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# **Etiology of Cancers**

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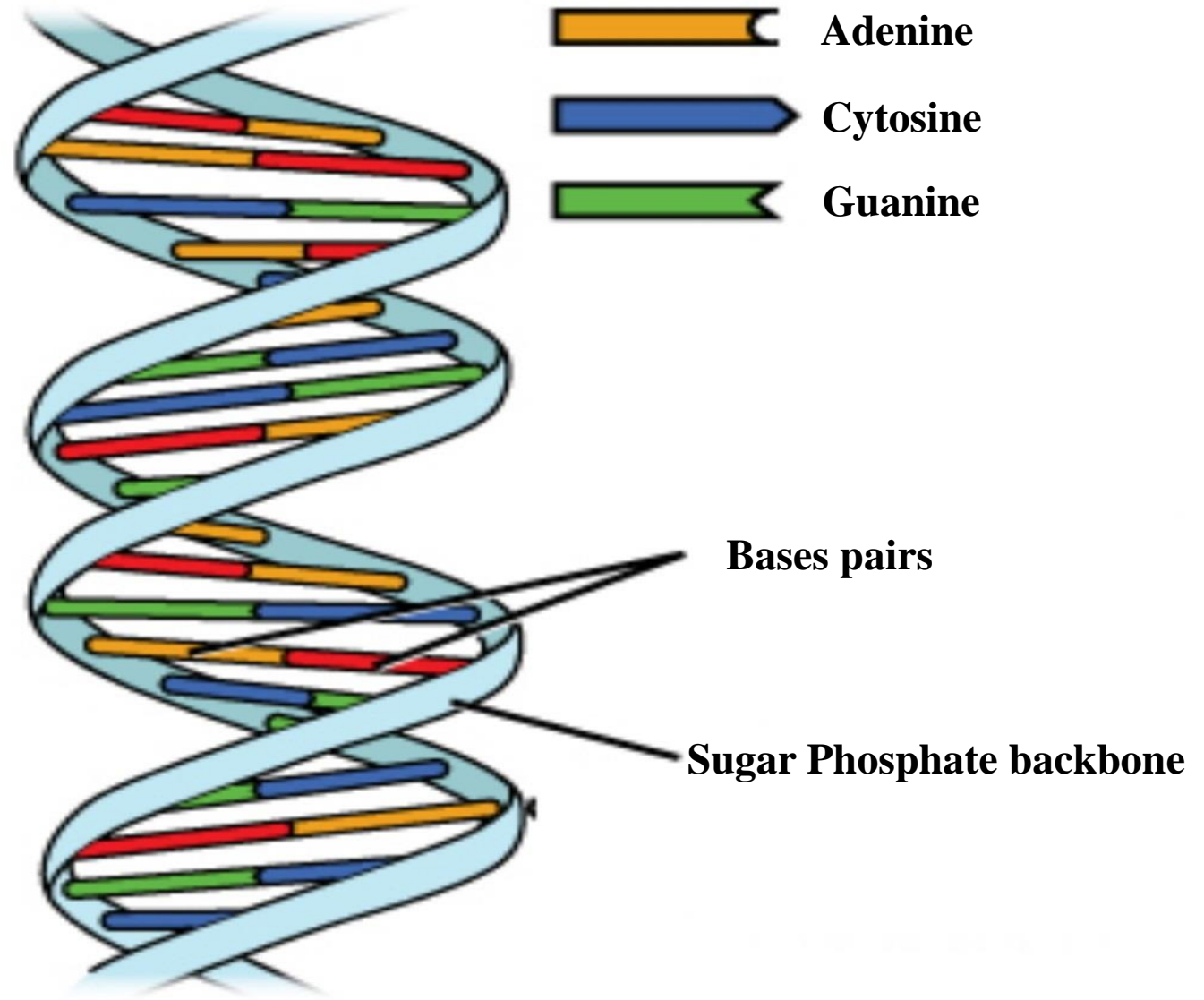
## Nitrogen Bases

Thymine

Adenine

Cytosine

Guanine



**Over 50% of mutations in Colorectal Cancer were C:G to T:A transitions**

**And 10% were C:G to G:C transitions**

**In Breast Cancers, only 35% of the mutations were C:G to T:A transitions**

**And 29% were C:G to G:C transitions**

Normal epithelium

Dysplastic

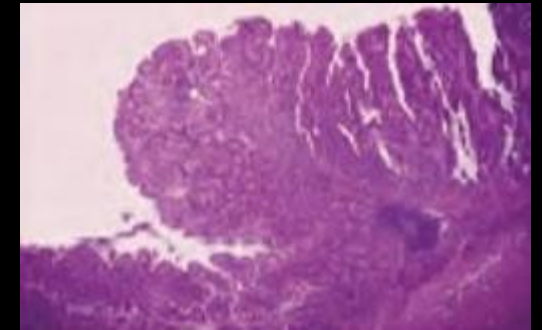
Early adenoma

Intermediate adenoma

Late adenoma

Carcinoma

Metastases



Normal epithelium

Adenoma

Carcinoma

# **Etiology of Cancer**

**Tobacco**

**Oncogenic Viruses**

**Inflammation**

**Chemical Agents**

**Physical Factors**

# Etiology of Cancer (Tobacco)

| <b>Level of Evidence for Smoking</b>                                       | <b>Cancer Site</b>  |
|--|---|
| <b>Evidence Sufficient to Infer Causal Relationship</b>                    | <b>Bladder, Cervix, Colorectal, Esophagus, Kidney, Larynx, Leukemia (AML), Liver, Lung, Oral cavity, pharynx, Pancreas and Stomach.</b> |
| <b>Evidence Suggestive but Not Sufficient to Infer Causal Relationship</b> | <b>Breast</b>   |
| <b>Inadequate to Infer Presence or Absence of Causal Relationship</b>      | <b>Ovary</b>  |
| <b>Evidence Sufficient to Infer No Causal Relationship</b>                 | <b>Prostate</b>   |

**Yearly Smoking Attributable Mortality**

# **Etiology of Cancer**

## **(Tobacco)**

**A common index of cancer risk is pack-years**

**Or the number of packs of cigarettes smoked per day multiplied by the number of years smoked in the lifetime**



# **Etiology of Cancer**

## **(Tobacco)**

**The pathway by which tobacco use leads to cancer**

- Carcinogen exposure leads to the formation of carcinogen– DNA adducts, then cause mutations, if not repaired or removed by apoptosis, will eventually give rise to cancer**
- Smoker tissues contain higher levels of DNA adducts than nonsmokers, and that DNA adduct levels are associated with cancer risk**

# **Etiology of Cancer**

## **(Oncogenic Viruses)**

**Viruses can cause cancer through either (or both) of two broad mechanisms**

**1- Direct**

**2- Indirect**

**Direct:** Inactivate of tumor suppressor proteins mechanisms, in which the virus-infected cell ultimately becomes malignant, then cancerous cell remains “addicted” to viral oncogene expression for ongoing growth and viability.

# **Etiology of Cancer**

## **(Oncogenic Viruses)**

**Viruses can cause cancer through either (or both) of two broad mechanisms**

**Indirect: The cells have never been infected by the virus.**

**Instead, the viral infection lead to cancer by attracting inflammatory immune responses that, lead to accelerated cycles of tissue damage and regeneration of non-infected cells.**

**- In some instances, virally infected cells may secrete paracrine signals that drive the proliferation of un-infected cells**

# Etiology of Cancer

## (Oncogenic Viruses)

**A variety of viruses can cause cancer**

**Human papillomavirus (types HPV16 & HPV18)**

**Cervix**

**Penis**

**Anus**

**Vagina**

**Vulva**

**Tonsils**

**Base of tongue**

**Hepatitis B virus (HBV) → Hepatocytes Cirrhosis, Hepatocellular Carcinoma**

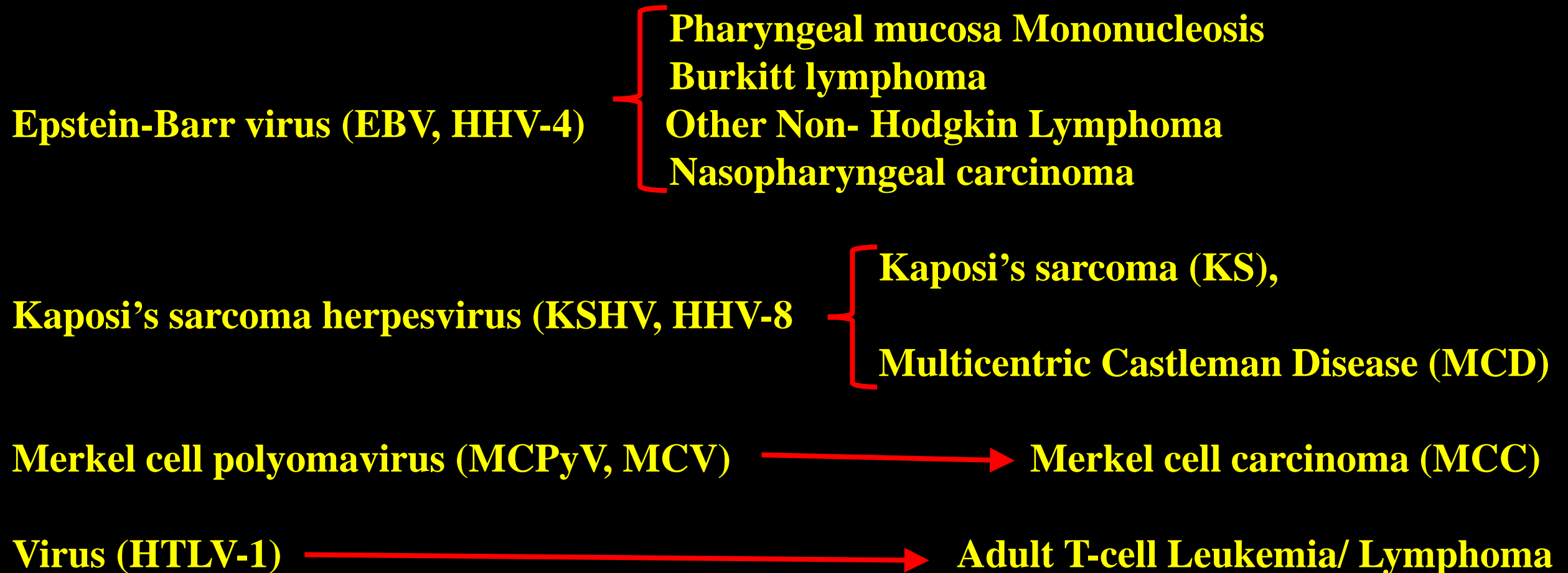
**Hepatitis C virus (HCV) →**

- Hepatocytes Cirrhosis**
- Hepatocellular carcinoma**
- Splenic marginal zone lymphoma**

# Etiology of Cancer

## (Oncogenic Viruses)

**A variety of viruses can cause cancer**





# **Etiology of Cancer** **(Oncogenic Viruses)**

## **Merkel cell carcinoma (MCC)**



# **Etiology of Cancer**

## **(Oncogenic Viruses)**

### **Vaccine**

- **Vaccine or anti viral agent targeting the virus demonstrate either prevents or treats human cancer**
- **This type of proof has fully validated the causal role of HBV in human liver cancer**
- **Also show that anti herpes virus therapeutics can prevent KSHV- or EBV-associated lymphoproliferative disorders**
- **Vaccination against HPV can prevent the development of precancerous lesions on the uterine cervix.**



# **Etiology of Cancer**

## **(Oncogenic Viruses)**

### **Summary**

**Oncogenic viruses are important causes of cancer, especially in less industrialized countries and in immunosuppressed individuals.**

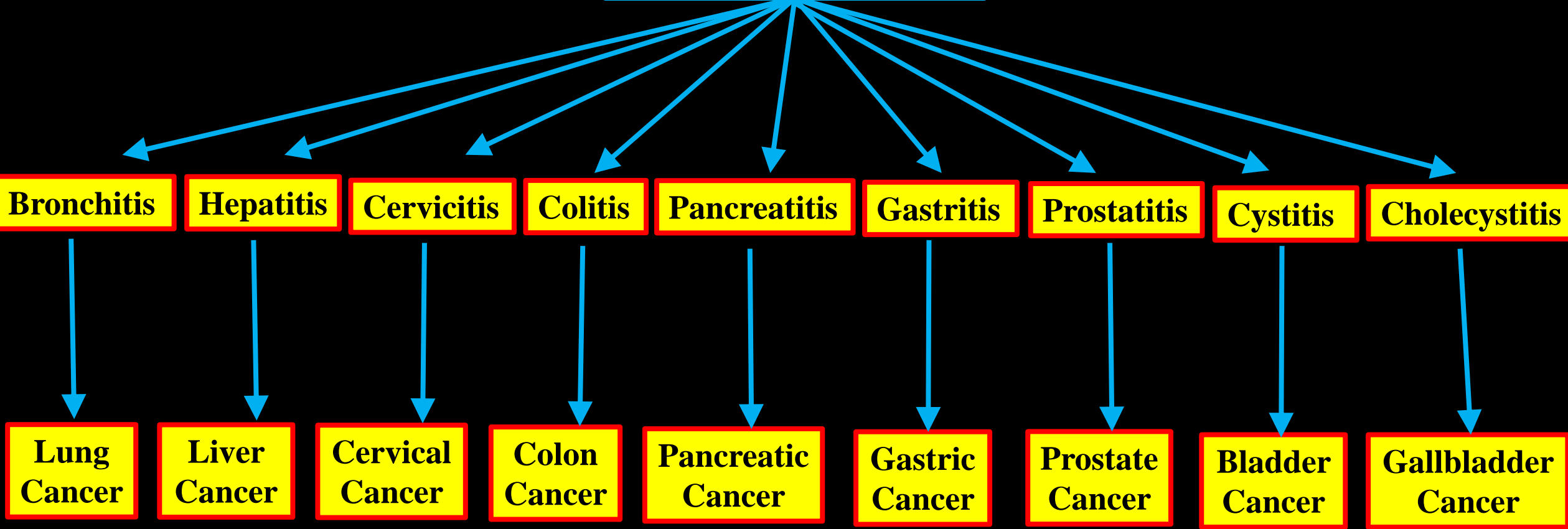
**Vaccines and antiviral agents play an important role in the prevention of virus-induced cancers**

# **Etiology of Cancer**

## **(Inflammation)**

- **Inflammation is closely linked to cancer, and the incidence of most cancers can be reduced by controlling inflammation.**
- **Pro-inflammatory conditions such as colitis, bronchitis, hepatitis, and gastritis can all eventually lead to cancer.**
- **Thus, one must find ways to treat these conditions before the appearance of cancer.**
- **All studies indicate that an anti inflammatory could play an important role in prevention of cancer.**

# Inflammation



# Etiology of Cancer

## (Chemical Agents)

| Target Organ | Agents  | Industries  | Tumor type   |
|--------------|---|---|--|
| Lung         | Tobacco Smoke<br>Arsenic<br>Asbestos<br>Chromium<br>Coal<br>Nickel Compounds<br>Soot<br>Mustard gas | Aluminum production<br>Coal gasification<br>Coke production<br>Painting | Squamous Cell Carcinoma<br>Large Cell Carcinoma<br>Small Cell Cancer<br>Adenocarcinoma |
| Pleura       | Asbestos<br>Painting  | Insulation<br>Mining  | Mesothelioma   |
| Oral Cavity  | Tobacco smoke<br>Alcoholic beverages<br>Nickel  | –   | Squamous cell cancer   |

# Etiology of Cancer

## (Chemical Agents)

| <b>Target Organ</b> | <b>Agents</b>  | <b>Industries</b>      | <b>Tumor type</b>                                   |
|---------------------|--|------------------------|---|
| <b>Esophagus</b>    | <b>Tobacco Smoke,<br/>Alcoholic Beverages</b>                                  | –                      | <b>Squamous cell cancer</b>                         |
| <b>Gastric</b>      | <b>Tobacco Smoking</b>   | <b>Rubber industry</b> | <b>Adenocarcinoma</b>                               |
| <b>Colon</b>        | <b>Alcohol,<br/>Tobacco Smoking</b>  | –                      | <b>Adenocarcinoma</b>                               |
| <b>Liver</b>        | <b>Aflatoxin<br/>Vinyl Chloride<br/>Tobacco Smoke,<br/>Alcoholic Beverages</b> | –                      | <b>Hepatocellular carcinoma<br/>Hemangiosarcoma</b> |
| <b>Kidney</b>       | <b>Tobacco Smoke<br/>Trichloroethylene</b>                                     | –                      | <b>Renal cell cancer</b>                            |

# Etiology of Cancer

## (Chemical Agents)

| <b>Target Organ</b> | <b>Agents</b>   | <b>Industries</b>                     | <b>Tumor type</b>   |
|---------------------|---|---------------------------------------|---|
| <b>Bladder</b>      | <b>Tobacco Smoke, Benzidine<br/>Phenacetin, Cyclophosphamide</b>                  | <b>Painting<br/>Rubber Production</b> | <b>Transitional Cell Ca.<br/>(TCC)</b>                          |
| <b>Prostate</b>     | <b>Cadmium</b>  | <b>—</b>                              | <b>Adenocarcinoma</b>   |
| <b>Skin</b>         | <b>Arsenic, Coal<br/>Mineral oils<br/>Soot<br/>Cyclosporin, Azathioprine</b>      | <b>—</b>                              | <b>Squamous Cell Ca.<br/>(SCC)<br/>Basal Cell Ca.<br/>(BCC)</b> |
| <b>Bone marrow</b>  | <b>Benzene<br/>Tobacco Smoke<br/>Ethylene Oxide<br/>Cyclosporin, Formaldehyde</b> | <b>Rubber workers</b>                 | <b>Leukemia<br/><br/>Lymphoma</b>                               |

# **Etiology of Cancer**

## **(Physical Factors)**

**Ionizing Radiation (IR) and Ultraviolet (UV)**

**Induce DNA damage and subsequent mutations, leads to Cancer**

**Mobile phone**

**In contrast, there is not correlation between mobile phone usage and incidences of glioma, meningioma, or non-central nervous system (CNS) cancers.**

**Electromagnetic fields**

**A low frequency EMF does not transmit energy high enough to break chemical bonds; therefore, it is not thought to directly damage DNA or proteins in cells**

# **Etiology of Cancer**

## **(Physical Factors)**

### **Asbestos**

**Asbestos** becomes a serious health hazard if the fibers are inhaled over a long period of time and these health effects are increased dramatically if the exposed individual is a **smoker**

It was first reported in 1935 that asbestos might be an occupational health hazard that could induce cancer

Asbestos-induced **DNA damage** has been shown to result in **chromosome aberrations**, micronuclei formation, and increased rates of sister chromatid exchanges

Asbestos can induce **Lung Cancer** and **Mesothelioma**



# Etiology of Cancer

## (Physical Factors)

### Nanoparticles

- The production of nanoparticles are found in many industrial and consumer products such as **Paint, Cosmetics, and Sunscreens**
- They also have many potential medical applications, such as delivery vehicles for specific drugs to specific target tissues or tumors.
- Many of the cellular effects of nanoparticles are **similar** to the effects exerted by **asbestos**, such as inflammation.
- Nanoparticles have been shown to induce oxidative **DNA damage**,

# Upcoming Webinar

## Nutrition & Cancer

**Alcohol**  
**Dietary fat & Red meat**  
**Dietary Fat and Breast Cancer**  
**Dietary Fat and Colon Cancer**  
**Dietary Fat and Prostate Cancer**  
**Dietary Fat and Other Cancer**  
**Milk, dairy products, and Calcium**  
**Vitamin D and Folate**  
**Carotenoids**  
**Selenium**  
**Soy products**  
**Carbohydrates**



*Thank you very much*



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