



# Cell Death and Cancer

SNC 2D

Ms. Papaiconomou

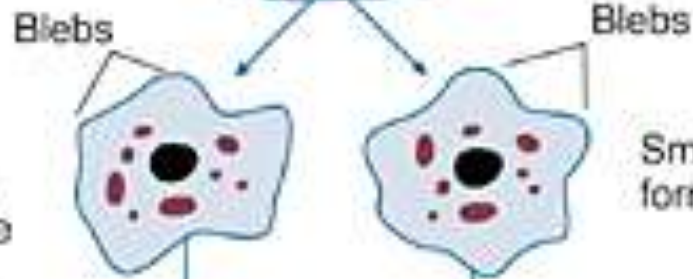
# How do cells die?

## **Necrosis**

- Death due to unexpected and accidental cell damage.
- This is an unregulated cell death.
- Causes: toxins, radiation, trauma, lack of oxygen due to the blockage of blood flow.

## **Apoptosis**

- A cell also dies as a normal part of the functioning of healthy multicellular organisms.
- This is a regulated, or controlled, cell death of cells that are no longer useful.
- Apoptosis also removes cells that have lost their ability to perform efficiently.



Small blebs form; the structure of the nucleus changes.

Small blebs form.

The blebs fuse and become larger; no organelles are located in the blebs.



The nucleus begins to break apart, and the DNA breaks into small pieces. The organelles are also located in the blebs.

The cell membrane ruptures and releases the cell's content; the organelles are not functional.



**Necrosis**

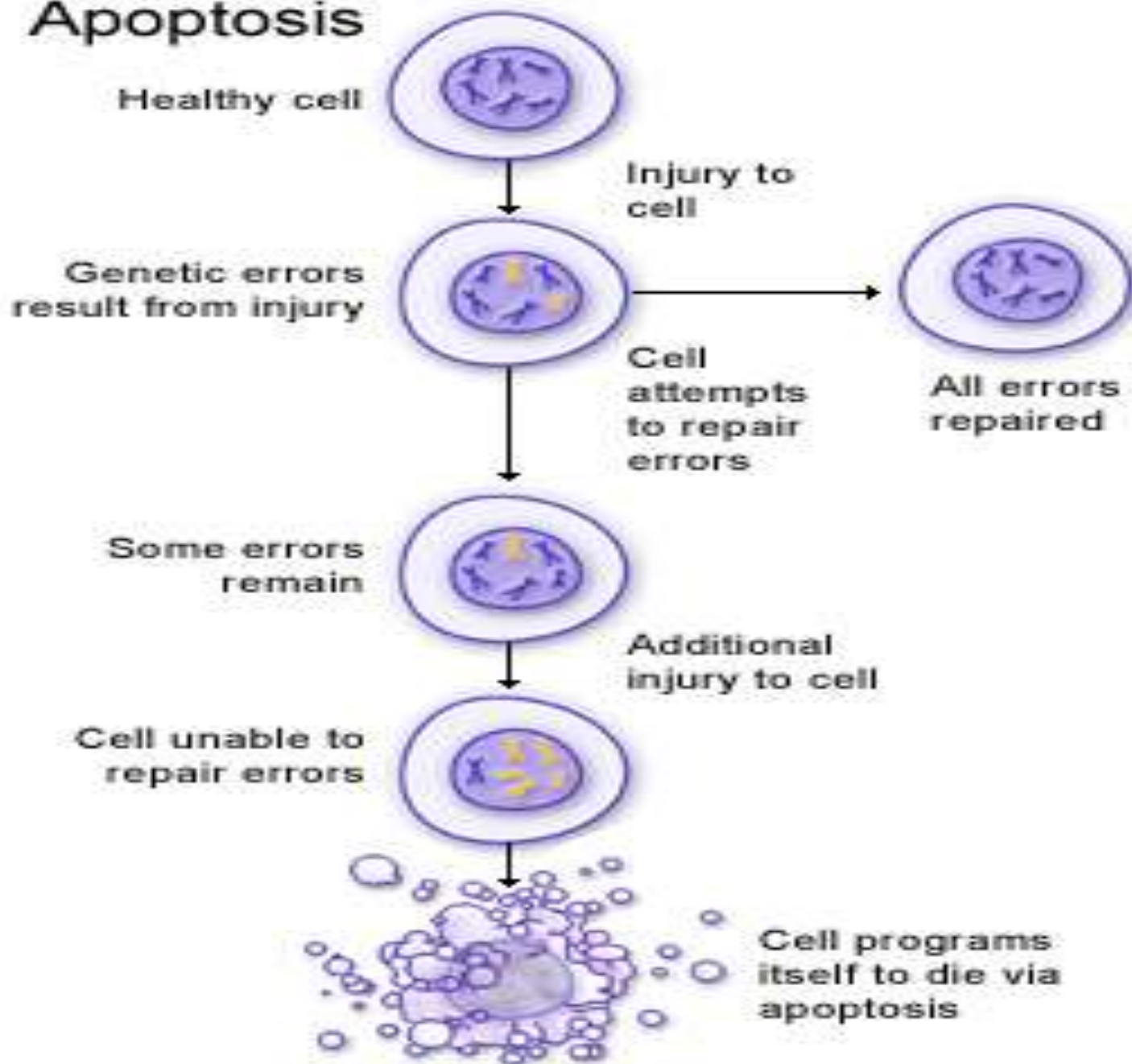


**Apoptosis**

The cell breaks into several apoptotic bodies; the organelles are still functional.

<b>Necrosis</b>	<b>Apoptosis</b>
Pathologic “Cell Homicide”	Physiologic “Cell Suicide”
Large number of cells Swelling	Few cells Shrinkage
Random, diffuse fragmentation of nucleus	Orderly nuclear condensation and fragmentation
Inflammation Surrounding normal tissue damage	No inflammation No secondary tissue damage

# Apoptosis



# Apoptosis Videos

- [http://www.youtube.com/watch?v=7WRkY8q\\_F3k](http://www.youtube.com/watch?v=7WRkY8q_F3k)
- [http://www.youtube.com/watch?v=gYWU\\_TBM8tTo](http://www.youtube.com/watch?v=gYWU_TBM8tTo)

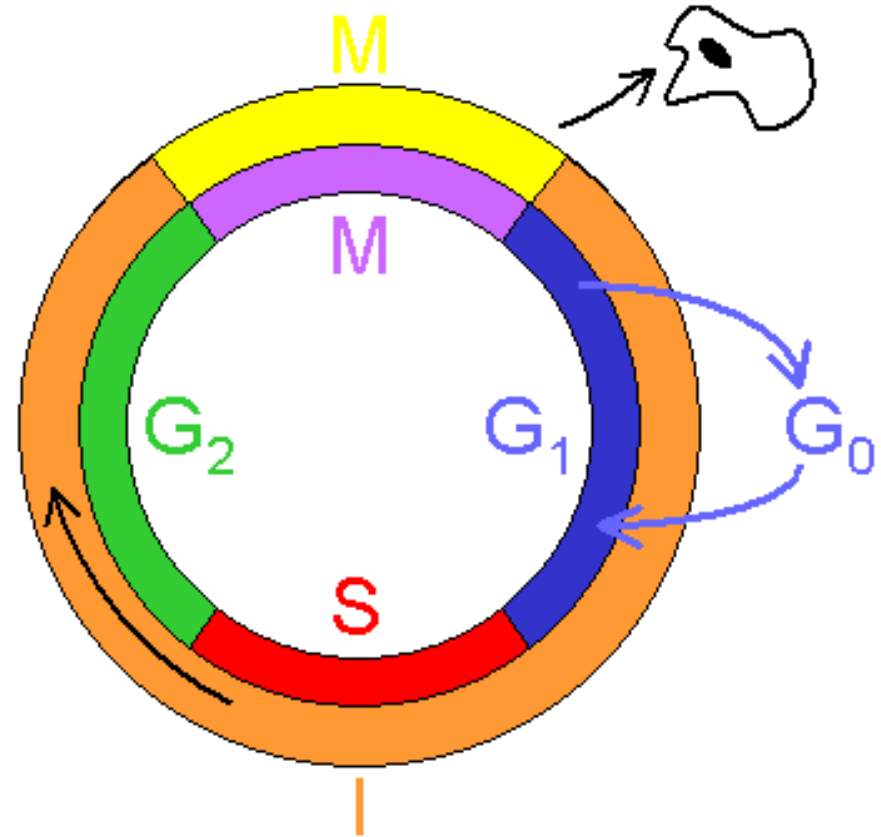
# Cell Lifespans

- Cells do not live forever. They can only divide a certain number of times until they receive a message or instructions to die. Cell division is necessary for cells to be replaced after they die.
- In your body, 3 billion cells die every minute.
- We undergo cell division as part of regeneration, a process essential for repairing damaged tissue.
- Why do we age?
  - It is believed we age because as cells die, they are not replaced or not replaced as quickly. This results in changes to the structure and function of major body systems.

# Review: The cell cycle has four phases and controls cell division

- Two gap or growth phases (G<sub>1</sub> and G<sub>2</sub>)
- S phase - DNA synthesis
- M phase - Mitosis

Interphase



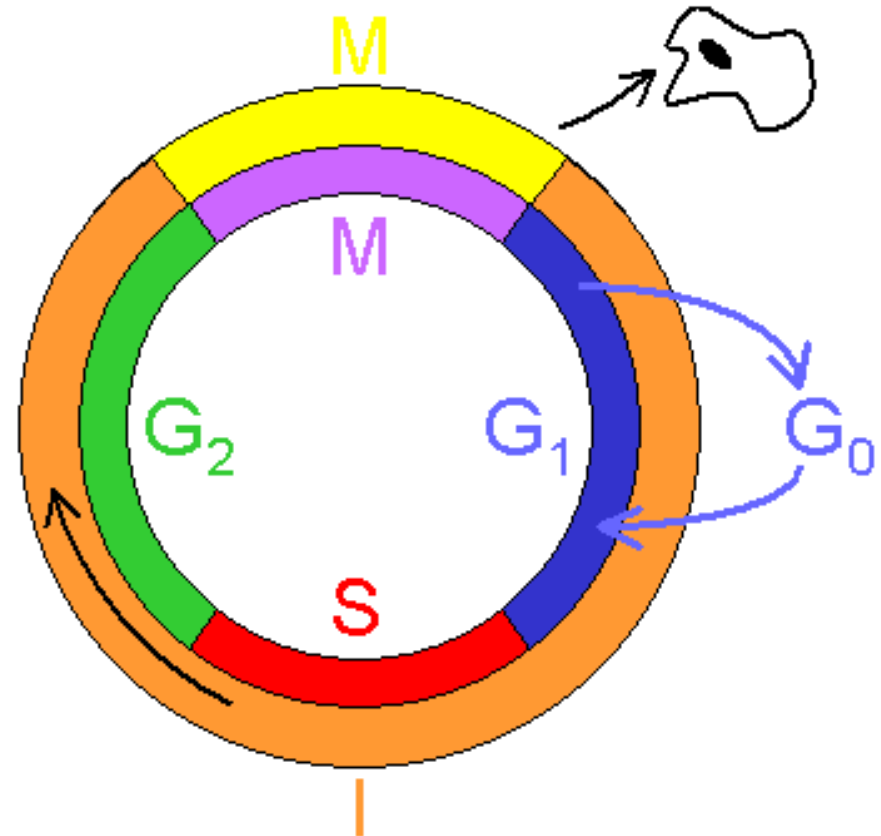


# Cell Cycle Checkpoints

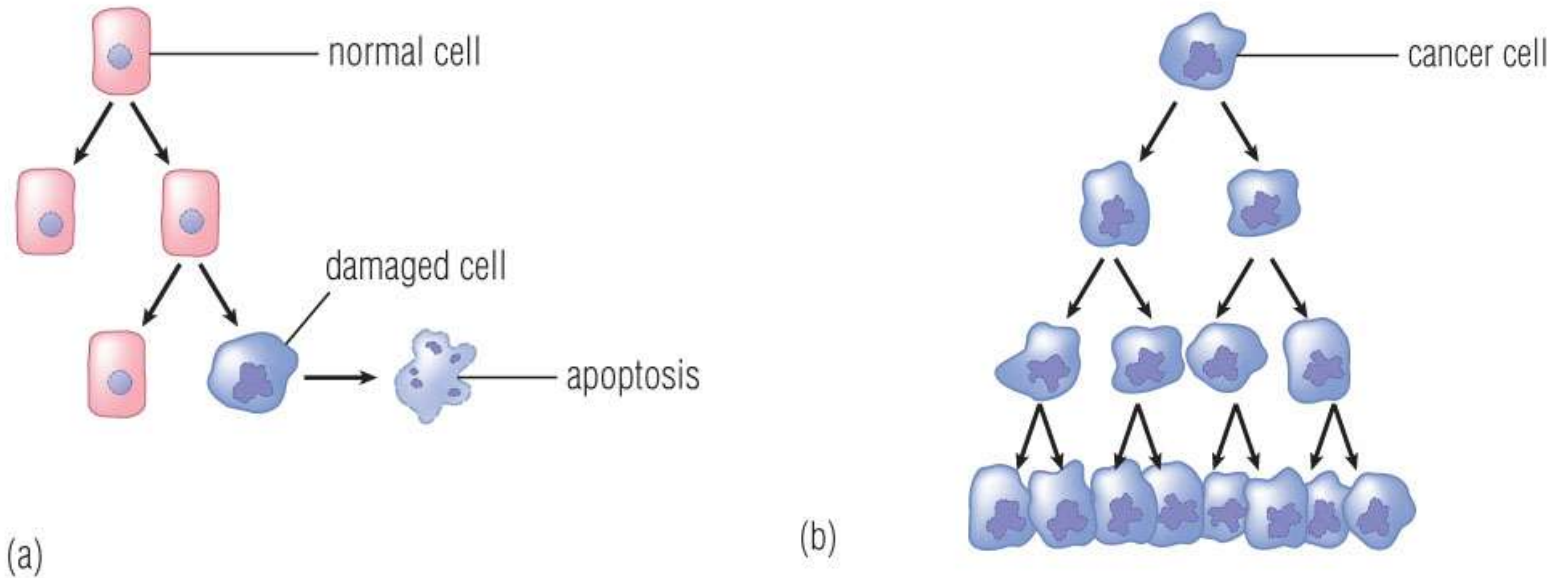
- A cell should remain in interphase and not divide if...
  - signals from surrounding cells tell the cell not to divide
  - there are not enough nutrients in the cell
  - the DNA has not yet been replicated
  - the DNA is damaged
- These checkpoints are regulated by special proteins like p53

# Cell Cycle Checkpoints

- Three checkpoints in cell cycle
  - **G1-S transition**
  - **G2-M transition**
  - **Exit M phase transition**
- Checkpoints are where the cell assesses whether conditions are favorable for cell division.
- When the environment is not favorable (for example, when the cell's DNA is damaged), a protein called **p53** can stop the cell cycle and cause the cell to die.
- When the proteins that regulate the cell cycle are mutated or absent, cells can divide uncontrollably, leading to cancer.



# Cell division in Normal Cells and Cancer Cells



**Figure 1.34** (a) Cell division and cell death in normal cells. (b) Cell division in cancer cells

# Cancer Cells

- A cell that divides uncontrollably and can seem to be “immortal”.
- Cancer arises from the accumulation of genetic changes or mutations.
- Most cancers have a minimum of 6-9 genes mutate.
- Not a hereditary disease – we do not pass on cancer to offspring.
- We can inherit dispositions (susceptibility) to cancer.
- Many genes that are mutated in cancer are involved in *regulating the cell cycle*.

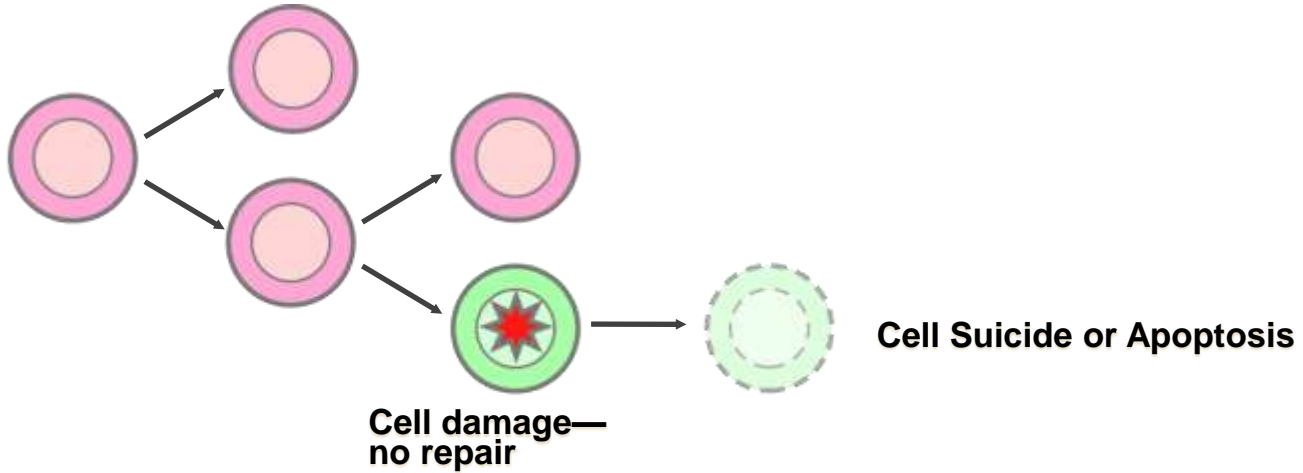
# Tumor suppressors and oncogenes

- Mutations in *oncogenes* and *tumor suppressor genes* can lead to cancer.
- [http://science.education.nih.gov/supplements/nih/cancer/activities/activity2\\_animations.htm](http://science.education.nih.gov/supplements/nih/cancer/activities/activity2_animations.htm)

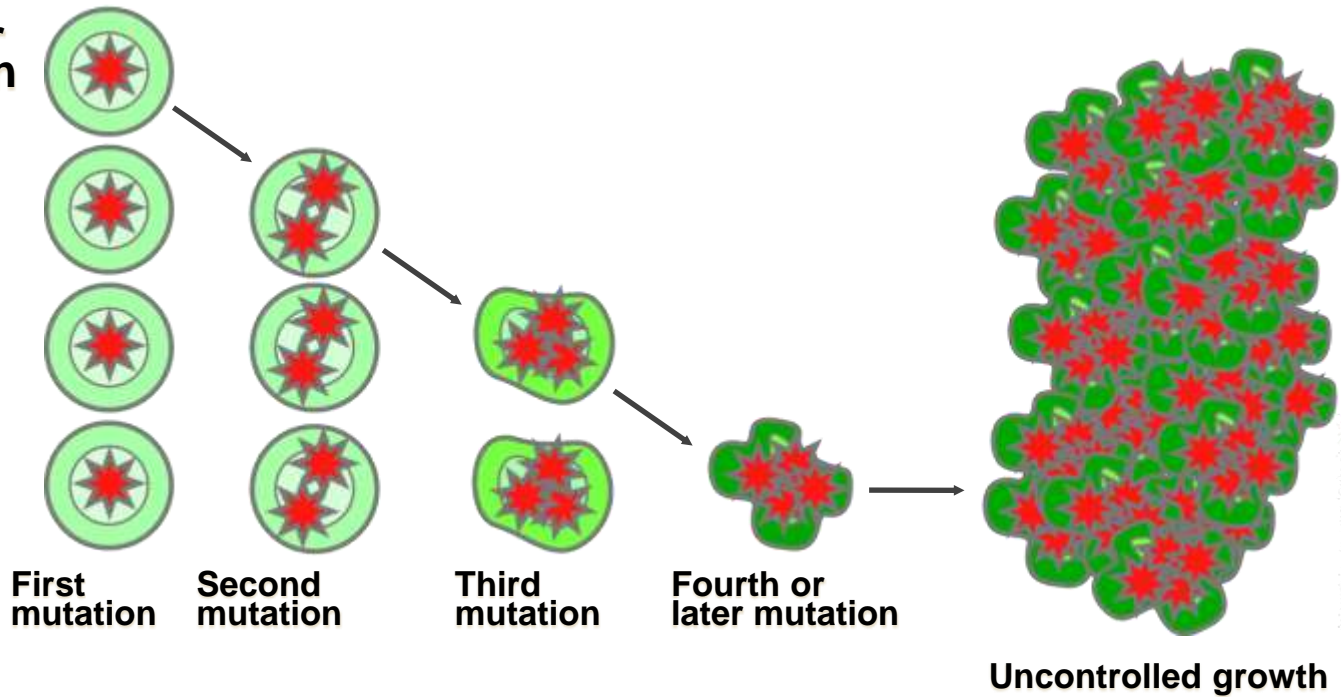
(Animation #5)

# Cell division in Normal Cells and Cancer Cells

**Normal cell division**



**Cancer cell division**

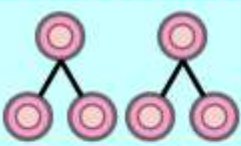















# Comparing Normal Cells with Cancer Cells

Normal Cells	Cancer Cells
Make exact copies of themselves through mitosis	Make exact copies of themselves through mitosis
Reproduce for about 50-60 cell divisions	Do not stop reproducing
Stick together to form masses of cells as appropriate	Do not stick to other cells Behave independently
Self-destruct when too old or too damaged	May move to another location of the body



# Microscopic Appearance of Cancer Cells

Normal	Cancer	
		Large number of irregularly shaped dividing cells
		Large, variably shaped nuclei
		Small cytoplasmic volume relative to nuclei
		Variation in cell size and shape
		Loss of normal specialized cell features
		Disorganized arrangement of cells
		Poorly defined tumor boundary



# Different Kinds of Cancer

## *Some common carcinomas:*

Lung  
Breast (women)

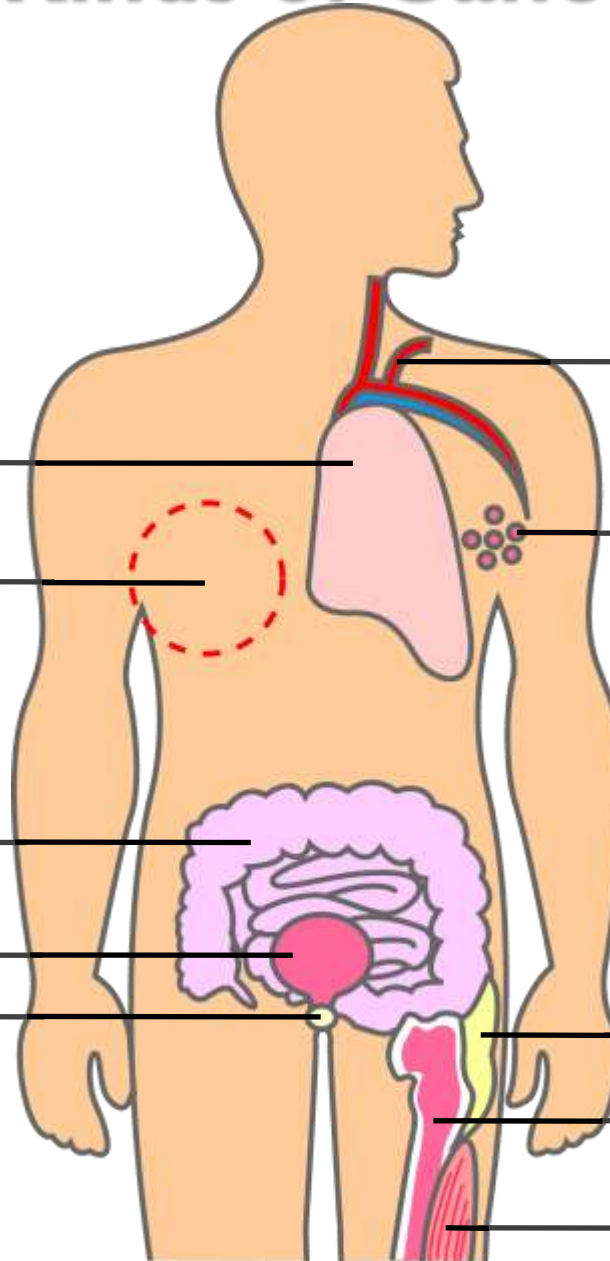
*Leukemias:*  
Bloodstream

*Lymphomas:*  
Lymph nodes

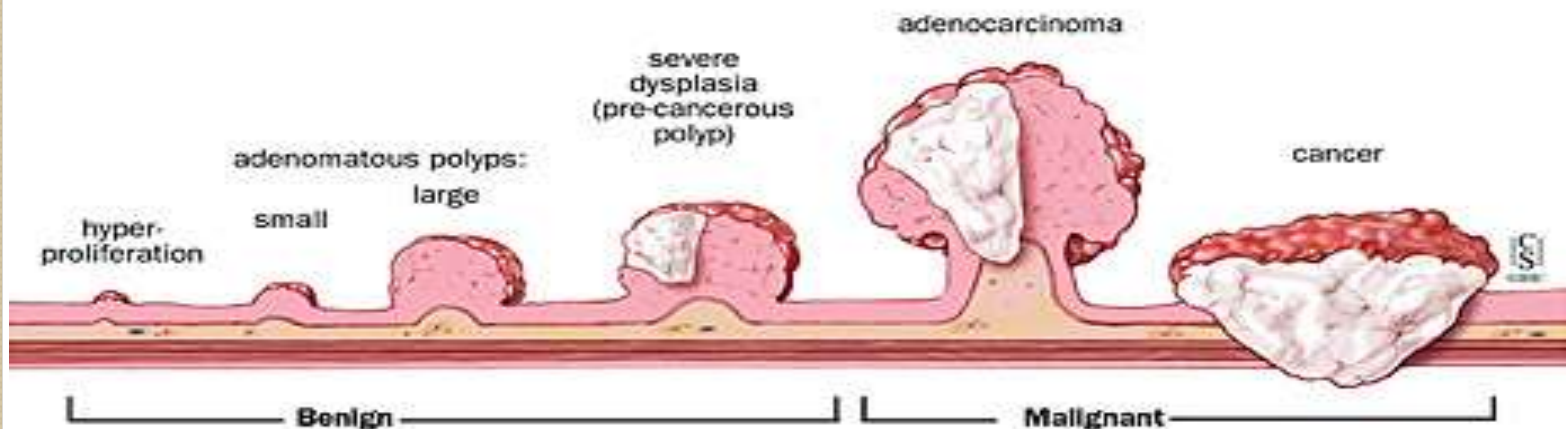
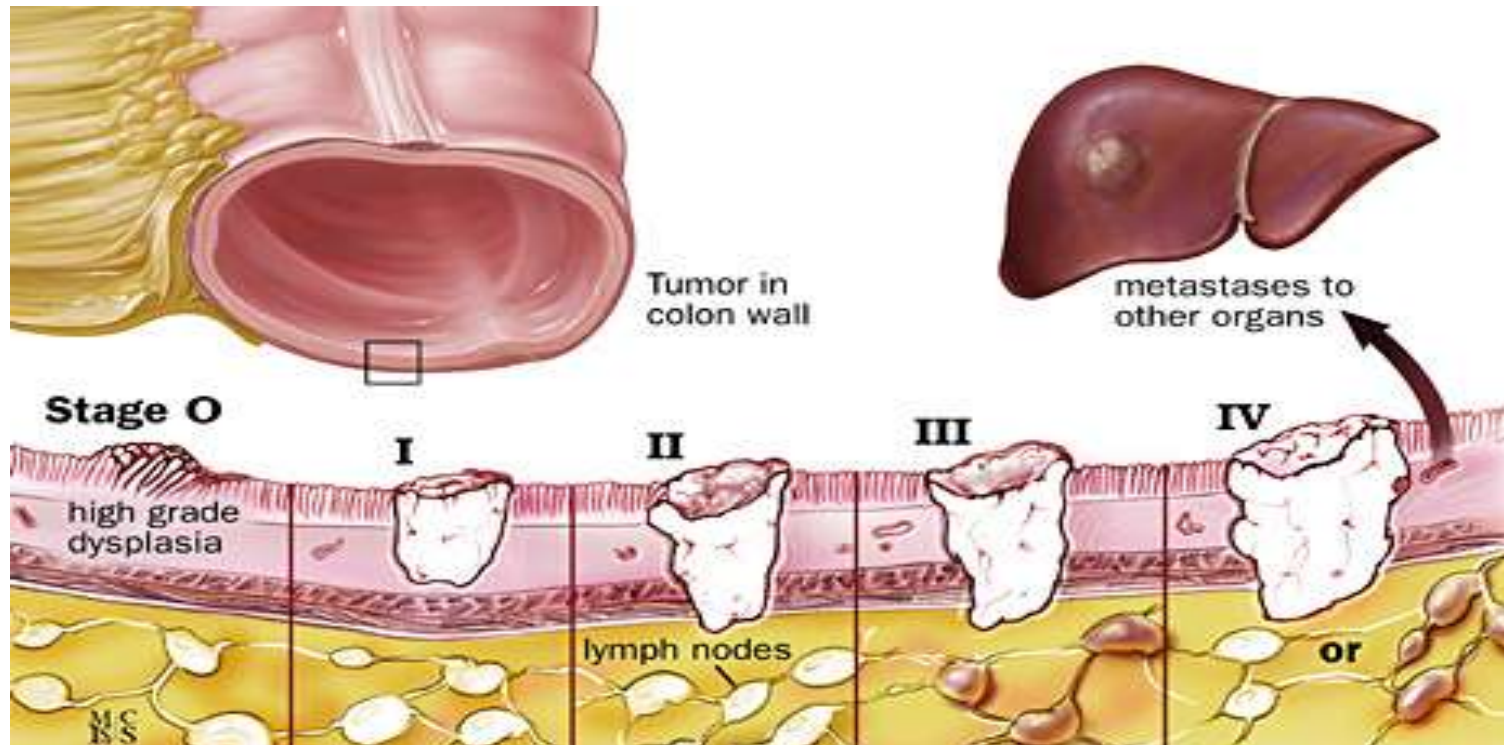
Colon  
Bladder  
Prostate (men)

## *Some common sarcomas:*

Fat  
Bone  
Muscle



# Stages of Colon Cancer



# Definitions

- Tumour: a mass of cells resulting from rapid cell growth



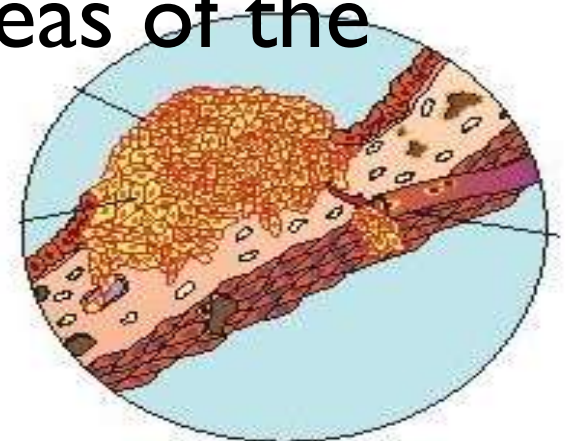
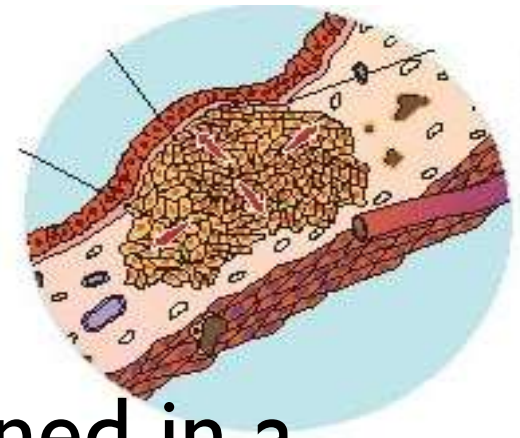


- **Benign:**

- tumours that stay confined in a small area, causing little damage

- **Malignant:**

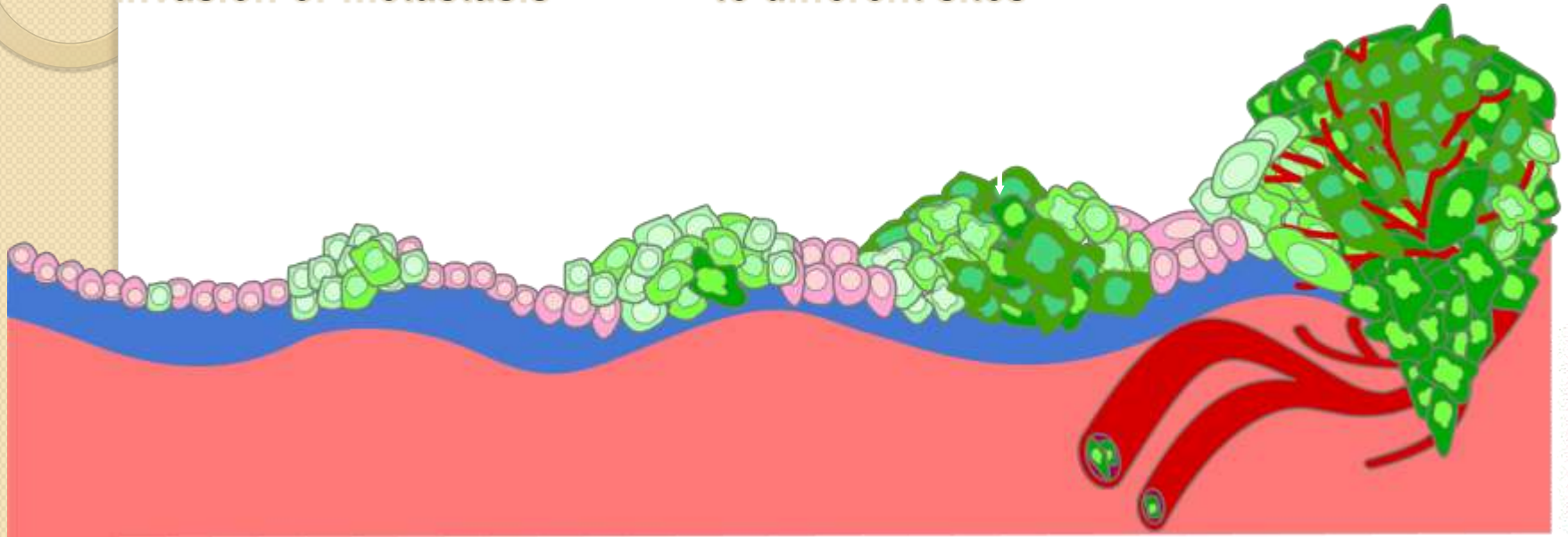
- dangerous tumours that break away and move to other areas of the body



# Cancer Tends to Involve Multiple Mutations

Benign tumor cells grow only locally and cannot spread by invasion or metastasis

Malignant cells invade neighboring tissues, enter blood vessels, and metastasize to different sites



Time



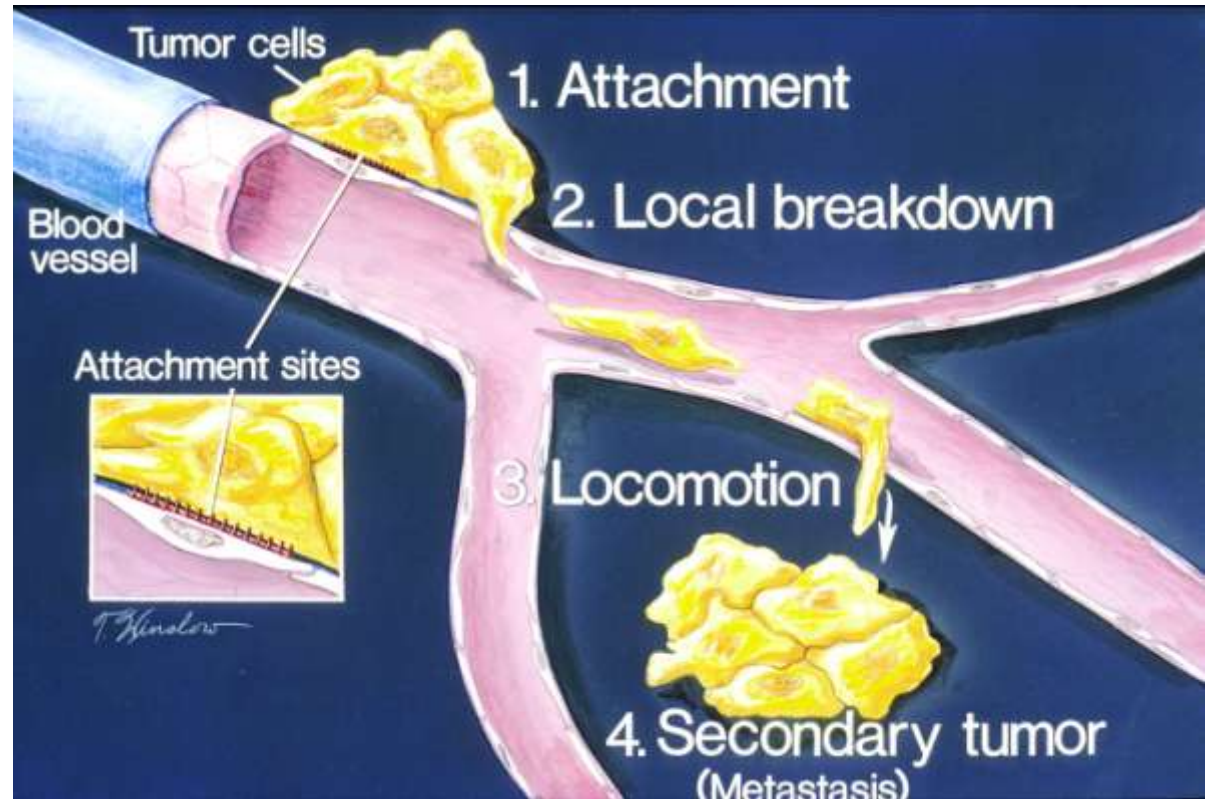
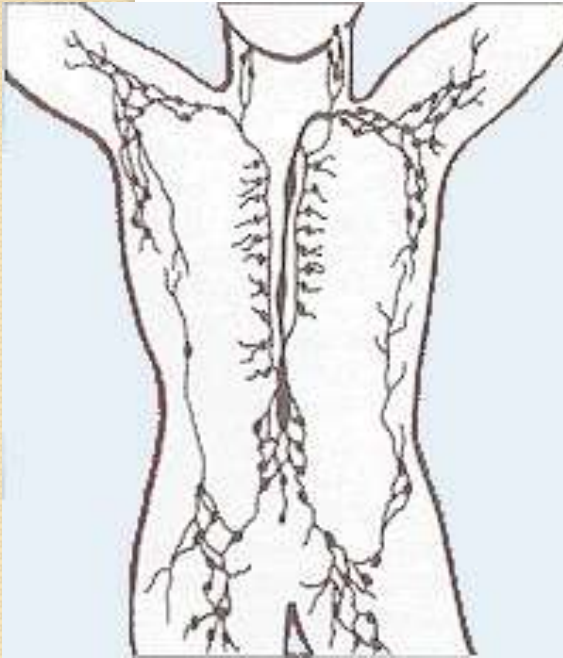
Mutation inactivates suppressor gene

Cells proliferate

Mutations inactivate DNA repair genes

Proto-oncogenes mutate to oncogenes

More mutations, more genetic instability, metastatic disease



The vessels of the circulatory and lymphatic systems provide a pipeline for cancer cells to move to other locations in the body through a process called *metastasis*.

# Conventional Methods of Treating Cancer

- **Surgery**
  - physically removing cancerous tissue
- **Chemotherapy**
  - using drugs to slow or stop cancer cells from dividing
- **Radiation**
  - damaging rapidly dividing cancer cells by ionizing radiation

# If cancer is treated, can it come back?

- There might be a risk of cancer recurring, even when surgery is performed to remove a malignant tumour because
  - if the tumour hasn't been completely removed, it will continue to divide
  - if the tumour has already migrated through the blood vessels, it is free to travel to other areas of the body



# Cancer Detection and Treatment

- Earlier detection and treatment of cancer greatly increase the odds of survival.
- Therefore, knowing the warning signs of cancer is important to health.

**C** Change in bowel or bladder habits

**A** A sore that does not heal

**U** Unusual bleeding or discharge

**T** Thickening or lump

**I** Indigestion or difficulty swallowing

**O** Obvious change in wart or mole

**N** Nagging cough or hoarseness

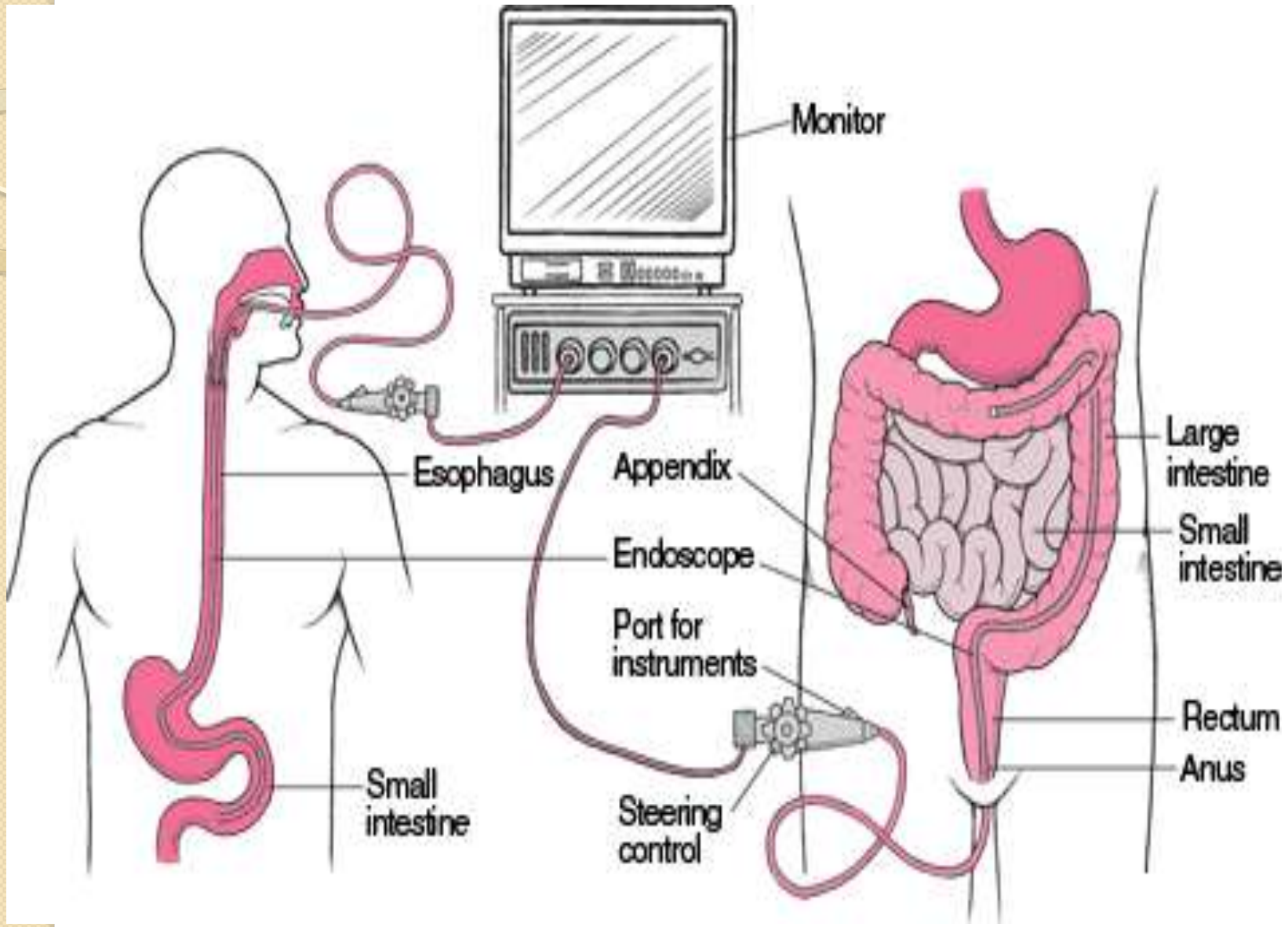
# Cancer Screening Tests

- breast self-examination
- Pap test
- PSA test
- colonoscopy
- regular skin checks (ABCDE of moles)
  - Assymetry
  - Border
  - Color
  - Diameter
  - Elevation

# Diagnosing Cancer

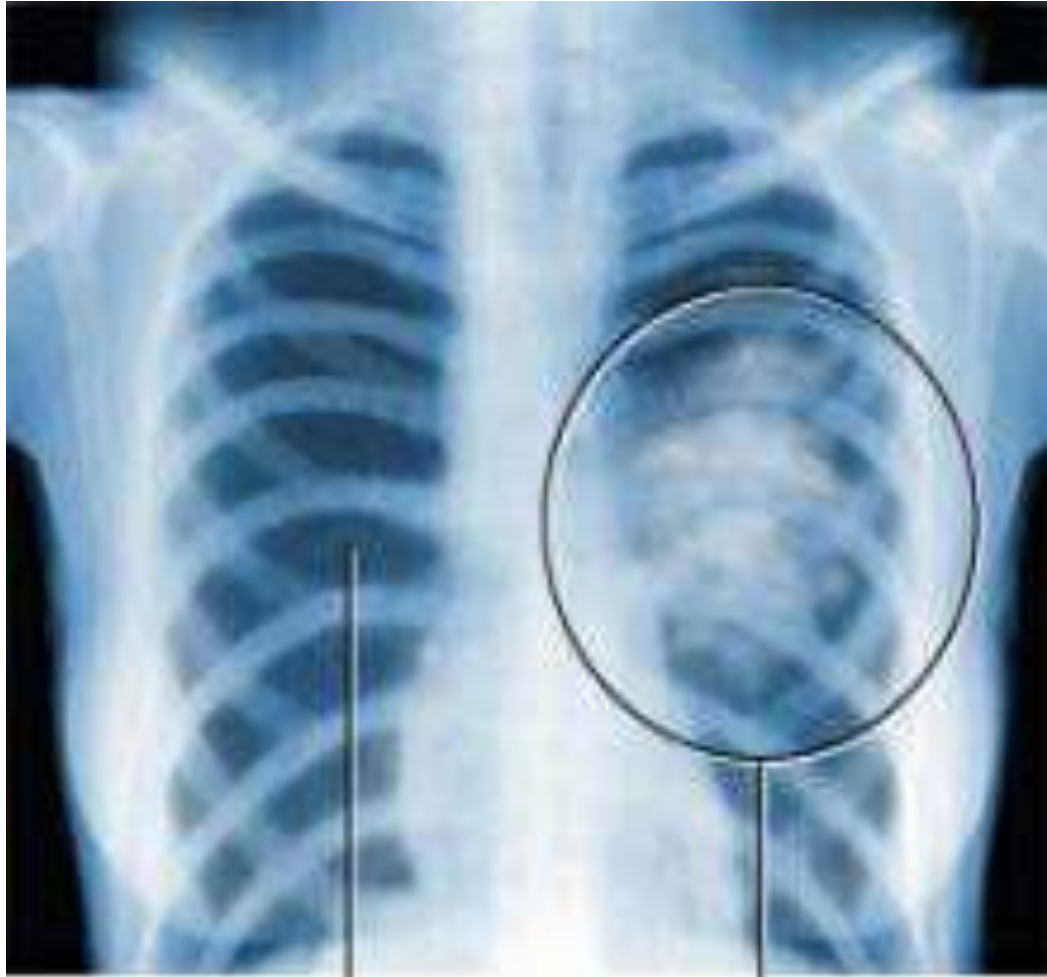
## Endoscope;

- is used to screen cancers such as colon cancer
- is made up of a fiber optic cable to give light and a tiny camera that can send images to a screen.



## **X-rays:**

- are used to view parts of the body such as bones and lungs
- a mammogram is a specialized X-ray technique for imaging breast tissue



Normal  
lung

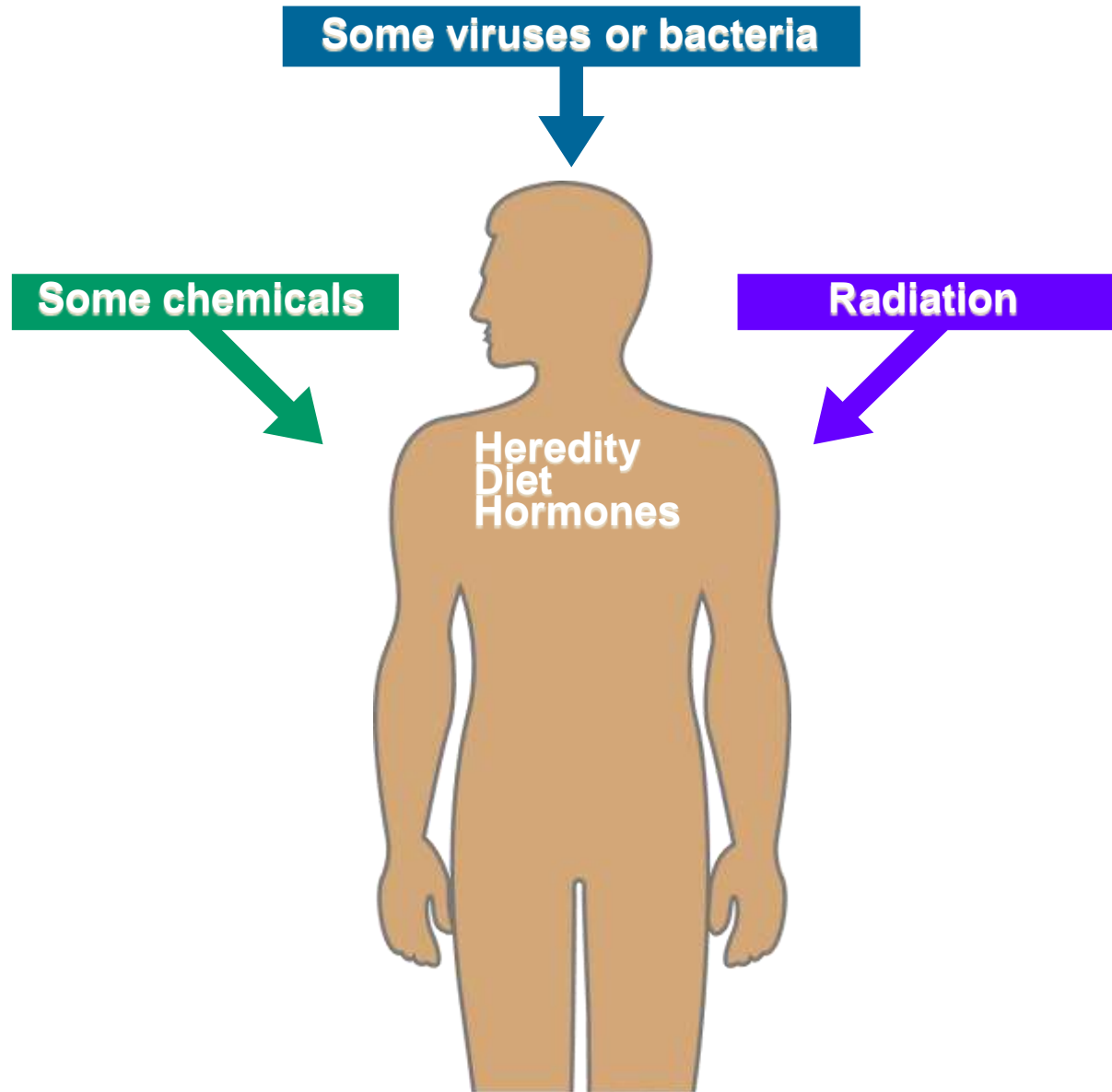
Cancerous  
tumour

## MRI (Magnetic Resonance Imaging):

- radio waves and a strong magnetic field create detailed 3D images.



# What Causes Cancer?

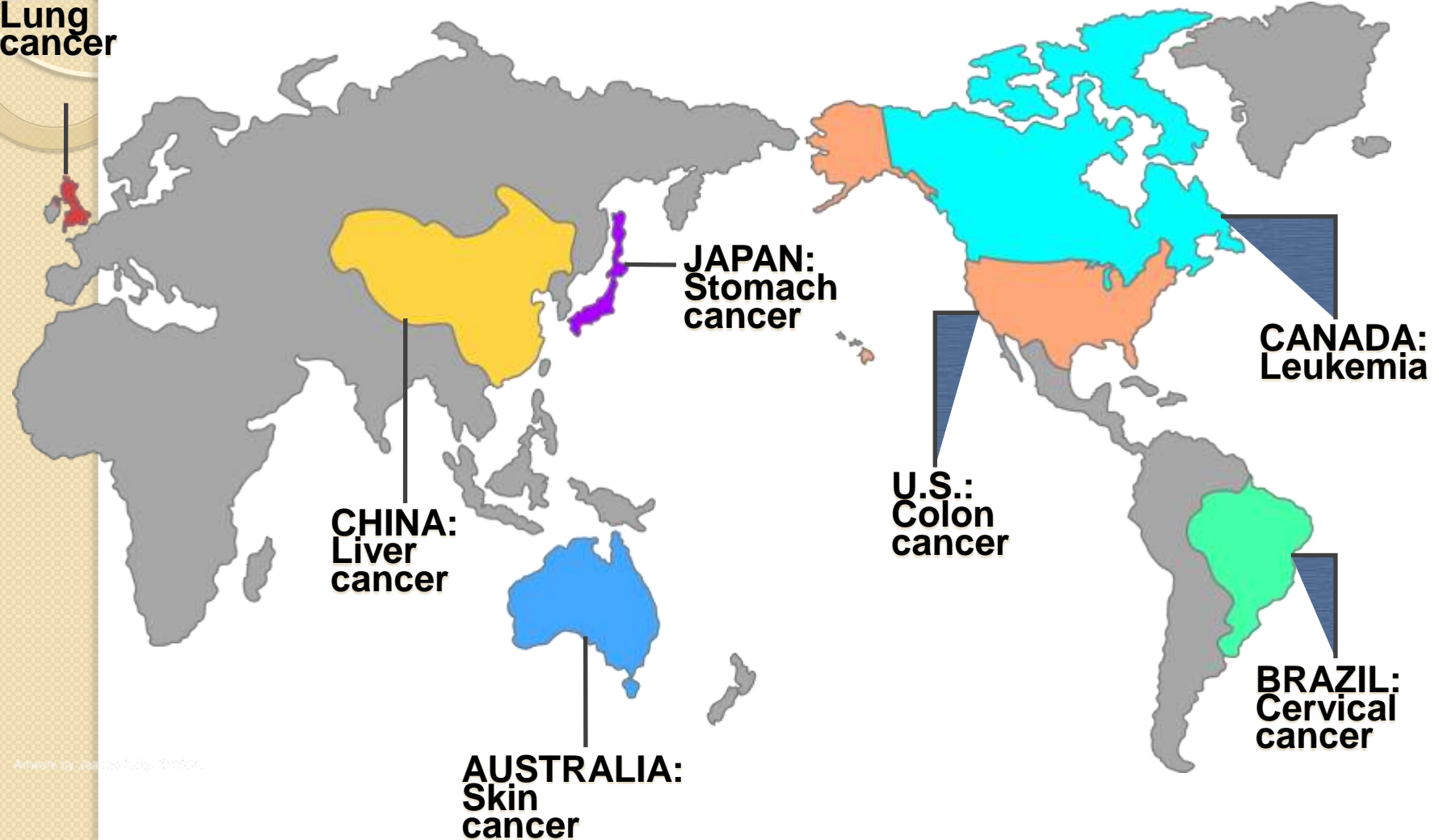




# Population-Based Studies

## Regions of Highest Incidence

**U.K.:**  
Lung  
cancer



**JAPAN:**  
Stomach  
cancer

**CHINA:**  
Liver  
cancer

**U.S.:**  
Colon  
cancer

**CANADA:**  
Leukemia

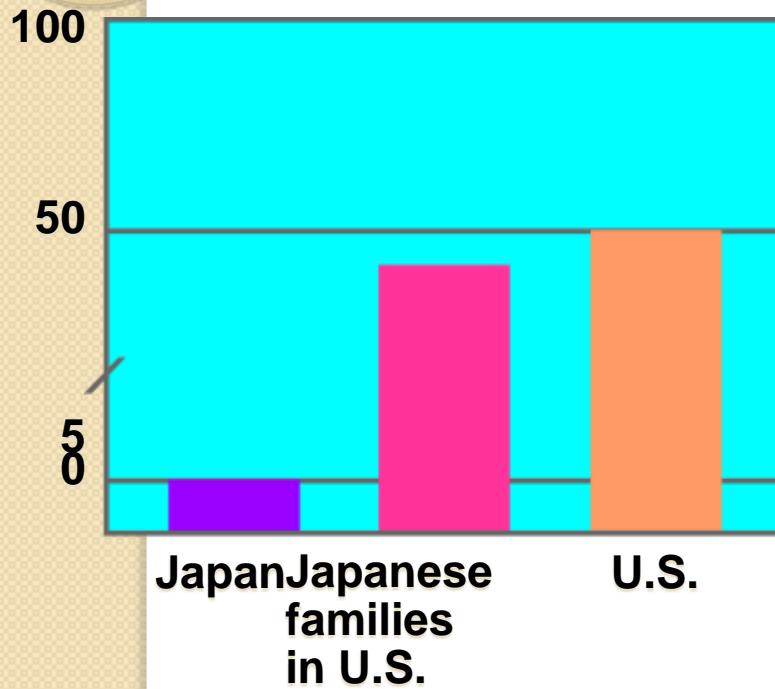
**BRAZIL:**  
Cervical  
cancer

**AUSTRALIA:**  
Skin  
cancer

# Heredity? Behaviors? Other Factors?

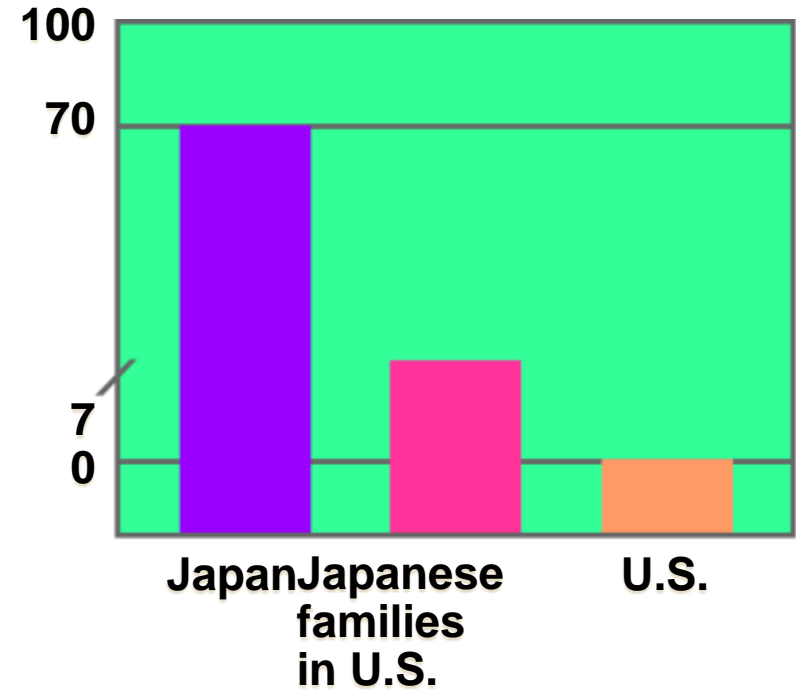
## Colon Cancer

(Number of new cases per 100,000 people)



## Stomach Cancer

(Number of new cases per 100,000 people)



# Tobacco Use and Cancer

## Some Cancer-Causing Chemicals in Tobacco Smoke

aminostilbene  
arsenic  
benz[a]anthracene  
benz[a]pyrene  
benzene

benzo[b]fluoranthene  
benzo[c]phenanthrene  
benzo[f]fluoranthene  
cadmium

chrysene  
dibenz[a c]anthracene  
dibenzo[a e]fluoranthene  
dibenz[a h]acridine  
dibenz[a j]acridine  
dibenzo[c g]carbazone  
N-dibutyl nitrosamine  
2,3-dimethylchrysene

indeno[1,2,3-c d]pyrene  
S-methylchrysene  
S-methylfluoranthene  
*alpha*-naphthylamine  
nickel compounds  
N-nitrosodimethylamine

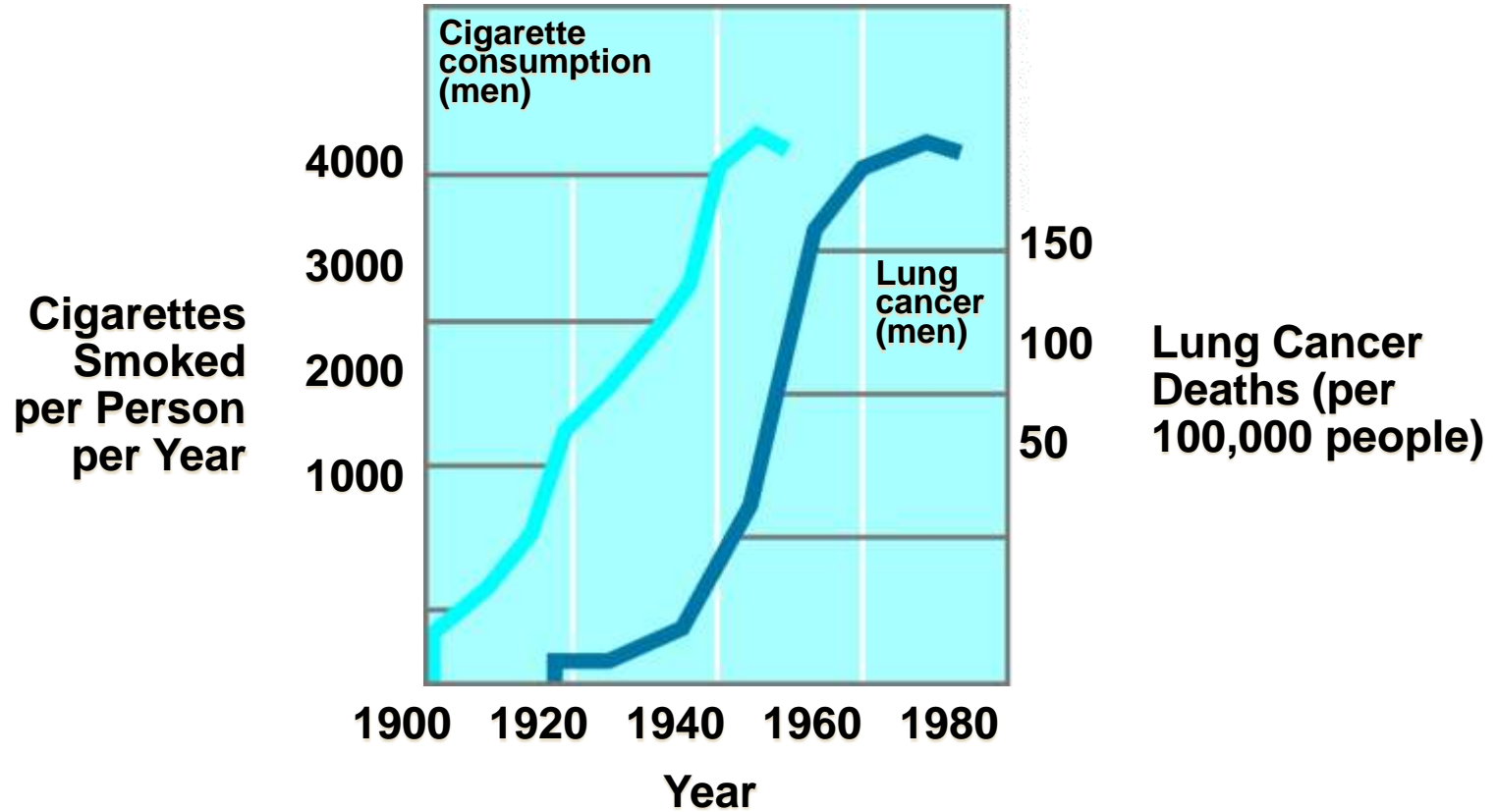
N-nitrosomethylethylamine  
N-nitrosodiethylamine  
N-nitrosornicotine  
N-nitrosoanabasine  
N-nitrosopiperidine  
polonium-210





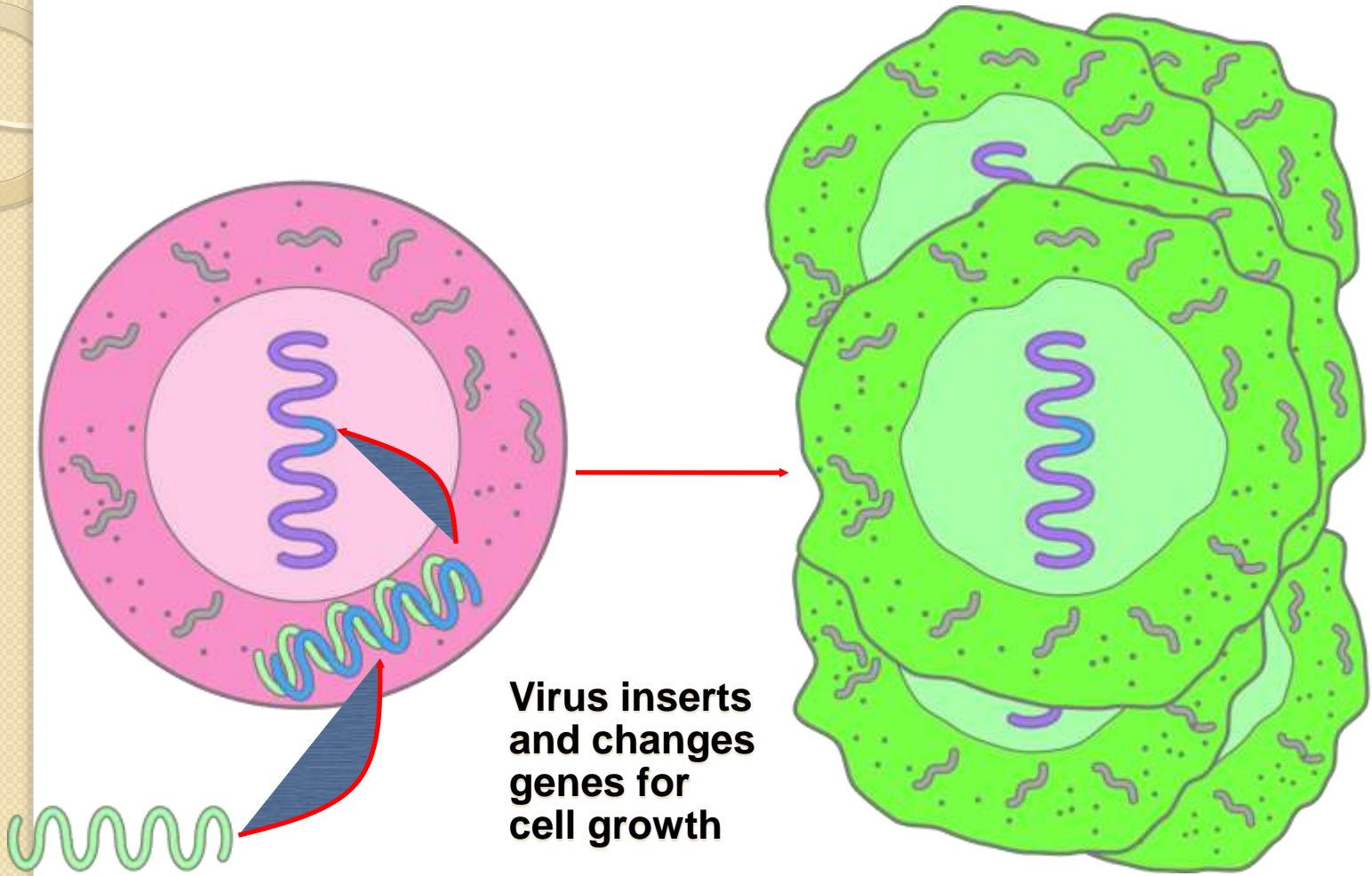
# Lag Time

## 20-Year Lag Time Between Smoking and Lung Cancer





# Viruses



Cancer-linked virus

Virus inserts and changes genes for cell growth

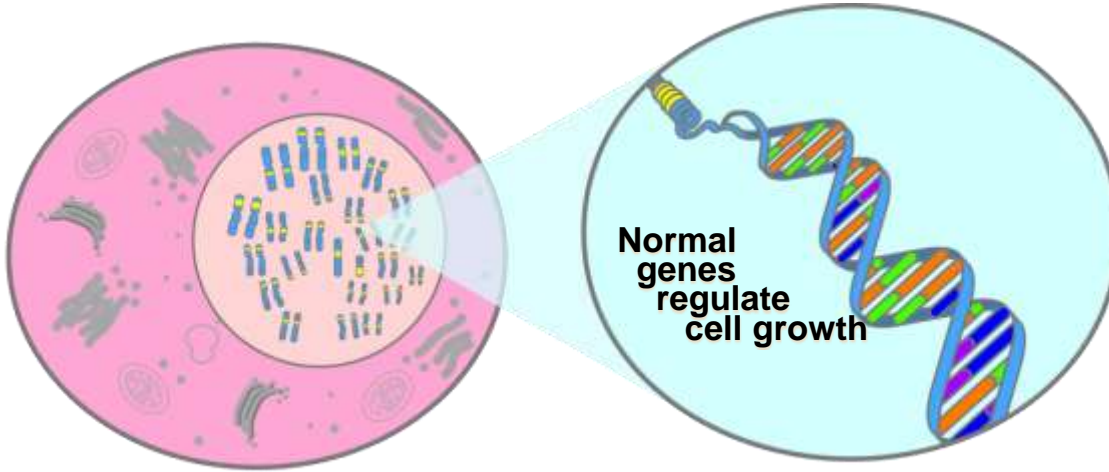
# Examples of Human Cancer Viruses

## Some Viruses Associated with Human Cancers

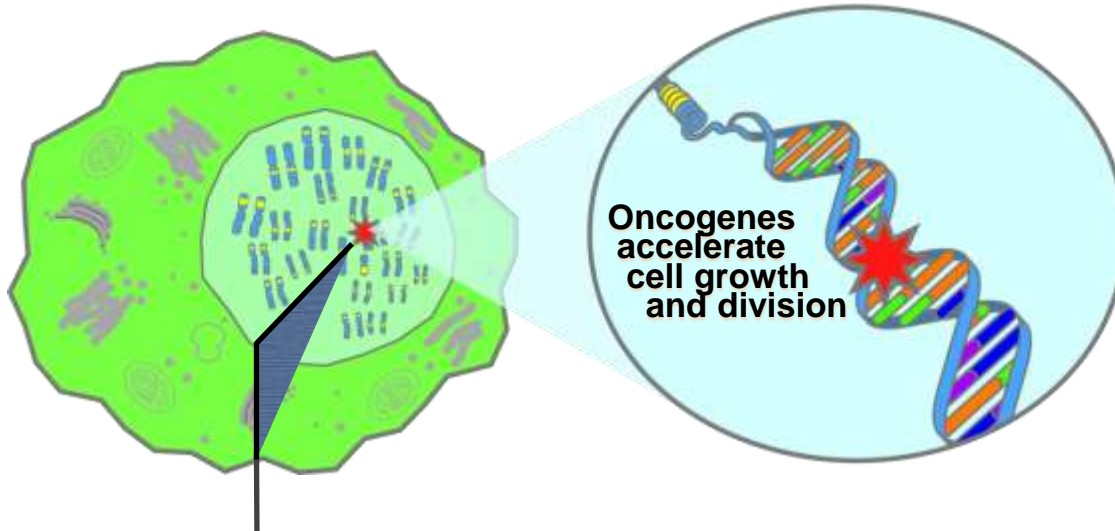
<i>Virus</i>	<i>Type of Cancer</i>
Epstein-Barr virus	Burkitt's lymphoma
Human papillomavirus	Cervical cancer
Hepatitis B virus	Liver cancer
Human T-cell lymphotropic virus	Adult T-cell leukemia
Kaposi's sarcoma-associated herpesvirus	Kaposi's sarcoma

# Oncogenes

Normal cell




Cancer cell



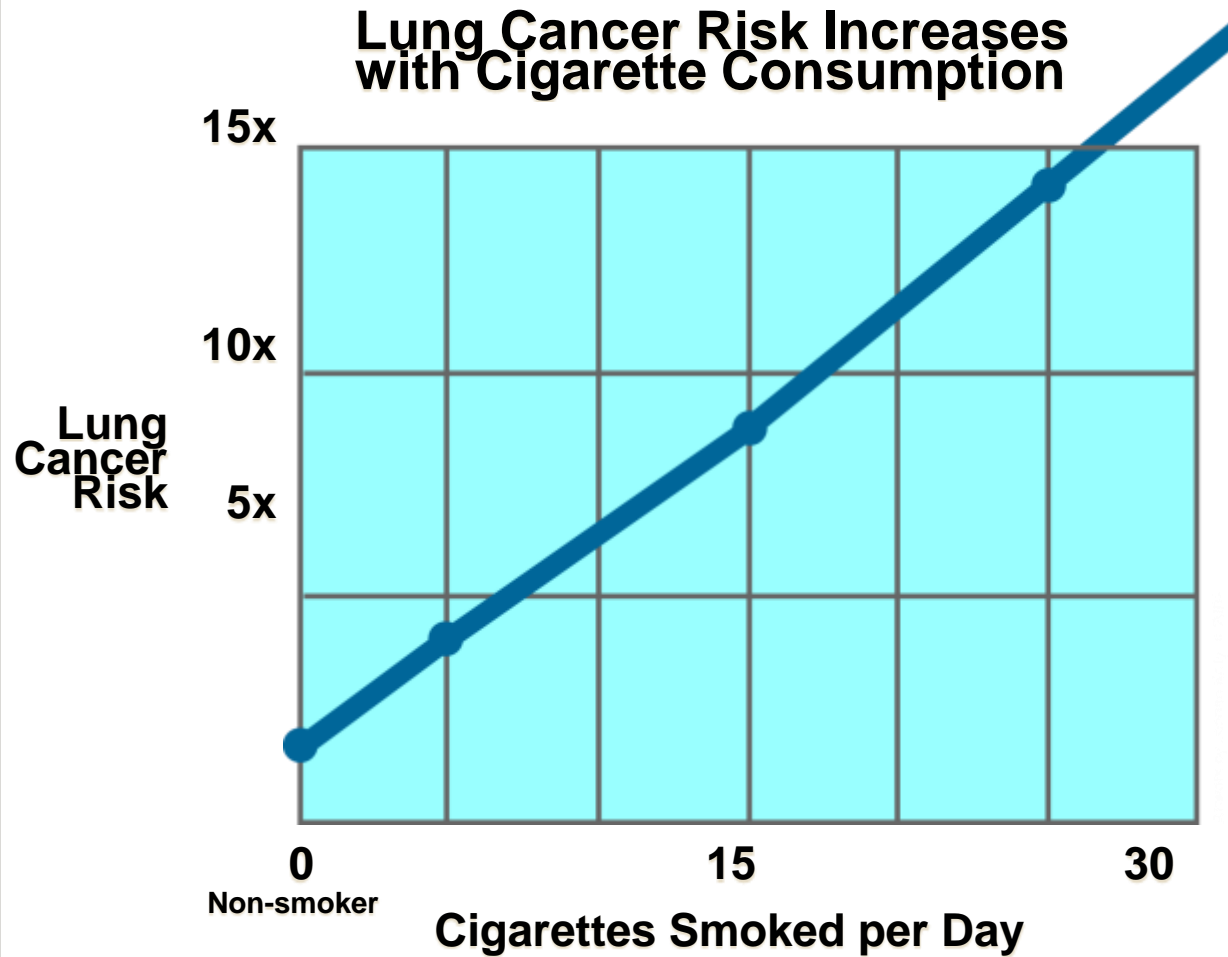
Mutated/damaged oncogene





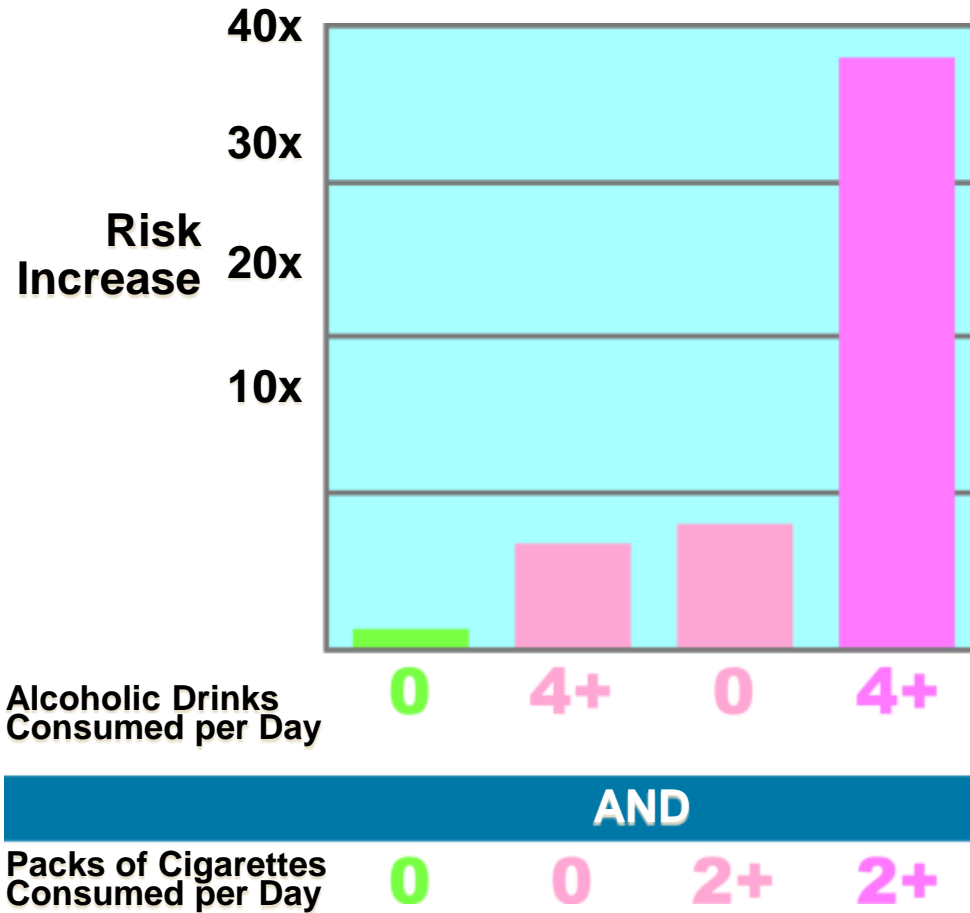
**How to decrease your risk of  
developing cancer?**

# Avoid Tobacco



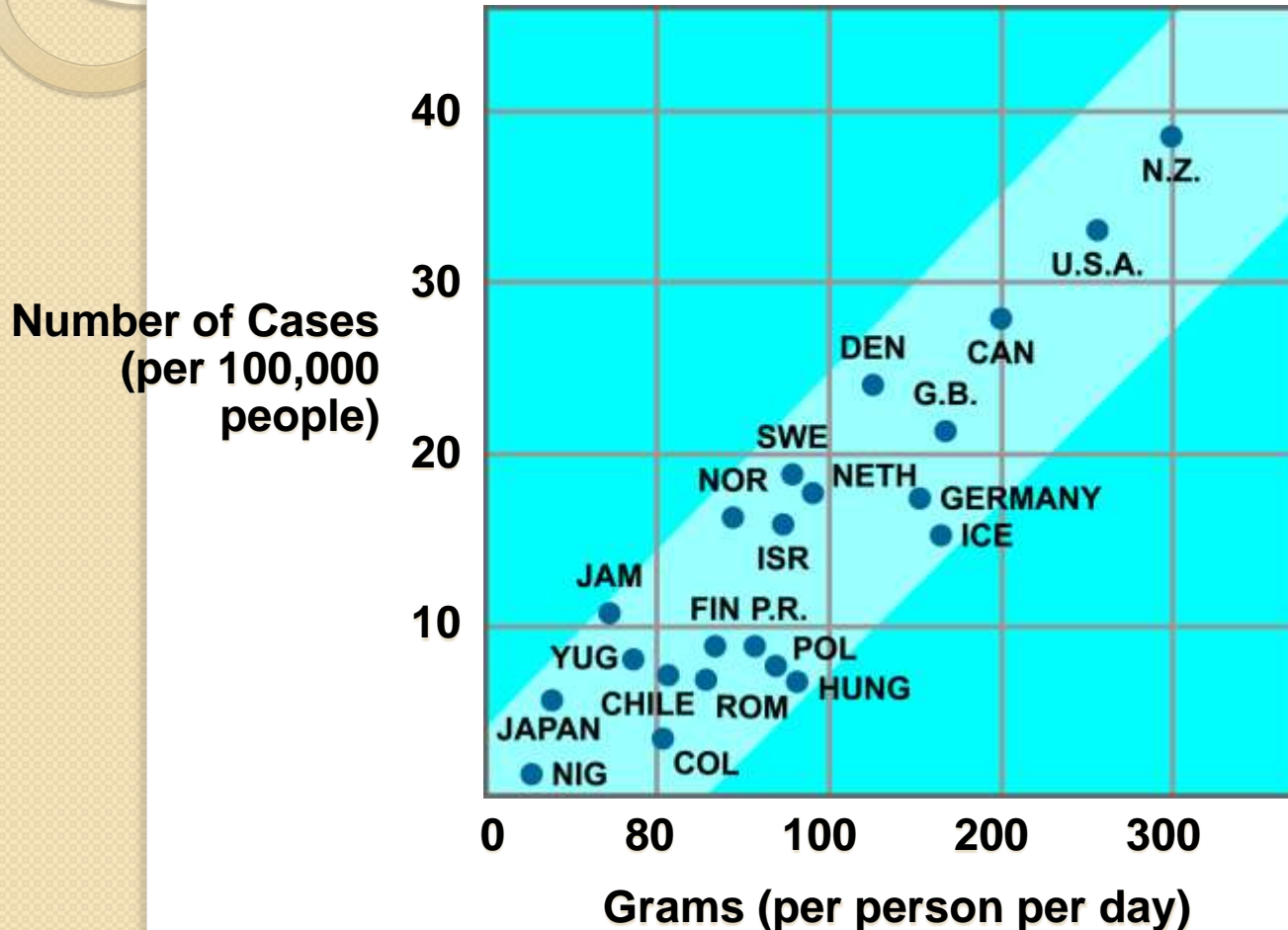
# Limit Alcohol and Tobacco

## Combination of Alcohol and Cigarettes Increases Risk for Cancer of the Esophagus

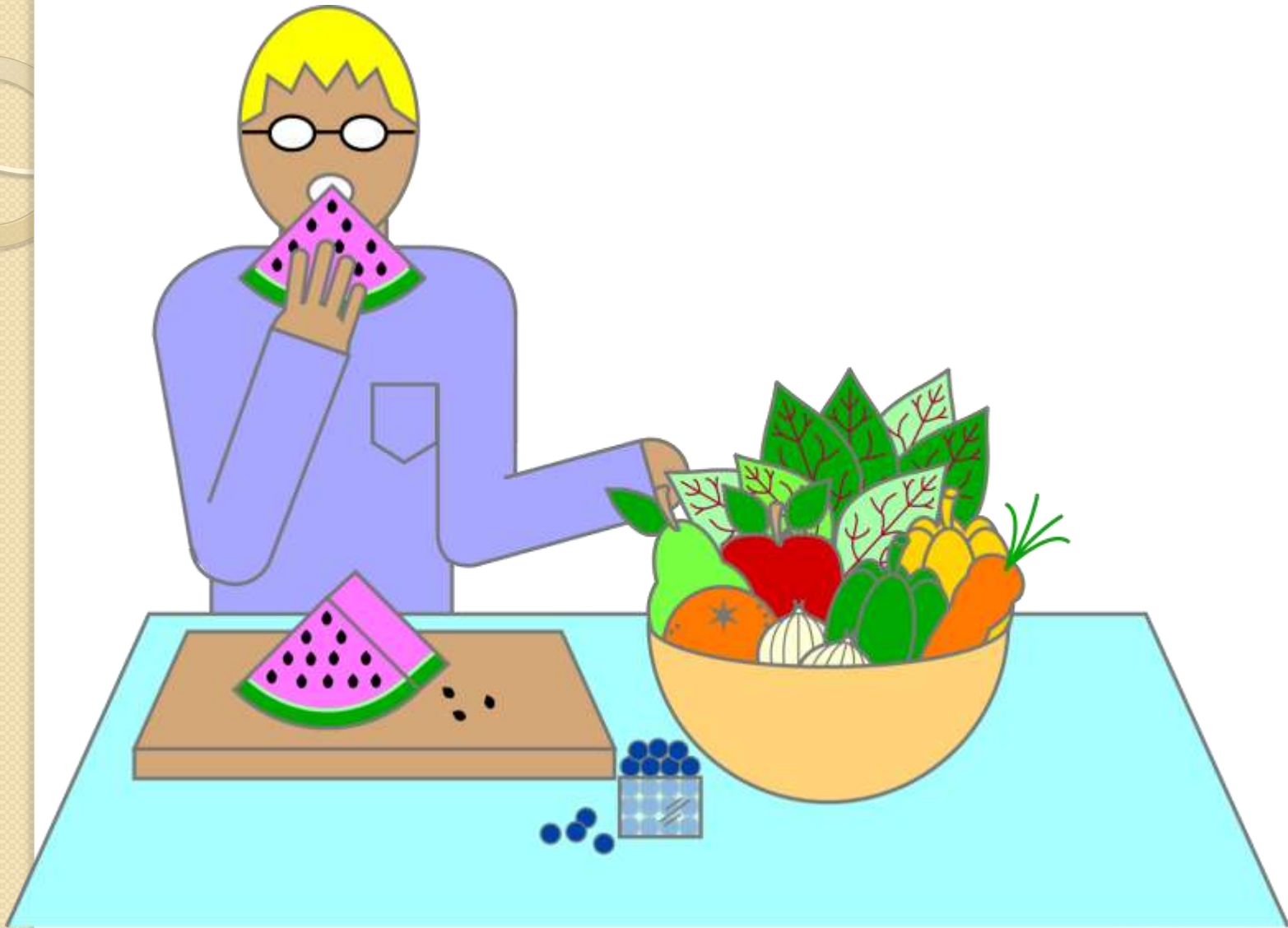


# Diet: Limit Fats and Calories

## Correlation Between Meat Consumption and Colon Cancer Rates in Different Countries



# Diet: Consume Fruits and Vegetables



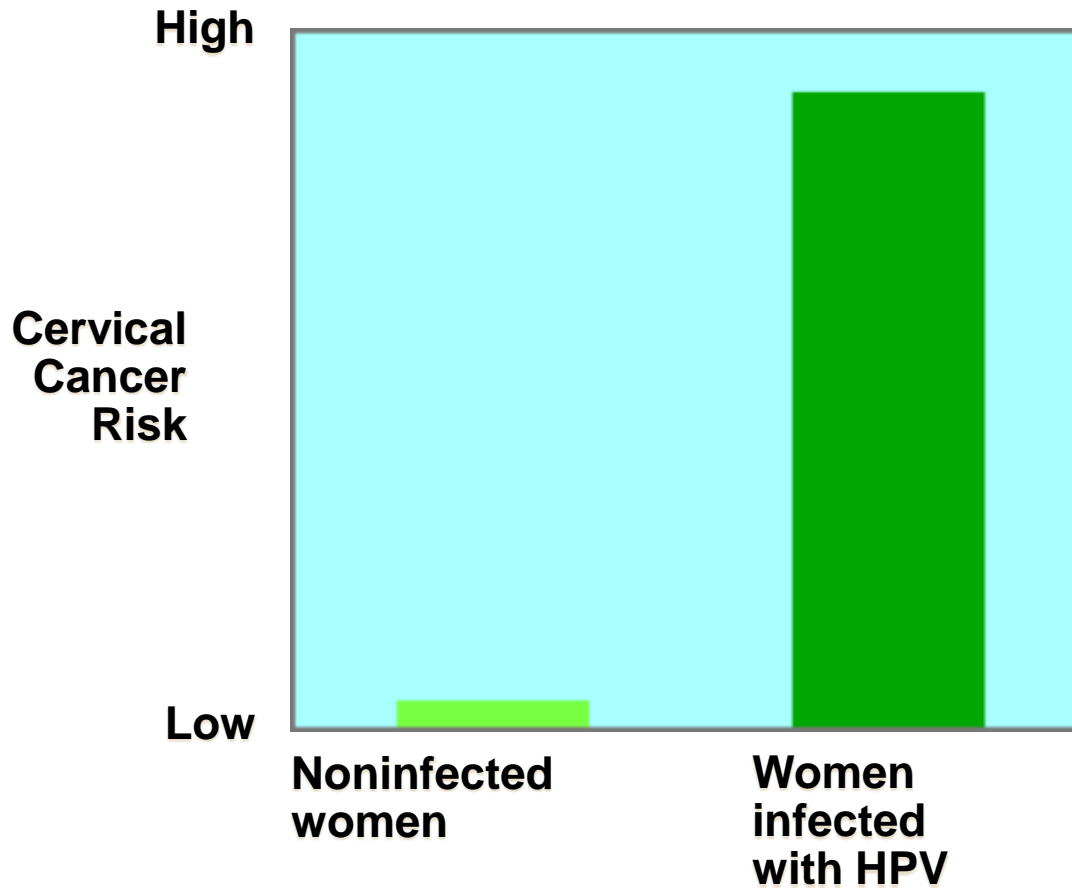
# Protect Yourself From Excessive Sunlight





# Avoid Cancer Viruses

## HPV Infection Increases Risk for Cervical Cancer



# Avoid Carcinogens

## Some Carcinogens in the Workplace

Carcinogen	Occupation	Type of Cancer
Arsenic	Mining, pesticide workers	Lung, skin, liver
Asbestos	Construction workers	Lung, mesothelioma
Benzene	Petroleum, rubber, chemical workers	Leukemia
Chromium	Metal workers, electroplaters	Lung
Leather dust	Shoe manufacturing	Nasal, bladder
Naphthylamine	Chemical, dye, rubber workers	Bladder
Radon	Underground mining	Lung
Soots, tars, oils	Coal, gas, petroleum workers	Lung, skin, liver
Vinyl chloride	Rubber workers, polyvinyl chloride manufacturing	Liver
Wood dust	Furniture manufacturing	Nasal

# Videos on Cancer

- <http://www.youtube.com/watch?v=LEpTTolebqo>
- [http://www.youtube.com/watch?v=j\\_wRp\\_a2b5XI](http://www.youtube.com/watch?v=j_wRp_a2b5XI)
- <http://www.youtube.com/watch?v=8n0ijZpYXwo>
- <http://www.pbs.org/wgbh/nova/body/how-cancer-grows.html>