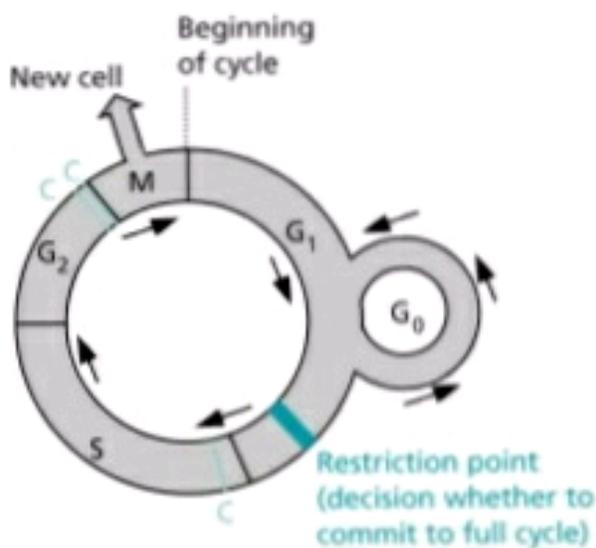


# ANTICANCER DRUGS



Cancer is a disease defined as the abnormal cell divide uncontrollably and destroy Body tissue and some times leads to abnormal growth of cell.

## Phases of the Cell Cycle

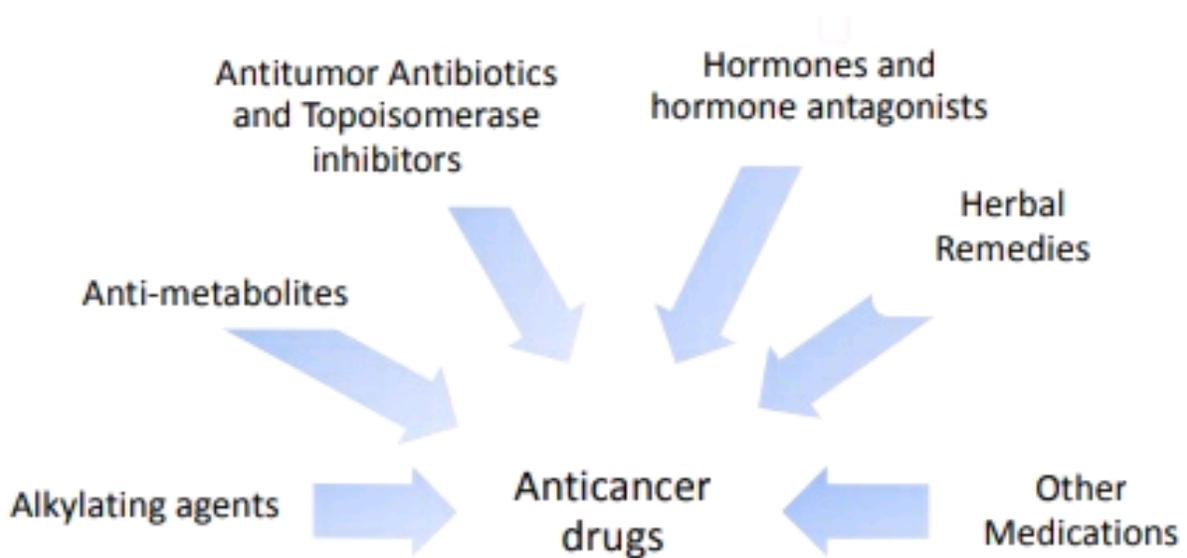


- G<sub>1</sub> phase (gap 1): Cell grows in size and prepares to copy its DNA in response to various growth factors
- S phase (synthesis): Replication of DNA, copying of the chromosome
- G<sub>2</sub> phase (gap 2): Preparation for cell division. Check copied DNA and repair damaged copies.
- M phase (mitosis): Formation of the mitotic spindle, and separation into two individual cells (cell division).

# TUMOR VERSUS CANCER

<p>Tumor is a development of a lesion or lump in the body due to an abnormal cellular growth</p>	<p>Cancer is a disease caused by an uncontrolled division of abnormal cells in a part of the body</p>
<p>Can be benign or malignant</p>	<p>Malignant</p>
<p>May not be fatal</p>	<p>Can be fatal</p>
<p>Can be treated by watchful waiting or surgical removing</p>	<p>Can be treated by surgical removal, chemotherapy, &amp; radiotherapy</p>

## CLASSIFICATION OF DRUGS



### 1) ALKYLATING AGENTS

#### Alkylating agents

CLASS	DRUGS	MAJOR USES
<b>Nitrogen Mustards</b>	Meclorethamine	HL, NHL
	Melphalan	Multiple myeloma; breast, ovarian cancer
	Chlorambucil	ALL, CLL, HL, NHL, Multiple myeloma; Neuroblastoma; Breast, Ovary, Lung cancer; Wilms' tumor; cervix, testis cancer;
	Cyclophosphamide	
<b>Etylenimine</b>	ThioTEPA	Bladder, breast, ovarian cancer
<b>Alkyl sulfonate-</b>	Busulfan	CML
<b>Nitrosoureas</b>	Carmustine	Primary brain tumor; Melanoma, HL, NHL,
	Streptozocin	Pancreatic insulinoma; Malignant carcinoid
<b>Triazine</b>	Dacarbazine	Malignant melanoma;

## **CHLORAMBUCIL:**

**Dose:**-4- 10mg(0.1-0.2mg/kg)daily for 3-6weeks then 2mg daily for maintenance dose .

**MOA:**-They alkilate the cell constituents such as cell membrane,proteins,amminoacid and damaging the genetic material of cancer cells(DNA,RNA) Which leads to stop their growth and multiplication.

**Pk:-**

- well absorbed orally
- Completely metabolised by liver
- Bio availability is 70%
- Completely excreted in urine with in 24hours

**SE:-**

- Bone marrow suppression, infertility
- Thrombocytopenia(low platelets), neutropenia(low neutrophills)

## **BUSULFAN**

**Dose:**-2-6mg/day(0.06mg/kg/day)orally.

**MOA:**- same as chlorambucil.

**Pk:-** It is administered orally as well as iv.

- 60-80% Bio availability .
- metabolised by liver and approx. 25-60% excrete in urine

**SE:-**

- Amenorrhoea(absence of menses)
- Anorexia(Loss of appetite)
- anxiety,Nausea and vomiting

## 2) ANTI-METABOLITES

### Antimetabolites

CLASS	DRUGS	MAJOR USES
Folic acid analogue	Methotrexate	ALL; choriocarcinoma breast, head, Lung cancer; osteogenic sarcoma; bladder ca
	Pemetrexed	Mesothelioma, lung cancer
Pyrimidine analogue	Fluorouracil Capecitabine	Breast, colon, esophageal, stomach cancer.
	Cytarabine	AML, ALL, NHL
	Gemcitabine	Pancreatic, ovarian, lung ca.
Purine analogue and related inhibitors	Mercaptopurine	AML, ALL
	Pentostatin	Hairy cell leukaemia; CLL, small cell NHL.
	Fludarabine	CLL

#### METHOTREXATE:

It is used in the treatment of lung cancer, Breast cancer, Blood cancer .

- Methotrexate is apparently curative in choriocarcinoma(uterus cancer) :15–30 mg/day for 5 days orally
- 20–40 mg/m<sup>2</sup> BSA i.m. or i.v. twice weekly. It is highly effective in maintaining remission in children with acute leukaemias, 2.5–15 mg/day.
- It is also useful in other malignancies, rheumatoid arthritis, psoriasis and as immunosuppressant

#### MOA

Folic acid is converted into active form tetra hydro folate(THF) by the enzymes folate reductase which required for the synthesis of purine, pyrimidine, and some amino acid. These components are required for the synthesis of DNA and RNA

- Drugs inhibiting this synthesis leads to inhibition of cell replication and act as anti cancer

### P.K

- It is administered orally as well as parenterally.
- Hepatic and intracellular metabolism
- .Approx 80% excrete in urine, small amount in faeces

### SE

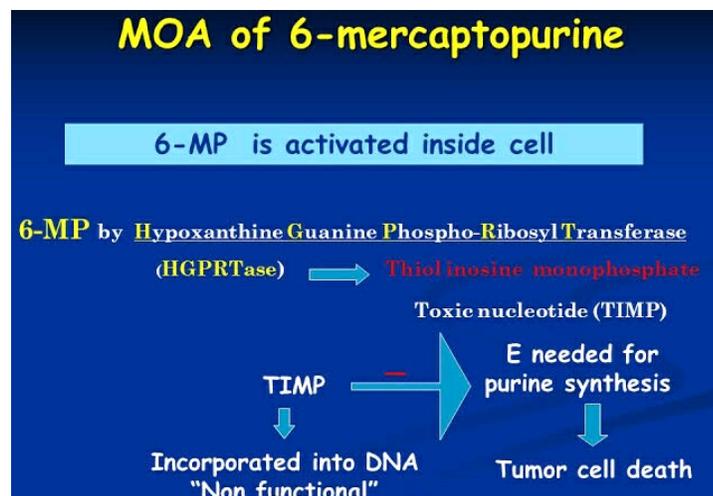
- Stomatitis( inflammation of mouth),
- Nausea and vomiting
- Dyspepsia(indigestion)

### 6-MERCAPTOPURINE

**Dose :-**Useful in the treatment of Blood cancer. Dose is 50mg /Day  
Or 2.5mg/kg

### MOA

It inhibiting the purine synthesis and metabolism by inhibiting an enzyme called phospho ribosyl pyrophosphate amido transferase .This enzyme is helpful for the purine synthesis and alters the synthesis and function of DNA and RNA and inhibit their growth



## P. K:-

- Absorption by the oral route is unpredictable and incomplete. Once it enters the blood circulation widely distributed in body tissue
  - Metabolised by liver
  - Penetration into CSF is poor.
  - Bioavailability varies approx 5-40%.
  - Excrete in urine

## SE

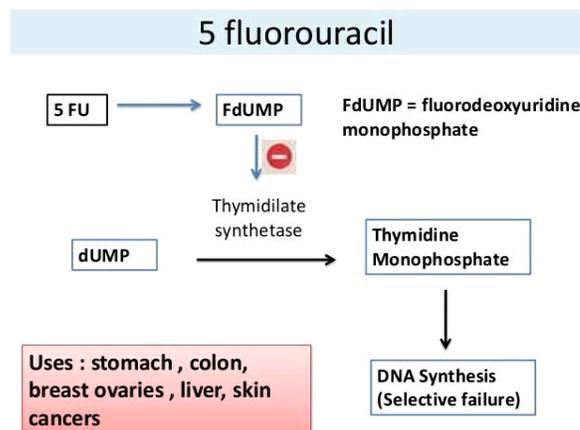
- Neutropenia, Anaemia, Jaundice,
- anorexia, Thrombocytopenia
- Bone marrow suppression

## 5-FLUOROURACIL

**Dose:** 1 g orally on alternate days (6 doses) then 1 g weekly  
or 12 mg/kg/day i.v. for 4 days—6 mg/kg i.v. on alternate days

## MOA:-

Binding with enzyme thymidilate synthetase, thus preventing the formation of thymidine an essential component of DNA and act as anti cancer drug



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## P.k

- Because of its severe toxicity to the GI tract, 5-FU is given IV or, in the case of skin cancer, topically
- The drug penetrates well into all tissues, including the CNS. 5-FU is rapidly metabolized in the liver, lung, and kidney.
- Bioavailability varies from 30-100%.
- Metabolised by liver.
- Excrete through urine

## SE

- Inflammation of mouth,
- anorexia, alopecia,
- pancytopenia, proctitis (inflammation of anus)

## 3) NATURAL AGENTS

### Natural Agents

CLASS	DRUGS	MAJOR USES
Vinca alkaloids	Vinblastine	HL, NHL, Testis cancer
	Vinorelbine	Non small cell lung cancer
	Vincristine	ALL, Neuroblastoma; Wilms' tumor;
Taxanes	Paclitaxel, Docetaxel	Metastatic ovarian, breast ca.
Epipodophyllotoxins	Etoposide	Testicular tumour, lung cancer ,HL, NHL
Camptothecins	Topotecan, Irinotecan	Ovarian cancer; small-cell lung cancer; colon ca.

## VINCRISTINE/VINBLASTINE

It is obtained from catharanthus roseus. Used in the treatment of cancer of nerve tissues, blood cancer, lung cancer.

**Dose:** 1.5-2 mg/m<sup>2</sup> BSA i.v. weekly (vincristine). Dose: 0.1-0.15 mg/kg i.v. weekly × 3 doses. (vinblastine)

# Dosages Based on BSA (cont.)

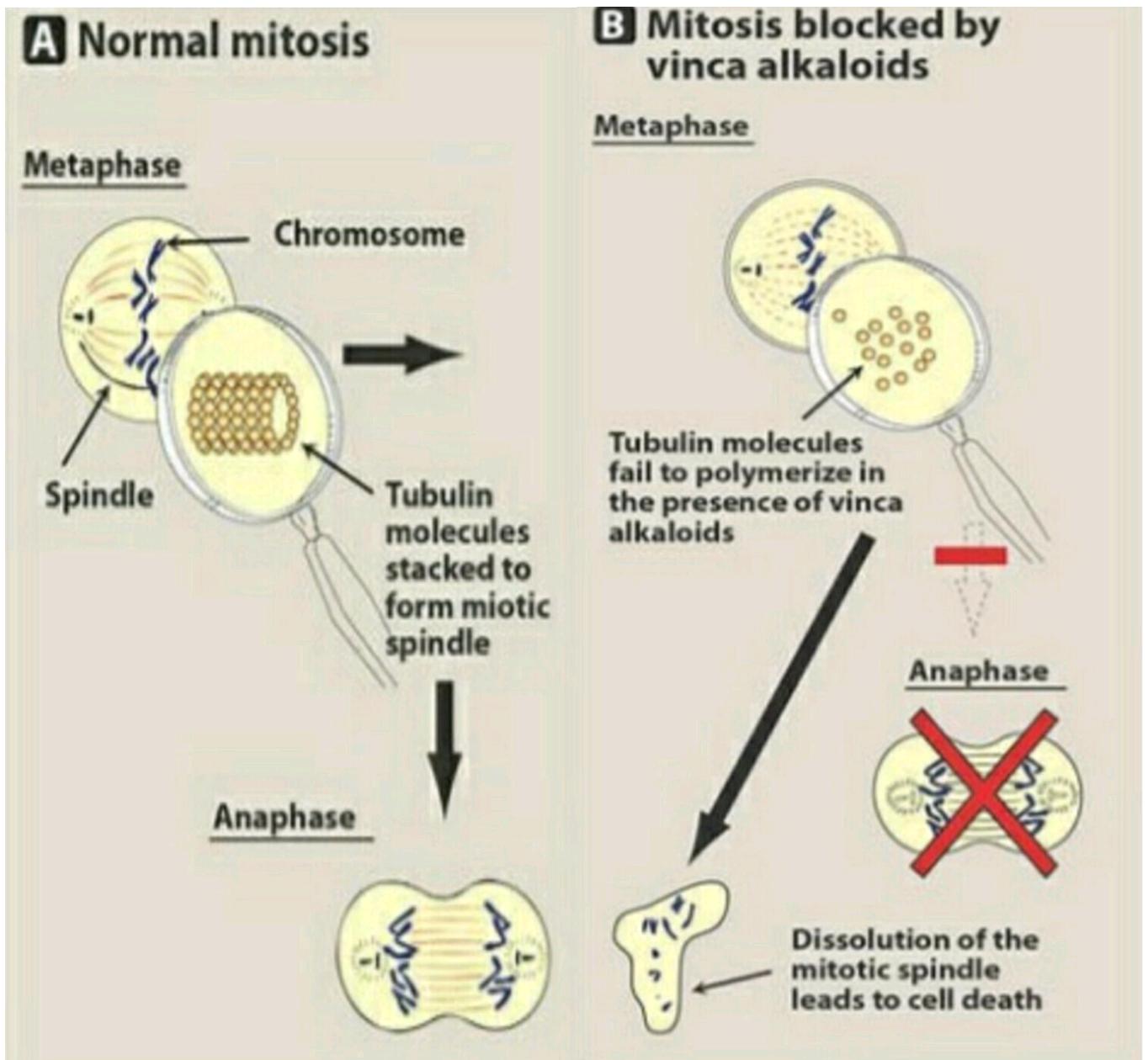
## Rule 17-5 Calculating the BSA using a formula:

1. If you know the height in cm and weight in kg, calculate

$$BSA = \sqrt{\frac{\text{height (cm)} \times \text{weight (kg)}}{3600}} \text{ m}^2$$

**MOA:-**

it binds with tubulin (cancer cell protein) and inhibiting the cell division



## PK

- It is administered parenterally partially absorbed by git, metabolised by liver.
- Approx 70% excrete in urine and 10% in faeces

## SE

- Neuotoxicity, alopecia ,
- anorexia, constipation

## 4 ANTIBIOTICS and ENZYMES

### Antibiotics and enzymes

CLASS	DRUGS	MAJOR USES
Antibiotics	Dactinomycin (actinomycin D)	Choriocarcinoma; Wilms' tumor; Rhabdomyosarcoma
	Daunorubicin	AML, ALL.
	Doxorubicin	Soft-tissue, osteogenic, and other sarcoma; HL, NHL , AML, ALL. Breast, Genitourinary, Thyroid, lung, stomach cancer; Neuroblastoma
	Mitoxantrone	AML, breast and prostate cancer
	Bleomycin	Testis, cervical cancer; HL, NHL
	Mitomycin	Stomach, anal, and lung cancer
Enzymes	L-Asparaginase	ALL

### ACTINOMYCIN-D

It is also called Dactinomycin. It is used in cancer of kidneys, cancer of testis and ovary, cancer of bones etc.

- **Dose** 0.5mg/Day, 15 µg/kg i.v. daily for 5 days.

### MOA

It damages the genetic materials (DNA, RNA) of the cancer cells and stops their growth and multiplication

## Pk

- Administered parenterally. Metabolised by liver.
- Excrete in urine

## SE

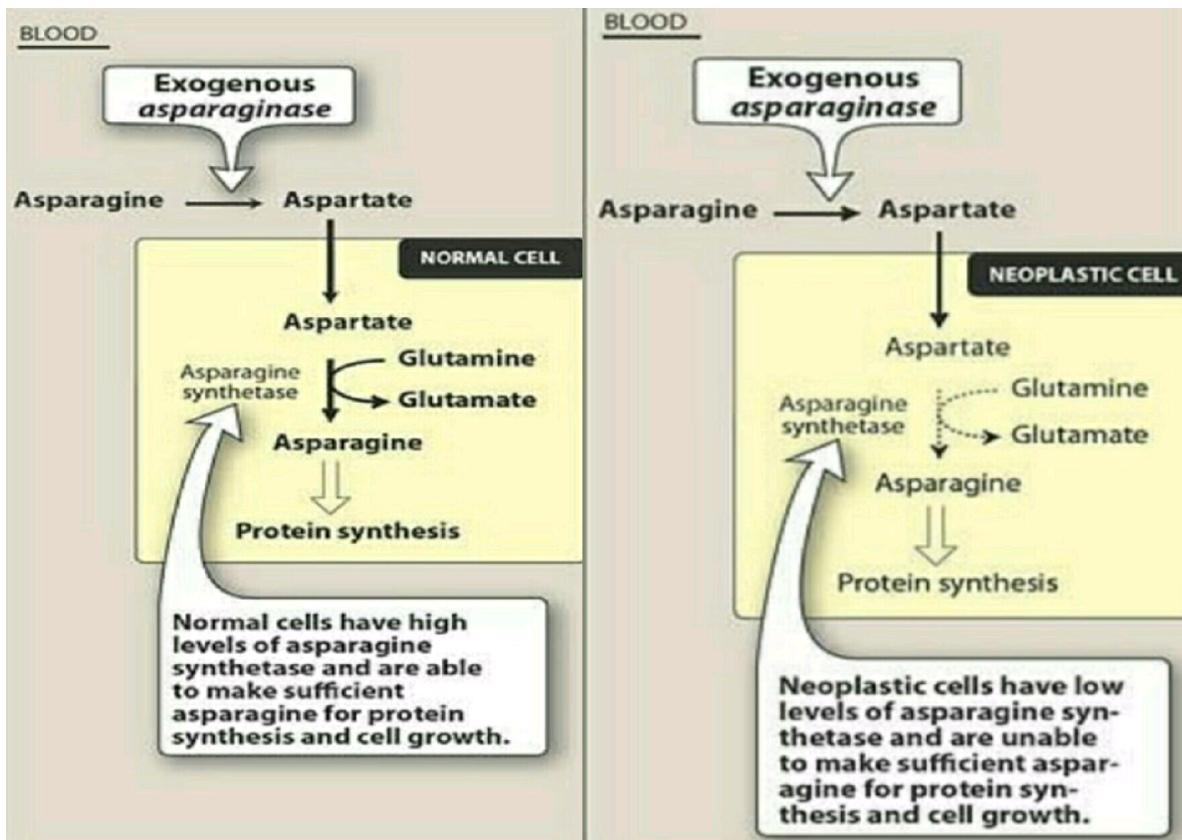
- Glossitis(inflammation of tongue)
- Diarrhoea, Anorexia

## L-ASPARAGINASE

**Dose:** 50–200 KU/kg i.v. daily for 2–4 weeks.(ku-killo units)

## MOA

The enzyme L-asparaginase (from E. coli) degrades L-asparagine to L-aspartic acid, depriving leukaemic cells of an essential metabolite may Cause cell death.



**PK:**

- The enzyme must be administered either IV or intramuscularly, because it is destroyed by gastric enzyme.
- Metabolised in liver
- Excreted in urine and faeces.

**SE**

- decrease in clotting factors, liver abnormalities, pancreatitis,
- Anaphylaxis(sudden severe allergic reactions)

**5) HORMONES and ANTAGONIST****Hormones and antagonists**

<b>CLASS</b>	<b>DRUGS</b>	<b>MAJOR USES</b>
<b>Glucocorticoides</b>	Prednisone	ALL, CLL, HL, breast cancer, multiple myeloma
<b>Progestins</b>	Hydroxyprogesterone caproate, Medoxyprogesterone acetate, Megestrol acetate	Endometrial, breast cancer
<b>Estrogens</b>	Diethylstilbestrol, Ethinyl estradiol	Breast, prostate cancer
<b>Anti-estrogens</b>	Tamoxifen, Toremifene,	Breast cancer
<b>Aromatase inhibitors</b>	Anastrozole, Letrozole,	Breast cancer
<b>Androgens</b>	Testosterone propionate	Breast cancer
<b>Antiandrogen</b>	Flutamide , casodex	Prostate cancer
<b>GnRH analogue</b>	Leuprolide	Prostate cancer

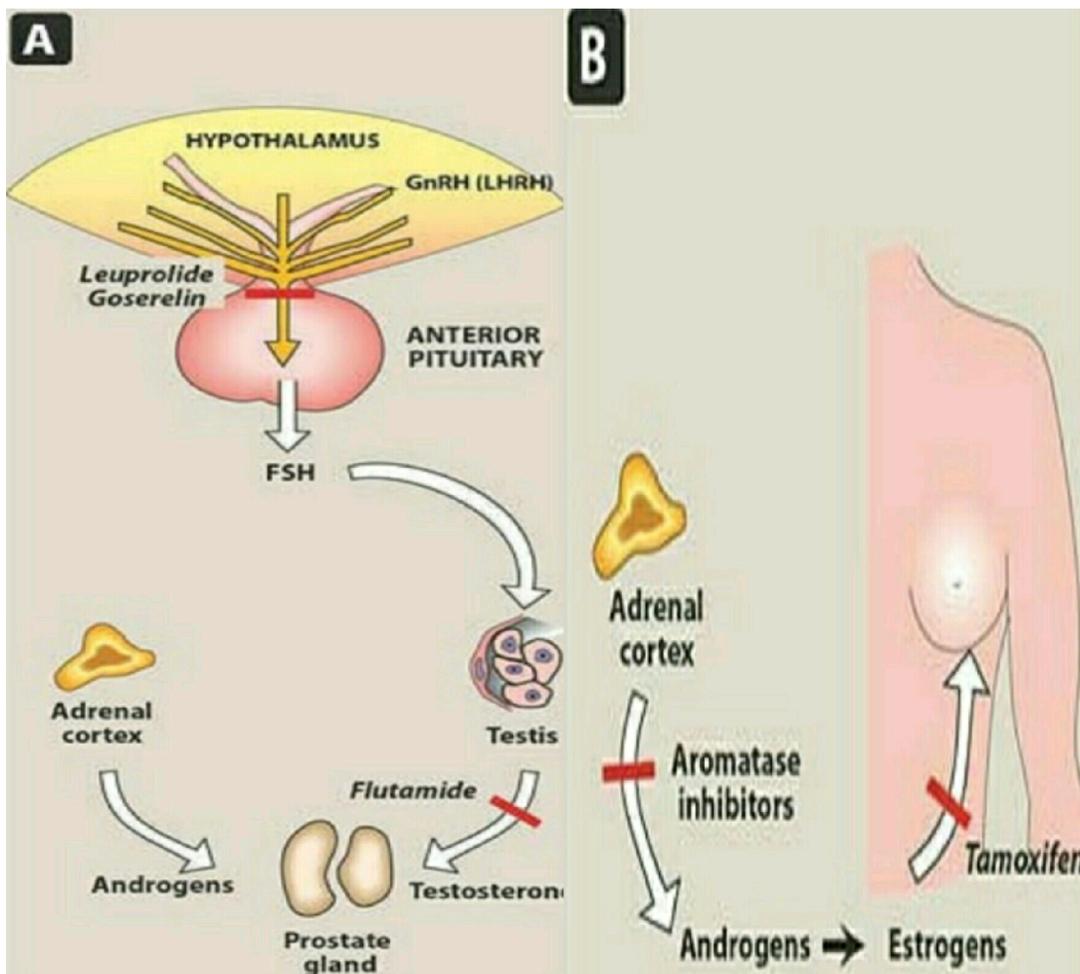
**FLUTAMIDE, NILUTAMIDE, and BICALUTAMIDE**

**Dose**-Flutamide requires dosing three times a day and the others once a day.flutamide 250mg and other two drugs 50mg tablets are available.

These are synthetic, nonsteroidal antiandrogens used in the treatment of prostate cancer. They compete with the natural hormone for binding to the androgen receptor

## MOA

blocks the action of both endogenous and exogenous testosterone by binding to the androgen receptor.



## Pk

- This drug taken orally
- Rapidly absorbed and completely absorbed on oral

- Metabolised in liver
- These agents clear through kidneys and some parts through stool.

**SE**

- Gynaecomastia(fluid deposit around the male Areola)
- Gi discomfort
- Liver failure

**6)RADIOISOTOPES:-**

- These are the isotopes of various element which act because of their physical properties of eliminating beta and gamma radiation .it produce ionization in the cells. There by disrupting cellular metabolism and cause cell destruction
- Radio iodine, Radio gold, Radio phosphorus are used.

Common Radioisotopes in Treating Cancer <sup>1</sup>		Common Radioisotopes Used to Detect Cancer <sup>1</sup>	
Radioisotope	Cancer Used to Treat	Type of Isotope	What type of Cancer it Detects
Technetium-99	Liver disorders, brain tumors	Technetium-99	Brain Tumors
Holmium-166	Liver Tumors	Iodine-131	Thyroid Cancer
Iodine-131	Thyroid Cancer	Phosphorus-32	Skin Cancer
Cesium-137, and Cobalt-60 are used to destroy other types of cancer		Holmium-166	Liver Cancer
		Gallium-68	Pancreatic Cancer

