Pediatrics TeamWork

437

Common Pediatric Oncological Diseases

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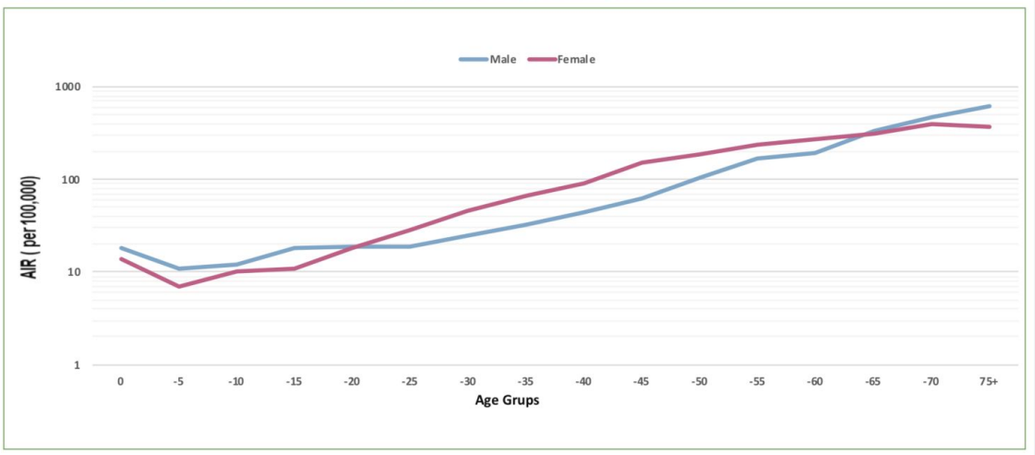
Notes Previous Notes Book Important!

Epidemiology

- Childhood cancer is rare
- Cancer incidence in among US children aged 0-14 years was 16.7/100,000 in 2012-2016 (SEER data)
- Childhood cancer occurs in about 10/100,000 children in Saudi Arabia about 1 in every 10000 cases.

Figure 2.2: Age-Specific Incidence Rate (AIR) for all cancers among Saudis, 2015



- As you can see in the diagram, the incidence of cancer increases with age.
- Most common types of cancer are different between children and adults.

Table 2.8.2: Top ten cancers among Saudi Children, 2015

Site	No.	%
Leukaemia	255	35.0
Brain, CNS	89	12.2
NHL	89	12.2
Hodgkin's lymphoma	66	9.1
Kidney	43	5.9
Bone	32	4.4
Adrenal gland	28	3.8
Eye	26	3.6
Connective,Soft tissue	23	3.2
Ovary	12	1.6

Table 2.7.3: Top ten cancers reported among Saudi Adults by gender, 2015

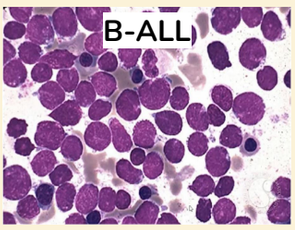
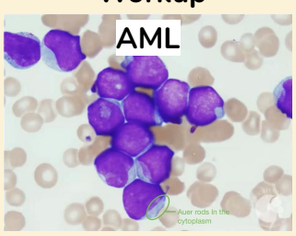
Male	5036	%
Colorectal	808	16.0
NHL	437	8.7
Prostate	340	6.7
Lung	323	6.4
Liver	266	5.3
Leukaemia	262	5.2
Hodgkin's lymphoma	226	4.5
Thyroid	224	4.4
Bladder	192	3.8
Stomach	184	3.7

Female	6275	%
Breast	1978	31.5
Thyroid	785	12.5
Colorectal	655	10.4
Corpus Uteri	403	6.4
NHL	303	4.8
Ovary	208	3.3
Leukaemia	185	2.9
Hodgkin's lymphoma	144	2.3
Stomach	131	2.1
Cervix Uteri	102	1.6

Causes

- Unknown in majority of cases. The most common question the parents will ask when we diagnose the child with cancer is why? unfortunately in 90% of the cases we don't know, it's usually due to interaction between genetics and environmental factors.
- Cancer predisposition syndromes:
  - Down syndrome: leukemia
  - Neurofibromatosis: gliomas mainly optic nerve giloma
  - Fanconi anemia: myeloid leukemia
  - Li-Fraumeni syndrome (germline P53 mutation) P53 is tumor suppressor gene
- Environmental factors:
  - Ionizing radiation
  - Infectious etiology e.g:EBV
  - Chemical exposures (e.g. pesticides, benzene)
- Prior treatment:
  - Chemotherapy (e.g. etoposide or alkylating agents e.g; cyclophosphamide) Patient receiving etoposide or alkylating agents like cyclophosphamide or any phosphamides are at risk of secondary cancer such as acute myeloid leukemia.
  - Radiotherapy develops cancer at the same site Children who receive chest radiotherapy for cancer Hodgkin lymphoma are at increased risk of breast cancer in adulthood.

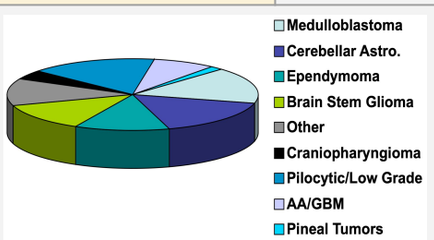
Leukemia

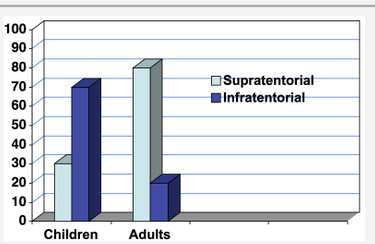
Types	(1) Acute lymphoblastic leukemia (ALL) most common (2) Acute myelogenous leukemia (AML) less common (3) Chronic myelogenous (CML) not common in children
Symptoms	Lethargy – Anorexia – Fever – Infection – CNS signs Bone / Joint pain could be the most initial presentation – Bleeding – Abdominal pain due to hepatosplenomegaly
Signs	Pallor – Hepatosplenomegaly – Petechiae – Purpura – Lymphadenopathy – Testicular involvement you have to do testicular examination
 **Workup** 	• CBC and differential + peripheral smear which is very important • LFT, electrolytes (K, Ph), uric acid, LDH for tumor lysis syndrome • CxR to assess if there is any mediastinal mass • Bone marrow study gold standard of diagnosis: o Morphology o Flow cytometry to define the type of leukemia based on surface antigen: B-ALL "CD10, CD19, CD20, CD22, CD79a, HLA-DR, CD34 & TdT" T-ALL "CD2, CD3, CD5, CD7, CD1a, TdT" AML "CD13, CD15, CD33, CD117, MPO, HLADR, CD34" o Molecular studies (e.g. BCR-ABL) o Cytogenetics e.g. t (9;22) • Lumbar puncture for any CNS or CSF involvement
Prognostic Factors ALL only	• NCI Risk Grouping: o Standard Risk: Age 1-9 yr and WBC <50,000/µl o High Risk: Age <1 or > 10 yr and/or WBC > 50k (initial WBCs) • Immunophenotype b better than T, T better than myeloid. • Cytogenetics The presence of Philadelphia translocation is a high risk feature and there are other cytogenetic features that help in the prognosis. • Response to induction therapy • CNS disease poor prognosis
Differential diagnosis	• Non-Malignant: o Infectious mononucleosis, as it has atypical lymphocytes which could lead to mistakenly diagnosing leukemia o Juvenile rheumatoid arthritis we do bone marrow biopsy because bone and joint pain can be common presentation of leukemia. o ITP no hepatosplenomegaly or lymphadenopathy o Aplastic anemia pancytopenia, no blast, empty bone marrow o Pertussis as it can lead to very high WBCs • Bone marrow study: o Lymphoma (BM blasts < 20%) o Neuroblastoma due to BM infiltration o Rhabdomyosarcoma due to BM infiltration
Treatment	• Supportive care: important in acute leukemia o Tumor lysis syndrome o Hyperleukocytosis o Superior vena cava syndrome o Infections • Chemotherapy Is the main treatment • Cranial radiation if CNS positive • Hematopoietic stem cell transplant (rarely) preserved for refractory cases • New immunotherapy: genetically modified T cell,

Brain tumors

- 2nd most common cancers in children
- **Low grade gliomas** are **most common** (non-malignant) type of brain tumor in children
- **Medulloblastoma** is the **most common malignant** brain tumor in children

Clinical presentation	• General and non-localizing symptoms: o headache, vomiting, behavioral changes, learning problems could be the first sign of brain tumor, weight loss/gain • General and non-localizing symptoms: o irritability, vomiting, bulging fontanelle, papilledema, parinaud syndrome • Localizing signs: o depend on tumor location e.g. ataxia in cerebellum)
Workup	• Brain MRI/Spine medulloblastoma can invade the spine • CSF cytopathology if not contraindicated • Surgical biopsy gold standard • CSF tumor markers (B-HCG/AFP) if germ cell tumor is suspected rare
Treatment	• Surgery (gross total resection if feasible) • Radiotherapy • Chemotherapy



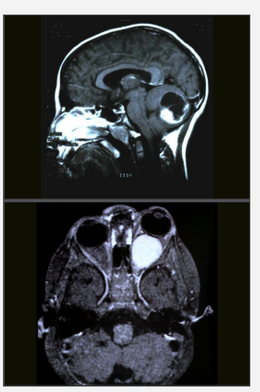


Astrocytoma (Glioma)

Site: cerebellum (pic1), Cerebral hemispheres, optic nerve* (pic2)& Cerebral white matter
Treatment:

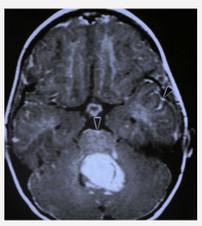
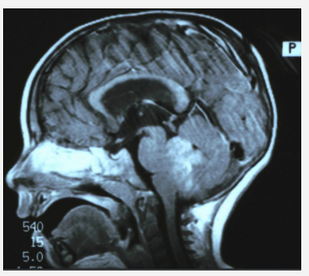
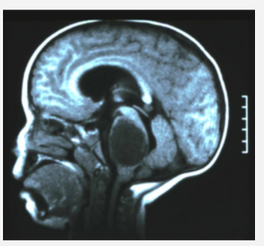
Prognosis:

- Low grade: good prognosis:
  o WHO grade I (juvenile pilocytic astrocytoma) fully resected no need for chemo or radiation
  o WHO grade II ((diffuse fibrillary astrocytoma)
- High grade: v. poor prognosis:
  o WHO grade III (anaplastic astrocytoma)
  o WHO grade IV (Glioblastoma multiforme) rare in children



*Optic nerve glioma (low grade) is seen frequently in neurofibromatosis patients.
Here surgical management is not an option because patient may lose his vision.
In NF patients we do annual MRI to look for tumors especially in the optic nerve
with ophthalmological examination even if the tumor is small to see whether it is affecting visual field or not

Brain tumors

Medulloblastoma	Ependymoma	Brain stem glioma
Common in pediatrics **Site:** posterior fossa (PNET) On microscope: small round cell tumor **Treatment:** surgery & radiation* 85% survival(non metastatic) 50% survival (metastatic) 	**Site:** ventricular lining **Treatment:** surgery, radiation & chemotherapy **Prognosis:** 50-60% if fully resected 	Eg: glioblastoma multiforme. Highly aggressive tumor. You cannot respect it. It progresses very quickly Site: **Treatment:** radiation **Progression:** at 12 months 

*The problem with radiation it might lead to learning or behavioral problems later on life, they might have difficulties in learning or in getting a job in the future.

From illustrated

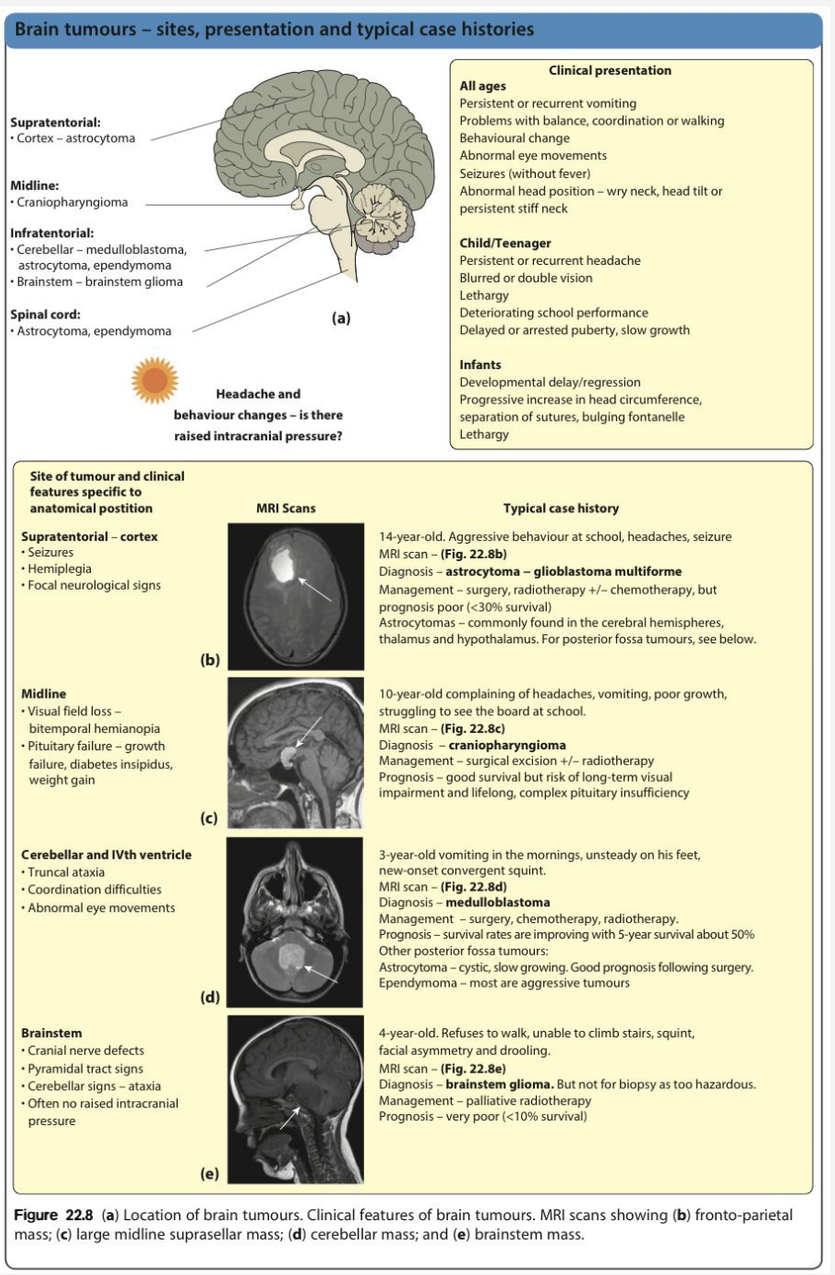


Figure 22.8 (**a**) Location of brain tumours. Clinical features of brain tumours. MRI scans showing (**b**) fronto-parietal mass; (**c**) large midline suprasellar mass; (**d**) cerebellar mass; and (**e**) brainstem mass.

Lymphoma

Hodgkin Lymphoma

Reed sternberg cell in hodgkin lymphoma
Epidemiology: Bimodal 15-34 years & after 50 years (rare under the age 5 years) If we see lymphoma in children younger than 5 years we always question if the child has immunodeficiency.
Staging (Ann Arbor Staging):
[Stage I]: single site/nodal region of involvement
[Stage II]: 2 or more sites/nodal regions on same side of diaphragm
[Stage III]: sites/nodal regions involved on both sides of diaphragm
[Stage IV]: diffuse or disseminated involvement in one or more extralymphatic organs
[E]: designation for extralymphatic involvement in any stage
[S]: splenic involvement
Symptoms: b symptoms are important in staging, more aggressive disease in case of B symptoms.
[A]: no associated symptoms
[B]: • Fever (>38o C) usually > 3 consecutive days | • Night sweats "Drenching"
• Unexplained weight loss of 10% - preceding 6 months
[X] bulky disease: mediastinum > 1/3 intrathoracic diameter – > 10 cm other nodal site
[E] extranodal involvement: • Pruritus • Alcohol-induced pain • Autoimmune disorders e.g. ITP When a child presents with ITP you need to R\O: - SLE -Lymphoma

Workup:
• Labs: CBC - ESR - LDH - uric acid- LFT - renal
• Biopsy of the lymph node
• Bone marrow biopsy (Bilateral) in case of advanced disease.
• CT scan / PET scan for staging
Treatment:
• 90-95% of all children/adolescence with HD can be cured
• Chemotherapy +/- radiotherapy
• Aims is to minimize late effects

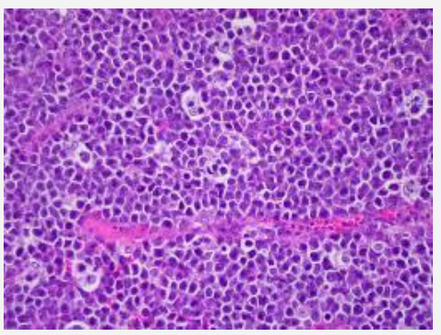
Non-Hodgkin Lymphoma

- No peak in incidence
- Immunodeficiency (10-100x increased risk over general population):
  - o Inherited or Acquired (HIV, post-transplant)
  - o Often EBV associated
  - o NHL in < 3 years of age – suspect immunodeficiency
- Environmental Exposures:
  - o Insecticides/pesticides – adult NHL only
  - o Viruses – EBV (endemic malaria regions and Burkitt lymphoma and immunodeficiency)

Potential complications:
• Superior vena cava syndrome
Symptom: Cough, dyspnea, orthopnea, dysphagia, wheezing, hoarseness, facial edema, chest pain
Treatment: Tissue diagnosis if possible | Emergency XRT +/- steroids
• Tumor lysis syndrome
Treatment: Chemotherapy

Burkitt Lymphoma

Clinical picture might look like appendicitis, it has starry sky appearance.



- Mature B-cell
- C-MYC +ve
- Abdominal disease most common presentation
- Head & neck second most common site
- Extranodal disease very common
- Almost all Burkitt lymphoma is associated with EBV in endemic Africa
- Very rapidly growing (t1/2 = 18-24 hr)

Potential complications: Superior vena cava syndrome | Tumor lysis syndrome
Treatment: Chemotherapy

- **The difference between Hodgkin and non-Hodgkin:**
  - In Hodgkin: the family tells you that their child had lymph nodes increasing slowly for the last 3-6 months and they thought it's nothing (slowly increasing in size).
  - In Burkett we approach it as an emergency because it can increase in size very quickly, especially if it's in the mediastinal area it can cause significant compression on their airway and can be life threatening, we try our best to do quick diagnosis so we can start therapy.

Because it's rapidly growing the risk of tumor lysis syndrome is even higher than in leukemia and this is why it's almost routine to give rasburicase not only allopurinol because we can't control the hyperuricemia

- Superior vena cava syndrome is also frequent because of the of the reasons I mentioned above.

- **Superior vena cava syndrome:**

Compression of SVC by the cancer mass (on chest X Ray you would see widening mediastinum) this compression causes SOB and congestion of the face and upper limb.
Venous flow to the heart is reduced because of the compression, so the patient will be leaning forward and refusing to lie down as s/he is trying to decrease the compression.
Making the patient lying down might cause significant drop in venous return and the patient might collapse.
It is contraindicated to intubate these patients because when you sedate them you may decrease venous return to the heart as well.

- **Tumor lysis syndrome:**

When you have lysis of the cancer cells because they are multiplying quickly or because of the effect of the initial therapy. Everything inside the cell will be elevated (high potassium, high phosphate, and high uric acid "product of DNA destruction") and hypocalcemia
Mnemonic: PUKE calcium (Phosphate, Uric acid and potassium (K) will be Elevated, calcium will be low)
For the uric acid we give allopurinol (oxidase inhibitor that decreases formation of uric acid), if the volume of leukemia or lymphoma cells is huge then allopurinol alone might not be enough so we give rasburicase (rasburicase clear the uric acid it's not an enzyme inhibitor so it will give quick drop in uric acid, the disadvantage of it is if the patient G6PD we can can't give it). If we don't treat the uric acid it will precipitate in the kidney and cause renal failure. Potassium can cause life threatening hyperkalemia, so we give kayexalate and limit the potassium and phosphate intake . For phosphate we give phosphate binder. And the first few week we check tumor lysis lab more frequently

Febrile neutropenia

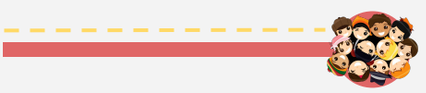
- High mortality when antibiotics started after blood cultures became positive, so once you suspect it give the patient broad spectrum antibiotics that covers pseudomonas, the first dose has to be STAT (received within 20 to 30 minutes)
- Narrow spectrum antibiotic coverage results in associated with poor outcomes
- Antibiotics in neutropenic patients should be started at the onset of fever
- **Treatment:**
  - o Use monotherapy with an antipseudomonal b-lactam, a fourth-generation cephalosporin, or a carbapenem as empirical therapy in pediatric high risk Febrile neutropenia
  - o Reserve the addition of a second gram negative agent or who are clinically unstable, when a resistant infection is suspected, or for centers with a high rate of resistant pathogens
- **Indication for adding VANCOMYCIN:**
  - o High dose cytarabine because of risk of step. viridans
  - o Sepsis
  - o Cellulitis
  - o Central line infection

And hypotensive we have to give both gram -ve and +ve coverage.
Here an e.g from 2019 if you see the pseudomonas : Piperacillin- Tazobactam (TZP) (77%) alone is not enough we will miss 23% of pseudomonas cases, as for Amikacin it has (94%) sensitivity which is very good, so in general we combine them now. We use 2 Abx TZP and Amikacin, but this is after discussing with ID and with microbiology lab. if you see in the past we used to give gentamicin instead of amikacin but now with resistance evolving you can see gentamicin is not as good as Amikacin. In general for gram negative Amikacin is better

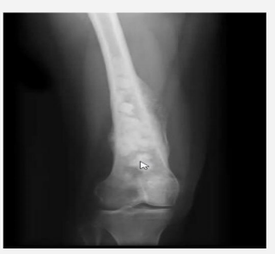
Neuroblastoma

- Second most common solid neoplasm in childhood
- Originates from neural crest tissue (sympathetic nerve pathway) e.g: adrenal glands
- Median age of diagnosis is 22 months
- **Clinical Presentation:**
  - Asymptomatic mass (e.g. abdomen or chest)
  - Horner's Syndrome
  - Spinal Cord Compression (medical emergency)
  - "Racoon eyes"
  - Systemic symptoms (hypertension,intractable diarrhea (VIP), opsoclonus/myoclonus)
  - Bone pain
  - Skin lesions
- **Workup:**
  - Asymptomatic **mass** (e.g. **abdomen** or chest)
  - **Urine catecholamine levels (VMA/HVA)**
  - Imaging (**CT**/MRI, CxR, MIBG important nuclear scan) CT scan of the head, neck and chest. MIBG because the nuclear materials will be up-taken by the neuroblastoma tissue so it's a very useful way to assess the staging of neuroblastoma
  - Biopsy: MYCN
  - Bone marrow
  - Bone scan
- **Treatment:**
  - Low risk → Surgery +/- chemotherapy
  - Intermediate risk → surgery + chemotherapy
  - High risk → High dose chemo / autologus stem cell transplant + surgery + radiation + immunotherapy

Bone cancers



- Malignant bone tumours are uncommon before puberty.
- Osteosarcoma is more common than Ewing sarcoma, but Ewing sarcoma is seen more often in younger children. Both have a male predominance.
- **Clinical Presentation:**
  - The limbs are the most common site
  - Persistent localized bone pain is the characteristic symptom
- **Workup:**
  - Plain X-ray is followed by MRI and bone scan
  - CT is used to assess for lung metastases, bone scan, whole body
  - MRI or PET for bony metastases and bone marrow sampling to exclude marrow involvement.
- **Treatment**
  - Chemotherapy given before surgery
  - Radiotherapy (in Ewing sarcoma)
- **Codman triangle:** triangular area of new subperiosteal bone that is created when the tumor raises the periosteum away from the bone. Seen in primary bone tumors



What makes you worry is that it's a severe thigh pain after minimal trauma and this is frequent when the patient comes with bone tumor. The degree of trauma doesn't explain the severity of the symptoms, and they don't usually respond to over the counter pain medications. So this is a red flag when you assess a child who has severe bone pain.
Bone tumor can also present without trauma, they will have bone pain.

Wilms tumor

- Most common primary malignant renal tumor of childhood
- 5-10% of patients have bilateral tumors
- Median age at presentation: Unilateral tumors: 44 months | Bilateral tumors: 31 months
- **Clinical Presentation:**
  - Asymptomatic abdominal mass most common presentation
  - Hypertension
  - Hematuria
  - Pain
- **Associated anomalies:**
  - WAGR syndrome: (wilms tumor, aniridia, genitourinary malformation, mental etardation) In ophthalmology when they see a child with aniridia they do abdominal US every 3 months to screen for wilms tumor. In general the risk decreases after 5 years so most screening should be done in the first 5 years.
  - Hemihypertrophy
  - Beckwith-Wiedemann syndrome
- **Workup:**
  - CBC, renal and liver functions
  - CT abdomen We do CT chest because wilms usually metastasize to the lungs and less likely to other organs.
- **Treatment:** Surgery + Chemotherapy +/- radiotherapy

It is well circumscribed lesion, which doesn't cross the midline

Hepatoblastoma

- **Most common type of <u>hepatic cancer</u>** in children (A rare pediatric tumor)
- Age: usually < 3 years
- **Clinical Presentation:**
  - Abdominal mass, distension
  - Abdominal pain
- **Workup:**
  - CBC, renal and liver functions (thrombocytosis) ddx of thrombocytosis: 1. Reactive (most common) 2.IDA 3. Abdominal tumor.
  - Serum alpha fetoprotein (increase)
  - CT abdomen

Retinoblastoma

- Non-hereditary **(unilateral)** →2-3 yrs of age
- Hereditary **(bilateral)** → 6-18 months of age (Germline mutation of RB1)
- **Clinical Presentation:**
  - Leukocoria
  - Strabismus (squint)
  - White pupillary reflex (replace the normaal red one)
- Absent red reflex
- **Workup:**
  - Examination under anesthesia
  - MRI orbit and brain
  - Bone scan, BM, and CSF in advanced disease
- **Treatment:** Focal therapy +/- chemotherapy +/- Enucleation Enucleation is done if other measures failed because the priority is to save the child no only the eye.

Others

Tables from dr slides

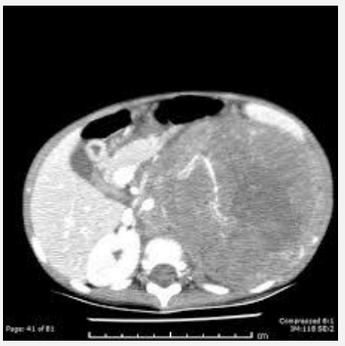
TABLE 1

Characteristics of Various Bone Cancers

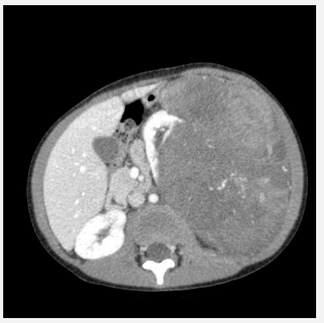
Cancer	Malignant cell origin	Patient demographics[2,3]	Locations (in order of common occurrence)[8]	Sites of metastases
Osteosarcoma	Mesenchymal cells, osteoblasts	Typically five to 25 years of age (median age: 16 years in males, 12 years in females); rare after 60 years of age More common in males and in blacks	Metaphyses of long bones: Distal femur Proximal humerus Proximal tibia Pelvis Skull	Bone, lung
Ewing sarcoma	Unconfirmed; thought to be from primitive stem cells or neural crest cells	Median age: 15 years Slightly more common in males and in whites and Asians	Diaphyses of long bones: Proximal femur Proximal humerus Proximal tibia Pelvis Ribs Scapula	Bone, lung
Chondrosarcoma	Chondrocytes	Typically 40 to 75 years of age Slightly more common in males; no racial predominance	Pelvis Proximal long bones Ribs Scapula Vertebrae	Lungs

Information from references 2, 3, and 8.

Parameter	Neuroblastoma	Wilms tumour
Age	Younger age group: < 2 years of age commonly	Slightly older age group : peak 3 - 4 years of age
Presentation	Painful abdominal mass	Painless abdominal mass
Calcification	Calcification very common: 80-90%	Calcification uncommon: 10%
Tumour composition	Solid mass lesion, rarely cystic components on US	Often cystic components at US
Tumour margin	Poorly marginated mass that may extend up into chest Adrenal NBL displaces the kidney	Well circumscribed mass - claw sign demonstrating it arises from the kidney
Vessel involvement	Encases vascular structures but does not invade them - elevates the aorta away from the vertebral column	Displaces adjacent structures – invades the vasculature with extension into renal vein/IVC
Metastatic sites	Bone/bone marrow (common) Liver Lung/pleura	Lung (common) Liver Local lymph nodes

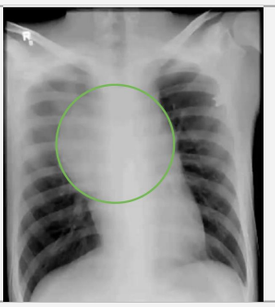
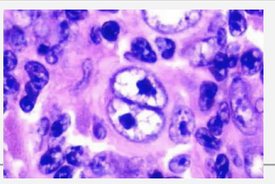
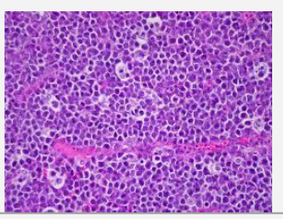
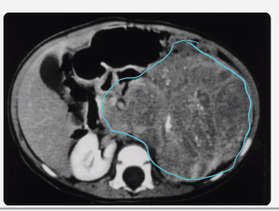
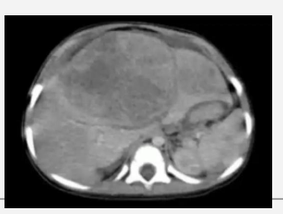
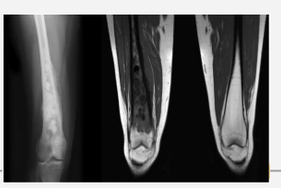
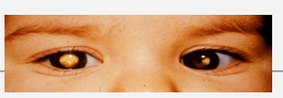


It crosses midline



It doesn't cross midline

Cases

Case	Image	Notes
A **5 year old girls** presented with a history of cough, SOB & fever. On exam she is leaning forward & refusing to lay on her back. You also noted swelling of her face, hepatosplenomegaly & lymphadenopathy. CBC: WBC = 150,000/ULC Hg= 7 g/dl | platelet= 20,000/ul with blasts in peripheral blood		Dx: leukemia
A **10 year old girls** with acute lymphoblastic leukemia presented to ER with a history of fever. On exam vital signs are normal, no evidence of cellulitis or line infections CBC: severe neutropenia		Dx: Febrile neutropenia Treatment?
A **10 year old boy** presented with right supraclavicular lymphadenopathy. On exam there is 5 cm non tender lump. Lymph node biopsy showed abnormal cells		Dx: Hodgkin Lymphoma
A **8 year old boy** presented with a 1 week history of intermittent abdominal pain, vomiting & gastrointestinal bleeding. On exam there is right lower quadrant tenderness. CT demonstrates an ileocecal mass & intussusception		Dx: Burkitt Lymphoma
A **1 year old boy** presented was discovered by his mother to have abdominal mass. On exam there is abdominal mass that crosses the midline. CT showed large calcified mass as shown in the figure. Urine VMA & HVA are high		Dx: Neuroblastoma
A **18 month old boy** presented with abdominal distension & hepatomegaly. CT demonstrates a large heterogeneously enhancing lesion in the liver and ascites. There is increase in serum alpha fetoprotein & thrombocytosis		Dx: Hepatoblastoma
A **12 year old boy** presented with severe right thigh pain after he sustained minimal trauma. The pain awake him at night & is not responding to over the counter pain medications.		Dx: Bone tumor
A **3 month old infant** presented with leukocoria & strabismus		Dx: Retinoblastoma

Book!

Treatment of cancer

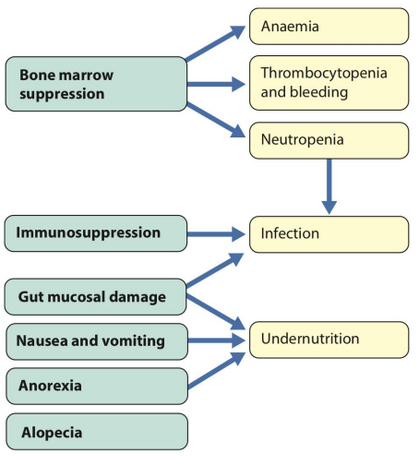


Figure 22.4 Short-term side-effects of chemotherapy.

Table 22.3 Some problems that may occur following cure of childhood cancer

Problem	Cause
Specific organ dysfunction	Nephrectomy for Wilms tumour
	Toxicity from chemotherapy, e.g. renal from cisplatin or ifosfamide, cardiac from doxorubicin or mediastinal radiotherapy
Growth/endocrine problems	Growth and other pituitary hormone deficiencies from irradiation
	Bone growth retardation and deformity at sites of irradiation
Infertility	Gonadal irradiation
	Alkylating agent chemotherapy (cyclophosphamide, ifosfamide)
Mental health disorders	Post-traumatic stress disorder, healthcare-related anxiety
Neuropsychological problems	Cranial irradiation (particularly at age <5 years)
	Brain surgery
Second malignancy	Irradiation
	Alkylating agent chemotherapy
Social/educational disadvantage	Chronic ill health Absence from school

Chemotherapy side effects

- Doxorubicin: cardiotoxicity
- Cisplatin: renal failure and deafness
- Cyclophosphamide: hemorrhagic cystitis
- Vincristine: neuropathy

Summary

Presentation of malignant disease in children

Brain tumours:

All ages
- Persistent or recurrent vomiting
- Problems with balance, coordination or walking
- Behavioural change
- Abnormal eye movements
- Seizures (without fever)
- Abnormal head position – wry neck, head tilt or persistent stiff neck

Child/Teenager
- Persistent or recurrent headache
- Blurred or double vision
- Lethargy
- Deteriorating school performance
- Delayed or arrested puberty, slow growth

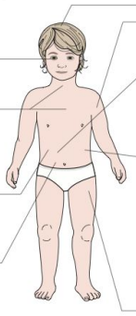
Infants
- Developmental delay/regression
- Progressive increase in head circumference, separation of sutures, bulging fontanelle
- Lethargy

Retinoblastoma:
- Screening if positive family history
- White pupillary reflex or squint

Lymphomas:
- Enlarged lymph nodes in the neck or abdomen
- Mediastinal mass – may cause superior vena caval obstruction

Wilms tumour:
- Large abdominal mass in a well child
- Occasionally anorexia, abdominal pain, haematuria

Langerhans cell histiocytosis:
- Seborrhoeic rash
- Widespread soft tissue infiltration
- Bone pain, swelling or fracture
- Diabetes insipidus



Soft tissue sarcomas:
- Mass any site

Neuroblastoma:
- Abdominal mass
- Spinal cord compression
- Weight loss and malaise
- Pallor, bruising
- Bone pain

Acute lymphoblastic leukaemia (ALL):
- Malaise, anorexia
- Pallor, lethargy
- Infections
- Bruising, petichiae, nose bleeds
- Lymphadenopathy
- Hepatosplenomegaly
- Bone pain

Malignant bone tumours:
- Localized bone pain

Preschool (<5 years old)	School-age	Adolescence
Acute lymphoblastic leukaemia (ALL) – peak incidence Non-Hodgkin lymphoma	Acute lymphoblastic leukaemia (ALL)	Acute lymphoblastic leukaemia (ALL) Hodgkin lymphoma
Neuroblastoma	Brain tumours	Malignant bone tumours
Wilms tumour		Soft tissue sarcomas
Retinoblastoma		

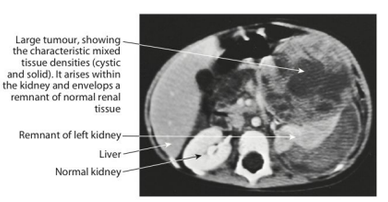


Figure 22.15 Large Wilms tumour arising within the left kidney, showing characteristic cystic and solid tissue densities.

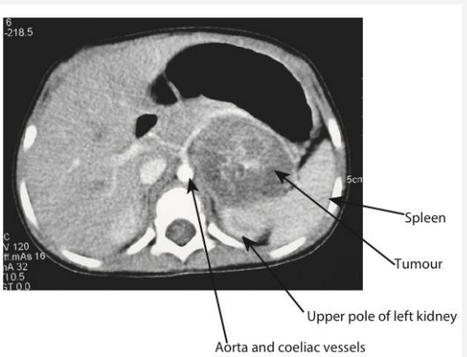


Figure 22.13 Transverse MRI image showing a large left-sided primary neuroblastoma arising from the adrenal region and distorting coeliac and mesenteric blood vessels.

Acute leukemia

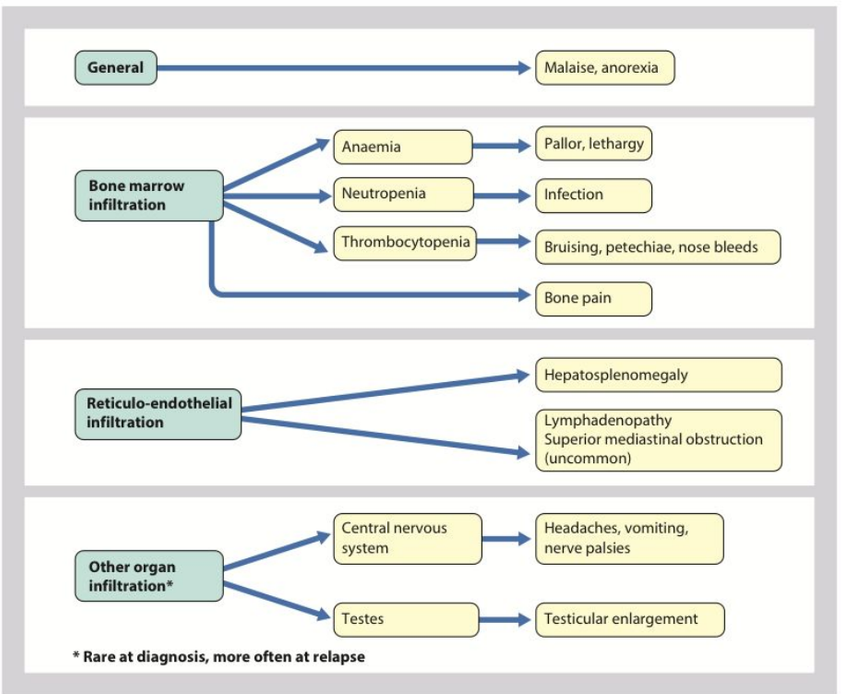


Figure 22.6 Signs and symptoms of acute leukaemia.

Oncological emergencies

Table 22.1 Oncological emergencies

Haematological	Bone marrow failure – anaemia, thrombocytopenia, neutropenia Hyperleukocytosis (white cell count $>100 \times 10^9$/L) Coagulopathy – bleeding, DIC
Infection	Bacterial, viral, fungal Sepsis
Neurological	Raised intracranial pressure (obstructive hydrocephalus) Spinal cord compression
Metabolic/ Endocrine	Tumour lysis syndrome (on initiating chemotherapy; risk of acute renal failure) Hypercalcaemia SIADH (syndrome of inappropriate anti-diuretic hormone) Diabetes insipidus
Other	Superior vena cava obstruction (SVCO) Airway obstruction Cardiac tamponade

Peds Cases!

FEBRILE NEUTROPENIA

FEVER: > 38.3°C once OR > 38°C for ≥ 1 hour OR two temperatures > 38°C within 12 hours

+

NEUTROPENIA: Absolute Neutrophil Count (ANC) < 0.5 x 10^9 cells/L

Fever and neutropenia is a medical emergency

Febrile neutropenia is a **common complication** in children receiving **chemotherapy** for cancer

ETIOLOGY OF FEVER

- **Bacterial**: bacteremia, line infection, meningitis, pneumonia, UTI, etc.
  - **Gram positive** (most common): *Coagulase-negative Staphylococcus, Staphylococcus aureus, Streptococcus viridans*
  - **Gram negatives**: *E.coli, Klebsiella, Pseudomonas*
- **Viral**: respiratory viruses, *Herpes simplex, Varicella zoster*
- **Fungi**: *Candida, Aspergillus, Cryptococcus*
- **Non-infectious**: drug fever, cancer-related, deep vein thrombosis/ pulmonary embolism, transfusion reaction

There may be no etiology of fever found!

ETIOLOGY OF NEUTROPENIA

- **Highest risk**: chemotherapy
- **High risk**: ill-appearing child with neutropenia (any cause), aplastic anemia, severe congenital neutropenia (ex: Kostmann syndrome)
- **Low-moderate risk**: chronic benign neutropenia, cyclic neutropenia
- **Low risk**: well-appearing transient neutropenia (ex: viral or drug-induced)

HISTORY

Infectious symptoms:
- Site-specific symptoms of **localized infection**
  - Headache, skin changes, oral ulcers, sore throat, cough, SOB, abdominal pain, vomiting, diarrhea, perianal lesions, dysuria, rashes
- **Sick contacts**

Immunization history

Past medical history:
- Underlying diagnosis
- Established central line
- Date of last chemotherapy
- Most recent ANC count
- Previous febrile neutropenia, infections, & antibiotics

Medications & allergies:
- Recent antipyretics
- Antimicrobial prophylaxis and compliance

PHYSICAL EXAM

Careful physical examination to determine site of infection.

Findings may be subtle or none at all!

- **Vitals**: tachycardia & tachypnea often accompany fever
- **Skin**: erythema, temperature, central venous catheter
- **HEENT**: gingivitis, oral ulcers, pharyngitis, cervical lymphadenopathy, meningismus
- **Respiratory**: work of breathing, signs of pneumonia
- **Cardiovascular**: new murmur, cap refill, pulses
- **Abdomen**: tenderness, distension, masses, hepatosplenomegaly
- **Perineum**: perianal and labial lesions

INVESTIGATIONS

INITIAL LABS

- **CBC with differential**
- **Blood cultures** from central line
- Electrolytes
- Urea
- Creatinine
- CRP
- Type & Screen

OTHER CONSIDERATIONS

- +/- urine culture
- +/- swab sites with purulent drainage
- +/- stool cultures
- +/- chest x-ray
- +/- NP swab if respiratory symptoms present

MANAGEMENT ALGORITHM FOR FEBRILE NEUTROPENIA IN CANCER PATIENTS

Initial investigations → **EMPIRIC ANTIBIOTICS** (Goal: 1st dose within 60 minutes of arrival) → **BROAD SPECTRUM ANTIBIOTICS (e.g: piperacillin-tazobactam & tobramycin)*** → **Transfer to tertiary care center** for further management by Pediatric Hematology/Oncology.

Recognizing a child who is UNWELL / HEMODYNAMICALLY UNSTABLE:

Early symptoms of shock: lethargy/irritability, poor feeding, fever, ↓ urine output.

Early signs of shock: ↑ HR, ↑ RR ↓ BP, orthostatic BP/pulse changes, delayed cap refill, ↓ level of consciousness. ***Early recognition is critical!***

*Antibiotic treatment is unique to each site based on local sensitivities.

- Inpatient treatment generally involves **empiric antibiotics** until the **ANC has recovered** and the **fever subsides**. If the ANC is not improving or the fever persists, a **fungal/extended fever workup** is initiated. An **antifungal agent** may be added.
- For **non-cancer neutropenia**, management is determined by **level of risk**. Consider Pediatric or Pediatric Hematology consultation.
- **The recurrence of fever in a neutropenic host should be approached as a *new fever* and be *re-evaluated*.**

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