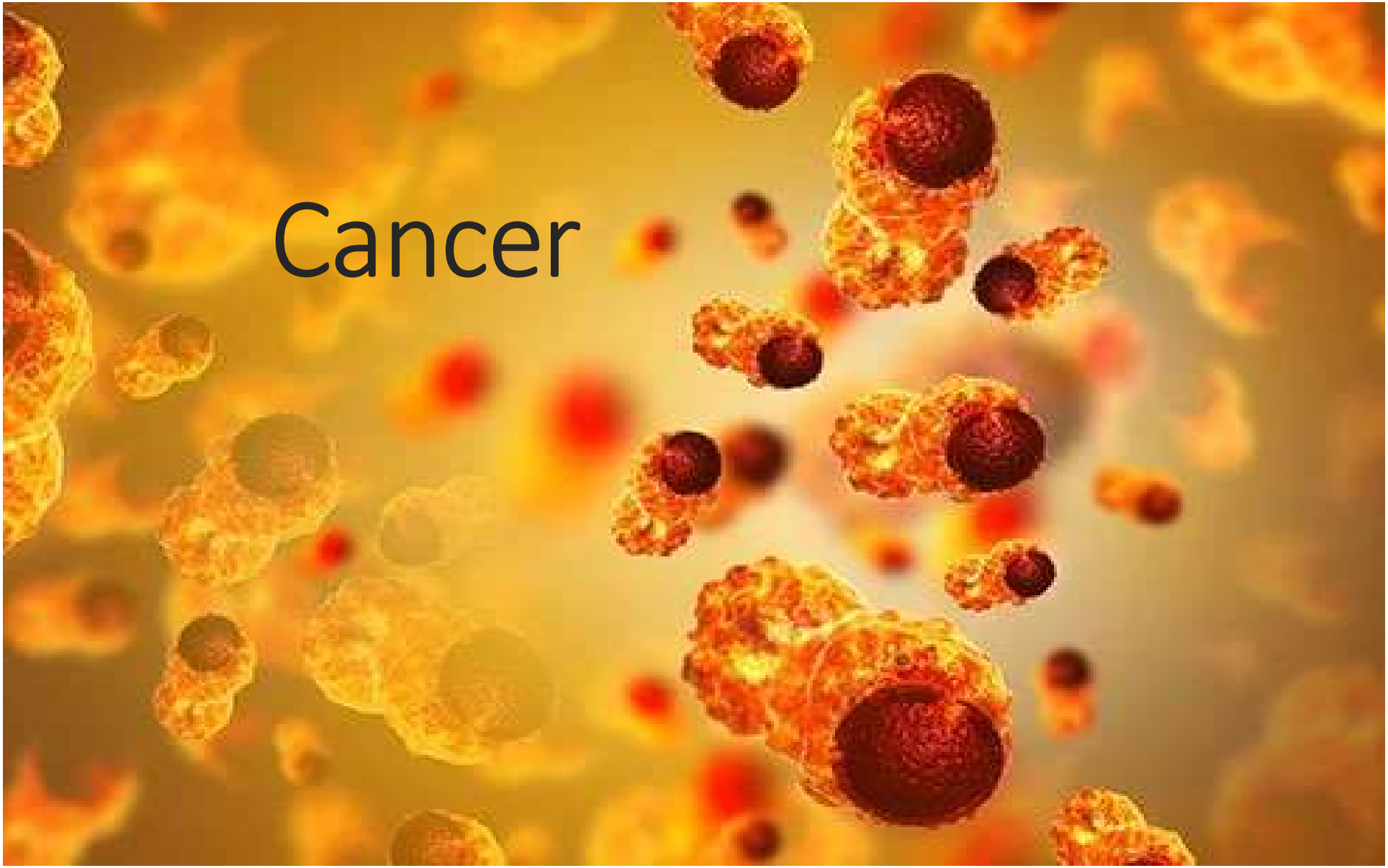


DR. SOBIA NOREEN

Assignment Titles

1. COVID-19 and Pakistan: what next? Naila

2. Outbreak of a novel coronavirus in Pakistan: momentous decisions along with many uncertainties Sumbal

3. COVID-19 Vaccine on way of development Anum

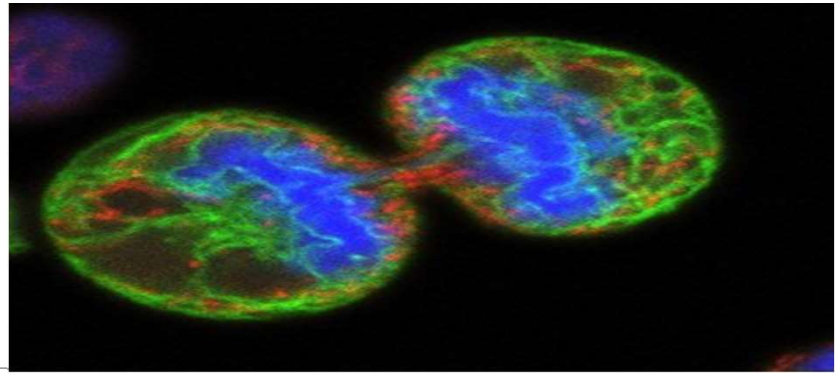
4. Environment before after COVID-19 Saman

5. Coronavirus and CRISPR-Cas Asma

6. Recent update Clinical applications of circulating tumour cells Sehrish

7. COVID-19 therapeutics on way of development Fakhar

What is cancer?



- Cancer is the uncontrolled growth of abnormal cells anywhere in a body.
- There are over 200 types of cancer
- All cancers derive from single cells that have acquired the characteristics of continually dividing in an unrestrained manner and invading surrounding tissues.
- Terrifying illness
- Heterogenous group of diseases
- A complex problem in health care delivery and public problems.

Cancer symptoms

Unable to **wee**, or has blood in their wee

An **unexplained lump**, firmness or swelling anywhere in their body

Persistent **abdominal** pain or swelling

Back pain or **bony pain** that doesn't go away

Unexplained **seizures** or changes in behaviour

Headaches that don't go away

Frequent or unexplained **bruising,** unusual paleness or a rash of small red or purple spots that can't be explained

Unexplained **bleeding**

Feeling **tired** all the time

Frequent **infections** or **flu-like** symptoms

Unexplained **vomiting** (being sick)

Unexplained **fever** (high temperatures) or sweating

Unexplained **weight loss**

Feeling **short of breath**

Changes in **appearance of the eye** or unusual eye reflections in photos

Cancer Research UK

Known Causes of Human Cancer

Chemical Exposure
- Tobacco smoke
- Environmental (PCBs)
- Occupational (coal tar, asbestos, aniline dye)
- Diet (aflatoxin)

Radiation (UV, ionizing)

Infection
- Viruses (EBV, hepatitis B, papilloma)
- Bacteria (Helicobacter)

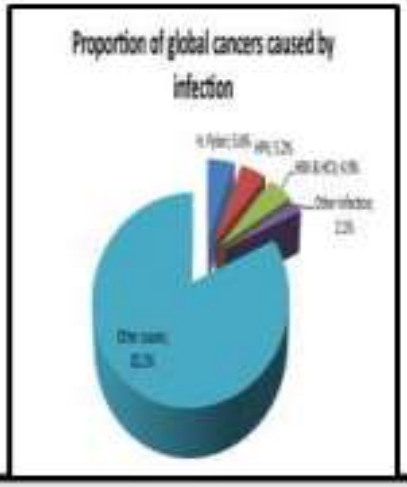
Inherited familial cancer syndromes

COMMON ENVIRONMENTAL FACTORS LEADING TO CANCER DEATH INCLUDE:

tobacco (25-30%)

diet and obesity (30-35%)

infections (15-20%)



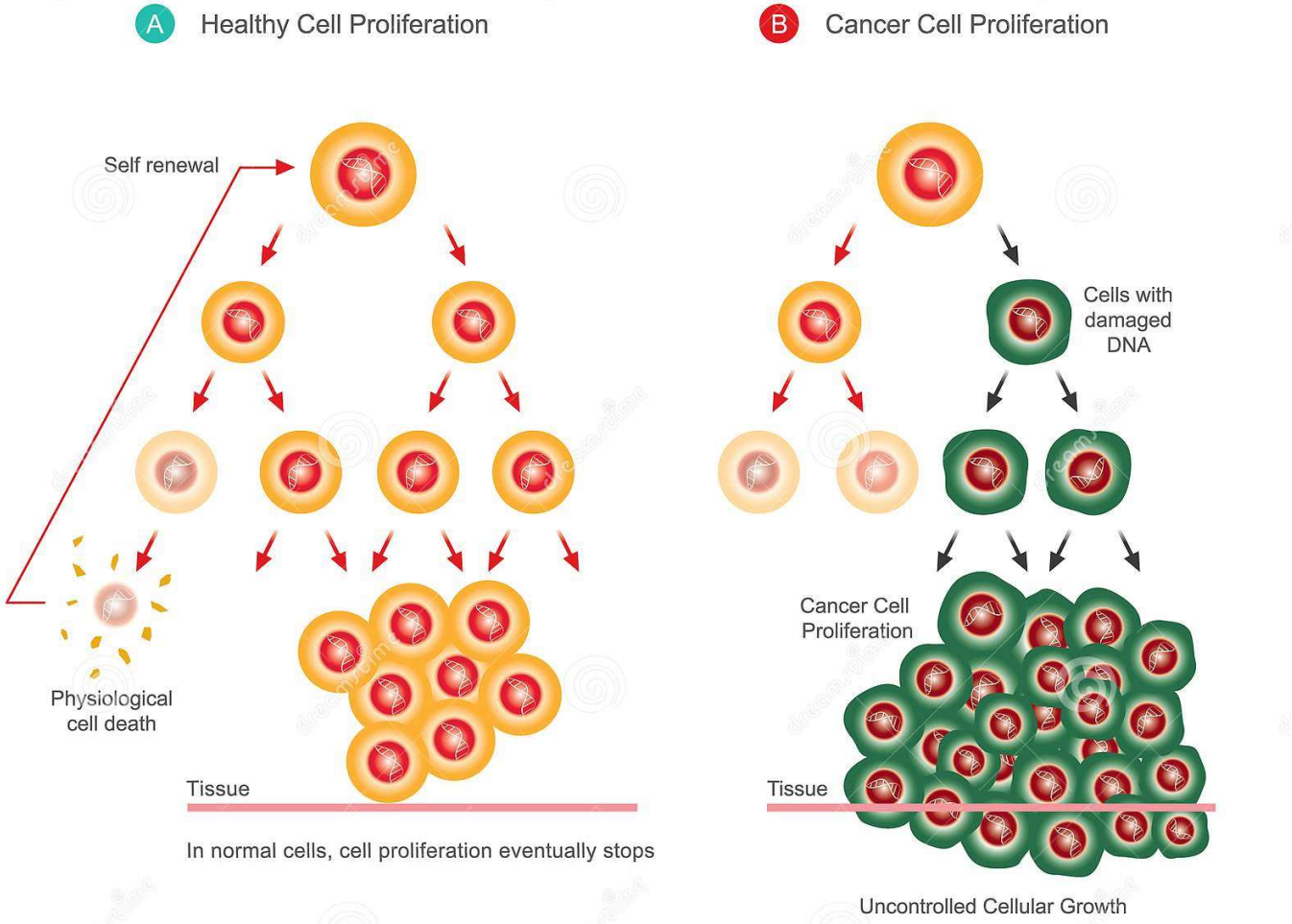
Radiation
Stress
lack of physical activity
environmental pollutants

Cell proliferation

Cell proliferation produces two cells from one, and it requires cell growth followed by cell division.

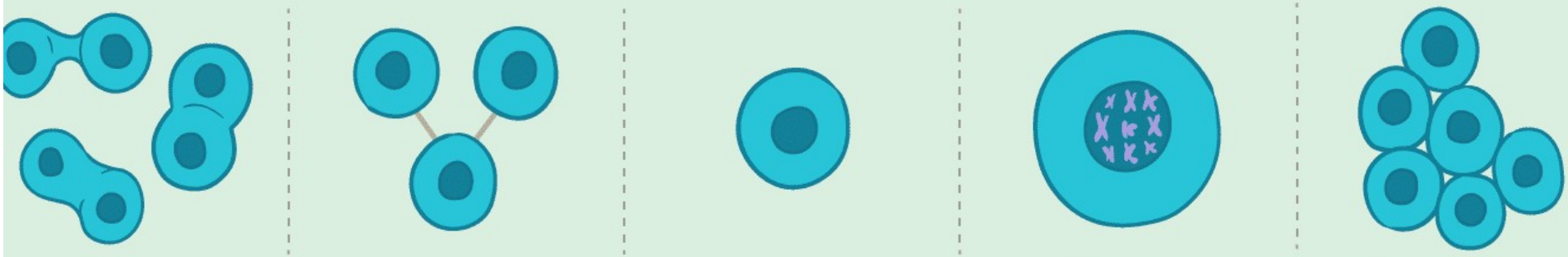
Uncontrolled cell proliferation is a hallmark of cancer.

Proliferation of Healthy Cells and Cancer Cells

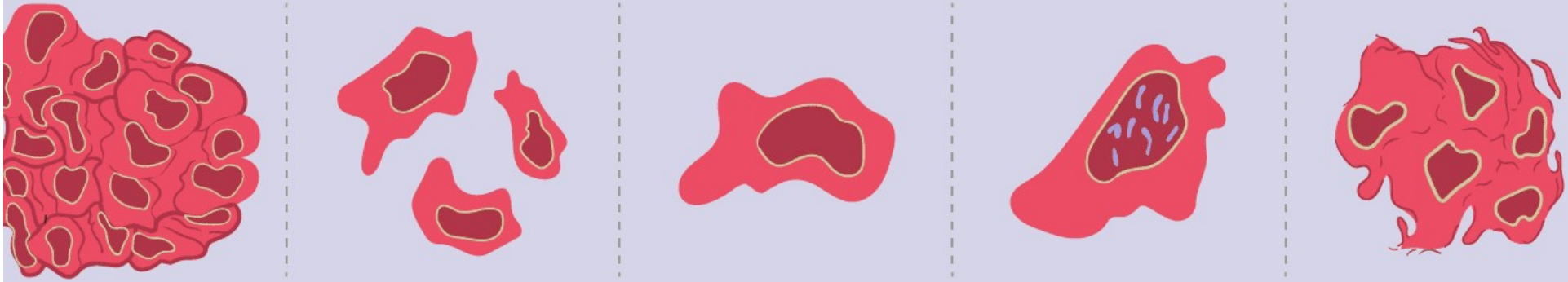


- In normal tissues, cell proliferation is generally restricted to cells that replenish the tissue.
- Most tissues are thought to contain stem cells that have this replenishment function
- Progenitor cells divide to produce cells that undergo terminal differentiation to produce the mature cells that make up a tissue or organ.

NORMAL CELLS



CANCEROUS CELLS



Many cells that ontinue to grow and divide

Variations in size and shapes of cells

Nucleus that is larger and darker than normal

Abnormal number of chromosomes arranged in a disorganized fashion

Cluster of cells without a boundry

What is a mutation?

- **Germline mutation**
  - A change in the DNA sequence that can be inherited from either parent
- **Somatic mutation**
  - A change in the DNA sequence in cells other than sperm or egg
  - The mutation is present in the cancer cell and its offspring, but not in the patient's healthy cells

Types of mutations

- Substitution
- Deletion
- Insertion
- Inversion
- Duplication

Mutations & cancer genes

Cancer genes are causally implicated in *oncogenesis*

Mutations in cancer genes can occur somatically or can be inherited.

Mutations in some cancer genes can be inherited from parents, in which case they are present in every cell of the body. Such people are at a higher risk of developing cancer.

Somatic mutations can occur in any of the cells of the body except the germ cells (sperm and egg) and therefore are not passed on to children.

Cancer genes

There are two types of cancer genes:

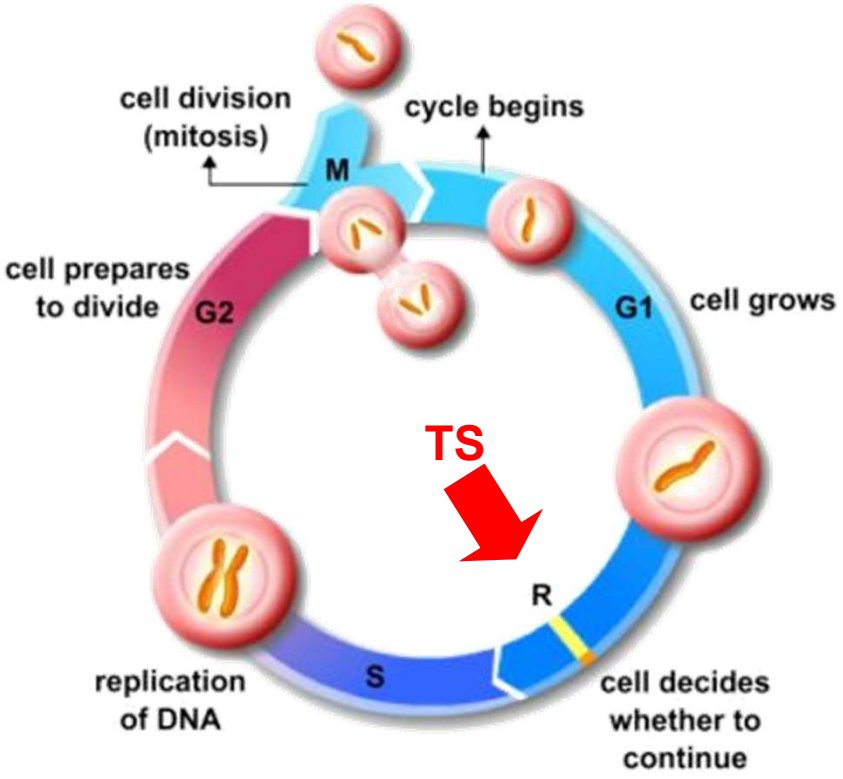
- **Tumour suppressor genes** (Gene encode RB associated and P53 proteins.
- **Oncogenes (ras, myc)**

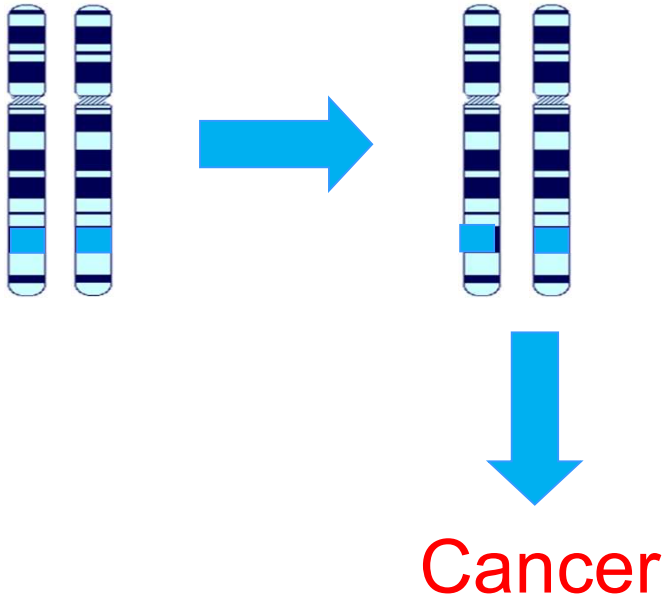
To date, we know of approximately 400 somatic “cancer genes” * but there are almost certainly more to be found

- Defect in genes regulate **apoptosis (**inactivation of p53 or overexpression of anti-apoptotic proteins)
- Defect in **DNA repair genes (**Principal DNA repair mechanisms include: mismatch repair, base and nucleotide excision repair, repair of depurinated sites and repair of double-strand breaks)

Tumour suppressor gene

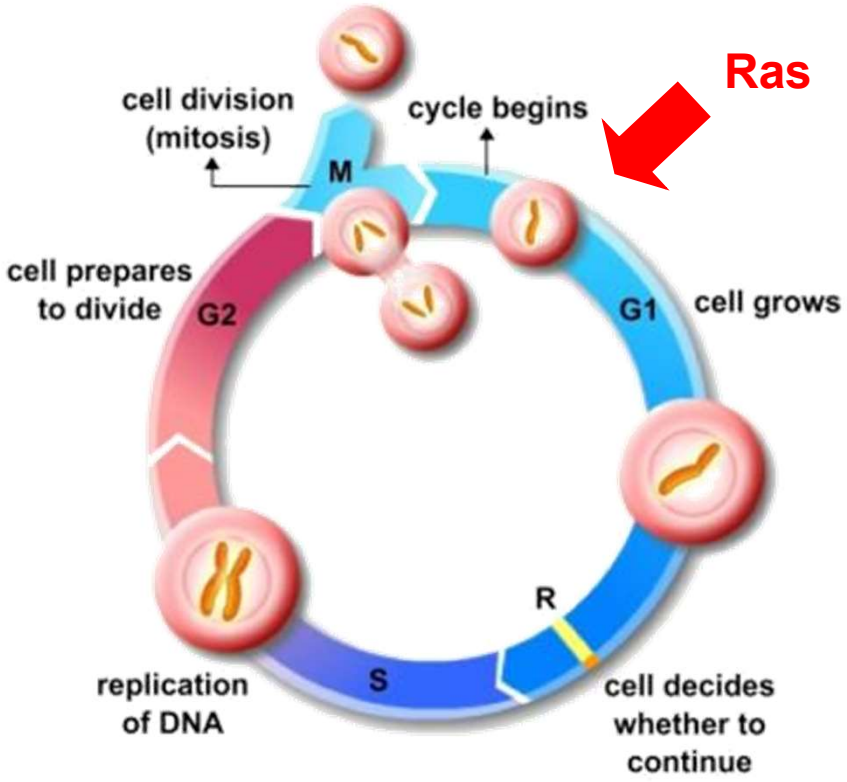
These genes normally function to PREVENT cell growth/division

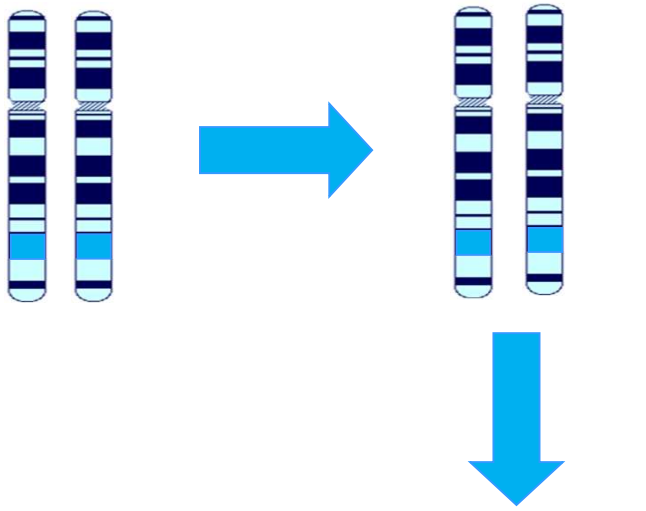




Oncogene

Genes which normally function to PROMOTE cell growth/division in a controlled manner





Cancer

Mechanisms which convert a proto-oncogene into an oncogene

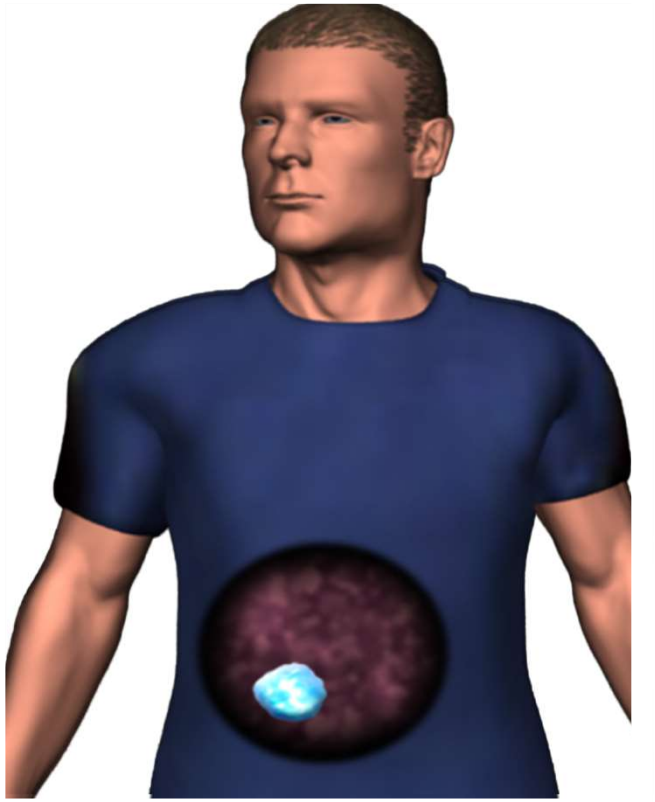
- Changes in the structure of **proto-oncogenes**
  (point mutation ,translocation,deletion)
  Abnormal gene product
- i.e.Translocation;Philadelphia chromosome (chronic myelogenous leukemia
- Activation **by gene amplification**
  Normal product is overexpressed

N-myc amplification (700 times increase)
in neuroblastoma

Cancer progression

Mutations in multiple cancer genes are required for the development and progression of a single cancer

Type



Benign Tumour

In situ cancer

Invasive cancer

Metastatic cancer

Genetic Basis of Cancer:-

Cancer causing mutation

1. Germline cells
2. Somatic cells (spradic)

Genes(Noncoding RNAs)---microRNAs(miRNA)

- Overexpressed
- Downregulated

In tumors(Oncomirs)

Oncogene initiated

Cancer progress by addtion al genetic damage(mutation in caretaker gene)

Produce an everwinding casecade of mutation in gene that control

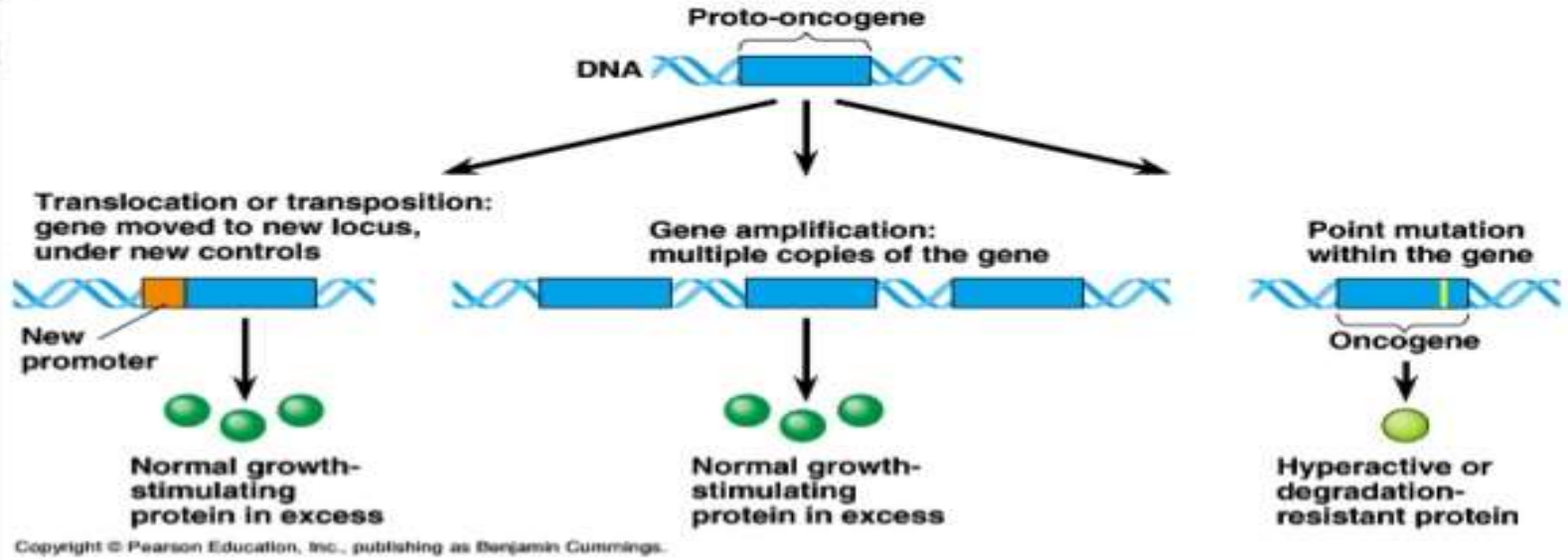
- Repair DNA damage
- Cellular proliferation

Produces an cancer stem cell

Cause malignancy

Cancer will taken place

Proto-oncogenes



Diagnosis of cancer

- There are several methods of diagnosing cancer with advantages in technologies that understand cancer better
- There are rises of number of diagnostic tools that can help detect cancers
- Diagnosis is usually made by pathologist and oncopathologist.
- Some type of cancers, particularly lymph nodes, can be hard to classify even for an expert. Most cancer needs a second opinion regarding diagnosis before being sure of diagnosis or stage & type.

Main methods of cancer diagnosis

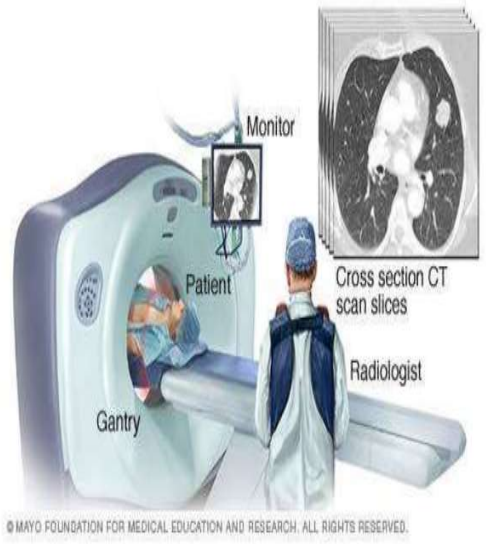
1. Radiological diagnosis
2. Cytological diagnosis
3. Histological diagnosis
4. Frozen section
5. Heamatogical diagnosis
6. Immunohistochemistry
7. Molecular diagnosis
8. Tumour markers

1.RADIOLOGICAL DIAGNOSIS

- It include,
- X-ray
- Ultrasound
- CT scan
- MRI
- These are one of the best early, non-invasive methods of cancer diagnosis.
- **X-ray** – it is a most common technique. These is used for detection of stomach & small intestinal growths & cancer.

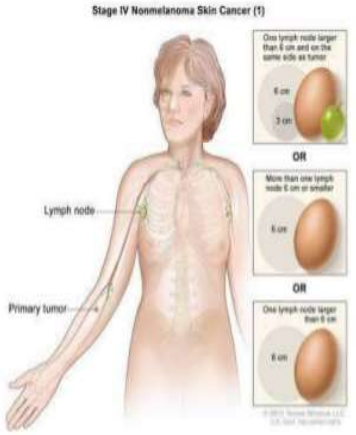
- **Ultrasound**- an exam in which the sound waves are bounced off tissue and echoes are Converted into picture
- **CT scan** – (computerized tomography)
  It uses radiographic beams to create detail Computerized picture.
  It is more preserise than a standered X-ray .

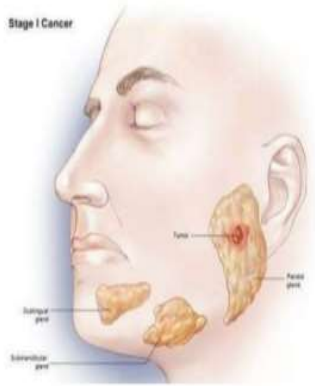
- **MRI**- (Magnetic resonance imaging)
  It uses powerful magnetic field to create Detail computerized images of the body's Soft tissue, large blood vessels & major organe.

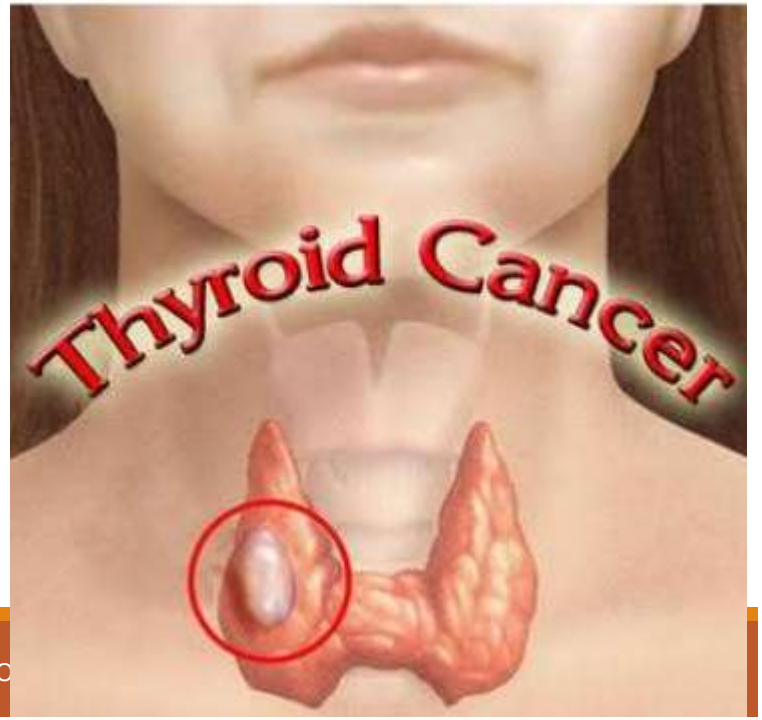


2.CYTOLOGICAL DIAGNOSIS

- **1. Fine needle aspiration cytology (FNAC)**
- Fine needle aspiration cytology is a popular method of tumor diagnosis particularly for palpable tumors
- Lymph nodal tumors
- Breast tumors
- Salivary gland tumors
- Thyroid tumors







- **Procedure :** the skin over the area is cleaned with antiseptic solution like sprit. Tumor is fixed by holding it.
  A 24 g needle is pushed inside the tumor and
  The material is sucked by a syringe is prepared
  from the. aspirated material.
  It is increased by putting the needle under CT or Ultrasound guidance. The smear is stained **Giemsa Stain.**

3.HISTOLOGICAL DIAGNOSIS :

- For histological diagnosis the following methods of sampling is done:
- **Biopsy**- biopsy is a surgical removal of small piece of tissue For microscopic examination for the presence of cancer cell.

There are three ways tissues can be removed for

- **Biopsy:-**
- Endoscopy
- Needle biopsy
- Surgical biopsy

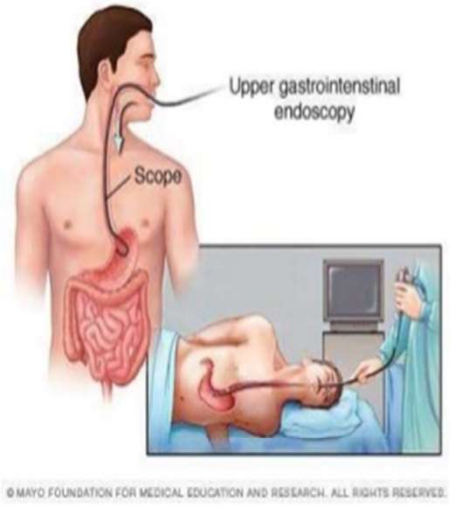
- **Endoscopy-** in this process ,

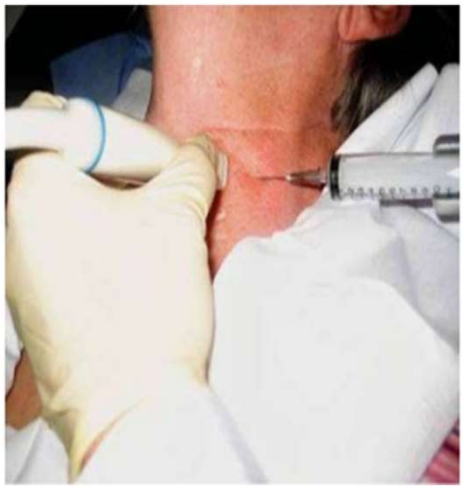
  A thin, flexible tube with a tiny camera on the end is inserted into the body cavity. This allows the doctor to view the abnormal area.

- **Needle biopsy** - the doctor takes a small tissue sample by Inserting a needle into abnormal area. Different types of needles are used, EX:Vim Silverman needle for liver biopsy
- Renal biopsy needle for renal tissue
- True cut biopsy needle for prostatic Tissue or breast tissue

Surgical Biopsy:-

- There are two types of surgical biopsies.
- **An excisional biopsy** :it is performed when the doctor removes the entire tumor, often with some surrounding normal tissue.





- **An incisional biopsy**: it is performed when the doctor removes just a portion of the tumor. If cancer is found to be present, the entire tumor may be removed immediately or during another operation.

  The processing of tissue and its diagnosis takes a two or three days.

4. FROZEN SECTION:-

- Frozen section is quick diagnosis method. The tissue is quickly frozen at around -20’ c in frozen section
- cryostant which makes the tissue hard.

  -tissue is immediately sectioned & stained

  -the whole process from receiving, staining to diagnosis can be completed within 10 to 15 days.

5. HAEMATOLOGICAL DIAGNOSIS:-

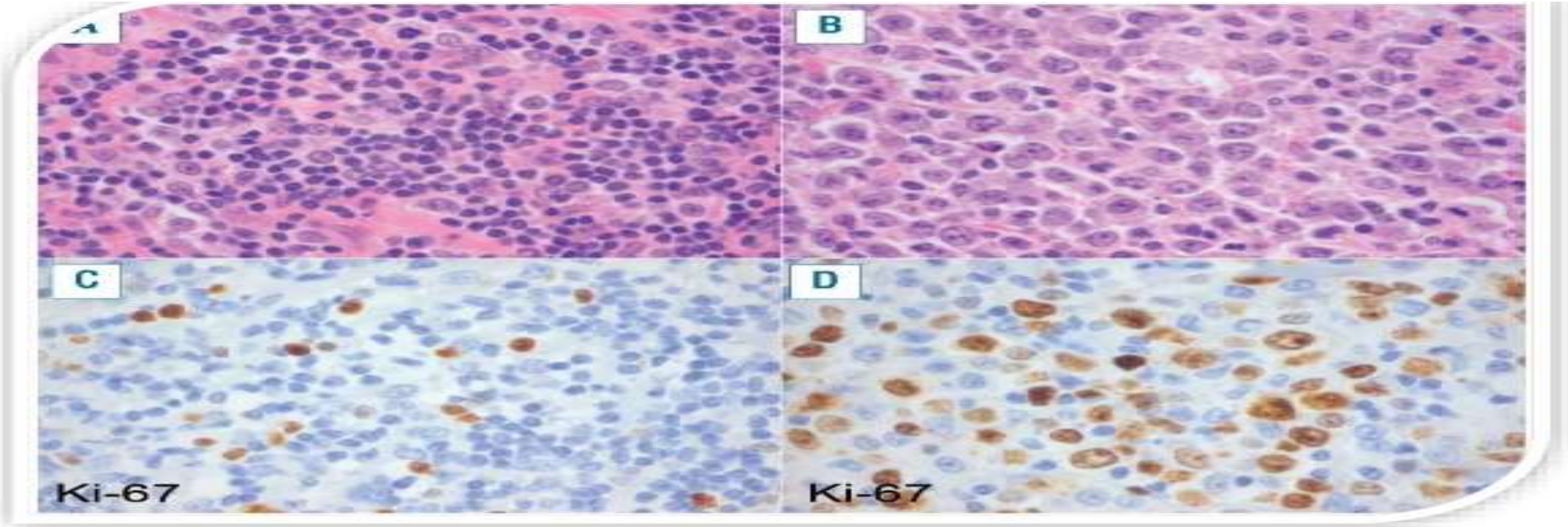
- -Marrow is aspirated by bone marrow aspiration needle biopsied by trephine needle. It is useful in the diagnosis of Leukemia
- Metastasis from lymphoma or solid tumors. This is needed for staging
- Leukemia

6.IMMUNOHISTOCHEMISTRY

Large number of monoclonal antibodies are available which are useful for:

- typing of a malignant tumour. Poorly differentiated tumours are difficult to morphologically type but if it shows positivity for cytokeratin antibody then it can be typed as carcinoma.
- T cell or B cell monoclonal antibody positivity in the T cell or B cell lymphoma.
- classification of leukemia and lymphomas.

Determination of site of primary in metastatic tumour.



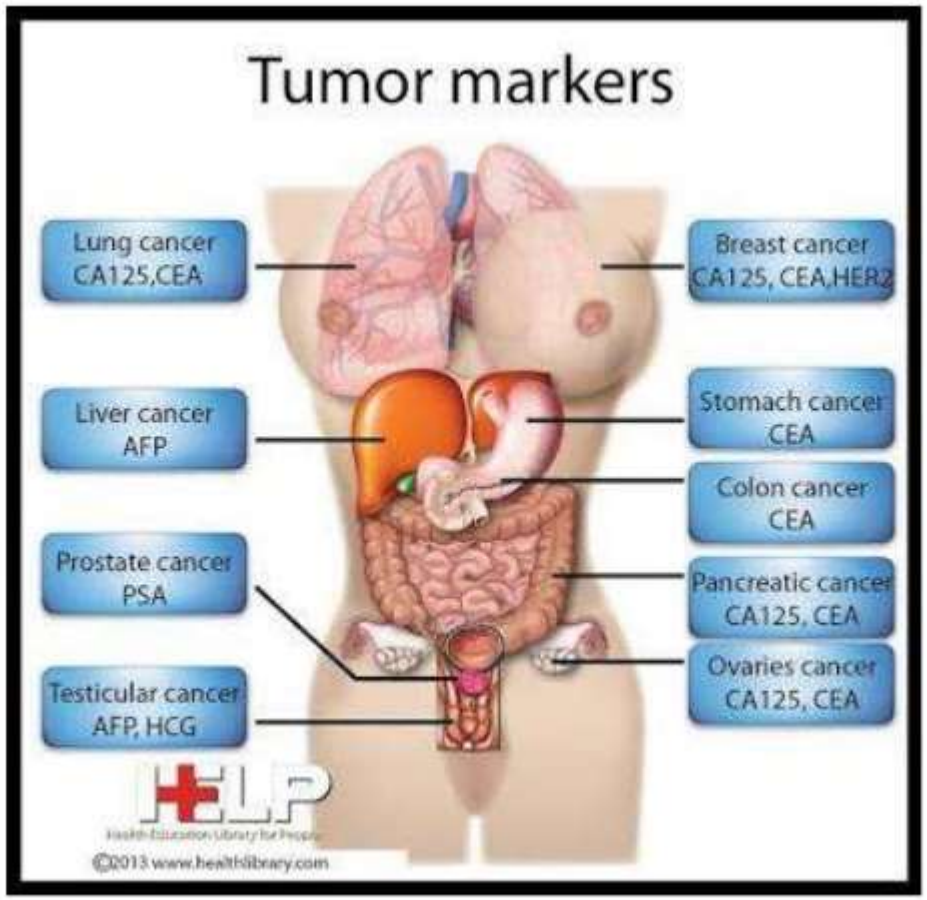
7.MOLECULER DIAGNOSIS

- Molecular diagnosis is an ever emerging field.
- These are useful in detection of : Minute translocations Minimal residual disease.

8. TUMOR MARKER:-

- Some tumors release substance is called **tumor markers**
- Blood test can be performed to detect the blood Cells as well as for specific tumor markers
- Tumor marker is biochemical indicators of

  Tumors .these may be:
- Antigens
- Cytoplasmic proteins
- Enzymes
- Hormones
- Use in support diagnosis


Tumor markers
Lung cancer
CA125,CEA
Breast cancer
CA125, CEA,HER2
Liver cancer
AFP
Stomach cancer
CEA
Colon cancer
CEA
Prostate cancer
PSA
Pancreatic cancer
CA125, CEA
Ovaries cancer
CA125, CEA
Testicular cancer
AFP, HCG
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Treatment of Cancer

Many cancer treatments are available.

Treatment options will depend on several factors, such as

the type and stage of cancer,

patient general health, and preferences.

Together Patient and his doctor can weigh the benefits and risks of each cancer treatment to determine which is best for him.

Goals of cancer treatment

Cure. The goal of treatment is to achieve a cure for your cancer, allowing you to live a normal life span. This may or may not be possible, depending on your specific situation.

Primary treatment. The goal of a primary treatment is to completely remove the cancer from your body or kill the cancer cells.

Any cancer treatment can be used as a primary treatment, but the most common primary cancer treatment for the most common cancers is surgery. If your cancer is particularly sensitive to radiation therapy or chemotherapy, you may receive one of those therapies as your primary treatment.

Adjuvant treatment. The goal of adjuvant therapy is to kill any cancer cells that may remain after primary treatment in order to reduce the chance that the cancer will recur.

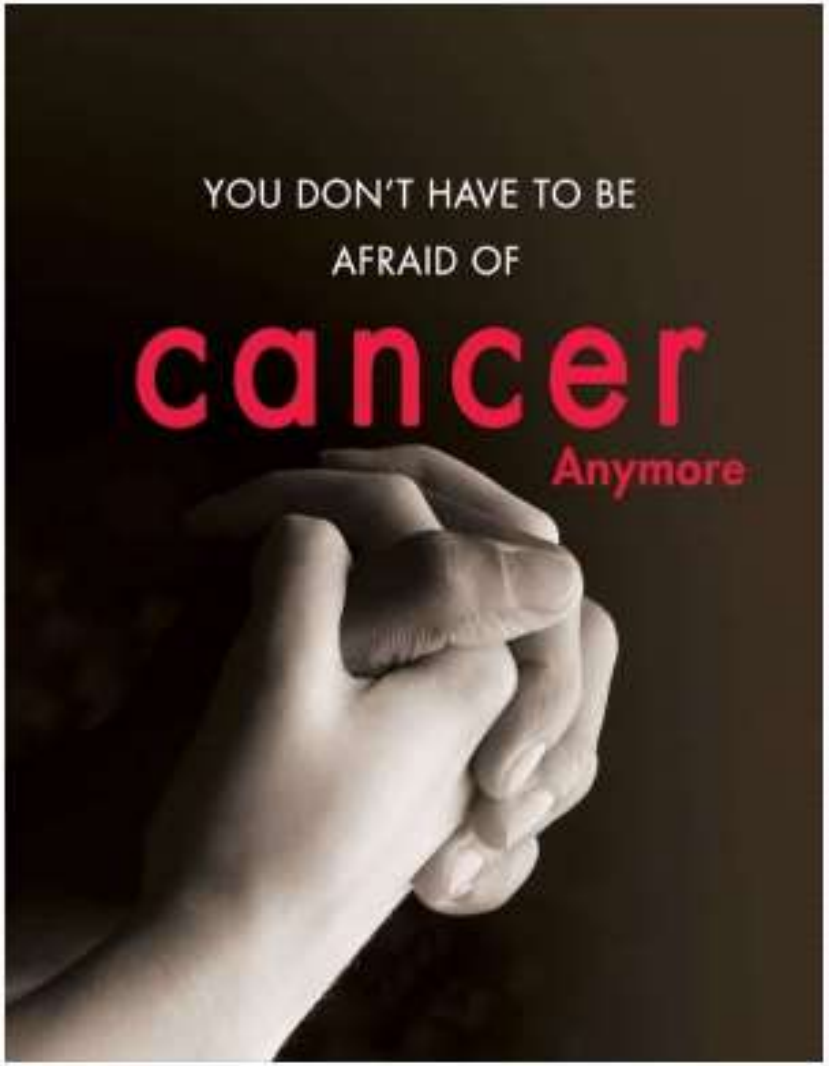
Any cancer treatment can be used as an adjuvant therapy. Common adjuvant therapies include chemotherapy, radiation therapy and hormone therapy.

Palliative treatment. Palliative treatments may help relieve side effects of treatment or signs and symptoms caused by cancer itself. Surgery, radiation, chemotherapy and hormone therapy can all be used to relieve signs and symptoms. Medications may relieve symptoms such as pain and shortness of breath.

Palliative treatment can be used at the same time as other treatments intended to cure your cancer.

TREATMENT

- Surgery
- Chemotherapy
- Radiation
- Targeted Cancer Treatments
- Small Molecule Inhibitors
- Antibodies
- Cell Based Immunotherapy
- Gene Therapy



•**Surgery.** The goal of surgery is to remove the cancer or as much of the cancer as possible.

•**Chemotherapy.** Chemotherapy uses drugs to kill cancer cells.

•**Radiation therapy.** Radiation therapy uses high-powered energy beams, such as X-rays, to kill cancer cells. Radiation treatment can come from a machine outside your body (external beam radiation), or it can be placed inside your body (brachytherapy).

•**Bone marrow transplant.** Bone marrow transplant is also known as a stem cell transplant. Your bone marrow is the material inside your bones that makes blood cells. A bone marrow transplant can use your own cells or cells from a donor.

•A bone marrow transplant allows your doctor to use higher doses of chemotherapy to treat your cancer. It may also be used to replace diseased bone marrow.

•**Immunotherapy.** Immunotherapy, also known as biological therapy, uses your body's immune system to fight cancer. Cancer can survive unchecked in your body because your immune system doesn't recognize it as an intruder. Immunotherapy can help your immune system "see" the cancer and attack it.

•**Hormone therapy.** Some types of cancer are fueled by your body's hormones. Examples include breast cancer and prostate cancer. Removing those hormones from the body or blocking their effects may cause the cancer cells to stop growing.

•**Targeted drug therapy.** Targeted drug treatment focuses on specific abnormalities within cancer cells that allow them to survive.

Other treatments may be available to you, depending on your type of cancer.

•**Clinical trials.** Clinical trials are studies to investigate new ways of treating cancer. Thousands of cancer clinical trials are underway.

Alternative medicine

No alternative cancer treatments have been proved to cure cancer. But alternative medicine options may help you cope with side effects of cancer and cancer treatment, such as fatigue, nausea and pain.

Some alternative medicine options found to be helpful for people with cancer include:

- Acupuncture
- Hypnosis
- Massage
- Meditation
- Relaxation techniques
- Yoga

Chemotherapy

- Drugs used to kill cancer cells; disrupt some aspect of cell division.
- Toxic to healthy cells; hair, bone marrow, lymphocytes, and epithelial cells of intestinal lining .
- Side effects include hair loss, nausea, vomiting, and reduced immune responses.

Radiation therapy

- High-energy rays are used to kill cancer cells
- Stop them from growing and dividing.
- radiotherapy is a local treatment; it can affect cancer cells only in the treated area.

- side effects–
- Tiredness, skin reactions such as rash or redness, and loss of appetite.
- Temporary lowering of the WBC count.

Surgery therapy

- In localized cancer surgery typically attempts to remove the entire mass.

Biological therapy/immunotherapy

- Monoclonal antibodies, interferon, interleukin-2, and colony-stimulating factors.

- **Side effects - Temporary flu-like symptoms such as fever and chills, muscle aches and weakness, loss of appetite and diarrhea.**

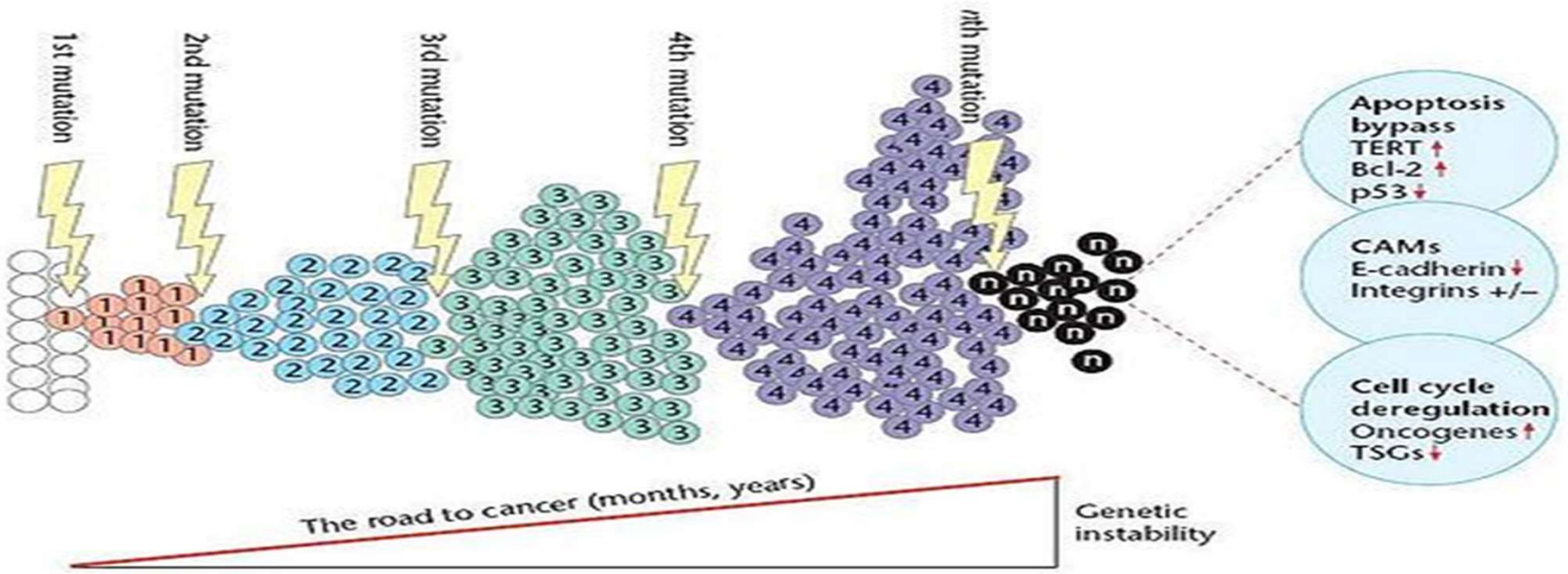
PREVENTION

- ✓Eating a healthy diet.
- ✓Exercising regularly.
- ✓Limiting alcohol.
- ✓Maintaining a healthy weight.

- ✓Minimizing your exposure to radiation and toxic chemicals.
- ✓Not smoking or chewing tobacco
- ✓Reducing sun exposure, especially if you burn easily.

Conclusion

It is a multi-step process that requires the accumulation of many genetic changes over time . These genetic alterations involve activation of proto-oncogenes to oncogenes, deregulation of tumour suppressor genes and DNA repair genes and ‘immortalisation’



Cancer and the Cell Cycle

Proto-oncogenes
The genes that code for the positive cell cycle regulators

Proto-oncogenes are normal genes that, when mutated in certain ways, become **oncogenes**, genes that cause a cell to become cancerous.

Oncogenes differ from proto-oncogenes in three basic ways

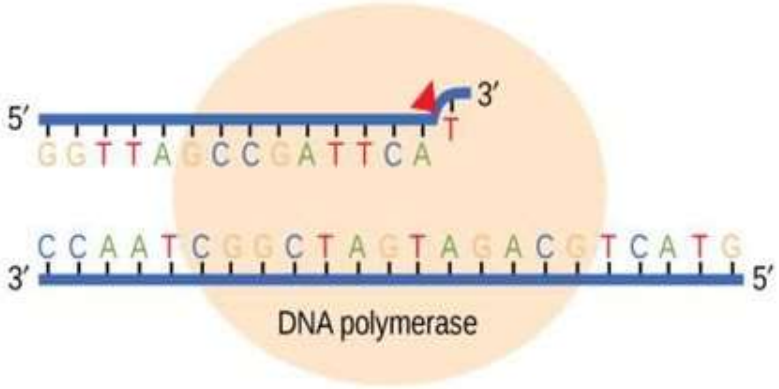
1- Timing and quality of expression

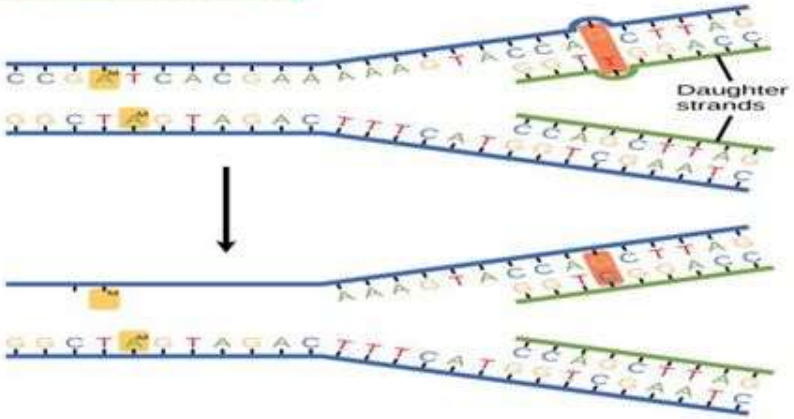
2- Structure of protein products

3 - Degree to which their protein products are regulated by cellular signals

DNA mutations

- DNA replication is a highly accurate process, but mistakes can occasionally occur
- **Uncorrected mistakes may sometimes lead to cancer..**



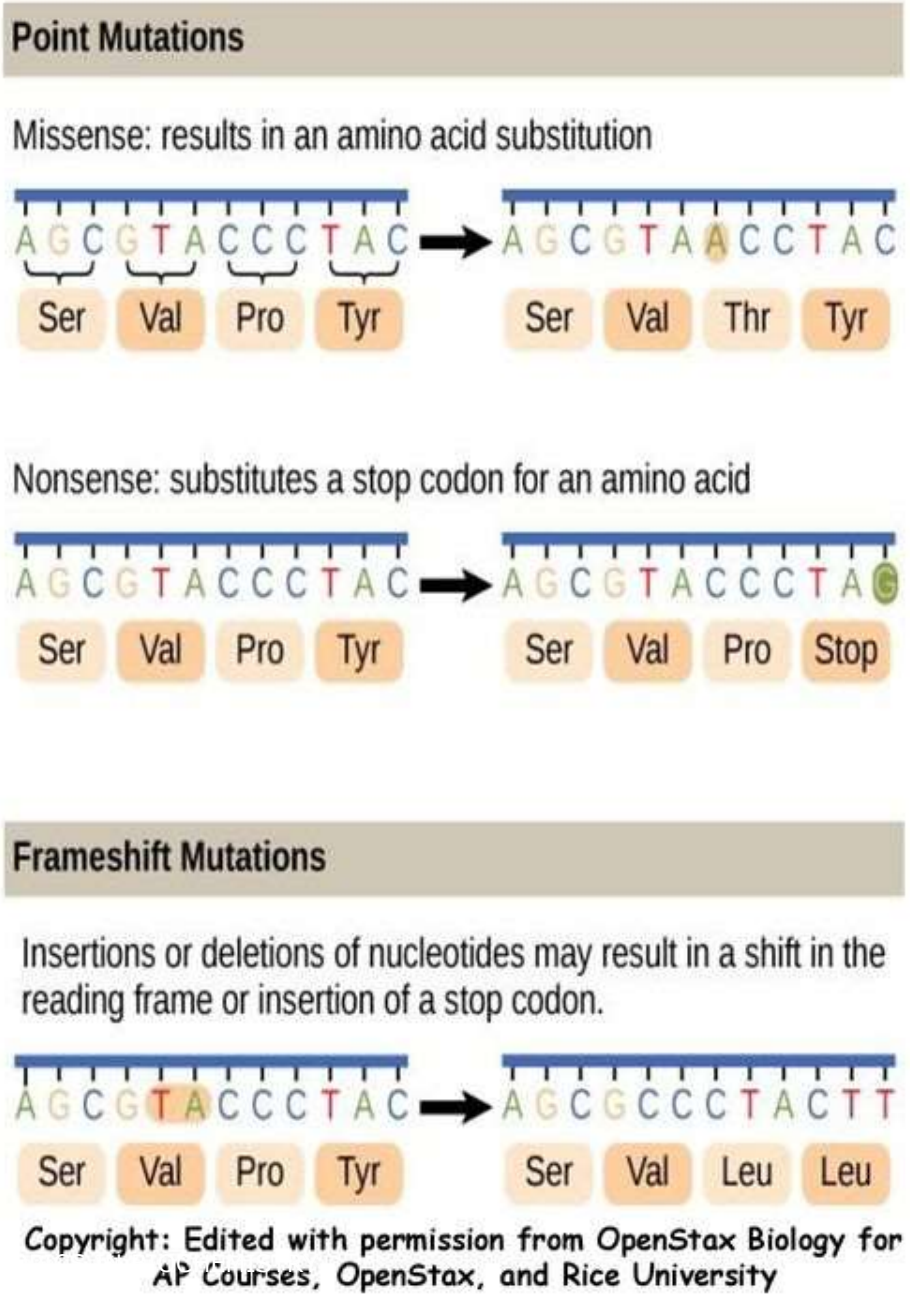


- **Proofreading failure**: The polymerase ***is unable to determine*** if the newly added base has paired correctly with the base in the template strand.
- The altered reading frame codon brings in a different amino acid.
- ***The alternate resulting protein could induce cancer***

- **Mismatch mutation**: The incorrectly added base goes ***undetected*** after replication.
- Mismatch repair proteins ***do not remove*** it from the newly synthesized strand
- The altered reading frame codon brings in a different amino acid.
- ***The alternate resulting protein could induce cancer***

DNA mutations

- In rare cases, mistakes are not corrected, leading to mutations and the induction of cancer.
- A point mutation in the RNA template can result in the coding for a alternate amino acid in the growing peptide chain during translation
  - ***if the new codon is for a different amino acid***
- An unwanted STOP command would change or stop protein function which could induce cancer formation
- Insertions or deletions resulting in a major frameshift of the reading frame can drastically alter protein translation and induce cancer.



Progression of cancer

- A tumor is said to be ***benign*** if it is contained in one location and has not broken through the basement membrane to which normal cells are attached

- Benign tumors often cause no health problems to an individual

- Can grow big enough to interrupt the functioning of normal tissue

- Removal is generally successful as they are not intermingled with other tissue

Progression of cancer

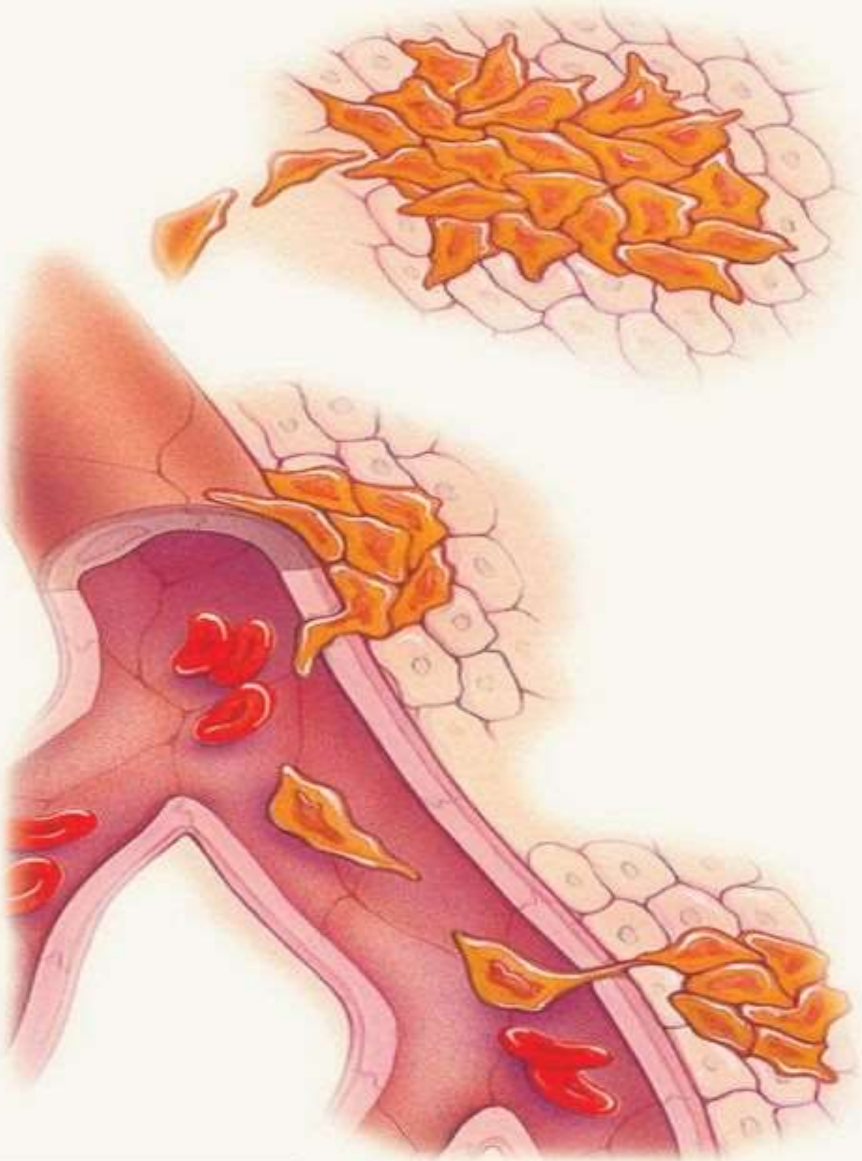
- *Malignant* tumors invade normal tissue
- Do not just push healthily cells out of the way
- Tumor cells produce protein-degrading enzymes that breaks down the connective tissue that holds cells together
- As Malignant tumors invade normal produce that allow them to invade other tissue, they spread to other locations
- *Metastasis* – one or more transformed cells spread to the rest of the body via the blood system

The Characteristics of Cancer

- **A cancer cell's structure is abnormal.**

  - Cancer is a result of a series of mutations in the cell's genes
    - Larger cell nucleus and less cytoplasm
    - Loss of structural specialization
    - Cytoskeleton shrinks
    - Plasma membrane proteins could be lost or altered
    - New plasma membrane proteins may appear
    - Changes passed on to cell's descendants

The Characteristics of Cancer



·A Cancer cells break away from their home tissue.

·B The metastasizing cells become attached to the wall of a blood vessel or lymph vessel. They secrete enzymes that break down part of the wall. Then they enter the vessel.

·C Cancer cells creep or tumble along inside blood vessels, then leave the bloodstream the same way they got in. They start new tumors in new tissues.

Tests and Procedures

The most common diagnostic tests and what to expect before, during, and after them. Information about **diagnostic tests for a specific type of cancer** can be found in a separate area of this website.

Barium Enema

Procedure used to find health conditions in the colon and rectum

Biopsy

How a tissue sample is used to diagnose cancer

Bone Marrow Aspiration and Biopsy

Procedures that can provide information about blood cells

Bone Scan

Used to find cancer or see how well treatment is working

Breast MRI

Imaging test used to look at breast tissue

Colonoscopy

Used to view a part of the large intestine

Computed Tomography (CT) Scan

Type of imaging test used to find and learn more about cancer

Types of Endoscopy
Procedures used to view the inside of the body
Fecal Occult Blood Tests
Used to find blood in the stool
Magnetic Resonance Imaging (MRI)
Imaging test done without using x-rays
Mammography
X-ray that checks for breast cancer
MUGA Scan
Test for checking if the lower chambers of heart are pumping blood properly
Pap Test
Procedure to find changes in cells that can lead to cervical cancer
Positron Emission Tomography and Computed Tomography (PET-CT) Scans
Used to find cancer and learn its stage
Sigmoidoscopy
Test to examine the lower part of the large intestine
Tumor Marker Tests
Types of tests that look for substances made by cells in the body in response to cancer
Ultrasound
Imaging test that can show tumor's location in the body
Upper Endoscopy
Used to examine the esophagus, stomach, and top of small intestine