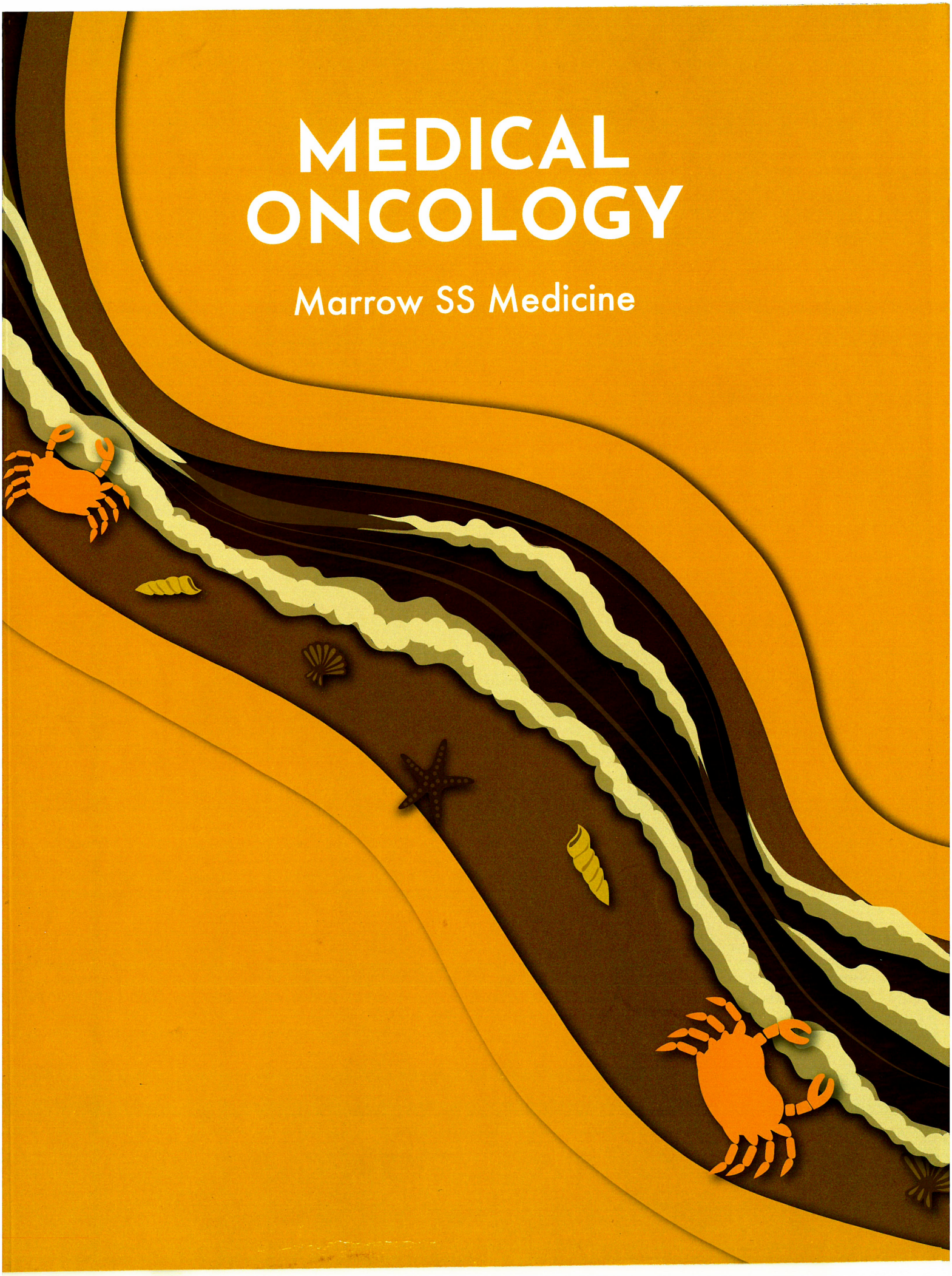
# MEDICAL ONCOLOGY

Marrow SS Medicine



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Dr. Vishnu Sreedath is an ESMO Certified Medical Oncologist. He completed his MBBS from Government Medical College, Kozhikode, followed by MD in General Medicine from Stanley Medical College, and DM (Medical Oncology) from Madras Medical College. He is actively involved in oncology research and patient care and currently consults at Meitra Super Specialty Hospital, Kozhikode.

# Medical Oncology

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## Pharmacology

# BASICS OF PAEDIATRIC ONCOLOGY

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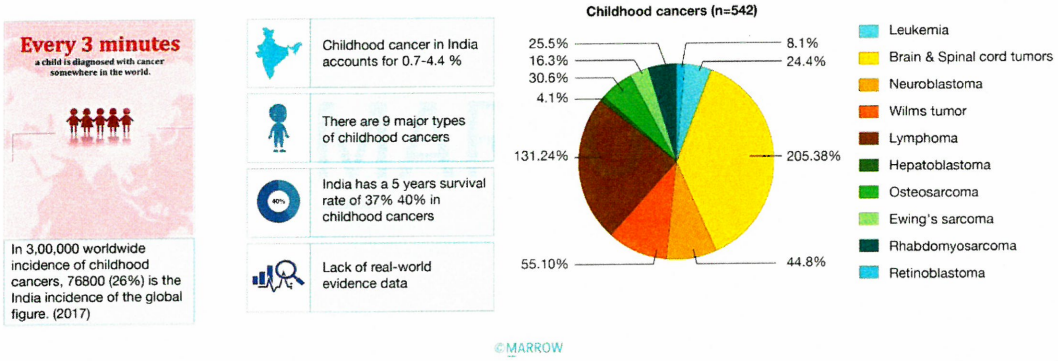
## Introduction 00:00:23

### Statistics :




80% of children with cancer will survive in high-income countries.

Only about 20% of children with cancer will survive in some low and middle income countries.

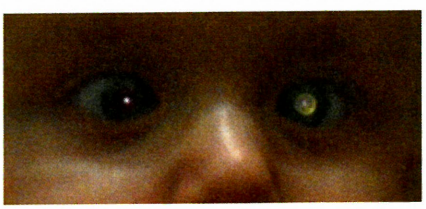
### Roadblocks to improved cancer survival :

- Delayed diagnosis/misdiagnosis/no diagnosis.
- Lack of awareness.
- Overlap of signs and symptoms of cancer with other infectious diseases.
- Lack of diagnostic facilities.
- Symptoms of leukemia/lymphoma are often mistaken for more common nutritional deficiency/tuberculosis.
- Many patients are empirically started on ATT.
- Steroids are often used in peripheral centres without a diagnosis.

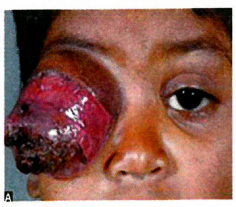
Retinoblastoma :

Early diagnosis : 100% survival.

Late diagnosis (Extraocular retinoblastoma) : 20-30% survival.



Loss of red reflex : Early retinoblastoma.



Extraocular retinoblastoma (Late).

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Cost of late diagnosis :

- Poor survival rates.
- High treatment cost.

### Factors related to late diagnosis :

Patient related factors :

- Infants : Dependent on caregivers for a diagnosis.
- Adolescents : Ignoring the symptoms.

Health related factors :

- Lack of diagnosis.
- Lack of availability of cancer centres within reach.

### Children at risk :

1. Infections :
    - EBV infection : Hodgkin Lymphoma, Burkitt lymphoma, Post transplant lymphoproliferative disorder (PTLD), nasopharyngeal cancer.
    - HIV : Kaposi sarcoma, B cell lymphoma.
    - Hep B and C : Hepatocellular carcinoma.
    - HPV : HPV associated cancer.
2. Immunodeficiency syndromes.
3. Patients receiving immunosuppressive therapy : Higher risk of malignancy (PTLD and lymphomas).
4. Pediatric solid organ transplant recipients who are on prolonged thiopurine therapy : PTLD.
5. Childhood cancer survivors.
6. Exposure to alkylating agent, anthracycline, topoisomerase inhibitors.
7. Exposure to radiation.

## Signs and symptoms 00:10:31

### Fever :

- Non specific symptom.
- One of the causes of prolonged fever of unknown origin (FUO) : Occult malignancy.
- 10% or less of patients with FUO as the only symptom are later diagnosed with a malignancy.

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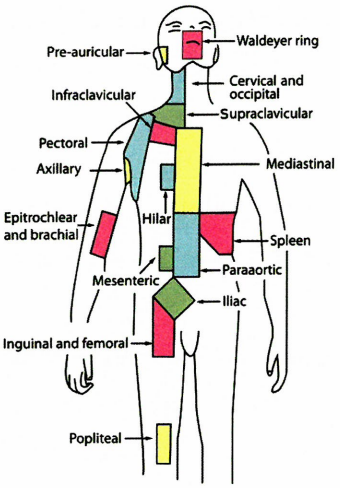
## Lymphadenopathy :

m/C cause : Reactive hyperplasia (Benign).

Enlarged lymph node could be due to :

- Intrinsic cellular components.
- Extrinsic cellular infiltration.




Lymphadenopathy.

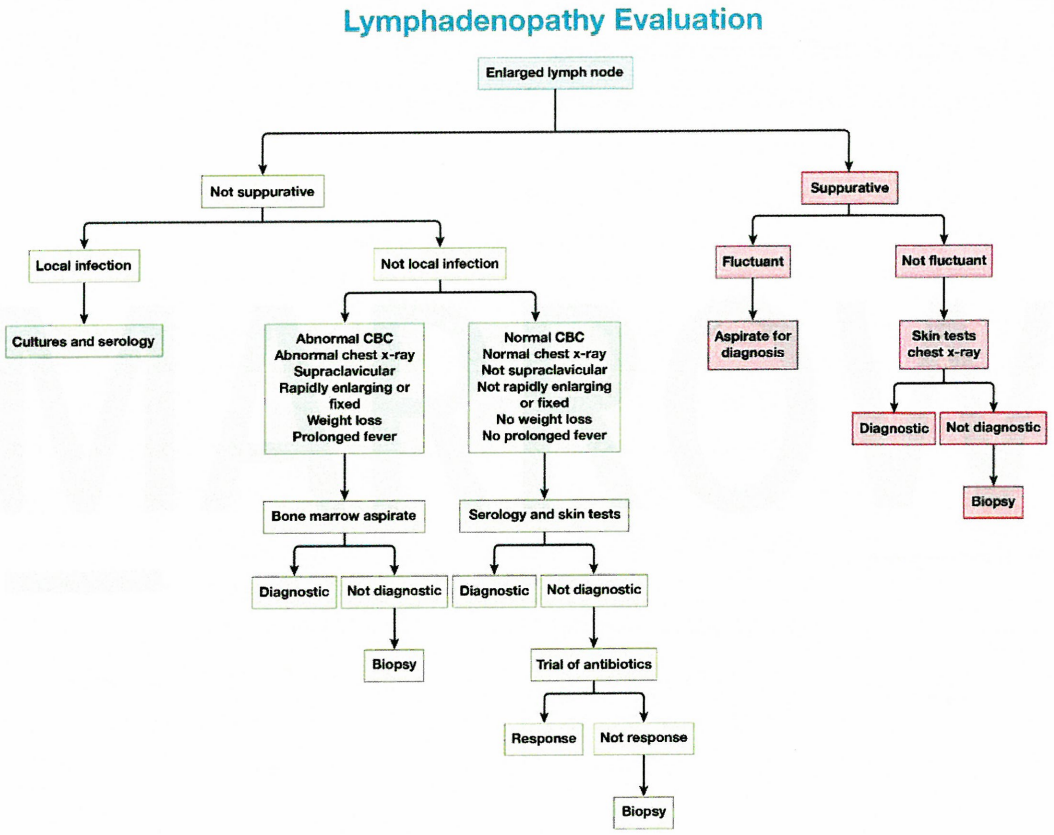
Significant lymphadenopathy :

- Cervical >1 cm.
- Axillary >1 cm.
- Epitrochlear >0.5 cm.
- Inguinal >1.5 cm.

Generalized lymphadenopathy : Significant lymphadenopathy of 2 or more noncontiguous lymph nodes.

Note :

- Palpable supraclavicular nodes should always be considered abnormal.
- Left-sided (Virchow) nodes suggest metastases from an intra-abdominal malignancy (Neuroblastoma).
- Right-sided nodes suggest intrathoracic disease.



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Indications of lymph node biopsy :

- Chronic, persistent, progressive adenopathy in the absence of any infectious etiology.
- Any nodes >2.5 cm in diameter in the absence of signs of infection.
- Supraclavicular adenopathy.
- Systemic symptoms.

Cautions for lymph node biopsy :

- Avoid upper cervical and inguinal areas : Commonly d/t infections.
- Lower cervical and axillary nodes are more reliable.
- Largest node should be biopsied.
- Node should be removed intact with the capsule.
- Lymph node should be immediately submitted to the pathologist fresh or in sufficient tissue culture to prevent the tissue from drying out.
- The node must not be left in strong light (Subject to heat) and should not be wrapped in dry gauze (Drying) : may produce a drying artefact.
- Fresh and frozen samples should be set aside for additional studies, as noted later.

**Intracranial mass :**

Red flag signs of headache :

- Recurrent early morning vomiting.
- Headache that awakens the child from sleep.
- Incapacitating headache.
- Enlargement of head size (In infants).
- C/F associated with raised ICT (Intracranial tension).

| Risk group | Clinical definition | Probability of brain tumor % | Diagnostic strategy |
|---|---|---|---|
| Low | Headache >6 months and no neurologic symptoms. | 0.01 | No imaging. Clinical follow-up and medical treatment. |
| Intermediate | Migrane HA and no neurologic symptoms. | 0.4 | CT, MRI followed by biopsy or surgery. |
| High | Headache <6 months and one clinical predictor of space occupying lesion. | 4 | MRI followed by biopsy or surgery. |

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## Abdominal masses :

Palpable abdominal mass : m/c presenting feature.

Age of patient :

- Neonatal period : Congenital malformation of GI and GU system.
- Childhood : Malignant.

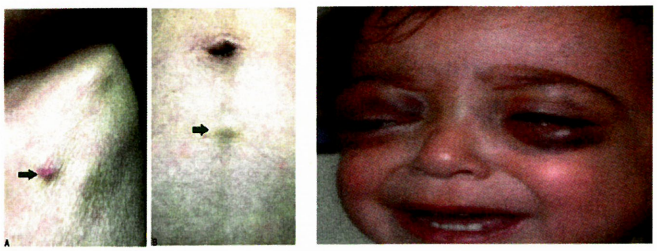
Site :

| Upper abdomen | mid abdomen | Lower abdomen |
|---|---|---|
| Neuroblastoma.<br>Wilms tumor.<br>Hepatoblastoma.<br>Lymphoma. | Lymphoma.<br>Sarcoma.<br>Germ cell tumor. | Germ cell tumor.<br>Sarcoma.<br>Lymphoma. |

History and physical examination :

Systemic symptoms :

- Periorbital ecchymosis (Racoon eyes).
- Subcutaneous nodules.
- Bone pains.



Subcutaneous nodules, periorbital ecchymosis.

Investigations :

- Ultrasound abdomen.
- Mass arising from liver : Serum alpha fetoprotein (AFP).
- Tumour markers : β-HCG.

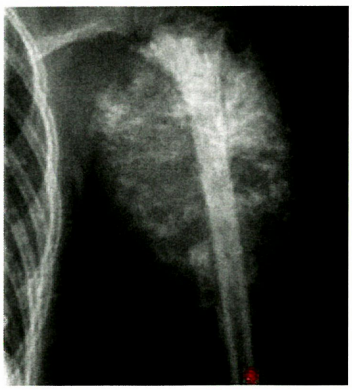
## Bone pain :

Localized bone pain with limping :

- Osteosarcoma.
- Ewing sarcoma.

Features of malignant bone tumor :

- Cortical erosion.
- Irregular mass.
- Periosteal reaction.
- White zone of transition.



Malignant bone tumor.

Diffuse bone pain is a cardinal feature of acute leukemia.

Differential diagnosis : Juvenile rheumatoid arthritis.

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| | Acute leukemia | JRA |
|---|---|---|
| Symptom manifestation | Worse at night. | Morning stiffness. |
| Involvement | Bones and joints. | Joints. |
| Constitutional symptoms | Present. | Present/absent. |

Acute leukemia vs juvenile rheumatoid arthritis (JRA).

## Mediastinal tumors

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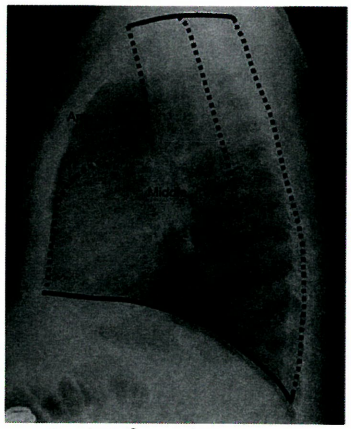
### Parts of mediastinum :



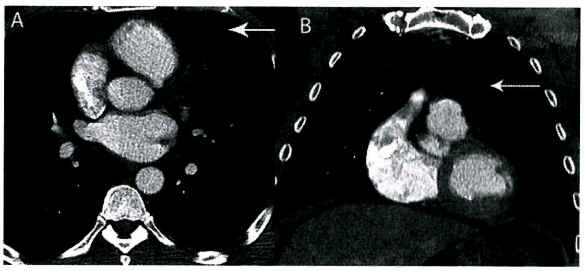
Parts of mediastinum.

Anterior mediastinum : Anteriorly by the sternum and posteriorly by pericardium.

Middle mediastinum : Between the anterior border of pericardium and an imaginary line drawn 1 cm posterior to the anterior border of the vertebral bodies.

Posterior mediastinum : Anteriorly by an imaginary line drawn 1 cm posterior to the anterior border of the vertebral bodies and posteriorly by the posterior paravertebral gutters.

Anterior mediastinal mass :




Anterior mediastinal mass.

| Benign | Malignant |
|---|---|
| Teratoma | Non-Hodgkin's lymphoma |
| Cystic hygroma | Hodgkin's disease |
| Haemangioma | Teratoma with yolk sac tumour |
| Thymic cyst | Seminoma |
| | Desmoid |
| | Sarcoma |
| | Thymoma |

Causes of anterior mediastinal mass.

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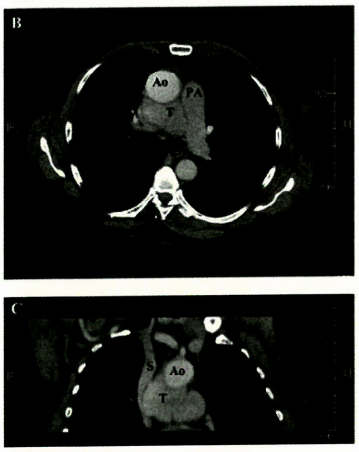
Middle mediastinal mass :

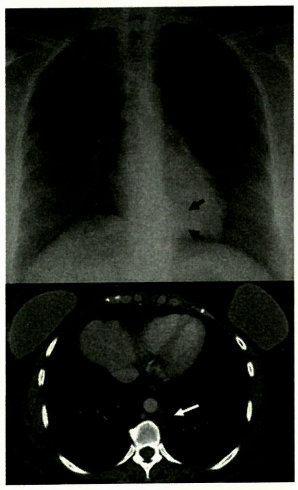



Middle mediastinal mass.

| Benign | Malignant |
|---|---|
| Bronchogenic cyst<br>(Tracheal duplication cyst)<br>Teratoma<br>Plasma cell granuloma<br>Cardiac rhabdomyoma | Hodgkin's disease<br>Non-Hodgkin's lymphoma<br>Teratoma<br>Rhabdomyosarcoma<br>Other sarcomas |

Causes of middle mediastinal mass.

Posterior mediastinal mass :



Posterior mediatinal mass.

| Benign | Malignant |
|---|---|
| Ganglioneuroma<br>Neurofibroma<br>Enterogenous cyst<br>Teratoma (Rare)<br>Lipoma<br>Leiomyoma | Neuroblastoma,<br>Ganglioneuroblastoma<br>Neurofibrosarcoma<br>Sarcoma<br>Liposarcoma<br>Leiomyosarcoma<br>Sarcoma |

Causes of posterior mediastinal mass.

## Lung tumors

00:26:03

- Primary malignancies of the lung and tracheobronchial tree : Rare.
- Inflammatory myofibroblastic tumor : m/c lung tumor in pediatrics.
- Bronchial carinoid : Intense contrast enhancement related to their fibrovascular stromal component.
- Mucoepidermoid carcinoma.
- Bronchogenic carcinoma.

### Pleuropulmonary blastomas (PPB) :

Type I :

- Purely cystic tumors occurring <2 years of age.
- Median age of 10 months, 5-year DFS : 90%.

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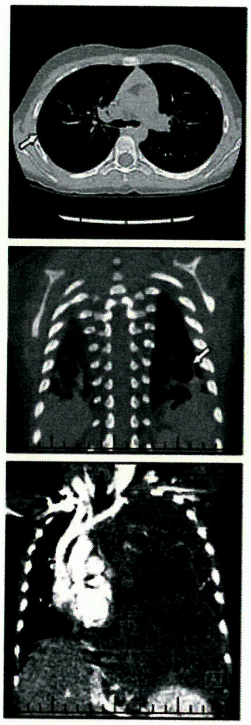
Type II :

- Cystic and solid tumors.
- Median age of 35 months.

Type III :

- Solid tumors, median age of 41 months.
- Surgical resection is recommended if feasible, followed by chemotherapy and/or radiation therapy, intracavitary chemotherapy.
- 5-year DFS : 50-60%.
- Associated with germline pathogenic DICER1 variants.
- Susceptible to other tumors :
  - Cystic nephromas.
  - Ovarian stromal sex cord tumors.
  - Thyroid and other endocrine tumors.
  - Embryonal rhabdomyosarcoma.
  - Brain tumors.



Pleuropulmonary blastomas.

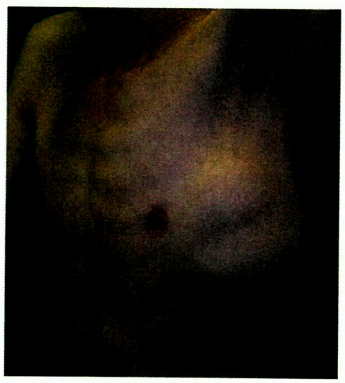
## Chest wall tumors

00:27:22

May arise from bone or soft tissues.
m/c : metastatic rib lesions (Neuroblastoma, Langerhans cell histiocytosis, lymphoma, leukemia).

m/c paediatric chest wall primary malignancies :

- Rhabdomyosarcoma.
- Extraosseous Ewing sarcoma.
- PNET of the chest (Askin tumor).



Chest wall tumor.

Primary bone malignancies :

- Ewing sarcoma.
- Osteosarcoma.

May arise from the ribs, thoracic vertebrae, or scapulae and manifest as chest wall masses.

Non malignant chest wall masses :

- Neurofibromas.
- Hemangiomas, vascular malformations.

- Aneurysmal bone cysts.
- Osteochondromas.
- Healing rib fractures.
- Osteomyelitis.
- Developmental variations of the thoracic cage.

### Indications of immediate evaluation of back pain :

- Bowel/bladder dysfunction.
- Paresis.
- Gait abnormalities.
- Paraesthesia.

Risk of spinal cord compression : Emergency.

Immediate MRI scanning.

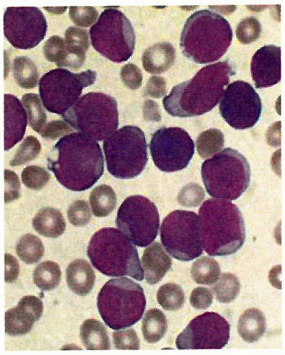
Start dexamethasone.

## Peripheral blood abnormalities

00:29:33

### Investigations :

1. Complete blood counts :
   - Pancytopenia/bicytopenia.
   - Leukocytosis.



Blast cells on PS.

2. Peripheral smear (PS) : Presence of blasts.

3. Bone marrow studies :

Indications for bone marrow studies :

- Patients with pancytopenia/more than one depressed cell line.
- Presence of blasts on peripheral smear.
- Presence of leucoerythroblastic changes on PS.
- Association with unexplained lymphadenopathy, bone pain, or hepatosplenomegaly.
- Association with an anterior mediastinal mass.

Diagnosis of leukemia :

- ≥20% bone marrow lymphoblasts in bone marrow study.
- Peripheral blood sample may be substituted if a sufficient level of circulating lymphoblasts is present.

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Stains to distinguish lymphoblasts from myeloblasts :

- Wright-Giemsa-stained bone marrow aspirates.
- Hematoxylin and eosin (H&E) stained biopsies.

Features of lymphoblast :

- High nucleus-to-cytoplasm ratio.
- Absence of nucleoli.
- Smaller size.

4. Flow cytometry.

5. Immunophenotyping :

B cells : CD10, CD19, CD20, CD45, kappa, lambda.

T cells : CD2, CD3, CD4, CD5, CD7, CD8, CD45.

myelomonocytic cells : CD11b, CD13, CD14, CD15, CD16, CD33, CD34, CD45, CD117, HLA-DR.

6. Chromosomal analysis and banding :

Essential for the identification of aneuploidy, microscopic chromosomal anomalies, and some translocations.

Common translocation in ALL :

- t(12 ; 21) : m/c translocation in childhood ALL, favorable prognosis.
- t(1 ; 19) : Bad prognosis.
- t(9;22) : very poor outcome.
- 11q23 rearrangements : Poor outcome.
- t(5;14).

Used for risk stratification.

Note :

In case of suspicion of leukemia, do not give steroids during a blood transfusion or in case of transfusion reaction as it can delay the diagnosis.

## Modalities of treatment :

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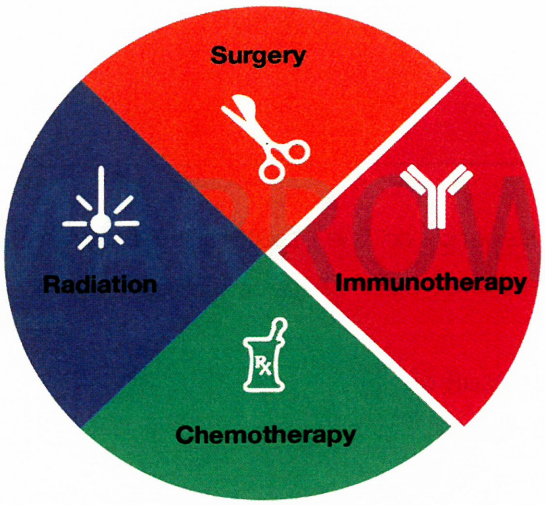


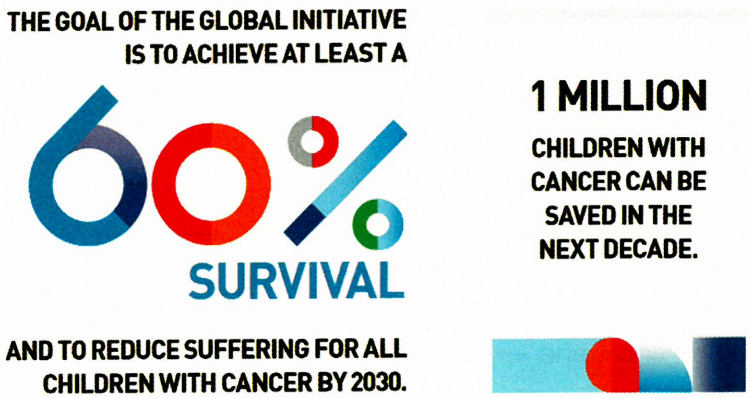


## Key home message :

- Childhood cancer is a highly curable disease.
- Increase awareness about symptoms and signs of childhood cancer.
- Early diagnosis.
- Early referral to the pediatric oncology unit.

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# EPIDEMIOLOGY AND MOLECULAR BIOLOGY OF PAEDIATRIC CANCER

## Introduction

00:00:17

Tissue homeostasis depends on the regulated cell division and self-elimination (Programmed cell death) of each of its constituent members except its stem cells.

A tumor arises as a result of :

- Uncontrolled cell division.
- Failure for self-elimination.

Alterations in genes responsible for the deregulated control mechanisms that are the hallmarks of cancer cells :

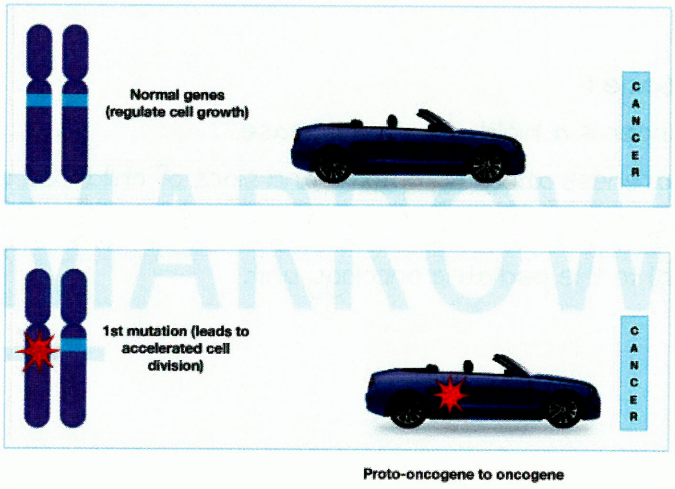
- Proto-oncogenes.
- Tumor supressor genes.
- DNA stability genes/DNA repair genes.

## Genes involved

00:01:18

### Oncogenes :

It is a proto-oncogene → Mutated → Leads to signals that cause uncontrolled growth i.e., cancer.




mechanism of oncogenes