Paediatric Hemato-Oncology

MARROW
Super Speciality

Instructions

- The notes must be used in conjunction with the Marrow SS Paediatrics videos and should not be considered standalone material.

Please note:

- The information in this book has been printed based on the transcript of the Marrow SS Paediatrics videos.
- The information contained in this book is for educational purposes only. The content provided is not intended to substitute for professional medical advice, diagnosis or treatment.
- This book cannot be sold separately. It has been made available to only select eligible users who have an active subscription to Marrow SS Paediatrics videos.
- The text, images, slides, and other materials used in this book have been contributed by the faculty, who are subject matter experts. We have merely reproduced them as video transcripts in this book.
- The notes have been consciously designed in a way that is concise and revisable. To ensure this, we have intentionally added only the most relevant modules and images that are needed for you.
- Reasonable care has been taken to ensure the accuracy of the information provided in this book. Neither the faculty nor Marrow takes any responsibility for any liability or damages resulting from applying the information provided in this book.
- This set contains notes of all main videos published in the app until October 2025. You can find notes for any additional videos published after this date within the app under the videos section.

All Rights Reserved

No part of this publication shall be reproduced, copied, transmitted, adapted, modified or stored in any form or by any means, electronic, photocopying, recording or otherwise.

© Marrow

// ME811-PPL

Contents

Basics of Paediatric Oncology

1. Basics of Paediatric Oncology 1
2. Epidemiology and Molecular Biology of Paediatric Cancer 11
3. Principles of Cancer Therapy 25
4. Chemotherapy 43

Malignant Haematological Disorders

5. Paediatric ALL 59
6. Paediatric AML 67
7. CML and JMML 73
8. Hodgkin Lymphoma 88
9. Non-Hodgkin's Lymphoma 102

Benign Haematological Disorders

10. Approach to Child With FN 111
11. Macrocytic Anaemia 117
12. Iron Deficiency Anaemia 129
13. Immune Thrombocytopenia 143
14. Lymphadenopathy and Splenic Disorders 162
15. Aplastic Anaemia 182
16. Hemolytic Anaemias 194
17. IBMFS 215
18. Hemophilia 232
19. Thalassemia 251
20. Sickle Cell Disease 272
21. Von Willebrand Disease 296

22. Disseminated Intravascular Coagulation 310
23. Polycythemia 327

Systemic Paediatric Oncology

24. Neuroblastoma 341
25. Wilms Tumor 353
26. Retinoblastoma 363
27. Hepatic Tumors in Paediatrics 379
28. Brain Tumours : Part I 389
29. Brain Tumors : Part II 405
30. Osteosarcoma 423
31. Soft Tissue Sarcoma 435
32. Ewing Sarcoma 444
33. Paediatric Germ Cell Tumour 450

HSCT

34. Basics of HSCT 467
35. Complications of HSCT 480

Oncologic Emergencies

36. Oncological Emergencies 495

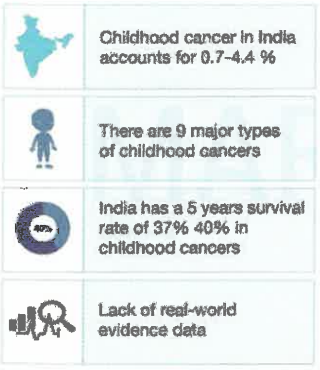
BASICS OF PAEDIATRIC ONCOLOGY

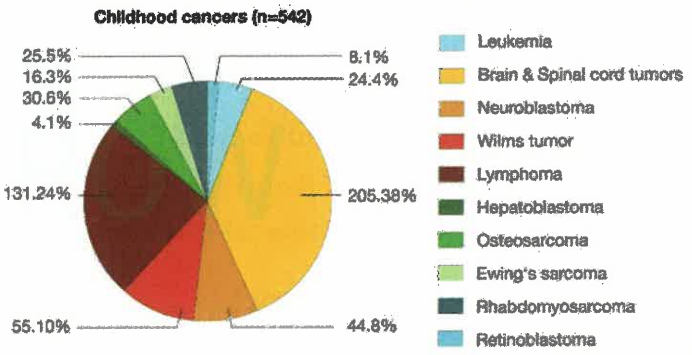
----- Active space -----

Introduction

00:00:23

Statistics :





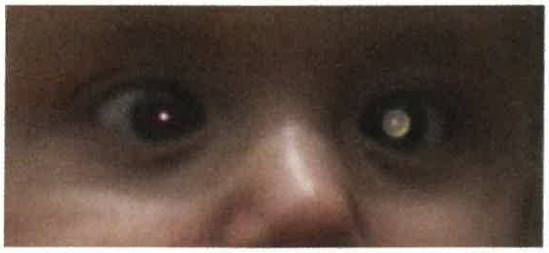
- 80% of children with cancer will survive in high-income countries.
- Only about 20% of children with cancer will survive in some low and middle income countries.

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 leukaemia/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.

Example : Retinoblastoma.

- Early diagnosis : 100% survival rate.
- Late diagnosis (Extraocular retinoblastoma) : 20-30% survival rate.



Loss of red reflex : Early retinoblastoma

Extraocular retinoblastoma (Late)

----- Active space -----

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 :

- Infections :
  - EBV infection : Hodgkin Lymphoma, Burkitt lymphoma, post transplant lymphoproliferative disorder (PTLD), nasopharyngeal cancer.
  - HIV : Kaposi sarcoma, B cell lymphoma.
  - Hepatitis B and C : Hepatocellular carcinoma.
  - HPV : HPV associated cancer (Vaccines are available).
- Immunodeficiency syndromes.
- Patients receiving immuno-suppressive therapy : Higher risk of malignancy (PTLD and lymphomas).
- Paediatric solid organ transplant recipients who are on prolonged thiopurine therapy (PTLD).
- Childhood cancer survivors.
  - Exposure to alkylating agent, anthracycline, topoisomerase inhibitors.
  - Exposure to radiation.

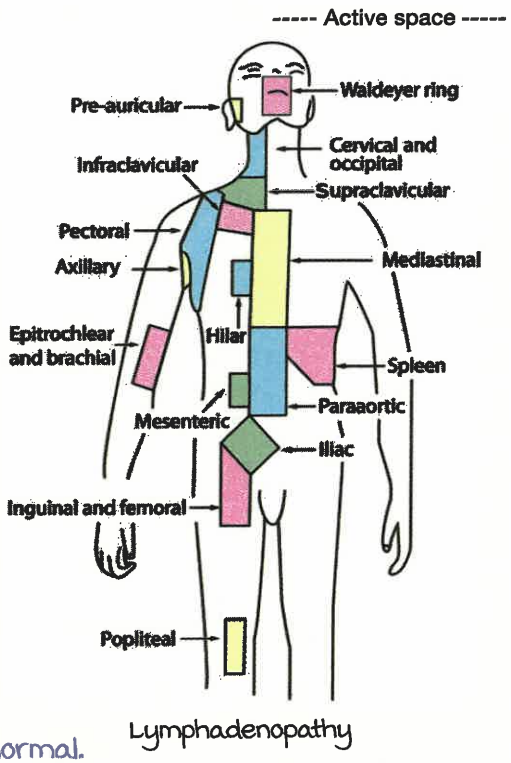
Signs and symptoms 00:10:31

Fever :

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

Lymphadenopathy :

m/c cause : Reactive hyperplasia (Benign).



Lymphadenopathy

Enlarged lymph node could be due to :

- Intrinsic cellular components.
- Extrinsic cellular infiltration.

Significant lymphadenopathy :

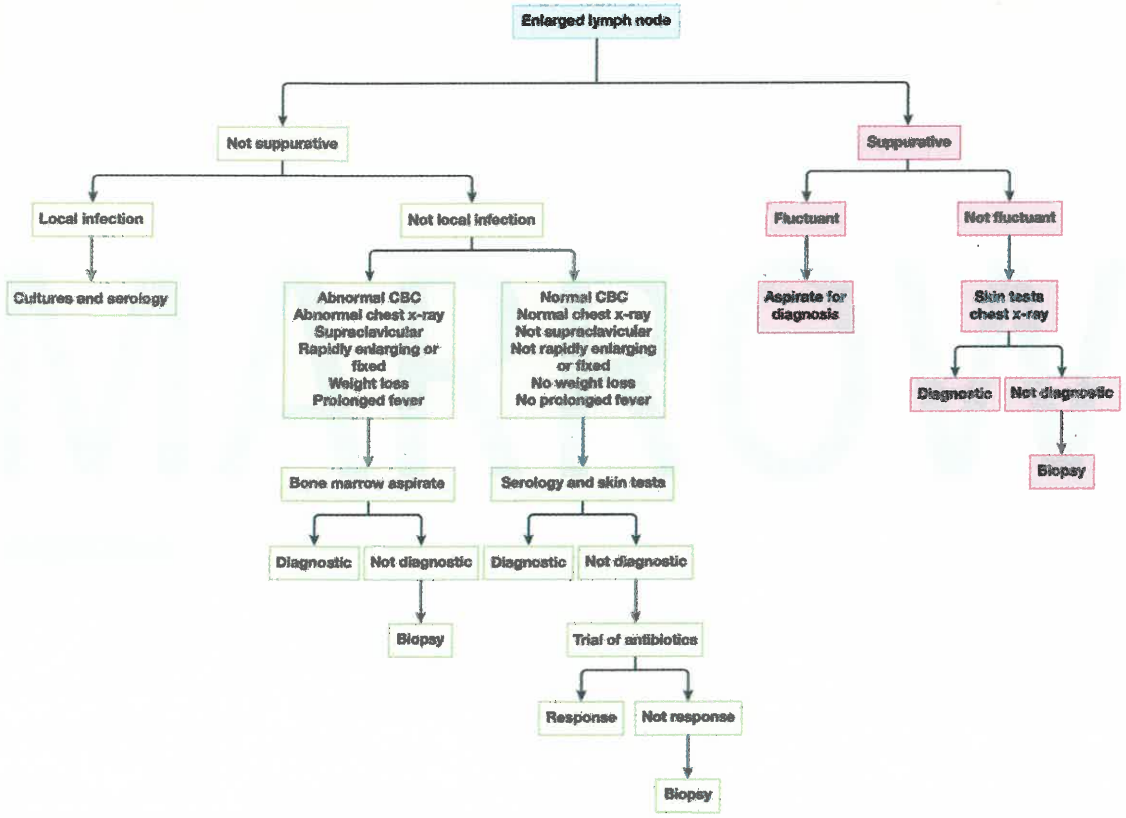
- Cervical >1 cm.
- Supraclavicular nodes.
- Axillary >1 cm.
- Epitrochlear >0.5 cm.
- Inguinal >1.5 cm.

Generalized lymphadenopathy : Significant lymphadenopathy of 2 or more non-contiguous 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.

Evaluation of patients with lymphadenopathy :



----- Active space -----

Lymph node biopsy :

Indications :

- 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.

Note :

Most common malignancies which presents with lymph adenopathy include : Leukaemia/lymphoma (NHL/HL).

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 & medical treatment
Intermediate	Migrane HA & 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

----- Active space -----

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 Wilms tumor Hepatoblastoma Lymphoma	Lymphoma Sarcoma Germ cell tumor	Germ cell tumor Sarcoma Lymphoma

History and physical examination :

Systemic symptoms :

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

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.

Malignant bone tumor

Features of malignant bone tumour :

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

Diffuse bone pain is a cardinal feature of acute leukaemia.

Differential diagnosis : Juvenile rheumatoid arthritis.

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

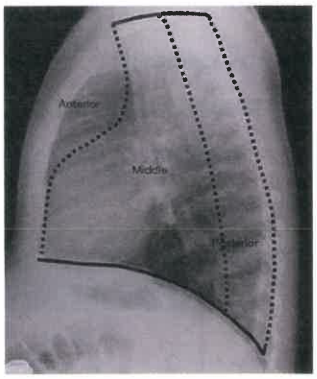
----- Active space -----

Mediastinal tumors

00:23:11

Parts of mediastinum :

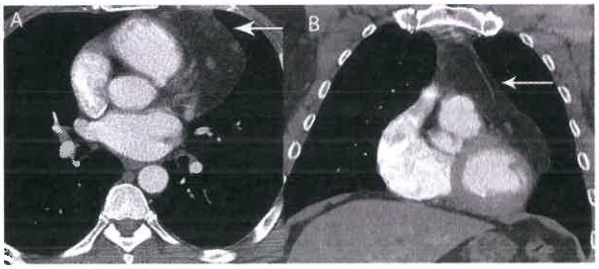
- Anterior mediastinum : Anteriorly by sternum & posteriorly by pericardium.
- Middle mediastinum : Between the anterior border of pericardium and an imaginary line drawn 1 cm posterior to the anterior border of the vertebral bodies.
- Posterior mediastinum : Anteriorly by an imaginary line drawn 1 cm posterior to the anterior border of the vertebral bodies and posteriorly by the posterior paravertebral gutters.



Parts of mediastinum

Anterior mediastinal mass :

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



Anterior mediastinal mass

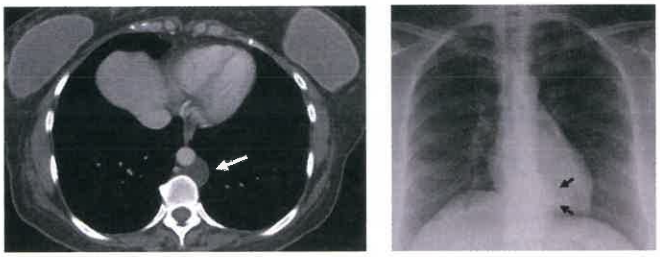
Middle mediastinal mass :

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

Middle mediastinal mass

Posterior mediastinal mass :

Benign	Malignant
• Ganglioneuroma • Neurofibroma • Enterogenous cyst • Teratoma (Rare) • Lipoma • Leiomyoma	• Neuroblastomaw • Ganglioneuroblastoma • Neurofibrosarcoma • Sarcoma • Liposarcoma • Leiomyosarcoma • Sarcoma


Posterior mediastinal mass

Lung tumors

00:26:03

----- Active space -----

Overview :

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

Pleuropulmonary blastomas (PPB) :

Type I :

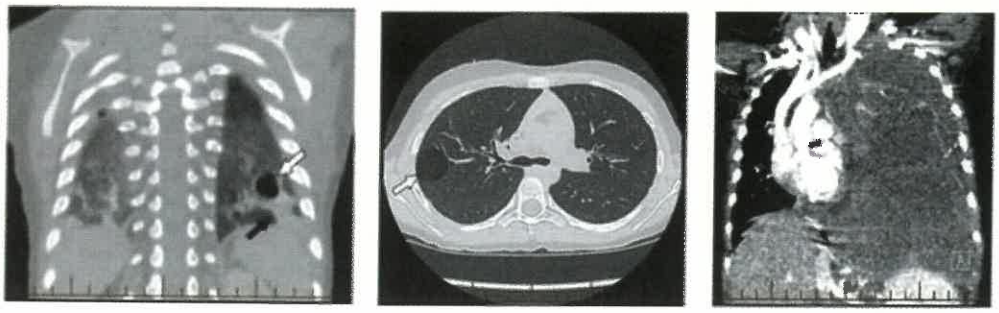
- Purely cystic tumours occurring <2 years of age.
- Median age of 10 months, 5-year DFS : 90%.

Type II :

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

Type III :

- Solid tumours, 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 tumours :
  - Cystic nephromas.
  - Ovarian stromal sex cord tumours.
  - Thyroid and other endocrine tumours.
  - Embryonal rhabdomyosarcoma.
  - Brain tumours.



Pleuropulmonary blastomas

----- Active space -----

Chest wall tumors

00:27:22

Overview :

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

Malignant chest wall masses :

Chest wall tumor

m/c paediatric chest wall primary malignancies :

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

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.

Approach :

CT/MRI, followed by biopsy.

Indications of immediate evaluation of back pain :

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

Risk of spinal cord compression : Emergency.

Immediate MRI scanning.

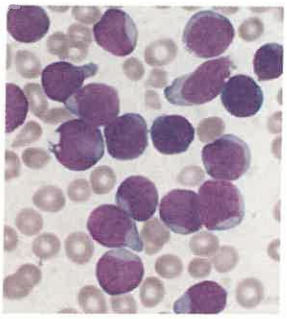
Start dexamethasone.

Peripheral blood abnormalities

00:29:33 ----- Active space -----

Investigations :

- Complete blood counts :
  - Pancytopenia/bicytopenia.
  - Leukocytosis.
- Peripheral smear (PS) : Presence of blasts, high N:C ratio.
- Bone marrow studies :



Blast cells on PS

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 leukaemia :

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

Flow cytometry.

- 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.
- Chromosomal analysis and banding :
  - Essential for the identification of aneuploidy, microscopic chromosomal anomalies, and some translocations.

----- Active space -----

Common translocation in ALL :

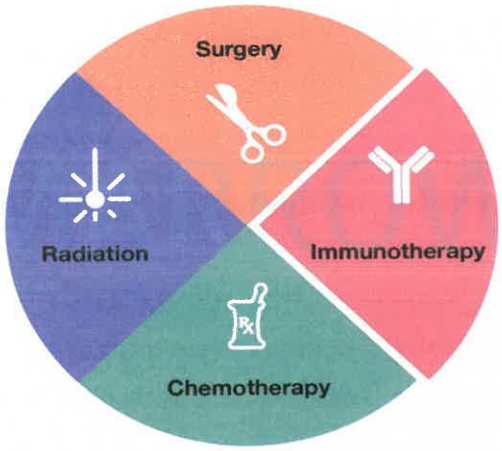
- t(12 ; 21) : m/c translocation in childhood ALL, favourable prognosis.
- t(1 ; 19) : Bad prognosis.
- t(9;22) : Very poor outcome.
- 11q23 rearrangements : Poor outcome.
- t(5;14).

Used for risk stratification.

Note :

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

Modalities of treatment :



Note :

The goal of WHO global initiative is to :

Achieve at least a 60% cancer survival and to reduce suffering of all children with cancer by 2030.

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 paediatric oncology unit.

EPIDEMIOLOGY AND MOLECULAR BIOLOGY OF PAEDIATRIC CANCER

----- Active space -----

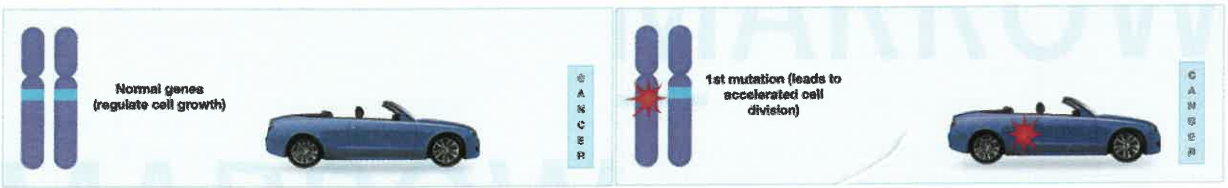
Introduction 00:00:17

- 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 suppressor genes.
  - DNA stability genes/DNA repair genes.

Genes involved 00:01:18

Oncogenes :

Proto-oncogene → Mutation → Signals causing uncontrolled growth i.e., cancer.



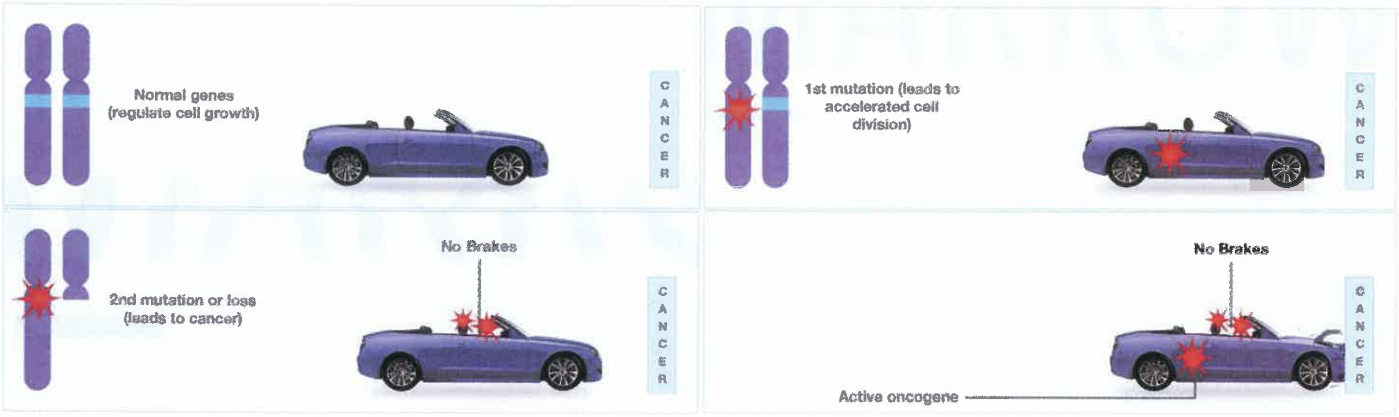
Proto-oncogenes to oncogenes

Important oncogenes	
Oncogene	Function
HER-2/neu	Encodes cell surface receptor that stimulate cell division
	Amplified in up to 30% of human breast cancers
RAS	Involved in Kinase signalling pathways → Controls transcription of genes, regulating cell growth and differentiation
MYC	Encodes transcription factor & controls expression of several genes
SRC	First oncogene ever discovered
	Is a tyrosine Kinase → Regulates cell activity
hTERT	Codes for telomerase → Maintains chromosome ends

----- Active space -----

Tumor suppressor gene :

- Segments of DNA that code for negative regulator proteins which keep the cell from undergoing uncontrolled division.
- Braking signals during phase G1 of the cell cycle, to stop or slow the cell cycle before S phase.
- Mutations in tumor suppressor genes cause loss-of-function, resulting in uncontrolled cell growth, i.e, cancer.



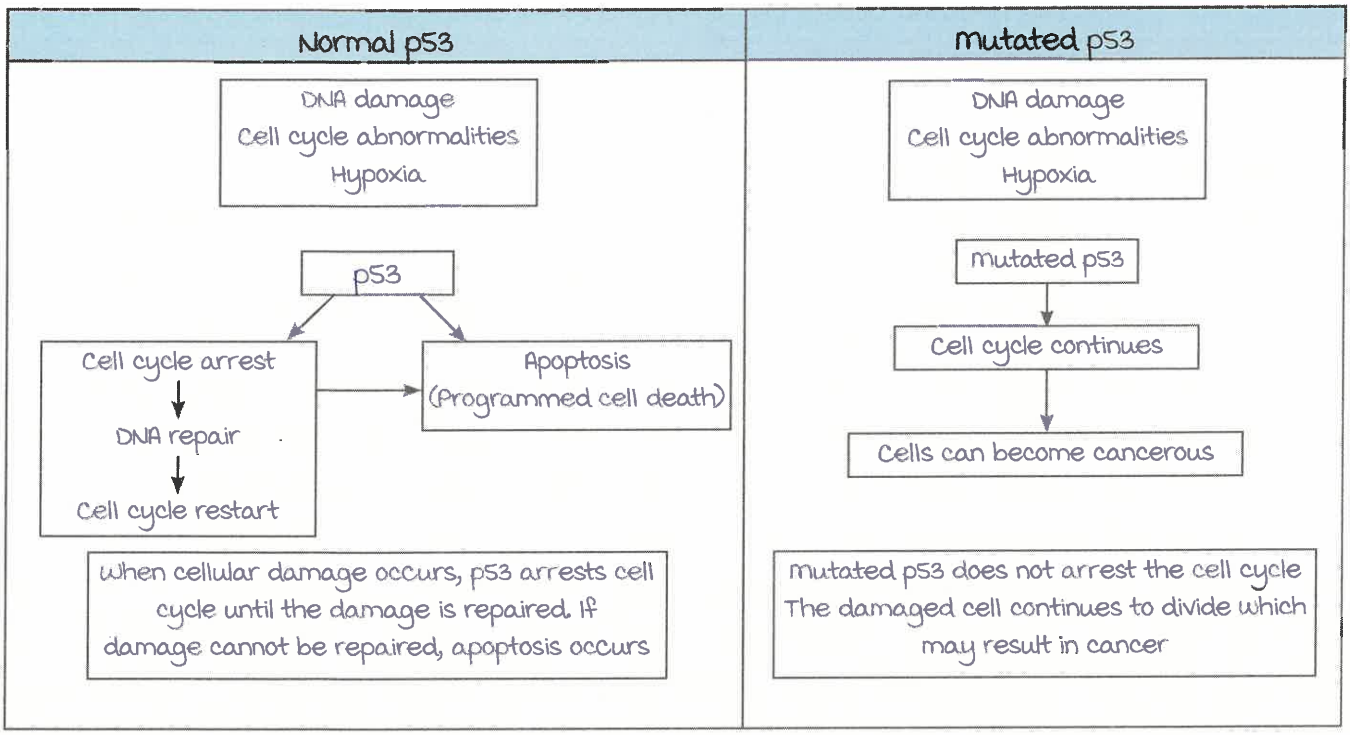
Tumor suppressor genes are normal genes whose absence leads to cancer

Examples of cancer predisposition genes and their associated syndromes :

Tumor suppressor gene	Syndrome	Tumor
Rb	Retinoblastoma	Retinoblastoma
WT 1	Familial Wilm's tumor	Wilm's tumor
NIF 1	Neurofibromatosis type 1	Neurofibroma, sarcoma
NIF 2	Neurofibromatosis type 2	Schwannoma, meningioma
APC	Familial adenomatosis polyposis	Tumors of colon, stomach and intestine
p53	Li-Fraumeni syndrome	Breast, lung, brain tumors, sarcoma
VHL	Von Hippel-Lindau disease	Tumors of kideny, adrenal
E-CAD	Familial gastric cancer	Tumor of stomach, breast
PTCH	Gorlin syndrome	Basal cell carcinoma
PTEN	Cowden syndrome	Hamartoma
MEN 1	Multiple endocrine neoplasia	Tumors of pituitary, pancreas and parathyroid

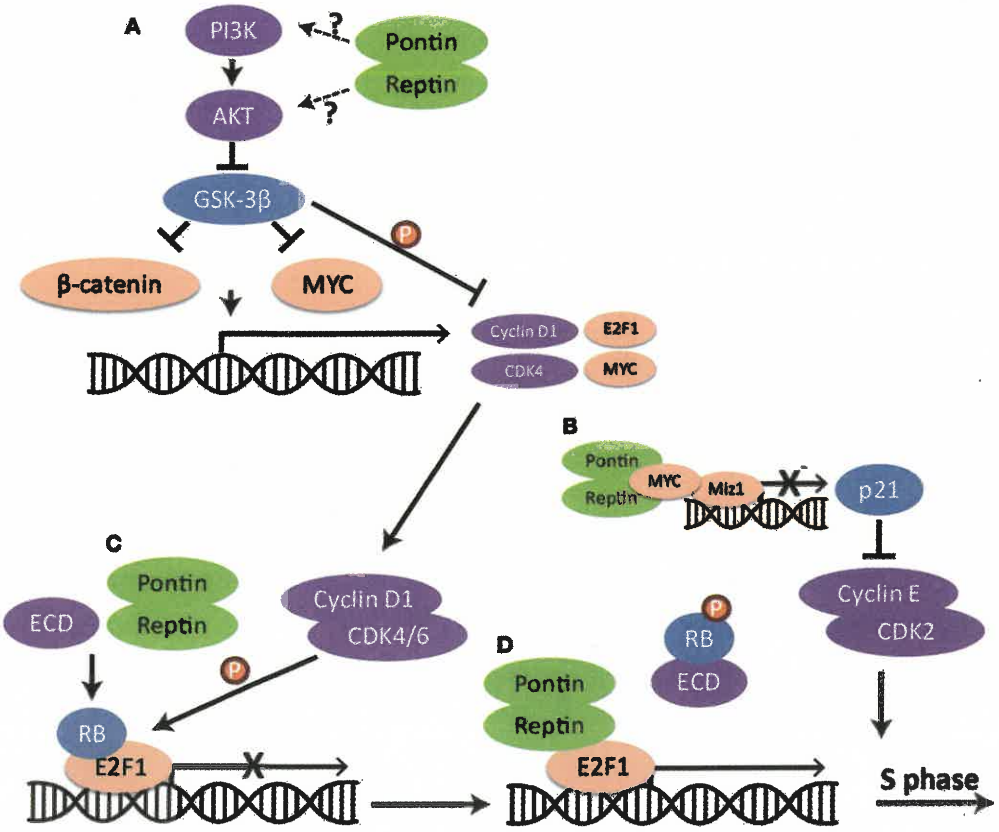
P53 gene :

----- Active space -----



Rb gene :

Also known as 'governor of the genome'.



mechanism of Rb gene

----- Active space -----

Mechanism :

- Rb is phosphorylated by cyclin D/CDK4/6 complexes as cells leave G0 phase and enter the cell cycle.
- Moving through G1 phase, Rb becomes progressively more phosphorylated until R is reached.
- Hyperphosphorylated Rb : Unable to bind & inhibit its primary target, the E2F transcription factors.
- Derepressed E2Fs are free to up regulate expression of cell cycle related genes, cyclins E/A and CDK1.
- Beyond the R point, Rb remains hyperphosphorylated throughout cell cycle until dephosphorylated by protein phosphatase type 1 (PP1) at end of mitosis.
- Homozygous deletions of Rb are necessary for the genesis of Rb.
- Rb gene mutations are also seen in :
  - Subsets of osteosarcoma.
  - Burkitt lymphoma.
  - Glioblastoma multiforme.

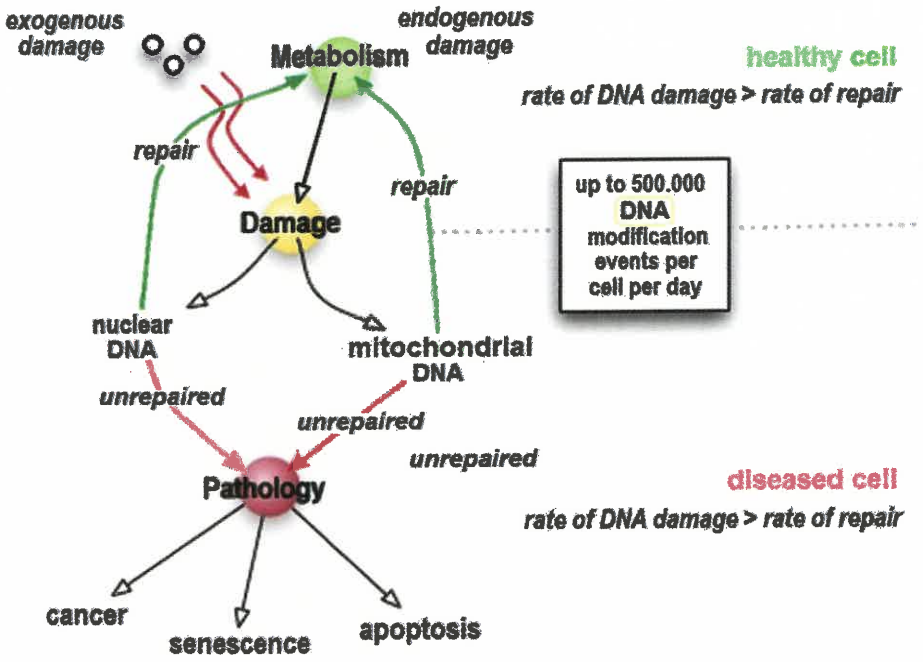
Difference between tumor suppressor genes and oncogenes :

Property	Tumor suppressor genes	Oncogenes
Alleles mutated in cancer	Both alleles	One allele
Germline transmission of mutant alleles	Frequently seen	Rare
Somatic mutation involved in tumor formation	Yes	Yes
Function of mutant allele(s)	Loss of function (Recessive allele)	Gain of function (Dominant allele)
Effects of cell growth	Inhibit cell growth	Promote cell growth

DNA repair genes :

- Code for proteins that function to correct errors that arise when cells duplicate their DNA prior to cell division.
- Active throughout the cell cycle, particularly during G2 phase.
- Eg : BRCA 1 and BRCA 2.

----- Active space -----



BRCA I and BRCA mechanism

Hallmark of cancer

00:09:16

The important hallmarks are :

- Sustained proliferative signaling.
- Evading growth receptors.
- Avoiding immune destruction.
- Enabling replicative immortality.
- Tumor promoting inflammation.
- Activating invasion and metastasis.
- Tumor angiogenesis.
- Genome instability and mutation.
- Resisting cell death.
- Deregulating cellular metabolism.

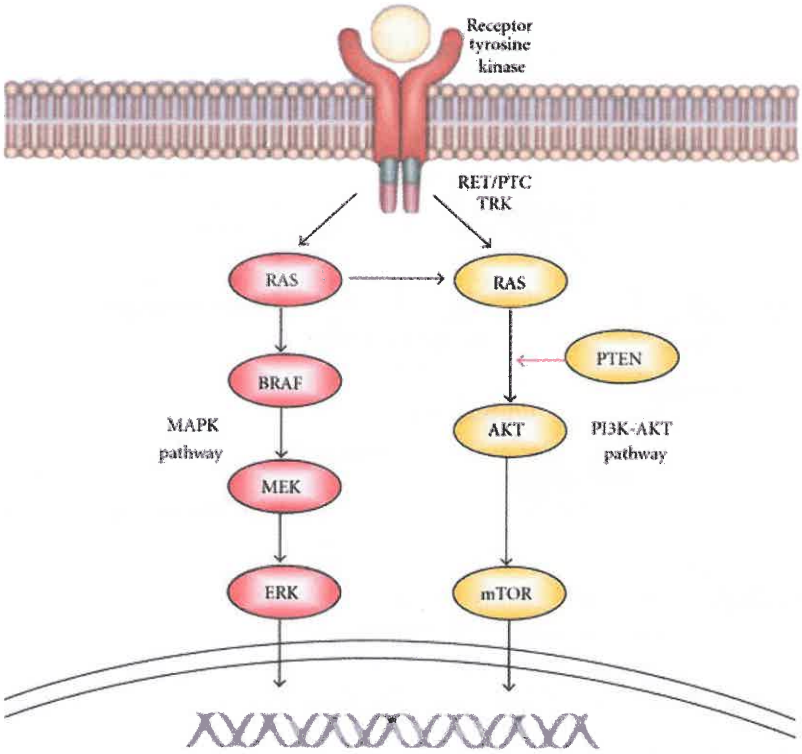
Sustained proliferative signaling :

Normal cells carefully control growth and division.

Cancer cells deregulate these signals of cell proliferation by :

- Synthesis of growth factors (Autocrine stimulation). E.g. : PDGF and TGF-β .
- Over express receptors E.g. EGFR.
- Show ligand-independent receptor activation by structural changes.
- Express different extracellular receptors.
- Independent from growth factors.
- Activation of downstream signaling pathways or the disruption of negative feedback mechanisms.

----- Active space -----



Mechanism of cell proliferation by RAS gene

Antiproliferation :

- Normal tissues have multiple antiproliferative signals.
  Eg : Soluble growth inhibitors and immobilized inhibitors embedded in extracellular matrix & on surfaces of surrounding cells → These signals transition cell out of cell cycle to resting state (G0).
- Cancer cells evade the growth suppressor genes.
  E.g. : Rb and p53 gene → Overrule initiation or "turning off" of cell division.

Enabling replicative immortality :

- Normal cells → Limited replicative potential. After a number of divisions, they stop growing (Senescence).
- Mechanism of senescence : Due to limited number of telomeres (Restricting number of divisions).
- Telomerase adds hexanucleotide repeats (-TTAGGG) to end of telomeric DNA and prevent telomer shortening.
- Tumor cells have high telomerase enzyme → Telomere shortening prevented → Unrestricted cell division.