

Biomedical
Science

Cancer
Biology II



BMS 44130A | Fall 2026-2027

Cancer Biology II
Environmental Causes of Cancers I



Free Session

A+ is more than just a platform



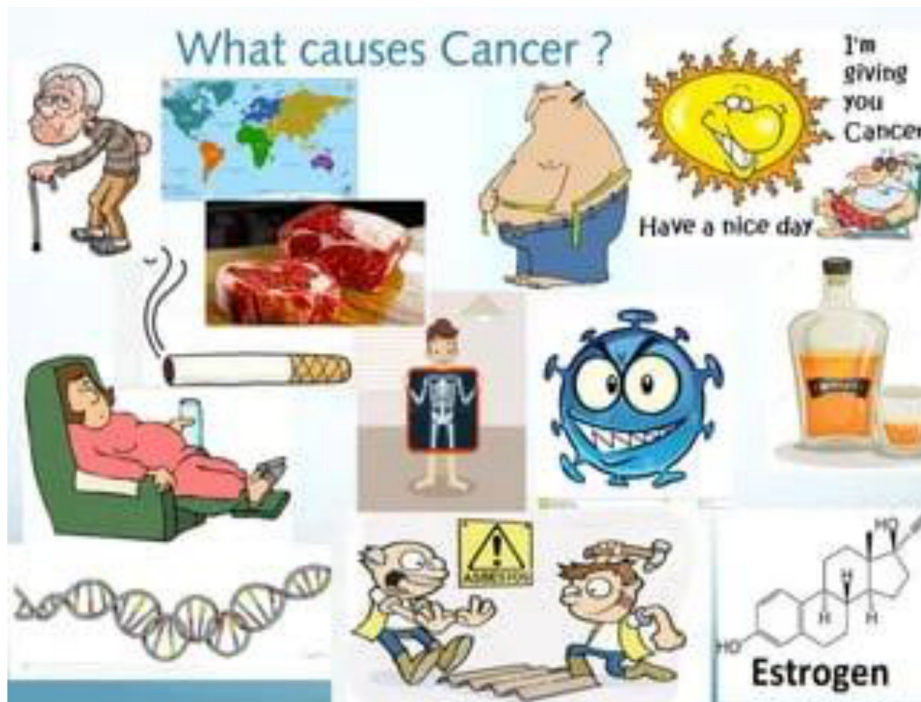
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What Causes Cancer?



Increasing Cancer Risk

FIGURE 2

Increasing Cancer Risk

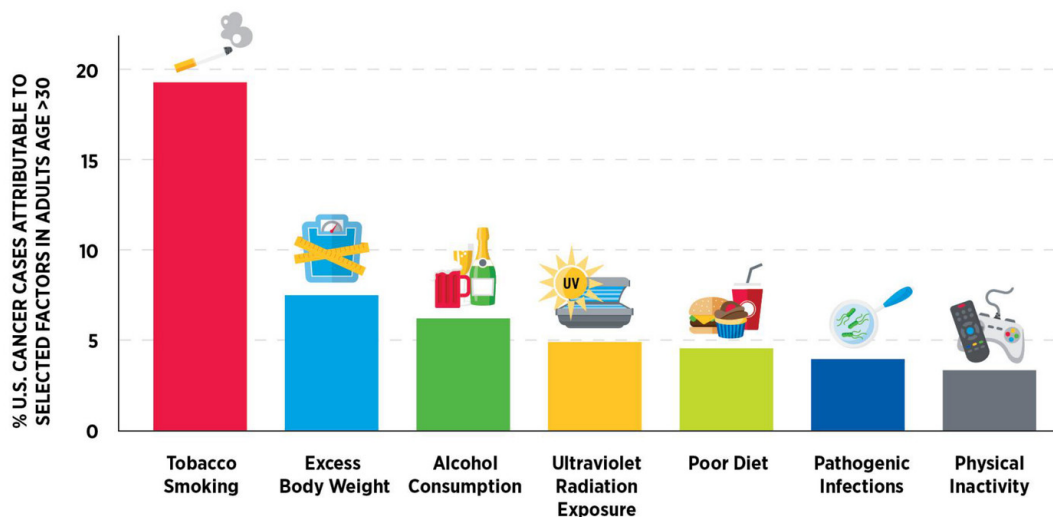
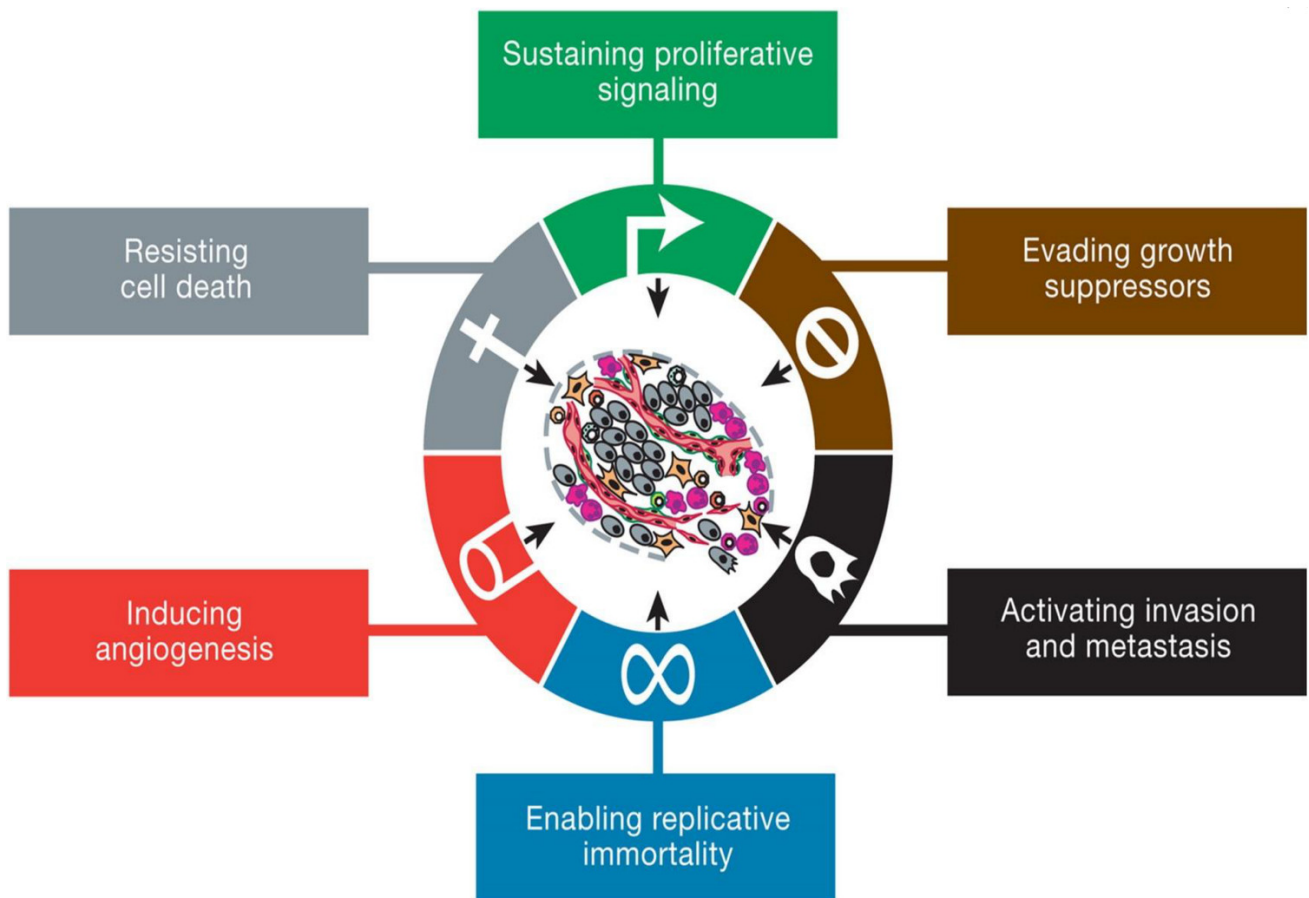


Figure 2 — % of U.S. cancer cases attributable to selected factors in adults aged over 30. AACR Cancer Progress Report 2022.



Hallmarks of Cancer



Genetic Factors

1 • Oncogenes

Many cellular genes can act as **oncogenes** when expressed inappropriately or mutated. They act in a **dominant way** at the cellular level to drive proliferation or prevent normal differentiation.

2 • Tumour Suppressor Genes

Genes that provide **negative regulatory signals** in the normal cell are associated with cancer via **loss or inactivation**, contributing to the transformation process.



Genetic Factors — DNA Repair

THE CORE IDEA

Genetic changes in the components of the **DNA repair machinery** cause altered repair capacity and an **increased risk of cancer**.

A defect in DNA repair machinery is **one of the most common mechanisms** through which cancers occur — once the DNA repair machinery is disrupted, the risk of accumulating mutations becomes high.

A **high mutational burden** can lead to alteration in the cell cycle and uncontrolled replication and proliferation of the cancer cells.

Repair defect



Mutations accumulate



High mutational burden

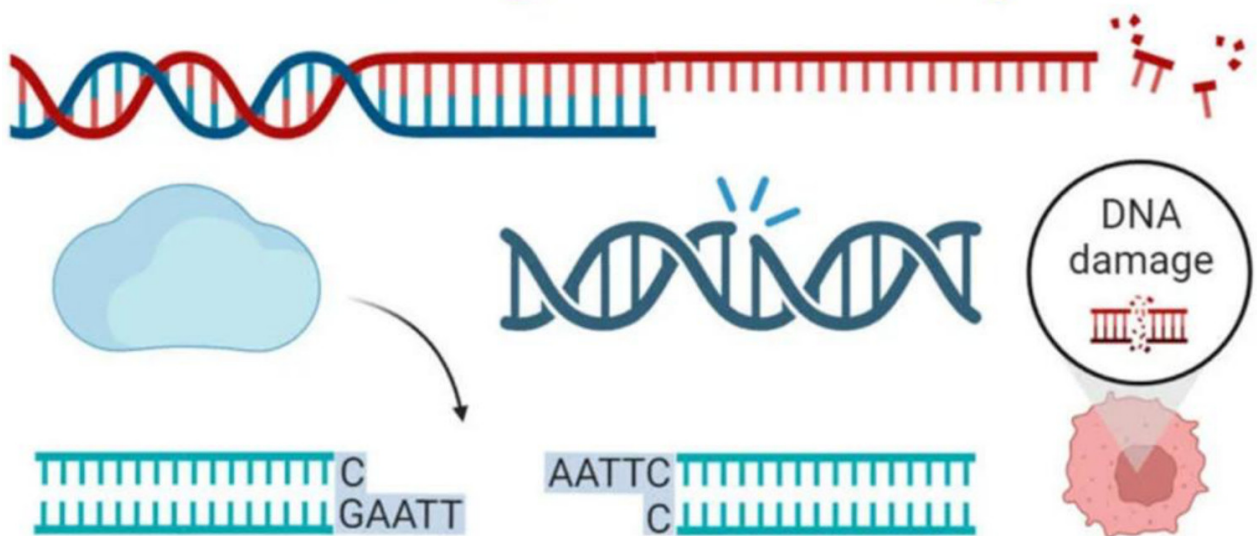


Cell-cycle alteration



Uncontrolled proliferation

DNA Damage and DNA Repair





'Mutator' Genes

DEFINITION

The genes that are associated with altered DNA repair are called **'mutator' genes**.

- Because of their altered function, mutator genes increase the capacity of cells to **accumulate mutations in other genes** as well — germline mutations leading to accumulation of somatic mutations.
- This increases the individual's **lifetime risk of cancer**.

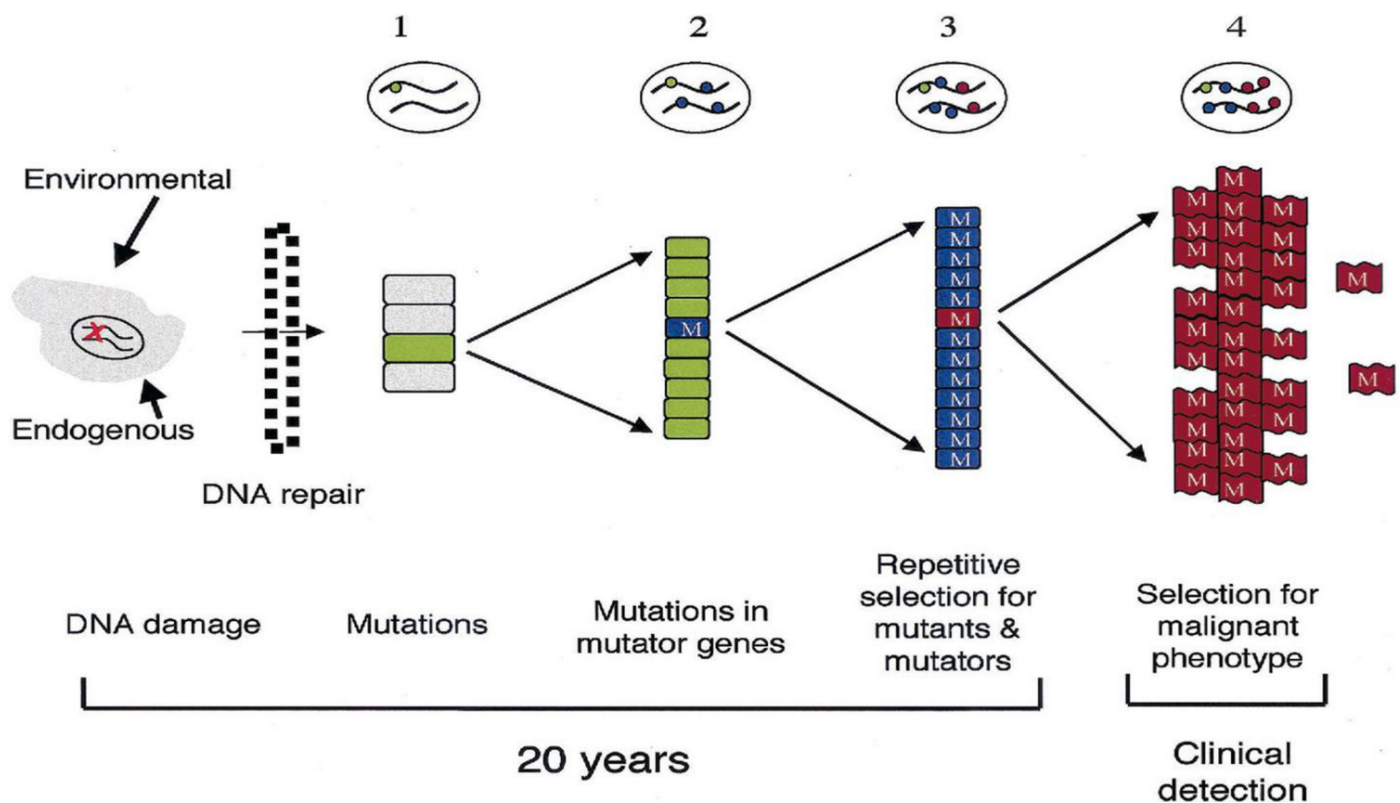


Fig. 1 — Mutation accumulation during tumour progression. Random mutations result when DNA damage exceeds the cell's capacity for error-free DNA repair.



Example of a Mutator Gene: MSH2

MSH2 · MUTS HOMOLOG 2

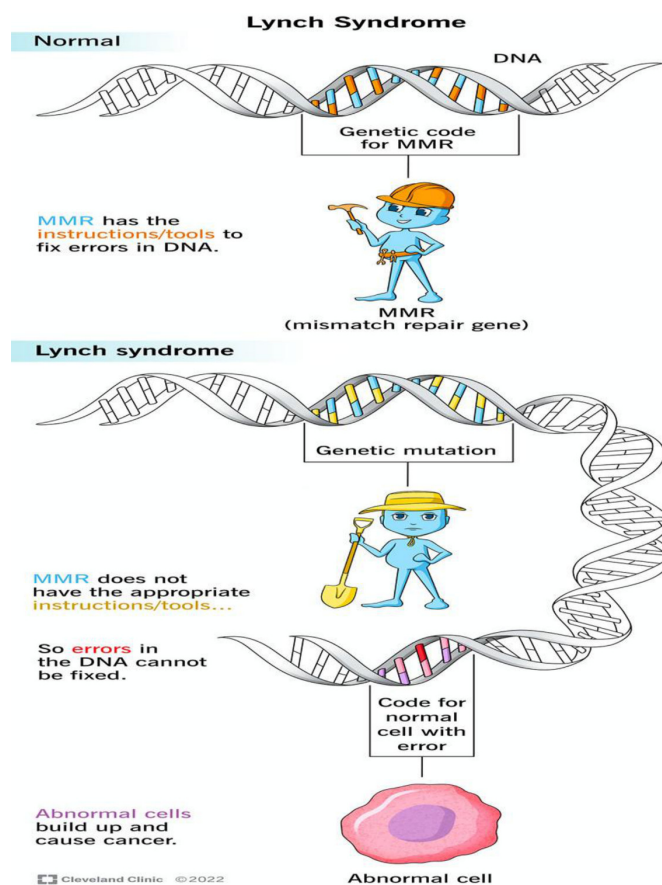
A **mismatch repair gene**. It provides instructions for making a protein involved in DNA repair, correcting errors that occur during DNA copying.

Lynch syndrome

Mutation in MSH2 can cause **Lynch syndrome**, also known as Hereditary Non-Polyposis Colorectal Cancer (**HNPCC**) syndrome.

Lifetime risk

People born with an inherited defect in this gene have a high risk of developing **colorectal cancer at young adult age** — around 40 years.



Normal mismatch repair versus Lynch syndrome. Cleveland Clinic, 2022.



'Young Adult Cancers' List

THINK IT THROUGH

- ? Can you think of any other **mutator gene** that can cause cancers at a young age (between the ages of 18 and 39 years old)?
- ? Do you think cancer in young adults can be **more aggressive** and have a worse prognosis compared to cancer in older adults?

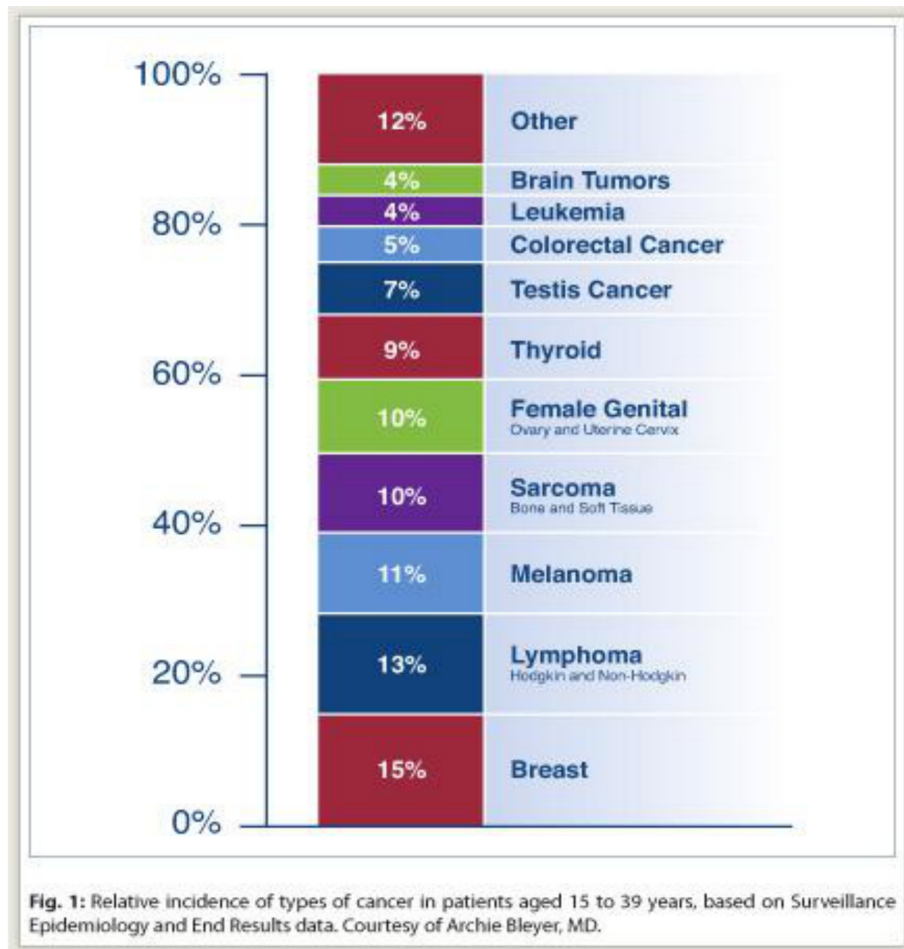


Fig. 1 — Relative incidence of types of cancer in patients aged 15 to 39 years, based on Surveillance Epidemiology and End Results data. Courtesy of Archie Bleyer, MD.



Gene–Environment Interaction

The actions of environmental factors are **not independent of cancer genes.**

There is a link between **genetic mutations** and **environmental factors** that increase cancer risk.

FOR EXAMPLE

Sunlight

Causes mutations in **tumour suppressor genes** in skin cells.

Cigarette smoke

With its carcinogenic compounds, makes **abnormal changes in the lung cells**, leading to cancers.

These factors act **directly or indirectly** on the oncogenes or tumour suppressor genes that are known to be involved in causing cancer.

Environmental factor



Oncogenes / tumour suppressor genes



Cancer



Hereditary & Sporadic Cancers

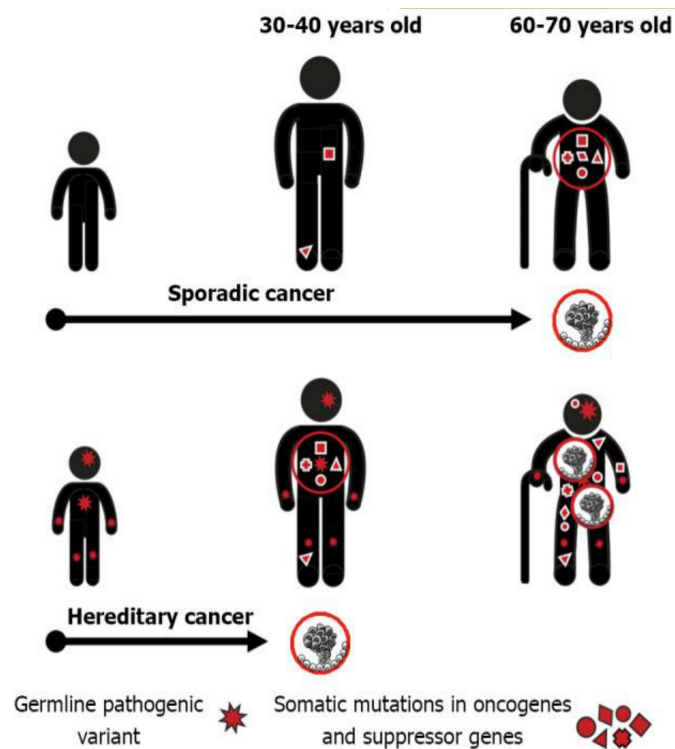
STILL UNCLEAR

How do hereditary factors contribute to the development of **sporadic cancers**?

Individuals who are carriers of **germline pathogenic mutations** do not remain healthy for a prolonged period of time.

BECAUSE

Every cell in the target organ **already contains one alteration** in a cancer gene, increasing the probability of accumulating a critical mass of additional oncogenic mutations — leading to cancer manifestation often occurring at a relatively young age.



DOI: 10.5306/wjco.v14.i2.40 Copyright ©The Author(s) 2023.

Sporadic versus hereditary cancer.



Aflatoxin B₁, HBV & p53

In addition to environmental factors, **individual genetic differences** also affect the susceptibility of an individual to the carcinogenic effects of environmental agents.

EXAMPLE — STUDIES ON LIVER CANCER

- 1 In geographic areas where **aflatoxin B₁** (a carcinogenic mycotoxin produced by *Aspergillus* fungi) and **hepatitis B virus** are common, a mutation in **codon 249** of the tumour suppressor **p53** gene is commonly observed.
- 2 A **dose-dependent relationship** between dietary aflatoxin B₁ intake and codon 249 p53 mutations is observed in liver cancer in these people.
- 3 In people living in areas without aflatoxin B₁ and hepatitis B exposure this specific mutation was **not** observed — indicating that the mutant p53 protein (codon 249) gives a **growth or survival advantage** to liver cancer cells.

This implicates that **genetic risk factors work in combination with environmental factors** to cause cancers.

THINK IT THROUGH

- ? Can you think of any other example that links specific genetic changes to environmental factors that can lead to increased risk of cancers? (hint: smoking, sunlight)



Migration & Cancer Patterns

Epidemiological studies of **migrant populations** have shown that migrants often acquire the **disease profiles of their adopted country**, indicating the role of environmental factors in cancer.

● On first arrival

- Immigrant populations show unique cancer incidence patterns reflecting both risk factors from their **countries of origin** and new exposures after migration.
- In high-income countries (United States, Canada, Western Europe) they typically have **lower rates** of many common solid tumours — breast, prostate and colorectal — than native-born residents.
- This **"healthy immigrant effect"** is attributed to selection biases, healthier lifestyles, and different environmental or reproductive exposures before migration.



OVER TIME

Longitudinal cohort studies from Canada and Europe indicate that as immigrants **acculturate** and adopt the dietary patterns, tobacco use and lifestyle behaviours of their new country, the risk of **"Western" cancers** such as lung and colorectal cancer rises and can eventually **match or even surpass** rates in the host population.

This gradual shift demonstrates that the **adoption of lifestyle risk factors after migration** plays a major role in shaping cancer patterns among immigrants.



Risk Factors of Cancers

MAJOR FACTORS ASSOCIATED WITH CANCER RISK

1. Age

2. Hormones

3. Alcohol use

4. Poor diet

5. Lack of physical activity,
or being overweight

6. Family history of cancer



Environmental Risk Factors

- 1 Smoking / tobacco use
- 2 Exposure to ultraviolet radiation
- 3 Exposure to ionizing radiation
- 4 Exposure to chemicals
- 5 Exposure to certain viruses and bacteria

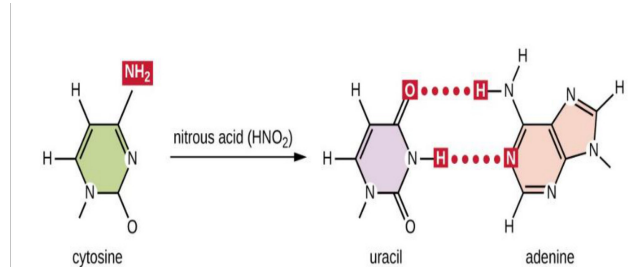




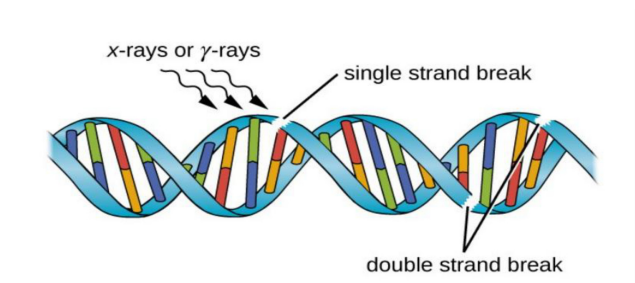
How Risk Factors Damage the DNA

These factors initiate cancers by **interacting directly or indirectly with the DNA molecule**, introducing :

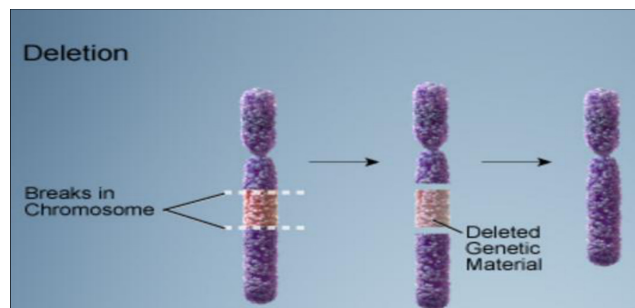
- 1 **Changes in the chemical structure of DNA bases** — causing incorrect bases to pair up that can then be misread during replication.



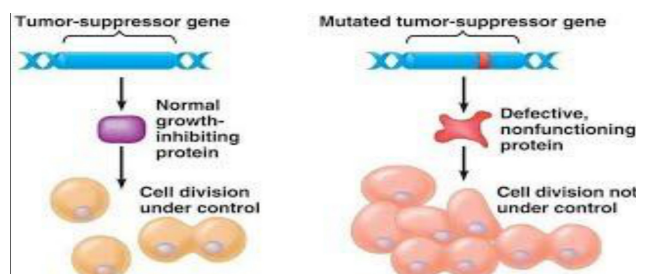
- 2 **Mutations that distort the DNA double helix** — causing it to be replicated inaccurately.



- 3 **Breaks in chromosomes** — that lead to deletions and other types of aberrations.



- 4 **Mutations in several genes** — that can lead to cell cycle disruption.





Smoking & Tobacco Use

IN CIGARETTE SMOKE, THERE ARE

- 1 Over **60 carcinogens** — cancer causing chemicals.
- 2 **Polycyclic aromatic hydrocarbons** and **aromatic amines** that are known carcinogens in humans.

RISK PROFILE

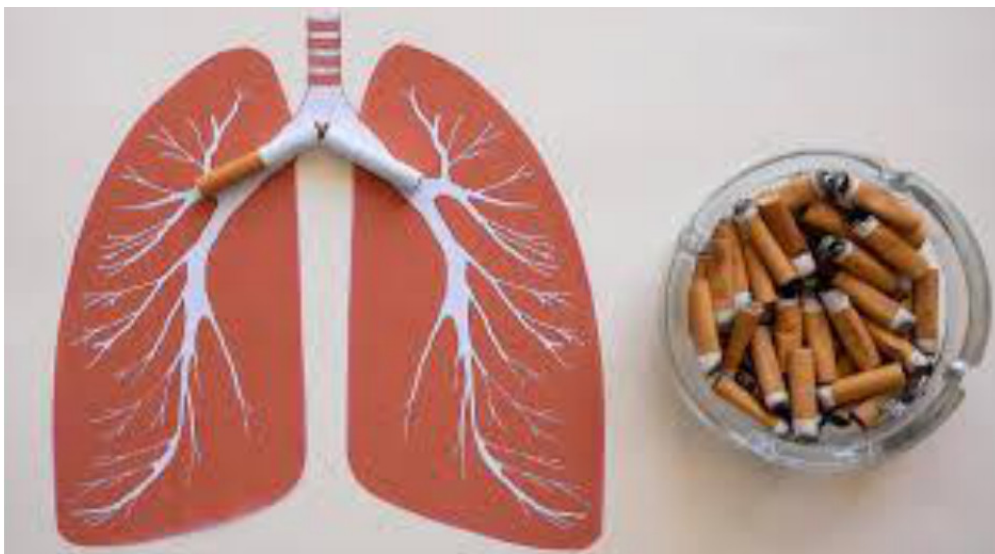
The risk of lung cancer increases rapidly among current smokers, being **highest in those who begin to smoke at an early age** and who continue to smoke throughout life.

60+

carcinogens — cancer causing chemicals — in cigarette smoke

2

named classes of known human carcinogens: PAHs and aromatic amines





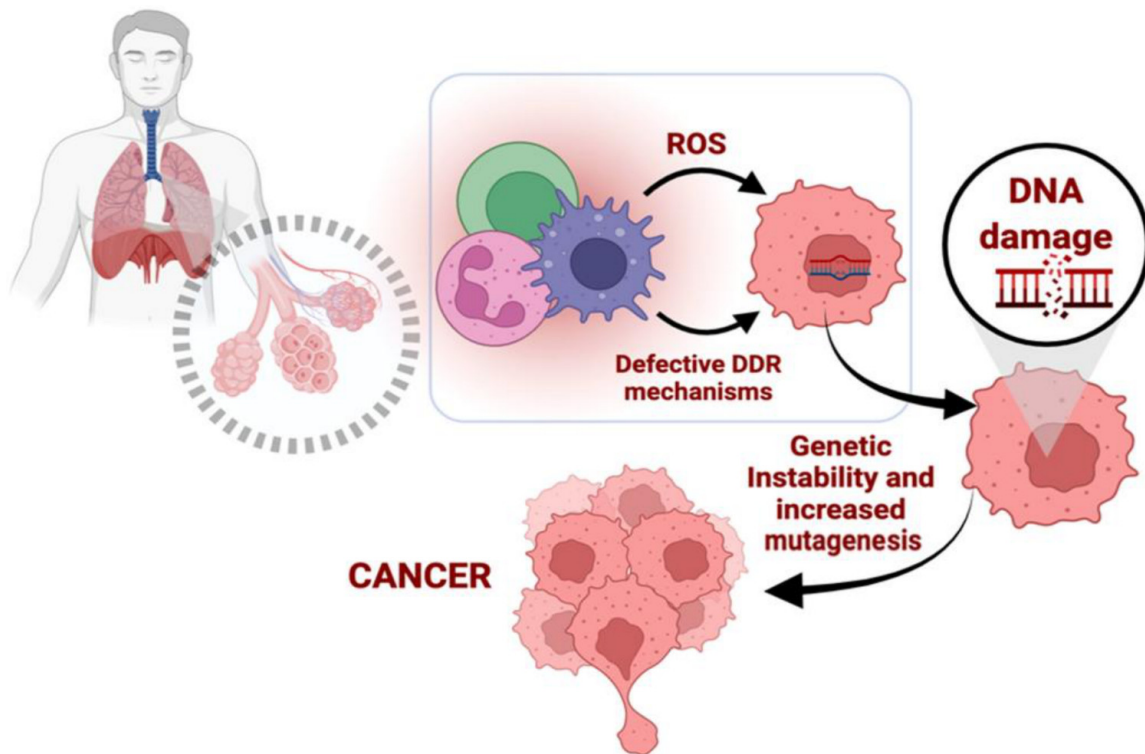
Smoking — Damage to the Cell

When smoking, carcinogens in cigarettes **enter our lungs and affect the entire body.**

IT CAUSES DAMAGE TO

- 1 **DNA structure**
- 2 **DNA repair machinery** and the production of reactive oxygen species (ROS) proteins
- 3 The body's **immune system**, making it harder to kill cancer cells

This **build-up of DNA damage in the same cell** over a long period of time can lead to various types of cancers.





Passive Smoking

Exposure to **environmental tobacco smoke** (passive smoking) is also **carcinogenic**.

- Passive smoking, or **second hand smoking**, means breathing in other people's tobacco smoke.
- Second hand tobacco smoke comes from **cigarettes, pipes, cigars and shisha pipes (hookah)**.
- Smoke is breathed out by a person who is smoking and spreads easily to be inhaled by other people in the same room, as smoke **can stay in the air for hours**.
- It can also build up on surfaces, furniture and clothes — known as **third hand smoke**.
- Passive smoking is harmful and can cause **many of the same health effects as active smoking** does.





Smoking & Cancers

There is a risk of **16 cancer types** due to smoking. These include cancer of the :

1 Lung

2 Mouth, throat, nose and sinuses, oesophagus

3 Bladder, kidney and ureter

4 Pancreas

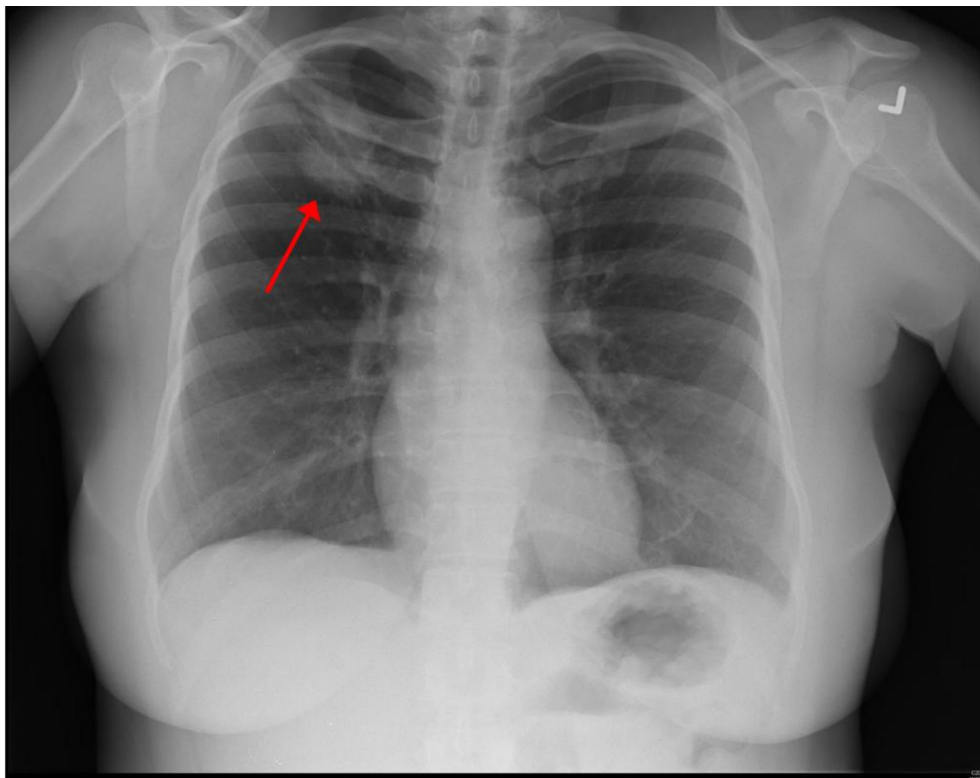
5 Stomach

6 Liver

7 Cervix and ovary

8 Bowel (colorectal cancer)

9 Acute myeloid leukemia





Exposure to Ultraviolet Radiation

DEFINITION

Ultraviolet (UV) radiation is a type of energy released **naturally by the sun** and artificially from other sources.

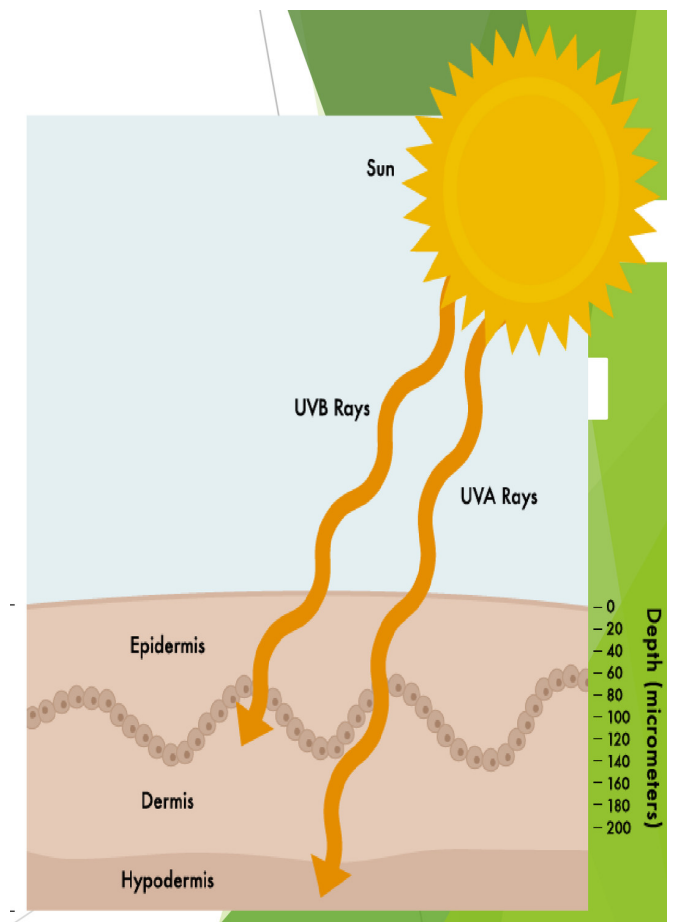
TWO MAIN TYPES OF UV RAYS

UVB

Reaches the **outer layer** of the skin — the **epidermis**.

UVA

Reaches **deeper** into the inner layer of the skin — the **dermis**.



Both UVA and UVB rays can damage the skin and cause **sunburn, aging and skin cancers**.



UV Exposure & Skin Cancers

THE AMOUNT OF UV EXPOSURE A PERSON GETS DEPENDS ON

- 1 **Strength of the rays**
- 2 **Length of time** the skin is exposed
- 3 Whether the skin is **protected** with clothing, sunscreen or personal protective equipment



Skin cancers: squamous cell carcinoma, basal cell carcinoma, melanoma and Merkel cell carcinoma.



Ionizing Radiation & Mobile Phones

Mobile phones also carry **low-frequency electric and magnetic fields** and radiofrequencies.

KEY DISTINCTION

Unlike ionizing radiation (such as X-rays or UV rays from the sun), **non-ionizing radiation does not have enough energy to break chemical bonds or damage DNA**. Because it cannot damage DNA, it **cannot trigger the cell mutations that lead to cancer**.

● Brain glucose metabolism

- Two small studies examined brain glucose metabolism in people after they had used cell phones.
- One study showed **increased** glucose metabolism in the region of the brain close to the antenna compared with tissues on the opposite side of the brain.
- The other study found **reduced** glucose metabolism on the side of the brain where the phone was used.



As to date, data on mobile phones does not show association with cancer.



Interphone Case–Control Study

● How the study was done

- The **largest case–control study** of cell phone use and the risk of head and neck tumours.
- Conducted by a consortium of researchers from **13 countries**.
- Data came from questionnaires completed by study participants in Europe, Israel, Canada, Australia, New Zealand and Japan.

WHAT THE STUDY SHOWED

- 1 Most published analyses showed **no overall increase** in brain or other central nervous system cancers (glioma and meningioma) related to higher amounts of cell phone use. One analysis found a statistically significant but small rise in glioma risk among the heaviest callers — the researchers considered this finding **inconclusive**.
- 2 Data pooled from all 13 countries showed a statistically significant association between where tumours sat inside the brain and the **self-reported location of the phone**. The authors noted that firm conclusions about cause and effect cannot be drawn.
- 3 Data from **five Northern European countries** showed an increased risk of **acoustic neuroma** in those who had used a cell phone for 10 or more years.
- 4 Later analyses asked whether tumours formed where exposure was highest: one found **no relationship** between tumour location and radiation level, while another found evidence that glioma — and to a lesser extent meningioma — were more likely to develop where exposure was highest.



Exposure to Chemicals

Exposure to chemicals **in the outdoors, at home, and at work** may add to your chances of getting cancer.

KNOWN HUMAN CARCINOGENS

- 1 Benzene
- 2 Beryllium
- 3 Asbestos
- 4 Vinyl chloride
- 5 Arsenic



Natural and anthropogenic sources of arsenic.

GETTING CANCER FROM A CHEMICAL DEPENDS ON

1. The **kind** of chemical you were exposed to

2. The **amount** you were in contact with

3. **How long** the contact lasted

4. **How often** you were exposed

Chemical exposures **in the workplace** can happen at high levels and over long periods of time, **making it a cancer risk.**



Case Study: Hexavalent Chromium

Erin Brockovich alleged that the **Hinkley compressor station** used **hexavalent chromium** in a cooling tower system to fight corrosion.

1

Cooling tower

Hexavalent chromium used to fight corrosion

2

Unlined ponds

Wastewater with the chemical discharged on site

3

Groundwater

Waste water percolated down into the aquifer

4

Drinking water

Supply contaminated with hexavalent chromium

5

Cancers

In the population drinking the contaminated water



Mechanism of Action

- Chemical carcinogens taken up by cells are usually **metabolized**. These metabolites may sometimes be **retained by the cell**.
- Such internalized carcinogenic compounds can then directly or indirectly **alter gene expression**.
- Some carcinogens are **genotoxic**, inducing various DNA and chromosomal abnormalities.
- Others have **non-genotoxic** effects and cause cancer via inflammation, suppressing immunity, forming damaging reactive oxygen species (ROS), or by activation of signaling pathways.

DAMAGE CAUSED BY CARCINOGENIC CHEMICALS

1. DNA structure

2. DNA repair machinery and proteins

3. The immune system — harder to kill cancer cells

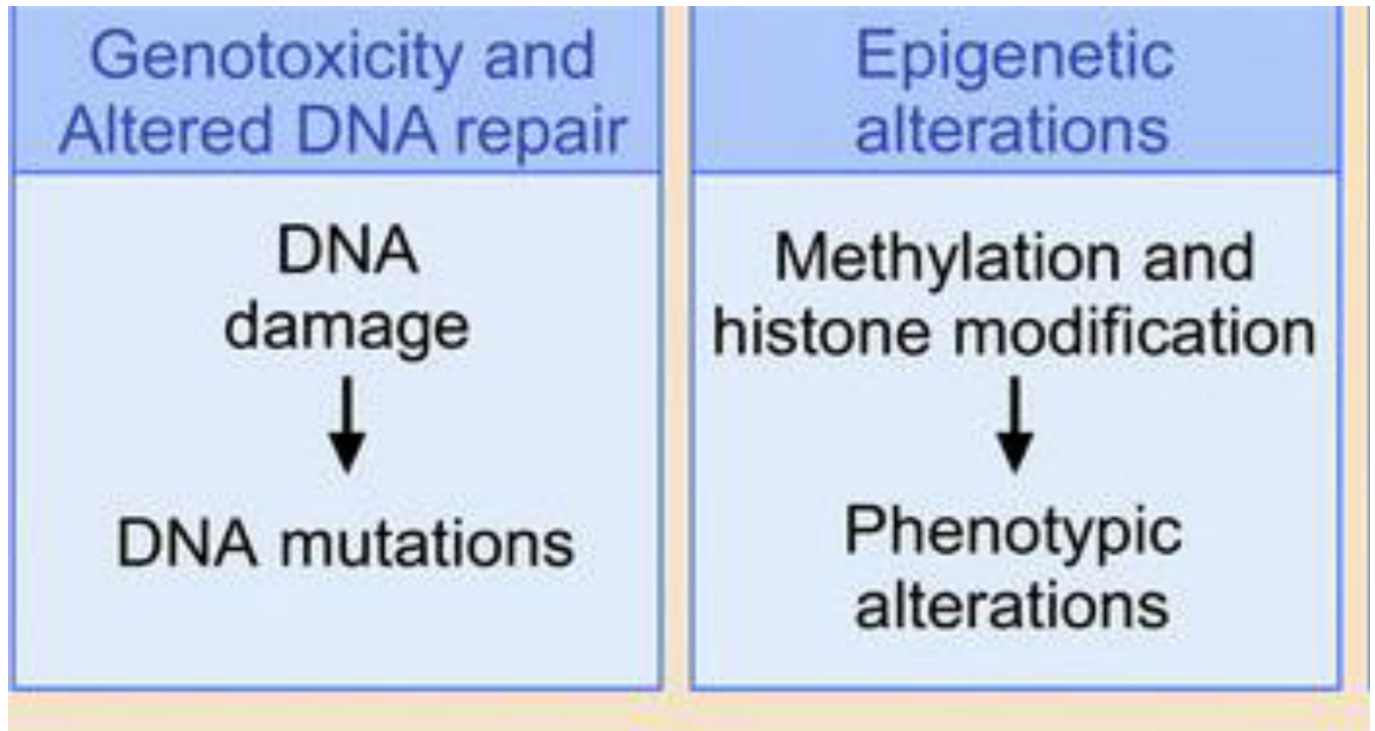
4. Induce mutations and cell cycle disruption

This **build-up of DNA damage in the same cell** over a long period of time can lead to various types of cancers.



Genotoxic vs Non-Genotoxic

GENOTOXIC CARCINOGENS — MECHANISM OF ACTION



Genotoxicity and altered DNA repair lead to DNA mutations; epigenetic alterations lead to phenotypic alterations.

NON-GENOTOXIC CARCINOGENS — MECHANISM OF ACTION

● Metabolic activation

Aflatoxin B₁ → CYP3A4 / CYP2A13 →

AFB₁-8,9-epoxide

An electrophilic compound.

● Oxidative stress

Reactive oxygen species → Tissue damage

Damage accumulates in the exposed tissue.

IN-CLASS READING



"This cancer-causing chemical may be lurking in your bread"

[ewg.org/news-insights/news/2026/07/cancer-causing-chemical-may-be-lurking-your-bread](https://www.ewg.org/news-insights/news/2026/07/cancer-causing-chemical-may-be-lurking-your-bread)

Read this article in class — we will discuss.



Occupational Exposures & Cancers

Cancers associated with various **occupations or occupational exposure.**

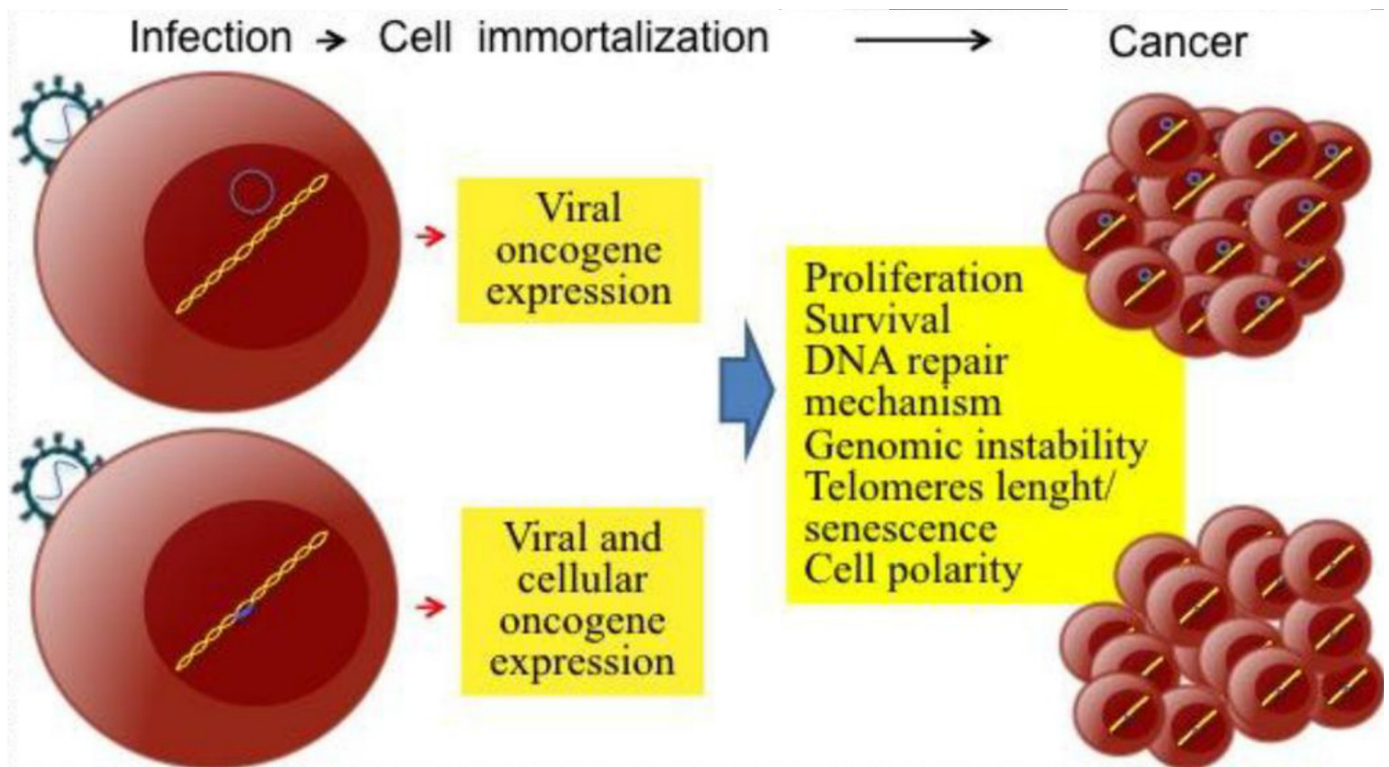
CANCER	SUBSTANCES OR PROCESSES
Lung	Arsenic, asbestos, cadmium, coke oven fumes, chromium compounds, coal gasification, nickel refining, foundry substances, radon, soot, tars, oils, silica
Bladder	Aluminum production, rubber industry, leather industry, 4-aminobiphenyl, benzidine
Nasal cavity & sinuses	Formaldehyde, isopropyl alcohol manufacture, mustard gas, nickel refining, leather dust, wood dust
Larynx	Asbestos, isopropyl alcohol, mustard gas
Pharynx	Formaldehyde, mustard gas
Mesothelioma	Asbestos
Lymphatic & hematopoietic	Benzene, ethylene oxide, herbicides, x-radiation system
Skin	Arsenic, coal tars, mineral oils, sunlight
Soft-tissue sarcoma	Chlorophenols, chlorophenoxy herbicides
Liver	Arsenic, vinyl chloride
Lip	Sunlight



Exposure to Viruses & Bacteria

Certain viruses and bacteria have been associated with **causing cancers** by :

- 1 **Directly affecting genes** associated with cell cycle regulation
- 2 **Introducing mutations** in the DNA molecule
- 3 **Chronic inflammation** — inducing a high influx of immune cells that damage the host organs and allow uncontrolled cell division
- 4 **Weakening of the immune system** so the body cannot fight cancer

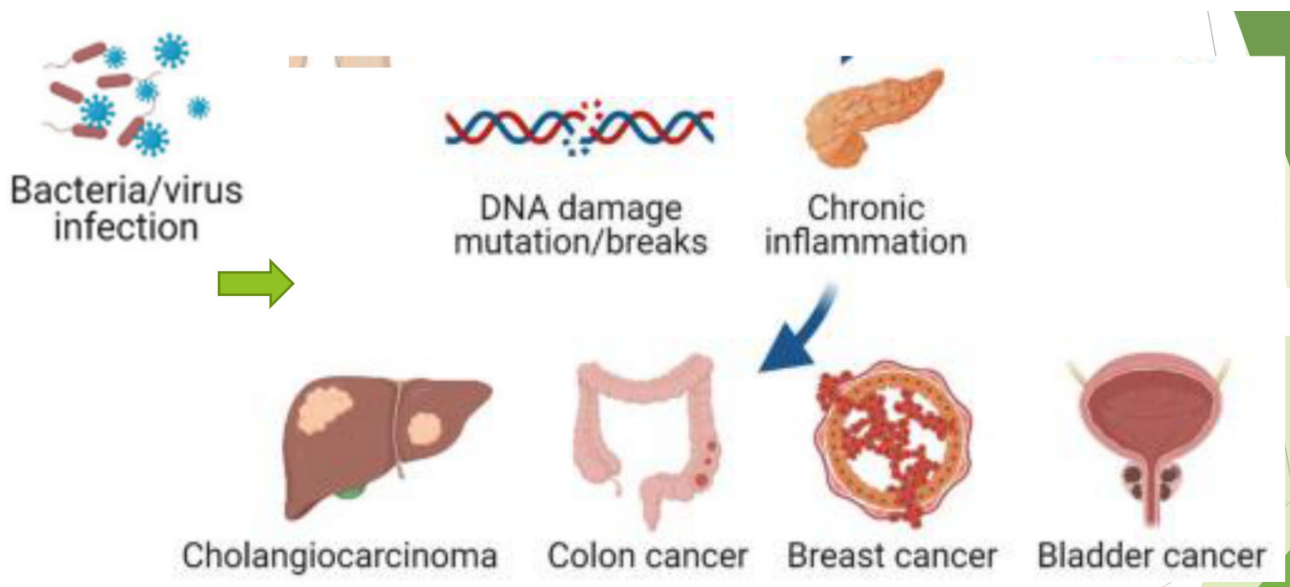


Infection → cell immortalization → cancer, via viral and cellular oncogene expression.



Infectious Agents & Cancers

TYPE	INFECTIOUS AGENT	ASSOCIATED CANCER
VIRUS	Hepatitis B virus	Hepatic carcinoma
VIRUS	Hepatitis C virus	Hepatic carcinoma, lymphomas
VIRUS	Human papilloma virus	Genital and oral carcinoma
VIRUS	Human Immunodeficiency Virus, type I	Kaposi's sarcoma, lymphomas, eye cancer
VIRUS	Human T-cell lymphotropic virus, type I	Adult T-cell leukemia
VIRUS	Epstein Barr Virus (EBV)	Pharyngeal carcinomas and lymphomas
VIRUS	Kaposi Sarcoma Herpes virus (KSHV)	Kaposi sarcoma
BACTERIA	Helicobacter pylori	Gastric carcinomas and lymphomas
PARASITE	Schistosoma haematobium	Bladder cancer
PARASITE	Opisthorchis viverrini	Cholangiocarcinoma
PARASITE	Opisthorchis sinensis	Cholangiocarcinoma



Bacterial and viral infection → DNA damage, mutation and breaks, chronic inflammation → cholangiocarcinoma, colon, breast and bladder cancer.

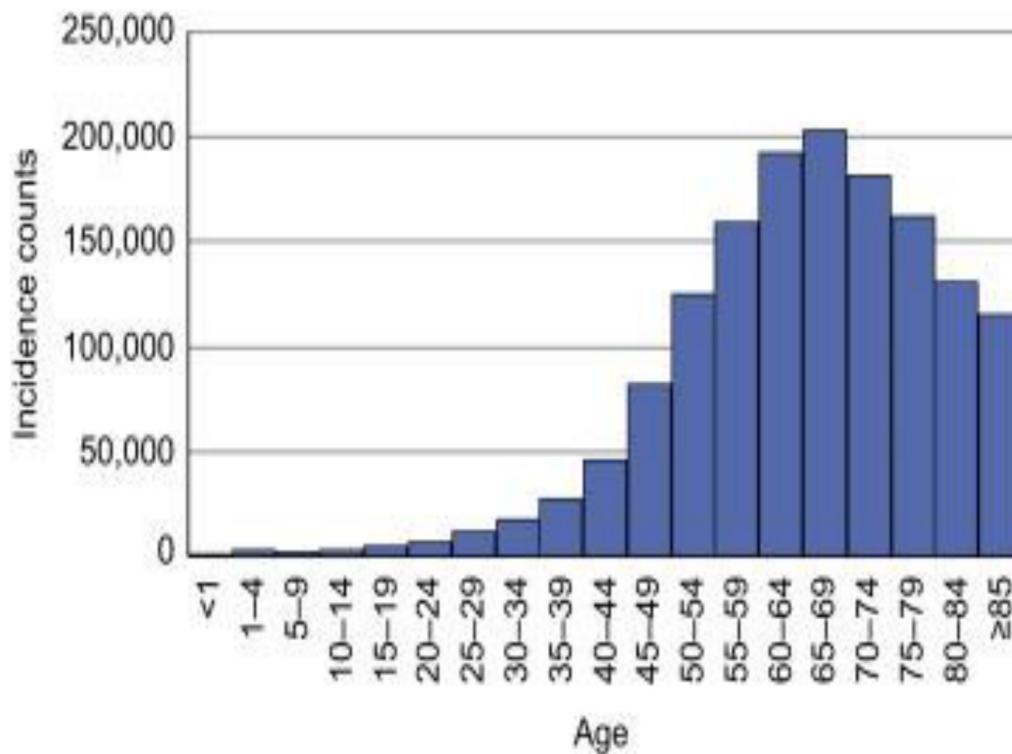


Age

THE HEADLINE

Age is the **biggest risk factor for developing cancer.**

- 1 **Continuous exposure throughout life** to low levels of exogenous carcinogens, accumulation of multiple genetic changes, and multiple phases of clonal selection.
- 2 **Reactive oxygen species (ROS)** produced as byproducts of normal metabolism. ROS such as superoxide and hydrogen peroxide are the same mutagens produced by radiation, and can damage DNA, proteins and lipids.
- 3 **Decline in DNA repair capacity** with an associated increase in mutation rate.



Cancer incidence counts by age group.



Certain **medical treatments may increase the risk of cancers.**

- 1 **Radiation and chemotherapy** may result in secondary cancers and increased aggressiveness of those cancers not fully cured by such treatments.
- 2 Some **immunosuppressive drugs** used for chronic inflammatory diseases or after transplantation can cause **lymphoma**.
- 3 Women exposed to **excess estrogen** are at increased risk for some gynecological cancers (e.g. breast, uterus), because estrogens can stimulate cell proliferation in these tissues.

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SCIENCEINSIDER | HEALTH

Gene therapy clinical trial halted as cancer risk surfaces

Virus carrying corrective gene may have caused study participant's bone marrow disorder

11 AUG 2021 • 10:40 AM • BY KELLY SERVICEK

IN-CLASS GROUP ACTIVITY

? "Study reveals why DNA damage from smoking and UV rays may cause cancer in some people but not others"

Scientists have found the first direct evidence of the powerful role our genetic makeup plays in influencing our risk of cancer, with inherited genes interacting with acquired genetic mutations to shape how tumours evolve.

cam.ac.uk/research/news/study-reveals-why-dna-damage-from-smoking-and-uv-rays-may-cause-cancer-in-some-people-but-not-others



To Summarise...

GENETIC 2

Two classes of cancer gene

- Oncogenes act dominantly to drive proliferation
- Tumour suppressors lost or inactivated
- Defective DNA repair genes = 'mutator' genes

INHERITED MSH2

Lynch syndrome (HNPCC)

- Mismatch repair gene
- Inherited defect → high colorectal cancer risk
- Presents at young adult age, around 40 years

ENVIRONMENT 5

Environmental risk factors

- Smoking / tobacco and UV radiation
- Ionizing radiation and chemicals
- Certain viruses and bacteria

SMOKING 60+

Carcinogens in cigarette smoke

- PAHs and aromatic amines are known carcinogens
- Risk across 16 cancer types
- Second and third hand smoke also harmful

CHEMICALS 5

Known human carcinogens

- Benzene, beryllium, asbestos, vinyl chloride, arsenic
- Act by genotoxic or non-genotoxic routes
- Workplace exposure: high level, long duration

AGE #1

Biggest risk factor

- Lifetime low-level carcinogen exposure
- ROS from normal metabolism damage DNA
- DNA repair capacity declines with age

THE THROUGH-LINE

DNA damage



Mutations



Mutations in mutator genes



Repetitive selection for mutants



Malignant phenotype



Clinical detection