NEOPLASIA

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EPIDEMIOLOGY of CANCER

-The branch of medicine deals with the incidence and prevalence of disease in large populations and with detection of the source and cause of epidemics.

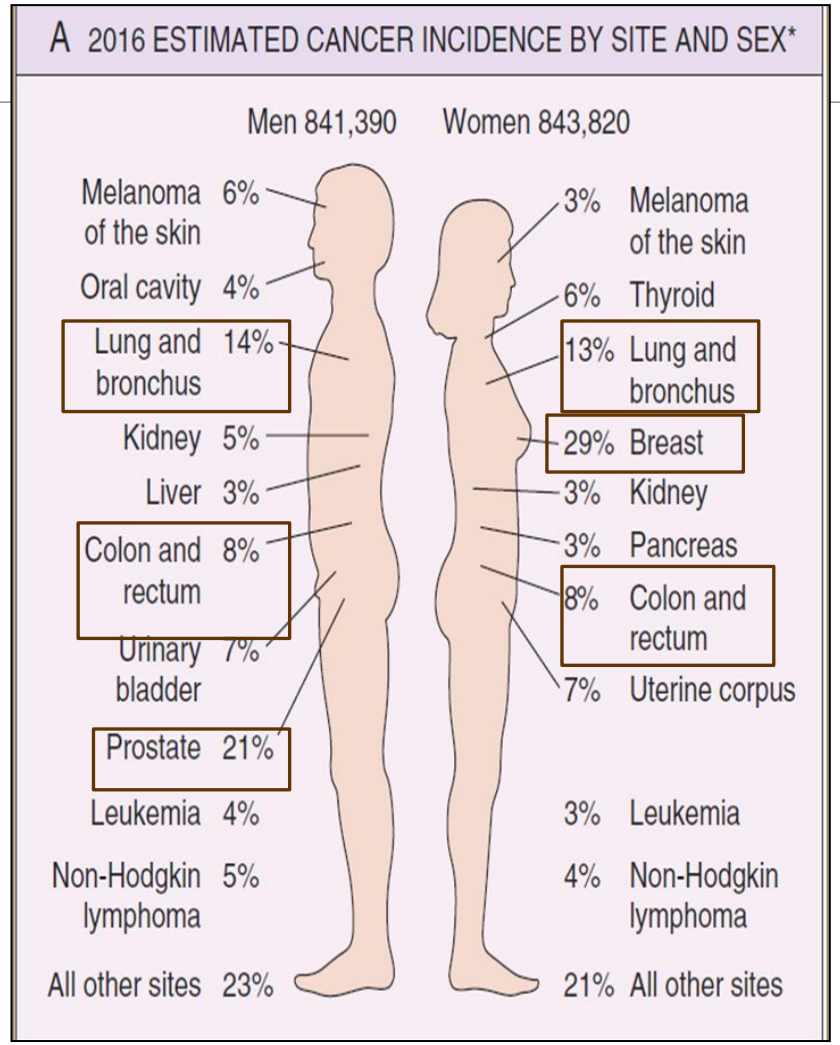
- Contributes substantially to the knowledge about the origin of cancer.

-The concept that **cigarette smoking is** causally associated with **lung cancer** arose from epidemiologic studies.

CANCER INCIDENCE:

- Worldwide Problem
- Increasing
- Due to genetic mutations in cells, which may be spontaneous or environmentally induced.

2016. *American Cancer Society.*



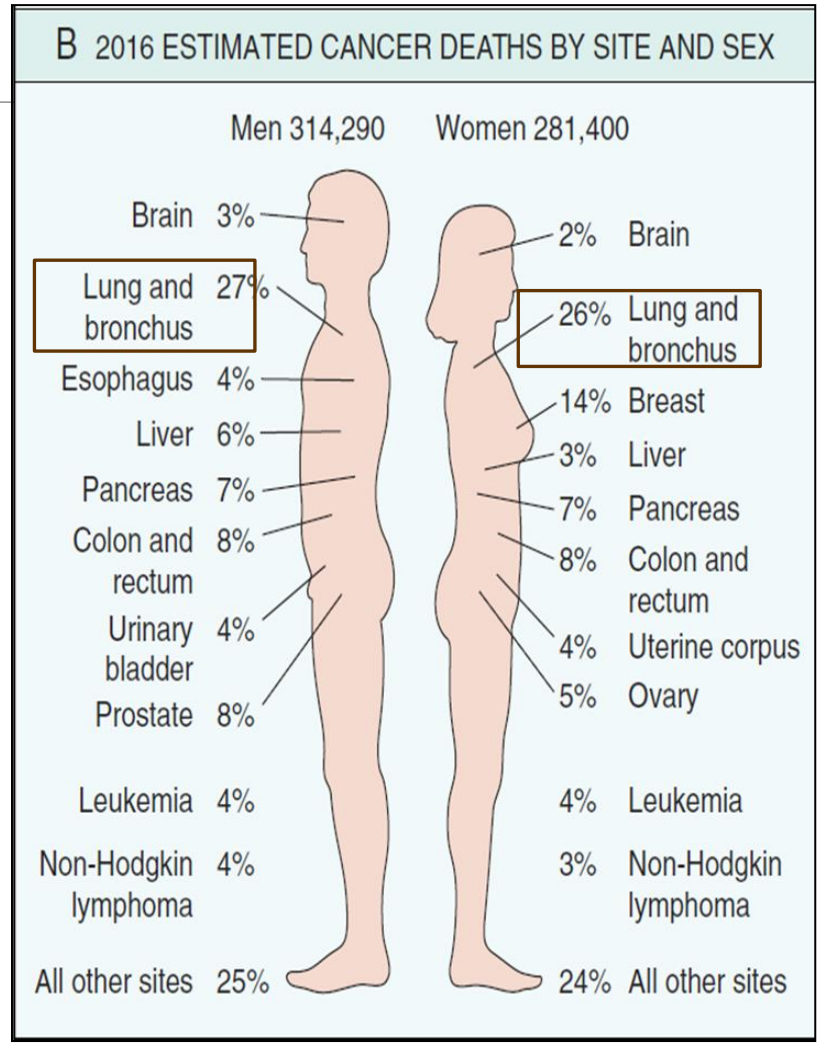


Table (7) Ten most common cancers among Jordanians, Males, 2014

Rank	Site	Frequency	Percent
1	Colorectal	371	13.6
2	Lung	326	12.0
3	Urinary Bladder	244	9.0
4	Prostate	229	8.4
5	Non-Hodgkin lymphoma	153	5.6
6	Leukemia	129	4.7
7	Hodgkin disease	113	4.2
8	Stomach	99	3.6
9	Kidney	93	3.4
10	Larynx	85	3.1

Table (8) Ten most common cancers among Jordanian Females , 2014

Rank	Site	Frequency	Percent
1	Breast	1174	39.4
2	Colorectal	287	9.6
3	Thyroid	173	5.8
4	Uterous	161	5.4
5	Non-Hodgkin lymphoma	121	4.1
6	Ovary	88	3.0
7	Hodgkin disease	78	2.6
8	Lung	77	2.6
9	Leukemia	66	2.2
10	Brain, Nervous system	60	2.0

JORDAN CANCER REGISTRY

- **WHAT FACTORS may influence the incidence of cancer?**

Incidence may be related to:

1. Geographic and Environmental factors.
2. Age.
3. Hereditary factors.
4. Acquired predisposing factors.

Genetic polymorphism is responsible for:

- ❖ Individual predisposition to disease
- ❖ Individual response to environmental agents
- ❖ Individual response to drugs

1. Geographic & environment (Multifactorial)

-Environmental factors are the predominant determinant of the most common sporadic cancers

- **Prostatic CA ---- High in USA**
- **Colorectal CA ----High in USA**
- **Breast CA ---- High in USA**
- **Gastric CA ---High in Japan**
- **Skin CA----High in New Zealand**
- **Hepatocellular CA --- High in Africa & China**
- **Nasopharyngeal CA --- Far East**
- **Burkitt Lymphoma --- Africa**

Nearly all the evidence indicates that these geographic differences are environmental rather than genetic in origin.

Environment:

-In the workplace, in food, and in personal practices.
-They can be as universal as sunlight or be largely restricted to urban settings (e.g., asbestos) or particular occupations

- Diet
- Obesity/Overweight
- Occupation (asbestos, radon….)
- Sunlight
- Personal habits (smoking and alcohol consumption).
- Reproductive history (age at first sexual intercourse and the number of sex partners)
- **Infectious** agents (cause **~15% of cancers worldwide**)

2.Age:

- In general, cancer incidence increases with AGE

- The rising incidence with age may be explained by:

1. The accumulation of somatic mutations associated with the emergence of malignant neoplasms
2. The decline in immune competence that accompanies aging.

- However, certain cancers occur more in children:

Acute Leukemia

Some Lymphomas

Some CNS Tumors

Blastomas

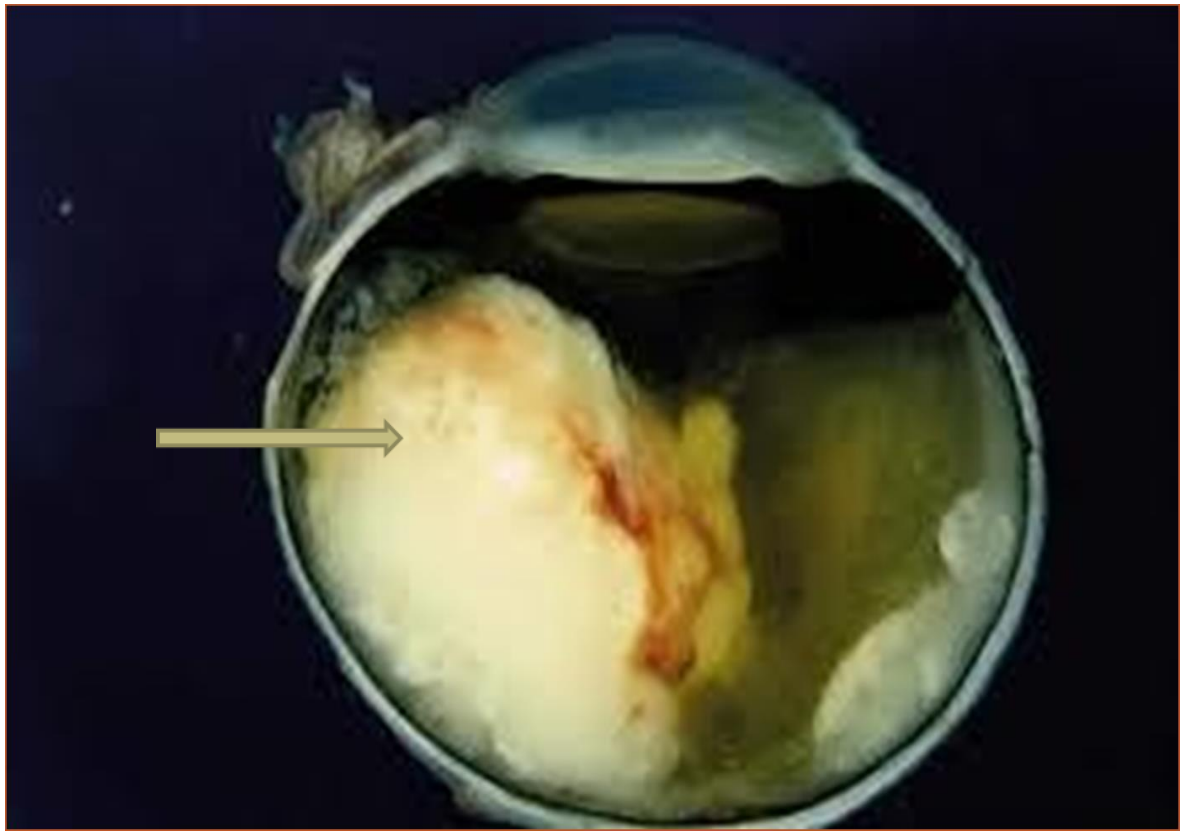
3. Heredity (5%-10% of cancers are familial)

Table 6.4 Inherited Predisposition to Cancer

Inherited Predisposition	Gene(s)
Autosomal Dominant Cancer Syndromes	
Retinoblastoma	*RB*
Li-Fraumeni syndrome (various tumors)	*TP53*
Melanoma	*CDKN2A*
Familial adenomatous polyposis/colon cancer	*APC*
Neurofibromatosis 1 and 2	*NF1, NF2*
Breast and ovarian tumors	*BRCA1, BRCA2*
Multiple endocrine neoplasia 1 and 2	*MEN1, RET*
Hereditary nonpolyposis colon cancer	*MSH2, MLH1, MSH6*
Nevoid basal cell carcinoma syndrome	*PTCH1*
Autosomal Recessive Syndromes of Defective DNA Repair	
Xeroderma pigmentosum	Diverse genes involved in nucleotide excision repair
Ataxia-telangiectasia	*ATM*
Bloom syndrome	*BLM*
Fanconi anemia	Diverse genes involved in repair of DNA cross-links

A. Inherited AD Cancer Syndromes:

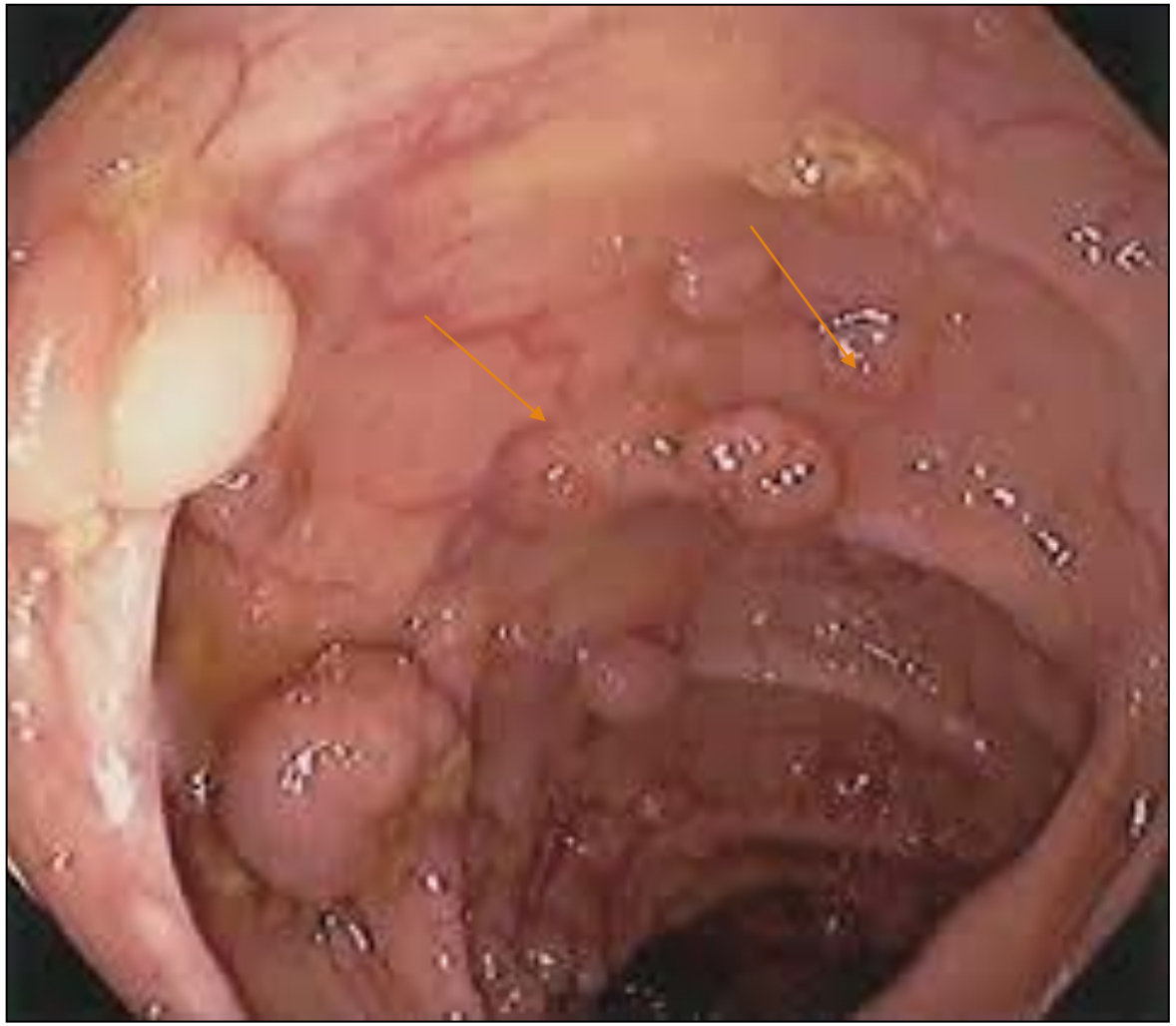
White tumor in the retina of the eyeball (gross view).



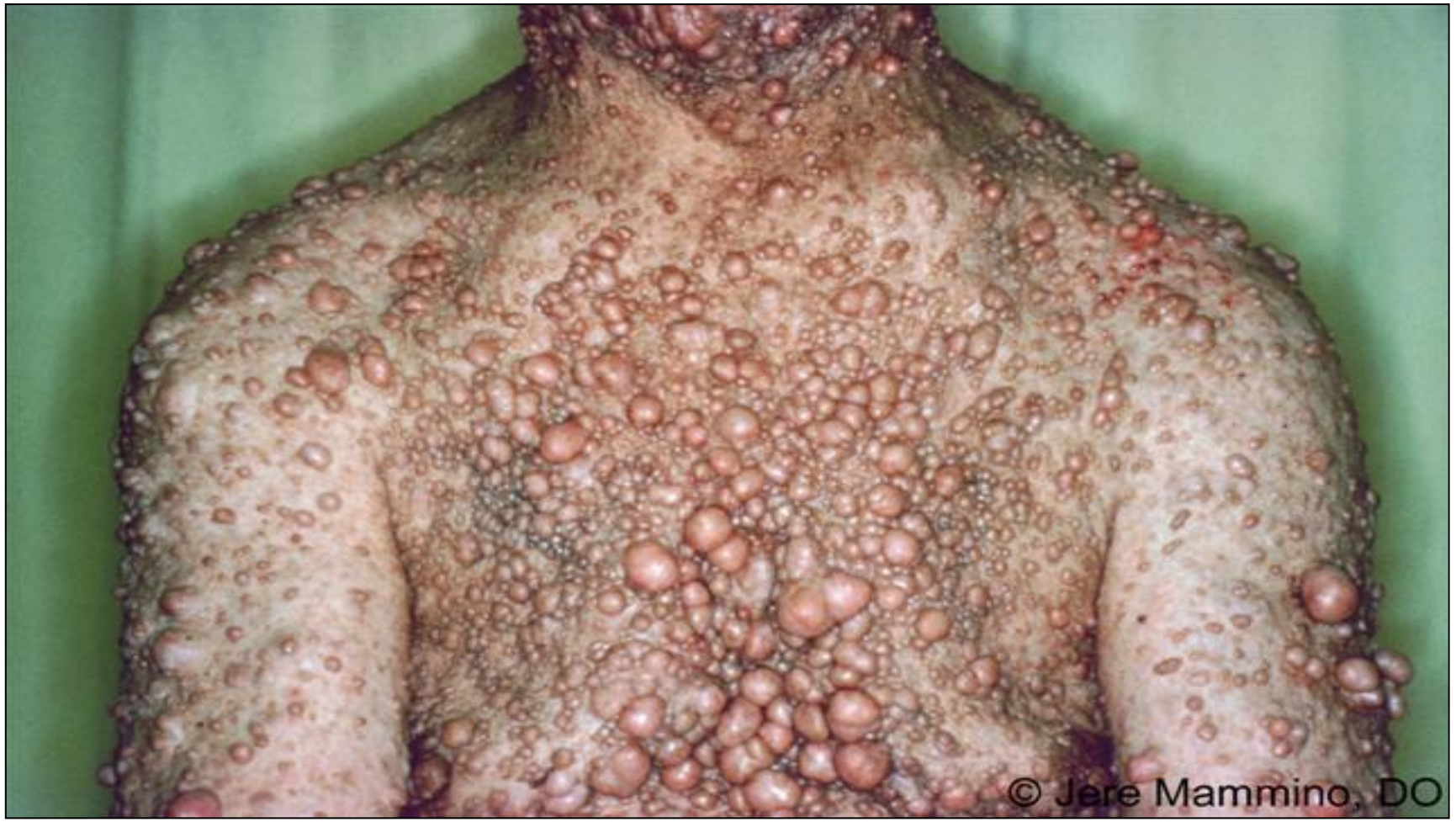
Retinoblastoma (malignant tumor) in the right eye of a child, is seen as a white patch.

Gross view of **familial polyposis coli (FAP),** the colon is studded with hundreds of mucosal polyps.

Endoscopic view of **familial polyposis coli (FAP)** showing numerous mucosal adenomatous polyps of the colon .



- **Neurofibromatosis** is an autosomal dominant hereditary neoplastic disease.
- Hundreds of neurofibromas with café aulait pigmentation of the skin



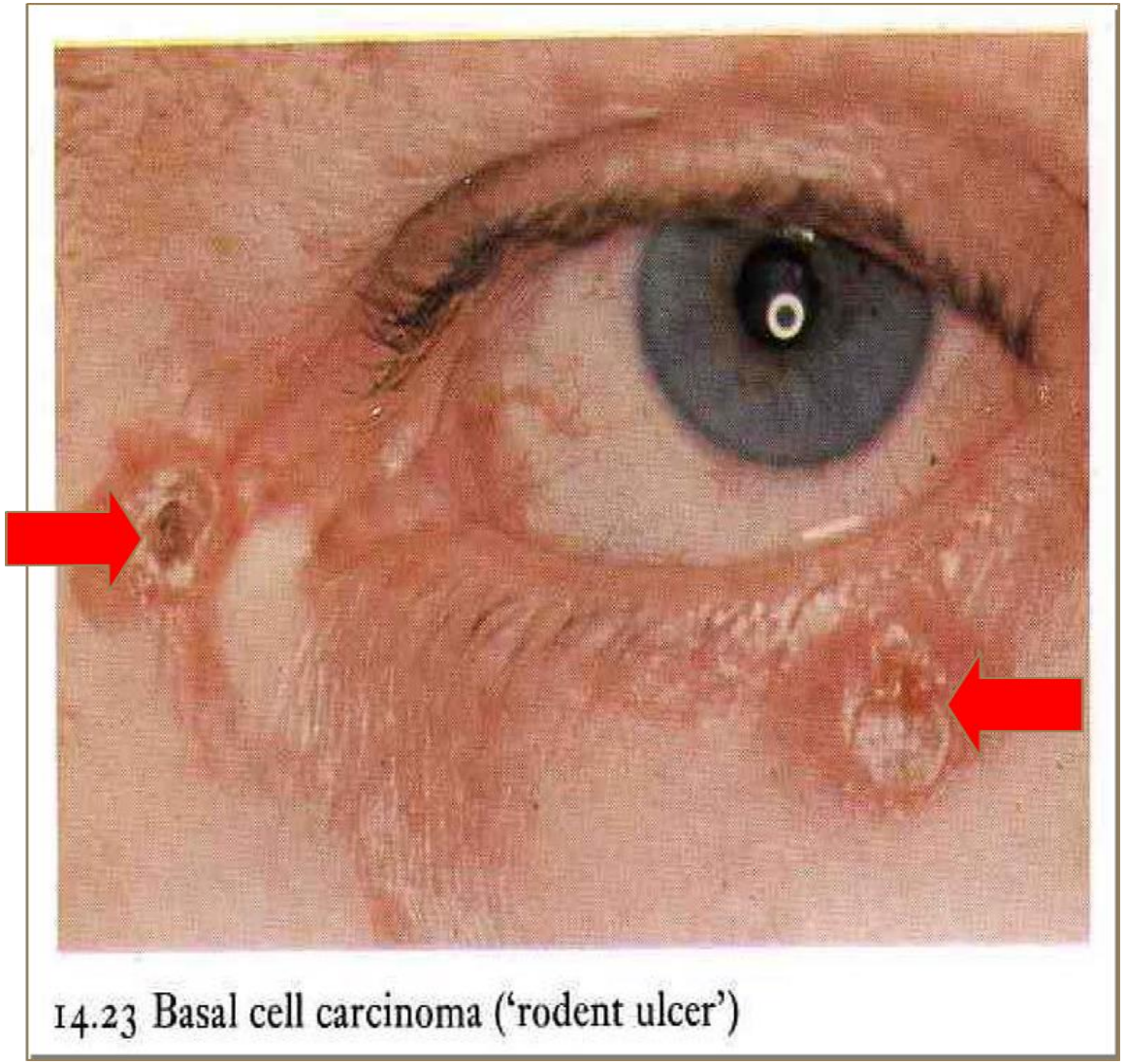
B. AR syndromes of Defective DNA Repair:

1.Xeroderma Pigmentosum

- Great predisposition to skin cancers, including (basal C. Ca, squamous C. Ca, & malignant melanoma) in sun-exposed areas like the face, hands & feet.

2. Ataxia Telangiectasia
3. Bloom Syndrome
4. Fanconi Anemia.

A child with XERODERMA PIGMENTOSUM , a recessively inherited disease, there are hundreds of pigmented nevi in the skin with squamous cell carcinoma in the lower lip of a young boy.



14.23 Basal cell carcinoma ('rodent ulcer')

C. Familial cancers with no specific phenotype

- Evident familial clustering of cancer, but the role of inherited predisposition is not clear.
- There is a familial predisposition to:
- CA of COLON
- CA of BREAST (Not linked to BRCA1 or BRACA2)
- CA of OVARY

- **Younger age groups**
- **Multiple or bilateral**
- **Two or more family members are affected.**
- **The transmission pattern of familial cancers is not clear.**
- **In general, relatives have a relative risk between 2 & 3**

4. Acquired predisposing conditions

- These are associated with increased risk for CA and most are related to rapid or abnormal cell proliferation due to either:
  - **Chronic inflammation**
  - **Immunodeficiency states**
  - **Precursor lesions**

❑ Are benign tumors precancerous?

- In general, the answer is **no**, but there are exceptions
- It is better to say that each benign tumor is associated with a particular risk, ranging from high to virtually nonexistent.

- **For example, large colon villous adenoma can undergo malignant transformation.**

However, the leiomyomata of the uterus do not transform into malignancy.

Acquired Preneoplastic Disorders:

(1) Persistent regenerative cell replication:

- e.g.: - Hepatocellular ca in liver cirrhosis

- SCCa in the margins of a chronic skin fistula like in osteomyelitis; or in a long-unhealed skin wound.

***(*2) Hyperplastic & dysplastic proliferation**

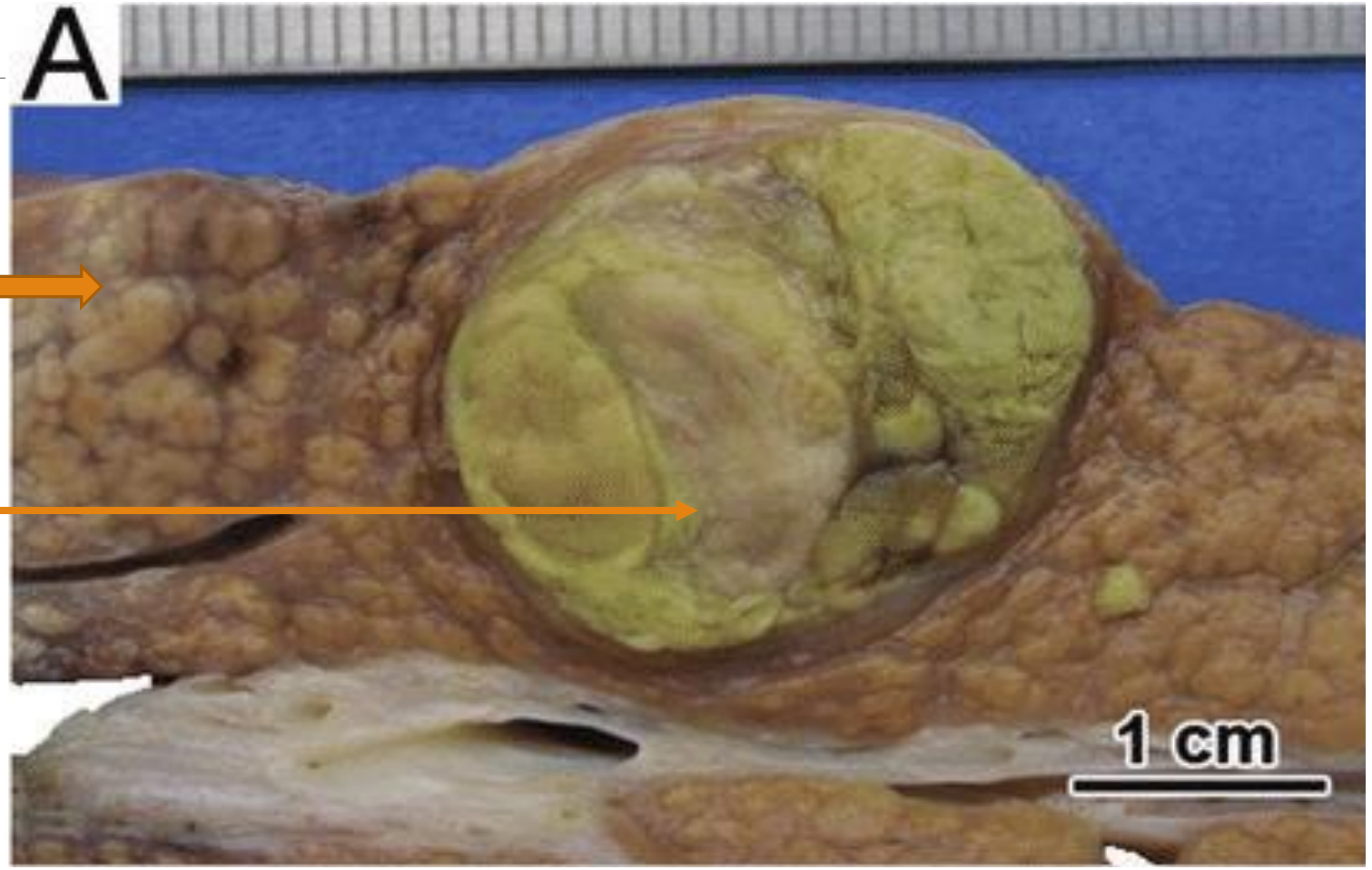
-e.g.: - Endometrial ca in atypical endometrial hyperplasia

- Bronchogenic lung ca in the dysplastic bronchial mucosa of smokers

Macronodular cirrhosis

Liver: Large number of hyperplastic nodules, separated from each other by fibrous trabeculae

Hepatocellular carcinoma



(3) Gastric ca in chronic atrophic gastritis

(4) An incidence (5%) of colorectal cancer in long-standing chronic ulcerative colitis.

(5) Leukoplakia of the oral cavity, vulva, or penis increases the risk of SCCa.

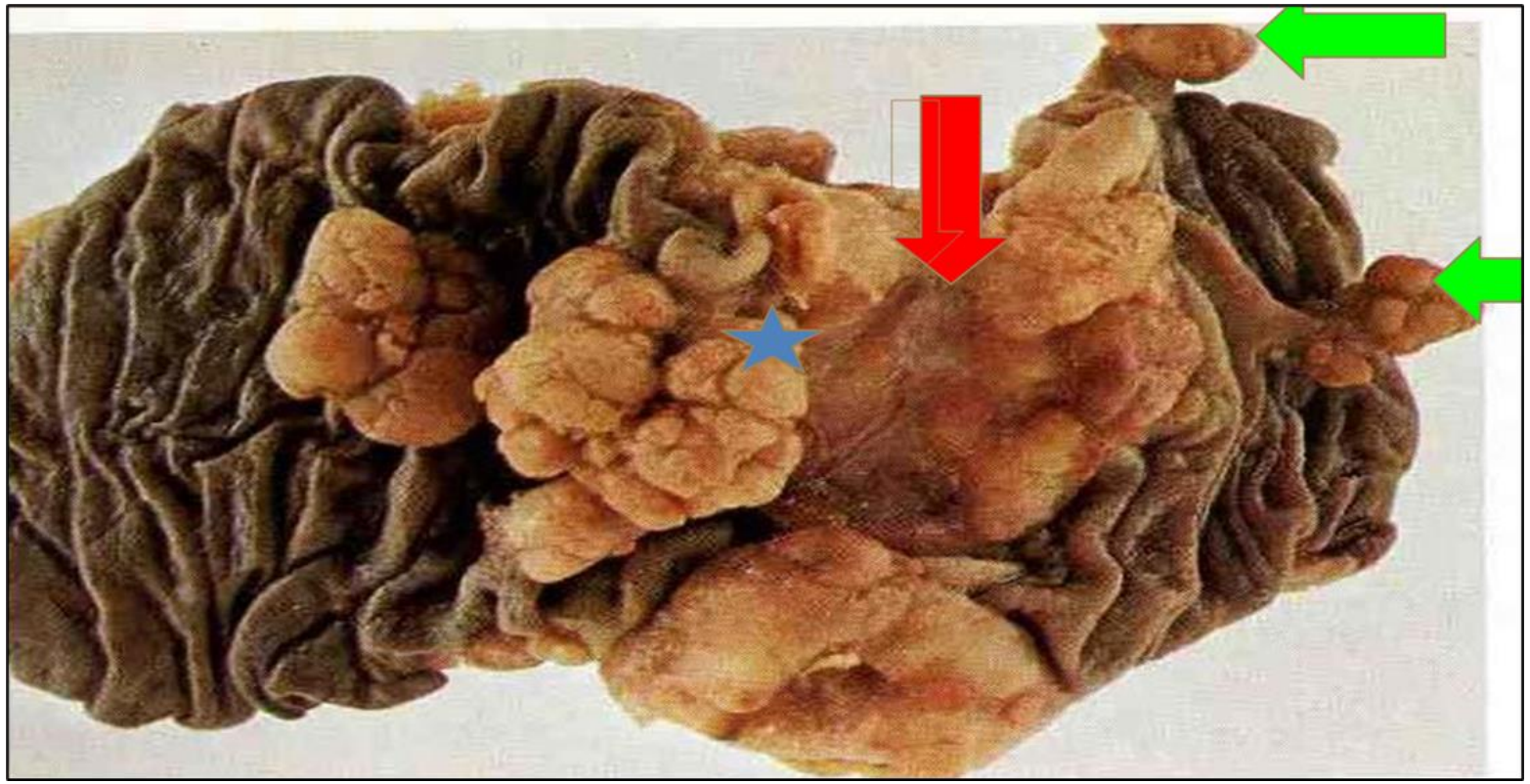
(6) Villous adenoma of the colon has a high risk of transformation to colorectal ca.

(7) Some benign tumors, e.g. colonic tubular adenomas, as they enlarge to more than 2 cm, can undergo a malignant transformation in 50% of cases.

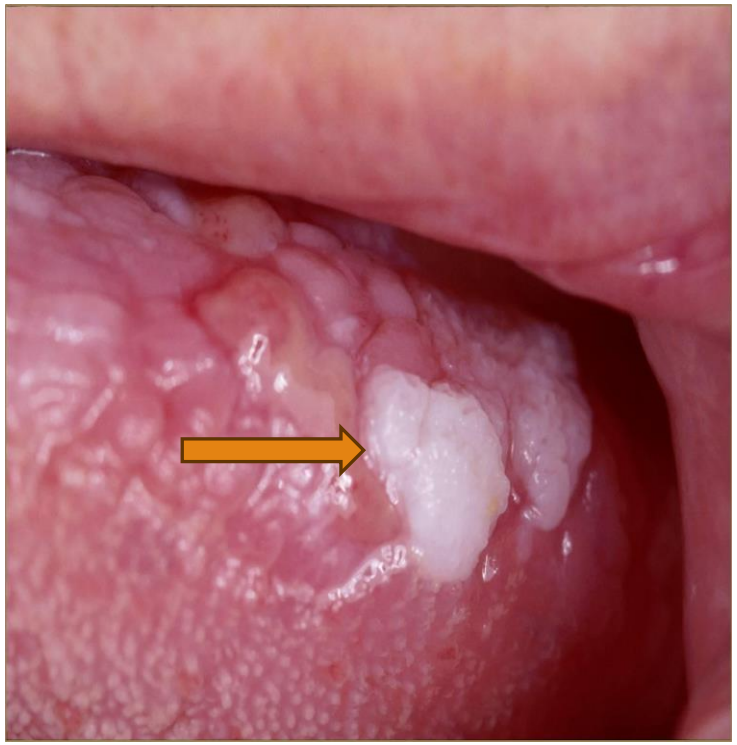
(8) Marjolin's ulcer (squamous cell carcinoma of the skin) arising in an old burn.

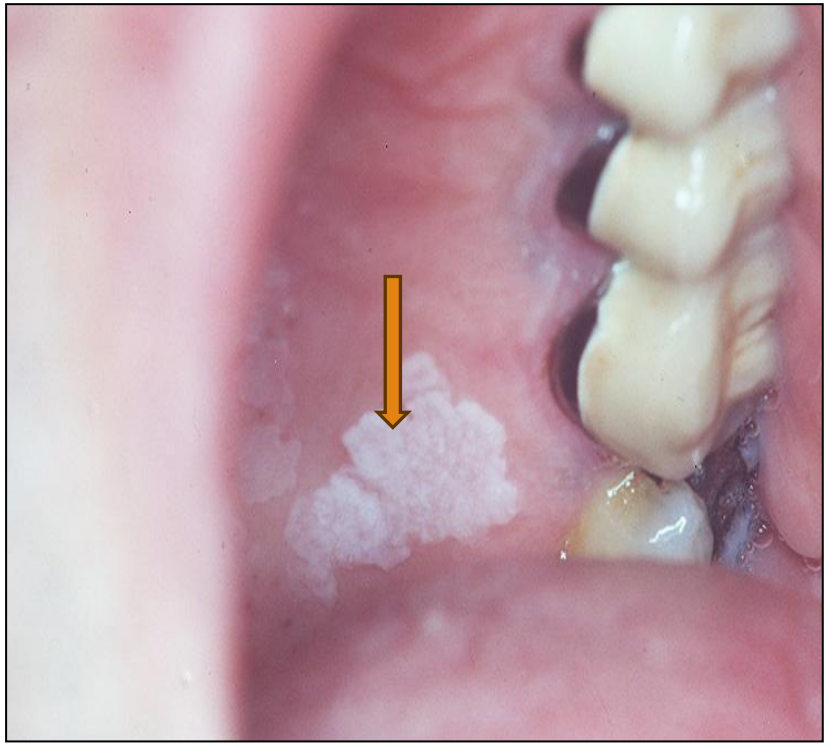
Colon: Papillary (Tubular) adenoma & carcinoma.

A circumferential ulcerating cancer is present (right center, red arrow) in direct continuity with large sessile adenomas to its left (blue star), also, there are two small pedunculated polypoidal adenomas (green arrows)

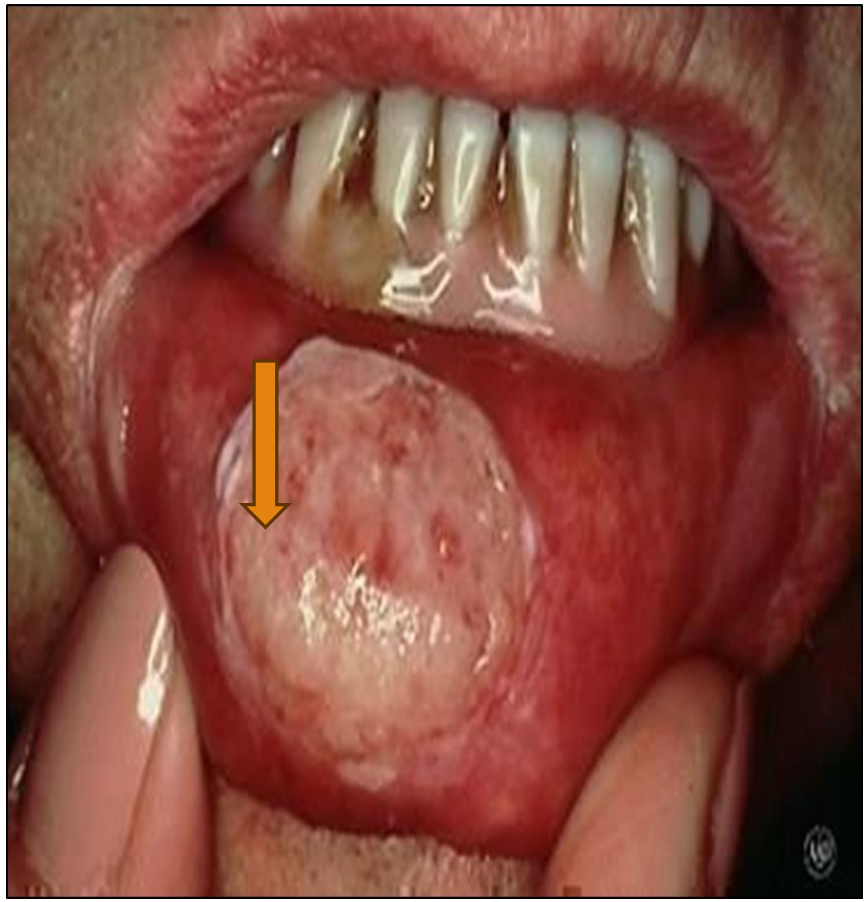


Leukoplakia in oral mucosa,white patch of mucosal thickening caused by irritation induced by ill-fitted denture. **A precancerous lesion**.





Squamous cell carcinoma arises in leukoplakia at the lower lip.



Carcinogenic agents

1- Chemical carcinogens

2- Radiant carcinogens

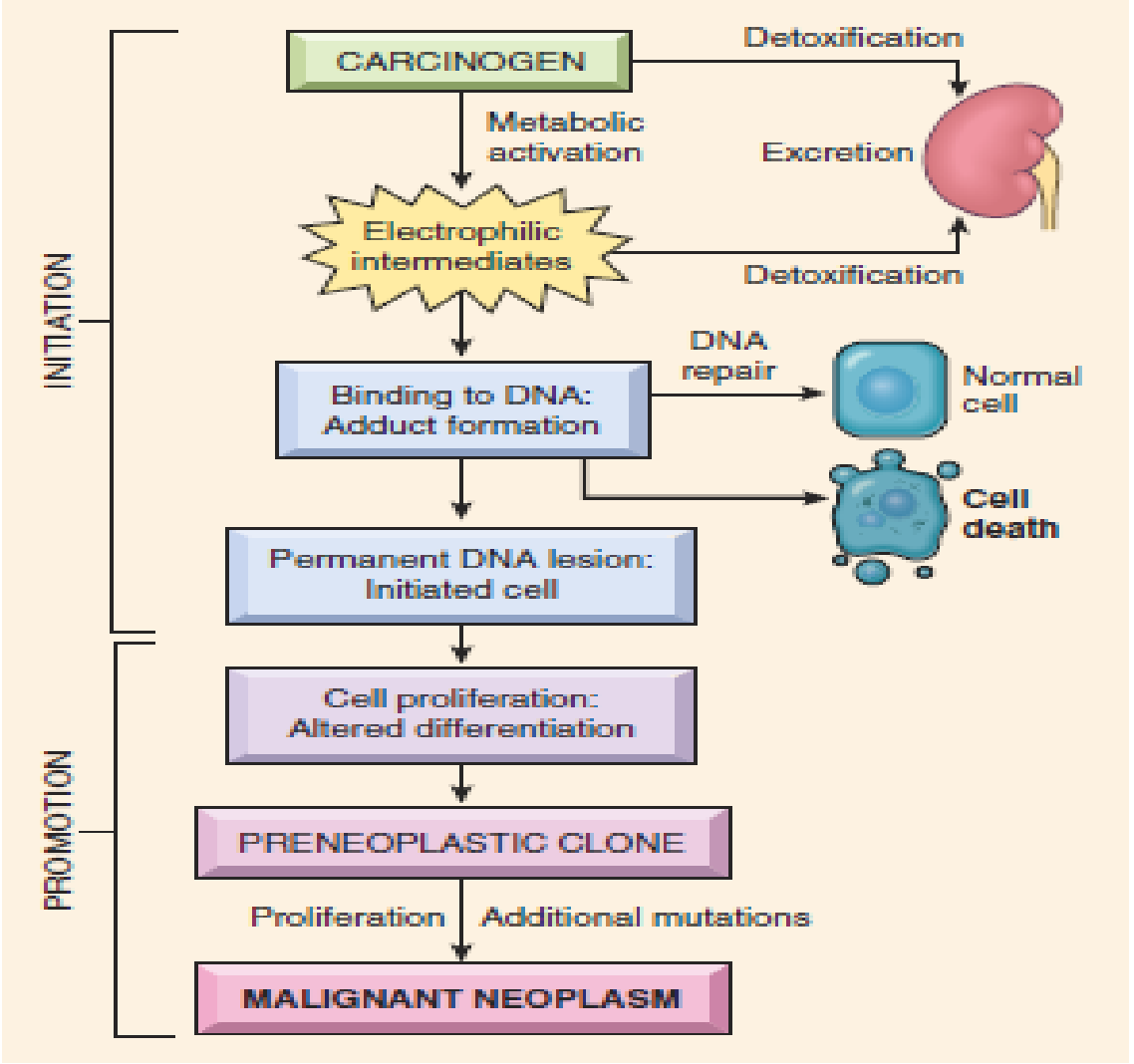
3- Microbial carcinogens, mainly viral

1. Chemical carcinogens:

- Chemical carcinogens are electrophilic and enter nucleus, damage DNA→ mutation → **Initiated Cell.**

❖ **Initiator (Mutagen)**– A chemical inducing irreversible DNA damage.

❖ **Promoter**- A chemical augmenting effect of the initiator by promoting cell growth and division.



Mechanisms of Action of Chemical Carcinogens:

- Chemical carcinogens contain highly reactive electrophile groups (i.e., have electron-deficient atoms) that react with the electron-rich atoms) that combine to DNA, RNA or protein-producing mutations.

- Genes commonly affected are RAS & TP53

---May be very specific ’ Signature Mutation,’ e.g. Aflatoxin-induced TP53 mutation.

- Some strong chemicals act as initiators and promoters.

❑ Promoters

- Act by stimulating cell **proliferation**.
- Promotors are NOT carcinogenic by themselves

- They have to **FOLLOW** the application of the initiator.

Examples:

- **HORMONES**
- **PHORBOL ESTERS**
- **PHENOLS**
- **DRUGS**

❖ Chemical Carcinogens are divided into:

1. Direct-Acting Agents:

- Directly produce damage without prior metabolic conversion to become carcinogenic.
- They are, in general, **weak** carcinogens.

2. Indirect-Acting Agents (most of them):

- **(Procarcinogen):** Need metabolic conversion in the liver by cytochrome P-450 dependent mono-oxygenases → **ultimate carcinogen**

Major types of chemical carcinogens:

1- Alkylating Agents: Direct, used in chemotherapy of cancer - may induce Leukemia.

2- Polycyclic Hydrocarbons: Indirect & very strong - include benzopyrene in cigarette smoke → CA Lung

3- Aromatic Amines & Azo dyes: Indirect -Rubber & Food Industry e.g. β-naphthylamine → Bladder CA

4- Natural plant and microbial products: includes Aflatoxin B1 produced by the fungus Aspergillus flavus (a mold that grows on improperly stored grains and nuts). → Hepatocellular CA.

5- Nitrosamines: Endogenous or food preservatives cause Gastric & Colon CA


THANK
YOU