Nutrition and the Pediatric Oncology Population

The Oncology Nutrition Dietetic Practice Group
Academy of Nutrition and Dietetics
Webinar - May 12, 2015

Nancy Sacks, MS, RD, LDN
The Children’s Hospital of Philadelphia
Learning Objectives

I. Identify common nutrition issues for children with cancer while receiving therapy
II. Evaluate nutritional status of the pediatric oncology population
III. Examine research and "best practice" standards related to nutrition and the pediatric oncology population
IV. Review medications used to improve appetite and manage side effects
V. Discuss nutrition-related health problems in childhood cancer survivors
Reminder: Children are Supposed to Grow!

“THE PRIMARY OUTCOME OF NUTRITIONAL STATUS”

Mehta et al, 2013

Adult and Pediatric Cancers
Adult and Pediatric Cancers

- Like adults, cancer in children due to mutations in genes
  → uncontrolled cell growth
  → eventually cancer

- 5% childhood cancers due to inherited mutations
  ➢ 25-30% cases of retinoblastoma from RB1 gene

- Inherited mutations associated with certain familial syndromes
  ↑risk of childhood cancer: Li-Fraumeni, Beckwith-Wiedemann, Fanconi and Noonan

- Children with Down syndrome (extra copy of chromosome 21)
  ➢ 10-20 X more likely to develop leukemia

Cancer - Incidence by Age (2001-2007)

- **32.1** per 100,000 children (0-14 years)
- **138.6** per 100,000 adolescents/young adults (15-39 years)
- **2,053.8** per 100,000 people (> 40 years)

## Environmental Risk Factors for Cancer

<table>
<thead>
<tr>
<th>Adults</th>
<th>Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cigarette smoke, asbestos, UV radiation (sun)</td>
<td>• Difficult to identify - cancer rare</td>
</tr>
<tr>
<td>• Radiation from nuclear power plant accidents ↑ risk thyroid cancer</td>
<td>Hard to determine exposure early in dev’t</td>
</tr>
<tr>
<td>• X-rays while pregnant, children ↑ risk cancer</td>
<td>• Ionizing radiation → damage DNA → leukemia/cancers</td>
</tr>
<tr>
<td>• World War II atomic bomb ↑ risk for leukemia</td>
<td>• World War II atomic bomb ↑ risk for leukemia</td>
</tr>
<tr>
<td>• Accelerated fetal growth, higher birth wt ↑ risk ALL, CNS &amp; Wilms tumor, NH lymphoma, RMS</td>
<td></td>
</tr>
</tbody>
</table>

### Mixed results:
- Parental exposure cancer causing chemicals
- Prenatal exposure pesticides
- Childhood exposure infectious agents
- Living near nuclear power plant

### Other Factors

- Family hx & genetic syndromes
- Parental smoking → ↑ risk hepatoblastoma
- Accelerated fetal growth, higher birth wt → ↑ risk ALL, CNS & Wilms tumor, NH lymphoma, RMS
- Lower birth weight → ↑ risk AML & some CNS tumor subtypes

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Cancer in Children and Adolescents. National Cancer Institute, National Institutes of Health. Reviewed
http://www.cancer.gov/cancertopics/types/childhoodcancers/child-adolescent-cancers-fact-sheet#r1
Pediatric Cancers
Introduction – Pediatric Cancer

- Leading cause of death by disease in U.S (0-14 yrs) in children
- 5-yr survival rate childhood cancers (80%)
- In 2014, 15,780 estimated new cases (0-19 yrs)
  - 1,960 expected to die
- 1:530 young adults (20-39 years) is childhood cancer survivor
- 379,112 childhood cancer survivors (0-19 years) living in U.S.
- 24% of childhood cancer survivors are alive > 30 years from diagnosis

Ward 2014; Murphy 2013; Howlander 2013; Mariotto 2009, Snapshot of Pediatric Cancers (SEERS) Surveillance Epidemiology and End Results (SEER) Program and the National Center for Health Statistics.
Introduction – Pediatric Cancer (cont.)

- Childhood cancer rates by site (0-14 yrs)
  - **Brain** (27%)
  - **Other Solid** (22%)
  - **Liquid** (51%)

- At diagnosis, incidence of malnutrition (8-60%)
  - Common in advanced/metastatic tumors

- Treatment results in side effects impacting nutritional status

- Atypical growth and development (physical and cognitive) and altered body composition may occur

- Interpretation of nutrition indices used in typical children/adults may not accurately reflect nutritional status during treatment and in childhood cancer survivors

<table>
<thead>
<tr>
<th>Cancer Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukemia</td>
</tr>
<tr>
<td>Lymphomas and Reticuloendothelial Neoplasms</td>
</tr>
<tr>
<td>Central Nervous System (CNS)</td>
</tr>
<tr>
<td>Sympathetic Nervous System Tumors</td>
</tr>
<tr>
<td>Retinoblastoma</td>
</tr>
<tr>
<td>Renal Tumors</td>
</tr>
<tr>
<td>Hepatic Tumors</td>
</tr>
<tr>
<td>Malignant Bone Tumors</td>
</tr>
<tr>
<td>Soft-Tissue Sarcomas</td>
</tr>
<tr>
<td>Germ-Cell, Trophoblastic and other Gonadal Neoplasms</td>
</tr>
<tr>
<td>Carcinomas and other Malignant Epithelial Neoplasms</td>
</tr>
<tr>
<td>Other and Unspecified Malignant Neoplasms</td>
</tr>
</tbody>
</table>

Major Types of Cancer in Children and Adolescents

- Leukemia and Lymphoma
  - Acute Lymphocytic Leukemia
  - Acute Myeloid Leukemia
  - Hodgkin Lymphoma
  - Non-Hodgkin Lymphoma

- Embryonal Tumors
  - Neuroblastoma
  - Wilms Tumor
  - Retinoblastoma

- Bone and Soft Tissue Sarcomas
  - Osteosarcoma
  - Ewing Sarcoma
  - Rhabdomyosarcoma

- Brain and Central Nervous System Tumors
  - Astrocytoma
  - Medulloblastoma
  - Ependymoma

- Gonadal Germ Cell Tumors
  - Ovarian Germ Cell Tumors
  - Testicular Germ Cell Tumors

### Estimated New Cases of Childhood and Adolescent Cancers, United States, 2014

#### Children (Ages 0-14)

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute lymphocytic leukemia</td>
<td>2,670</td>
<td>26%</td>
</tr>
<tr>
<td>Brain and CNS</td>
<td>2,240</td>
<td>21%</td>
</tr>
<tr>
<td>Neuroblastoma*</td>
<td>710</td>
<td>7%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>620</td>
<td>6%</td>
</tr>
<tr>
<td>Wilms tumor</td>
<td>510</td>
<td>5%</td>
</tr>
<tr>
<td>Acute myeloid leukemia</td>
<td>500</td>
<td>5%</td>
</tr>
<tr>
<td>Bone tumors†</td>
<td>450</td>
<td>4%</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>380</td>
<td>4%</td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>340</td>
<td>3%</td>
</tr>
<tr>
<td>Retinoblastoma</td>
<td>280</td>
<td>3%</td>
</tr>
<tr>
<td><strong>All sites</strong></td>
<td></td>
<td><strong>10,450</strong></td>
</tr>
</tbody>
</table>

#### Adolescents (Ages 15-19)

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hodgkin lymphoma</td>
<td>800</td>
<td>15%</td>
</tr>
<tr>
<td>Thyroid carcinoma</td>
<td>570</td>
<td>11%</td>
</tr>
<tr>
<td>Brain and CNS</td>
<td>540</td>
<td>10%</td>
</tr>
<tr>
<td>Testicular germ cell tumors</td>
<td>430</td>
<td>8%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>420</td>
<td>8%</td>
</tr>
<tr>
<td>Acute lymphocytic leukemia</td>
<td>410</td>
<td>8%</td>
</tr>
<tr>
<td>Bone tumors†</td>
<td>370</td>
<td>7%</td>
</tr>
<tr>
<td>Melanoma</td>
<td>310</td>
<td>6%</td>
</tr>
<tr>
<td>Acute myeloid leukemia</td>
<td>230</td>
<td>4%</td>
</tr>
<tr>
<td>Ovarian germ cell tumors</td>
<td>110</td>
<td>2%</td>
</tr>
<tr>
<td><strong>All sites</strong></td>
<td></td>
<td><strong>5,330</strong></td>
</tr>
</tbody>
</table>

 Estimates are for malignant cancers only and are rounded to the nearest 10. In addition, 730 children and 630 adolescents will be diagnosed with benign and borderline brain tumors in 2014.

CNS=central nervous system

*Includes ganglioneuroblastoma. †Bone tumors include osteosarcoma and Ewing sarcoma.
Trends in Pediatric Cancer Incidence Rates by Site, Ages Birth to 19 Years, 1975-2010

CNS=central nervous system.
Note: Lines represent joinpoint fitted trends. Benign and borderline brain tumors are not included. Malignant bone tumors include osteosarcoma and Ewing sarcoma. Source: Surveillance, Epidemiology, and End Results (SEER) program, 9 SEER Registries, National Cancer Institute.
Trends in Pediatric Cancer Mortality Rates by Site, Ages Birth to 19 Years, **1975-2010**

ONS=other nervous system.
Note: Lines represent joinpoint fitted trends. Source: National Center for Health Statistics, Centers for Disease Control and Prevention.
ALL=acute lymphocytic leukemia, HL=Hodgkin lymphoma, NHL=Non-Hodgkin lymphoma, CNS=central nervous system, TGCT=testicular germ cell tumor
*Cases were followed through 2010.
Note: Does not include benign and borderline brain tumors.
Source: National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) program, 9 SEER registries.
Nutrition Care
Pediatric Oncology and Survivorship
Children’s Oncology Group

- Children’s Cancer Centers treat patients 0-20 yrs

- Children’s Oncology Group (COG) – supported NCI
  - World’s largest organization - conducts research for children/adolescents w/cancer
  - 8,000 experts, 200 children’s hospitals, universities, cancer centers in North America, Australia, New Zealand, Europe
  - 90% children/adolescents diagnosed in US cared for at COG member institutions

Children’s Oncology Group - https://childrensoncologygroup.org/
Joining the COG - https://childrensoncologygroup.org/index.php/joiningcog
Nutrition Assessment

Nutrition-Focused Physical Findings

- Evaluation of body systems
- Muscle wasting
- Subcutaneous fat wasting
- Oral health
- Suck / swallow
- Appetite
- Affect

Assessment parameters (IDNT, 2012):

- Overall appearance (PD-1.1.1)
- Body language (PD-1.1.2)
- Cardiovascular-pulmonary (PD-1.1.3)
- Extremities, muscles and bones (PD-1.1.4)
- Digestive system (PD-1.1.5)
- Head and eyes (PD-1.1.6)
- Nerves and cognition (PD-1.1.7)
- Skin (PD-1.1.8)
- Vital signs (PD-1.1.9)
<table>
<thead>
<tr>
<th>Body Composition Component</th>
<th>Area Assessed</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Subcutaneous fat</strong></td>
<td>Infraorbital fat pad</td>
<td>• Sunken appearance</td>
</tr>
<tr>
<td></td>
<td>Triceps skinfold (pinch test)</td>
<td>• Excessive or normal to fingers touching</td>
</tr>
<tr>
<td></td>
<td>Midaxillary line at the level of the lower ribs</td>
<td>• Excessive or normal to fingers touching</td>
</tr>
<tr>
<td><strong>Skeletal Muscle</strong></td>
<td>Temporalis muscle</td>
<td>• Temporal wasting</td>
</tr>
<tr>
<td>(Loss of muscle bulk and tone by palpitation)</td>
<td>Deltoid muscles</td>
<td>• Squaring of the junctions of neck and shoulder and at the shoulder joint (ie, loss of normal curvature); prominent acromial process; prominent infraclavicular fossa along its lateral aspect; depression above scapula when hand extended against wall</td>
</tr>
<tr>
<td></td>
<td>Pectoral muscles</td>
<td>• Prominent infraclavicular fossa along its medial aspect; loss of chest wall muscle mass</td>
</tr>
<tr>
<td></td>
<td>Latissimus dorsi muscle</td>
<td>• Depression medial to scapula or at axillary border when hand extended against wall</td>
</tr>
<tr>
<td></td>
<td>Thenar interosseous muscles</td>
<td>• Flattening of the prominence between thumb and index finger when patient is asked to press the pads of these digits together</td>
</tr>
</tbody>
</table>
Nutrition Assessment

- **Comorbid disorders** (i.e. obesity, autism, diabetes)
- **Food/Nutrition-Related History** – food intake (Infants), CAM use, beliefs/attitudes (cultural), access to food, physical activity and function
- **Nutrition Impact Symptoms** – difficulty chewing/swallowing, age-appropriate oral/feeding skills, N/V/D, constipation, dysphagia, taste aversions, mucositis, altered sense of smell, pain, fatigue, infection
- **Anthropometric Measurements** – Height/length, weight, weight change, BMI, weight for length, growth patterns (growth charts)
  - Growth Assessment – weight for age, length/height for age, weight for length, BMI for age/sex, frontal occipital circumference (FOC), triceps skinfold (TSF), mid-arm circumference (MAC)
  - CDC and WHO growth charts
Categories of Nutritional Status for the Pediatric Oncology Patient

- Identify appropriate category:
  - Age > 2 years - choose either BMI (Body Mass Index) or IBW (Ideal Body Weight)
  - Age < 2 years - choose either WT/LT (Weight for Length) or IBW (Ideal Body Weight)

- Weight loss/gain may or may not be present

<table>
<thead>
<tr>
<th>Underweight</th>
<th>Normal</th>
<th>Risk of Overweight / Overweight</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 5th % ile</td>
<td>5 - 85th % ile</td>
<td>&gt; 85 - 95th % ile</td>
</tr>
<tr>
<td><strong>WT/LT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 10th % ile</td>
<td>10 - 90th % ile</td>
<td></td>
</tr>
<tr>
<td><strong>IBW</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 70% Severe</td>
<td>&gt; 70-80% Moderate</td>
<td>&gt; 90 - 110 %</td>
</tr>
</tbody>
</table>

Children's Oncology Group, Cancer Control - Nutrition Sub-committee 10.25.04. Currently being revised
COG – Resources (free)

The Children's Oncology Group Family Handbook 2nd Edition
• Information: treatment, support, follow-up care. (English, Spanish, French)
  https://childrensoncologygroup.org/index.php/cog-family-handbook

Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers – Version 4.0
• Recommendations screening/management of late effects due treatment
• Increase awareness of potential late effects
• Standardize and enhance follow-up care provided to survivors
  https://childrensoncologygroup.org/index.php/survivorshipguidelines

Health Links (English, some in Spanish and French)
Information about some of the more common late effects (use above link)
• General and Psychosocial: Diet and Physical Activity
• Cardiac System: Heart Health, Cardiovascular Risk Factors
• Endocrine System: Growth Hormone Deficiency
• Gastrointestinal System: Gastrointestinal Health
• Musculoskeletal System: Bone Health, Osteonecrosis
Late Effects of Treatment for Childhood’s Cancer – 3 of 5 survivors develop late effects; Links on AVN, bone health, hormones, secondary cancers, heart problems
https://childrensoncologygroup.org/index.php/lateeffectsoftreatment

Coping With Cancer - guidance for parents, family members, friends, teachers, others who care for and about a child with cancer

Treatment Side Effects – Weight gain/loss, GI problems, appetite, constipation, fatigue, dehydration
https://childrensoncologygroup.org/index.php/weightgainorweightloss

COG - Cancer Control, Nutrition Sub-committee (see publications)
Elena Ladas, PhD, RD, Chair  ejd14@cumc.columbia.edu


Defining and Developing an Oncology Nutrition Program in a Cancer Center

Nutritional Management of the Pediatric Oncology Patient:

- Methods used to diagnose malnutrition
- Energy/protein needs equations and recommendations
- Nutritional risk screening and assessment
- Integrative Oncology
- PN and Enteral
- HSCT
Treatment Modalities and Complications
Treatment Modalities

- Chemotherapy, Surgery, Radiation, Hematopoietic Stem Cell Transplant
- Immunotherapy:
  - Help pt’s immune system recognize/destroy cancer cells more effectively
  - Several types used w/ neuroblastoma (NBL)
  - Monoclonal antibodies: man-made versions of immune system proteins attack specific target
    - Inject into the body → seek out/attach → to cancer cells
  - Dinutuximab (Unituxin) - antibody attaches to GD2, substance on surface of NBL cells
    - Given w/cytokines (immune system hormones) → GM-CSF & interleukin-2 (IL-2) help immune system recognize/destroy NBL cells
    - Antibody part of tx for many children w/ high-risk NBL after HSCT


https://www.nutritioncaremanual.org/topic.cfm?ncm_category_id=13&lv1=144629&lv2=255473&ncm_toc_id=255473&ncm_heading=Nutrition%20Care
Complications of Cancer and Treatment

- Anorexia
- Vomiting
- Mucositis
- Diarrhea
- Constipation
- Malabsorption
- Malnutrition
- Infection
- Organ toxicity
- Mechanical gut problems
- **Altered energy needs**
- **Altered taste / smell**
- Metabolic changes
- Psychological

**Performance Status**
- Karnofsky performance scale (100-0)
- Lansky play-performance for pediatric patients (1-16 yrs) (100-0)
- ECOG (WHO/Zubrod Score) (1-5)

http://hemonc.org/Performance_status
Malnutrition

- Incidence at diagnosis in children with cancer ranges from 5-50%
- Can increase as a result of treatment, often persists when therapy completed
- Complications of malnutrition:
  - Impaired immune function (increased risk of infection)
  - Treatment toxicity and delays in treatment
  - Decreased survival rates
  - Poor tumor response to therapy
  - Lethargy, apathetic, may appear sad

A new way of defining malnutrition
The spectrum of malnutrition

**Undernutrition**
- 14% of children/adolescents
- Hospitalization
- Chronic Illness
- Special Needs

Grover, 2009; US Department HHS, 2007

**Overweight/Obese**
- 17% of children/adolescents
- Excessive energy imbalance

Ogden, 2010; U.S. statistics

Defining pediatric malnutrition: a paradigm shift toward etiology-related definitions.

**Consensus Statement of the Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition: Indicators Recommended for the Identification and Documentation of Pediatric Malnutrition (Undernutrition).**

Table 3. Primary Indicators When Single Data Point Available.\(^{71-74,76,77}\)

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Mild Malnutrition</th>
<th>Moderate Malnutrition</th>
<th>Severe Malnutrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight-for-height z score</td>
<td>-1 to -1.9 z score</td>
<td>-2 to -2.9 z score</td>
<td>-3 or greater z score</td>
</tr>
<tr>
<td>BMI-for-age z score</td>
<td>-1 to -1.9 z score</td>
<td>-2 to -2.9 z score</td>
<td>-3 or greater z score</td>
</tr>
<tr>
<td>Length/height-for-age z score</td>
<td>No data</td>
<td>No data</td>
<td>-3 z score</td>
</tr>
<tr>
<td>Mid-upper arm circumference</td>
<td>Greater than or equal to -1 to -1.9 z score</td>
<td>Greater than or equal to -2 to -2.9 z score</td>
<td>Greater than or equal to -3 z score</td>
</tr>
</tbody>
</table>

BMI, body mass index.

Table 4. Primary Indicators When 2 or More Data Points Available.\(^{71-74,76,77}\)

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Mild Malnutrition</th>
<th>Moderate Malnutrition</th>
<th>Severe Malnutrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight gain velocity (&lt;2 years of age)</td>
<td>Less than 75%(^{a}) of the norm(^{b}) for expected weight gain</td>
<td>Less than 50%(^{a}) of the norm(^{b}) for expected weight gain</td>
<td>Less than 25%(^{a}) of the norm(^{b}) for expected weight gain</td>
</tr>
<tr>
<td>Weight loss (2–20 years of age)</td>
<td>5% usual body weight</td>
<td>7.5% usual body weight</td>
<td>10% usual body weight</td>
</tr>
<tr>
<td>Deceleration in weight for length/height z score</td>
<td>Decline of 1 z score</td>
<td>Decline of 2 z score</td>
<td>Decline of 3 z score</td>
</tr>
<tr>
<td>Inadequate nutrient intake</td>
<td>51%–75% estimated energy/protein need</td>
<td>26%–50% estimated energy/protein need</td>
<td>(\leq25%) estimated energy/protein need</td>
</tr>
</tbody>
</table>


Nutritional Status - Studies
## Challenges Evaluating Nutritional Status – Clinical vs. Research?

<table>
<thead>
<tr>
<th>Location</th>
<th>Sample</th>
<th>Age</th>
<th>Time Points</th>
<th>Measurements</th>
<th>Criteria</th>
<th>Outcomes*</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>Homogenous vs. Heterogenous</td>
<td>Range within study</td>
<td>Dx</td>
<td>Weight</td>
<td>CDC</td>
<td>Clinical: Anthropometric parameters (height, weight, HC, MUAC)</td>
</tr>
<tr>
<td>Other country</td>
<td></td>
<td>Specific to Dx</td>
<td>Treatment time varies based on dx and study</td>
<td>WFAZ</td>
<td>WHO</td>
<td>Biochemical (acute phase protein)</td>
</tr>
<tr>
<td>Developed vs.</td>
<td></td>
<td>Age changes - indices change</td>
<td>Dx 3m, 6m, End Survivorship: Varies</td>
<td>Percentile/Z-Score</td>
<td>International</td>
<td>Re-hospitalization</td>
</tr>
<tr>
<td>Underdeveloped</td>
<td></td>
<td>Survivor studies</td>
<td>Dx → End of Tx</td>
<td>Percent IBW</td>
<td></td>
<td>Developmental milestones</td>
</tr>
<tr>
<td>War</td>
<td></td>
<td>Time span varies</td>
<td>Dx → Survivor 5 yr s/p Dx</td>
<td>HFAZ</td>
<td></td>
<td>Lean body mass</td>
</tr>
<tr>
<td></td>
<td></td>
<td>→ Survivor 5,10,15+yrs &gt; Dx</td>
<td>Dx</td>
<td>Percent / Z-Score</td>
<td>Specific to country Guidelines</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Dx</td>
<td>% absolute loss</td>
<td>Guidlines</td>
<td>Databases change</td>
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<tr>
<td></td>
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<td></td>
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<td>Wt to Ht/Lt</td>
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<td>Cut-off’s change</td>
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<td></td>
<td></td>
<td>BMI</td>
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<td>Prevalence changes</td>
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<td></td>
<td></td>
<td>BMI for age/sex</td>
<td></td>
<td>Underweight</td>
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<td></td>
<td></td>
<td></td>
<td>Percentile/Z-Score</td>
<td></td>
<td>Over/Obese</td>
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<td></td>
<td></td>
<td>Body Composition</td>
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<td></td>
<td></td>
<td>DXA</td>
<td>CDC</td>
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<td>BIA</td>
<td>WHO</td>
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<td></td>
<td>MUAC</td>
<td>International</td>
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<td></td>
<td></td>
<td>TSF</td>
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</tbody>
</table>

Different methodologies used for ages (0-2y, >2-20y, >20y)

Nutritional Status of Pediatric Oncology Patients with Sarcomas (unpublished data)

Sacks N, Norris C, Rheingold S, Zhao H, Womer R

Aims:
- Describe NS of pediatric pts w/ new dx sarcoma (RMS, Ewings, osteo and NOS)
- Evaluate relationship of NS with relapse, survival and infection

Results
- Majority of patients lose wt
- ↑ in pts who become undernourished
- Pts w/ higher BMIZ at dx had less infections vs. pts w/ lower BMIZ (<p>.001)
- Smaller ↓ in BMIZ from dx was associated w/ less infections vs. those w/ larger ↓ (<p>.004)

Percent malnutrition at various time points

<table>
<thead>
<tr>
<th></th>
<th>Low Weight</th>
<th>End of Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;90% IBW for Height</td>
<td>18.9 (N=40)</td>
<td>44.1 (N=93)</td>
</tr>
<tr>
<td>&lt;5th percentile BMI</td>
<td>11.2 (N=21)</td>
<td>38.4 (N=71)</td>
</tr>
<tr>
<td>&lt;10th percentile Wt/Length</td>
<td>35.0 (N=7)</td>
<td>59.7 (N=40)</td>
</tr>
<tr>
<td></td>
<td>23.4 (N=48)</td>
<td>17.7 (N=32)</td>
</tr>
<tr>
<td></td>
<td>26.7 (N=16)</td>
<td></td>
</tr>
</tbody>
</table>
Changes in nutritional status in childhood cancer patients: A prospective cohort study

**Aim:** Determine when changes in NS occur during tx

**Methods:**
- New dx: hematological, solid, brain (N=133)
- Time points: 0, 3, 6, 12 mths s/p dx

**Measures:** WFA, HFA, BMI, TSF, MUAC, FM, %FM, FFM
- Undernutrition: BMI < -2SDS or FFM < -2SDS
- Overnutrition: BMI > 2SDS or FM > 2SDS
- Weight ↓ or ↑: >5% between 2 times

**Pt characteristics:** (age, gender, dx)

**Nutrition:** % needs, TF (y/n)

**Tx intensity**

**Corticosteroids**

**Physical Activity**

Brinksma A et al, 2015
Conclusions:

- 3 mths > dx: ↓WFA solid/hemat.
- 12 mths >dx: ↓HFA brain/hemat
- 12 mths % obese patients doubled
- 45.1% had NG in 1st yr:
  - Younger: (P = 0.005)
  - Lower initial WFA (P=0.033)
  - More intensive tx (P < 0.001)
- Low initial NS and TF contributed to ↑ BMI
- Catch-up growth or overfeeding?
- No association w/BMI and corticosteroids
Impact on Survival and Toxicity by Duration of Weight Extremes During Treatment for Pediatric Acute Lymphoblastic Leukemia: A Report From the Children’s Oncology Group

- Other studies evaluated weight at diagnosis: event-free survival (EFS) & treatment related toxicity (TRT) in childhood ALL

- Current study
  - Cumulative time receiving tx at extreme weight (obese or underweight)
  - End of induction & start of maintenance tx (CCG-1961, n=2,008)

**Results**
- Obese/underweight at dx and >50% of time between end of induction and start of maintenance tx → **inferior EFS**
- Normalization of wt during that period → **mitigation risk**, same as never being obese/underweight
- Influence of wt extremes on EFS and TRT is **not set at dx**, as previously reported
- Weight may be a risk factor that can be impacted with intervention

Orgel E et al. J Clin Oncol 32:1331-1337
Nutrition Intervention
Type of Enteral Tube Feeding - Reactive vs Proactive?

GASTRIC FEEDS - (0.5 - 2 mL/kg/hour and ↑ 0.5-1 mL/kg/day)
- Nasogastric tubes (NG) - 6 or 8Fr
- Gastrostomy tube (GT) – IR vs. surgical, dx (i.e. NP-RMS), preference

POST-PYLORIC
- Nasoduodenal tube (ND)- reflux/aspiration, emesis not very successful
- Nasojunal tube (NJ) – pancreatitis, emesis
- Gastrojejunostomy (GJT) – vomiting/aspiration
- Jejunostomy (JT) - needed > 6 months

Formula – Age, GI function (Standard, pre-digested, lactose-free)
- WIC (< 5 yrs), Medical Assistance, LOMN

Fluid - Provide fluid via tube (60 ml syringe, bag, flush)

Algorithm: Nutritional intervention in the pediatric oncology patient (Sacks et al 2015)

PN guidelines: see references/resources below
Nutrition Intervention

**Oral Intake** → weight loss / unable to maintain nutritional status ↔ 1970 - 1980’s

**PN** → Weight/muscle ↑, reversed PEM, but infection rate concerning ↔ 1980’s - 1993

**ETF** → Reverses weight loss/prevents weight loss, well tolerated ↔ 1995 - current

<table>
<thead>
<tr>
<th>Enteral Tube Feeding (ETF)</th>
<th>Author / Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>All children gained/maintained wt (GT)</td>
<td>Aquino V et al 1995</td>
</tr>
<tr>
<td>82% achieved IBW with some complications (GT)</td>
<td>Mathew P et al 1996</td>
</tr>
<tr>
<td>Protocolized ETF resulted in children achieving IBW</td>
<td>den Broeder E et al 1998</td>
</tr>
<tr>
<td>NG tube generally well tolerated</td>
<td>Pietsch J et al 1999</td>
</tr>
<tr>
<td>Wt gain using ETF associated with reduced rate of nonleukopenic infections in children with solid tumors</td>
<td>den Broeder E et al 2000</td>
</tr>
<tr>
<td>ETF initiated prior to second course of therapy helps prevent acute malnutrition and supports repletion of nutritional stores</td>
<td>Sacks et al 2008</td>
</tr>
<tr>
<td>PEG reversed early wt loss and infectious complications did not usually lead to PEG removal</td>
<td>Parbhoo PM 2011</td>
</tr>
<tr>
<td>Early PEG tube placement was safe, prevented malnutrition, restored weight for height z scores</td>
<td>Schmitt F et al 2012</td>
</tr>
<tr>
<td>Proactive ETF is feasible and improved NS at end of therapy</td>
<td>Sacks et al 2014</td>
</tr>
</tbody>
</table>

ETF is a safe method and cost-effective way to provide nutrition support.
Proactive Enteral Tube Feeding in Pediatric Patients Undergoing Chemotherapy

- Pilot study
  - n=20 participants
  - n=49 chart collection only
- Determine feasibility/safety of proactive enteral tube feeding (ETF)
- New Dx: brain or solid tumors, AML
- Start ETF before cycle 2 chemo
- Barriers: MD, pt/family
- Proactive ETF is feasible
- Improved NS at end of therapy

Sacks et al PBC 2014;61:281–285
Gastrointestinal Supportive Care Medications and Appetite Stimulants
## Medications: GI and Anti-emetics

| Motility Agents | • ↑ forward peristalsis in stomach/duodenum  
| • Macrolide antibiotic, increases proximal gut motility |
| --- | --- |
| Acid-blocker medications | **H-2 receptor Antagonists**  
| • Block histamine-induced acid secretion |
| **Proton Pump Inhibitors**  
| • Block hydrogen/potassium ATPase (“proton pump”) |
| Antiemetics | **Serotonin Receptor (5HT3 or 5-hydroxytryptamine-3) Antagonists**  
| • Block effects of serotonin at 5HT3 receptors in GI tract & chemo receptor trigger zone in brain |
| **Aprepitant**  
| • Neurokinin-1 receptor antagonist  
| • Small ↓ acute N/V, larger r↓ delayed N/V |
| **Glucocorticoids**  
| • Used w/ serotonin receptor antagonist or metoclopramide  
| • Single agent mildly emetic regimens |
| **Phenothiazines**  
| • Block dopamine receptors vomiting center & chemo receptor trigger zone in brain  
| • Acute N/V mild/mod emetic chemo breakthrough N/V |
| **Cannabinoids**  
| • Typical antiemetic haven’t worked  
| • Psychoactive component of marijuana |
| **Atypical antipsychotics**  
| • Similar to dopamine blockers  
| • Less likely to cause extrapyramidal side effects |
| **Antihistamines and Bensodiazepines**  
| • Adjunctive agents for chemo-induced N/V  
| • Sedation helps sleep through treatment |

Appetite Stimulants

**Megestrol/Megace™ and Medroxyprogesterone/Provera™**
- Progestins $\uparrow$ appetite and cause weight gain
- Potential adverse effects: thrombophlebitis, photosensitivity, impotence in men, Cushing’s syndrome with adrenocortical suppression and Addisonian crisis

**Dronabinol/Marinol™**
- Synthetic THC in sesame oil (capsule)
- Weight gain in adults, FDA approved (anorexia in AIDS)
- Little data on use in cancer pts w/ anorexia or pediatrics.
- Doses for appetite stimulation lower vs. N/V; fewer adverse effects

**Nabilone/Cesamet™**
- Synthetic cannabinoid - synthetic molecule similar to THC (capsule)

**Cyproheptadine/Periactin™**
- Serotonin antagonist and antihistamine – side effect is appetite stimulant

Literature Review
Appetite Stimulants
Appetite Stimulants - studies

**Megestrol/Megace™ and Medroxyprogesterone/Provera™**

- Randomized, double-blind, placebo-controlled trial in peds:
  - 20% mean weight gain; fat mass > LBM; adrenocortical suppression frequent
  (Cuvelier et al. 2014)

**Dronabinol/Marinol™ (but not nabilone)**

- Minimal evidence for efficacy with weight gain or reducing weight loss in cancer patients
  (Jatoi et al. 2002; Yavuzsen et al. 2005; Strasser et al. 2006; Taketomo et al. 2007)

**Cyproheptadine/Periactin™**

- Adults with advanced malignancies; increased appetite but no less weight loss vs. placebo
  (Kardinal et al. 1990)

- Children with cancer; weight gain, but drowsiness as common side effect
  (Couluris et al. 2008)
Cannabis
Cannabis – Medical Marijuana
Using the internet .....search medical marijuana

Benefits of **Sativa**
(higher THC, low CBN/CBD):
- Reduces nausea
- Stimulates appetite
- Fights depression
- Positive, uplifting, cerebral effect
- Energizes and stimulates
- Promotes creativity
- Relieves headaches and migraines
- Relaxes muscles, relieves pain
- Acts as an expectorant

Benefits of **Indica**
(lower THC, higher CBN/CBD):
- Muscle relaxant
- Relieves spasms, reduces seizures
- Reduces inflammation #006600
- Aids sleep
- Reduces anxiety and stress
- Reduces nausea
- Stimulates appetite
- Relieves headaches and migraines
- Reduces intra-ocular pressure
- Broncho-dilator and expectorant

Which one would you buy ????

[http://patientsmarijuana.org/Sativa_or_Indica.html](http://patientsmarijuana.org/Sativa_or_Indica.html)

Patient's Marijuana Caregiver Services are offered in strict accordance with the Michigan Medical Marihuana Act of 2008, and within the guidelines set forth for this program by the Michigan Department of Community Health.
Cannabis in the U.S

- Legal in 24 states for medical use, 7 states pending
- Schedule 1 Drug under Controlled Substance Act (CSA) – illegal under federal law

### 23 Legal Medical Marijuana States and DC
Laws, Fees, and Possession Limits

#### I. Summary Chart

<table>
<thead>
<tr>
<th>State</th>
<th>Year Passed</th>
<th>How Passed (Yes Vote)</th>
<th>Possession Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alaska</td>
<td>1998</td>
<td>Ballot Measure 8 (58%)</td>
<td>1 oz usable; 6 plants (3 mature, 3 immature)</td>
</tr>
<tr>
<td>Arizona</td>
<td>2010</td>
<td>Proposition 203 (50.13%)</td>
<td>2.5 oz usable; 0-12 plants</td>
</tr>
<tr>
<td>California</td>
<td>1996</td>
<td>Proposition 215 (56%)</td>
<td>8 oz usable; 6 mature or 12 immature plants</td>
</tr>
<tr>
<td>Colorado</td>
<td>2000</td>
<td>Ballot Amendment 20 (54%)</td>
<td>2 oz usable; 6 plants (3 mature, 3 immature)</td>
</tr>
<tr>
<td>Connecticut</td>
<td>2012</td>
<td>House Bill 5389 (96-51 H, 21-13 S)</td>
<td>One-month supply (exact amount to be determined)</td>
</tr>
<tr>
<td>DC</td>
<td>2010</td>
<td>Amendment Act B18-622 (13-0 vote)</td>
<td>2 oz dried; limits on other forms to be determined</td>
</tr>
</tbody>
</table>

#### II. Details by State

#### III. Sources

http://legalmedicalmarijuanastates.com/2015/
Cannabis classification

- Cannabis
- Family: Cannabaceae (Hemp)
- Genus: Cannabis L.
- Species:
  - C. sativa
  - C. indica
  - C. ruderalis
- Psychoactive chemical: delta-9-tetrahydrocannabinol (THC)

http://plants.usda.gov/core/profile?symbol=CASA3
**Cannabinoids** – Family of complex chemicals in Cannabis

**Classification** (Chakravarti B, 2014)

Pre-clinical studies:
- Cannabinoids have the ability in targeted killing of tumors
- Effects are mediated via cannabinoid receptors

Cannabinoids bind to cannabinoid receptors (protein-coupled receptors):
- CB1 (Central): highest amount in CNS; mediate cannabinoid psychoactive effects
- CB2 (Peripheral): restricted to parts of immune system (enriched area of B lymphocytes)
Cannabis – Types of Cannabinoids:

**Phytocannabinoids** - 60 types - active constituents
- Only occur naturally in significant quantity in cannabis plant (viscous resin)

$\Delta^9$-tetrahydrocannabinol (THC) - contribute to the psychoactive properties of marijuana
- Cannabinol (CBN) (metabolite of THC) - lack this property (psychoactive)
- Cannabidiol (CBD) (isomer of THC) - lack this property (psychoactive)

Cannabigerol (CBG) (alpha 2 adrenergic receptor agonist)
- Tetrahydrocannabivarin (THCV; THV; TCH homolog)
- Cannabichromene (CBC)

**Endocannabinoids** (endogenous cannabinoid agonists)
- 2-AG (2-arachidonoyl glycerol)
- Anandamide (arachidonoyl ethanolamide)

**Synthetic cannabinoids**
- **Dronabinol** (Marinol®) - synthetic THC in sesame oil: Schedule III drug
- **Nabilone** (Cesamet®) - synthetic molecule similar to THC: Schedule II – more potent
- **Nabiximols** (Sativex®) - THC/CBD (phytocannabinoid) - Oral mucosal spray (Canada)

- Dronabinol: 10–20% reaching circulatory system vs. Nabilone: rapid complete absorption in GI tract
Research - Cannabis
Cannabis and Cannabinoids

Antitumor activity
- Lab/animal - inhibit tumor growth, cause cell death, block cell growth & dev’t of blood vessels needed by tumors, protect normal cells
- Mouse - potential ↓ risk colon cancer
- Lab/Mouse: $\Delta^9$-THC damaged/killed cancer cells (hepatocellular carcinoma, non-small cell lung cancer & breast cancer)
- Lab/Mouse: Cannabidiol (CBD)
  - Estrogen receptor+/- breast cancer - Cancer cell death, little effect normal cells
  - Metastatic breast cancer - may lessen growth, number, spread of tumors
- Lab/Mouse: Cannabidiol (CBD):
  - Glioma cells: CBD may make chemotherapy (i.e.) temozolomide more effective
  - ↑ cancer cell death without harming normal cells

Stimulating appetite:
- Animal studies: $\Delta^9$-THC & other cannabinoids ↑ appetite/intake

Pain relief: Cannabinoid receptors (molecules that bind cannabinoids)
- May play role in pain relief (evaluating in brain, spinal cord, nerve endings)
Cannabis - Clinical Trials.gov

Search for Studies:

Cannabinoids – 463  Cannabidiol and cancer – 14

Cannabinoids and glioma – 3
1  Completed
   Has Results: A Pilot Study of Dronabinol for Adult Patients With Primary Gliomas
   Conditions: Brain Neoplasms; Nausea; Vomiting
   Intervention: Drug: Dronabinol

2  Active, not recruiting
   A Safety Study of Sativex in Combination With Dose-intense Temozolomide in Patients With Recurrent Glioblastoma
   Condition: Cancer
   Intervention: Drug: Sativex

3  Recruiting
   A Safety Study of Sativex Compared With Placebo (Both With Dose-intense Temozolomide) in Recurrent Glioblastoma Patients
   Condition: Cancer
   Interventions: Drug: Sativex; Drug: Placebo

Cannabis and epilepsy – 2 studies

https://clinicaltrials.gov/
Cannabis – Things to know

- Oral: cookies, brownies, tea, capsule
- Smoke plant parts: leaves, stems, tops
- Cigarette (joint) contains approximately 20 mg of THC from a gram of the plant’s leaves and buds
- Smoke hashish, hashish oil, sensimilla
- “Boosting”: add marijuana to tobacco or other drugs
- Hookah pipe “Dabbing” (uses butane hash oil)
- Hot boxing (cannabis smoking in a closed car with peers)

- Pharmacokinetics influenced: THC content, smoking and puff duration, inhalation volume, breath-holding, gastric acidity, first-pass metabolism.
Medical Marijuana

Since cultivating medical marijuana is already legal in a lot of states in the U.S., as well as in a number of other regions, there have been an increasing number of customers considering to grow these plants for medical purposes. The ever-growing support for making marijuana legal for medical use will hopefully give rise to more countries changing their laws. The most uncomplicated method to start cultivating medical marijuana is by purchasing seeds on the internet – and are in the perfect place: Buy Dutch Seeds!

Medical marijuana can eliminate pain and reduce the symptoms of a wide variety of ailments and illnesses. As doctors, researchers, growers and patients continue to look for the potentials of medical marijuana, the understanding is starting to dawn that marijuana has few to no side effects. Specifically when set side by side with prescription drugs.

30 item(s)
Indica:  Sativa:

Night Time Use  Day Time Use
Body High     Cerebral High
Sedative      Energetic
Relieves Anxiety  Stimulate Appetite
Causes Sleepiness  Enhances Creativity
Relieves Pain  Relieves Depression
High CBD Level  Higher THC Level
Childhood Cancer Survivors
Childhood Cancer Survivors

- Two of three 5-year survivors develop a chronic health condition
- More than one-third will develop a condition that is severe or life threatening
- Late effects often occurring in survivors:
  - cardiopulmonary disease
  - subsequent malignant neoplasm
  - musculoskeletal problems
  - endocrine and neurosensory problems
- Many children diagnosed with cancer are alive at least 5 years after diagnosis and are considered cured, but many experience late effects from therapy affecting their lives long after therapy is completed.

A Retrospective, Longitudinal Evaluation of Nutritional Status in a Cohort of Childhood Cancer Survivors

Background:
- Children with cancer - suboptimal weight gain and linear growth during therapy
- Survivors - demonstrate atypical growth patterns after therapy completion

Objective:
- Describe WFAZ, HFAZ and categories of nutritional status at specified time points
- Analyze changes in nutritional status between Dx (T1) and five years from Dx (T2)

Design/Subjects: Retrospective pilot study (Brain tumor: n= 61; Other solid tumor: n=61)

Results:
- Significant ↓ mean HFAZ at T1 vs. T2 in entire and brain cohorts (p=0.010, p=0.004) respectively
- Significant difference between nutrition category T1 and T2
  - Entire cohort (p<0.0001)
  - Brain tumor cohort (<0.05)
  - Other solid tumor cohort (p<0.05)
- 35% of survivors were overweight or obese at initial survivorship visit

Sacks N (Submitted in partial fulfillment of the requirement for the Doctorate in Clinical Nutrition, Rutgers – The State University of New Jersey – SHRP (unpublished results), 2014.)
The mean WFAZ and HFAZ at each time point in the entire cohort

Error bars indicate 95% Confidence Intervals for Different Time Points

Over: D 8.0% → 19.0% SUR
The mean WFAZ and HFAZ at each time point in the brain tumor cohort

Error bars indicate 95% Confidence Intervals for Different Time Points

Under: D 2.0% → 10.0% SUR
Over: D 9.0% → 23.0% SUR
Obese: D 13.0% → 20.0% SUR
The mean WFAZ and HFAZ at each time point in the other solid tumor cohort

Error bars indicate 95% Confidence Intervals for Different Time Points

Under: D 9.0% → 2.0% SUR
Over: D 7.0% → 15.0% SUR
Conclusions: Nutritional Status in Childhood Cancer Survivors

- First study to evaluate NS using WFAZ, HFAZ and categories of NS at these time points
  - Trends: inadequate weight gain and linear growth at end of therapy
  - Trends: for increase in overweight/obesity at survivorship
- Catch-up growth may not be occurring in some patients
- Atypical growth patterns persist for weight and/or height
- Limitations: small sample size, heterogeneity, age ranges
- Research is needed to better understand changes in weight and height
- Develop proactive strategies to support optimal nutritional status
Case Study
Childhood Cancer Survivor with Neuroblastoma
Case Study - NBL

- Female cancer survivor: 20y 3m (survivorship visit)
- Diagnosis - Stage IV Neuroblastoma (3yr 8m)
- Primary site adrenal to right kidney w/metastases to bone marrow; n-myc non-amplified
- Treatment
  - Chemo: Cisplatin, VCR, Carboplatin, VP-16, Cytoxan
  - Surgery: Partial Resection (11/29/95) s/p 3 cycles chemotherapy
  - Autologous BMT (12/20/95)
    - Carboplatin, Melphalan, VP-16, Total Body Irradiation - TBI (1,000 cGy)
    - Post BMT consolidative XRT to celiac region (1080 cGy) May 1996
  - Off therapy: 4y 6m (on tx 10 mths)

Mahoney 2006 and Barhelowmew 2011
Characteristics at Presentation

Secretory diarrhea (resolves after tumor removal)
- Hormones secreted by tumor (vasoactive intestinal peptide – VIP)
- Dehydration and hypokalemia

Hypertension (often requires treatment)
- Renovascular compression
- Elevated catecholamine levels

Increased heart rate and fever
- Pain, disease and bone marrow (BM) involvement

Suppression of normal cell lines
- BM involvement (thrombocytopenia, anemia, leucopenia)
- Pallor, fatigue, increased infection and bleeding

Appearance
- Very ill appearing (more advanced disease), irritable
- Periorbital ecchymosis (raccoon eyes) and proptosis
- Bone – pain, decreased use of impacted extremity, limping
- Abdominal distension (fixed/firm mass)

Presentations of children with NBL

A) Infant with a large, distended abdomen and a right-sided abdomen mass.

B) Infant with stage 4-S NBL with multiple skin nodules, *blueberry muffin syndrome.*

C) Skin tumor on the scalp in another infant with stage 4-S NBL

MRI of a left adrenal mass. The mass was revealed by fetal ultrasonography at 30 weeks' gestation


Pizzo and Poplack 2010, Barhelowmew 2011
<table>
<thead>
<tr>
<th>Age</th>
<th>Birth</th>
<th>3 years 8 months</th>
<th>4 years 6 months</th>
<th>9 years 5 month</th>
<th>14 years 7 months</th>
<th>20 years 3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weight, height and nutritional indice</strong></td>
<td>Diagnosis 8/18/95</td>
<td>Off therapy 5/96</td>
<td>5/24/01</td>
<td>7/19/06 (Initial Nutritional Assessment Survivorship)</td>
<td>3/14/12 Survivorship</td>
<td></td>
</tr>
<tr>
<td>Weight (kilogram) / Height (centimeter)</td>
<td>3.7 / Length not available</td>
<td>14.7 / 101.5</td>
<td>18.3 / 104</td>
<td>25.4 / 121.5</td>
<td>33.5 / 142.7</td>
<td>40.6 / 146.5</td>
</tr>
<tr>
<td>Weight for Age Percentile (Hendricks, 2000)</td>
<td>50-75&lt;sup&gt;th&lt;/sup&gt;</td>
<td>25th</td>
<td>50-75th</td>
<td>10-25th</td>
<td>&lt;5&lt;sup&gt;th&lt;/sup&gt;</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Length/Height for Age Percentile (Hendricks 2000)</td>
<td>Not Available</td>
<td>75&lt;sup&gt;th&lt;/sup&gt;</td>
<td>25-50th</td>
<td>&lt;5&lt;sup&gt;th&lt;/sup&gt;</td>
<td>&lt;5&lt;sup&gt;th&lt;/sup&gt;</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Degree of Wasting (weight for height percent standard) (Waterlow 1972)</td>
<td>Unable to determine</td>
<td>92% (Normal Variation) IBW: 16.0 kg</td>
<td>107.6% (Normal Variation) IBW: 17.0 kg</td>
<td>110% (Normal Variation) IBW: 23.0 kg</td>
<td>93.1% (Normal Variation) IBW: 36.0 kg</td>
<td>101.5% (Normal Variation) IBW: 40 kg (20 yr)</td>
</tr>
<tr>
<td>Degree of Stunting (height for age percent standard) (Waterlow 1972)</td>
<td>Not Available</td>
<td>103% (Appropriate) Ht for age is 98.5 cm</td>
<td>99.5% (Appropriate) Ht for age is 104.5 cm</td>
<td>90% (Mild Stunting) Ht for age is 135.0 cm</td>
<td>88.4% (Moderate Stunting) Ht for age is 161.5 cm</td>
<td>90% (Mild Stunting) Ht for age is 163.5 cm (20 yr)</td>
</tr>
<tr>
<td>Body Mass Index (kg/m&lt;sup&gt;2&lt;/sup&gt;) (Center for Disease Control and Prevention 2007)</td>
<td>Not Available</td>
<td>BMI 14.3 (10-25th percentile)</td>
<td>BMI 16.9 (85th percentile)</td>
<td>BMI 17.2 (50-75th percentile)</td>
<td>BMI 16.5 (5-10th percentile)</td>
<td>BMI 18.9 (18.5-24.9 Normal Range)</td>
</tr>
</tbody>
</table>
Nutrition challenges – PN/TF for 10 years

Diagnosis
- Wt loss, wasted, large tumor (up to 10% body wt)
- 50% present undernourished at dx
- Difficult to assess NS due to tumor burden
- GI: N/V/D, decreased intake, electrolyte abnormalities

During/After therapy
- Oral: High calorie diet, oral supplements, small frequent meals, Lactose free
- Enteral Tube Feeding (NG, NJ, GT)
- Formula: Standard, predigested, elemental; with/without fiber, high calorie
- Parenteral Nutrition
- Medication: Reglan, Immodium, calcium/Vitamin D, Multi vitamin mineral supplement
Growth Charts for NB (Stature-for-age, Weight-for-age and Body Mass Index-for-age percentiles)
Endocrine
• Hypothyroidism
• Growth Hormone Deficiency
• Premature Ovarian Failure
• Gonadal Dysfunction
• Infertility
Cardiac
• Hypertension
Respiratory
• Restrictive lung disease
Kidney
• Radiation nephritis
• Loss of kidney and/or function
Musculoskeletal
• Exotoses
• Bone integrity
• Short roots/crowded teeth
Skin
• Pigmented nevi

Hearing
• High frequency hearing loss
Vision
• Cataracts
Gastrointestinal (clinical observations)
• Weight loss and poor weight gain
• Diarrhea, vomiting, abdominal pain
• Failure to thrive
• Decreased appetite and poor intake
• Short stature
• Radiation esophagitis
• Lactose intolerance
• Reflux
• Poor tolerance to tube feeding

Psychosocial
• Problems with anxiety, attention, performance
• Post traumatic stress disorder

Childhood Cancer Survivors – Education information

- Importance of nutrition (macro and micronutrients)
- Dietary Recommendations for each food group
- Tips for making healthy choices
- Exercise Recommendations
- Tips for gaining or losing weight
- Calcium and vitamin D recommendations
- Complementary and Alternative Medicine

Children’s Oncology Group, http://www.childrensoncologygroup.org/
Oncology Nutrition Dietetic Practice Group
Pediatric Sub-Unit
Recently formed group within ONDPG
Focus on pediatric oncology population and childhood cancer survivors
New sub-unit of ONDPG aims to unite pediatric cancer dietitians:
  ➢ Improve networking and collaboration
  ➢ Disperse the latest pediatric oncology nutrition research
  ➢ Share evidence-based resources
  ➢ Develop nutrition guidelines
  ➢ Collaborate with other pediatric and/or oncology-specific nutrition groups to coordinate efforts

To join this group and receive the latest group notifications, please email Katie.Badgett@STJUDE.ORG.

Contacts: Rachel Hill, Chair: Rachel.Hill@cookchildrens.org
          Nancy Sacks, Chair-elect: sacks@email.chop.edu
Summary

- Children with cancer continue to struggle to meet their nutritional needs
- Growth is suboptimal at the end of therapy in some children, particularly those who receive aggressive therapy
- Problems related to nutrition persist long after therapy is completed
- Be an advocate for the patient and family - it’s ok to “push back”
- Reach out to others for support
- Become involved in research to demonstrate that nutrition makes a difference in improving outcomes
Thank You
Thank You
**Estimated New Cancer Cases* in the US in 2015  (Adults)**

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>26%</td>
<td>29%</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>14%</td>
<td>13%</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>8%</td>
<td>8%</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>Melanoma of skin</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td>Oral cavity &amp; pharynx</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>All other sites</td>
<td>21%</td>
<td>21%</td>
</tr>
</tbody>
</table>


**Source:** SEERS, NCI 2014.

**Trends in Five-year Cancer Survival Rates (%), 1975-2010 (Adults)**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>49</td>
<td>55</td>
<td>68</td>
</tr>
</tbody>
</table>

All sites 1 in 2 risk

All sites 1 in 3 risk
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites</td>
<td>49</td>
<td>55</td>
<td>68</td>
</tr>
<tr>
<td>Breast (female)</td>
<td>75</td>
<td>84</td>
<td>91</td>
</tr>
<tr>
<td>Colon</td>
<td>51</td>
<td>60</td>
<td>65</td>
</tr>
<tr>
<td>Leukemia</td>
<td>34</td>
<td>43</td>
<td>60</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>12</td>
<td>13</td>
<td>18</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>82</td>
<td>88</td>
<td>93</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>47</td>
<td>51</td>
<td>71</td>
</tr>
<tr>
<td>Ovary</td>
<td>36</td>
<td>38</td>
<td>45</td>
</tr>
<tr>
<td>Pancreas</td>
<td>3</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Prostate</td>
<td>68</td>
<td>83</td>
<td>100*</td>
</tr>
<tr>
<td>Rectum</td>
<td>48</td>
<td>58</td>
<td>68</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>72</td>
<td>79</td>
<td>79</td>
</tr>
</tbody>
</table>


*99.6%

Source: Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute, 2014.
Trends in Cancer Incidence Rates*, US, 1975-2011 (Adults)

*Age-adjusted to the 2000 US standard population and adjusted for delays in reporting.
Source: Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute, 2014.
**Diffuse intrinsic pontine glioma:** < 1 yr from dx
Medulloblastoma 70% at 5 yrs
Astrocytoma: 80% at 5 yrs

**5-year relative survival rate (%)**

Cancer in Children and Adolescents. NCI, NIH.
http://www.cancer.gov/cancertopics/types/childhoodcancers/child-adolescent-cancers-fact-sheet#r1
<table>
<thead>
<tr>
<th>Symptom</th>
<th>Strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea/vomiting</td>
<td>• Small frequent meals&lt;br&gt;• Cold foods and beverages&lt;br&gt;• Avoid extreme temperatures and highly seasoned items&lt;br&gt;• Avoid high-fat content items</td>
</tr>
<tr>
<td>Anorexia</td>
<td>• Small frequent meals&lt;br&gt;• Nutrient-dense foods&lt;br&gt;• Homemade shakes</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>• Low-fat, cold or room temperature foods&lt;br&gt;• Encourage adequate fluid intake - avoid caffeine&lt;br&gt;• Lactose reduced/free products&lt;br&gt;• Limit raw fruits (except bananas) and raw vegetables&lt;br&gt;• Include easy to digest foods</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>• Herbs, spices, and marinades&lt;br&gt;• Cold non-odorous foods&lt;br&gt;• Fruit and lemon flavored beverages and sour candy&lt;br&gt;• Good oral hygiene and mint mouthwashes</td>
</tr>
<tr>
<td>Mucositis</td>
<td>• Soft diet and smooth bland moist foods&lt;br&gt;• Frozen slushes/ices/ice cream&lt;br&gt;• High-calorie liquid beverages</td>
</tr>
<tr>
<td>Xerostomia</td>
<td>• Moist foods, encourage liquids with meals&lt;br&gt;• Sauces/gravy/butter/broth, add vinegar/lemons to stimulate saliva, good oral hygiene</td>
</tr>
</tbody>
</table>
Grade 1 Mild; asymptomatic/mild symptoms; clinical or diagnostic observations only; intervention not indicated.

Grade 2 Moderate; minimal, local, noninvasive intervention indicated; limiting age-appropriate instrumental ADL*.

Grade 3 Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care ADL**.

Grade 4 Life-threatening consequences; urgent intervention indicated.

Grade 5 Death related to AE.

(Publish Date: May 28, 2009 Quick Reference)
Descriptive terminology utilized for Adverse Event (AE) reporting for severity
Body Mass Index (BMI) at Diagnosis is Associated With Surgical Wound Complications in Patients With Localized Osteosarcoma: A Report From the Children’s Oncology Group

Aim: Role of BMI on incidence of surgical wound complications in pts with localized osteosarcoma.

Procedure: Pts enrolled on COG trial INT-0133
- Remained on protocol therapy for definitive surgery 6–16 wks after study entry
- Adequate ht, wt, and surgical complication data for analysis
- Wound complications within 30 days after definitive surgery were considered post-operative
- BMI calculated at start of neoadjuvant chemotherapy

Results: 498 patients met criteria for analysis
- Low BMI (≤10th percentile) in 73 (14.7%)
- Middle BMI (11th–94th percentile) in 382 (76.7%)
- High BMI (≥95th percentile) in 43 (8.6%)
Wound infection or slough seen in low BMI pts (OR=2.0, p=0.07).
Arterial thrombosis more common in high BMI patients (OR=9.4, p=0.03)

Conclusions:
- Abnormal BMI at start of tx associated w/ increased risk of post-operative wound complications like arterial thrombosis.
- Evaluate if maintenance of age-appropriate BMI reduces risk of surgical complications.

Hingorani P et al. PBC. 2011 December 1; 57(6
Evaluation - Laboratory tests

Complete blood count with differential and platelets
Full chemistry panel

- Lactate dehydrogenase (LDH) elevated with Neuron-specific enolase (NSE) rapid tumor growth / Ferritin advanced disease
- Prothrombin time (PT) baseline value
- Partial Thromboplastin Time (PTT) for surgery
- Urine catecholamines
  - Vanillymandelic Acid (VMA) elevated in 90-95% of patients
  - Hemovanillic Acid (HVA)

## International Neuroblastoma Staging System (INSS) – National Cancer Institute

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tumor</th>
<th>Resectable</th>
<th>Disease Spread</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>Localized</td>
<td>Complete gross excision, with or without microscopic residual disease</td>
<td>Ipsilateral lymph nodes negative for tumor microscopically</td>
</tr>
<tr>
<td>Stage 2A</td>
<td>Localized</td>
<td>Incomplete gross excision</td>
<td>Ipsilateral lymph nodes negative for tumor microscopically</td>
</tr>
<tr>
<td>Stage 2B</td>
<td>Localized</td>
<td>With or without complete gross excision</td>
<td>Ipsilateral nonadherent lymph nodes positive for tumor. Enlarged contralateral lymph nodes must be negative microscopically</td>
</tr>
<tr>
<td>Stage 3</td>
<td>Unilateral tumor crosses midline (vertebral column)</td>
<td>Unresectable</td>
<td>With or without regional lymph node involvement Contralateral regional lymph node involvement Infiltration by lymph node involvement</td>
</tr>
<tr>
<td></td>
<td>Localized unilateral tumor</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Midline tumor with bilateral extension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 4</td>
<td>Primary tumor with dissemination to distant lymph nodes, bone, bone marrow, liver, skin, and/or other organs, except as defined for stage 4S.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 4S Age &lt; 12 months</td>
<td>Localized primary tumor (stage 1, 2A, or 2B) with dissemination limited to skin, liver, and/or bone marrow (infants &lt; 18 months). Marrow involvement minimal (&lt;10% of total nucleated cells identified as malignant by bone biopsy or by bone marrow aspirate). More extensive bone marrow involvement is stage 4. MIBG scan should be negative for disease in the bone marrow.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Cannabinoid: Name (abbreviation), target, structure, role in physiological process
Role in different cancers and its associated signaling

<table>
<thead>
<tr>
<th>Cannabinoid</th>
<th>Structure</th>
<th>Role in Physiological Process</th>
<th>Role in Different Cancers and Associated Signaling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ⁹-tetrahydrocannabinol (Δ⁹-THC)</td>
<td><img src="image" alt="Molecule" /></td>
<td>Analgesic, antiemetic, appetite stimulant tumour growth inhibitor [159].</td>
<td>1) Breast cancer: mitogenic effect in cells expressing low levels of CB1/CB2 receptors. 2) Prostate cancer: PI3K/Akt and Raf-1/ERK1/2 pathway. Mitogenic at low doses. 3) Lung cancer: EGFR/ERK1/2, c-Jun-NH2-kinase1/2, and Akt pathway. Mitogenic at low doses. 4) Glioma: MMP-2 pathway</td>
</tr>
<tr>
<td>Cannabidiol (CBD), CB1 agonist</td>
<td><img src="image" alt="Molecule" /></td>
<td>Anti-tumor agent, attenuate catalepsy, immunosuppressive, inflammatory or anti-inflammatory agent (depends upon used concentration of drug), antipsychotics [164-168]</td>
<td>1) Breast cancer: ER stress/ERK and reactive oxygen species (ROS) pathways. 2) Prostate cancer: ERK1/2 and AKT pathways. 3) Lung cancer: up-regulation of TIMP-1, Cox-2 and PPAR-γ regulation. 4) Cervical cancer: Up-regulation of TIMP1</td>
</tr>
</tbody>
</table>

From: Chakravarti B, 2014 | Table I: Cannabinoid’s structure and its role in different physiological processes | Table II: Role of cannabinoid in different cancers and its associated signaling |
Neuroblastoma (NBL)

- Cancer of primitive cells from which sympathetic nervous system arises
- Localized disease or multiple organs with metastatic involvement
- Metastatic disease in 70% of children at diagnosis
- Location of primary tumor and sites with metastases affect types and severity of symptoms at presentation

Incidence
- Second most common extracranial solid tumor in children
- Accounts for 15% of all childhood cancer deaths
- 700 new cases of NBL diagnosed each year in the US
- 5 yr survival (Stage IV) approximately 40%
- Occurs more in young children (< 19 months), most < 5 years of age

Cervical and high thoracic masses
- Stellate ganglion - can cause Horner syndrome (sympathetic palsy) - unilateral ptosis (eye lid prolapse), anhydrosis (lack of sweat production) and miosis (pupil contraction)

Masses in thoracic area
- Tracheal deviation, superior vena cava syndrome resulting in dyspnea, jugular distention, cough, facial flushing, upper-extremity edema or cyanosis

Tumors in paraspinal area
- May invade through neural foramina compressing spinal cord
- Weakness of extremity and paralysis
- Bowel and bladder dysfunction may require emergency treatment

Mahoney 2006 and Barhelowmew 2011
<table>
<thead>
<tr>
<th>Results - Oral Nutrition (Volitional)</th>
<th>Author / Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wt loss 16%-22% in 1st mth of treatment</td>
<td>Rickard K 1979</td>
</tr>
<tr>
<td>Wt loss in 1st month in well nourished children with NBL</td>
<td>Rickard K 1985</td>
</tr>
<tr>
<td>Low oral intake &amp; less able to maintain body weight vs. receiving PN</td>
<td>Hays 1983</td>
</tr>
<tr>
<td>Only 2/12 maintained or improved nutritional status</td>
<td>Donaldson S 1982</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parenteral Nutrition (PN)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>28 days PN normalized wt/ht, skinfold percentiles &amp; albumin</td>
<td>Rickard K 1979</td>
</tr>
<tr>
<td>9-14 days PN ineffective in reversing PEM</td>
<td>Ghavimi 1982</td>
</tr>
<tr>
<td>Central &amp; peripheral PN reversed PEM (NBL/Wilms)</td>
<td>Hays D 1983</td>
</tr>
<tr>
<td>PN reversed/prevented PEM</td>
<td>van Eys J 1980</td>
</tr>
<tr>
<td>Infection rate with TPN 0.5 / 100 days</td>
<td>Christensen M et al 1993</td>
</tr>
</tbody>
</table>
# Nutrition Intervention

## Enteral Tube Feeding (ETF)

<table>
<thead>
<tr>
<th>Description</th>
<th>Author / Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>All children gained/maintained wt (GT)</td>
<td>Aquino V et al 1995</td>
</tr>
<tr>
<td>82% achieved IBW with some complications (GT)</td>
<td>Mathew P et al 1996</td>
</tr>
<tr>
<td>Protocolized ETF resulted in children achieving IBW</td>
<td>den Broeder E et al 1998</td>
</tr>
<tr>
<td>NG tube generally well tolerated</td>
<td>Pietsch J et al 1999</td>
</tr>
<tr>
<td>Wt gain using ETF associated with reduced rate of nonleukopenic infections in children with solid tumors</td>
<td>den Broeder E et al 2000</td>
</tr>
<tr>
<td>ETF initiated prior to second course of therapy helps prevent acute malnutrition and supports repletion of nutritional stores</td>
<td>Sacks et al 2008</td>
</tr>
<tr>
<td>PEG reversed early wt loss and infectious complications did not usually lead to PEG removal</td>
<td>Parbhoo PM 2011</td>
</tr>
<tr>
<td>Early PEG tube placement was safe, prevented malnutrition, restored weight for height z scores</td>
<td>Schmitt F et al 2012</td>
</tr>
<tr>
<td>Proactive ETF is feasible and improved NS at end of therapy</td>
<td>Sacks et al 2014</td>
</tr>
</tbody>
</table>

ETF is a safe method and cost-effective way to provide nutrition support.
<table>
<thead>
<tr>
<th>Motility Agents</th>
<th>Metoclopramide/Reglan™</th>
<th>↑ forward peristalsis in stomach/duodenum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acid-blocker medications</td>
<td>Erythromycin</td>
<td>Macrolide antibiotic, increases proximal gut motility</td>
</tr>
<tr>
<td>H-2 receptor Antagonists</td>
<td>(famotidine/Pepcid™,</td>
<td>Block histamine-induced acid secretion</td>
</tr>
<tr>
<td>Proton Pump Inhibitors</td>
<td>famotidine/Zantac™, nizatidine/Acid™, cimetidine/Tagamet™</td>
<td></td>
</tr>
<tr>
<td>Antiemetics</td>
<td>Proton Pump Inhibitors</td>
<td>Block hydrogen/potassium ATPase (the “proton pump”), effectively blocking acid secretion</td>
</tr>
<tr>
<td>Serotonin Receptor (5HT3 or 5-hydroxytryptamine-3) Antagonists</td>
<td>(ondansetron/Zofran™, granisetron/ Kytril™, dolasetron/Anzemet™, palonosetron/Aloxi™)</td>
<td>Block effects of serotonin at 5HT3 receptors in GI tract and chemotherapy receptor trigger zone in brain</td>
</tr>
<tr>
<td>Aprepitant (Emend™ and fosaprepitant, the IV Emend™)</td>
<td>Neurokinin-1 receptor antagonist produce small reduction in acute N/V, larger reduction in delayed N/V</td>
<td></td>
</tr>
<tr>
<td>Glucocorticoids</td>
<td>(dexamethasone/Decadron™, methylprednisolone sodium succinate/Medrol™)</td>
<td>In combinations w/ serotonin receptor antagonist or metoclopramide, as single agent mildly emetic regimens</td>
</tr>
<tr>
<td>Phentothiazines</td>
<td>(prochlorperazine/Compazine™, promethazine/ Phenergan™, chlorpromazine/Thorazine™), butyrophenones (haloperidol/Haldol™, droperidol/Inapsine™)</td>
<td>Block dopamine receptors in vomiting center and chemotherapy receptor trigger zone; acute N/V from mildly/moderately emetic chemotherapy breakthrough N/V</td>
</tr>
<tr>
<td>Cannabinoids</td>
<td>(dronabinol/Marinol™, nabilone/ Cesamet™)</td>
<td>Used when typical antiemetic haven’t worked; psychoactive component of marijuana</td>
</tr>
<tr>
<td>Atypical antipsychotics</td>
<td>(olanzapine/Zyprexa™)</td>
<td>Similar to dopamine blockers, less likely to cause extrapyramidal side effects</td>
</tr>
<tr>
<td>Antihistamines and Bensodiazepines</td>
<td>(diphenhydramine/Benadryl™) and Benzodiazepines (lorazepam/Ativan™)</td>
<td>Adjunctive agents for chemotherapy-induced N/V; sedation helps sleep through treatment</td>
</tr>
</tbody>
</table>