**What is Cancer?**

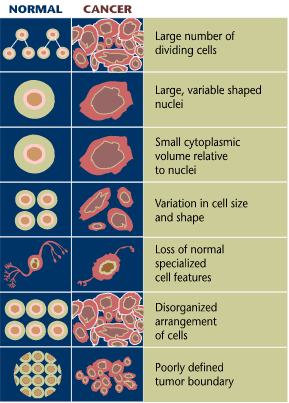
**Neoplasia:** new, uncontrolled cell growth

**NORMAL CELL PROLIFERATION:**

1. during fetal, childhood, and adolescent growth
2. in tissues requiring rapid cell turnover (blood cells, skin, GI epithelial cells)
3. during tissue repair or regeneration
4. synthesis of sperm cells

**Normal Cell Division is regulated by**:

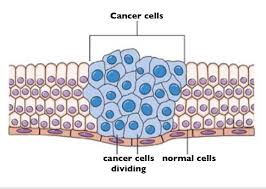
1. growth promoting factors
2. space (contact inhibition)
3. growth inhibiting factors **(**apoptosis regulating genes if DNA is damaged)
4. **limited lifespan** - programmed death of aged, damaged, or excess cells

**CANCER CELLS LOOK DIFFERENT THAN NORMAL CELLS:**

**Undifferentiated**

Abnormal nuclei:

* enlarged,
* may contain abnormal number of chromosomes. Chromosomes may be mutated (duplicated/deleted, extra copies of certain genes)

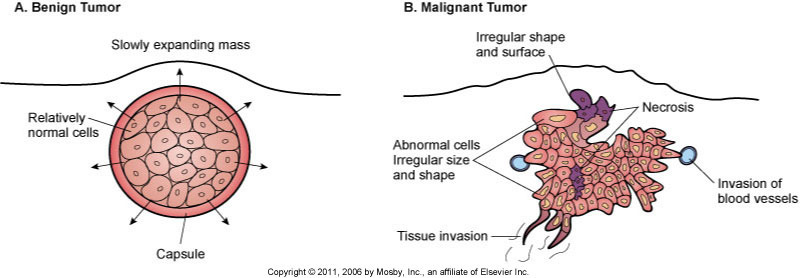


**CANCER CELLS BEHAVE DIFFERENTLY THAN NORMAL CELLS:**

|  |  |
| --- | --- |
| **Normal** | **Cancer** |
| * + - * require positive signals from growth factors or signalling proteins * obey inhibitory signals, may undergo apoptosis if DNA is damaged * Have limited life span (telomeres) * Stay in one place * Contact inhibition:   Adhere to neighbours,  Stop dividing   * Differentiate to perform a specific function | * Reduced need for stimulatory growth factors * no longer respond to inhibitory growth factors * can keep dividing (produce telomerase) * don’t stick together very well and can spread to other parts of the body🡪 metastasis * Lack contact inhibition - will pile on top of each other. * do not perform any function like surrounding tissue * Angiogenesis- release growth factors causing neighbouring vessels to branch into cancerous tissue |

**Tumours are classified in two ways:**

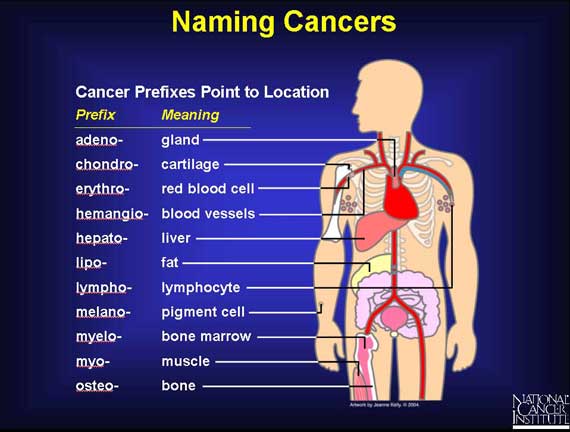
1. **Clinical classification** (features and outcome)
   * benign
   * malignant
2. **Histologic classification**
   * named according to the tissue and cell type from which they arise



**Difference between Benign and Malignant:**

|  |  |  |
| --- | --- | --- |
|  | **benign** | **malignant** |
| Morphology  (appearance) | * encapsulated by connective tissue –**defined border** * clearly separated from surrounding tissue * cells are **well-differentiated** * **resemble the tissue of origin** * **uniform** in size and shape | * not encapsulated * **lack** sharp borders * cells are **poorly differentiated** (**anaplasia**) * **do not** resemble cells of origin * cells and nuclei are **variable** in size and shape |
| Functional | * **slower growing** * stay in one place * (**do not metastasize**) * usually not **life-threatening**. | * **Faster growing** * **invade** nearby tissues * can spread to other parts of the body (**metastasis**). * Potential for **causing death** |

Naming: 5 Main Categories named for site of origin



* **Carcinoma** – begins in tissues that line or cover internal organs.
* **Adenocarcinoma** - glandular structures in epithelial tissue.
* **Sarcoma** – begins in the connective or supportive tissues such as bone, cartilage, fat, muscle, or blood vessels
* **Leukemia** – starts in blood forming tissue eg. bone marrow
* **Lymphoma and myeloma** – begin in the cells of the immune system (lymphatic tissue)
* lung cancer that has spread to the brain is called metastatic lung cancer,

Carcinoma ***in situ*** – in place of origin- has not spread.

**GENETICS OF CANCER**

**Cancer is Caused by Cumulative Gene Mutations:**

* **inherited** or
* **spontaneous/acquired (**caused by **repeated** exposure **mutagens)**:
  + **errors in DNA replication (🡪mutated genes assoc with cancer)**
  + **External Factors:** 
    - **Smoking**
    - **Diet** - high fat, low fibre diet, lacking in fruits and veg (antioxidants)
    - excessive **alcohol** consumption
    - **Radiation** – UV, X-rays,
      * *leukemia in Hiroshima and Nagasaki*
      * *thyroid cancer after the Chernobyl nuclear disaster*
    - **Chemicals** from occupational hazards (asbestos –>lung and colon cancer)
    - **Viruses (HPV, Hep B)**

### **GENES ASSOCIATED WITH CANCER:**

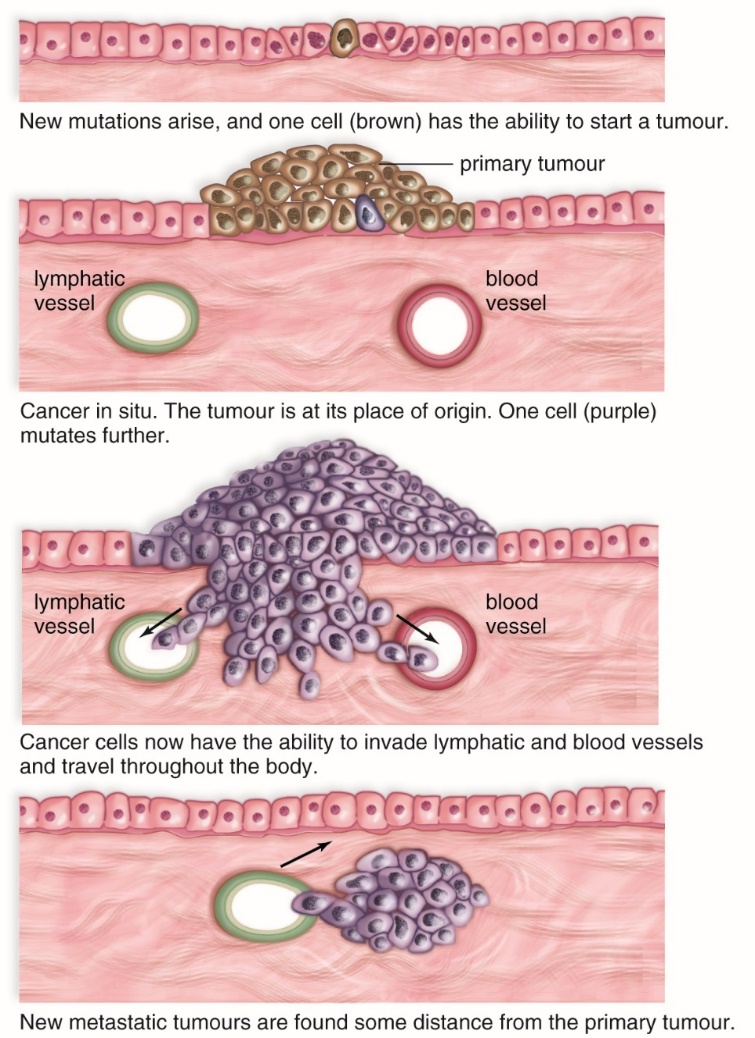
### **DNA repair genes -** https://upload.wikimedia.org/wikipedia/commons/thumb/d/de/Oncogenes_illustration.jpg/300px-Oncogenes_illustration.jpg become damaged/mutated no repair 🡪 damage DNA replicated, mutations may not be repaired and **will build up**.

[**Proto-oncogenes**](javascript:popGlossary('../../glossary/proto_oncogene.html','yes')) - Code for growth factors, or signalling proteins (promote growth)

* **stimulate cell division** or
* **inhibit apoptosis**.
* **Normally inactive**
* When Activated by mutagen🡪 become [**oncogenes**](javascript:popGlossary('../../glossary/oncogene.html','yes')). (*activated)* 🡪 accelerate growth

[**Tumor suppressors**](javascript:popGlossary('../../glossary/tumor_suppressor.html','yes'))

* **inhibit** **cell division**
* **trigger apoptosis**.
* **Mutated** 🡪 become inactivated 🡪uncontrolled growth
* Nearly 50% of all cancers are thought to involve a damaged or missing tumour suppressor gene.
* **TP53**, a tumour suppressor gene that triggers cell death, is commonly damaged or missing in many types of cancer.

**HOW DOES CANCER SPREAD?**

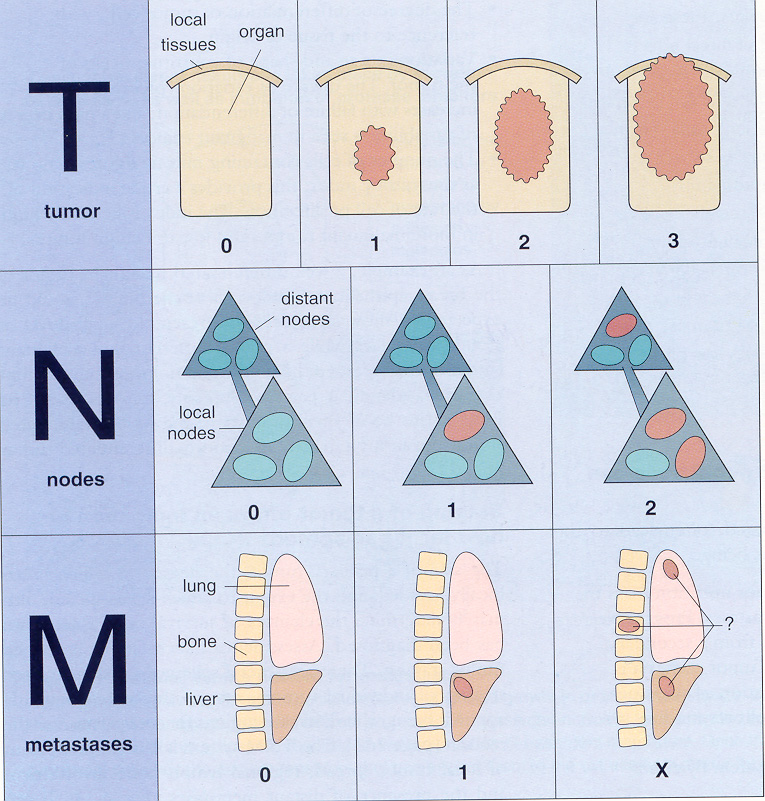
**Invasion**- tumor grows into surrounding tissue

**Metastasis-**

* **Degrade** basement membrane,
* **invade** underlying tissue,
* **break away** from the tumour,
* **enter** the **bloodstream** or **lymphatic system** and
* travel to a **new location** in the body.

(Basement membrane isthin, fibrous, extracellular matrix separating epithelium from connective tissue.)

**STAGING**

* based on **location**, **size,** **number**, **spread** to nearby lymph nodes.
* **TNM classification**:

**T = tumour size and local invasion**;

T0 = carcinoma *in situ* (no local invasion),

T1-T4 increasing in size

**N = regional lymph node involvement**.

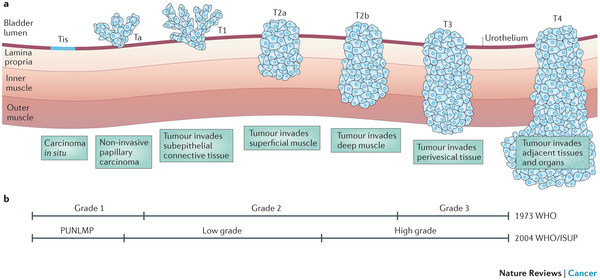
N0 = no nodes,

N1-N3 in increasing number of nodes

**M = distant metastases**;

M0 = no metastasis,

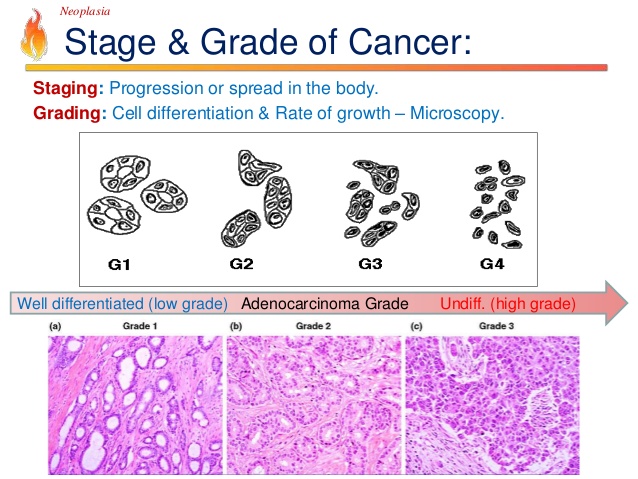
M1 = metastasis



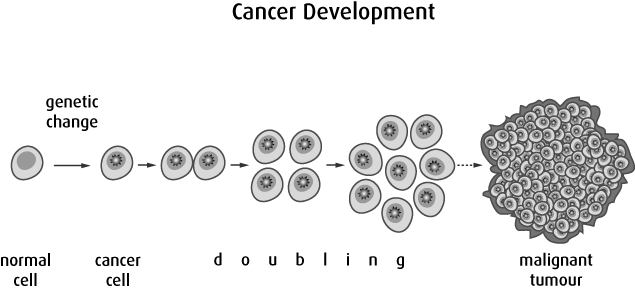
**GRADING**:

* degree of **differentiation** in the tumour cells (1,2,3,4)
* Grade 1: cells and the organization appear **close to normal**, **grow and spread slowly**.
* Grade 3 and Grade 4: tumors **do not look like normal** cells or surrounding tissue (less differentiated), grow **rapidly** and **spread faster** (**more aggressive**) than tumors with a lower grade.

Grading an Unspecified tumor:

* GX: Grade cannot be assessed (undetermined grade)
* G1: Well differentiated (low grade)
* G2: Moderately differentiated (intermediate grade)
* G3: Poorly differentiated (high grade)
* G4: undifferentiated (high grade)

**CANCER DEVELOPMENT**



1. **Initiation**: **Mutations/Failed repairs/Carcinogens (initiators**)

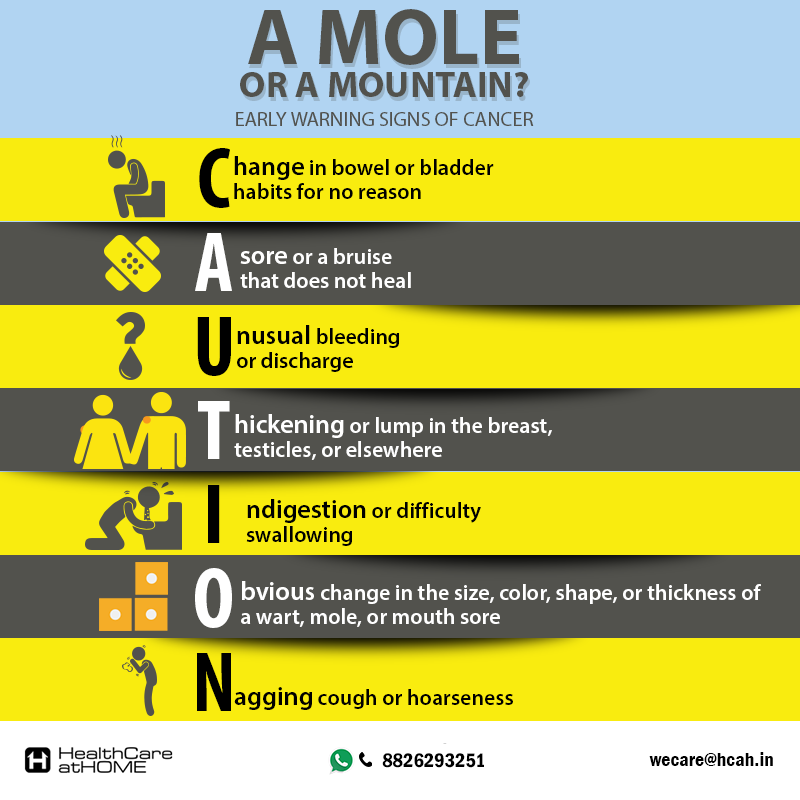
**a**. **Activate oncogenes**: Mutation of proto oncogenes can cause them to become oncogenes 🡪 uncontrolled cell division

**b**. **Inactivate Tumor Suppressor** genes 🡪 active cell division

1. **Promotion:** 
   1. Further and **repeated damage** may be caused by hormones / drugs (***promoters****)*.
   2. Abnormal cells actively divide
2. **Progression** (**transformation** of normal cell causes it to behave, grow and function quite **differently** and turn into a cancer cell.
3. **Angiogenesis**
4. **Metastasis** – when tumor becomes malignant, cancer cells break away from tumour and travel via lymphatic system to other areas of body to form a secondary tumour.

**PROGNOSIS** (Probably Outcome) depends on:

1. Invasion of surrounding tissue
2. Lymph node involvement
3. Metastasis

**WARNING SIGNS OF CANCER:**



A – assymetry

B – border irregularity

C – colour

D – diameter

**DETECTION**

* monthly breast self-examinations and regular **mammography** and **Pap tests**
* regular self-examination of the testes for young men,
* older men: examination of the prostate gland
* Colonoscopy

**TREATMENT**

* **surgery** (localized)
* **chemotherapy** (system-wide)
* **radiation therapy** (localized) (X rays and gamma rays)
* **therapeutic vaccines** (agents that stimulate the immune system to attack cancerous cells)
* **Drug therapy** - inhibits certain kinase receptors that become hyperactive in cancer cells, resulting in the cells' rapid reproduction

**CHARACTERISTICS OF CANCER**

1. Abnormal Cell morphology
2. Lack of Contact Inhibition
3. Growth in absence of growth signals:
4. Insensitivity to growth inhibitors
5. Avoid detection
6. Evade apoptosis
7. Limitless replicative potential- Activate telomerase
8. Stimulate angiogenesis
9. Tissue invasion and metastasis

**RETROVIRUSES AND CANCER**

Retrovirus RNA copied into DNA which then is inserted into host genome.

4 ways viral DNA can cause cancer:

1. Virus could carry **oncogene** directly
2. Viral DNA causes a normal host gene to **translocate** elsewhere
3. Viral DNA causes **over expression of a gene** causing overproduction of a protein
4. Viral DNA causes **normal gene to mutate** or change so it no longer functions

Gleason 1-5

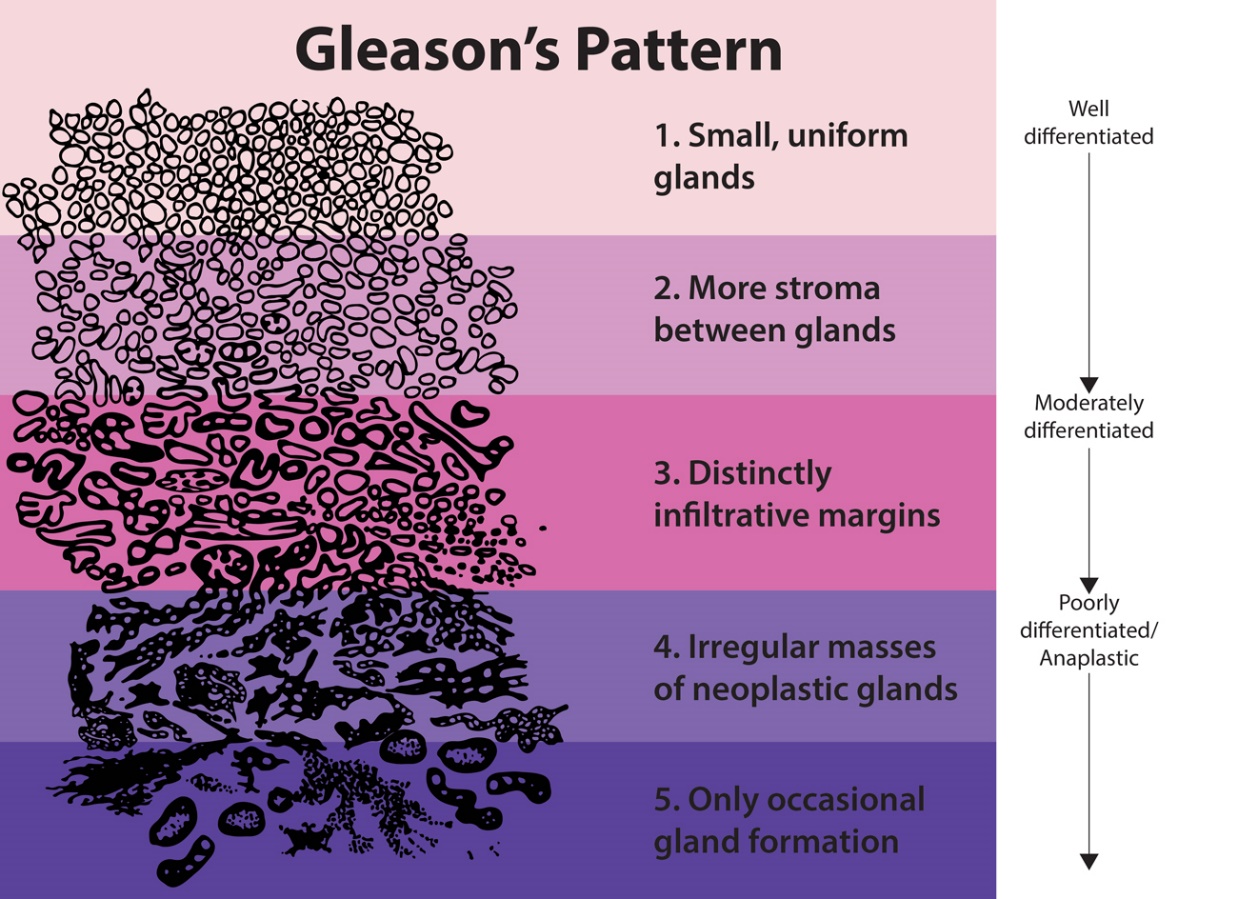
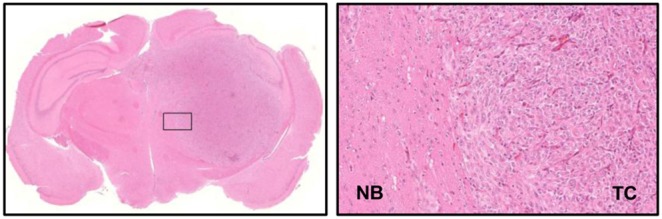
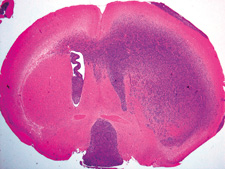
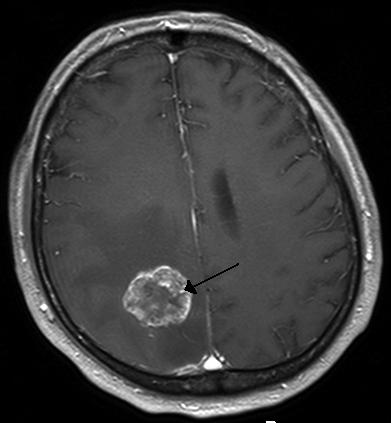
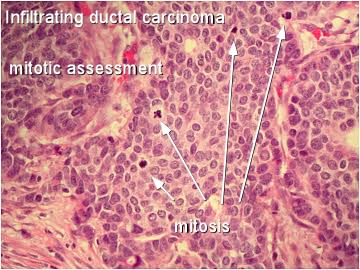


FIG. 1. (A) Low-grade endometrial stromal sarcoma (ESS). (B) High-grade ESS showing uniform nuclei. (C) A circular arrangement of tumor cells around small vessels in low-grade ESS. (D) High-grade ESS showing circular arrangement around the small vessel (A to D, hematoxylin-eosin staining; magnification: 40 Â ). 
                









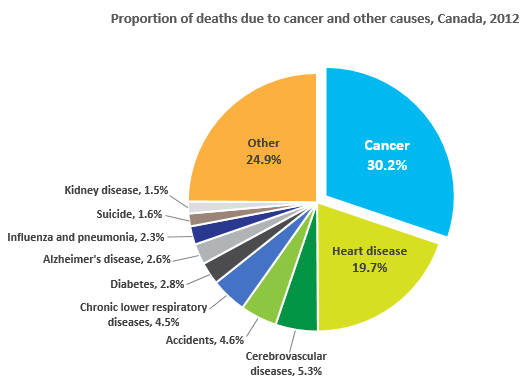
## Incidence and mortality

Incidence is the total number of new cases of cancer.

Mortality is the number of deaths due to cancer.

An estimated 202,400 new cases of cancer and 78,800 deaths from cancer will occur in Canada in 2016. (does not include non-melanoma skin cancer cases.)n(2016 pop is 36.4 million)

Cancer is the leading cause of death in Canada and is responsible for 30% of all deaths.



Read more: <http://www.cancer.ca/en/cancer-information/cancer-101/cancer-statistics-at-a-glance/?region=on#ixzz4TfsB5941>