC CANCER PAIN MANAGEMENT

*Pediatric Pain PRN
Curriculum*

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The
MAYDAY
Fund

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Objectives

- Recognize the variety of reasons for pain and barriers to optimal pain management for children with cancer.
- Develop evidence-based multimodal and interdisciplinary individualized plans of care to treat children with pain and cancer.

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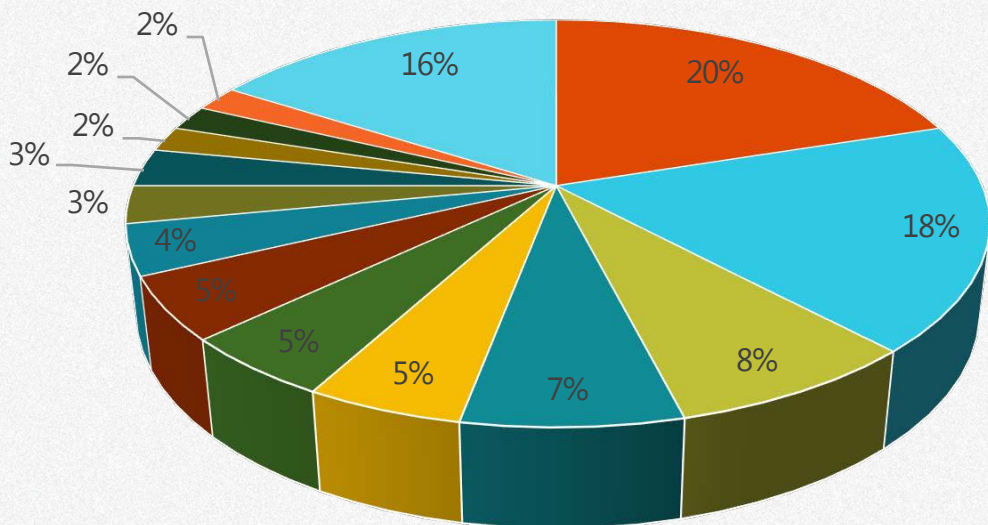
Pediatric Cancer Pain

Pediatric Cancer: Prevalence

We do not know what causes most childhood cancer. Overall survival rate for childhood cancer was just 10 % 50 years ago and is nearly 90 % today. Yet, the number of cases diagnosed annually has not declined in nearly 20 years. Each year > 15,000 children are diagnosed with cancer; and 40,000 are in active treatment in the US.

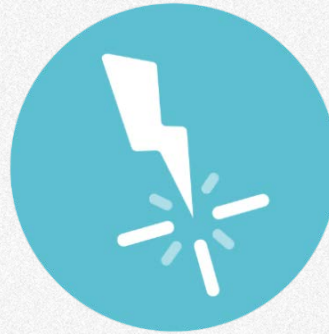
Source: American Cancer Society, Cancer Facts and Figures (2017) Includes: osteosarcoma and Ewing sarcoma

Number of diagnosis 0-19 years of age per year (N=15,780)



- Acute Lymphoblastic Leukemia (ALL)
- Brain and Central Nervous System
- Hodgkin Disease
- Non-Hodgkin Lymphoma
- Acute Myeloid Leukemia (AML)
- Neuroblastoma
- Bone Tumors*
- Thyroid Carcinoma
- Wilms/Kidney
- Germ Cell Tumors
- Rhabdomyosarcoma
- Retinoblastoma
- Melanoma
- Other 16%

Pediatric Cancer Pain Prevalence



Why is this significant?

- Pain causes the greatest source of anxiety for children (more than the fear of not being cured).
- Inadequately controlled pain decreases quality of life and increases morbidity, mortality, and care costs.

49% of children reported pain at diagnosis

In advanced disease, pain is the most common physical symptom of cancer.

Primary sources of pain are related to chemotherapy, radiation and medical procedures:

- Mucositis
- Dermatitis or burns
- Lumbar Punctures
- Bone Marrows
- Venipuncture/Accessing of ports

Barriers to Cancer Pain Relief



Common barriers

- Healthcare professionals
- Expectations
- Knowledge
- Fear of tolerance
- Lack of interdisciplinary cooperation

Patients and families

- Most families believe pain is an unavoidable part of treatment
- Assume treatment team would address pain if it could be reduced or relieved.
- Reluctant to “complain” about pain to treatment team

The healthcare system

- Low priority
- Few treatments approved by FDA for children
- Lack of evidence and funding for research for most biobehavioral treatments.



What is your response?

What additional questions might you ask to obtain a complete initial pain assessment and history?

Billy

Billy is a 4-year-old who presents to the pediatrician with his mother. He has refused to walk for the last 2 days and has complained of leg pain for the last week with fatigue and dyspnea with mild exertion.

Lab results initially revealed anemia and decreased platelets. Blood pathology revealed Billy has B cell ALL.

ALL is the most common cancer diagnosed in children and represents approximately 25% of cancer diagnoses among children younger than 15 years.

Causes of Pediatric Cancer Pain

Planning for Pediatric Cancer Pain Management: Procedures



Pain associated with diagnostic procedures

- Lab draws
- Implanted venous or intrathecal pump access
- Lumbar punctures
- Bone marrow aspirates/biopsies

How do you consistently and systematically prevent and manage the pain from these and other common cancer-related diagnostic procedures?

Does your healthcare system provide optimal management of procedural pain with every procedure, the first to the last?



Planning for Pediatric Cancer Pain Management: Operative

Predictable acute pain from oncologic surgeries

- Post-operative pain
- Phantom Limb Pain
- Others?

Surgical intervention may be aggressively pursued to cure or as an important component of treatment for some childhood cancers.

Is anesthesia consulted pre-operatively?

Are pain management expectations and plans developed with the patient, family and interdisciplinary teams, including anesthesia, surgery, oncology, nursing, pharmacy, child life, physical therapy, etc.?

Is there plan to continually assess and address persistent post-operative pain or phantom limb pain?



Pain Associated with Cancer Treatment

Pain associated with cancer treatment (chemotherapy/radiation)

- **Mucositis**
- Peripheral neuropathy
- Granulocyte colony-stimulating factor
- Immunotherapy
- Infection
- Acute herpetic neuralgia (shingles)

Mucositis may occur in the mouth, esophagus, stomach, intestine, rectal, and vaginal areas after chemotherapy, radiotherapy, or bone marrow transplantation.

- Timing of mucositis depends on the type and duration of chemotherapy/radiation, but maximum expression generally occurs 7 - 10 days after chemotherapy and then gradually subsides over a period of 2 - 3 weeks after cytotoxic treatment (Chaveli-López, 2016).
- Mucositis may be prolonged after bone marrow transplant. Mouth care and function (swallowing and oral hygiene) exacerbates mucositis pain and therefore drinking, eating and talking are functional outcomes that may guide therapy for patients who can and cannot self-report pain intensity.
- There are no effective treatments to adequately relieve mucositis pain and adherence to topical treatments, like diphenhydramine, lidocaine, and Carafate or Maalox solutions is poor due to lack of efficacy and burning with use. Therefore, mucositis pain is typically treated with systemic opioids at escalating doses, often delivered by intravenous patient-controlled analgesia (IV PCA).

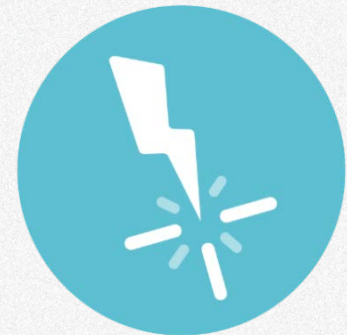
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Children may experience painful treatment-related peripheral **neuropathies** after administration of chemotherapy like vincristine. Radiation therapy to the central and peripheral nervous systems can cause long term chronic peripheral neuropathy that may not present until years after treatment.

- Patients will describe neuropathies as “burning,” “tingling,” “electrical,” or “numbness”.
- Children experience neuropathic pain in their jaw, legs, hand, feet, and abdomen.
- Neuropathic pain occurs in 26% of adolescents and young adults receiving cancer therapy and persists in 11% of adolescent and young adult cancer survivors following completion of therapy.



Pain Associated with Cancer Treatment

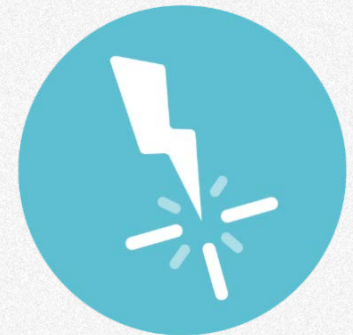
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- infection
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Medullary bone pain is associated with administration of granulocyte colony–stimulating factor and pain may be associated with **immunotherapy**.

Shingles is not unique to cancer; however, the immunosuppression seen in cancer and its treatment can lead to a shingles outbreak.

- *While shingles is rare in children with cancer when compared to the prevalence in adults treated for cancer, it can occur, most commonly in the acute phase and following a stem cell transplant.*
- The initial outbreak is an example of severe acute pain, yet some patients may develop chronic shingles pain.



Pain from Advancing Cancer

Tumors involving organ invasion

- Capsular Wall Stretching
- Organ Compression
- Intestinal Obstruction
- Metastasis



Tumor involvement and tumor metastasis in the abdomen are unfortunately the cause of most visceral pains in children with cancer.

- Described as “squeezing” or “cramping,” this pain is often diffuse rather than localized and can be referred (e.g., liver involvement can lead to right shoulder pain).
- Judicious use of steroids along with escalating doses of opioids, chemotherapy, and radiation therapy can cause relief by reducing tumor size or slowing the rate of growth; for example, for spinal cord compression or increased intracranial pressure from brain tumors.
- If chemotherapy and radiation are effective, providers need to perform continuous pain assessments in an effort to wean opioid doses to match the effectiveness of the tumor reduction.
- Pain caused by metastases is the most common cause of pain in advanced cancer. Usually described as “aching” or “throbbing.”



What is your response?

What can be done immediately to relieve Billy's leg pain?

What pain medications would be indicated for persistent pain?

Billy

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Pediatric Cancer Pain Treatment

Goals of Cancer Pain Treatment

Prevention

Reduce pain that can not be relieved

Prevent/manage adverse effects associated with cancer pain treatment

Promote patient safety and function

Enhance quality of life

As with other types of pain, the goals of cancer pain treatment include:

- preventing pain whenever possible,
- relieving or reducing pain that can not be relieved, preventing side effects associated with cancer treatment like phantom limb pain
- preventing adverse effects associated with cancer pain treatment, like opioid-induced constipation,
- promoting patient safety, optimizing function, and enhancing quality of life to the end of life.

Pharmacological Management of Cancer Pain



Cancer treatments, such as chemotherapy, biotherapy, and radiation can decrease tumor burden and therefore alleviate pain in select patients.

Develop an evidence-based multimodal, interdisciplinary, individualized plan of care to treat children with pain and cancer.



Cautious use of Non-opioids in Children with Cancer



Nonsteroidal anti-inflammatory drugs

Analgesic, antipyretic and anti-inflammatory

Contraindicated in thrombocytopenia due to chemotherapy, so consider selective Cox-2 inhibitors

Acetaminophen

Analgesic

Antipyretic, may mask fever

Use with caution in primary liver or metastatic disease

Acetaminophen may mask a fever. Fever must be treated immediately with antibiotics when cancer patients are neutropenic to prevent septic shock.

Because of potential for hepatotoxicity, acetaminophen should be used with caution in patients with primary or metastatic liver tumors.

Most NSAIDs are contraindicated in patients who are thrombocytopenic from chemotherapy, because most NSAIDs reduce platelet function.

More selective cox-2 inhibitors like celecoxib could be considered.

Cautious use of Opioids in Children with Cancer

Analgesia from Opioids

- PO: peak 1 hour
- duration 3-4 hours
- IV: peak 10-15 minutes
- duration 1-2 hours



Initiate opioid treatment with short-acting intravenous (IV) or oral (PO) opioids at recommended starting doses for opioid-naïve children.

While there are subtle differences, most opioids administered by the IV route reach peak analgesia at 10-15 minutes and doses can be repeated if appreciable pain reduction is not achieved.

Anticipated duration of analgesia is only 1 to 2 hours after IV administration as compared to 3 to 4 hours after PO doses. References of longer duration are typically based on intramuscular (IM) parenteral injection rather than IV administration.

Relative potency of opioids is different; but ineffectiveness is typically related to dose rather than opioid choice. Some pain management specialists recommend rotating opioids when treatment is over several weeks to prevent tolerance to an opioid and the consequential need for larger and larger doses.

Methadone has a long and unpredictable half-life

Long-acting opioids

Many opioid agonists are available in long-acting formulations for persistent pain in children with cancer who are opioid tolerant

Opioid tolerant patients may benefit from long-acting opioids. Both extended release oxycodone and transdermal fentanyl patch have been approved by the FDA for use with children with persistent pain.

Expertise in prescribing and monitoring of methadone and long-acting opioids is required to prevent unintended death.

Other Options

Anticonvulsants

Antidepressants

Local Anesthetics

Ketamine

Corticosteroids

- Usually reserved for use during postoperative period, or at the end of life
- Administer in morning, since sleeplessness may occur if doses are given in the evening.
- May improve energy and appetite

Like NSAIDs, corticosteroids inhibit prostaglandin synthesis and reduce edema. Therefore steroids may be useful when treating neuropathic pain, bone pain, and visceral pain.

Cannabinoids

- Several trials suggest that marijuana or cannabinoids may provide relief of chronic pain, especially neuropathic pain
- The primary cannabinoids in marijuana are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD)
- 2 THC formulations are approved by the FDA for the treatment of nausea and vomiting associated with cancer chemotherapy (but not for children)
- One THC and CBD formulation is available in Canada for the treatment of spasticity in MS patients
- There are **NO** trials of good quality published with use of children with cancer or at the end of life

Given the survival rates of childhood cancer and the effects of marijuana, THC, and CBD on the developing brain, pediatric recommendations are limited to case-by-case or forbidden in many areas.



What is your response?

What bio-behavioral therapies might be useful for Billy?

What education should be provided to the patient and his family?

How would you treat his peripheral neuropathic pain?

Billy

Billy is started on IT chemotherapy with methotrexate, weekly administration of vincristine, and daily dexamethasone.

A week after completing the first cycle of chemotherapy, Billy refuses to put socks or shoes on.

**In
Summary...**

Key Points



Cancer pain management

- Consider the variety of causes of children's cancer pain
- Conduct a thorough pain assessment
- Develop evidence-based, multimodal, interdisciplinary, individualized plans of care to treat children with pain and cancer.
- Prevent or promptly treat adverse effects
- Evaluate treatment efficacy and modify treatment plan as necessary
- Address existential distress
- Educate patients, families, other caregivers
- Lead organizational efforts to reduce barriers to optimal pain management for children's pain.

Appendix

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