# Pediatric Oncology Update

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TSNO 14th Annual Conference
November 4th 2016

# Outline

- Historical Perspective
- Pediatric Cancer Statistics
- Acute Leukemia
- CNS Tumors
- Lymphoma
- Solid Tumors (Including Bone Tumors)
- What's New
- Childhood Cancer Research Funding
- Closing

# Historical Perspective

- 1940: Average survival for ALL was 3 months (5% at 5 years)
- 1947: Sidney Farber noted accelerated cell growth induced by folic acid
- 1948: Folic acid antagonist induce temporary remissions in 10 of 16 pts with ALL (NEJM 1948; 238:787-93)
- 1949: Glucocorticoids as therapy for ALL
- 1956: Acute Leukemia Group A founded; later renamed the Children's Cancer Group.
- 6-mercaptopurine (1953), cyclophosphamide (1959), L-asparaginase (1961), Vincristine (1962)

# Historical Perspective

- 1964: Skipper publishes report of the synergistic effect of combination chemotherapy in animal models
- 1965: Freireich & Pinkel showed that combination chemotherapy improved remission length in ALL.
- 1967: Aur & Pinkel: ALL study with intensified continuation, cranio-spinal XRT and intrathecal chemotherapy.
- Protocols have since worked on maximizing therapeutic effects of chemotherapy while minimizing toxicities.
- Present: ALL survival > 90% at 5 years

# Pediatric Cancer

- 15,780 new cases per year (0-19 yrs of age)
- 2,000 will die from their disease
- Death rate declined by 70% in past 40 years
- Leading cause of death by disease in children
- Cause in unknown for most
- 5% caused by inherited mutation

# Pediatric Cancer

- Most are treated enrolled or following Children's Oncology Group (COG) protocols
- 200+ hospitals in the U.S., Canada and numerous international sites
- > 90% of children with cancer are treated at COG institutions
- 3 in San Antonio: Methodist Children's Hospital, Children's Hospital of San Antonio & UTHSCA

# Pediatric Mortality

- Causes of Death (Age 1-4)
- 1. Accidents (1,367)
- 2. Congenital Malformations
- 3. Homicide
- 4. Cancer (343)

- Causes of Death (15-24)
- 1. Accidents (12,015)
- 2. Homicide
- 3. Suicide
- 4. Cancer (1,594)

Causes of Death (5-14): 1. Accidents (1,626) 2. Cancer (913)

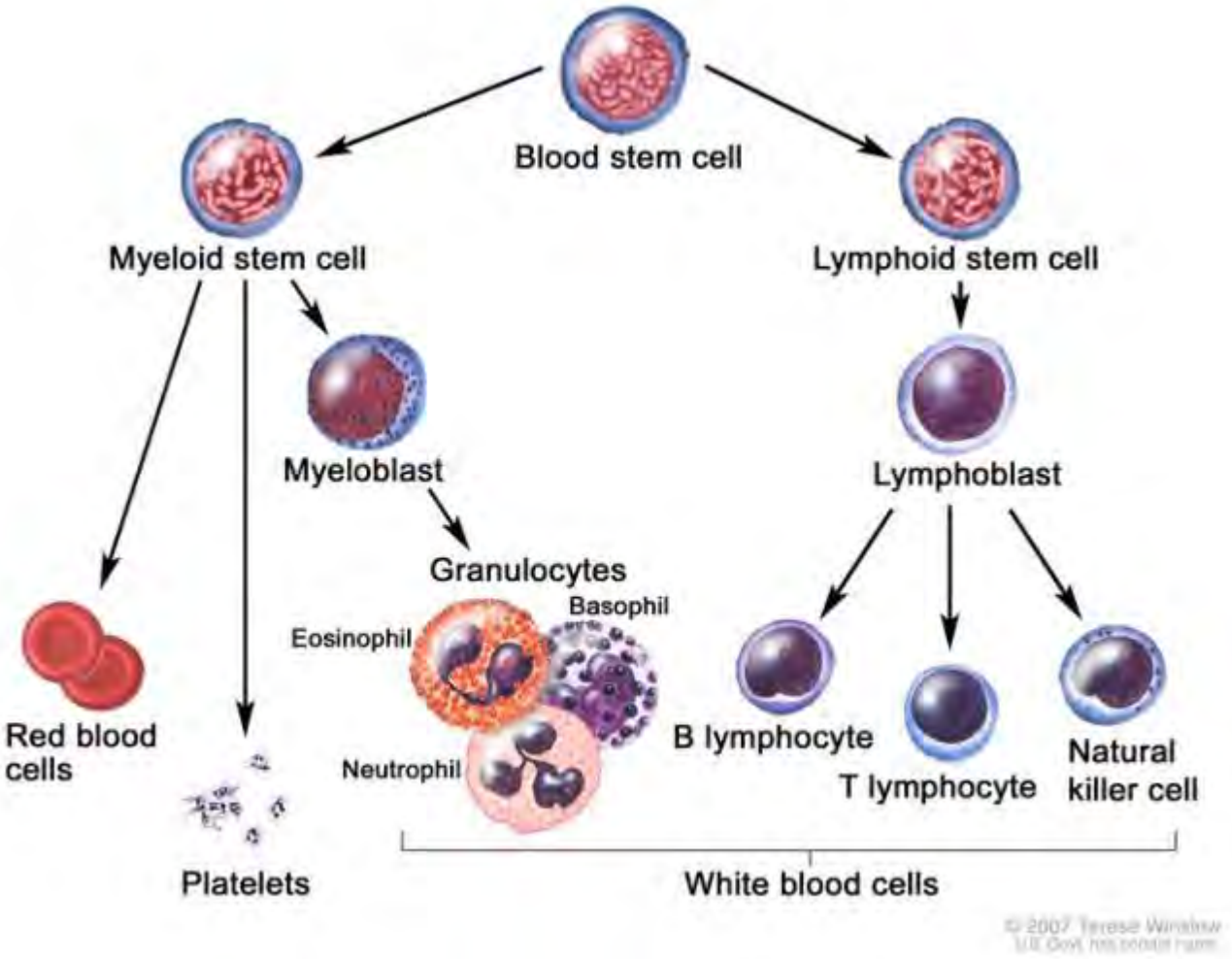
# Case 1

- 6 year old presents with a 1 week history of pallor and fatigue. Upon further questioning, she relates that he has been complaining of legs pain the past 3 weeks which now is affecting his daily playtime.
- Physical exam reveals a pale child. Diffuse small, non-tender lymph nodes involving neck and axilla. Liver and spleen are palpable. Occasional bruising and petechiae are noted.

# Acute Leukemia

- Most common malignancy of childhood
- Most common sub-types: Acute Lymphoid Leukemia (A.L.L.) and Acute Myeloid Leukemia (A.M.L.)
- ALL: Overall cure rate: 90%
- AML: Overall cure rate: 50-60%

# Leukemia Origins



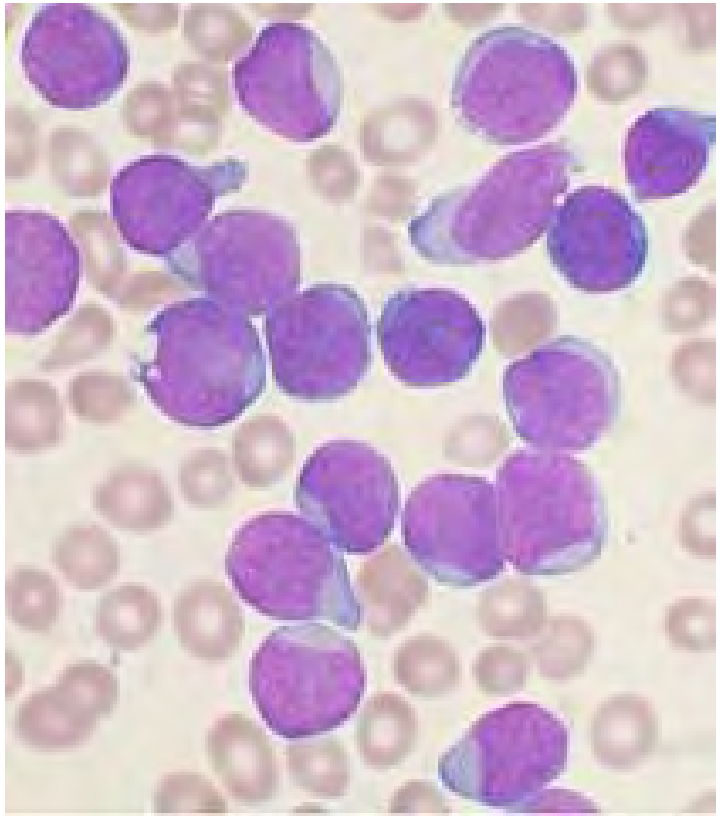
# Leukemia Clinical Presentation

- Fever
- Bone Pain/Arthralgias
- Fatigue/Pallor
- Petechiae or Ecchymosis
- Infections
- Organomegaly

# Diagnosis

- Complete Blood Count (CBC): Leukocytosis or Leukopenia, Anemia and Thrombocytopenia
- Circulating Blasts
- Bone Marrow Aspirate and Biopsy
- Comprehensive Metabolic Panel, LDH, ESR
- Flow cytometry: Acute Lymphoid (ALL) versus Acute Myeloid Leukemia

# What does it look like?



# ALL: Treatment

- Diagnosis Risk Stratification: WBC, Age, Immunephenotype, CNS disease
- Induction: Vincristine, Steroid, Peg-Asparaginase, CNS prophylaxis (intrathecal chemotherapy)
- Post Induction Risk: MRD, Cytogenetics
- Post Induction: Combination Chemotherapy Blocks based on risk.
- Complications: Low WBC, may require blood products, increased risk of acute side effects

# ALL Treatment

- Maintenance: longest phase of treatment
- Approximately 2 years for girls and 3 years for boys (likely changing with future protocols)
- Backbone drugs: steroids, methotrexate, mercaptopurine, vincristine and CNS prophylaxis
- Maintenance: Cleared by M.D. to return to school and play most sports

# AML: Treatment

- Risk Stratification based on cytogenetics
- Intensive Blocks of near-myeloablative chemotherapy
- Low risk: 4 cycles of chemotherapy
- High Risk require Matched Donor Bone Marrow Transplant
- Very High Risk for Invasive Infections

# Leukemia: Survivorship

- Obesity
- Diabetes
- Cognitive Dysfunction (Radiation Therapy)
- Behavioral Issues
- Cardiac Toxicity (Late Effect)
- Fertility

# Case 2

- Father brings 7 year old child to PCP with 1 week history of headaches, nausea and vomiting. Diagnosed with Viral Illness and instructed to return if symptoms persist.
- Symptoms persist. Headaches usually in the morning with associated vomiting.
- Parents start to notice child “walking funny” and losing balance.

# CNS Tumors

- Most common solid malignancy of childhood
- Approximately 4,300 new cases per year
- Classification based on histology and location
- Posterior Fossa: Astrocytoma, Medulloblastoma, Ependymoma, Brainstem gliomas
- Suprasellar: Astrocytomoas
- Parasellar: craniopharyngiomas, germ cell tumors, gliomas
- Spinal Cord: Astrocytomas, ependymomas

# CNS Tumors: Clinical Presentation

- Headaches
- Nausea and Vomiting
- Ataxia
- Seizures
- Neurologic Deficits: Blurred/Double Vision, facial asymmetry, weakness,

# CNS Tumors: Treatment

- Multimodal Approach
- Surgery: Gross versus Sub-total Resection
- Combination Chemotherapy
- Radiation Therapy
- Goals are to limit short and long term toxicity

# CNS Tumors Survivorship

- Cognitive Deficits
- Behavioral Issues
- Memory
- Chronic Neurologic Deficits
- Endocrine: thyroid, puberty, diabetes insipidus
- Growth and Developmental Delays

# Case 3

- 15 year old presents with a “lump” on the right side of his neck. Patient reports he noticed it about two months ago. Seen by PCP, given antibiotics and instructed to return if worsens. After 2 week summer camp, parents noticed that lump has gotten bigger. Patient said it doesn’t hurt.
- On exam: large lymph node is noted to be hard, non-movable and non-tender to palpation. Lymph nodes are noticed in the right supraclavicular region as well.

# Hodgkin Lymphoma

- 6% of all childhood cancers
- Incidence highest between 15-19 yrs of age
- Second peak after age 50
- 80% present with painless lymphadenopathy
- 20% are Stage IV at diagnosis
- 25% have constitutional (B) symptoms: fever, weight loss and drenching night sweats

# Hodgkin Lymphoma

- Risk adapted therapy
- Multi-modal treatment: chemotherapy +/- radiation therapy
- Cure rate 90-95%
- Survivorship: thyroid, heart, lung, bone mineral density deficit, infertility, secondary malignancies

# Non-Hodgkin Lymphoma

- 7% of all childhood cancers
- 800 cases per year
- More common in 2nd decade of life; rare in infants
- Can present with lymphadenopathy (head, neck chest, abdomen, CNS and bone marrow)

# Non-Hodgkin Lymphoma

- Burkitt lymphoma: combination chemotherapy in cycles given every 3 weeks with rituximab (monoclonal antibody that targets CD 20 cells)
- Lymphoblastic Lymphoma: leukemia-like combination chemotherapy
- CNS prophylaxis required
- Cure rate: 82-87%

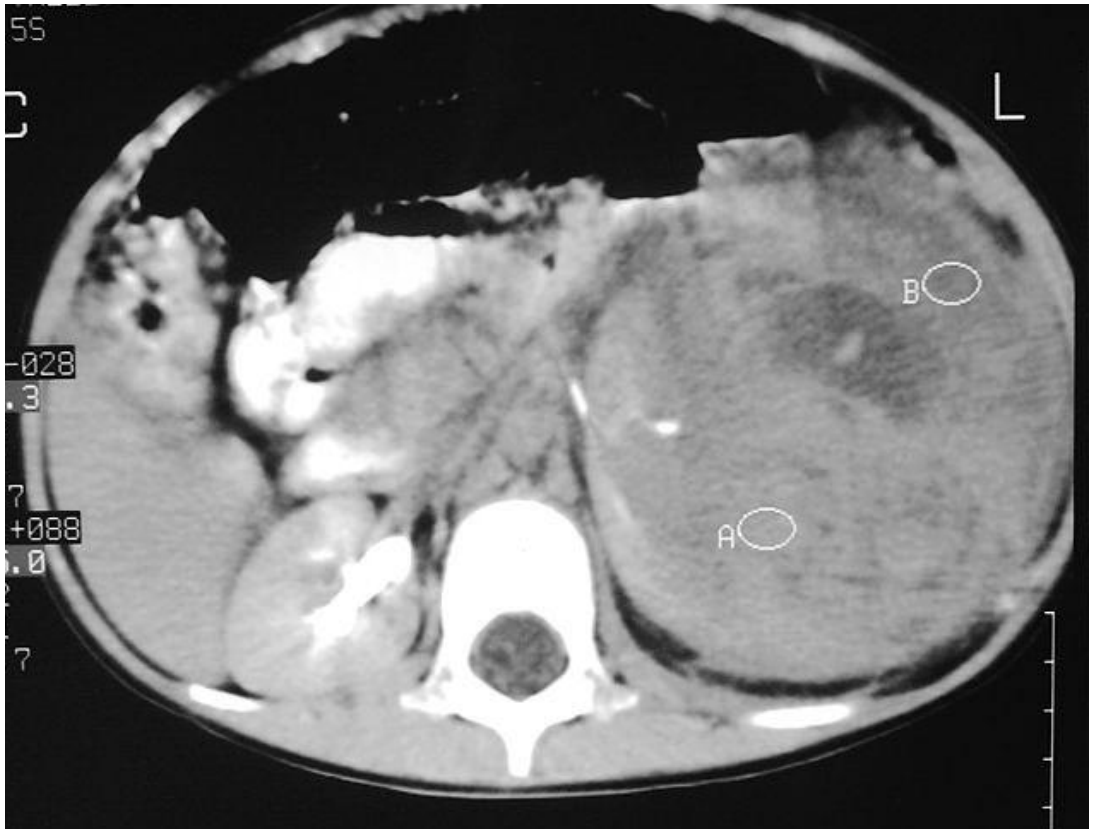
# Case 4

- 5 year old falls down in playground at school. When teacher helps to pick him up, she notices his belly is full and hard on one side.
- Teacher informs mother of this during pick-up. Mother reports that child has been having issues with constipation for the past 3 weeks.
- Urine appears red the following day.

# Wilms Tumor

- Most common primary malignant renal tumor of childhood
- 7.6 cases/million
- 500 cases/year with slight female predominance
- Uncommon in children > 10 yrs old & associated with worse prognosis
- Hereditary Wilms' uncommon (1-2%); 10% are associated with congenital anomalies

# Wilms Tumor



# Wilms Tumor

- Usually presents with painless abdominal mass
- Less frequent: fever, high blood pressure, hematuria
- Risk Adapted Multimodal: surgery, chemotherapy, radiation therapy
- Overall cure rate 90%
- Survivorship: heart, growth deformities, single kidney, second malignancies

# Neuroblastoma

- Most common extracranial solid tumor of childhood
- 650 cases per year
- 37% diagnosed as infants (most common malignancy during first year of life)
- 90% younger than 5 years of age at diagnosis
- May spontaneously regress in first year of life

# Neuroblastoma

- Sites: adrenal gland or paraspinal sites along sympathetic nervous system chain
- Usually presents with abdominal mass
- Other symptoms: proptosis, periorbital ecchymosis, bone pain, high blood pressure, paralysis
- Diagnosis: biopsy, imaging, bone marrow evaluation, urine VMA &HVA

# Neuroblastoma

- Stage and Risk Adapted Multimodal Treatment: surgery, chemotherapy, radiation therapy, high dose chemotherapy with stem cell rescue
- Cure rates:
  - < 1 yr: 95%
  - 1-4 yrs: 68%
  - 5-9 yrs: 52%
- Survivorship

# Almost there!

# Historical Perspective

- Stanford Kadinsky (1920): “If you do not operate they die, if you operate, they die just the same.”
- Historically, local control achieved by surgical amputation alone
- In spite of this, 50% developed distant metastasis by 6 months, 80% by 2 years
- Historical controls: < 20% 5 year survival

# Historical Perspective

- 1984: Mayo Clinic reports no benefit from adjuvant chemotherapy in osteosarcoma (JCO)
- They report relapse-free survival of 44% with surgery alone
- This questioned the accepted natural history of osteosarcoma and the need for adjuvant chemotherapy

# Historical Perspective

- 1986: Cooperative Randomized Control Trial comparing surgery alone versus surgery plus chemotherapy (NEJM)
- 113 pts: 36 accepted randomization
- 2 year relapse free survival:  control group (18): 17%, chemotherapy group (18): 66%
- Declined randomization (77 pts): 2 yr RFS: surgery (18): 17%, chemotherapy (59): 72%

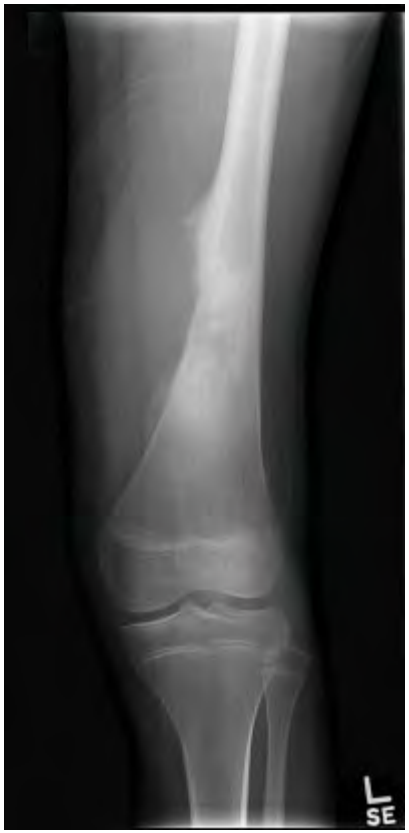
# Case 6

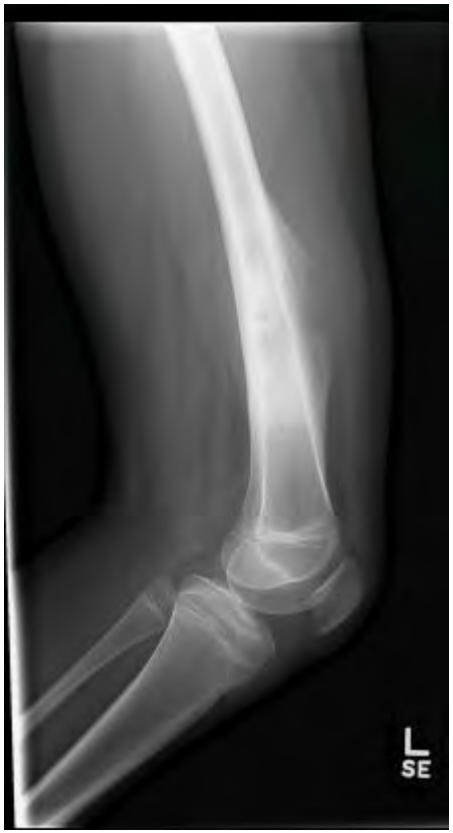
- High school basketball player notices ankle pain during practices.
- Takes OTC pain meds and applies ice.
- Pain persists and worsens. He notices hard swelling around his ankle.
- Orthopedic doctor sees patient and orders  plain x-ray.

# Bone Tumors

- Osteosarcoma and Ewing sarcoma: most common bone tumors; 450 and 200 cases per year respectively
- Most common symptoms are pain and swelling of involved bone (Ewing Sarcoma may present with extra-osseous mass).
- Rarely present with systemic symptoms.
- 25% present with metastatic disease at diagnosis

# Osteosarcoma



# Bone Tumors

- Osteosarcoma: 3 agent chemotherapy, local control (limb salvage versus amputation), post surgery chemotherapy
- Ewing Sarcoma: combination chemotherapy every 2 weeks, local control (surgery versus radiation therapy), post local control chemotherapy
- Survivorship: Infertility, heart, limb function, second malignancies (chemotherapy, radiation)

# What's next

- Immune therapy
- Antibody directed therapy in combination with established chemotherapy
- Proton radiation therapy
  - Limiting collateral damage & long term neurocognitive and endocrine toxicity
- Continued Risk Stratification
- Prevention
- Survivorship

# Childhood Cancer Reasearch Funding

- These Groups Donate at least $0.80 out of every $1:
  - St. Baldrick's Foundation
  - Alex's Lemonade Stand
  - Curesearch
  - The Rally Foundation for Childhood Cancer Research
  - Cookies for Kids Cancer
  - Bear Necessities
  - B+ Foundation
- $0.01-0.02 out of every dollar: ACS, NCI, LLS

www.childrensoncologygroup.org, www.cancer.gov, www.curesearch.org



# Thank You!

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