Surgical Oncology

Volume - 1

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- This set contains notes of all main videos published in the app until August 2025. You can find notes for any additional videos published after this date within the app under the videos section.

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PRINCIPLES OF CANCER STAGING

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Introduction

00:00:10

Purpose : To know the extent of the disease.

TNM Staging :

- Most widely used staging system (Anatomical staging system).
- 3 components : TNM.

T category (Primary tumour) :

- Invasive : T1/T2/T3/T4.
- Others : TX/T0/Tis.

N category : Regional Lymph nodes (LN).

- N0 : No nodes.
- N1.
- N2.
- N3.

M category : Distant metastasis.

- M0 : No distant metastasis.
- M1 : Distant metastasis present (Has sub-categories like a, b, c, d).

Note : It is an evidence based system (Upper stage → ↓ Survival).

Eg., Breast cancer :

- T1 : <2 cm. T2 : 2-5 cm. T3 : >5 cm.
- 1.8 cm and 1.9 cm tumours : No difference in survival.
- 1.9 cm and 2.1 cm tumours : Sharp difference in survival.
- Therefore cut-off for upper stage is 2 cm.

Staging groups :

Group	Based on	
cTNM	• Clinical/radiological examination • Surgical exploration without resection	
pTNM	Pathology of resected tumour	
yTNM	Post-Neoadjuvant therapy (NACT)	
	ycTNM	Clinical/radiological examination post-NACT
	ypTNM	Pathology of resected tumour post-NACT
rTNM	Recurrence	
	rcTNM	Clinical/radiological examination of recurrence
	rpTNM	Pathology of resected tumour of recurrence
aTNM	Autopsy (incidental detection)	

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TNM staging

00:09:40

T Primary tumor	N (Regional nodes)	M (Distant metastasis)
Tx : Cannot be assessed/information not available. • Eg., Primary tumour operated elsewhere with no records. • Extensive tumour where the 1° cannot be identified. T0 : No primary tumour. Tis : in situ. T1–T4 : invasive.	Nx : Cannot assess. N0 : No nodes. N1– N3 : Nodes present	M0 : No distant metastasis. M1 : Distant metastasis.

Multiple tumours :

Highest T mentioned

E.g., breast cancer : 3 tumours are present with largest being 6 cm.

- Staging : pT3 (m)/N0/M0 (or) pT3 (3)/N0/M0 where (m) means multiple.
- Actual number of tumours can also be specified like (3).

Synchronous Vs. Metachronous :

- Cut-off is 4 months.
- <4 months is synchronous and >4 months is metachronous.

Unknown primary :

- Evidence of nodal spread is present, expected primary site doesn't show up.
- Categorised as T0.
- Example. :
  - Axillary nodes present, no primary seen in breast, clinically → cT0.
  - Mastectomy is done and no primary is found → pT0.
  - Staging (As per suspected 1° site) → Ca. Breast, T0/N1/M0, Stage II.

Regional nodes :

Sentinel node :

- Represented as (sn).
- If only sentinel node biopsy is done then (sn) can be used.
- If complete dissection is done, then (sn) cannot be used.

FNAC proven nodes :

- Represented as (f).
- Eg.: FNAC proven N1 : pN1 (f).

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

Isolated tumour cells :

- Cluster of <200 cells.
- Size <0.2 mm.
- Represented as (i+). Eg.: pN1 (i+).
- It represents in-transit disease & not something that stations & proliferates.
- It is not considered as node positive.
- Except : Isolated cells are also considered node positive.
  - Melanoma.
  - Merkel cell carcinoma.

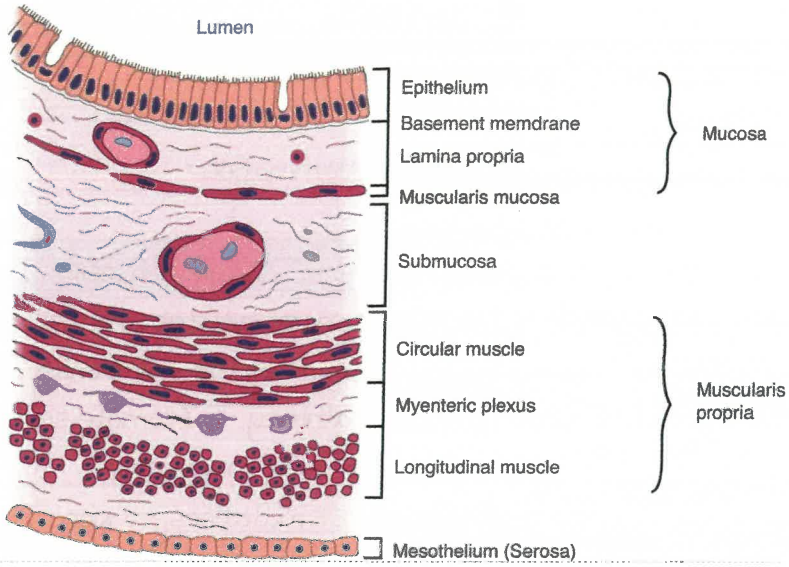
Stage 0 :

In situ and non-invasive cancers.

- Area below the serosa : Subserosa.
- If serosa is absent, it is called adventitia.

Definition :

- Non-invasive : Disease has not crossed basement membrane of epithelium.
- in situ : Disease has not attained spread potential.



Layers of GIT

In situ :

- Not crossed a boundary to attain spread.
- Boundary can be :
  - Basement membrane : Oral cavity.
  - Muscularis mucosa : Colon.
- No potential to spread.
- Nodal/Distant assessment not needed.

Complete pathological response :

- Seen when tumour disappears after NACT.
- Represented as : ycT0/N0/M0.

Non-invasive :

- Represented as Ta.
- Eg.: Bladder cancer : pTa/N0/M0.

DCIS :

- Can have nodal spread.
- invasive component maybe missed on pathology.

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ETIOLOGY OF CANCER I

Introduction

00:00:10

Factors responsible for carcinogenesis :

Inflammation :

Rudolf Virchow proposed that lymphoreticular infiltrate in a tumor originates from chronic inflammation.

Types of inflammation :

Tumor intrinsic	Tumor extrinsic
Cancer initiates and amplifies the inflammatory pathway → Promote survival growth & invasion	Macroscopic environment of tumor contributes to carcinogenesis
RET mutations → Non invasive follicular thyroid neoplasm → Promotes tumor development (Promotion of inflammatory pathway)	
E.g. : • Aflatoxin & aspergillus causing HCC. • RET mutations.	E.g. : • C/c pancreatitis → Pancreatic carcinoma • H pylori → Stomach cancer • GERD → Esophageal ca • Hepatitis → HCC

Infections causing cancer :

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Long standing infections can cause cancer.

Cancer	Infection
Bladder cancer	Schistosoma hematobium
Burkitt's lymphoma	EBV
Cervical cancer	HPV
Cholangiocarcinoma	Salmonella typhi, opisthorchis viverrini, clonorchis sinensis
Colorectal cancer	JC virus, Streptococcus bovis
Glioma	JC virus
HCC	Hepatitis B, C, D, Schistosoma japonicum, aflatoxin
Hodgkin's lymphoma	EBV
Merkel cell cancer	Merkel cell polyoma virus
Mesothelioma	SV 40
Adult T cell leukemia/lymphoma	HTLV I
Prostate cancer	Xenotropic murine leukemia virus

Inflammatory Mediators

00:08:48

Cytokines :

- Cytokines have a role in interaction b/w tumor & host immune cells.
- Cytokines are further divided into :
  - Chemokines.
  - Interleukins : IL-1, IL-6, IL-8, IL-17.
  - Interferons : I (α & β), II (γ), III ($\Delta 1, \Delta 2$ & $\Delta 3$).
  - Prostaglandins.
  - TNF α.
- TNF : 1° mediator of inflammation.

NFKB pathway :

- Major role in cancer.
- Activator : TNF.
- Initiation & transformation.

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Inflammation → Cytokines → Inflammatory cells → Oxidative damage, DNA mutation → Microenvironment in tissue is more conducive to increased cell growth, survival & transformation.

Survival of cell :

Pro-inflammatory cytokines :

- IL-1β, IL-8, TNFα & CRP.
- Increase in their levels results in reduced survival (Poor prognosis).
- STAT 6 & STAT 3 high expression showed inverse association of survival in mesothelioma.

Invasion :

- mmp 9 (matrix metalloproteinase 9) :
  - Gelatinase which degrades type IV collagen.
  - High expression shows poor prognosis (High chance of tumor invasion).
- HIFα : Increased vascular invasion in HCC → Poor prognosis.
- Cathepsin D : Increased association in inflammatory breast cancer.

Angiogenesis :

Pro-angiogenic factors
TNFα
IL-1β
IL-8

Factors for metastasis
VEGF
FGF 2
PDGF
ICAM-1
VCAM-1
E-selectin
P-selectin
mmp 9

Factors for angiogenesis
MIF : endothelial cell activation
TGFβ
Angiopoietin-2

Molecular mechanism of carcinogenesis 00:18:05

NFKB pathway : Protumorogenic.

C/c inflammation → EMT (Epithelial mesenchymal transformation) activation → Increased cell survival by promoting anti-apoptotic proteins → MYC & BCL-XL.

Extracellular matrix remodelling by mmp & VEGF.

STAT 1 & 3 : Persistent STAT 3 → Tumor inflammatory signal + NFKB → Tumor cell survival & angiogenesis

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Inflammasome :

- Silica & asbestos can trigger inflammasome.
- Activates IL-1β & IL-8 and other mediators (Pro-inflammatory).

Toll like receptors (TLR) :

- Role in :
  - Host defense mechanism.
  - Tissue injury.
- C/c inflammation → C/c TLR pathway activation → Carcinogenesis.

Chemical factors

00:23:09

Scrotal cancer in chimney sweepers : First environmental cancer discovered by Percivall Pott.

Cancer	Chemical factor
Lung	Tobacco, asbestos, nickel
Pleura	Asbestos
Oral cavity	Tobacco, alcohol
Esophagus	Tobacco, alcohol
Gastric	Tobacco
Colon	Tobacco, alcohol
Liver	Aflatoxin, vinyl chloride, tobacco, alcohol
Kidney	Tobacco, trichloroethylene
Bladder	Tobacco, 4-amino biphenyl, 2-naphthylamine, cyclophosphamide, phenacetin
Prostate	Cadmium
Skin	Arsenic, coal tar, PAH, benzopyrenes, cyclosporin A

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Mechanism of chemical carcinogens :

Genotoxic	Non-genotoxic
Directly altering genetic material	Independent of direct insult
Mechanism : • DNA adducts • Inducing DNA ssb (Single stranded breaks) & dsb (Double stranded breaks)	MAP (mitogen activated protein) Kinase pathway (or) NFKB pathway They are epigenetic modifiers : • Cytotoxic • Receptor mediated (Steroid receptors & tamoxifen)
• Direct genotoxic : Cause cancer at site of exposure. E.g : UV induced skin cancer • Indirect genotoxic : Requires metabolic transformation from procarcinogen to carcinogen. E.g : Aflatoxin	

Both can cause reactive oxygen species DNA damage alter gene expression.

Aristolochic acid :

- From genus of Aristolochia (Plant).
- Used as herbal remedy for weight loss.
- Class I carcinogen.
- Causes A:T to T:A transformation.
- Diseases caused :
  a. Balkan endemic nephropathy.
  b. Nephrotoxic : Interstitial fibrosis.
  c. Upper tract urothelial carcinoma.

PAH (Polycyclic aromatic hydrocarbons) :

- ≥3 fused benzene rings.
- >200 chemicals.

Benzopyrene :

- Most studied PAH.
- Metabolized by CYP4501A1 & CYP4503A4.
- Mechanism of action : DNA adducts.
- Excretion : Glutathione pathway.
- Increased lung & skin cancer.
- Found in overcooked food, coal burning and tobacco smoke.

IARC group 1 pharmaceutical carcinogens

00:35:14

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Drug	Cancer
Azathioprine	Non-hodgkin's lymphoma, SCC of skin, HCC, cholangiocarcinoma.
Cyclophosphamide	Bladder cancer, leukemia
Chlorambucil	Leukemia
Cyclosporine	Leukemia, lymphoma, non-melanomatous skin cancer
Tamoxifen	Endometrial cancer
Estrogen/OCP/HRT	Breast cancer, endometrial cancer

Physical factors

00:37:13

Radiations :

- Ionising radiations : Ionise molecules (Electron is displaced from orbit) by linear energy transfer (LET).
- X rays & γ rays have low LET.
- Particulate matter :
  - Electron, proton, neutron, C ion, α particles.
  - They have high LET.

m/c source of radiation exposure :

- 80% : Radon gas.
- 20% : Medical sources.

Mechanism of action of ionising radiations :

Direct action	Indirect action
High LET : Direct DNA damage	Low LET
Direct energy transferred to molecule.	Hydrolysis of H_2O releases OH^- radical which causes DNA damage.

Both causes similar lesions in DNA.

1 Gy of ionising radiation :

- 40 dsb.
- 1000 ssb.
- 1000 single base lesions.
- 150 DNA protein crosslinks per cell.

Dsb are critical lesions → Cell lethality.

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Cell response to radiation :

- Base excision repair : For ssb.
- Homologous repair :
  - High fidelity repair.
  - For dsb.
- Non homologous end joining repair :
  - m/c mechanism of repair in ionising radiations.
  - For dsb.
  - Not accurate → Results in mutation.

Theoretical risk models for radiation induced cancer :

Linear, no threshold model :

- Most accepted.
- Induction of cancer is directly proportional to dose of radiation even in low dose.

Sublinear/threshold model :

- Below threshold dose, risk is negligible.

Supralinear/stealth model :

- Doses below threshold can trigger activation of DNA damage surveillance & repair mechanism leading to suboptimal activation of cell cycle.

Linear quadratic model :

- Effect of radiation at low doses → Single tract of radiation hitting multiple targets quadratic induction rate.

Vulnerable cells :

- Most vulnerable :
  - Hematopoietic cell line (Leukemia except CLL) : m/c.
  - Thyroid gland.
- Intermediate : Breast, lung, salivary gland.
- Radioresistant : Skin, bone, GIT.

ETIOLOGY OF CANCER II

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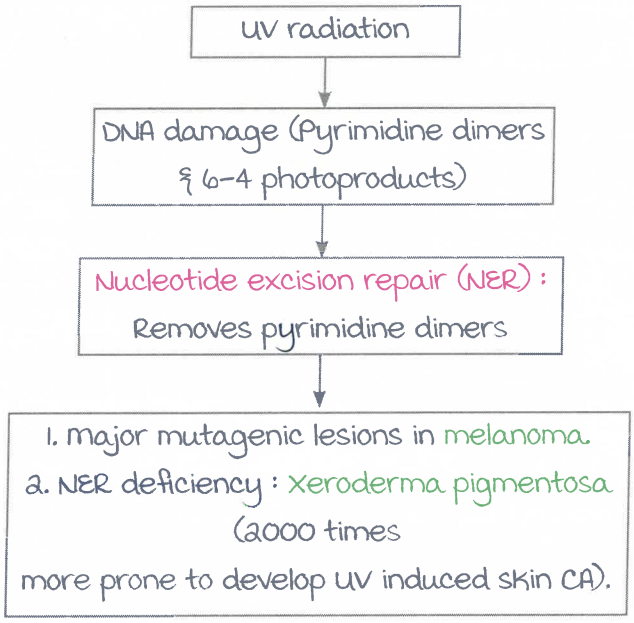
Physical factors leading to carcinogenesis 00:00:08

UV light :

- UV A (320 to 400 nm) : mainly produces ROS → Single strand breaks & base lesions in DNA.
- UV B (290 to 320 nm).
- UV C (240 to 290 nm) :
  - Most damaging to DNA.
  - Most of the UV C is absorbed by ozone layer.
- UV B & UV C :
  - Forms pyrimidine dimers.
  - And also 6 - 4 photoproducts that consists of covalent ring structures → Bending of DNA helix → Interfere in DNA synthesis.

Cellular reponse to UV radiation :



Asbestos :

- Contributes in causing 5 -7 % of all lung cancers.
- Mechanism of action : ROS → Single strand breaks + base lesions.
- Asbestos + tobacco : More chance of causing lung CA.
- Tumor suppressor genes p53 & p16INK4A + K-RAS oncogene are associated with lung CA caused by asbestos.

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- Malignant mesothelioma :
  - Major cause : Asbestos fibres.
  - Associated with p16INK4A & NF2 gene mutation.

Radiofrequency radiation and microwave radiation :

- Radiofrequency radiation : 3 KHz to 300 MHz.
- Microwave radiation : 300 MHz to 300 GHz.
- Cellphones :
  - Brain peak specific absorption rate : 4 to 8 W/Kg.
  - > 10 yrs of cellphone usage : Increased chance of glioma and acoustic neuroma.
  - It is inconclusive as large prospective studies have shown no risk.

Electromagnetic fields :

- Not carcinogenic (Energy is not high enough to break chemical bonds).

Dietary factors

00:09:33

Dietary fibre :

- All plant polysaccharide & lignin → Resistant to hydrolysis by the digestive enzymes.
- No association b/w dietary fibre and colorectal cancer.

	Increased incidence	Decreased incidence
Red meat	Colorectal CA	
Regular milk consumption	Prostate CA	Colorectal CA
Coffee		HCC Endometrial CA Prostate CA
Vit D		Colorectal CA Breast CA Prostate CA
Selenium (acc to SELECT RCT)	No protective effect in prostate CA.	

Mechanisms of redmeat being carcinogenic :

- ↑ Anabolic hormones in red meat.
- Polycyclic aromatic hydrocarbons (Cooking at high temperature).
- ↑ Heme in red meat.
- Nitrates → Nitrosamines (In smoked, salted and processed meat).