CHEMOTHERAPY OF ANTICANCER DRUGS

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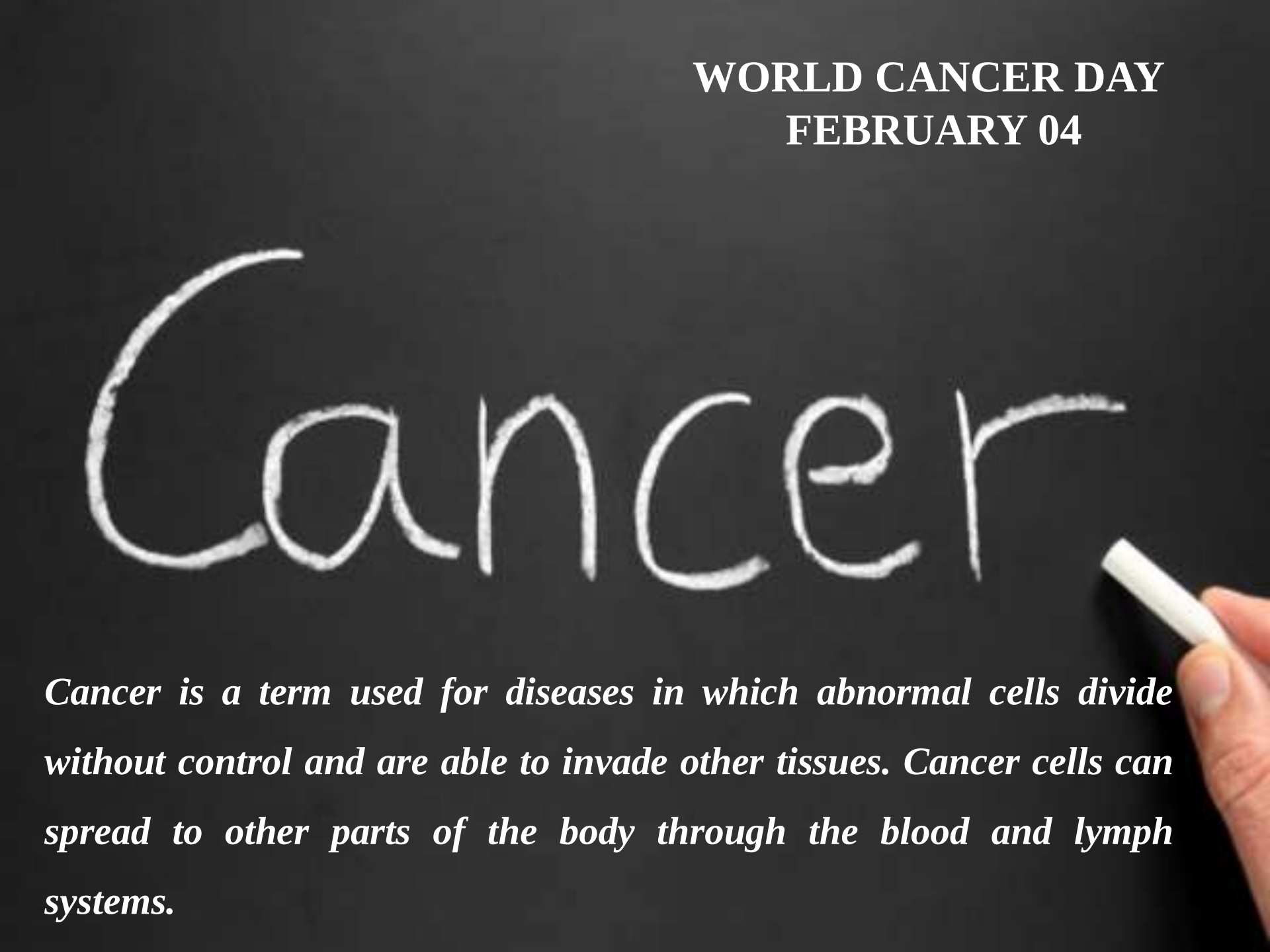
WORLD CANCER DAY
FEBRUARY 04



Cancer is a term used for diseases in which abnormal cells divide without control and are able to invade other tissues. Cancer cells can spread to other parts of the body through the blood and lymph systems.

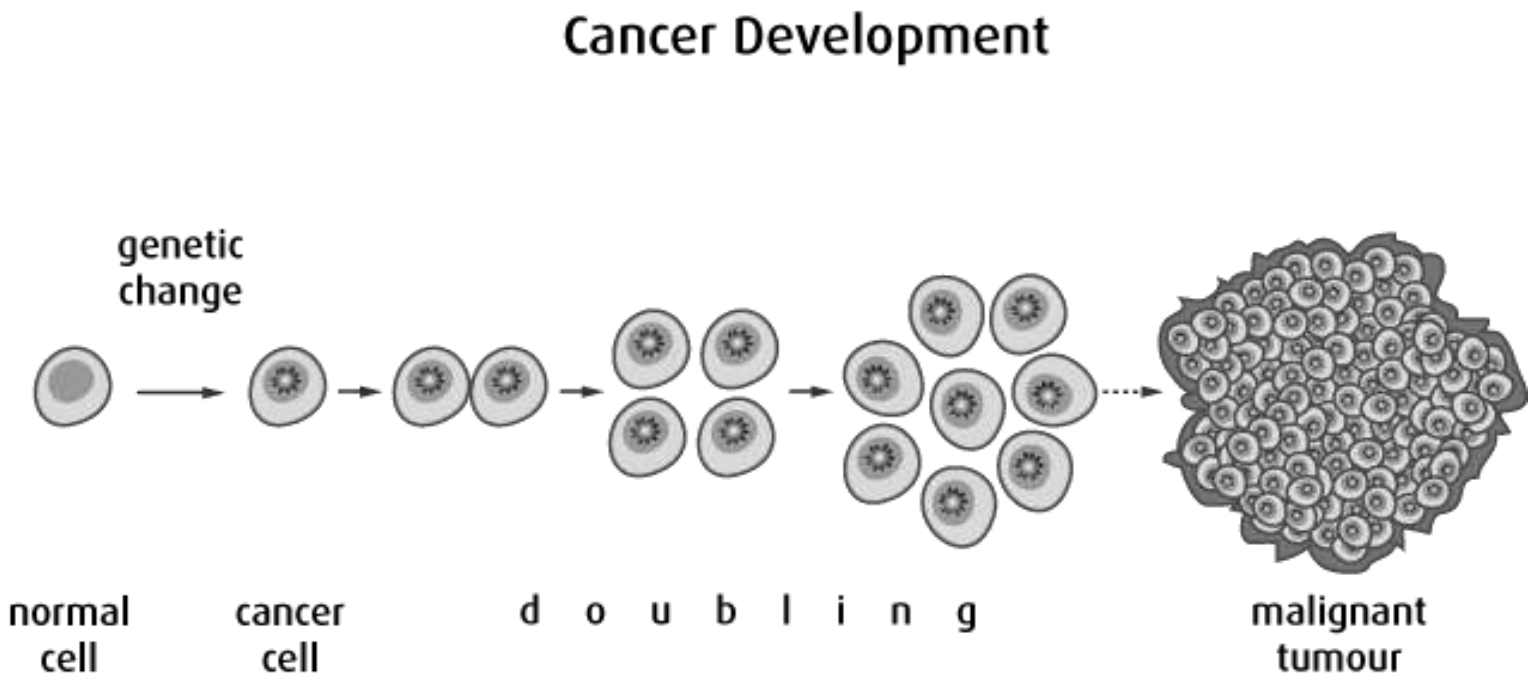
Cancer it is a class of disease characterized by uncontrolled proliferation of cells. Dedifferentiation, Loss of function, Invasion to local tissues, Spread or metastasis to other parts of the body.

- ***Cancer is not a single disease. It is a group of more than 200 different diseases.***
- ***Cancer may spread to other parts of the body.***
- ***Currently 1 in 4 deaths in USA are due to cancer.***
- ***1 in 17 deaths are due to lung cancer.***
- ***An estimated 2,22,520 people diagnosed lung cancer in the United States in 2010.***
- ***Lung cancer is the most common cancer in men.***
- ***Breast cancer is the most common cancer in women.***
- ***Around 15 lakh new cases are diagnosed every year in India.***

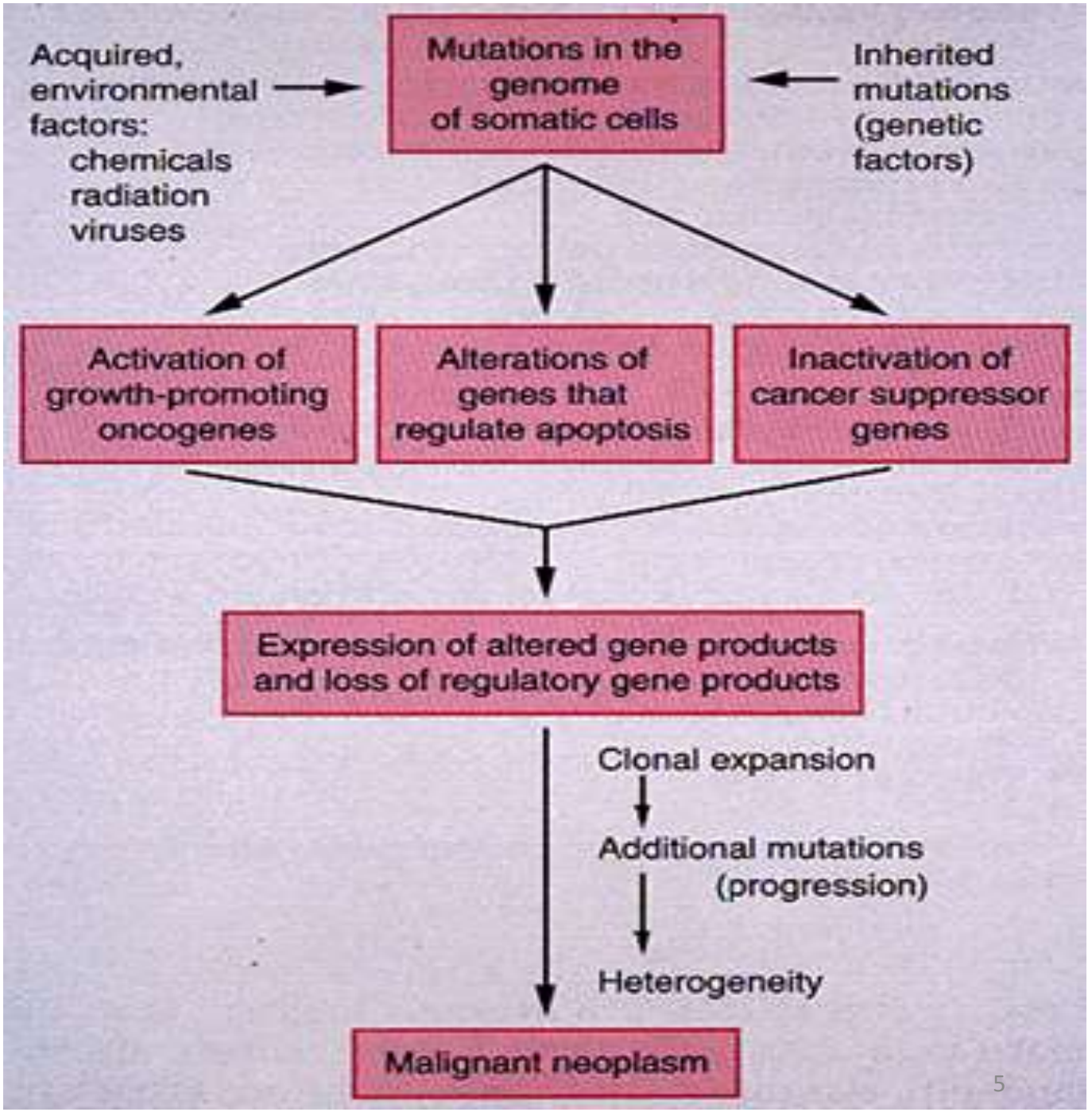
The medical term for tumor (or) cancer is Neoplasm, which means a relatively autonomous growth (or)un coordinated cell proliferation of body tissue.

The term Neoplasm means New growth & the process of cell proliferation is called Neoplasia.

The branch of medicine which deals with the excessive study of neoplasm (tumor) and its development diagnosis and treatment is called "Oncology."



MOLECULAR BASIS OF CANCER

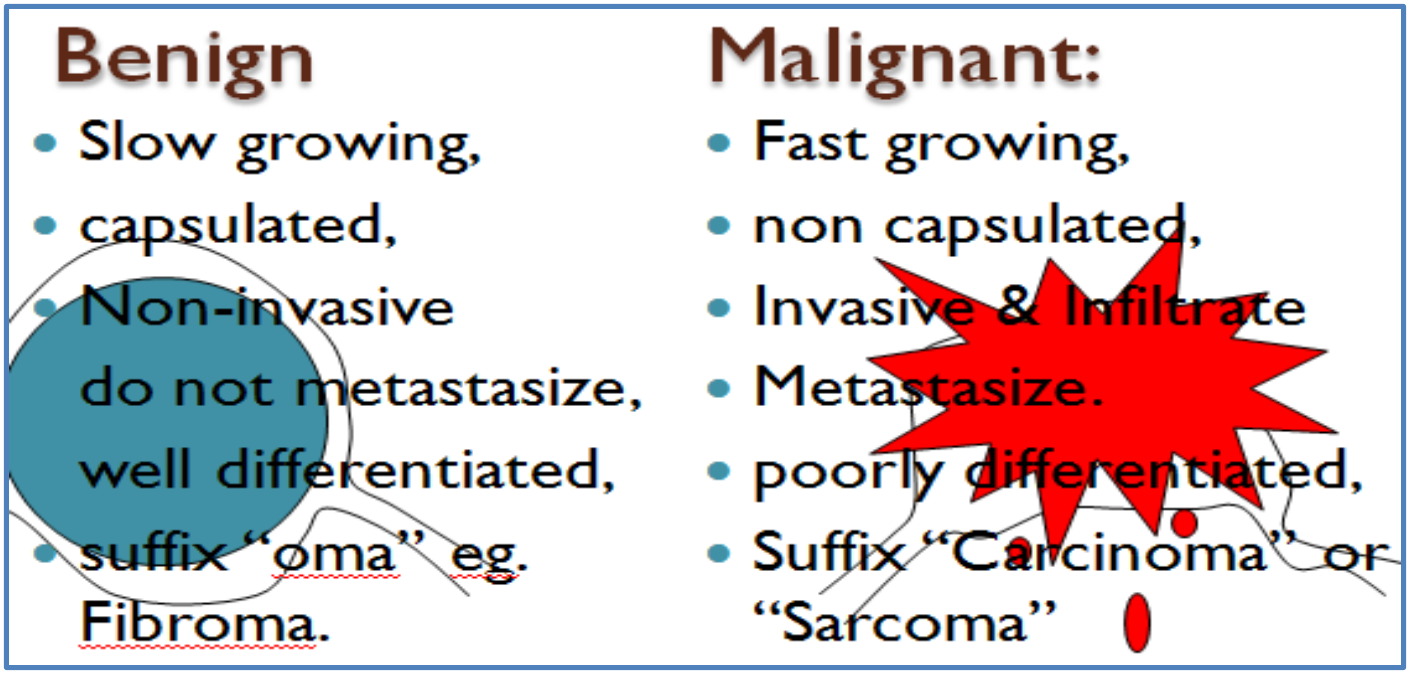


TYPES OF TUMORS

Not all tumors are cancerous; tumors can be benign or malignant.

Benign tumors aren't cancerous. They can often be removed, and, in most cases, they do not come back. Cells in benign tumors do not spread to other parts of the body.

Malignant tumors are cancerous. Cells in these tumors can invade nearby tissues and spread to other parts of the body. The spread of cancer from one part of the body to another is called metastasis.



TYPES OF CANCER

BASED ON ORIGIN:

Carcinoma - cancer that begins in the skin or in tissues that line or cover internal organs. There are a number of subtypes of carcinoma, including adenocarcinoma basal cell carcinoma, squamous cell carcinoma and transitional cell carcinoma.

Sarcoma - cancer that begins in bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue.

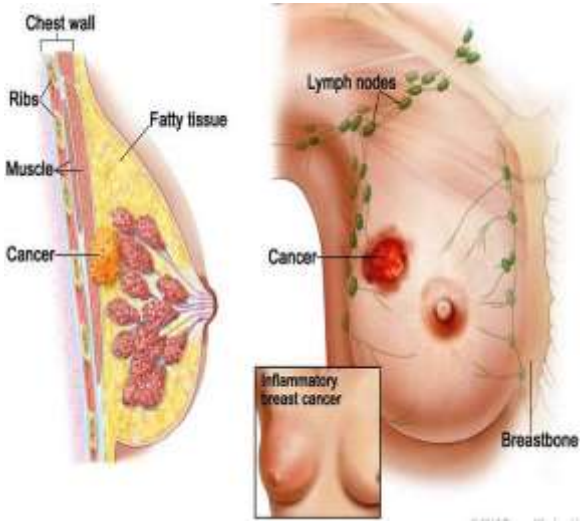
Leukemia - cancer that starts in blood-forming tissue such as the bone marrow and causes large numbers of abnormal blood cells to be produced and enter the blood.

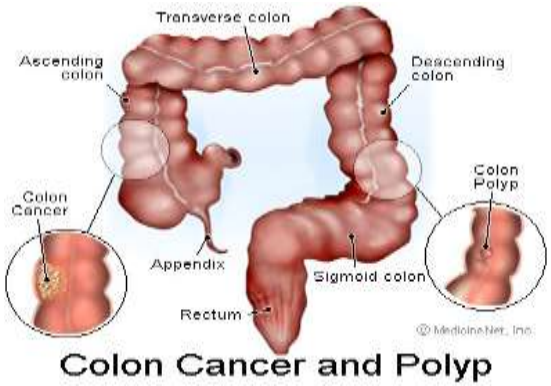
Lymphoma and myeloma - cancers that begin in the cells of the immune system.

Central nervous system cancers - cancers that begin in the tissues of the brain and spinal cord.

Germ cell cancer- germ cells; testicle and ovarian cancers.

Blastoma-resembles embryonic tissue.





Colon Cancer and Polyp

The agents which causes cancer is called carcinogenesis.

1. ***PHYSICAL AGENTS:*** *UV and ionizing radiations (x-ray, gamma and alpha and beta rays cause cancer, UV rays of sunlight, nuclear fission. These radiations have mutagenic effect. Ex: Leukaemias, skin, lung, breast, osteosarcoma, thyroid cancer*

2. ***BIOLOGICAL AGENTS:***

   a) Bacterial agents: peptic ulcers and chronic gastritis and if these are be left untreated for a long time leads to gastric cancer.

   b) Fungal agents: The fungus Aspergillus flavus releases aflatoxins in stored.

   c) Viral agents: Cervical cancer, Burkitt's lymphoma, hairy cell lukaemia, Haepatic carcinoma.

3. ***CHEMICAL AGENTS:*** *Alkylating agents, The acylating agents, Polyaromatic hydrocarbons, Aniline, arsenic, Anthracenes, dimethylsulphate, acetyl imidazole, dimethylcarbamyl chloride.*

4. ***GENETIC FACTORS:*** *Genetic inheritance plays a key role in causing some of the cancers (breast carcinoma, retino blastinoma).*

5. ***DIET AND HABITS:*** *People taking rich in fats, low fibre content.*

SYMPTOMS

- ***Significant weight loss***
- ***Poor appetite***
- ***Excessive sweating(night sweat)***
- ***Severe Pains***
- ***Neurological symptoms***
- ***Change in appearance***
- ***Blood in vomiting***
- ***Chronic cough (lung cancer)***
- ***Bowel Changes (Colon cancer)***
- ***Fever(Leukemia and lymphoma)***

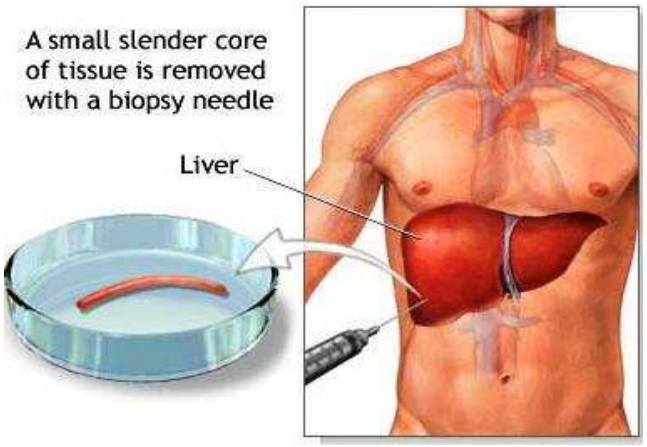
DIAGNOSIS

1. ***Physical examination***
2. ***Biopsy of the tumor***
3. ***Blood tests (Complete Blood Count-CBC)***
4. ***Newer molecular and Cellular diagnosis test***

- X-Ray

-MRI scanning (Magnetic resonance imaging)

-CT scan



TREATMENT OF CANCER

1. **CHEMOTHERAPY**

Rapidly dividing cells metastasised cancers (leukemia and lymphoma)

2. **RADIOTHERAPY**

In combination with other therapies iodine -131 (thyroid cancer)

iridium-192 (breast cancer).

3. **SURGERY**

not metastasized cancers prostate, breast or testicular cancers

4. **IMMUNOTHERAPY**

immune system made strong to fight against cancers

5. **HORMONE THERAPY**

killing cancer cells by altering hormone levels

6. **GENE THERAPY**

replacing defective genes

CLASSIFICATION OF ANTINEOPLASTIC AGENTS

There are two Major Groups of Anticancer Drugs:

1. CHEMICAL STRUCTURE AND RESOURCE OF THE DRUG

A) Cytotoxic Drugs (largest group)

- **-Alkylating agents**
- **-Antimetabolites**
- **-Antitumor antibiotics**
- **- Plant-derived products**
- **-Miscellaneous cytotoxic drugs**

B) Hormones and hormone antagonists

C) Immunomodulators

- **-Immunostimulants**
- **-Immunosuppressant**

2. CELL CYCLE OR PHASE SPECIFICITY OF THE DRUG

A) Cell cycle non- specific agents(CCNS)

Ex : Alkylating Agents, Platinum Compounds, Antibiotics

B) Cell cycle specific agents:

Drugs that act during a specific phase of the cell cycle

- **-S- Phase - Antimetabolites , Topoisomerase Inhibitors**
- **-M Phase - Vinca Alkaloids, Taxanes**
- **-G2 Phase – Bleomycin**

Chemical Classification of Anti-Cancer Agents

ALKYLATING AGENTS

A) Nitrogen Mustards

- -Mechlorethamine
- -Cyclophosphamide
- -Melphalan
- -Chlorambucil

B) Nitrosoureas

- -Carmustine
- -Lomustine
- -semustine

C) Alkyl Sulfonates

- -Busulfan

D) Triazine

- -Dacarbazine
- -Procarbazine

E) Ethylenimine

- -Thio-TEPA

ANTIMETABOLITES

A) Folate antagonist

- -Methotrexate

B) Purine antagonist

- -6-mercaptopurine
- -6-thioguanine
- -Azathioprine

C) Pyrimidine antagonist

- -5-Fluorouracil
- -Cytarabine

ANTIBIOTICS

-Actinomycin(D-actinomycin)

-Doxorubicin

-Daunorubicin(rubidomycin)

-Bleomycin

-Mitoxantrone

-Mitomycin C

-Mithramycin(plicamycin)

IMMUNOMODULATORS

A) Levamisole

B) Interferons

-Interferon alfa-2a and 2 b

C) Interleukins

-Aldesleukin

PLANT-DERIVED PRODUCTS

A) VINCA ALKALOIDS

-Vincristine

-Vinblastine

B) AXANES

-Paclitaxel

-Docetaxel

C) EPIPODOPHYLLO TOXIN

-Etoposide

-Teniposide

HORMONES AND HORMONE ANTAGONISTS

A) Glucocorticoids

-Prednisolon

-Prednisone

B) Estrogen

-Diethylstilbestreol

C) Anti-estrogen

-Tamoxifen

D) Androgens & Anti-androgens

-Testosteron

-Flutamide

E) Progestin

-Medroxy Progesteron Acetate

MISCELLANEOUS AGENTS

-Hydroxyurea (Hydrea)

-Mitotane

-Cisplatin

-Carboplatin

-Mitoxantrone

Enzymes:

-L- Asparaginase (Elspar)

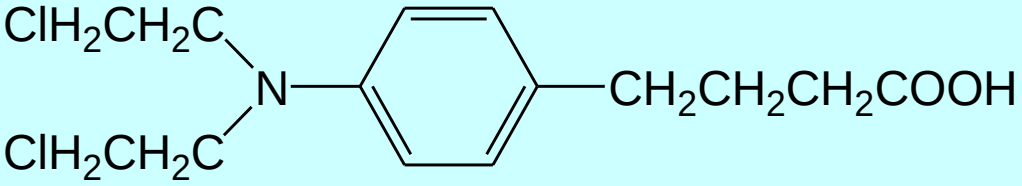
MONOCLONAL ANTIBODIES

- Trantuzumab

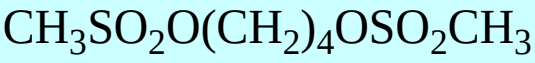
- Rituximab

-Imatinib

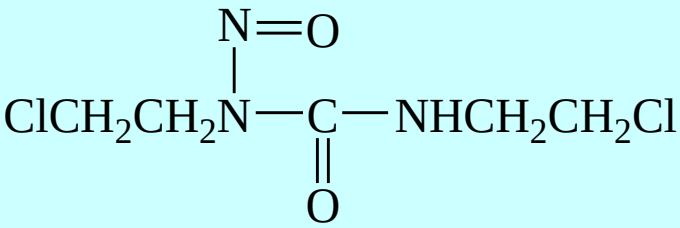
Structures of Alkylating Agents



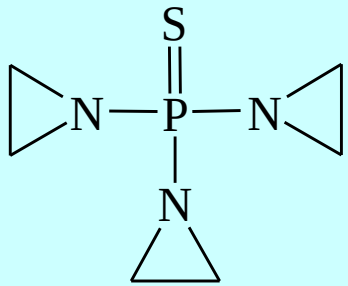
Chlorambucil



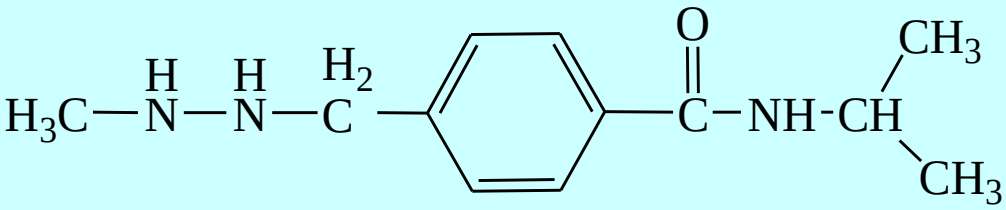
Buslulfan



Carmustine

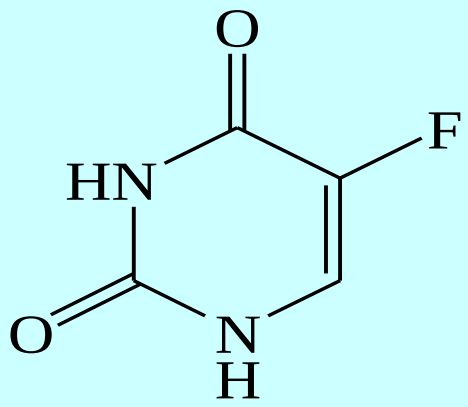


Thio-TEPA

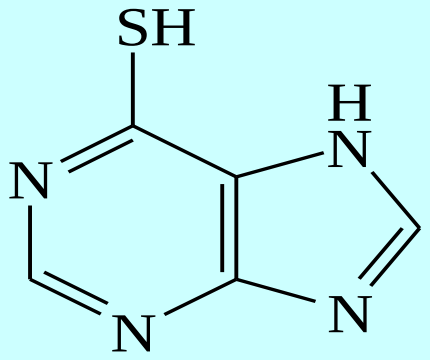


Procarbazine

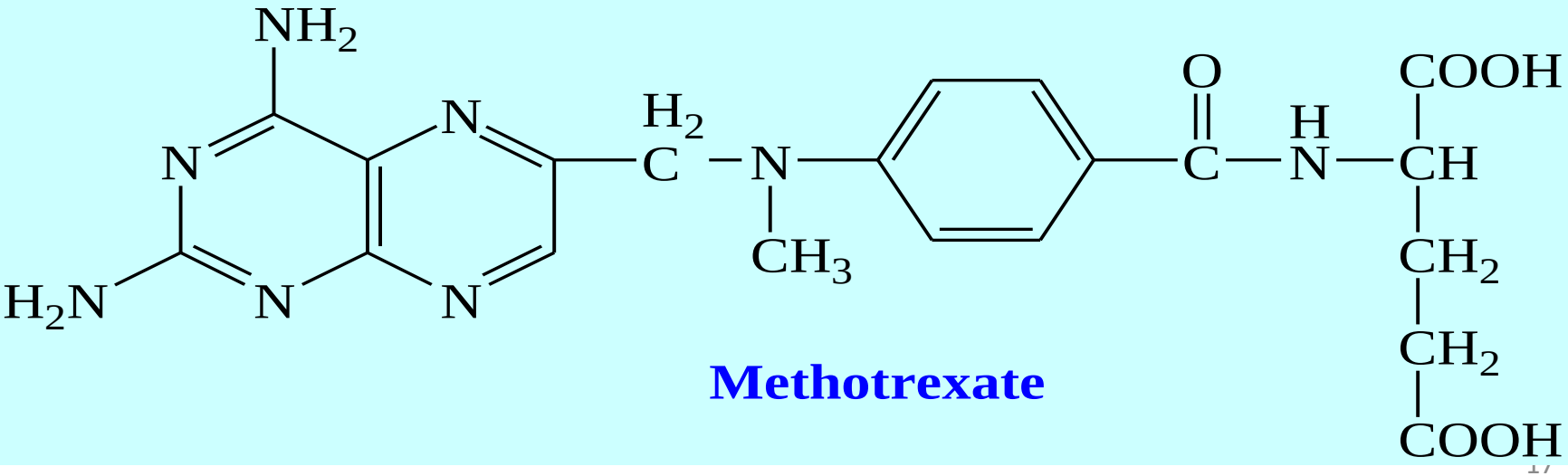
Structures of Antimetabolities



5-Fluoro uracil

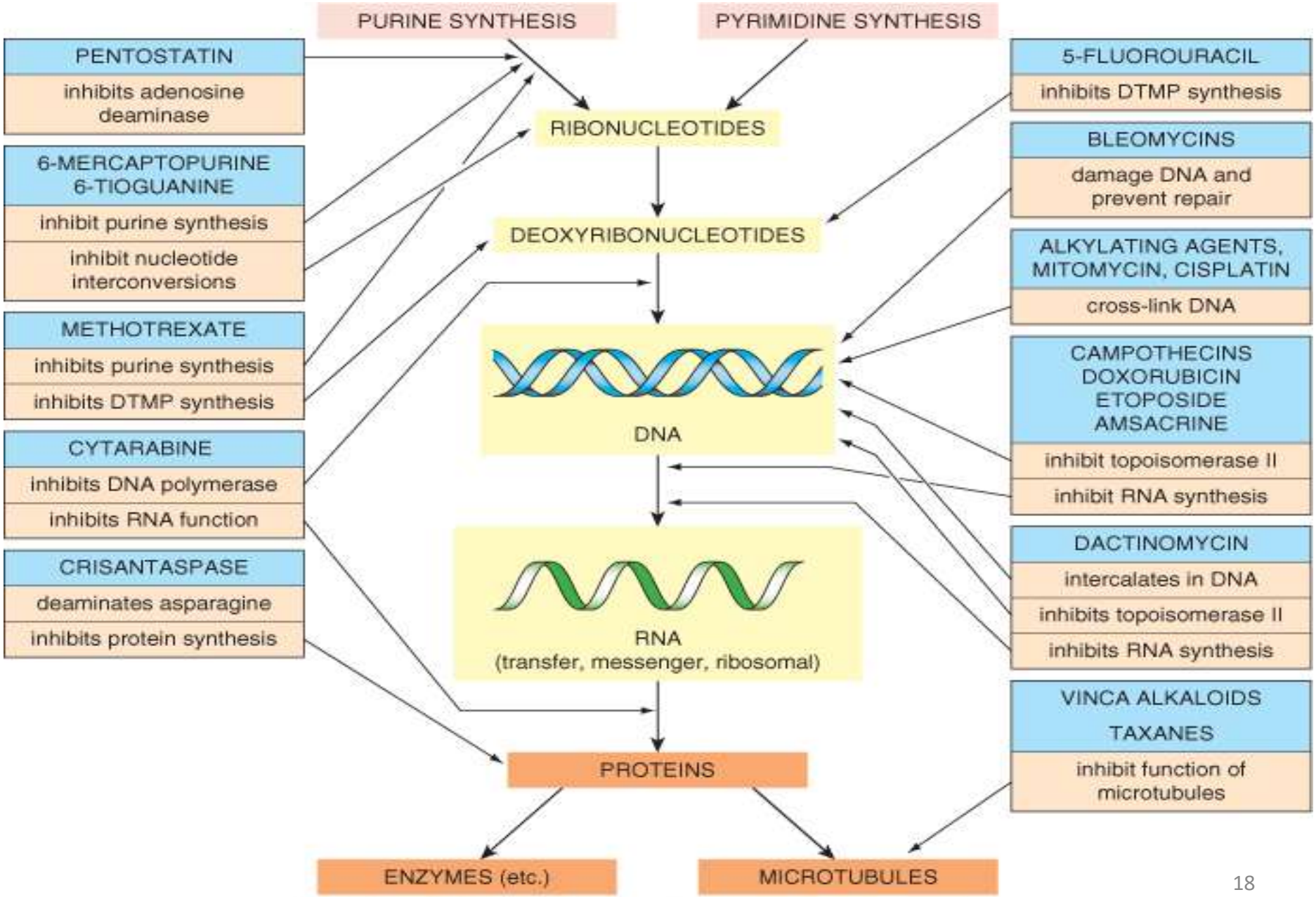


Mercaptopurine



Methotrexate

MECHANISIM OF ACTION OF CYTOTOXIC AGENTS

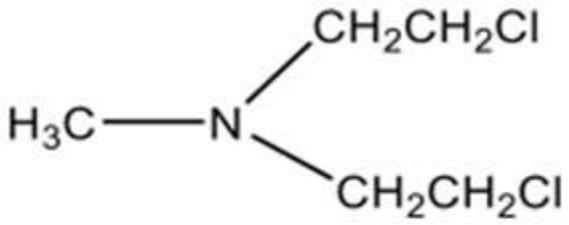


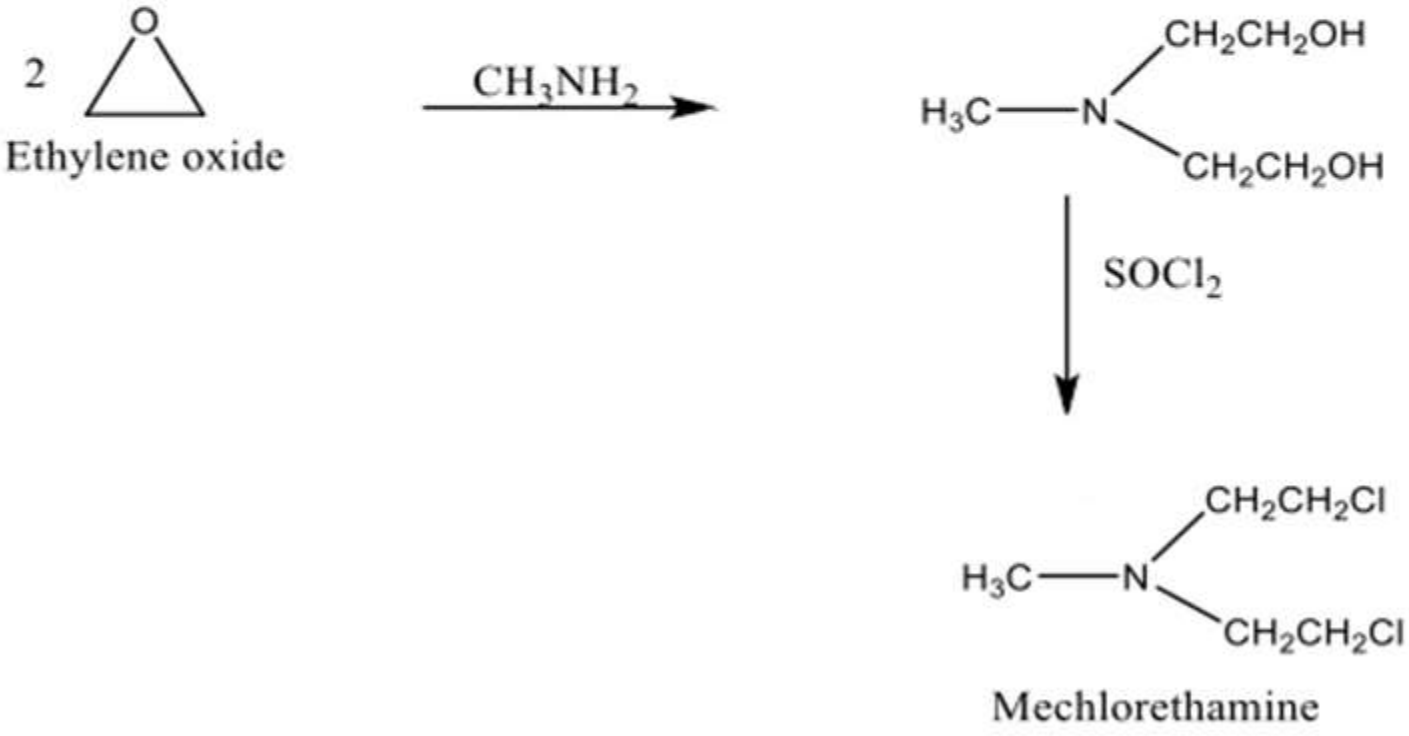
Anticancer agent	*1. Mechanism of Action*	*2. Clinical application*	*3. Route*	*4. Side effects*
		a. Nitrogen Mustards		
Mechlorethamine	*DNA cross-links, resulting in inhibition of DNA synthesis and function*	*Hodgkin's and non-Hodgkin's lymphoma*	*Must be given Orally*	*Nausea and vomiting, decrease in PBL count, BM depression, bleeding, alopecia, skin pigmentation, pulmonary fibrosis*
		b. Alkyl Sulfonates		
Busulfan	**Atypical alkylating agent.**	**Chronic granulocytic leukemia**	**Orally effective**	**Bone marrow depression, pulmonary fibrosis, and hyperuricemia**
		c. Nitrosoureas		
Lomustine	**Lomustine alkylates and crosslinks DNA, thereby inhibiting DNA and RNA synthesis. Lomustine is lipophilic and crosses the blood-brain barrier**	**Hodgkins and non-Hodgkins lymphoma, malignant melanoma and epidermoid carcinoma of lung**	**Orally effective**	**Nausea and vomiting, Nephrotoxicity, nerve dysfunction**

Aticancer agent	1. MOA	2. Clinical application	3. Route	4. Side effects
		Antimetabolites		
Pyrimidine Analogs: Cytosine	inhibits DNA synthesis	most effective agent for induction of remission in acute myelocytic leukemia; also used for induction of remission acute lymphoblastic leukemia, non-Hodgkin's lymphomas; usually used in combination chemotherapy	Orally effective	bone marrow depression
		Plant alkaloids		
A. Vincristine	Cytotoxic: Inhibition of mitotic spindle formation by binding to tubulin. M-phase of the cell cycle.	Metastatic testicular cancer, Hodgkins and non-Hodgkins lymphoma, Kaposi's sarcoma, breast carcinoma, neuroblastoma	I.V.	Bone marrow depression, epithelial ulceration, GI disturbances, neurotoxicity
		Antibiotics		
a. Dactinomycin (ACTINOMYCIN D)	It binds to DNA and inhibits RNA synthesis, impaired mRNA production & protein synthesis	Rhabdomyosarcoma and Wilm's tumor in children;	I.V.	Bone marrow depression, nausea and vomiting, alopecia, GI disturbances, and ulcerations of oral mucosa
		Epipodophyllotoxins		
A. Etoposide	Binds to and inhibits Topoisomerase II and its function. Fragmentation of DNA leading to cell death, apoptosis.	Testicular cancer, small-cell lung carcinoma, Hodgkin lymphoma, carcinoma of breast, Kaposi's sarcoma associated with AIDS	I.V.	Myelo suppression, alopecia

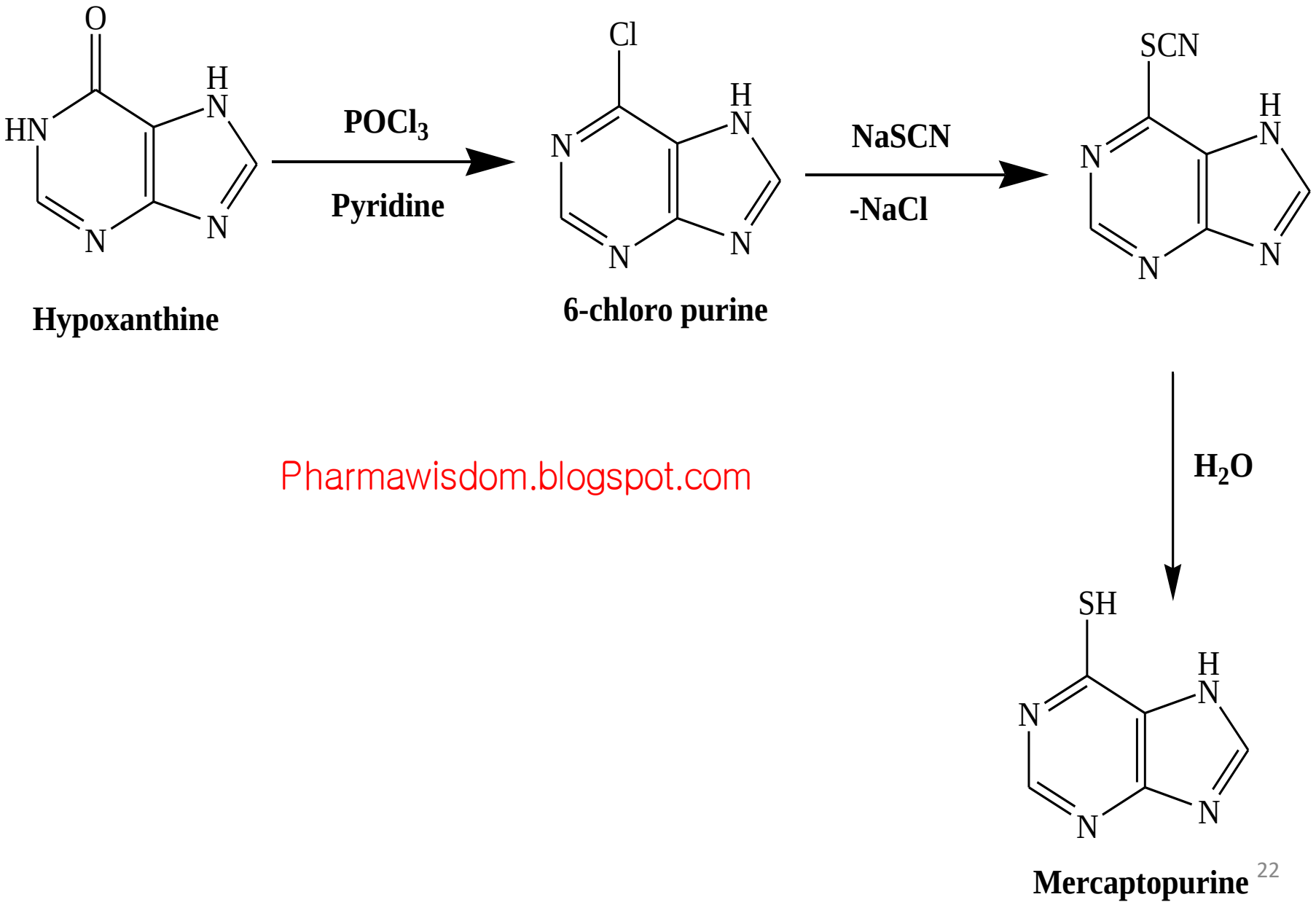
Synthesis of Mechlorethamine

Mechlorethamine

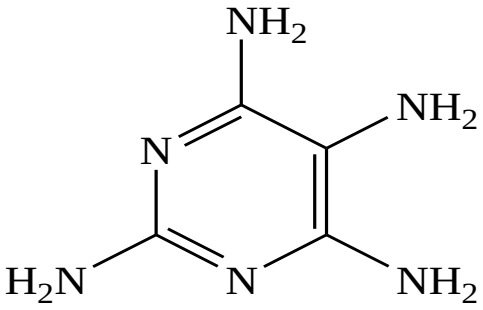




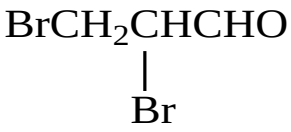
Synthesis of Mercaptopurine



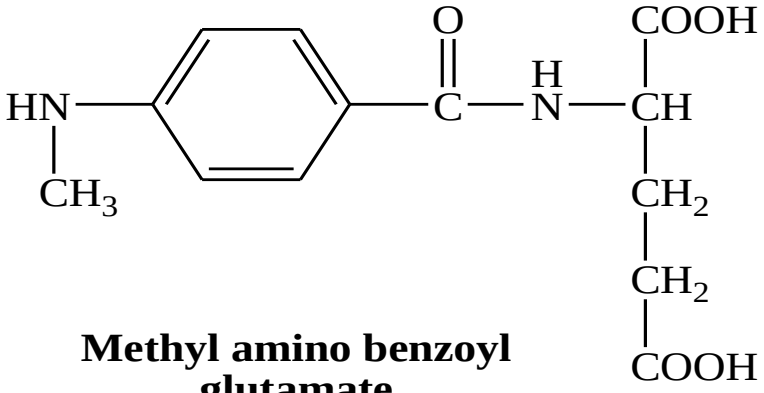
Synthesis of Methotrexate



2,4,5,6-Tetra amino pyrimidine



2,3-dibromo propionaldehyde

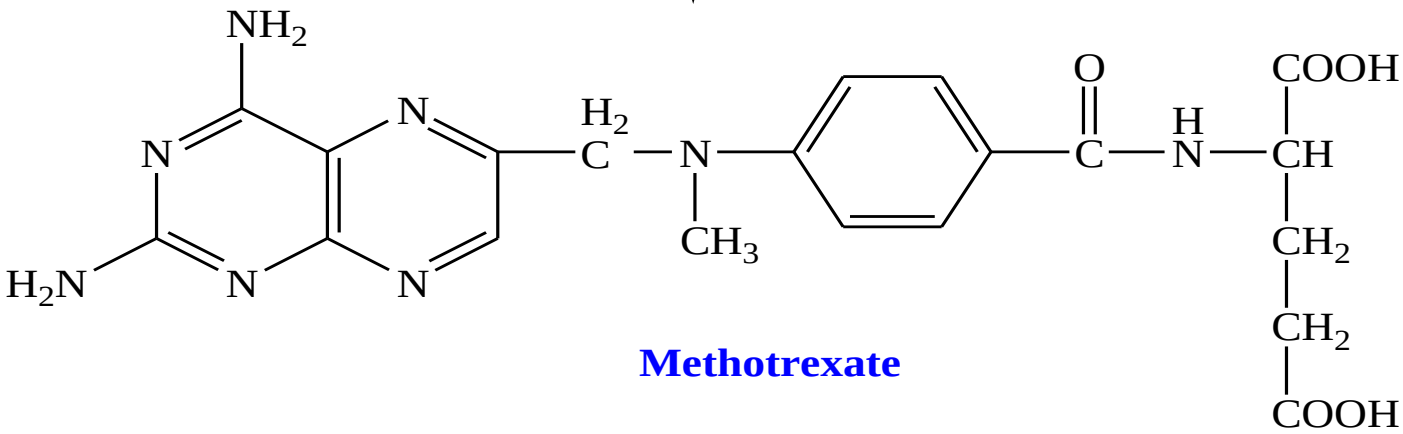


Methyl amino benzoyl glutamate

Cyclization
Dehydration

-2HBr/H_2O

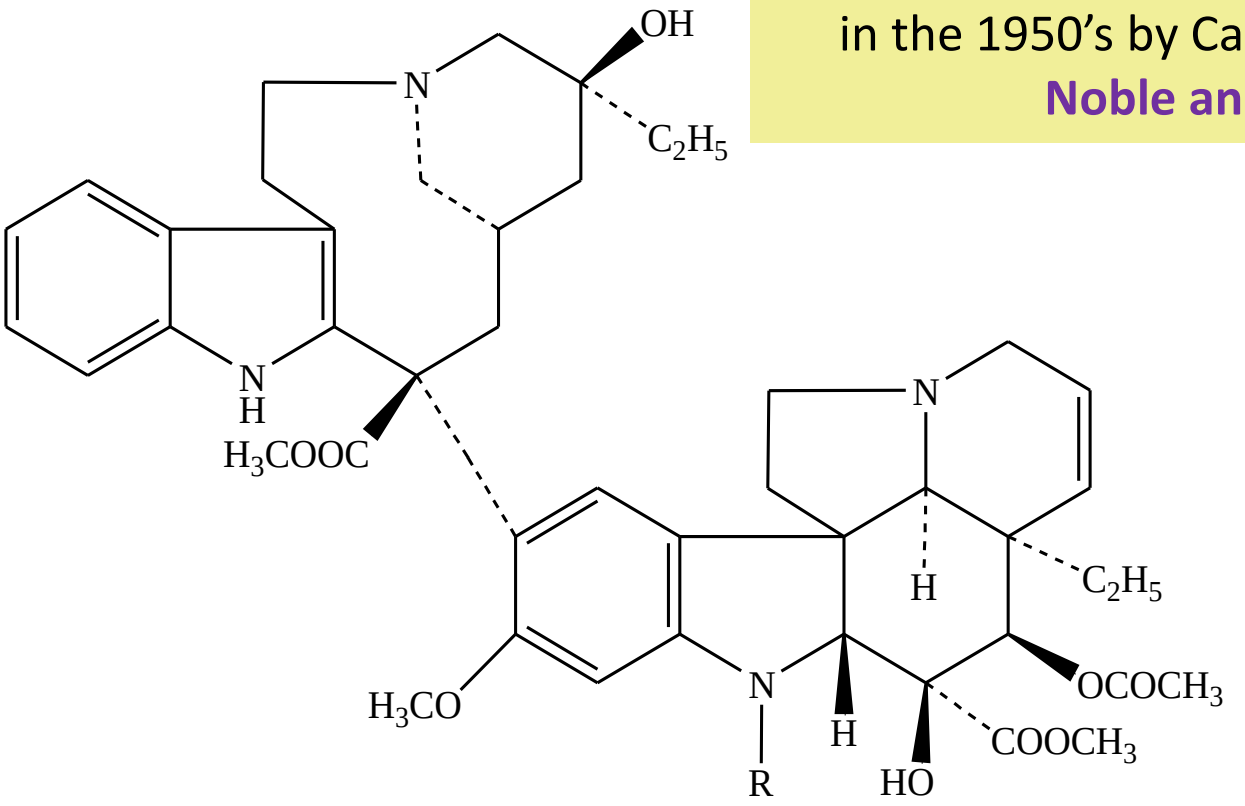
lime water
NaOH
CH_3COOH



Methotrexate

VINCA ALKALOIDS

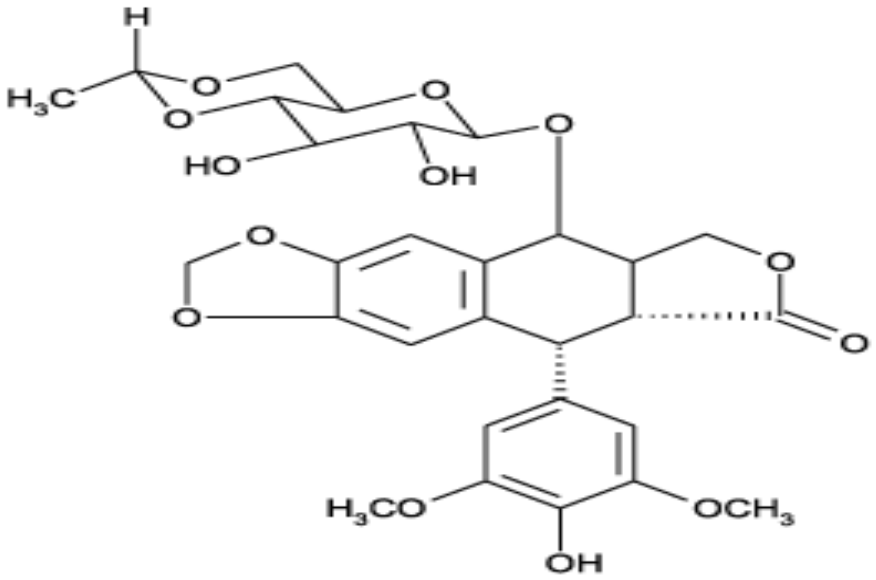
Vinca alkaloids are a set of anti-mitotic and anti-microtubule **alkaloid** agents originally derived from the Madagascar periwinkle plant **Catharanthus roseus** (basionym **Vinca** rosea) and other **Vinca** plants. **Vinca alkaloids** are used in chemotherapy for cancer. They were discovered in the 1950's by Canadian scientists, **Robert Noble and Charles Beer**.



R = CHO - Vincristine

R = CH_3 - Vinblastine

Etoposide, sold under the brand name Vepesid among others, is a chemotherapy medication used for the treatments of a number of types of cancer including testicular cancer, lung cancer, lymphoma, leukemia, neuroblastoma, and ovarian cancer. It is also used for hemophagocytic lymphohistiocytosis.



TOXICITIES

- ***Bone marrow deression***
- ***Buccal mucosa erosion***
- ***GIT:***
  - ***-Diarrhoea***
  - ***-Haemorrhage***
  - ***-Nausea***
  - ***-Vomiting***
- ***Alopecia***
- ***Carcinogenicity***
- ***Teratogenicity***
- ***Hyperuricemia***
- ***Folinic acid rescue***

Common combination chemotherapy drugs		
Cancer type	**Drugs**	**Acronym**
Breast cancer	Cyclophosphamide, Methotrexate, 5-fluorouracil	CMF
	Doxorubicin, Cyclophosphamide	DC
Hodgkin's disease	Mustine, Vincristine, Procarbazine, Prednisolone	MVPP
	Doxorubicin, Bleomycin, Vinblastine, Dacarbazine	DBVD
Non-Hodgkin's lymphoma	Cyclophosphamide, Doxorubicin, Vincristine, Prednisolone	CDVP
Germ cell tumor	Bleomycin, Etoposide, Cisplatin	BEC
Stomach cancer	Epirubicin, Cisplatin, 5-fluorouracil	ECF
	Epirubicin, Cisplatin, Capecitabine	ECC
Bladder cancer	Methotrexate, Vincristine, Doxorubicin, Cisplatin	MVDC
Lung cancer	Cyclophosphamide, Doxorubicin, Vincristine,	CDV
Colorectal cancer	5-fluorouracil, Folinic acid, Oxaliplatin	FFO

Seven Steps to Prevent Cancer

prevent cancer FOUNDATION

1. Don't use tobacco.
2. Protect your skin from the sun.
3. Eat a healthy diet.
4. Maintain a healthy weight and be physically active.
5. Practice safer sex and avoid risky behaviors.
6. Get immunized (HPV & hepatitis vaccines).
7. Know your family medical history and get regular cancer screenings.

To learn more, please visit www.preventcancer.org

Anti-cancer Super Foods


Turmeric


Cruciferous vegetables


Legumes


Garlic


Lemon

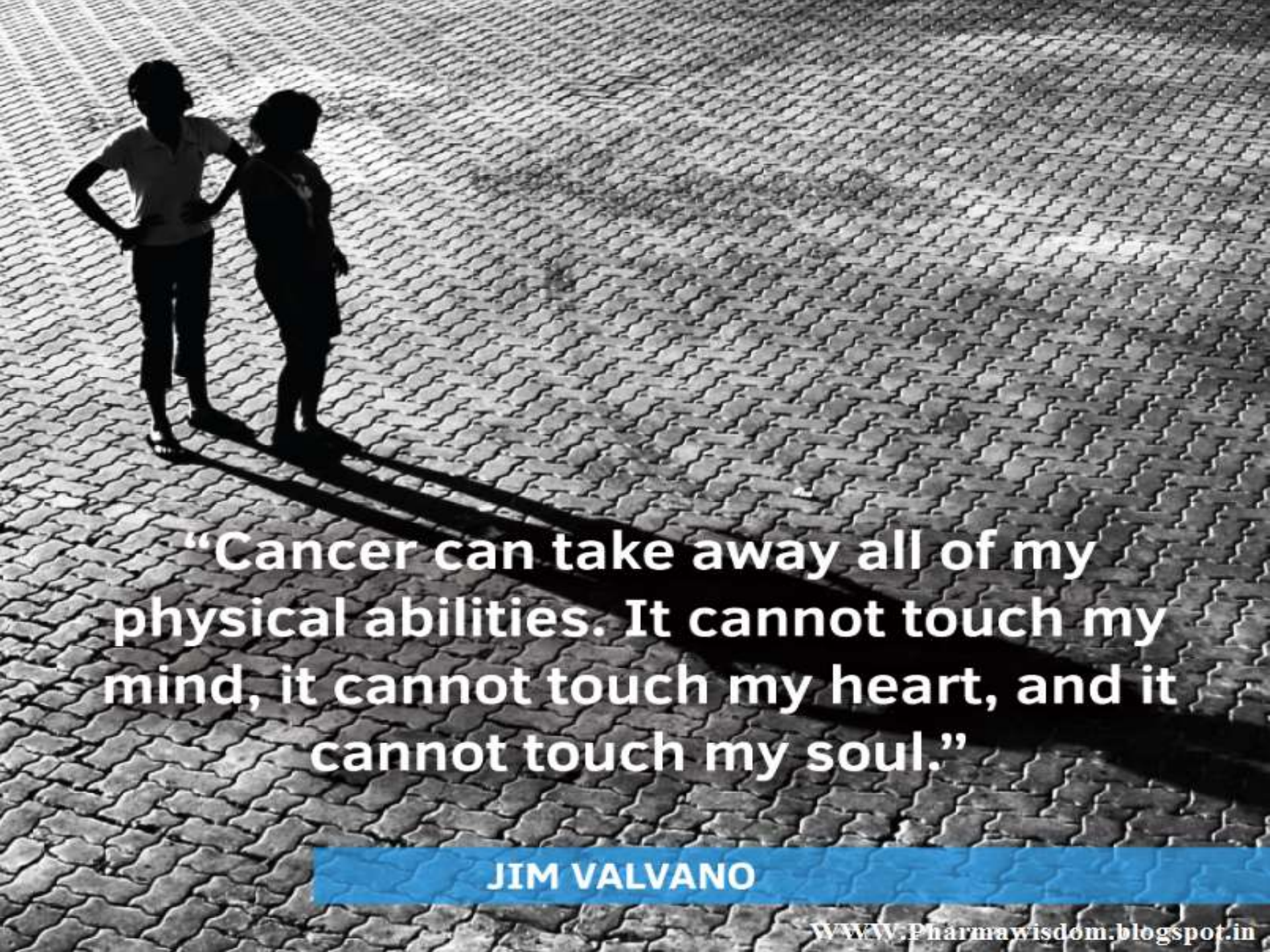

Berries


Oily Fishes like Tuna


Nuts like Almonds

www.siddham.in


“Attitude is a little thing that makes a big difference.”
WINSTON CHURCHILL
WWW.Pharmawisdom.blogspot.in


"Cancer can take away all of my physical abilities. It cannot touch my mind, it cannot touch my heart, and it cannot touch my soul."
JIM VALVANO
WWW.Pharmawisdom.blogspot.in

smoking and drinking is injurious to health……..