Chemotherapy of Neoplastic Disease

1. Which of the following drug acts on the S phase of cell cycle? (GPAT-2014, 2024)

(a) Methotrexate (b) Chlorambucil (c) Paclitaxel (d) Vincristine

2. Following anthracycline antibiotic is a synthetic derivative (GPAT-2014, 2024)

(a) Daunorubicin (b) Doxorubicin (c) Idarubicin (d) All of these

3. Hemorrhagic cystitis caused by (GPAT-2014, 2024)

(a) 5-FU (b) Methotrexate (c) Doxorubicin (d) Cyclophosphamide

4. Which of the following metabolite is used to inactivate the vesicotoxic metabolites leading to hemorrhagic cystitis by alkylating agents used in the treatment of cancer? (GPAT-2023 SHIFT-I)

(a) Acrolein (b) Alkophosphamide

(c) Cyclophosphamide (d) Mesna

5. Trastuzumab is a/an (GPAT-2023 SHIFT-I)

(a) EGFR/HER-2 inhibitor (b) Angiogenesis inhibitor

(c) EGF receptor (HER-1) inhibitor (d) BCR-ABL tyrosine kinase inhibitor

6. Which phase of cell cycle is the shortest phase in terms of time? (GPAT-2023 SHIFT-II)

(a) G_1 (b) S (c) M (d) G_2

7. Which of the following is a malignant type of tumor? (GPAT-2022)

(a) Lipoma (b) Adenoma (c) Melanoma (d) Osteoma

8. Mitomycin C is an antibiotic isolated from (GPAT-2020)

(a) Streptomyces peucetius (b) Streptomyces verticillus

(c) Streptomyces antibioticus (d) Streptomyces caespitosus

9. Match the following agents that cause cancer with the preferable sites for where it might cause (GPAT-2017)

Arsenic	**[P] Prostate**
Benzene	**[Q] Angiosarcoma**
Cadmium compounds	**[R] Leukemia**
Vinyl chloride	**[S] Hemangiosarcoma**

(a) 1-[S], 2-[R], 3-[P], 4-[Q]`
(b) 1-[Q], 2-[P], 3-[R], 4-[S]
(c) 1-[R], 2-[S], 3-[Q], 4-[P]
(d) 1-[P], 2-[Q], 3-[S], 4-[R]

10. Cisplatin having high (GPAT-2016)

(a) Neurotoxicity
(b) Hepatotoxicity
(c) Nephrotoxicity
(d) MAO inhibition

11. Secobarbital is drug [GPAT 2014]

(a) Mitomycin-C
(b) Doxorubicin
(c) Methotrexate
(d) Cyclophosphamide

12. Pulmonary fibrosis is the most common complication after treatment with (GPAT-2013)

(a) 6-Mercaptopurine
(b) Vincristine
(c) Bleomycin
(d) Adriamycin

13. Paclitaxel acts on which phase of cell cycle (GPAT-2013)

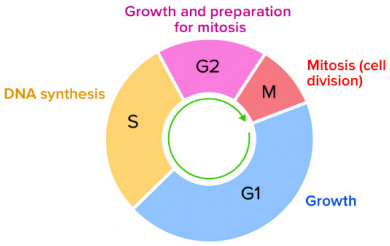
(a) G_1 (b) S (c) G_2 (d) M

ANTINEOPLASTICS

ANTINEOPLASTICS

ANTICANCER DRUGS

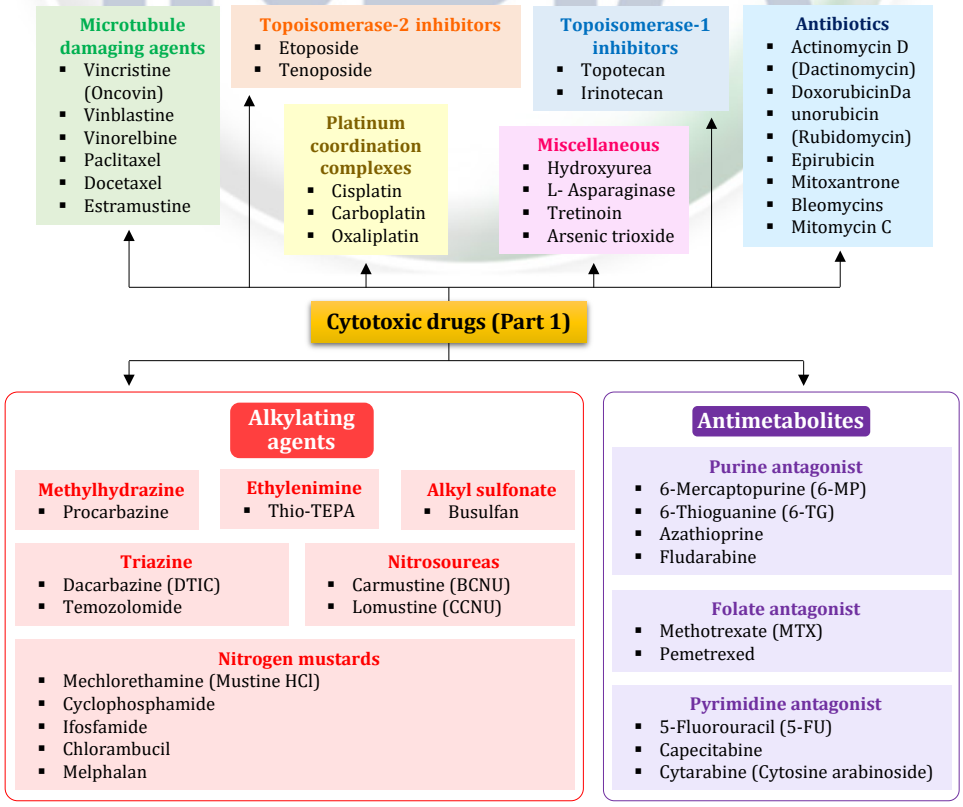
- The anticancer drugs either kill cancer cells or modify their growth.
- Cancer is a disease of cells characterized by Progressive. Persistent. Purposeless and uncontrolled Proliferation of tissues.
- Both normal as well as cancerous cells must pass through the following phases of cell cycle:

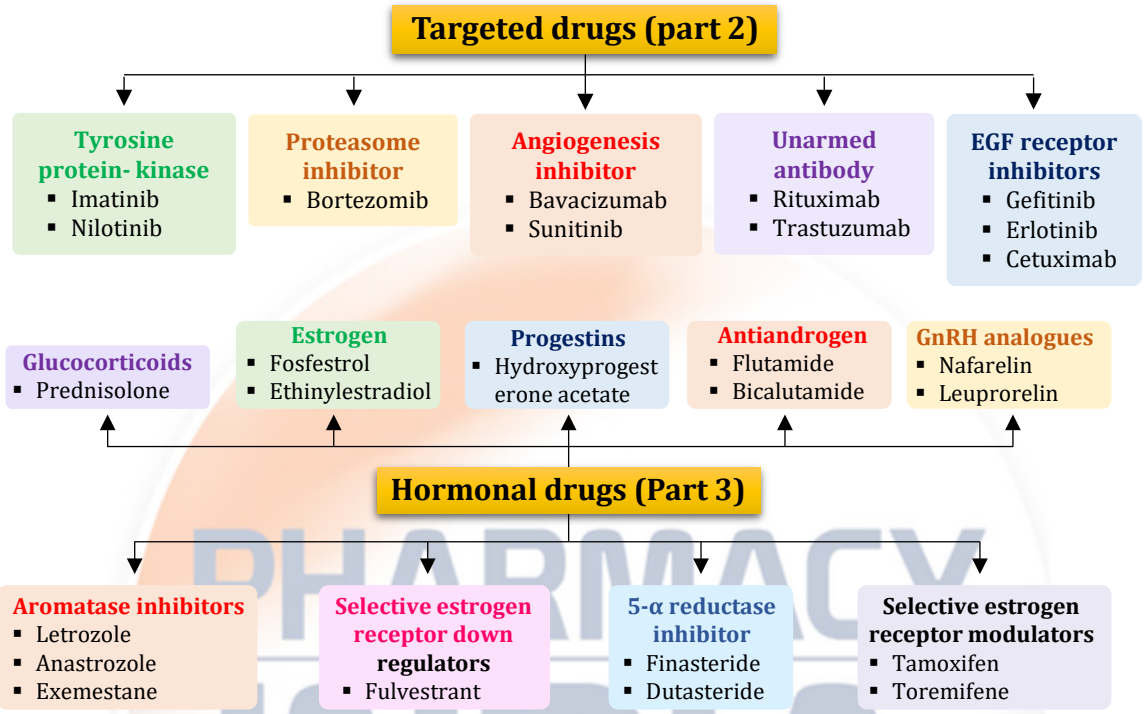


☐ CELL CYCLE SPECIFIC AND NON-SPECIFIC DRUGS

Phase	Cell cycle specific drugs	Cell cycle non-specific drugs
G1	Etoposide	Platinum compound
S	**ANTIMETABOLITE:** Methotrexate, 6- mercaptopurine, 5-Fluro-uracil, Capecitabine, Cytarabine, Cytosine arabinoside (G-05)	**ALKYLATING AGENT:** Melphalan, Cyclophosphamide, Nitrosoureas
G	**TOPOISOMERASE INHIBITOR:** Irinotecan, Topotecan, Etoposide, Bloemycin	**ANTHRACYCLINS:** Doxorubicin, Daunorubicin, Epirubicin, Mitoxantrone
M	**VINCA ALKALOIDS:** Vincristine, Vinblastine, Vinorelbine **TAXENES** • Paclitaxel • Docetaxel	**MITOMYCINS C:** • Dactinomycin • Camptothecin

☐ CLASSIFICATION





- The drugs that are used to treat malignant condition or neoplasm are called as Cytotoxic drugs/ Anti-neoplastic drugs/ Anti-cancer drugs.

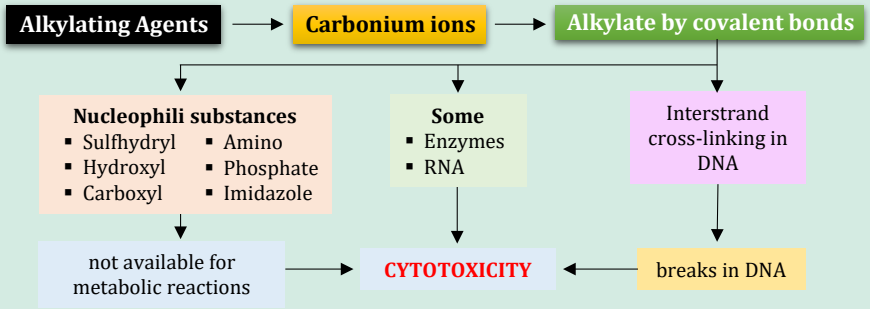
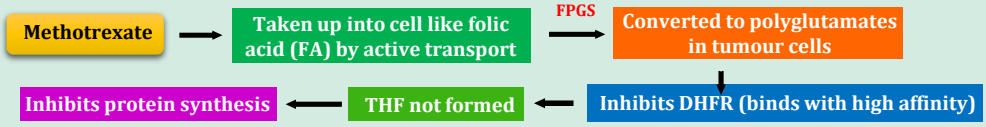
Types of cancer

Type	Description
Carcinoma	Cancer of epithelial tissue.
Sarcoma	Cancer of connective tissues.
Leukemia	Cancer of the white blood cells.
Myeloma	Cancer that starts in plasma cells.
Lymphomas	Cancer that starts in the lymph glands or cells of the lymphatic system.

☐ TOXICITY OF ANTICANCER DRUG

S.No.	Drugs	Toxicity
1.	Anthracycline (Doxorubicin Daunorubicin)	Cardiotoxicity
2.	Busulphan, Bleomycin(G-16)	Pulmonary fibrorsis
3.	Vincristine, vinblastine, Vinorelbine	Peripheral neuropathy
4.	Methotrexate (G-17)	Megaloblastic anaemia,Hepatotoxicity, Obstructive nephropathy
5.	Cyclophosphamide, Ifosfamide	Haemorrhagic cystitis, Alopecia
6.	Cisplatin (G16)	Emesis, Nephrotoxicity, Neuropathy, Ototoxicity
7.	5-Flourouracil, Capecitabine, Fludarabine, Cytarabine	Hand and foot syndrome, Neurotoxicity
8.	6- Mercaptopurine, 6-Thioguanine	Hepatotoxicity
9.	Paclitaxel, vincristine	Peripheral neuropathy, Hypersensitivity
10.	Docetaxel`	Peripheral neuropathy, Fluidretention
11.	Irinotecan, Gemcitabine	Diarrhea
12.	Doxifluridine	Bone marrow depression, Hearingloss, Neuritis.
13.	Cytarabine	Cerebral ataxia (neurotoxicity)

☐ INDIVIDUAL DRUGS

Drug	Description
Nitrogen Mustard	• Cyclophosphamide is a prodrug and is activated by hepatic biotransformation and converted into aldophosphamide & acrolein. • Acrolein is responsible for hemorrhagic cystitis, alopecia, vercotoxic (adverse effect). • Mesna (mercapto ethane sulfonic acid) is used to prevent cystitis & vericotoxic caused by acrolein. Cyclophosphamide is the drug of choice for Wegener's granulomatosis. • **Mechanism of Action of Alkylating Agents** • Metabolite Of Cyclo Phosphamide Hydroxy Cyclophosphamide 
Busulfan	• It causes adrenal insufficiency, pulmonary fibrosis, skin hyperpigmentation and hyperuricemia. • Busulfan is drug of choice for chronic myloid leukemia.
Platinum compounds	• Cisplatin is most nephrotoxic whereas carboplatin is more hematotoxic (bone marrow suppressant). • Cisplatin reduces all ions in serum i.e., causes hypomagnesemia, hypokalemia, hypocalcemia and hypophosphatemia. (Remember, cyclosporine, an immunosuppressive drug cause hyperkalemia). • Cisplatin - Maximum emetic effect **Cisplatin** → **forms highly reactive platinum complexes** → **Reacts with DNA (forms interstrand and intrastrand cross-links.)** → **DNA damage**
Methotrexate	• Methotrexate is the inhibitors of dihydrofolate reductase (DHFRase). • This drugs also inhibit thymidylate synthase (TS) and the enzymes involved in early purine synthesis. • Methotrexate is the drug of choice for the treatment of chorio carcinoma. • **Mechanism of Action** • Used in arthrits. 
Purine analogues	• 6-mercaptopurine (6-MP) and 6-thioguanine (6-TG) are the purine antimetabolites that are activated by hypoxanthine-guanine phosphoribosyl transferase (HGPRTase). • Use of 6MP /6TG → acute lymphatic leukemia in children. • Hyperuricemia can occur, reduced by allopurinol. • 6 Mercaptopurine - first used for the treatment of leukemia. **Purine Analogs** → **Active metabolite** → **Inhibits protein synthesis** → **Breaks in DNA strand**, **↓ DNA synthesis**
5-Fluorouracil	• 5- fluorouracil (prodrug) convert into 5 flouro deoxy guinosine monophosphate which inhibit thymidylate synthase • Cisplatin, oxalipaltin & leucovorin enhance the efficacy of 5-FU • Fludarabine is drug of choice for chronic lymphocytic leukemia (CLL). • Treatment of breast cancer colorectal cancer vs basal cell cancer of the skin **Fluorouracil (Pyrimidine Analog)** → **Active metabolite** → **Inhibits Thymidylate Synthetase** → **inhibits DNA and RNA synthesis**; **Incorporated into DNA and RNA** → **inhibits thymine synthesis**

Vincristine, vinblastine and vinorelbine	• Act by inhibiting polymerization of microtubules (tubilin protein). Vinca Alkaloids → bind to microtubules in the mitotic apparatus. → inhibit the assembly of microtubules → mitotic arrest in metaphase → cell division stops • Side effects of vincristine is alopecia & peripheral neuropathy • Vincristine with glucocorticoids is the treatment of choice for inducing remission in childhood leukemias. • It can also be used for pediatric solid tumors (Wilm's tumor, neuroblastoma and rhabdomyosarcoma) and lymphomas, lymplo cytic leukemia. • Vinblastine - Alopecia is less than vincristine • Vinblastine's most important clinical use is the curative therapy of metastatic testicular tumors.
Paclitaxel	• Promote polymerization of tubulin /prevent depolymerisation (opposite of vinca alkaloids) Used in advanced ovarian cancer, breast cancer head & neck cancer • Paclitaxel causes hypersentivity (abraxane is albumin bound formulation of paclitaxel which decrease the incident of hypersensitivity).
Docetaxel	• Semi synthetic derivative & more potent than paclitaxel • Used in advanced breast cancer • Docetaxel is formulated in polysorbate medium which produces less acute hypersentivity.
Estramustine	• Complex of estradiol with a nitrogen mustard normustine which has estrogenic but no alkylating property • Binds to tubulin (protein) & interferes • Gynecomastia, thromboembolism & impaired glucose tolerance are the side effects.
Irinotecan and topotecan	• Act by inhibiting topoisomerase I • Irinotecan • Prodrug • It has anti cholinesterase actyivity • Prior atropinisation is required • Used in advanced colo-rectal cancer in combination with 5-FU.
Etoposide and teniposide	• Act by inhibiting topoisomerase II resulting in DNA damage through strand breakage. (Cleaving of DNA is not interfered, resealing is prevented) • Etoposide is indicated for testicular, prostatic and oat cell carcinoma [of lung]. • Etoposide therapy can result in acute non-lymphocytic (acute monocytic or monomyelocytic) leukemia.
Doxorubicin & Daunorubicin	• These agents also generate semiquinone free radicals that are responsible for cardiotoxicity. • This adverse effect can be reduced by using a-tocopherol and dexrazoxane (a free radical scavenger). Liposomal forms of these drugs have decreased cardiac toxicity. • Block DNA dependent RNA synthesis • These drugs also can cause red coloured urine. • Both of these used in acute leukemia.
Bleomycin	• Produce superoxide ion by chelationn of copper and iron, this superoxide intercalalte between DNA strand and cause chain break. • Highly effective in testicular carcinoma and squamous cell carciunoma.
Mitomycin C	• Highly toxic act like a alkylating agent • It may be used as intravesical therapy to treat superficial bladder cancers and anal carcinoma • Mitomycin C is used in patients with treacheal or laryngeal stenosis. • It can cause hemolytic uremic syndrome.
Dactinomycin	Dactinomycin (Actinomycin-D) acts by inhibiting DNA dependent RNA synthesis. It is indicated for solid tumors in children (rhabdomyosarcoma and wilm's tumor) and choriocarcinoma.
Imatinib	MOA: - inhibit a specific tyrosine kinase labelled "Bcr-Abl" tyrosine kinase expressed by cells. Used in GIT TUMOUR DOC for CML & C-kit positive GIST (gastro intestinal stromal tumour). Also used in dermato fibrosarcoma protuberans

☐ BUSULFAN: FEATURES

TRICK – "ABCDEF"
- **A** → **A**lkylating agent
- **B** → **B**one marrow supperssion s/e
- **C** → **C**ML indication
- **D** → **D**ark skin (hyperpigmentation) s/e
- **E** → **E**ndrocrine insufficiency (adrenal) s/e
- **F** → **F**ibrosis (Pulmonary) s/e

☐ CANCER DRUGS: TIME OF ACTION BETWEEN DNA AND mRNA

TRICK – "ABCDEF"
- **A** → **A**lkylating agents
- **B** → **B**leomycin
- **C** → **C**isplastin
- **D** → **D**actinomycin Doxorubicin
- **E** → **E**toposide
- **F** → **F**lutomide and other steroids or their antagonists (e. g. tamoxifen, leuprolide)

☐ ETOPASIDE: ACTION, INDICATIONS, SIDE EFFECT

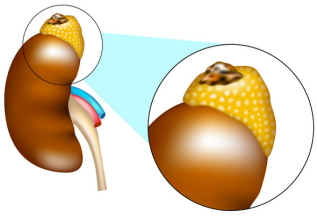
TRICK – "eTOPosIde" **Action:** Inhibits TOPoisomerase II
Indications: Out cell carcinoma of lung Testicular carcinoma Prostate carcinoma
Side effect: Affects TOP of your head, causing alopecia

☐ CYTOTOXIC DRUGS WITH HIGH POTENTIAL TO CAUSE VOMITING

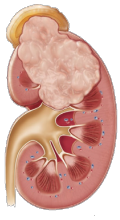
TRICK – "CADMIUM"
- **C** **C**isplatin Cyclophosphamide
- **A** **A**ctinomycin D
- **D** **D**acarbazine
- **Mi** **Mi**thramycin
- **UM** **Mu**stine

EXAM PUNCH

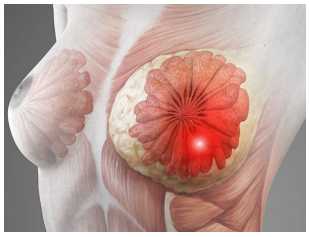
- **Pheochromocytoma -** High levels of circulating catecholamines generated due to catecholamines secreting tumours in adrenal medulla.
- **Iodine-131 -** therapeutically used as a radiopharmaceutical for the treatment of thyroid cancer.
- Azathioprine is a heterocyclic derivative of **6-Mercaptopurine.**
- Carcinogenicity of a chemical can be tested by its ability to **induce mutations in Salmonella typhimurium.**
- Anticancer drugs kill cancer cells by **first order kinetics.**
- **Trimethyl melamine** is an alkylating agent.
- **Neoplasia -** An increase in the size of an organ or a tissue that is not associated with cancer.
- Wilms tumor is also known as Nephroblastoma.
- **Chlorambucil -** used in autoimmune disease and transplant maintenance regimen.
- Disruption of the purine and pyrimidine base of DNA pairing occurs with **cyclophosphamide.**
- **Tacrolimus** specifically inhibits Calcineurin in the activated T-lymphocytes.
- **Actinomycin -** used in Wilm's Tumor.
- Leucovorin rescue is given to reduce the toxic effects of **methotrexate.**
- **Folinic acid** given for cancer patient who is under methotrexate therapy.
- PAP smear test is used in diagnosis of **cancer.**
- **Tamoxifen citrate -** used for treatment of Breast Cancer.
- Alopecia is the most common side effect of **anticancer drugs.**



Pheochromocytoma



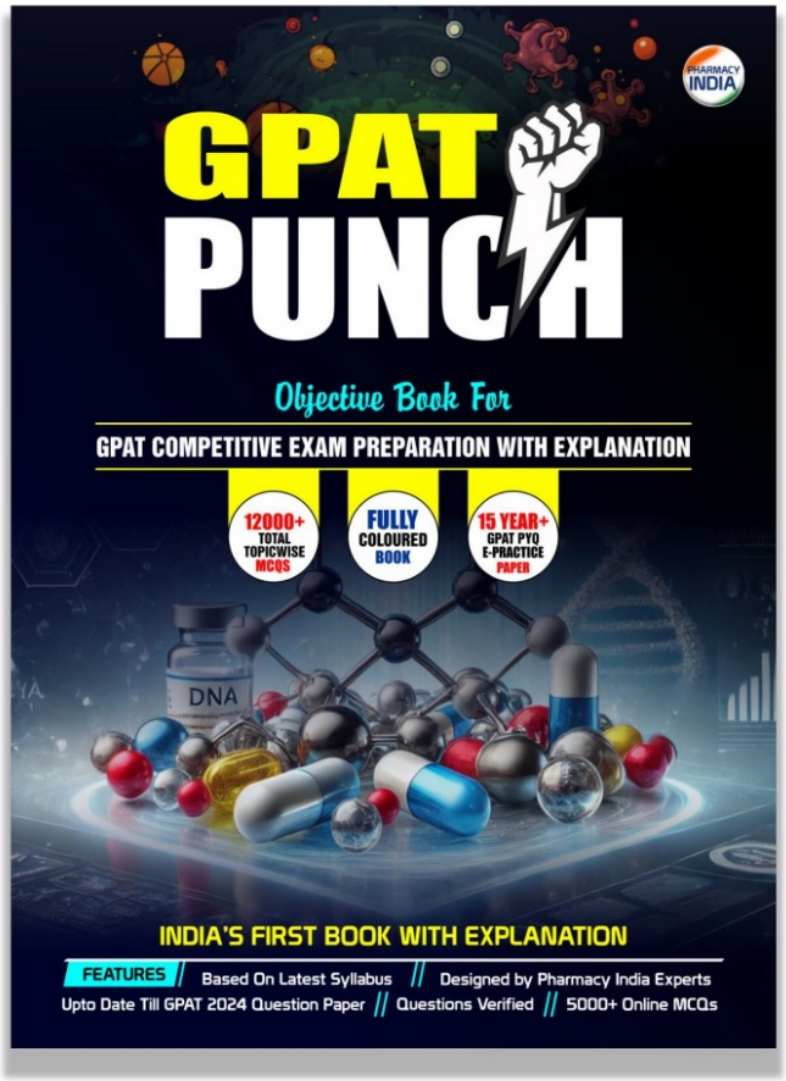
Wilms Tumor



Breast Cancer

Alopecia

BEST BOOK FOR GPAT PREPATRATION



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