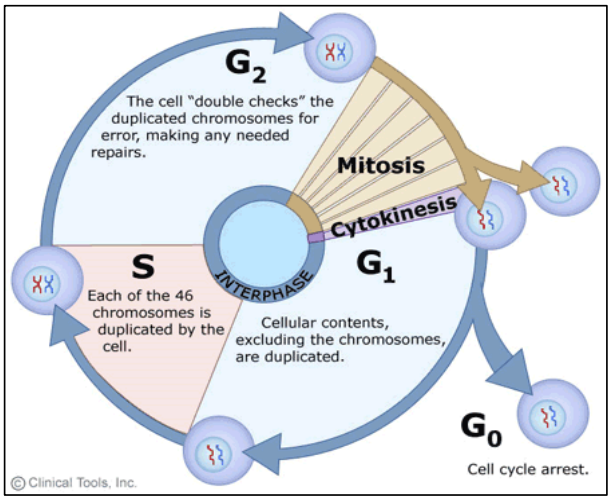
MITOTIC CELL DIVISION

MITOTIC DIVISION GENERATES EXACT CELL COPIES

- **CELL CYCLE** – *life of a cell from the time it was first formed during cell division of a parent cell until its own division into two daughter cells*
- **Mitotic (M) phase** – includes both mitosis and cytokinesis; usually the shortest part of the cell cycle
- **Interphase** – 90% of the cycle; G_1 phase *(first gap)*, S phase *(synthesis)* & G_2 phase *(second gap)*

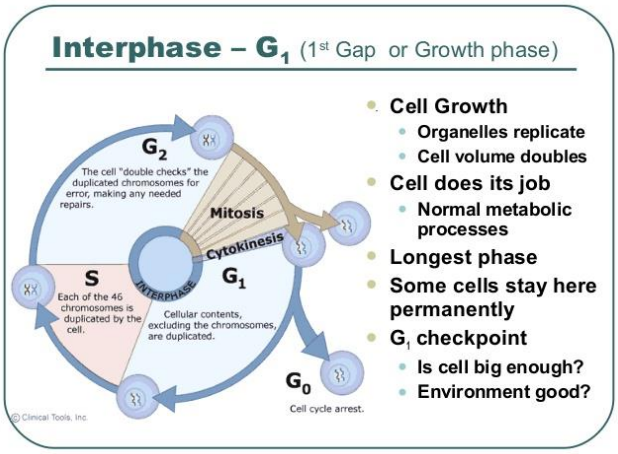


DNA IS COPIED DURING INTERPHASE

- **Interphase** is a very active time for the cell. The cell ***produces proteins*** and ***performs its functions*** in the organism, from photosynthesis to muscle contraction to insulin production to bone formation.
- ***DNA replication*** also occurs during this stage.
- Divided into **"gap"** phases (designated **G_1** and **G_2** separated by a **"synthesis" S** phase).

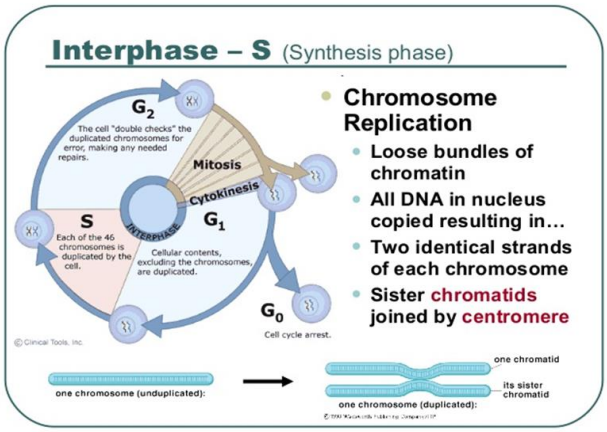
G_1 PHASE

- The **cell grows,** carries out its **basic functions,** and produces the **new organelles** and other components it will require if it divides.



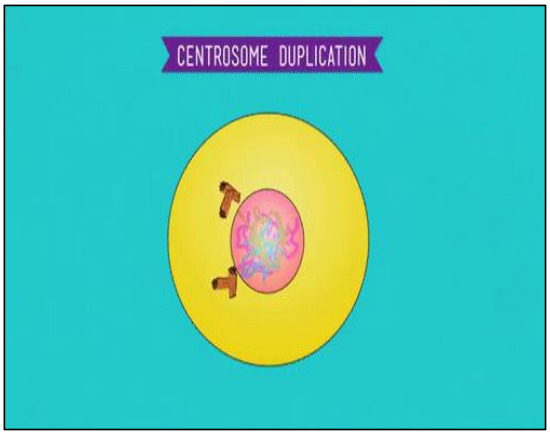
S PHASE

- Enzymes **replicate** the cell's genetic material & **repair** damaged DNA
- As S phase *begins*, each chromosomes include **one DNA molecule**
- By the *end* of S phase, each chromosome consists of **two attached sister chromatids**
- In an animal cell, **duplication of centrosome** also happens in this phase



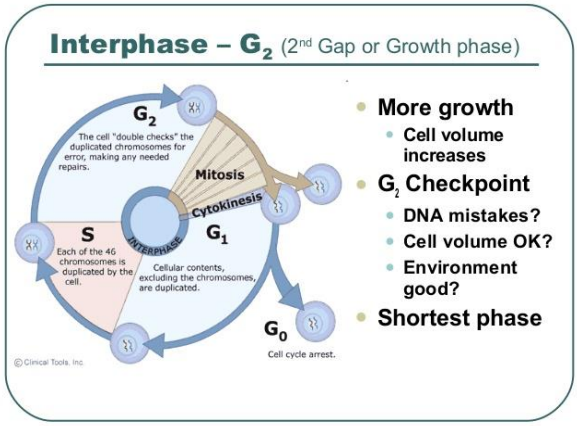
CENTROSOMES

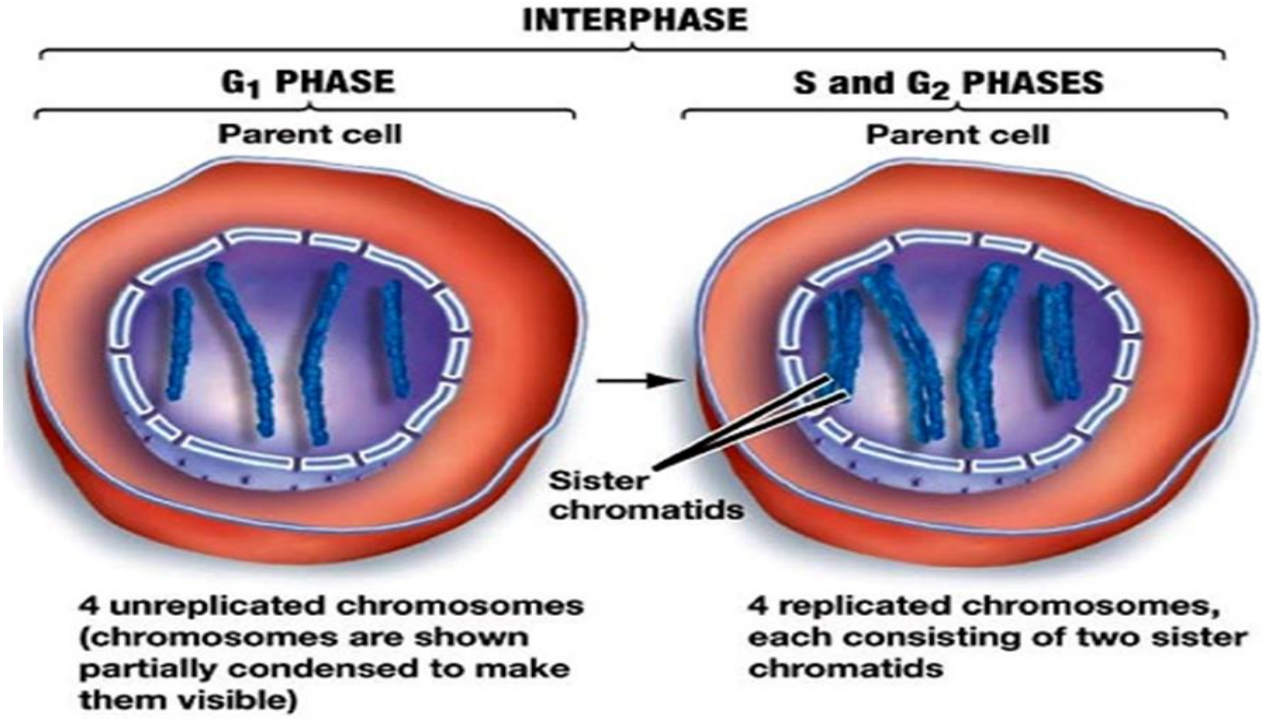
- Structures that **organize** the **mitotic spindle,** *a set of microtubule proteins that coordinate the movements of chromosomes during mitosis*
- Each centrosome includes proteins enclosing a pair of barrel-shaped **centrioles**
- Most plant cells lack centrosomes; they organize their spindle fibers throughout the cell



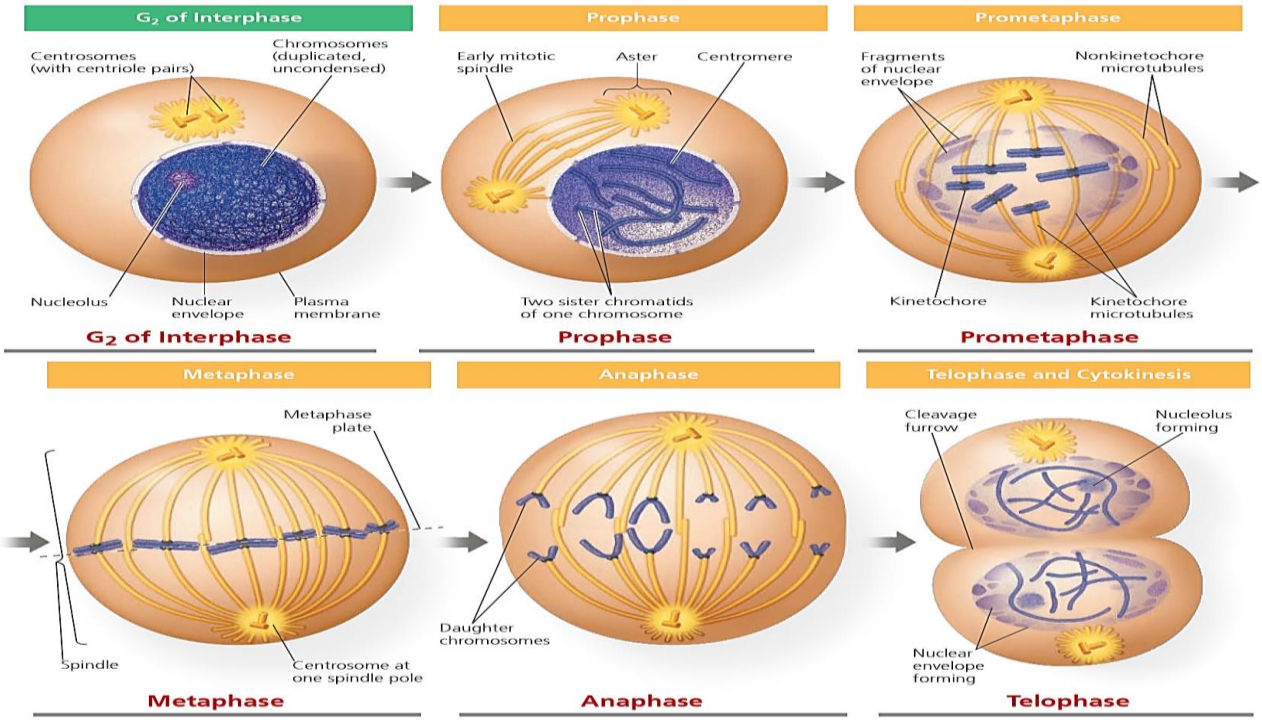
G_2 PHASE

- The cell **continues to grow** but also prepares to divide**, producing the proteins** that will help coordinate mitosis.
- The **DNA winds more tightly** around its associated proteins, and this start of **chromosome condensation** signals the start of mitosis.
- Interphase has ended.

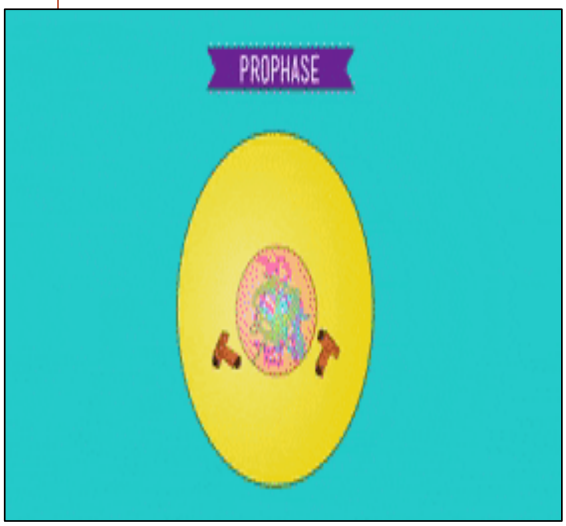




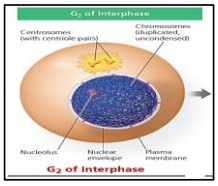
CHROMOSOMES DIVIDE DURING MITOSIS



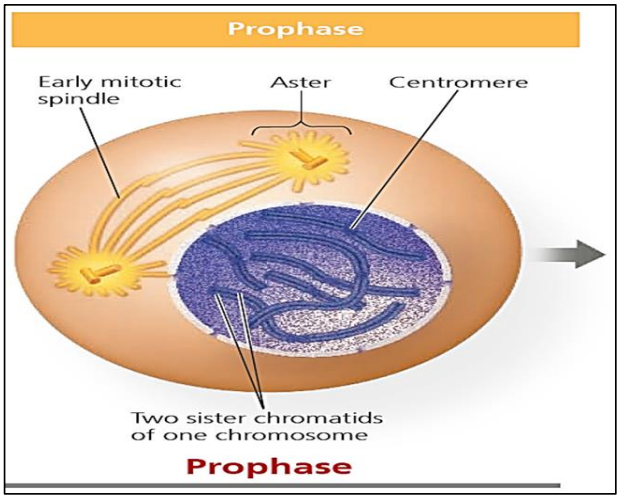
PROPHASE



- Chromatin fibers become more tightly coiled *(discrete chromosomes)*
- Nucleoli disappear
- Duplicated chromosomes appear as two identical sister chromatids joined at their centromeres & along their arms *(cohesins)* – ***sister chromatid cohesion***

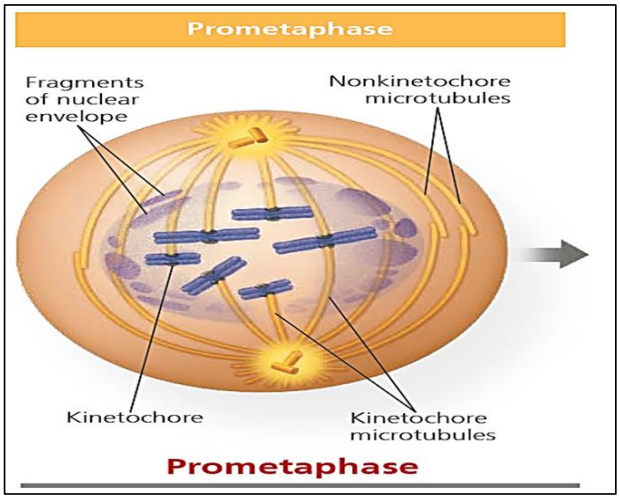


PROPHASE



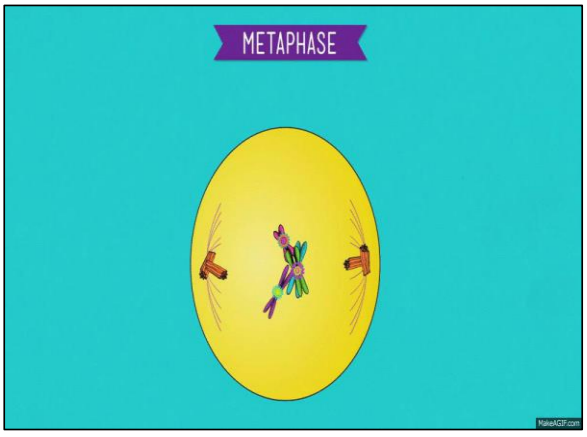
- **Mitotic spindle** begins to form – *composed of centrosomes & microtubules along with radial arrays of shorter microtubules called asters*
- Centrosomes move away from each other

PROMETAPHASE



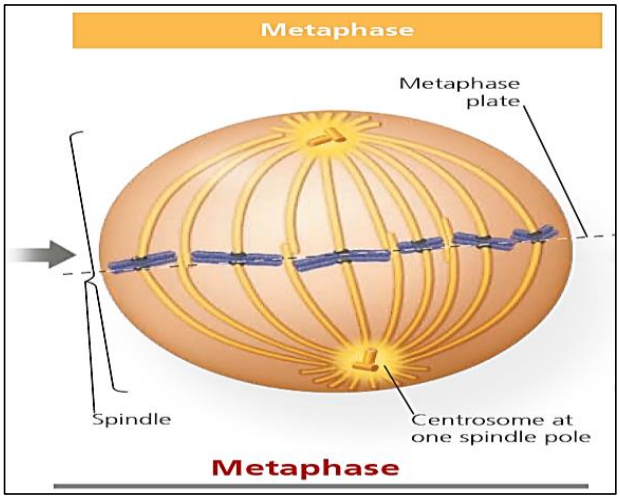
- Nuclear envelope fragments
- Microtubules invade the nuclear area
- Chromosomes – more condensed
- **Kinetochore** – *specialized protein structure,* forms at the centromere of each chromatid
- Nonkinetochore microtubules lengthens the cell

METAPHASE



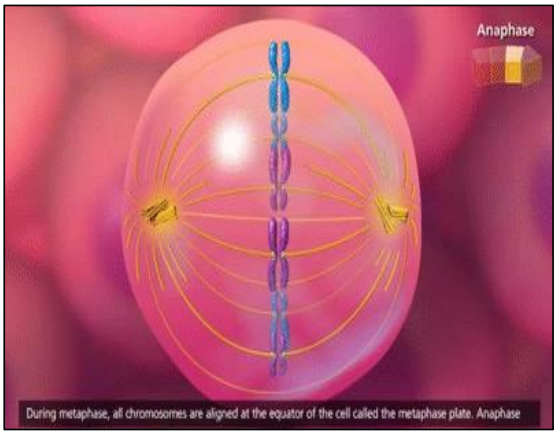
- Centrosomes are at the opposite poles of the cell
- Chromosomes have all arrived at the **metaphase plate,** *a plane that is equidistant between the spindle's two poles*
- Kinetochores are attached to ***kinetochore microtubules*** from opposite poles

METAPHASE



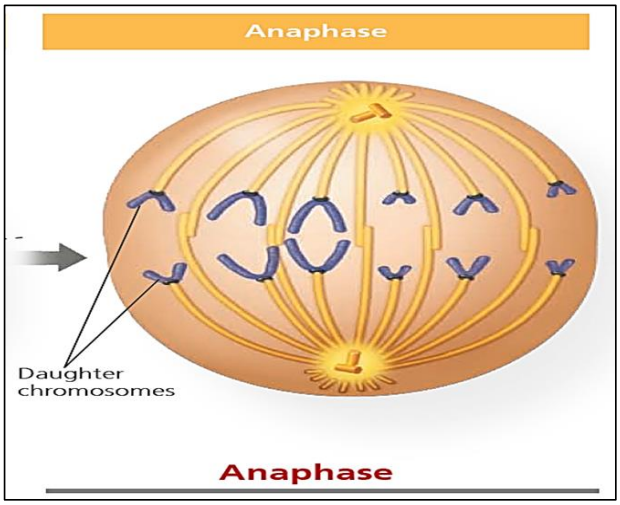
- Microtubules that do not attach to kinetochores overlap & interact with other ***nonkinetochore microtubules*** from the opposite pole of the spindle
- Microtubules of ***asters*** have also grown & in contact with plasma membrane
- Spindle is now complete.

ANAPHASE



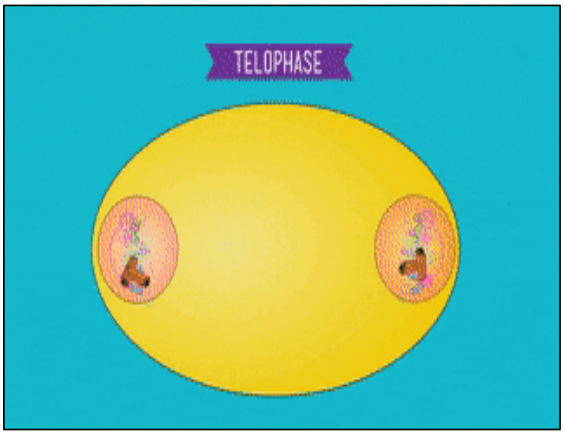
- Shortest stage of mitosis
- Cohesin proteins are cleaved ***(separase);*** sister chromatids part suddenly & become independent chromosome
- The two new daughter chromosomes move toward opposite ends of the cell *(kinetochore microtubules shorten)*

ANAPHASE



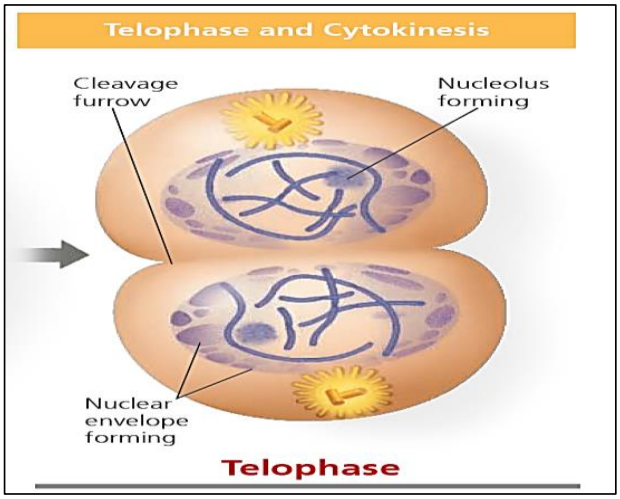
- Cell elongates as nonkinetochore microtubules lengthen
- By the end of anaphase, the two ends of the cell have identical—and complete—collections of chromosomes

TELOPHASE



- Two daughter nuclei form; nuclear envelope arise
- Nucleoli reappear
- Chromosomes – less condensed
- Remaining spindle microtubules – depolymerized
- Mitosis *(division of one nucleus into two genetically identical nuclei)* is now complete.

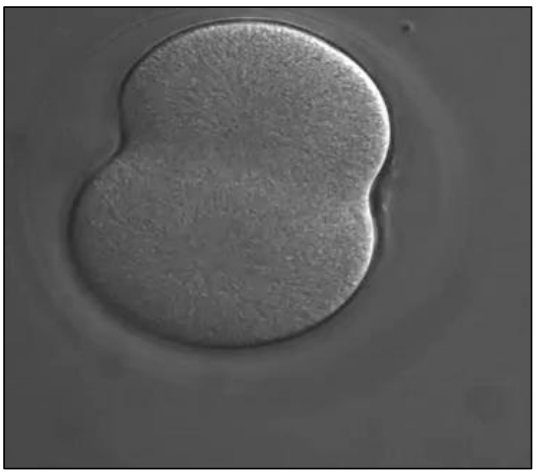
TELOPHASE & CYTOKINESIS



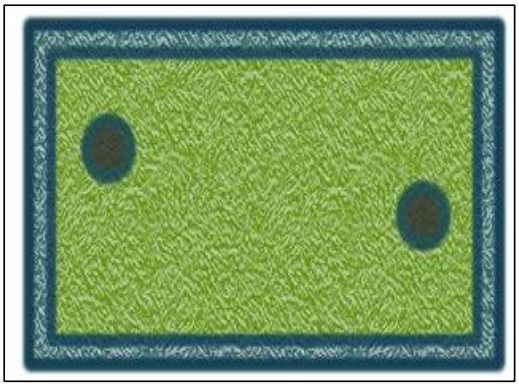
Cytokinesis

- Division of cytoplasm starts at late telophase
- In animal cells, cytokinesis involves formation of **cleavage furrow,** which pinches the cell in two

- In an animal cell, the first sign of cytokinesis is the **cleavage furrow,** *a shallow groove in the cell surface near the old metaphase plate*
- A ring of proteins beneath the cell membrane contracts like a drawstring, separating the daughter cells



- Cytokinesis in plant cells, which have cell walls, is markedly different. *There is no cleavage furrow.*
- Vesicles in Golgi bodies move along microtubules to the middle of the cell to merge, producing **cell plate**
- A new cell wall arising from the contents of the cell plate forms between the daughter cells



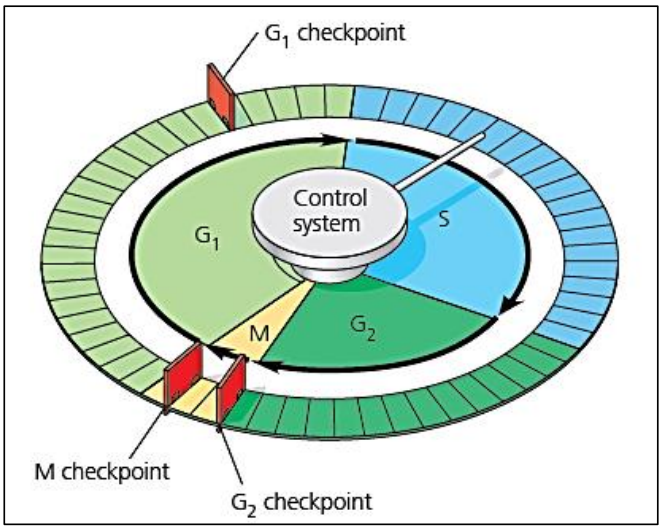
THE CELL CYCLE CONTROL CENTER

THE EUKARYOTIC CELL CYCLE IS REGULATED BY A MOLECULAR CONTROL SYSTEM

- ***Timing*** and ***rate*** of cell division in different parts of a plant or animal are crucial to normal growth, development and maintenance.
- *Human skin cells divide frequently, liver cells maintain ability to divide but keep it in reserve until need arises, nerve cells and muscle cells do not divide at all in a mature human*
- ***How do any of these cells "know" what to do?***

CHEMICAL SIGNALS REGULATE CELL DIVISION

- **Cell cycle control system** – *a cyclically operating set of molecules in the cell that both triggers and coordinates key events in the cell cycle*
- **Checkpoint** in the cell cycle – a control point where stop and go-ahead signals can regulate the cycle
- *Three important checkpoints:* **G_1, G_2** and **M phases**



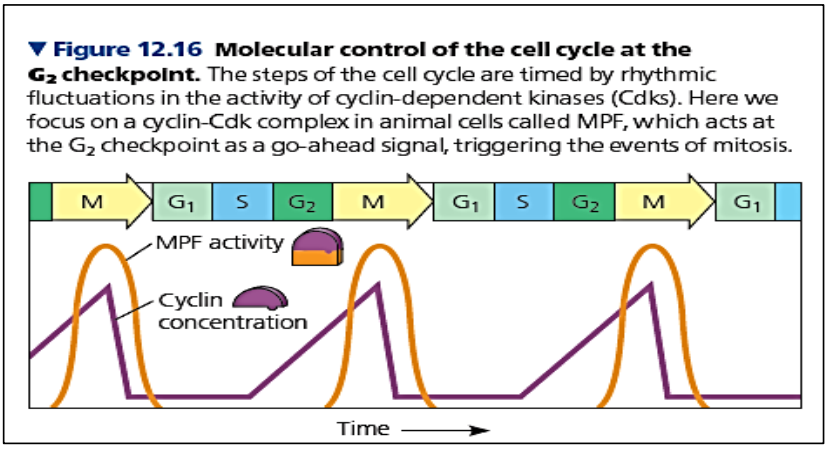
Mechanical Analogy for the Cell Cycle Control System

THE CELL CYCLE CLOCK: CYCLINS AND CYCLIN-DEPENDENT KINASES

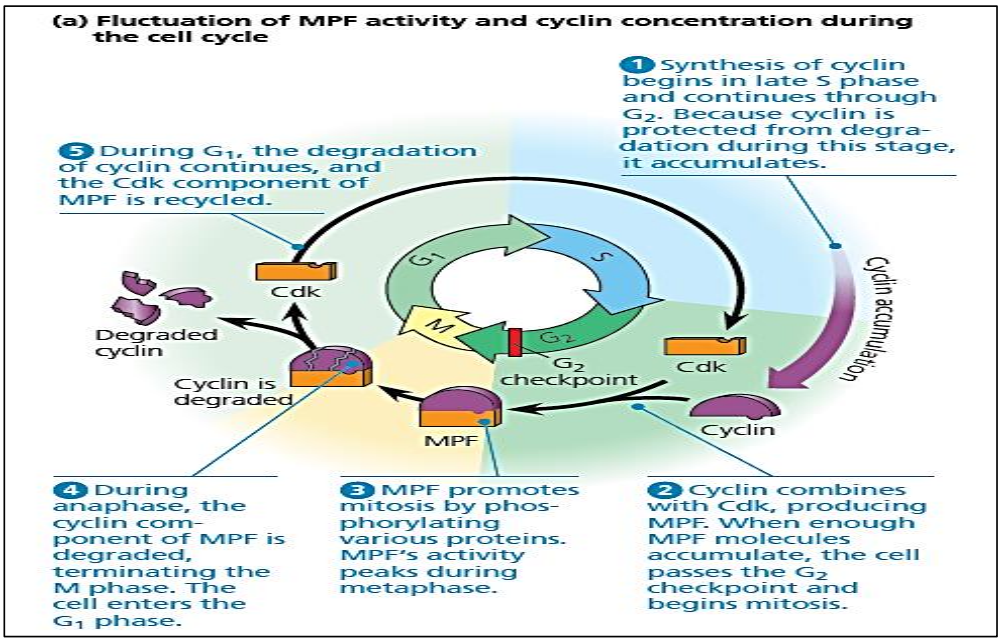
- Rhythmic fluctuations in the abundance and activity of cell cycle control molecules pace the sequential events of the cell cycle.
- Protein **kinases** & **cyclins** – *main proteins of the regulatory molecules*
- **Kinases** – often times inactive; present at a ***constant*** concentration in the growing cell

- To be active, a kinase must be attached to a **cyclin** – *a protein that has **cyclically fluctuating** concentration in the cell*
- D/t this requirement, these kinases are called ***cyclin-dependent kinases*** or **Cdks**
- Activity of a Cdk rises and falls with changes on the concentration of its cyclin partner

FLUCTUATING ACTIVITY OF MPF (MATURATION-PROMOTING FACTOR)



▼ **Figure 12.16 Molecular control of the cell cycle at the G_2 checkpoint.** The steps of the cell cycle are timed by rhythmic fluctuations in the activity of cyclin-dependent kinases (Cdks). Here we focus on a cyclin-Cdk complex in animal cells called MPF, which acts at the G_2 checkpoint as a go-ahead signal, triggering the events of mitosis.

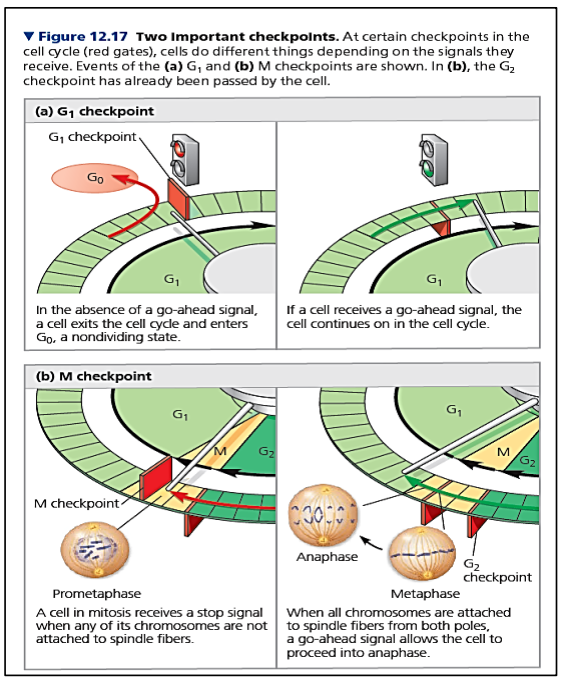


STOP AND GO SIGNS: INTERNAL AND EXTERNAL SIGNALS AT THE CHECKPOINTS

- Animal cells have built-in **stop signals** that halt the cell cycle at checkpoints until overridden by **go-ahead signals.**
- Signals come from cellular surveillance mechanisms ***inside*** the cell reporting crucial cellular processes that should have occurred by that point have in fact completed correctly and thus whether or not the cell cycle should proceed.
- Checkpoints also register signals from ***outside*** the cell.

FOR MANY CELLS, G_1 CHECKPOINT SEEMS TO BE THE MOST IMPORTANT.

- ***Go-ahead signal*** – usually complete the interphase and M phases and divide
- If it does not receive go-ahead signal at that point, it may exit the cycle and switch to *nondividing state* called **the G_0 phase** *(mature nerve and muscle cells; liver cells)*

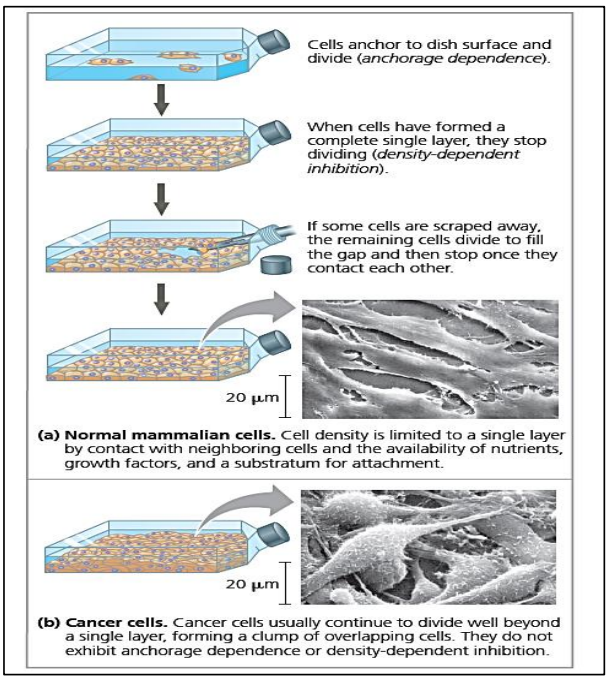


- **M checkpoint** – separation of the sister chromatids does not begin until all chromosomes are properly attached to the spindle at the metaphase plate *(internal signal)*
- *Once activated, the protein complex sets off a chain of molecular events that activates the enzyme* ***separase****. This mechanism ensures that daughter cells do not end up with missing or extra chromosomes.*

WHAT ABOUT THE **STOP AND GO-AHEAD SIGNALS**, WHAT ARE THE SIGNALING MOLECULES?

- Studies showed that many external factors, both chemical and physical, can influence cell division. *(Cells fail to divide when essential nutrient is lacking in a culture medium.)*
- **Growth factor** – protein release by certain cells that stimulates other cells to divide
- Different cell types respond specifically to different growth factors or combination of growth factors.

- **Density-dependent inhibition** – a phenomenon in which crowded cells stop dividing
- **Anchorage dependence** – to divide, animal cells must be attached to something, such as inside of a culture flask or extracellular matrix of tissue



LOSS OF CELL CYCLE CONTROLS IN CANCER CELLS

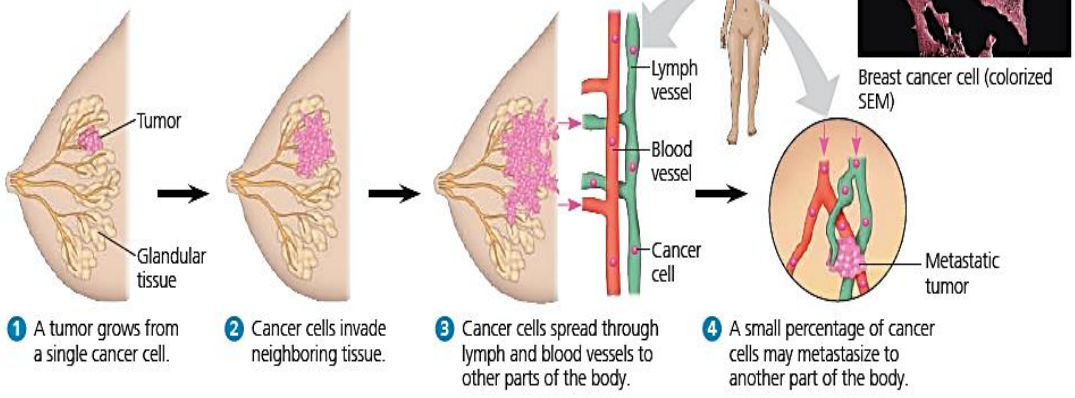
- Cancer cells do not heed the normal signals that regulate the cell cycle. They do not stop dividing when growth factors are depleted. Cancer cells do not need GF in their culture medium to grow and divide. *(logical hypothesis)*
- **Transformation** – a process in which cells in culture acquire the ability to divide indefinitely causing them to behave like cancer cells *(immortal)*

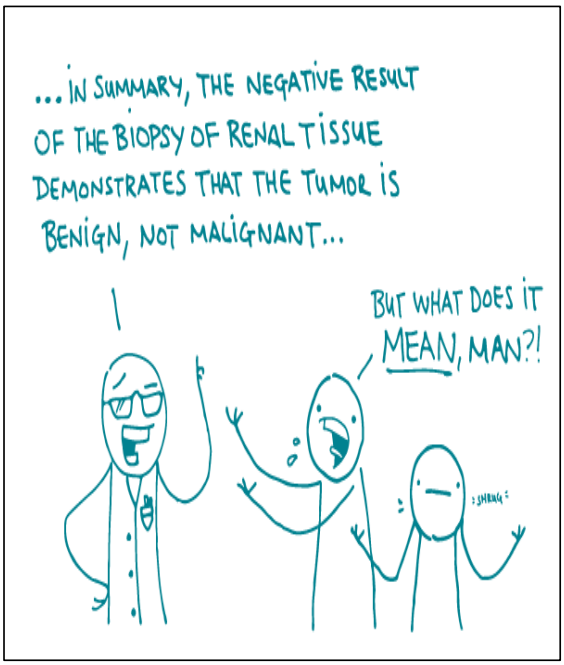
ABNORMAL CELL BEHAVIOR IN THE BODY CAN BE CATASTROPHIC.

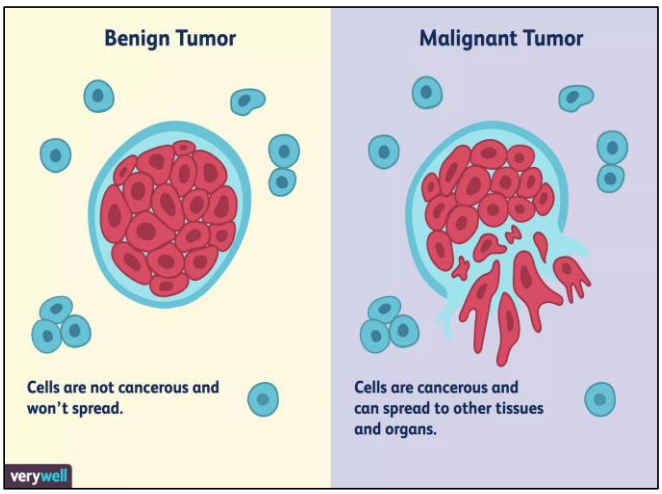
- When cells are converted to cancer cells, it often has ***altered proteins*** on its surface that the immune system normally recognizes as *"non-self"* and destroys it.
- If the cell evades destruction, it may proliferate and form a **tumor,** *a mass of abnormal cells within normal tissues*
- **Benign tumor** – abnormal cells that remain at the original site
- **Malignant tumor** – includes cells whose genetic and cellular changes allow them to spread to new tissues (also called transformed cells)

▼ Figure 12.20 The growth and metastasis of a malignant breast tumor. A series of genetic and cellular changes contribute to a tumor becoming malignant (cancerous). The cells of malignant tumors grow in an uncontrolled way and can spread to neighboring tissues and, via lymph and blood vessels, to other parts of the body (metastasis).

Mastering Biology HHMI Animation: How Tumors Grow

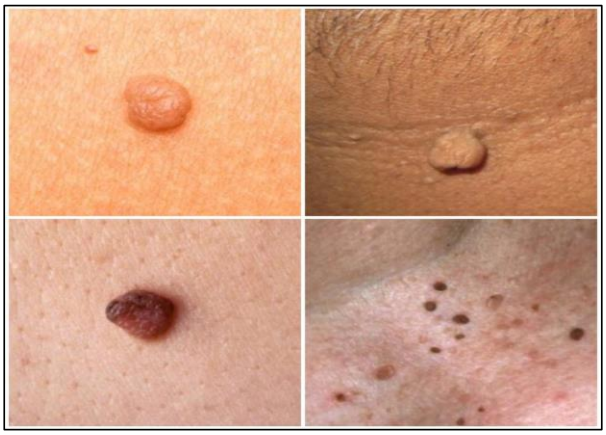






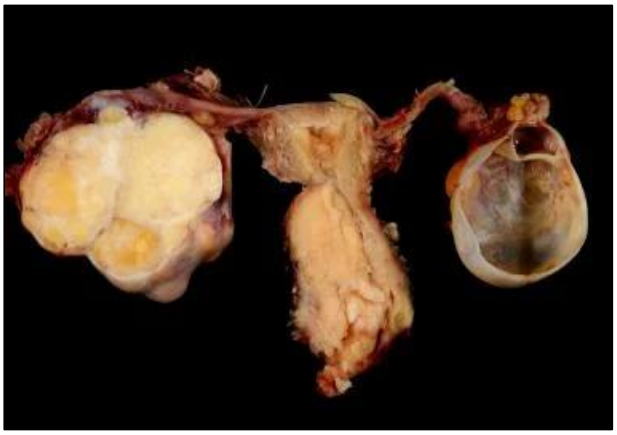
BENIGN TUMORS

- Usually **slow-growing** and **harmless,** unless they become large enough to disrupt nearby tissues or organs.
- A **tough capsule** surrounding the tumor prevents it from invading nearby tissues or spreading to other parts of the body.



MALIGNANT TUMORS

- Invades adjacent tissue
- Lacks surrounding capsule; likely to **metastasize**– meaning that its cells can break away from the original mass and travel in the bloodstream or lymphatic system to colonize other areas of the body.



Single cell – genetic mutations

Tumor develops

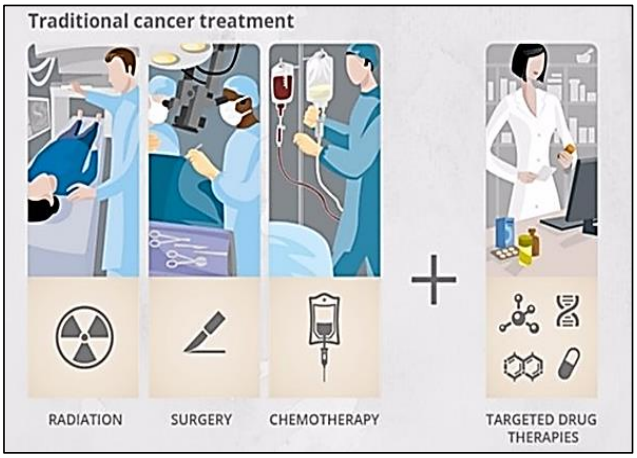
Daughter cells – no cell cycle control

Cancer cells divide uncontrollably

Crush vital organs, block passageways & divert nutrients from other body cells

CANCER TREATMENTS REMOVE OR KILL ABNORMAL CELLS

- Traditional cancer treatments include **surgical tumor removal,** drugs **(chemotherapy)** and **radiation.**



- **Chemotherapy drugs** usually delivered *intravenously,* are intended to stop cancer cells any where in the body from dividing.

- **Radiation therapy** uses directed steams of energy from *radioactive isotopes* to kill tumor cells in limited areas.

- ***Chemotherapy*** and ***radiation*** are relatively **"blunt tools"** that target rapidly dividing cells, whether cancerous or not.
- Examples of cells that divide frequently include those in the *bone marrow, digestive tract,* and *hair follicles.*
- The death of these cells accounts for the most notorious side effects of cancer treatment: *fatigue, weakened immune system, nausea and hair loss.*
- Fortunately, the healthy cells usually return after the treatments end.

- The success of any cancer treatment depends on many factors, including the **type of cancer** and the **stage** in which it is detected.
- **Surgery** can cure cancers that **have not spread.**
- Once cancer metastasizes, however, it becomes difficult to locate and treat all of the tumors.
- Moreover, DNA replication errors introduce mutations in rapidly dividing cancer cells.
- Treatments that shrank the original tumor may have no effect on this new changed growth.

GENES AND ENVIRONMENT BOTH CAN INCREASE CANCER RISK

- Proteins control both the cell cycle and apoptosis. Genes encode proteins, so **genetic mutations** *(changes in genes)* play a key role in causing cancer.
- So far, researchers know of hundreds of genetic mutations that contribute to cancer.
- *Where do the cancer-causing mutations come from?*
- Sometimes, a person **inherits mutated versions** of the genes from one or both parents.
- The parent may also have had cancer or mutations may have arisen spontaneously in sperm- or egg-producing cells.
- Often, however people develop cancer after **exposure to harmful chemicals, radiation,** and **viruses,** all of which may alter their genes.
- **Poor diet** and **exercise habits, sun exposure,** and **cigarette smoking** also raise cancer risks.

WHY WE CARE: SKIN CANCER

- Cancer has many forms, *some inherited* and others caused by *radiation or harmful chemicals.*
- **Exposure to ultraviolet radiation** from the sun or from tanning beds, for example, *increases the risk of skin cancer* because UV radiation damages DNA.
- If mutations occur in genes encoding proteins that control the pace of cell division, cells may begin dividing out of control, forming a malignant tumor on the skin.

HOW MIGHT A PERSON DETERMINE WHETHER A MOLE, SORE OR GROWTH ON THE SKIN IS CANCEROUS?

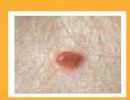
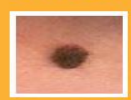
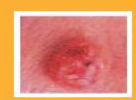
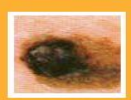
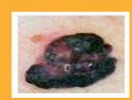
- The abnormal skin may vary widely in appearance and only a physician can tell for sure.
- Nevertheless, most skin cancers have a few features in common.
- "ABCDE" is a shortcut for remembering these four characteristics.

KNOW YOUR ABCDE's

A	B	C	D	E
ASYMMETRY	BORDER	COLOR	DIAMETER	EVOLUTION
				
One half does not match the other half	Uneven borders	Variety of colors like brown, tan, or black	Grows larger than the size of a pencil eraser (¼ inch)	Change in size, shape, color, elevation, another trait, or new symptom

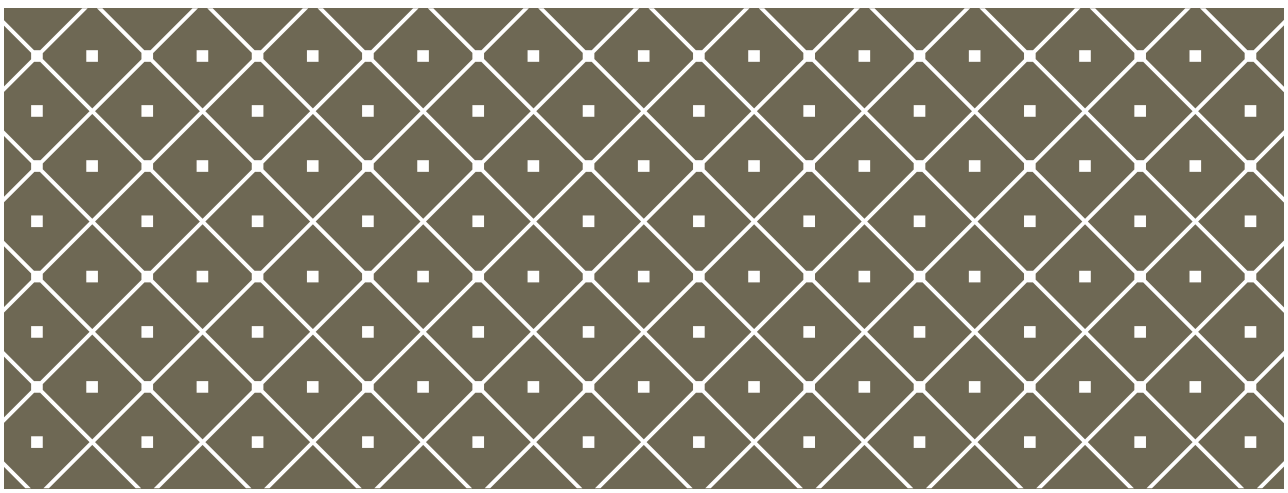
THE LAUREN SAVOY OLINDE FOUNDATION

KNOW YOUR ABCDE's

A	B	C	D	E
ASYMMETRY	BORDER	COLOR	DIAMETER	EVOLUTION
				
				
ONE HALF DOES NOT MATCH	UNEVEN BORDERS	VARIETY OF COLORS	LARGER THAN A PENCIL ERASER (1/4")	CHANGE IN SIZE, SHAPE, COLOR, ETC.

REDUCING CANCER RISK

RISK FACTOR	WAYS TO REDUCE RISK
Unhealthy diet	Eat less saturated fat; eat more fruits and vegetables
Obesity	Maintain healthy body weight; get regular, vigorous exercise
Tobacco use	Quit smoking or chewing tobacco or never start
Ultraviolet radiation	Avoid UV radiation from sunlight and tanning beds
Cancer-causing viruses	Use condoms to avoid sexually transmitted diseases (e.g. human papillomavirus associated with cervical cancer)
Detection time	Use self tests and medical exams for early detection
Family history	Cannot be avoided

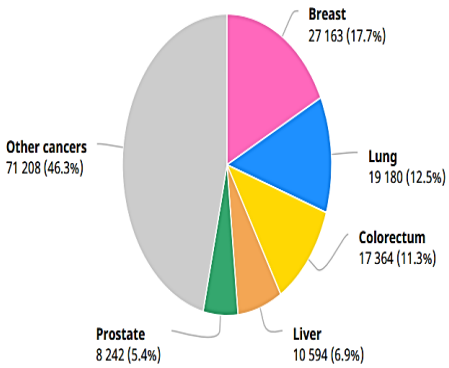


2020 PHILIPPINE CANCER FACTS AND ESTIMATES

Philippines

Source: Globocan 2020

Number of new cases in 2020, both sexes, all ages



Total: 153 751

Numbers at a glance

Total population

109 581 085

Number of new cases

153 751

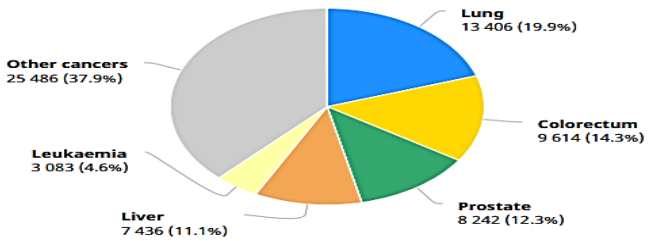
Number of deaths

92 606

Number of prevalent cases (5-year)

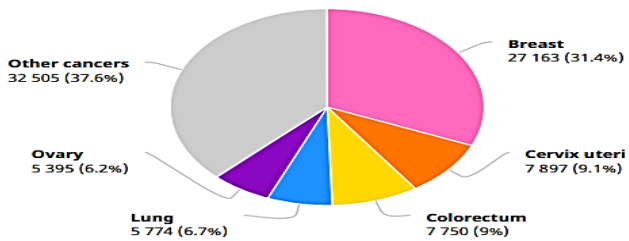
354 398

Number of new cases in 2020, males, all ages

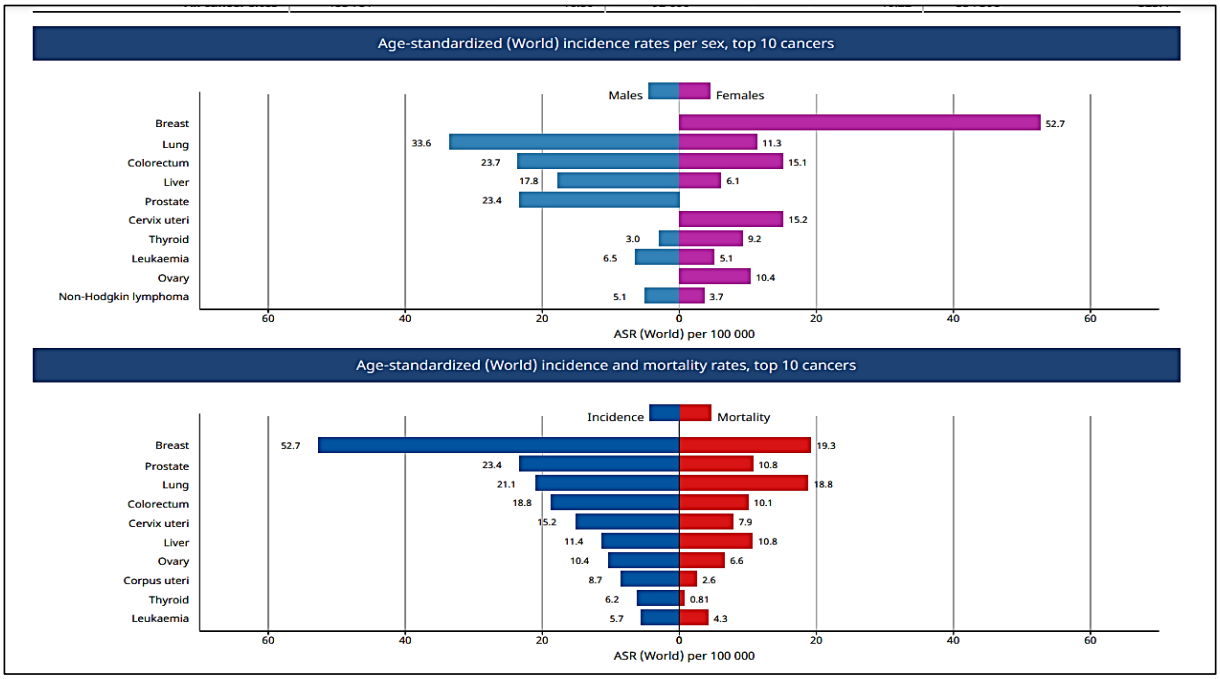


Total: 67 267

Number of new cases in 2020, females, all ages



Total: 86 484



CAN CANCER BE PREVENTED?

At least 1/3 of all cancers can be prevented.

Cancer protecting mechanisms prevent cancer. A healthy lifestyle that is started in childhood, particularly eating a HEALTHY DIET, maintaining PHYSICAL FITNESS and MINIMIZING/ PROPERLY COPING with STRESS may decrease the risk of cancer, coronary artery disease, hypertension, stroke and diabetes.

A **healthy diet** is ***low in animal fat, rich in starchy foods*** *(such as cereals, tubers and pulses)*, with ***substantial fruits*** and ***vegetables.***

The micronutrients found in fruits and vegetables, such as vitamins, minerals and trace elements, are essential in **maintaining the defense mechanisms** that protect the body.

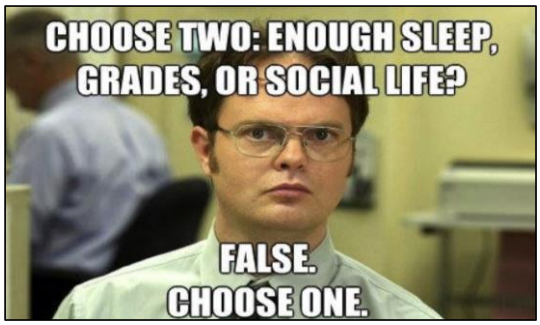
An unhealthy diet is rich in fat, salt and free sugars, and/or in smoked, salt-pickled/-preserved foods.

Physical fitness is achieved through a *lifelong active lifestyle*. Physically fit individuals are ***not overweight, quite productive,*** with ***high self-esteem,*** and ***successful in coping with stress.***

Formally **planned exercise** as well as usual walking, stair climbing, and myriad manual activities regularly performed result in physical fitness.

Increasing mental, social, psychological *and* ***spiritual stress*** seems to accompany economic progress, and at the same time coping mechanisms are eroded.

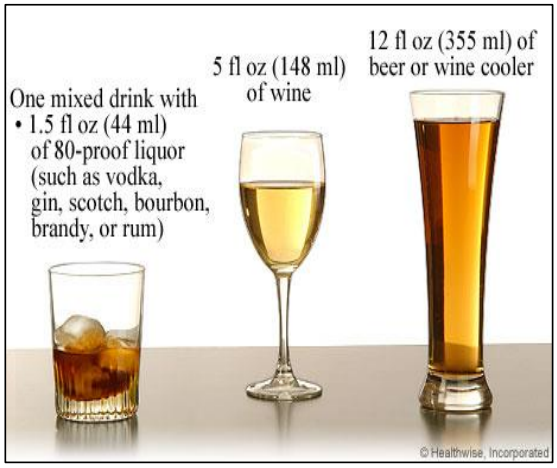
While increasing stress may be inevitable, *traditional support structures* within the family and community ought to be strengthened, and new institutional mechanisms established, to help individuals and families **cope with day to day stress.**

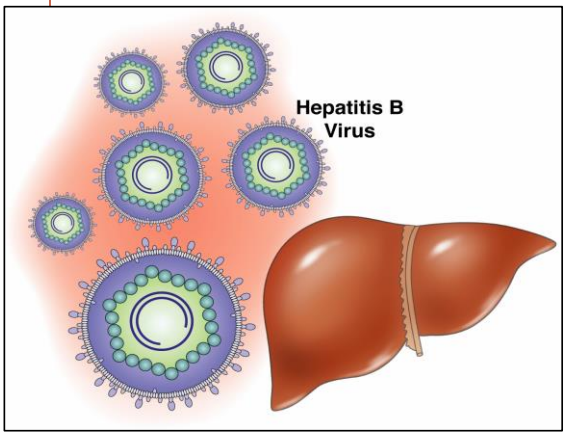


Cancer promoting agents should be avoided. **Cigarette smoke** is the most pervasive cancer causing substance. The numerous carcinogenic agents found in cigarette smoke cause cancers of the lung, mouth, pharynx, larynx, esophagus, other cancers, and other acute and chronic diseases.

The damage is not inflicted on the smoker alone but on everyone who inhales cigarette smoke (second hand smoke [SHS] or passive smoking).

High alcohol consumption also increases the risk of many cancers. Betel quid chewing causes cancer of the mouth and this habit should be avoided.





Some viral infections of the liver can result to chronic active hepatitis which can then lead to cirrhosis and liver cancer. **Hepatitis B virus (HBV)** is the most common cause of liver cancer in the Philippines. HBV vaccination should prevent majority of liver cancer in the country.

Human papilloma virus (HPV) causes cancer of the uterine cervix and is transmitted through sexual intercourse. Safe sex, including the use of barrier protective devices such as condoms, is currently the most effective means of preventing sexually transmitted diseases. HPV vaccines are available.

Ultraviolet rays from the sun are capable of causing skin cancer, particularly in fair-skinned persons. Excessive sun exposure should be avoided, and the use of umbrellas, wide-brimmed hats and sun-bloc preparations ought to be encouraged.

Many cancers of the LUNG, LIVER, CERVIX, ORAL CAVITY, STOMACH, COLON/RECTUM, LARYNX and SKIN MELANOMA, which comprise 42% of all cancers in both sexes, can be prevented.

CAN CANCER BE CURED?

At least 1/3 of all cancers can be cured.

Majority of cancers can be cured if they are **detected early.** However at present, not all cancers can be detected early enough to be cured. At least a third of all cancers can be cured when detected and treated early, and particularly when curative treatment is available.

These common cancers can be detected early and when treated properly can be cured - BREAST, CERVIX, COLON, RECTUM, ORAL, THYROID, PROSTATE. These comprise 42% of all cancers, 27% of cancers in males, and 58% of cancers among females.

WHAT ABOUT CANCERS THAT CAN NEITHER BE PREVENTED NOR DETECTED EARLY?

All cancer patients with distressful symptoms can have **adequate palliative care** that can result in an acceptable quality of life.

Palliative care is the active total care of patients whose disease is not responsive to curative treatment.

Palliative care affirms life and regards dying as a normal process that neither hastens nor postpones death, provides relief from pain and other distressing symptoms, integrates the psychological and spiritual aspects of patient care, offers a support system to help patients live as actively as possible until death, and offers a support system to help the family cope during the patient's illness and in their own bereavement.

7 SUCH BASICS SYMPTOMS INCLUDE:

C – change in bowel or bladder habits

A – a sore that does not heal

U – unusual bleeding or discharge

T – thickening or lump in breast or elsewhere

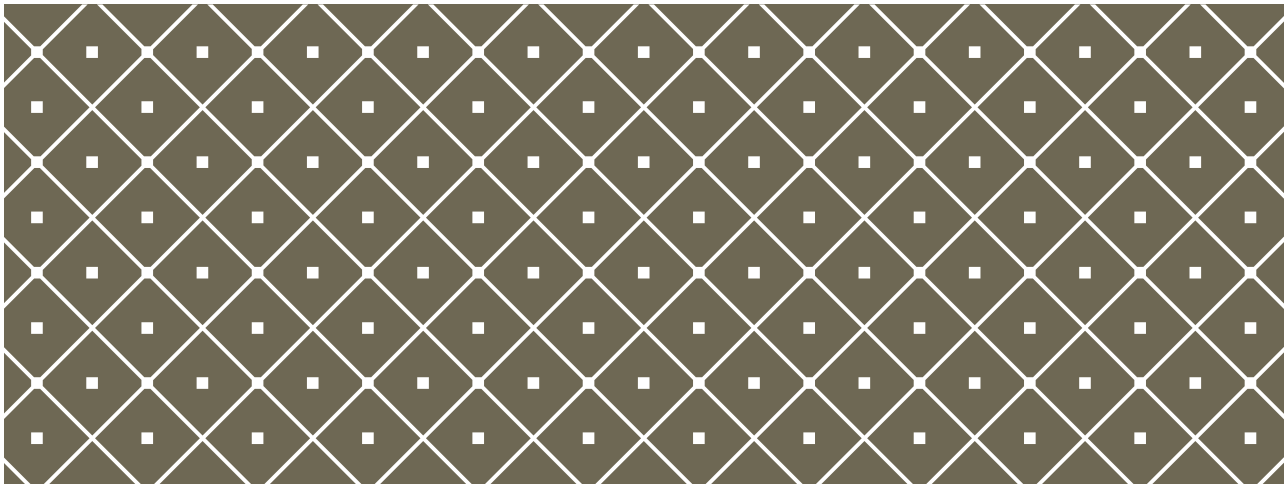
I – indigestion or difficulty in swallowing

O – obvious change in wart or mole

N – nagging cough or hoarseness

U – unexplained anemia

S – sudden unexplained weight loss



END OF LESSON 7