Epidemiology:
Roughly 8000 new cases of cancer in children under 1.5 years per year in the US. Acute leukemia accounts for about 25% of these, brain tumors, collectively account for slightly less than 25%. Lymphoma and Neuroblastoma are next most common.

Acute Lymphoblastic Leukemia
Acute Lymphoblastic Leukemia makes up 75% of all leukemia in children. AML accounts for 20%, CML and JCML account for about 4%, and Burkitt's leukemia accounts for 1%.

The peak age incidence of ALL is between 2 and 10 years of age, with a peak age of 2 years at diagnosis.

Diagnosis:
Duration of symptoms is usually short (2-3 months).
About half of all patients will present with a history of bruising or bleeding.
About a quarter of patients present with bone or joint pain.
61% present with a fever history (remember to include leukopenia in your FUO Ddx!)

Common Clinical Findings:

<table>
<thead>
<tr>
<th>Age</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; 2 years</td>
<td>15</td>
</tr>
<tr>
<td>2 &lt; Age &lt; 10 years</td>
<td>70</td>
</tr>
<tr>
<td>Age&gt; 10 years</td>
<td>15</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>70</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>75</td>
</tr>
<tr>
<td>Lymphadenopathy (moderate/marked)</td>
<td>45</td>
</tr>
</tbody>
</table>

Lab Features:
53% of patients present with a VVBC < 10,000, 30% between 10 and 49,000, and 17% above 50,000.
43% have severe anemia (< 7 gm/dL, 45% have moderate anemia (7 to 11 gm/dL, 12% have no evidence of anemia (hgb > 11.)
28% of patients have severe thrombocytopenia (<20,000). 47% have moderately low platelets (20-100,000). 25% have mild or no depression of platelet counts.

(Bottom line: No feature of a CBC can exclude the diagnosis completely)
Differential Diagnosis of Acute Leukemia

**Infectious**: Mono, toxoplasmosis, pertussis, infectious lymphocytosis, HIV

**Autoimmune**: JRA, ITP, autoimmune neutropenia

**Bone Marrow Failure**: Aplastic Anemia, MDS, Fanconi’s Anemia

**Other Malignancies**: Lymphoma, Neuroblastoma, Rhabdomyosarcoma

**Others**: Leukemoid reaction, Iron deficiency

Characteristics of Blast Cells:

- Acute Lymphoblastic Leukemia (Favorable Prognostic Factors)
  - Presenting WBC < 50,000
  - Presenting Hgb < 10 gm/dl
  - Age between 2 and 10 years
  - Absence of bulky extramedullary disease
  - Absence of CNS involvement
  - Hyperdiploid chromosome number
  - Absence of non-random translocations
  - No Myeloid markers
  - CALIA +
  - Rapid response to induction therapy

Acute Lymphoblastic Leukemia (Prognosis)

<table>
<thead>
<tr>
<th>Category</th>
<th>5 yr EFS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard Risk</td>
<td>80%</td>
</tr>
<tr>
<td>High Risk</td>
<td>50%</td>
</tr>
<tr>
<td>Infants</td>
<td>20%</td>
</tr>
</tbody>
</table>
Brain Tumors:

Location: Posterior Fossa 60%, Supratentorial 40% (15% midline, 25% hemispheric)

Most Common: Medulloblastoma (20%), Cerebellar Astrocytoma G 7%) (Nugget: medulloblastomas are common, but they are not the only game in town...)

Common Presenting Symptoms of Brain Tumors:

Posterior Fossa tumors present with increased intracranial pressure symptoms, and long tract symptoms (gait disturbances, ataxia) As the lesion encroaches on the brain stem, cranial nerve deficits become more common.

Common Symptoms: headache, vomiting, visual disturbances, gait disturbance

Evaluation of a headache:

History: Time of day, quality of headache, changes, associated symptoms (vomiting) visual changes, polydipsia, changes in growth rate.

Physical Exam: Neuro exam, visual exam, plot growth over multiple points.

Lab: urine specific gravity (esp with history of growth changes or polydipsia)

Indication for imaging: Any neurologic abnormality, eye findings (visual acuity change, papilledema) vomiting, wakes child from sleep, change in growth pattern, polyuria, polydipsia, Coexisting Neurofibromatosis
Neuroblastoma

Common Presenting Symptoms:
- Weight Loss
- Failure to Thrive
- Periorbital ecchymoses
- Bonefoint Pain

Anemia
Fever
Limp

Uncommon Presenting Symptoms:
- Diarrhea
- Hypertension
- Paresthesia
- Opso(m.yo)clonus
- Sweating
- Sensory Loss

Common Sites of Origin
- Abdomen (3/5 Adrenal, 2/5 non-Adrenal) 65%
- Chest (Posterior Mediastinum) 14.6%
- Pelvis 4.5%
- Neck 3.2%
- Head 0.2%
- Unknown Primary 12.3%

Staging, INSS
- Stage 1. Tumor confined to organ of origin, complete gross excision
- Stage 2A. Unilateral tumor with incomplete excision
- Stage 2B. 2A + positive ipsilateral lymph nodes
- Stage 3. Tumor crosses midline or contralateral nodes +
- Stage 4. Distant metastatic spread
- Stage 4S. Infant < 12 months, stage I or 2 primary, with mets to skin, liver, or bone marrow

Prognostic factors
- Stage (low is better)
- Age (Infants do better than older kids)
- Location (Adrenal primaries do worse than non-adrenal primaries)
- N-myc (1 copy is better than multiple copies)
- DNA index (hyperdiploid is better than either diploid or tetraploid)
- LDH (Low is better, over 1500 is a poor prognostic factor)

Prognosis
- Stage 1, 2, 4 S: 75-90% 2 yr EFS
- Stage 3, 4: 10-30% 2 yr EFS
Wilms' Tumor:

- Peak age incidence 2-3 years (contrast with NBL’s 0-2 year peak)
- 80% diagnosed before age 5 years
- 95% diagnosed before age 9 years

History: Painless mass found by accident
Physical exam: non-tender, unilateral mass filling flank.
Radiographic: complex cystic mass arising in kidney and distorting renal anatomy.
Ultrasound may reveal tumor thrombus in renal vein or IVC.

Associations with congenital anomalies:

- Aniridia, Hernihypertrophy (Beckwith Wiedemann syndrome).
- Cryptorchidism, and other genitourinary anomalies (+MR = Denys-Drash syndrome)

Genetics: deletion of I I p 13 gene and I I p 15

Staging:

- Stage 1. Confined to kidney, completely excised
- Stage 2. Confined to flank, completely excised
- Stage 3. Residual tumor in abdomen, lymph node involvement, tumor spillage
- Stage 4. Distant mets (lung, liver, bone, brain)
- Stage 5. Bilateral tumors

Prognostic factors:

- Flistology: Favorable versus Unfavorable
- Metastatic disease at diagnosis

Prognosis:

- Stage 1: 95%
- Stage 2: 90%
- Stage 3: 84%
- Stage 4: 54%

Favorable histology (all stages): 90%
Unfavorable histology (all stages): 54%