

Meeting the Unique Needs of Pediatric Oncology Patients

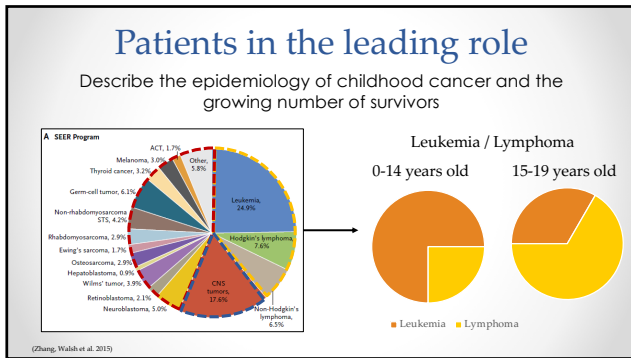
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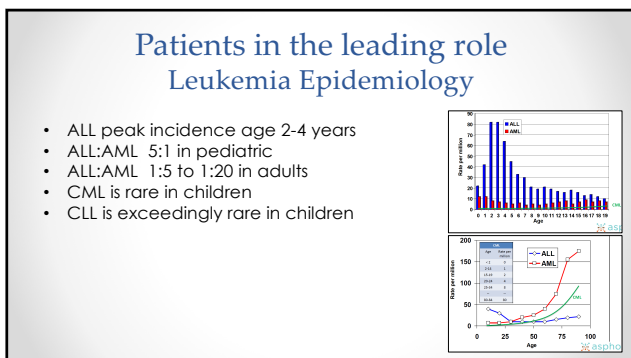
Learning Objectives

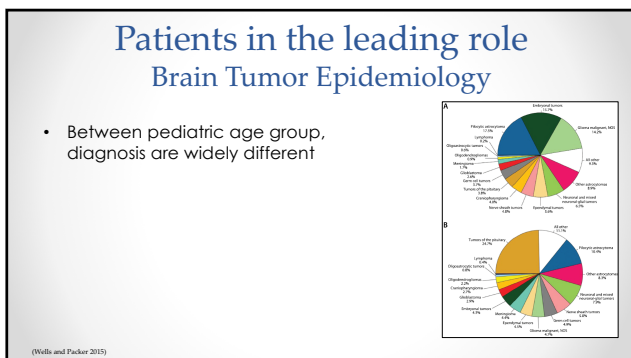
1. Describe the epidemiology of childhood cancer and the growing number of survivors
2. List the challenges and opportunities facing clinicians (and children and families) during intensive multi-modal therapy
3. Discuss novel frontier and precision medicine and immunotherapy in pediatric oncology.

Cast of characters

- Patients – babies, toddler, children, teenagers, young adults
- Community – mom, dads, step mom and step-dad, brothers, sisters, grandparents
- Care team – nurses, child life, case managers, social workers, school teachers, volunteers, nurse practitioners/physicians
- Researchers –
 - Clinical – research assistants, statisticians, clinical investigators
 - Translational – research technicians, graduate students, PhDs, donors, government.





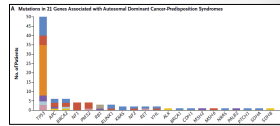
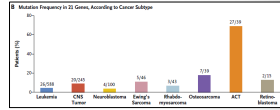


Children with cancer frequently have a genetic predisposition

Why did my child get this?

Did I cause this?

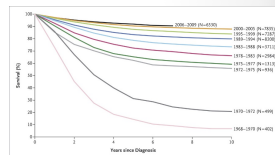
What should I have done differently?



(Zhang, Walsh et al. 2015)

ALL - Outcomes

- Treatment last ~3 years in best case scenario
 - 9 months of multi-agent intense, myelosuppressive treatment
 - 2-3 years of maintenance therapy
- Overall survival >90%
 - Standard Risk: > 90% OS
 - High Risk: 75-80% OS
- Common sites of relapse
 - Brain / spinal fluid
 - Testicles
 - Bone Marrow



Hunger SP, Mullighan CG. Acute Lymphoblastic Leukemia in Children. N Engl J Med. 2015 Oct 15;373(16):1541-52.

ALL - Treatment by Decade

- 1950s – Folic Acid? Whoops. Anti folate (a.k.a Methotrexate)?
- 1960s – CR achieved. Nearly universal relapse, usually CNS
- 1970s – Beginnings of cure with multi-agent therapy and XRT
- 1980s – Improved supportive care. PCP proph, blood products
- 1990s – Prognostic Factors, Cytogenetics, Delayed Intensification
- 2000s – Intrathecal therapy can replace XRT, MRD Evaluation
- 2010s – Precision Medicine, Genomic Revolution

Acute Lymphoblastic Leukemia Teachers and Child Life Specialists

- <https://youtu.be/GnKeMB8lxbY?t=174>

Curative therapy requires prolonged intensive treatment.
Patients are over and under treated.

Supportive teams provide age appropriate counseling and teaching.
Risk stratification is improving therapy selection

ALL – Late Effects

- Neuropathy – Vincristine
- Osteonecrosis – Steroids
- Meningioma – XRT
- Cognitive dysfunction – Intrathecal MTX
- Cardiac dysfunction – Anthracyclines
- Reproductive dysfunction – Cyclophosphamide
- Metabolic Syndrome - ?steroids, others

Acute Myeloid Leukemia Siblings and Parents

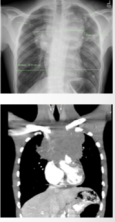
- Treatment – Maximally intense chemotherapy
 - Best case is 5 months of profound immune suppression
 - Majority of time is in the hospital
 - Hematopoietic Stem Cell Transplant is recommended for 40%
- Outcomes
 - Overall survival is 70% even with maximal therapy

Most patient remain hospitalized for most of therapy, affecting family jobs, schedules, activities
Many patient are incurable with current chemotherapy.

Counseling for siblings is critical
HSCT techniques provide more donor options and are safer

Hodgkin Lymphoma Clinical Researchers

- Case of Sarah
- Treatment -
 - 4 months of outpatient chemotherapy
 - +/- radiation therapy
- Outcomes
 - Survival rates are good (>90%)
 - Long term effects can be terrible



Long terms survivors have health consequences from chemotherapy and radiation

Risk stratification is identifying patients who can safely avoid radiation. Late effects guidelines have potential to improve long term health

Hodgkin Lymphoma Clinical Researchers

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Neuroblastoma Nursing

- Not a brain tumor. Tumor of sympathetic nerves, usually arising in adrenal gland leading to abdominal mass
- Presentation and prognosis vary widely
- Observation → Surgery/Chemo/Radiation/Immunotherapy
- Multimodal care requires

Neuroblastoma can have profoundly different biology in different patients. High-risk disease very often relapses after remission.

Improved risk stratification and biological prognostic scoring is improving. Immunotherapy has improved survival rates.

Bone Tumors

Surgeons, Physical Therapists

- Ewing Sarcoma
 - Pelvis, spine, long bones, other
 - Metastase to bones, lung
 - Chemotherapy /Surgery / XRT
- Osteosarcoma
 - Long bones
 - Metastase to lung
 - Chemotherapy / Surgery

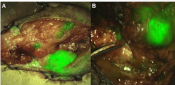
Large resection is often required
Outcomes for metastatic disease is poor even with maximal therapy.

Limb salvage surgery can be offered in placed of amputation for many cases
Physical therapy and counseling teams are critical

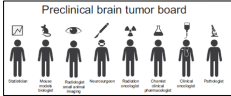
High Grade Brain Tumor

Translational Researchers

- High grade brain tumor are fast growing, infiltrative tumors
- Surgery is challenging because of the surrounding vital structures
- Chemotherapy is challenging because blood-brain barrier limits tumor exposure in many cases
- Radiation is challenge because of profound toxicity in early developing brains.



Preclinical brain tumor board



Therapy delivery for high grade brain tumors in children faces many challenges.

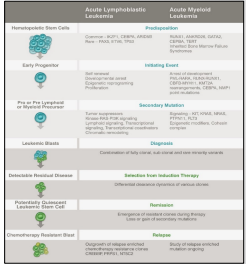
Newer preclinical models, diagnostic techniques, therapeutic modalities to study this disease are being developed

(Parrish-Novak, Byrne-Blake et al. 2017), (Nimmerjell, Boudou et al. 2018)

Precision Medicine

Translational Scientists

- Even within disease subtypes, different biology can drive pathology.
- Biology driving the cancer often changes over time. Both genetic and epi-genetic changes.



Precision Medicine Translational Scientists

- The explosion in sequencing has allowed improved understanding of ALL disease classification and pathogenesis
- Ph-like ALL is a subtype of ALL with a distinct gene expression pattern drive by alteration in cell signaling pathways.
- These altered signaling pathways can potentially be inhibited by adding targeted therapy to standard treatment.

(Jacobucci and Mullighan 2017)

Precision Medicine Translational Scientists

- Glioblastoma Multiforme
- BRAF V600E mutation

(Robinson, Chr et al. 2014)

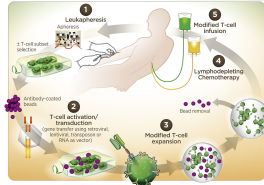
Cancer Molecular Dependency - AML

- Most precision medicine effort are based upon specific gene mutations.
- It has become clear that gene mutations are only part of the story.

CELL LINE

Immunotherapy Translational Scientists

- What is immunotherapy?
 - Hematopoietic Stem Cell Transplantation
 - Medications
 - Interferon, Checkpoint inhibitors
 - Antibody +/- conjugate medications
 - T-cell engagers
 - BiTE
 - DART
 - Autologous Chimeric T-cells



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