# Nutrition Risk Assessment and Interventions for Childhood Cancer

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## Objectives

After this presentation, the viewer should be able to:

- Discuss risk groups for pediatric oncology diagnoses
- Discuss how interventions are adjusted based on treatment intensity
- Describe one pediatric cancer diagnosis and its proposed interventions

## Disclosures

- No disclosures to report

## Pediatric Oncology & Nutrition Plans

- Children ≠ little adults
- Childhood cancer ≠ adult cancer
- Guidelines in this area are under-developed


## Important Tools for Dietitians

- Interventions vary based on treatment intensity and nutritional impact.
- Important tools for pediatric RDs to gain:
  - Working understanding of common pediatric cancers and their treatment plans
  - Ability to identify treatments that will adversely affect nutritional status
  - Relationship with providers and research team members

## Malnutrition During Childhood Cancer

Increased
- Treatment toxicity
- Infection risk

Decreased
- Survival
- Lean body mass
- Functional status
- Quality of life

# Acute Lymphoblastic Leukemia (ALL)

## Background

- Background
  - Cancer of blood and bone marrow
  - Most common childhood malignancy (25% of all new childhood cancers; 75% of childhood leukemia cases)
  - Average survival: 90%
- Presentation and work-up
  - Anemia (fatigue, pallor), thrombocytopenia (easy bruising, bleeding), neutropenia (fever, recent illness)
  - Hepatosplenomegaly may be present (infiltration of leukemia into the spleen and liver)
  - Blood work and bone marrow evaluation to confirm diagnosis and determine sub-type
    - B-cell (80-85% of cases)
    - T-cell (15% of cases)

# Acute Lymphoblastic Leukemia (ALL)

## Treatment Overview

- Treatment intensity is based on risk of treatment failure; high risk features include:
  - Age <1 year and ≥ 10 years
  - WBC at dx >50,000
  - Certain genetic markers (Philadelphia chromosome, hypodiploidy, etc.)
  - Response to treatment during induction therapy
- Treatment overview
  - Duration: 2-3.5 years (first 6-12 months is most intense)
  - Multiple therapy "phases": induction, consolidation, interim maintenance, delayed intensification, and maintenance/continuation
  - Several chemotherapy agents given during each phase

Rabin, 2016

# Acute Lymphoblastic Leukemia (ALL)

## Nutritional Considerations & Interventions

- Nutritional status at diagnosis:
  - Obesity at dx has been associated with poorer survival
  - If hepatosplenomegaly is present at dx, obtain mid-upper arm circumference (MUAC)
- Nutritional risk
  - High risk/very high risk patients at greatest risk for malnutrition
  - Greatest risk for malnutrition during: induction, consolidation, & delayed intensification
  - Significant risk for weight gain during: induction & maintenance therapy

Rabin, 2016

| Treatment Phase | Chemotherapy | Nutrition-Related Side Effects | Nutrition Interventions |
|---|---|---|---|
| Induction | Vincristine (IV)<br>Steroids (PO)<br>Asparaginase (IV)<br>Daunorubicin (IV)<br>Cytarabine (IT) | Constipation, jaw pain<br>Hyperphagia, weight gain<br>Hyperglycemia, pancreatitis<br>Anorexia, mucositis, nausea/ vomiting | Educate (food safety, nutrition risk)<br>Encourage physical activity<br>Monitor for hyperglycemia<br>Monitor for weight loss<br>- High risk patients<br>- Overweight/obese<br>- Down syndrome<br>- Hyperglycemia |
| Consolidation | Cyclophosphamide (IV)<br>Cytarabine (IV and/or IT)<br>Vincristine (IV)<br>PEG-asparaginase (IV)<br>Methotrexate (IT)<br>Mercaptopurine (PO) | Anorexia<br>Nausea/vomiting<br>Mouth sores<br>Constipation, jaw pain<br>Pancreatitis | Encourage hydration and exercise<br>Appetite stimulants<br>Oral supplements<br>Nutrition support |
| Interim Maintenance | Methotrexate (IV, high dose; IT)<br>Vincristine (IV)<br>Mercaptopurine (PO) | Mucositis/mouth sores<br>Decreased appetite<br>Constipation, jaw pain | Encourage healthy behaviors and exercise |
| Delayed Intensification | Vincristine (IV)<br>Steroids (PO)<br>Doxorubicin (IV)<br>PEG-asparaginase (IV)<br>Cyclophosphamide (IV)<br>Cytarabine (IV and/or IT)<br>Methotrexate (IT)<br>Thioguanine | Constipation, jaw pain<br>Increased appetite, weight gain<br>Anorexia, mucositis<br>Hyperglycemia, pancreatitis<br>Nausea/vomiting | Monitor for hyperglycemia<br>Monitor weight trends<br>Appetite stimulants<br>Oral supplements<br>Nutrition support |
| Maintenance | Steroids (PO)<br>Mercaptopurine (low dose, PO)<br>Methotrexate (low dose, PO)<br>Vincristine (IV) | Increased appetite, weight gain | Counsel proactively if able:<br>- Weight management<br>- Bone health<br>Monitor weight trends |

Burke, 2016; www.chemocare.com

## Acute Lymphoblastic Leukemia (ALL)

Nutritional Considerations & Interventions

- Significant and sustained weight gain begins in maintenance therapy
- Studies suggest that nutrition intervention is feasible and effective
- Essential components included:
  - Early intervention (toward beginning of maintenance)
  - Regular interaction with an RDN

Zhang, 2015; Li, 2017; Hill, 2017

## Acute Myeloid Leukemia (AML)

Background

- Background
  - Cancer of blood and bone marrow (20% of childhood leukemia cases)
  - Survival: 60-70%
  - Certain genetic markers can predict more or less favorable outcomes
- Presentation and work-up
  - Anemia (fatigue, pallor), thrombocytopenia (easy bruising, bleeding), neutropenia (fever, recent illness)
  - Blood work and bone marrow evaluation to confirm diagnosis

Arceci, 2016

## Acute Myeloid Leukemia (AML)

Treatment, Nutritional Considerations, & Interventions

- Chemotherapy: 4-5 cycles of ADE-based therapy
  - ADE (Ara-C/Cytarabine, Daunorubicin, Etoposide)
  - May also include additional anthracyclines like mitoxantrone
  - Cycles provided quickly upon count recovery; may require prolonged admissions
  - Side effects: significant anorexia, weight loss, nausea/vomiting, mucositis; early and regular nutrition evaluation warranted
- Under/overweight at diagnosis is associated with poor outcomes (Inaba, 2012)
- Early nutrition support +/- physical therapy may be warranted

Arrieci, 2016; Inaba, 2012

## Down Syndrome & Leukemia

- Children with Down Syndrome (DS) are more likely to develop leukemia (ALL and AML) than peers without DS.
- Patients with DS are treated on modified treatment plans.
- Outcomes:
  - Patients with ALL and DS have less favorable outcomes than patients without DS
  - Patients with AML and DS have more favorable outcomes than patients without DS
- Particularly sensitive to some chemotherapy agents (more likely to develop mucositis from methotrexate and hyperglycemia with steroids and asparaginase)

Rabin, 2016; Arrieci, 2016

## Central Nervous System Tumors

Background

- Background
  - Tumors of the brain and spine
  - May be benign or malignant or benign with "malignant" location
- Presentation and workup
  - Headache, nausea/vomiting, fatigue, abnormal gait, seizures, weight loss
  - Work up includes imaging and biopsy vs resection
- Treatment varies widely
  - Surgery or observation only
  - Intensive chemotherapy and radiation + autologous stem cell transplant

National Cancer Institute

## Central Nervous System Tumors

Treatment Overview

| Malnutrition Risk Group | Common Treatment | Examples |
|---|---|---|
| Low | Tumors that require observation or surgery +/- radiation or low impact chemotherapy (vinca alkaloid + carboplatin) | Astrocytoma<br>Low grade glioma<br>Germinoma<br>Craniopharyngioma (obesity risk) |
| Intermediate | Tumors or surgeries that impact swallowing function<br>Requirement for sedation w/ RT | Brainstem gliomas<br>Ependymoma (posterior fossa)<br>Young age + radiation<br>Non-germinomatous GCT |
| High | Intensive chemotherapy and radiation<br>High dose chemo + HSCT | Embryonal tumors (ATRT, medulloblastoma, ETMR, NOS) |

## Central Nervous System Tumors

Nutritional Considerations & Interventions

- Surgery: May cause dysphagia (posterior fossa & brain stem tumors) or motor issues
- Radiation: decreased appetite, fatigue, prolonged NPO status
- Chemotherapy:
  - Cisplatin: nausea/vomiting (continuous feeds may be helpful), anorexia
  - Cyclophosphamide: anorexia, nausea/vomiting
  - Vincristine: constipation, neuropathy
- Early enteral nutrition support may be warranted for high risk protocols

## Lymphoma

Background

- Cancer of the lymphatic system
- Two main types:
  - Hodgkin lymphoma
  - Non-Hodgkin lymphoma
    - B cell (diffuse large B cell, mature B-cell)
    - Lymphoblastic lymphoma (often T cell)
    - Anaplastic large cell lymphoma
    - Burkitt and Burkitt-like

www.cancer.gov

## Hodgkin Lymphoma
Background

- Background
  - Occurs most often in adolescents
  - Risk factors include immunodeficiencies and certain infections (ex: EBV)
  - Overall survival: 95%
- Presentation and work-up
  - Lymphadenopathy, significant weight loss very common at diagnosis
  - Work-up includes imaging and biopsy to stage disease
  - Higher risk features: multiple lymph node involvement, disseminated disease (bone, bone marrow, lung), and "B" symptoms (night sweats, unexplained fever, unintentional weight loss ≥10%)

Metzger, 2016

## Hodgkin Lymphoma
Treatment, Nutritional Concerns, & Interventions

- Treatment is adjusted to optimize outcomes and limit late effects
  - Chemotherapy: 3-5 cycles (commonly with ABVD-PC)
    - Adriamycin/doxorubicin, bleomycin, vincristine, etoposide, prednisone, cyclophosphamide
  - + Radiation for higher risk or slowly responding disease
- Excellent supportive care → low risk for malnutrition
  - Monitor initially until stable and adequately supported
  - Then monitor for weight gain due to frequent use of steroids

Metzger, 2016

## Non-Hodgkin Lymphoma
Background

- Background
  - Occurs mostly in children >5 years old
  - More aggressive than Hodgkin lymphoma
  - Overall survival: 80%
- Presentation and work-up
  - Lymphadenopathy and significant weight loss are common
  - Work-up includes imaging, biopsy, and bone marrow evaluations
  - Higher risk features: older age, mediastinal or bone marrow involvement, treatment response, higher stage disease

Allan, 2016

## Non-Hodgkin Lymphoma

Treatment, Nutritional Considerations, & Interventions

- Common chemotherapy regimens:
  - CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone)
  - EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
  - ALL-based therapy for lymphoblastic lymphoma
  - Targeted agents now being added: rituximab, brentuximab, crizotinib
- Common nutritional concerns include: nausea/vomiting, anorexia, constipation; mucositis and diarrhea less common but can be significant

Allen, 2016

## Rhabdomyosarcoma

Background

- Background
  - Tumor of soft tissue (sites: head/neck, genitourinary tract, extremities, and trunk)
  - Two main subtypes: embryonal and alveolar (alveolar is more aggressive)
  - Overall survival:
    - Low risk: >70%
    - Intermediate risk: 50-70%
    - High risk: ≤30%

Wexler, 2016

## Rhabdomyosarcoma

Treatment, Nutritional Concerns, & Interventions

- Surgery: initial resection if possible
- Chemotherapy:
  - VAC (vincristine, actinomycin-D/dactinomycin, cyclophosphamide) in 3 week cycles
    - All 3 agents together often results in anorexia; vincristine only: constipation, jaw pain
  - Additional agents for high risk patients: doxorubicin, irinotecan, ifosfamide, etoposide
    - May cause significant diarrhea, anorexia, and weight loss
- Radiation: impact depends on site; consider proactive TF if head/neck

Wexler, 2016

## Wilms' Tumor

Background

- Background
  - Tumor of the kidney
  - Overall survival: 90% for favorable histology
- Presentation and work-up
  - Often present with large abdominal mass, anorexia/early satiety, hematuria, or hypertension
  - Malnutrition often present at diagnosis but masked by large tumor (measure MUAC)
  - Work-up includes multiple scans to rule out metastatic disease and biopsy/resection
  - Risk determined by histology (favorable vs. unfavorable/anaplastic), age, stage

Fernandez, 2016

## Wilms' Tumor

Treatment, Nutritional Concerns, & Interventions

- Surgery: at diagnosis or after several cycles of chemotherapy
  - Monitor diet advancement and MUAC closely; consider parenteral nutrition if necessary
- Chemotherapy:
  - Lower risk: EE-4A (vincristine and dactinomycin) – low risk for nutritional issues
  - Higher risk: DD-4A (vincristine, dactinomycin, doxorubicin) – at risk for anorexia, N/V
  - High risk patients may receive cyclophosphamide and etoposide – at significant risk for anorexia, N/V
- Radiation: whole abdomen radiation often used (stage I and II – no RT)
  - Short duration but may cause radiation enteritis and malabsorption; eliminate lactose
  - If given in conjunction with chemotherapy, may be unable to tolerate enteral nutrition

Fernandez, 2016

## Osteosarcoma

Background

- Background
  - Most common bone tumor in children and adolescents
  - Occurs frequently in adolescents
  - Overall survival: localized disease: 60-70%; metastatic disease: 10-30%
- Presentation and work-up
  - Often presents as pain or fracture
  - Work-up includes biopsy and scans to assess for metastatic disease

Gorlick, 2016

## Osteosarcoma

Treatment, Nutritional Concerns, & Interventions

- Chemotherapy: MAP (methotrexate, Adriamycin/doxorubicin, cisplatin)
  - Cisplatin & doxorubicin side effects: N/V, anorexia, hypomagnesemia, taste changes
  - Methotrexate side effects: mucositis, decreased appetite
  - Ifosfamide and etoposide occasionally added if poor response is noted
  - Tenardi et al, 2012: 7.8% underweight at dx; 36.1% underweight one year later
- Local control: surgery
  - Often provided after 2 full cycles of MAP chemotherapy
  - Complete resection essential; often requires amputation or limb salvage

Gorlick, 2016; Tenardi, 2012

## Ewing Sarcoma

Background

- Background
  - Tumor of bone or soft tissue; most often in lower extremities, pelvis, or chest wall
  - Survival: 60-70% for local disease; significantly less for metastatic disease
- Presentation and work-up
  - Presenting symptoms include pain, mass, or weight loss
  - Work-up includes biopsy, scans to assess for metastasis, and bone marrow evaluation

Hawkins, 2016

## Ewing Sarcoma

Treatment, Nutritional Concerns, & Interventions

- Chemotherapy: alternating, compressed (q2 week) cycles of VDC/IE
  - VDC (vincristine, doxorubicin, cyclophosphamide)
  - IE (ifosfamide, etoposide)
  - Relapsed pts may receive topotecan/cyclophosphamide or irinotecan/temozolomide
- Local control: surgery or radiation therapy (radiation used for mets)
  - Often provided after about 6 cycles of chemotherapy
  - Underweight or overweight/obese status at diagnosis may impact tumor necrosis (Goldstein, 2015)

Hawkins, 2016; Goldstein, 2015

# Hepatoblastoma

## Background

- Background
  - Most common liver malignancy in children; mostly in children <3 years
  - Risk factors: prematurity, familial cancer syndromes
  - Prognostic indicators: tumor histology (favorable/unfavorable), age, local vs. metastatic disease, tumor rupture or invasion of surrounding tissue
- Presenting symptoms
  - Distended abdomen, early satiety/anorexia, elevated AFP (alpha fetal protein)
  - Malnutrition common at diagnosis; MUAC is important.

Meyer, 2016

# Hepatoblastoma

## Treatment, Nutritional Concerns, & Interventions

- Surgery: complete resection essential (may be delayed if too large/involved)
- Chemotherapy: cisplatin-based treatment
  - Low risk: cisplatin, 5-FU, vincristine
  - Intermediate risk: above + doxorubicin
  - High risk: above + irinotecan +/- temsirolimus being studied
  - Side effects: significant nausea/vomiting, anorexia, and hypomagnesemia for all; risk for mucositis and diarrhea increased with doxorubicin and irinotecan, respectively
- Liver transplant may be considered if tumor is unresectable

Meyer, 2016

# Summary

- "Pediatric cancer" represents many different diagnoses and treatment plans
- Higher intensity treatment is often equivalent to greater nutritional risk
- Understanding treatment protocols can improve nutrition plans
- Consider treatment intensity rather than diagnosis alone

## Additional Resources

- Online Pediatric Nutrition Care Manual – revised
- Oncology Nutrition for Clinical Practice, 2nd Edition – coming soon
- Intensity Rating Scale – 3 (CHOP)
- Treatment protocol schemas

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Questions?