



Pathology

Subject : 23

Lec no :

Done By : Lujain Zaareer

وَقُلْ رَبِّ زِدْنِي عِلْمًا

NEOPLASIA



Dr. Ola Abu Al Karsaneh



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

CANCER INCIDENCE:

2016. American Cancer Society.

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

يختلف نوع ال cancer التي بسبب death
 ① بين Female و Male
 ② بين الدول

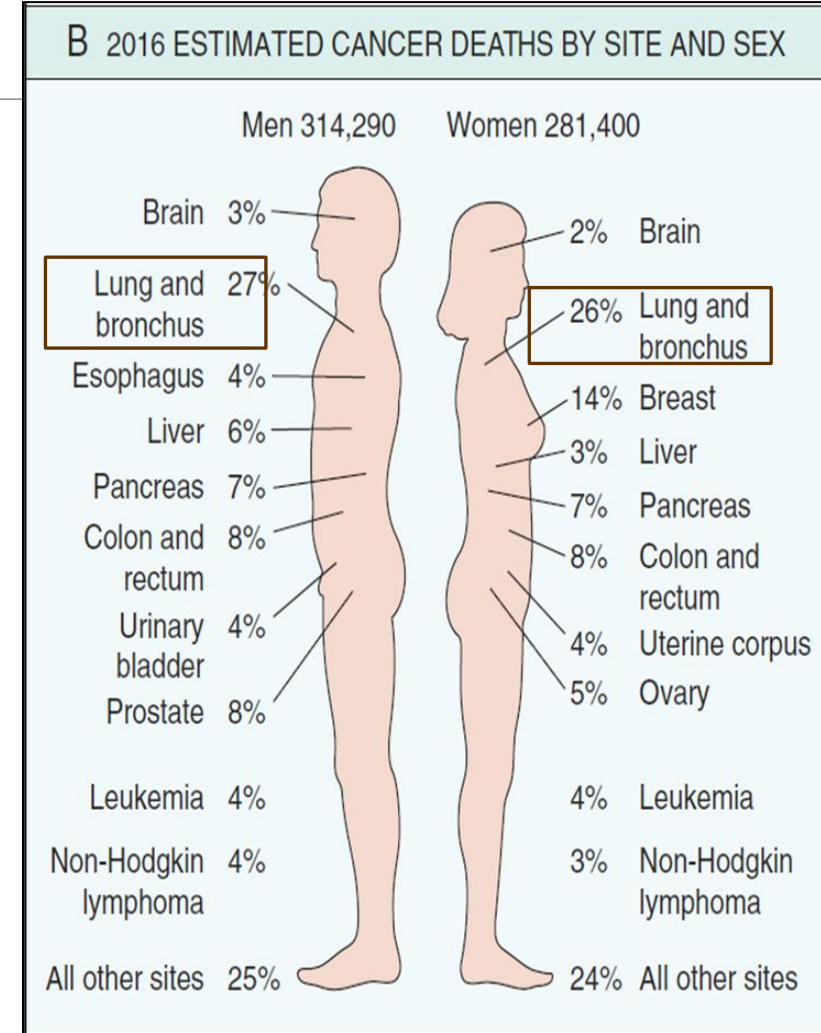
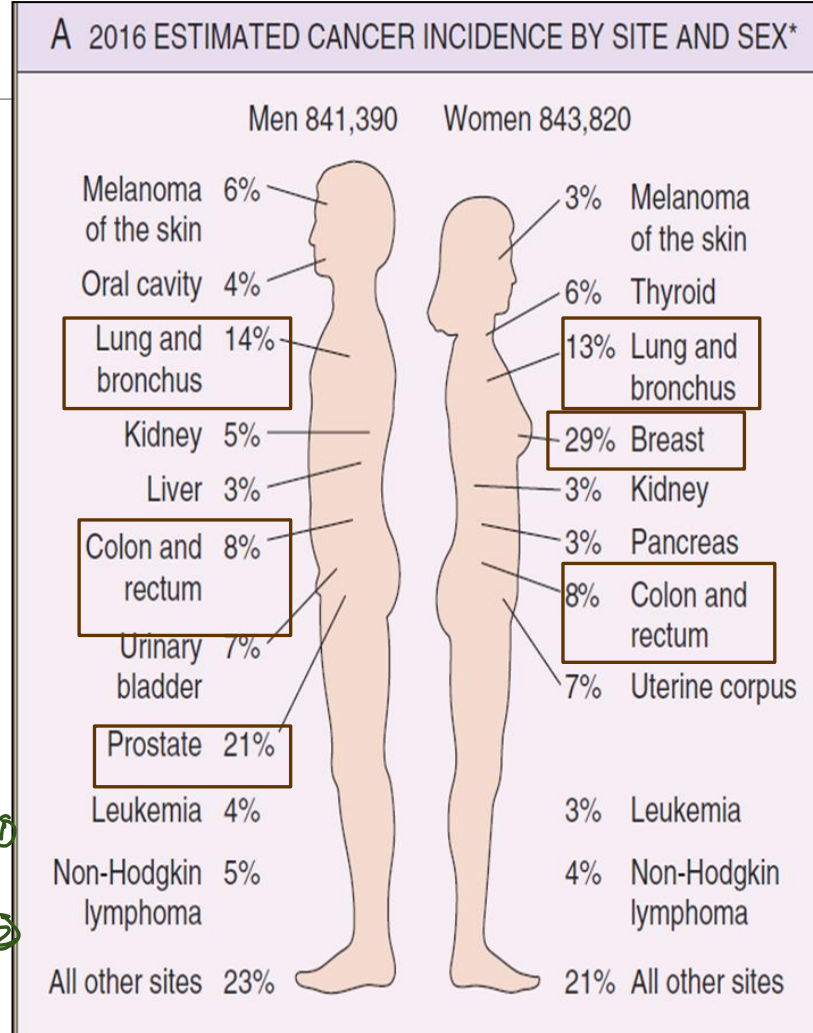



Table (7) Ten most common cancers among Jordanians, Males, 2014



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

JORDAN CANCER REGISTRY

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

➔ 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.

استجابة

العنصر

لهاي

العوامل

تعتمد على

Genetic

polymorphism

لذا في بعض

أنواع Cancer

بتصنيف ناسي وناسا

و كمان العلاج يختلف

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 →
صناطقه تعرفون بهن كيمي يودي
lung cancer
- Personal habits (smoking and alcohol consumption).
multiple sexual partners → ↑ cancer
- 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)

(5-10%)
 هنا Cancer
 بكونوا وراثياً

Table 6.4 Inherited Predisposition to Cancer

Inherited Predisposition	Gene(s)
Autosomal Dominant Cancer Syndromes <i>درامي بشكل سائد</i>	
Retinoblastoma	RB
Li-Fraumeni syndrome (various tumors)	TP53
Melanoma	CDKN2A
Familial adenomatous polyposis/colon cancer (FAP)	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 <i>درامي بشكل متنحي</i>	
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

نوعى
 نقص

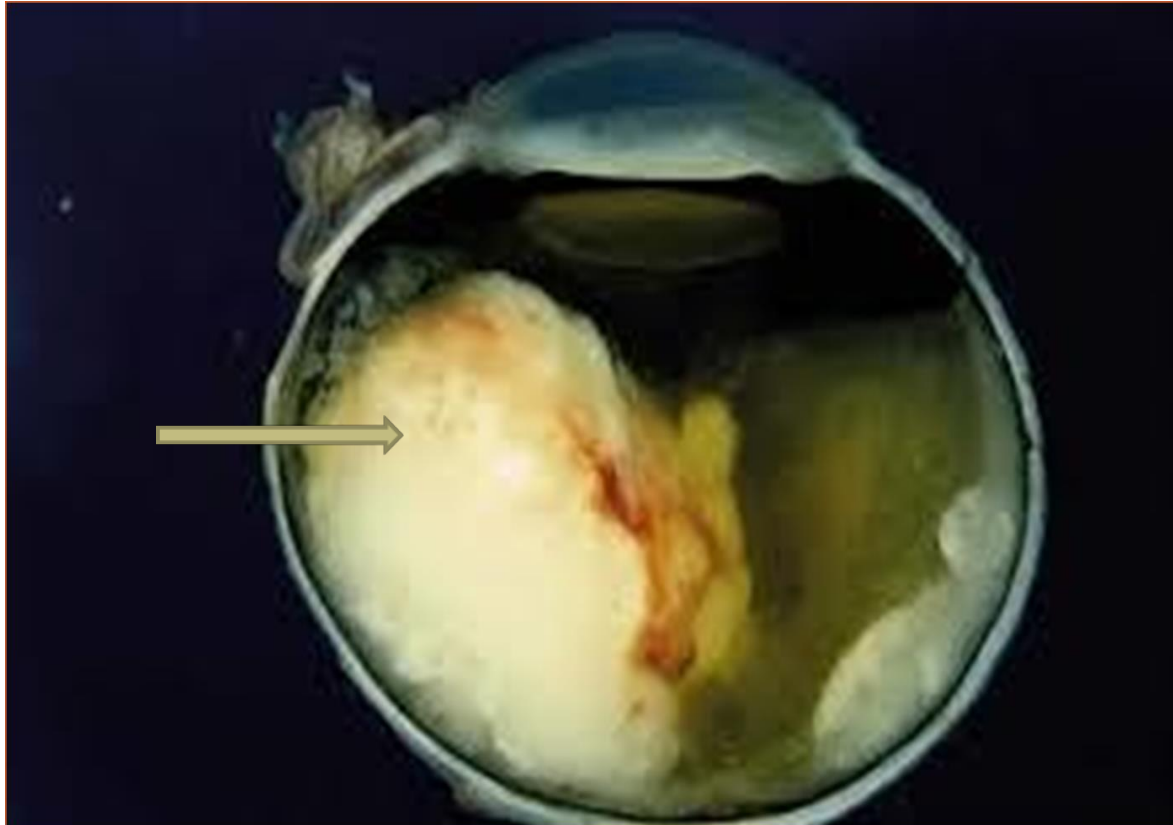
دكت التواجد و كثر صاهم
 للاسنان و اللكليبكال و الارزم
 دصوفه بس 2 نشرح منه Syndromes
 لقدهم فان هيك بزكره ليه

*
 بسلاهم

Autosomal dominant
↑

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.



osis = Multiple

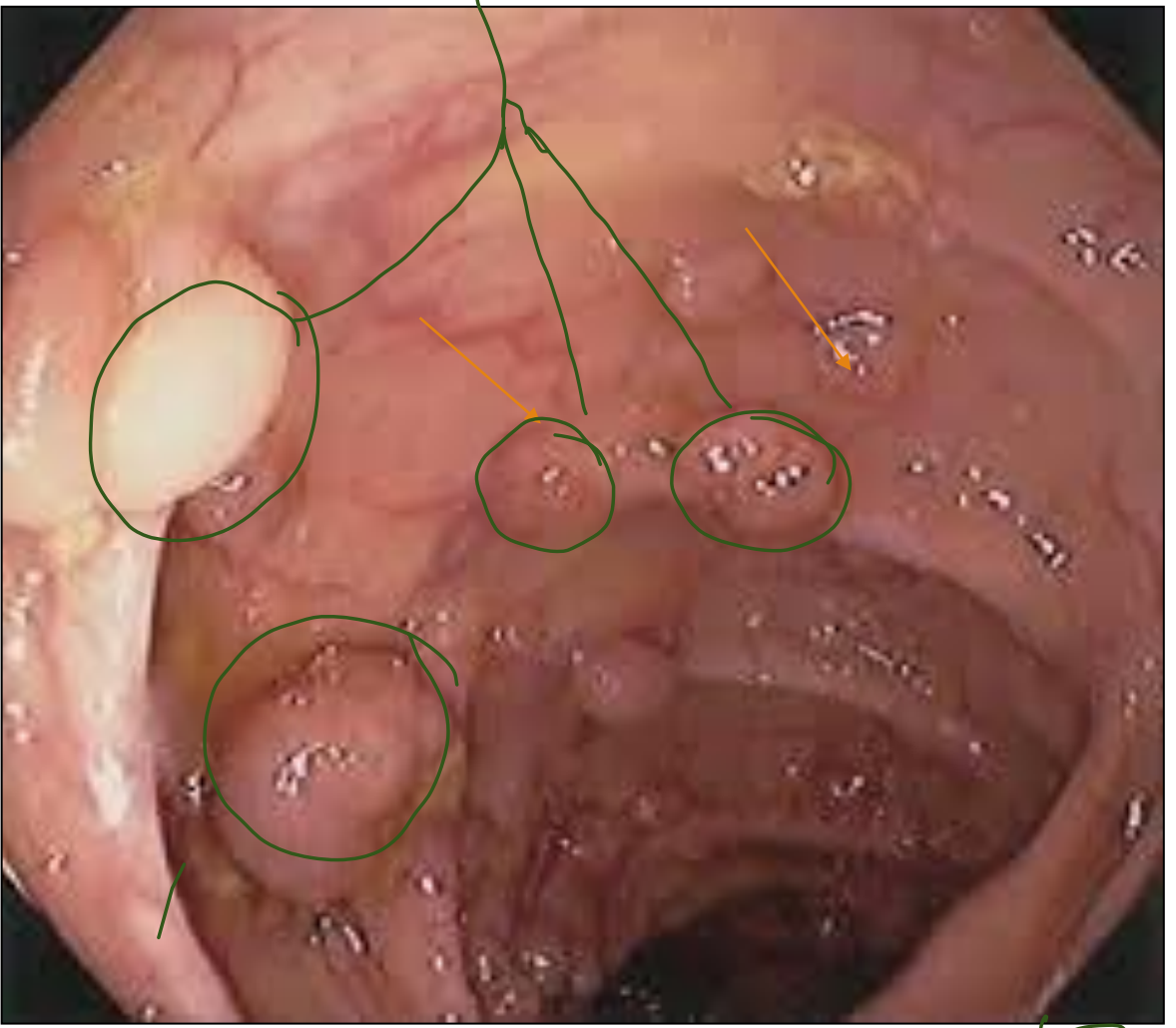
dominant multiple projection colon

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



Surgical resection colons 2

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



colons 2

- ^{class} ^{benign} ^{multiple}
- **Neurofibromatosis** is an autosomal dominant hereditary neoplastic disease.
 - Hundreds of **neurofibromas** with **café au lait pigmentation** of the skin



© Jere Mammimo, DO

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.

أنواعها المختلفة
Skin Cancer ←
Melanoma ← (بسر) defective DNA repair (mainly nucleotide) ←
Exgene

2. Ataxia Telangiectasia

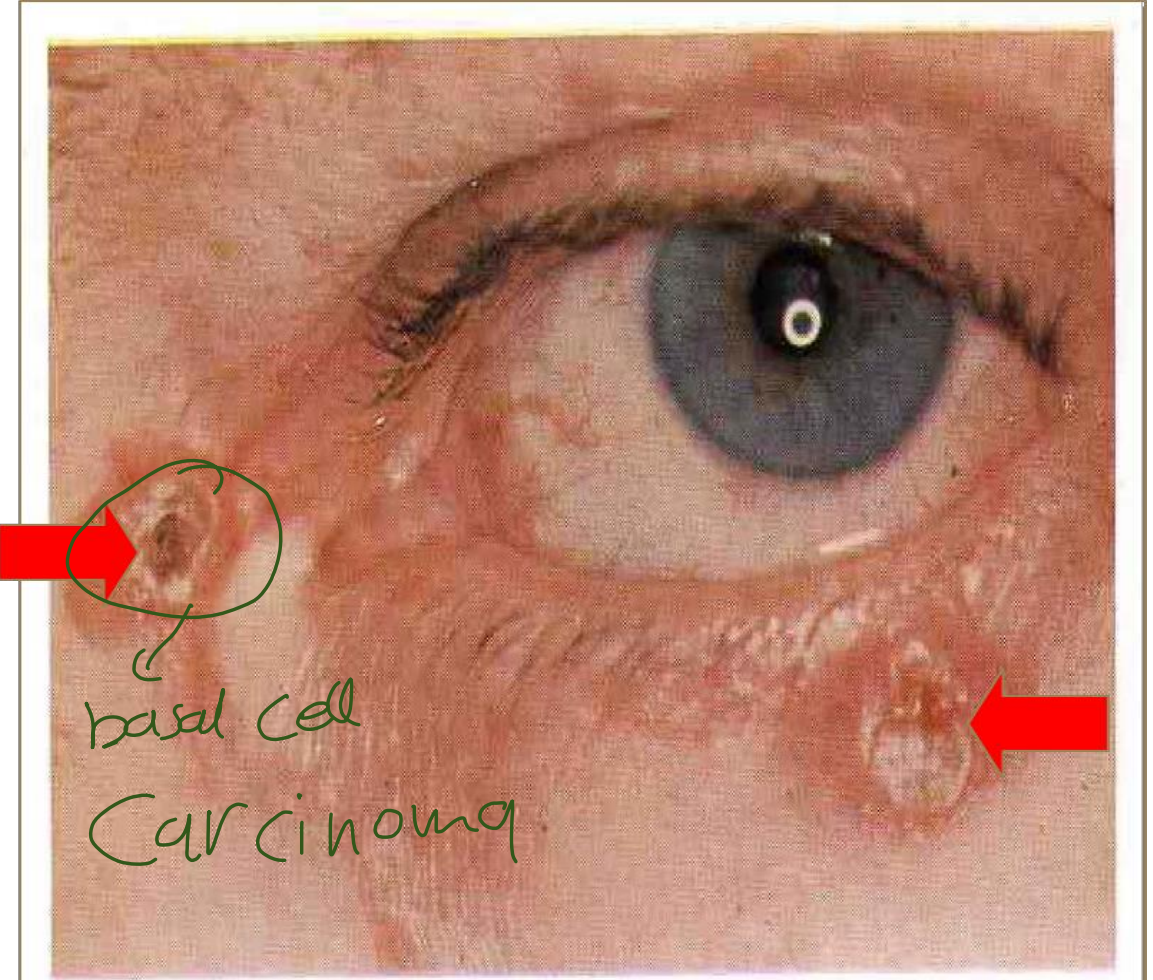
3. Bloom Syndrome

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.

لا يتعرضوا لأشعة الشمس



14.23 Basal cell carcinoma ('rodent ulcer')

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?

صب نوع ال benign في شي عنده risk دني
شلا ماعنده (risk)

- 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.

عوامل بتزيد حليته حدوث Cancer
↑

Acquired Preneoplastic Disorders:

(1) Persistent regenerative cell replication:

↑ عند
regenerative
rate

- 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. ←
unhealed infected wound (Wound) اللى بكون فيها بيراله التئام بالتالي
regeneration بعد

كل ما كان في regeneration و proliferation زكتر كل ما زادت ال Cancer risk

حغال

(2) Hyperplastic & dysplastic proliferation

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

- Bronchogenic lung ca in the dysplastic bronchial mucosa of smokers

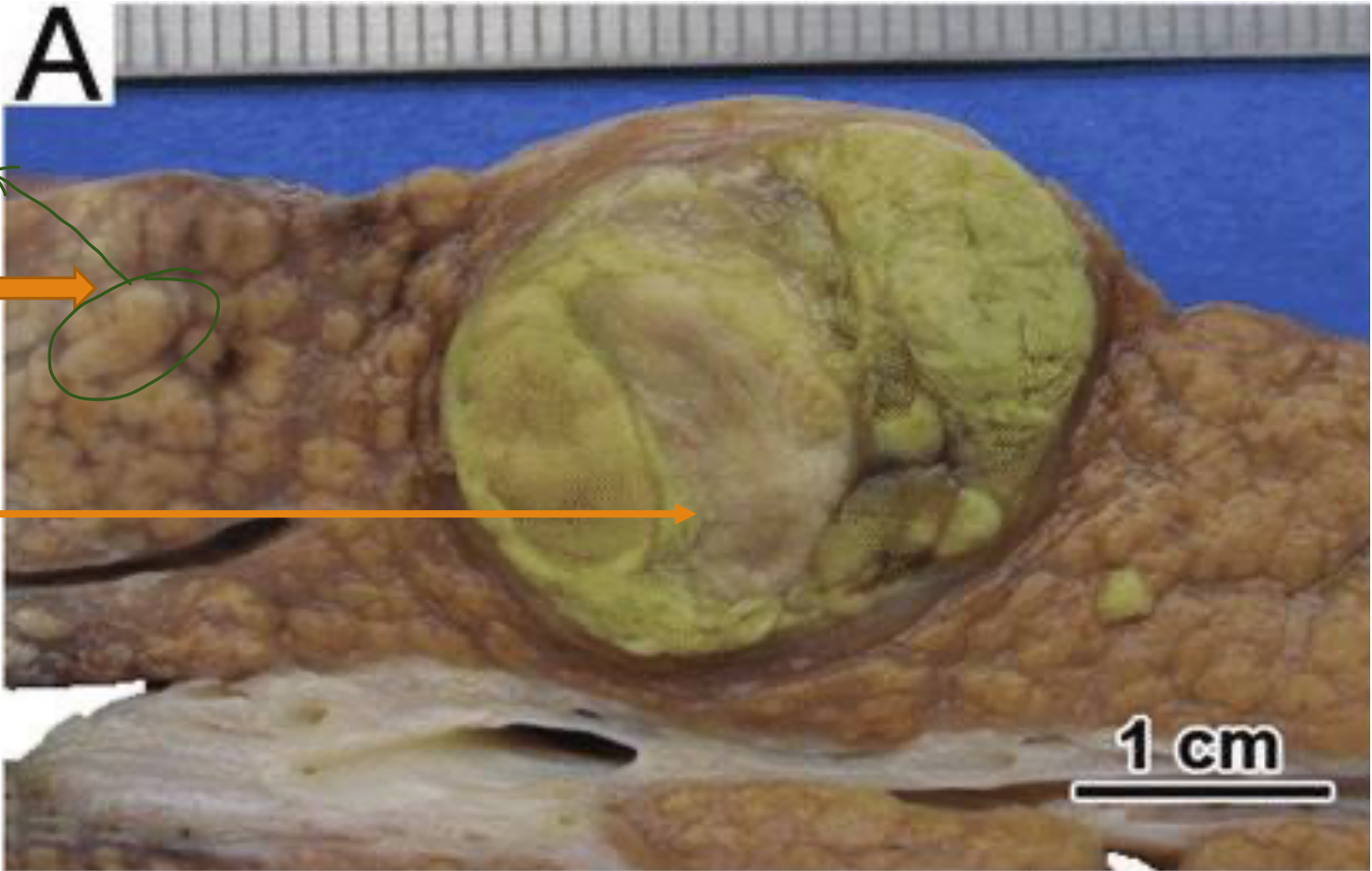
بزيد ال
risk
لل
Cancer

dysplasia = لا تعني Cancer

Macronodular cirrhosis

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

تليفات
تجدد
Fibrosis
Regeneration



(3) Gastric ca in chronic atrophic gastritis →

التهاب
بالمعدة

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

(ulceration + inflammation)

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

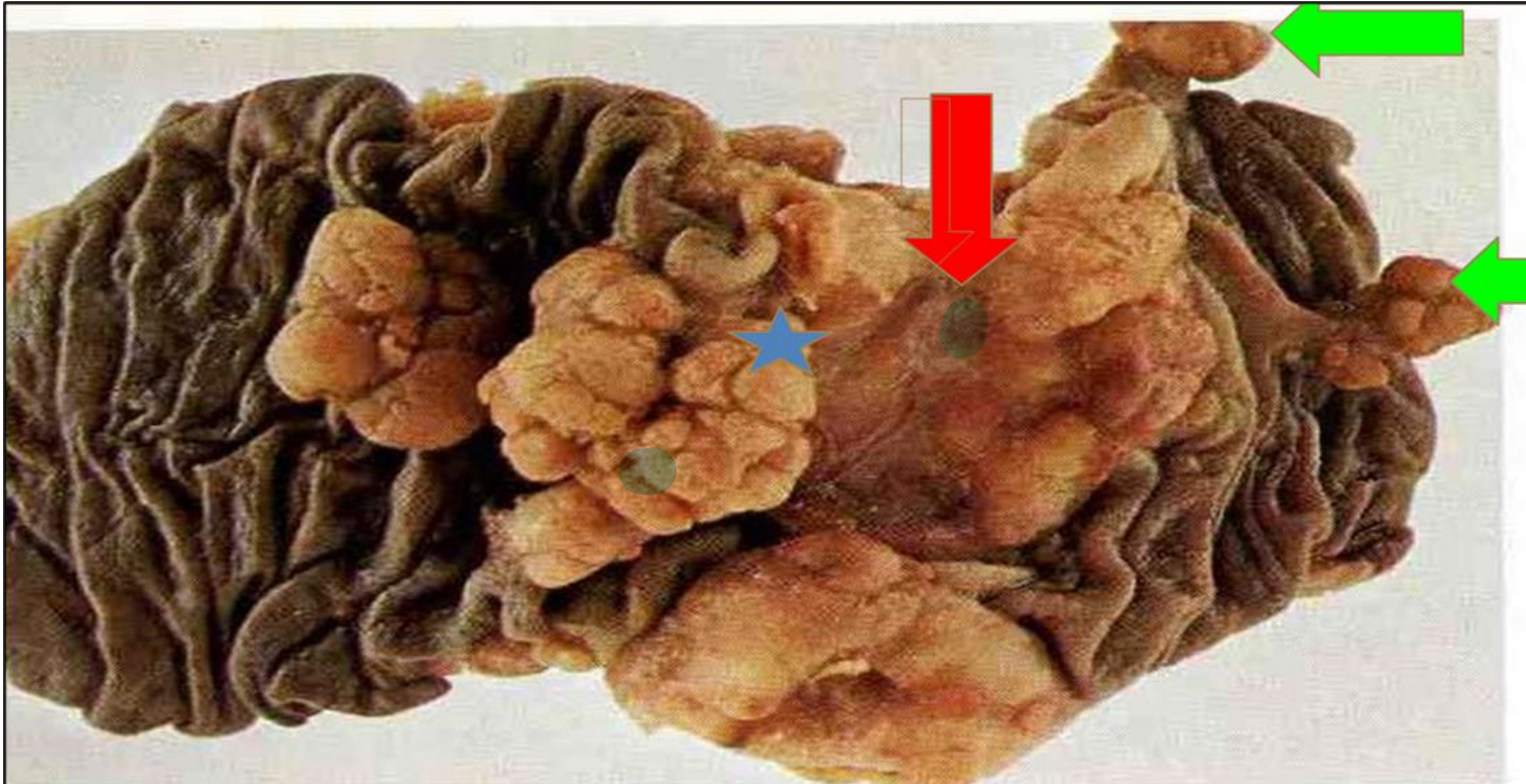
(6) ^{elongated} Villous adenoma of the colon has a high risk of transformation to colorectal ca.

(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.

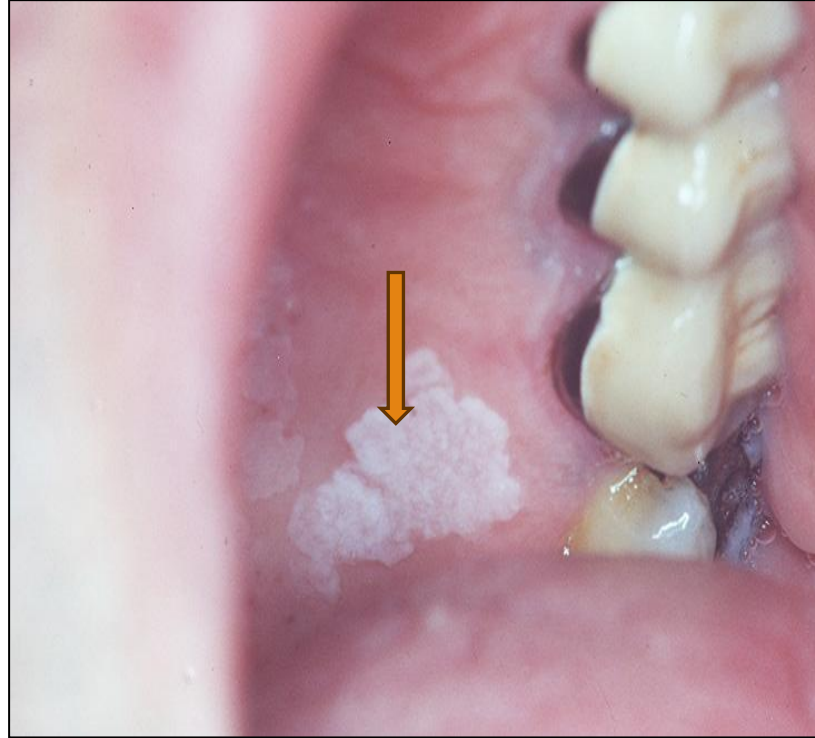
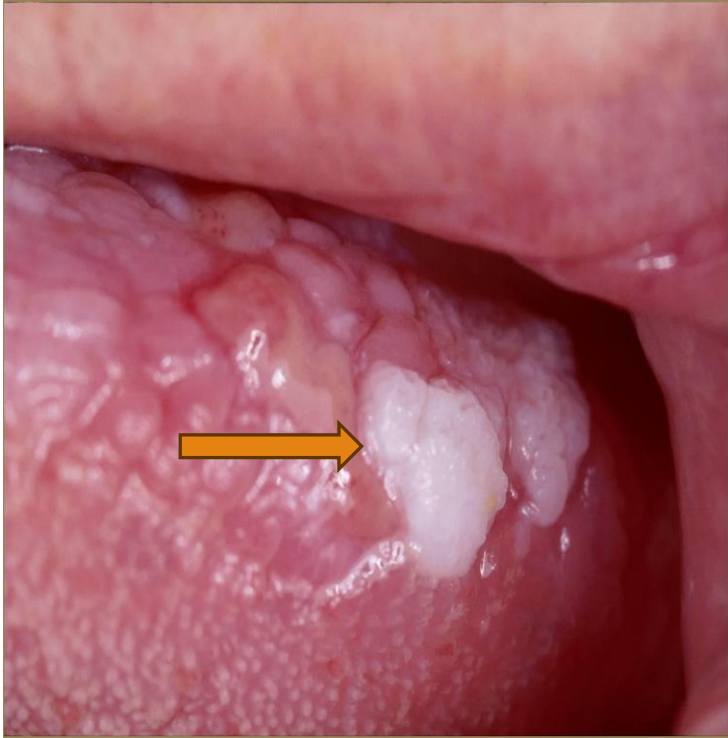
(8) Marjolin's ulcer (squamous cell carcinoma of the skin) arising in an old burn.

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.



agent تسبب سرطان cancer



Carcinogenic agents

- 1- Chemical carcinogens
 - 2- Radiant carcinogens
 - 3- Microbial carcinogens, mainly viral
-

1. Chemical carcinogens:

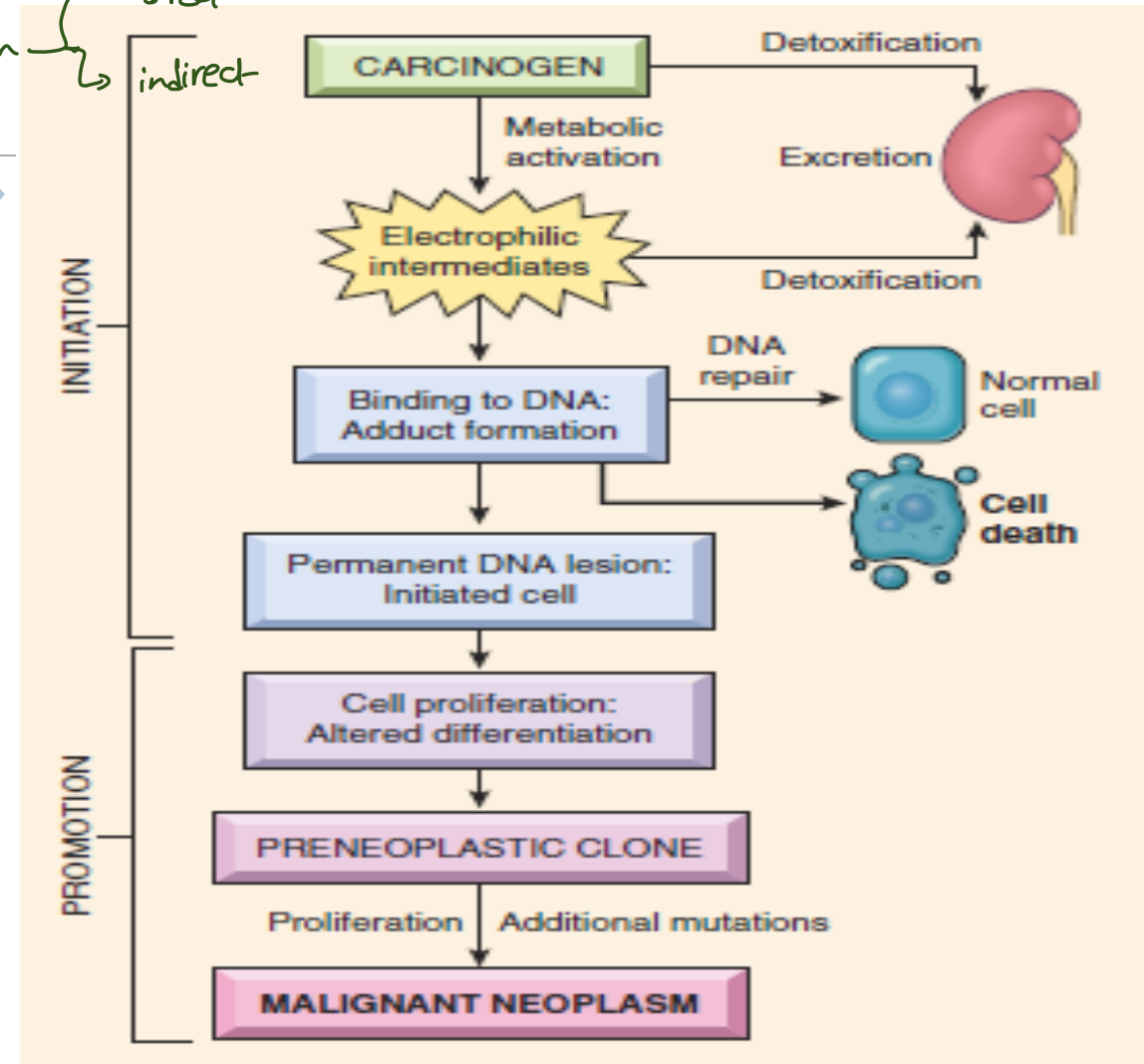
Cause → Initiator
 → promoter
action → direct
 → indirect

- Chemical carcinogens are electrophilic and enter nucleus, damage DNA → mutation → **Initiated Cell**
وجوده بالبيئة اذا تعرضنا اليها نضيق DNA و تعمل damage Cell

Types of chemical carcinogens:

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

❖ **Promoter** – A chemical ^{يعزز نسخ هاي الخلايا التي عندها damage} 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.**

← اصيانا فاده نفايتكون ك initiator و promoter

□ Promoters

- Act by stimulating cell **proliferation**.
- Promoters are **NOT** carcinogenic by themselves
لا يعقب Carcinogenic & نه هو فاعل mutation
- They have to **FOLLOW** the application of the initiator.

Examples:

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

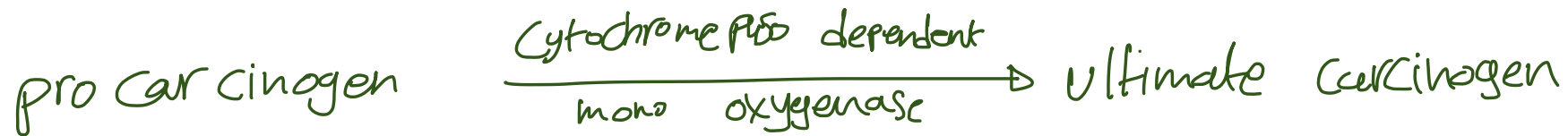
❖ Chemical Carcinogens are divided into:

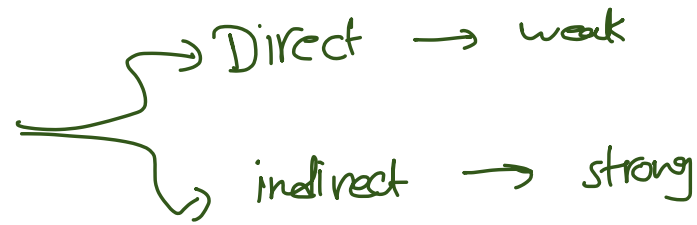
1. Direct-Acting Agents:

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

2. Indirect-Acting Agents (most of them): ^{الأغلب يكون indirect}

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





Major types of chemical carcinogens:

- 1- **Alkylating Agents:** **Direct**, used in chemotherapy of cancer - may induce **Leukemia**. ((side effect))
- 2- **Polycyclic Hydrocarbons:** **Indirect** & very strong - include benzopyrene in cigarette smoke
 → **CA Lung** (lung)
 بتلف دبتور فهي indirect يعني cyclic
- 3- **Aromatic Amines & Azo dyes:** **Indirect** - Rubber & Food Industry e.g. β -naphthylamine → **Bladder CA** رکز علیها
 تنتج Fungus التي عادة يتكون في المعلبات التي تخزینها علیها
- 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**.
 aflatoxin B₁ + hepatitis A/B = Hepatocellular CA
- 5- **Nitrosamines:** Endogenous or food preservatives cause **Gastric & Colon CA**



و بسى والله
دعواتكم ٧