

Subject: Biology

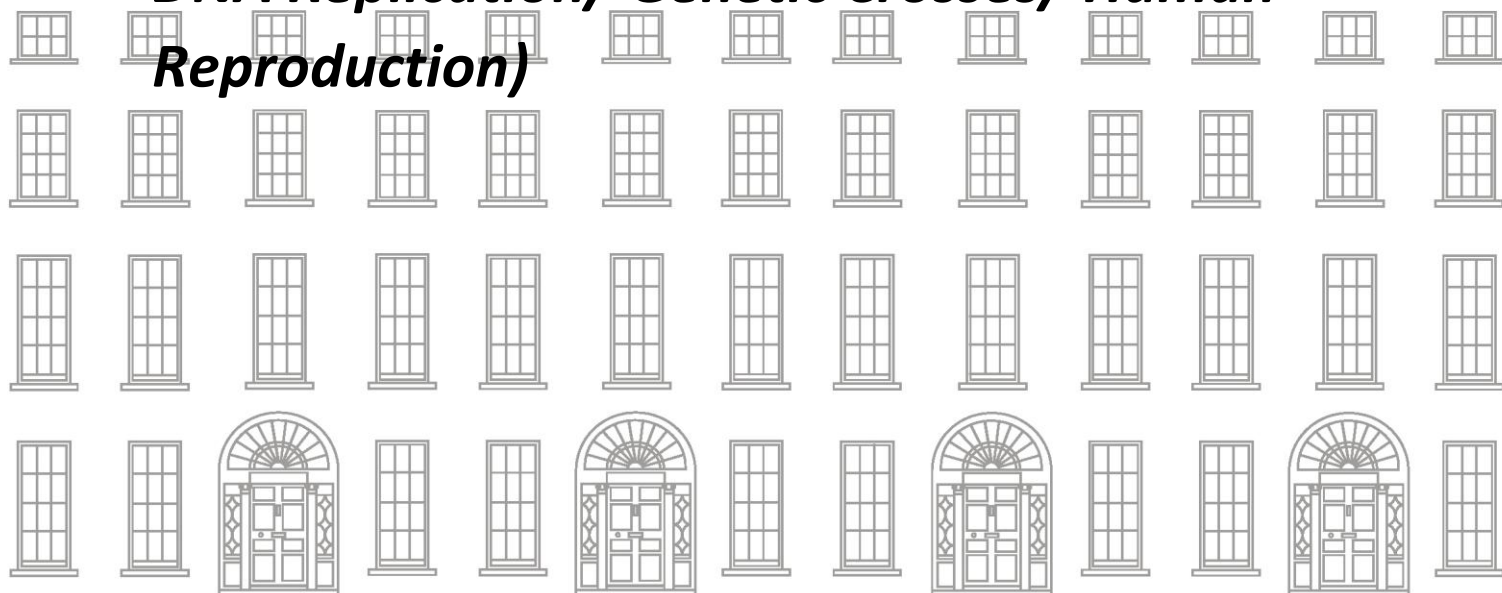
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COURSE: 5th/6th Year

ACADEMIC LEVEL: Higher

ACADEMIC YEAR: 26/27

***TOPIC: Strand 2.3 - Cell Division (linked to
DNA Replication/ Genetic Crosses/ Human
Reproduction)***



CONTENTS

Contents

Definitions.....	4
Science in Society	5
2 types of Cell Division.....	6
Comparing Mitosis Vs Meiosis.....	6
Sample Question.....	7
Cell Cycle.....	8
Sample Questions.....	9
Mitosis	11
Diagrams of stages of Mitosis.....	12
Sample Questions.....	13
Cancer.....	15
2 types of tumours.....	15
1. Benign	15
2. Malignant.....	15
Cancer Symptoms and Detection	16
Cancer Treatment.....	16
Cancer Prevention	16
Cancer Summary.....	16
Sample Question.....	17
Cell Division Revision Questions.....	18
New Course Exam Paper Questions	19
Old Course Exam Paper Questions	22



Definitions

Asexual reproduction: reproduction involving one parent

Cancer: cell loses control of the rate of mitosis

Cell continuity: cells arise from other pre-existing cells

Diploid: two sets of chromosomes or chromosomes in pairs

Haploid: a single set of chromosomes

Meiosis: type of cell division that results in four unidentical daughter cells; half the chromosomal number of the parent cell

Mitosis: type of cell division that results in two identical daughter cells; same number of chromosomes as the parent cell

Multicellular: a living organism composed of more than one (many) cells

Sexual reproduction: reproduction involving two parents

Species: interbreeding between organism to produce fertile offspring

Unicellular: a living organism composed of one cell

Variation: difference between member of the same species.



Science in Society

Health: Cancer

Technology: microscope to view cells undergoing cell division, X ray and MRI to cancer diagnostics

Sustainability: developing treatment for cancer and methods of cancer prevention e.g. HPV helps people live longer and not threaten life

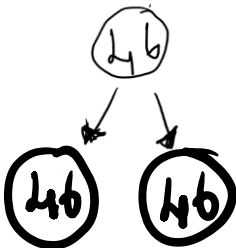
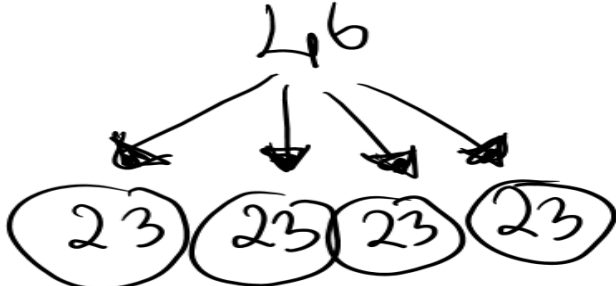


To ensure the ongoing existence of cells continuity is essential. Cell continuity is defined as cells arising from pre existing cells. This is achieved by cell division.

2 types of Cell Division

- Mitosis
- Meiosis

Comparing Mitosis Vs Meiosis

Mitosis	Meiosis
Location: nucleus of the cell (<u>cannot occur in cells that don't have genetic material e.g. red blood cells</u>)	Location: nucleus of a cell
Produces two genetically identical daughter cells. (daughter cells genetically identical to each other and to the parent cells). Daughter cells contain the same number of chromosomes as parent cells.	Produces four genetically unidentical daughter cells. (daughter cells different to the parent and to each other). Contain half the genetic information and half the chromosomal number of the parent cell
Products: same chromosomal number as parent (diploid to diploid or haploid to haploid)	Products: half chromosomal number of parents (diploid to haploid)
	
Functions: Unicellular Organism: <u>Asexual reproduction</u> Rhizopus: Sporulation Multicellular Organism: growth and repair Plants: meristem of root and shoot tip Animals: growth plate of bone	Functions: Unicellular: - <u>no function</u> Multicellular: 1. production of gametes in animals and plants. All gametes are haploid in their chromosomal content. • Animals: sex cells; sperm and egg. Sperm (location: testes) and egg (location: ovary). • Plants: sex cells; pollen and egg Pollen (location: anther) and egg (location: ovule) Mutations can only be passed on if they occur in a somatic cell which has undergone meiosis 2. gives rise to variation (<u>difference</u> between members of the <u>same species</u>)
Advantages of mitosis: Faster, genetically identical, desirable traits passed on	Advantages of meiosis: Gives rise to variation



Somatic cell: normal cells of the body containing pairs of chromosomes and carrying out normal body functions. Somatic cells contain 46 chromosomes (i.e. 23 pairs). **Chromosomes that appear in pairs or 2 sets of chromosomes are called diploid cells and are represented by the symbol $2n$.** **Therefore, diploid number of a typical human cell is $2n=23$**

Sex cell: examples include sperm and egg in animals, pollen and egg in plants. Contain half the genetic information of normal somatic cells (i.e. 23 chromosomes). **A single set of chromosomes is called a haploid cell and is represented by the symbol n . Therefore, the haploid number of a typical human sex cell is $n = 23$**

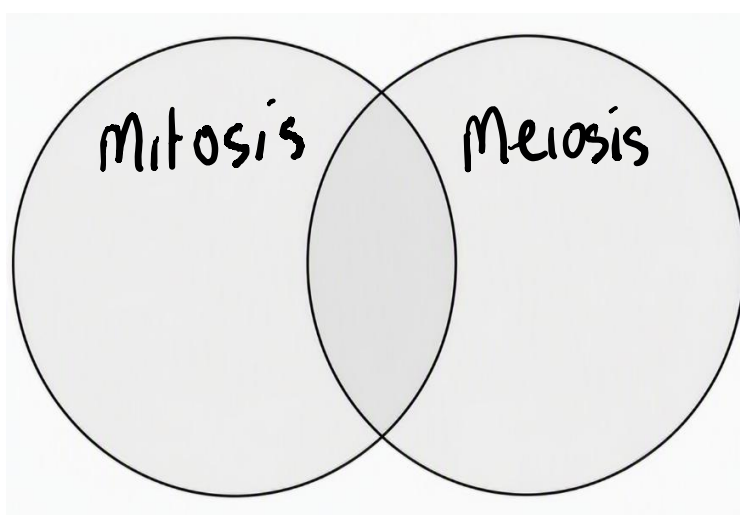
Sample Question

- (iv) Distinguish between mitosis and meiosis with reference to chromosome number and number of daughter cells by filling in the table below.

	Mitosis	Meiosis
Chromosome number		
Number of daughter cells		

- (v) Explain how meiosis contributes to genetic variation in multicellular organisms.

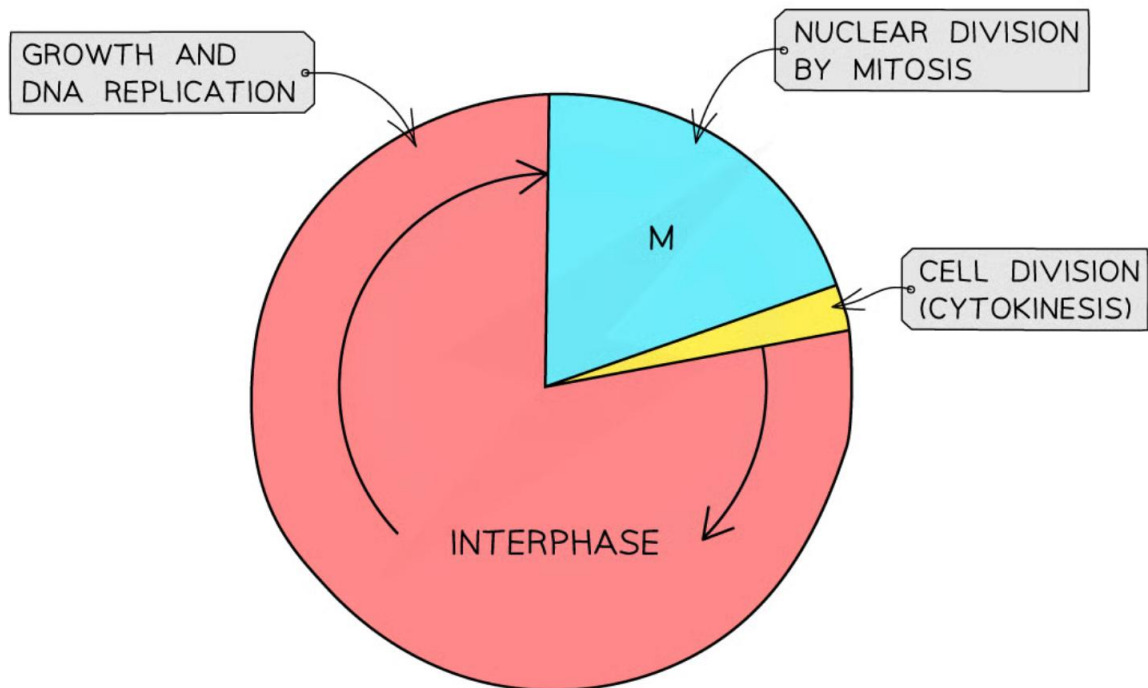
- a) Using the graphic, identify one similarity and two differences between mitosis and meiosis.



Cell Cycle

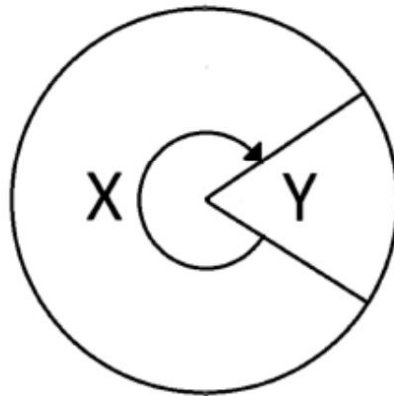
3 stages (100%):

1. Interphase (90%): cell metabolism, cell organelle replication, DNA replication
2. Mitosis (7%): nuclear division composed of prophase, metaphase, anaphase, telophase (PMAT).
3. Cytokinesis (3%): cell division: cleavage furrow formation (animal cell), cell plate formation (plant cell).



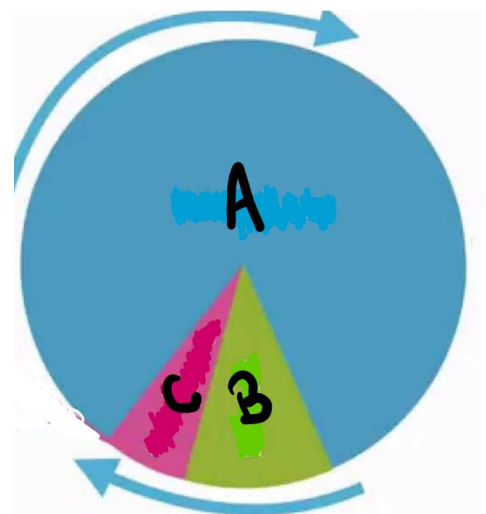
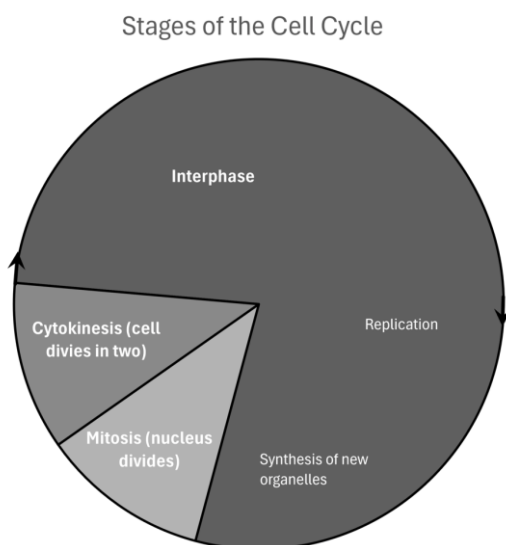
Sample Questions

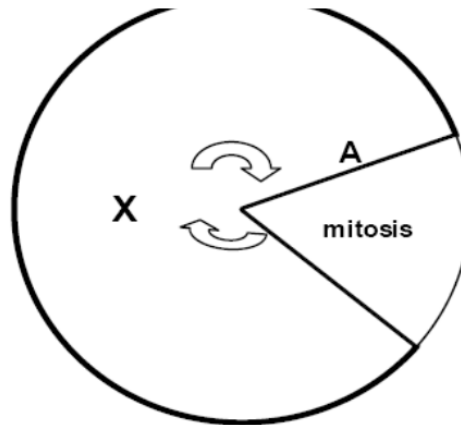
The diagram represents the cell cycle.



(a) What stage of the cell cycle is represented by X?

Label the parts of the graphic that represents the stages of cell cycle.





- (a) What stage of the cycle is represented by X?
- (b) Give the names of the two processes involving DNA which take place during stage X.
 1..... 2
- (c) For convenience of study, mitosis is divided into four stages. List these in order starting at A.

Mitosis

- Nucleus dividing
- Four stages: prophase, metaphase, anaphase, telophase
- To observe the stages of mitosis, the cells must be placed under a light microscope
- Cell from a root tip of an onion often used as they are easy to see under the microscope and their division is active and frequent increasing the chances of observing all four stages of mitosis.

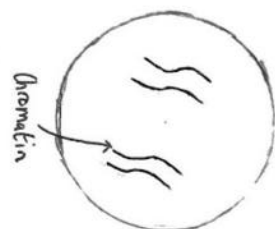
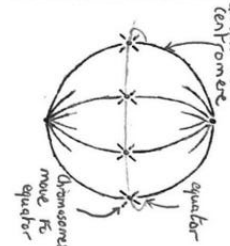
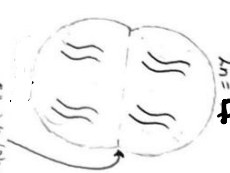
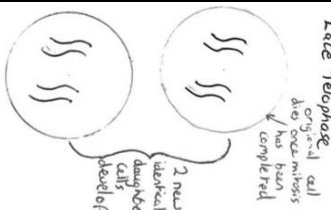
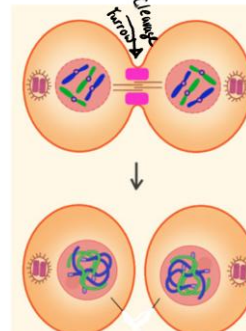
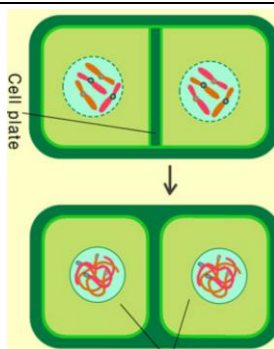
Sample Question

Explain why onion tips are commonly used when preparing slides to view mitosis under the microscope.



Diagrams of stages of Mitosis

Diagrams representative of $2n=4$ (diploid number adds up to 8 i.e. 4 pairs of chromosomes)

Interphase (90%)	Prophase	Metaphase	Anaphase	Telophase	Cytokinesis (3%)
Interphase $2n=2$ Diploid number  Chromatin	Early Prophase $2n=2$ Chromatin shorten/condense Nuclear membrane breaks down Late Prophase $2n=4$ Spindle fibres develop Centromere Chromosomes replicate + connected by centromere	Metaphase $2n=4$ Spindle fibres attach to centromere Equator Chromosomes move to equator 	Anaphase Spindle fibres contract separating chromosomes 	Early Telophase $2n=4$ Cell plate (don't) (large furrow/indent)  Late Telophase Original cell has been completed 2 new identical daughter cells develop 	Animal - Cleavage Furrow  Plant - Cell Plate 
Not a stage of mitosis. - Chromosomes appear as long skinny structures known as chromatin. - Cell carries out its regular function. Reactions that take place during this time include; respiration, protein synthesis (transcription), cell organelle replication, DNA replication.	- Nuclear membrane disintegrates and disappears. - Chromatins shorten, thicken to become known as chromosomes and become double stranded. - Point at which two chromosomes join called centromeres. - Spindle fibres develop.	Chromosomes line up on equator, and spindle fibres attach at centromere.	- Spindle fibres contract and shrivel causing the chromosomes to pull apart and separate. - Role of Spindle fibres: to separate chromosomes.	New membrane forms around separated chromosomes to form to two identical daughter nuclei.	- A membrane starts to burrow its way down through the cytoplasm to separate the two nuclei and create two identical daughter cells. This membrane formation in a plant cell is known as a "cell plate". In an animal cell is known as a "cleavage furrow". - The process of producing 2 new identical daughter cells is known as cytokinesis.

Sample Questions

Study the diagrams which show the stages of mitosis in plants and answer the following questions.
(The stages are not in the correct order.)

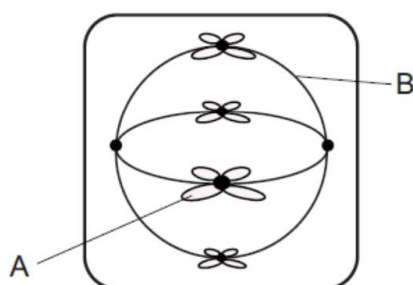


- (a) List the stages of mitosis shown in the diagrams above in the correct order, starting with interphase.

- (b) Name stage E and describe what is happening to the chromosomes in this stage.

E _____ What is happening _____

The diagram shows a stage of mitosis.



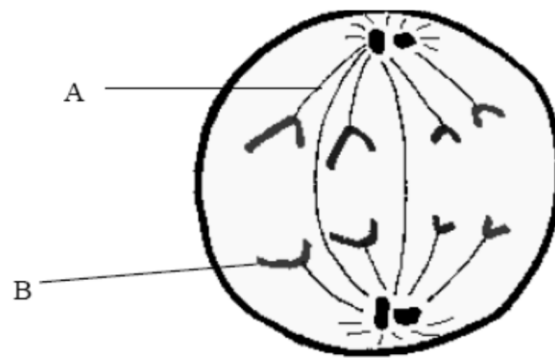
- (a) Identify the stage of mitosis shown in the diagram.

- (b) Name the parts labelled A and B.

A _____

B _____

The diagram shows a stage of mitosis.



(a) Name this stage of mitosis.

(b) Give a feature from the diagram which allowed you to identify this stage.

(c) Name the parts of the diagram labelled A and B.

A. _____

B. _____

Cancer

When cells lose control of the rate of mitosis (happens too fast). This often results in the formation of tumours (growth/mass of cells).

2 types of tumours

1. Benign
2. Malignant

1. Benign

- Tumour after some time stops dividing by mitosis and stops grow in size.
- It does not migrate (move away) from the tissue which it originated.
- Generally, not harmful
- e.g. wart, cyst (on ovaries)
- Causes: often unknown, genetics, mutations, hormones, environment (e.g. sun exposure) age, any other valid.

2. Malignant

- tumour never stops dividing by mitosis and never stops increasing in size.
- Known as cancer
- Part of the tumour can sometimes break away from the original tissue/tumour and migrate to a new location (secondary tumour/cancer)
- May be harmful and potentially cause death
- Causes:
 - Oncogenes (genes responsible for malignant tumour/ cancer e.g. BRCA genes responsible for types of breast and ovarian cancer)
 - Mutations
 - Infectious agents (viruses e.g. HPV responsible for cervical cancer)
 - Lifestyle carcinogens (chemical responsible for malignant tumour/cancer e.g. smoking cigarettes, drinking alcohol)
 - Environment carcinogens (environmental chemicals responsible for malignant tumours/cancer e.g. UV and radiation exposure)
 - Any other valid.



Cancer Symptoms and Detection

- Self-examination e.g. breast check for lumps, stool and urine observation for blood, change in bowel and bladder movements, loss of appetite, shortness of breath, deterioration of vision, fatigue
- Screening Programmes e.g. Breast check, prostate cancer screening
- Blood tests, urine tests, hormonal checks
- X ray and MRI

Cancer Treatment

- Surgery: physical remove the tumour
- Chemotherapy: chemicals that kill cancer cells
- Radiotherapy: radiation that kills cancer cells
- Immunotherapy: use of white blood cells to attack the tumour

Cancer Prevention

- Balanced diet
- Avoid alcohol
- Avoid smoking cigarettes
- Increase exercise
- Vaccines e.g. HPV vaccine prevents people getting cervical cancer caused by HPV virus. A vaccine is a small dose of an inactive virus that will stimulate an immune response.
Discussed in further detail in the immunity chapter.

Cancer Summary

Causes	Symptoms	Detection	Treatment	Prevention
• Oncogenes • Mutations • Infectious agents (e.g. viruses) • Lifestyle carcinogens e.g. smoking cigarettes, drinking alcohol) • Environment carcinogens (e.g. UV and radiation exposure) • Any other valid.	• Lumps • Blood in urine/stool • Fatigue • Loss of appetite • Shortness of breath • Impaired vision	• Blood Tests • X rays • MRI • Hormone	• Surgery • Chemotherapy • Radiotherapy • Immunotherapy	• Balanced diet • Avoid alcohol • Avoid smoking cigarettes • Increase exercise • Vaccines

Sample Question

Evaluating Cancer Risk Factors

1. Of the causes of malignant tumours listed above (oncogenes, mutations, infectious agents, lifestyle carcinogens, environmental carcinogens), identify **two** that an individual could realistically reduce through their own choices, and **two** that an individual has little or no control over. Justify your groupings.

2. Complete the table below for **two** different causes of cancer from the list above.

Cause	Type (genetic / infectious / environmental / lifestyle)	Degree of individual control (none / partial / high)	Example prevention or reduction strategy

3. Explain why early detection (e.g. screening programmes, self-examination) is described as a way to *manage the impact* of cancer, whereas lifestyle changes are described as a way to *reduce the risk* of cancer developing in the first place. What is the biological difference between these two approaches?



Cell Division Revision Questions

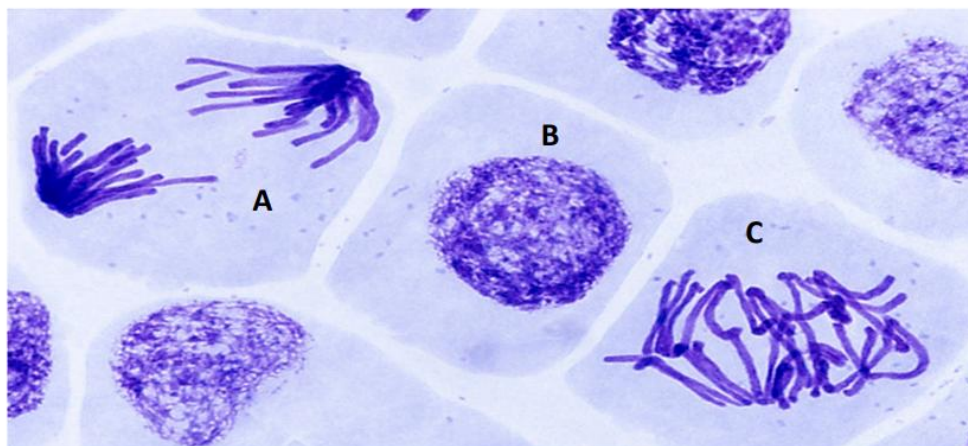
1. Define Mitosis.
2. State a function of mitosis in a single celled/unicellular organism.
3. State a function of mitosis in a multicellular organism.
4. Identify a location of mitosis in a flowering plant (a multicellular organism).
5. Identify the location of mitosis in an animal (a multicellular organism).
6. Explain the term unicellular with respect to living organisms.
7. Explain the term multicellular organism.
8. Mitosis occurs in eukaryotic organisms. Explain the term "eukaryote".
9. Explain why mitosis cannot occur in red blood cells.
10. Identify the type of cell division involved in tissue culturing.
11. What is the corresponding term to a eukaryotic organism.
12. Define the term "diploid number".
13. What is the symbol to represent diploid number?
14. The diploid number of the nucleus of a cell is $2n=6$. Identify how many pairs of chromosomes would be present in the cell
15. What is the diploid number of a typical human cell.
16. Identify the three stages of the cell cycle.
17. Use a labelled diagram to model the three stages of the cell cycle.
18. Name the stage of a cell's cycle when it is not engaged in mitosis.
19. Cell organelles replicate when the cell is not undergoing mitosis. Identify two such cell organelle.
20. Identify two biochemical reactions that are happening during the stage when the cell is not undergoing mitosis.
21. What percentage of a cell's life will the cell not engage in mitosis?
22. Identify the location of mitosis in a cell.
23. List the stages of mitosis in order.
24. Chromosomes are structures involved in mitosis. Identify the biomolecules from which chromosomes are composed.
25. Describe two events that are happening during prophase of mitosis.
26. Name the stage of mitosis where the chromosomes are lined up on the equator and spindle fibres are attached to the chromosomes at the centromeres.
27. Draw a labelled diagram of anaphase for $2n=5$.
28. Name the membrane formed in a plant cell towards the end of mitosis.
29. In what type of cell is a cleavage furrow formed toward the end of mitosis.
30. Identify the stage of the cell cycle when a cleavage furrow is formed.
31. Explain your understanding of "cytokinesis".
32. Define Cancer.
33. Identify 3 possible causes of cancer.
34. There is only one type of cell in the human body that chromosomes are not present in pairs (diploid number); identify this type of cell and the location of named cell
35. Explain the term haploid number.
36. What is the symbol to represent haploid number?
37. Explain the term "meiosis"
38. Identify a role of meiosis in a multicellular organism.
39. Does meiosis have a role in a unicellular organism?
40. A cell with a diploid number of $2n=6$ undergoes meiosis followed by mitosis. How many chromosomes will be present at the end of the cell division process?



New Course Exam Paper Questions

Sample Paper 2- HL

- (a) The light microscope image below is of cells in a garlic root tip at different stages in the cell cycle. Mitosis is one part of the cell cycle and is followed by cell division. Analyse the image and answer the questions that follow.



- (i) Identify **both** stages of **mitosis** that each of the cells labelled **A** and **C** are undergoing.

A:

C:

- (ii) Identify the stage of the **cell cycle** that the cell labelled **B** is undergoing.

- (iii) On the image above, write the letter **X** on the location of a cell membrane.

- (iv) Uncontrolled cell division can lead to cancer.

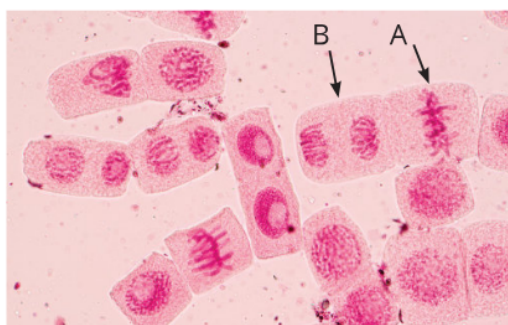
Name **two** environmental risk factors that increase the chance of cancer development.

1.

2.

Examcraft Sample Paper E

- (a) The diagram below shows onion root tip cells in different stages of division.



- (i) Name the **two** stages of mitosis labelled **A** and **B** in the diagram above.

A:
B:

- (ii) Describe **one** event that occurs in cells during **each** of the stages **A** and **B**.

A.	
B.	

- (iii) Explain why onion root tips are commonly used when preparing slides to study mitosis.

Examcraft Sample Paper H

- (iii) In the space below, draw a diagram to show a diploid cell, where $2n = 6$, during anaphase of mitosis.

- (iv) Distinguish between mitosis and meiosis with reference to chromosome number and number of daughter cells by filling in the table below.

	Mitosis	Meiosis
Chromosome number		
Number of daughter cells		

- (v) Explain how meiosis contributes to genetic variation in multicellular organisms.

- (vi) Name the process by which the cytoplasm divides **and** give a brief description of that process in an animal cell.

Process:
Description:

Old Course Exam Paper Questions

2022 Q14 (c)

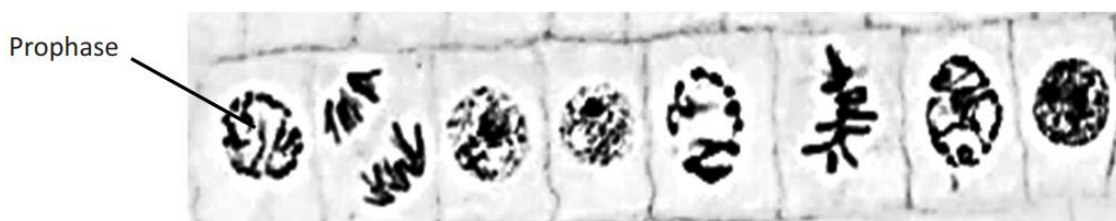
- (c) Interphase and mitosis occur during the cell cycle.
The process of mitosis occurs over four phases (prophase, metaphase, anaphase and telophase).
- (i) Describe **two** events that occur during prophase.
 - (ii) Describe **one** event that occurs during metaphase.
 - (iii) Draw a large labelled diagram of a cell with a diploid number of four at anaphase of mitosis.
 - (iv) At the end of mitosis, the cell divides.
Describe how cell division occurs in an animal cell **and** in a plant cell.

(24)

2019 Q4



- The photograph below is of plant cells undergoing different stages of mitosis. The cells are not shown in any particular order.



- (a) Which type of microscope is used in the school laboratory to observe cells like these?

--

- (b) The first cell is in prophase. Give two observable events that happen during prophase.

1.
2.

- (c) On the photograph, use the letter **M** to label a cell that is undergoing metaphase.

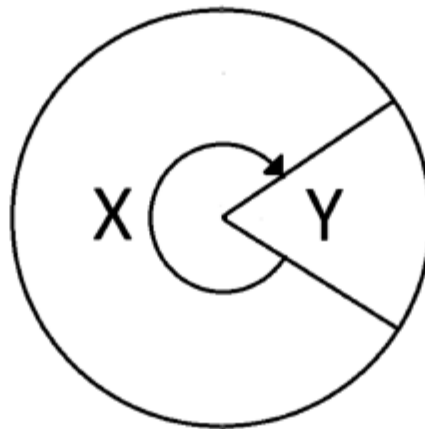
- (d) On the photograph, use the letter **A** to label a cell that is undergoing anaphase.

- (e) After mitosis, the cell divides in two.
This happens differently in animal cells and in plant cells.
Describe what happens in animal cells **and** in plant cells during this stage.

Animal cells.
Plant cells.

2018 Q3

3. The diagram represents the cell cycle.



(a) What stage of the cell cycle is represented by X?

(b) There are two types of cell division, mitosis and meiosis. Define *mitosis*.

(c) State **two** ways in which meiosis differs from mitosis.

1.

2.

(d) Explain the term *cancer*.

2017 Q6

- (a) What term is used to describe the long stage of the cell cycle when cell division is not occurring?

- (b) Name two types of biomolecule that are produced in the cell during this stage of the cell cycle.

(i) _____

(ii) _____

- (c) Name one organelle that is replicated at this stage of the cell cycle.

- (d) Give any two other changes which will have occurred in the cell by the end of this stage of the cell cycle.

(i) _____

(ii) _____

- (e) Suggest why mature human red blood cells do not undergo cell division.

2015 Q4

Indicate whether the following statements are true or false by placing a tick (✓) in the appropriate box in each case.

- (a) Meiosis is an important source of variation.
- (b) Mitosis occurs in mature red blood cells in humans.
- (c) During mitosis the nuclear membrane temporarily disappears.
- (d) Meiosis gives rise to the haploid condition.
- (e) In multicellular organisms mitosis functions primarily in growth.
- (f) In plants, a cell plate forms during telophase of mitosis.
- (g) The human zygote divides by meiosis.

True	False
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐



2013 Q11 (c)

(c) Answer the following questions, which relate to events in the cell cycle.

(i) What name is applied to the period of the cell cycle in which division is not taking place?

(ii) Give a cellular process that occurs during this period in which the nucleus is not dividing.

(iii) Draw a labelled diagram to show the position of the chromosomes during metaphase of mitosis in a nucleus in which $2n = 6$.

(iv) 1. State a function of one of the structures, other than chromosomes, that you have labelled in your diagram of metaphase.

2. How does the structure carry out this function?

(v) What term is used for the group of disorders in which control has been lost over the rate of mitosis?



2011 Q2

2. Use your knowledge of mitosis to answer the following questions:

(a) What is the role of mitosis in single-celled organisms?

(b) What medical term is used for the group of disorders in which certain cells lose normal control of Mitosis? _____

(c) Suggest a possible cause of one of the group of disorders referred to in (b).

(d) Name the stage of mitosis in which the chromosomes are located at the equator of the cell and before they begin to separate.

(e) To what are the chromosomes attached in the stage of mitosis referred to in (d)?

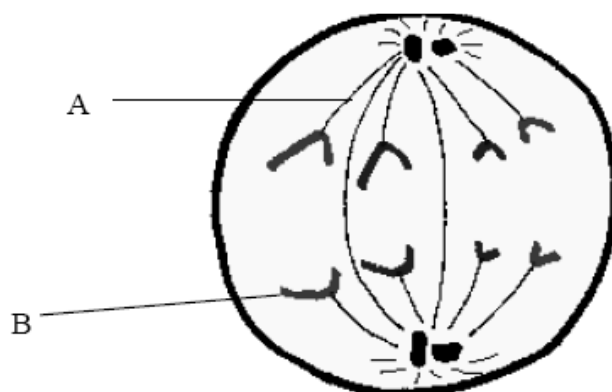
(f) Towards the end of mitosis, in what type of cell does a cell plate form?

(g) Give one way in which mitosis differs from meiosis.



2009 Q5

The diagram shows a stage of mitosis.



(a) Name this stage of mitosis.

(b) Give a feature from the diagram which allowed you to identify this stage.

(c) Name the parts of the diagram labelled A and B.

A. _____

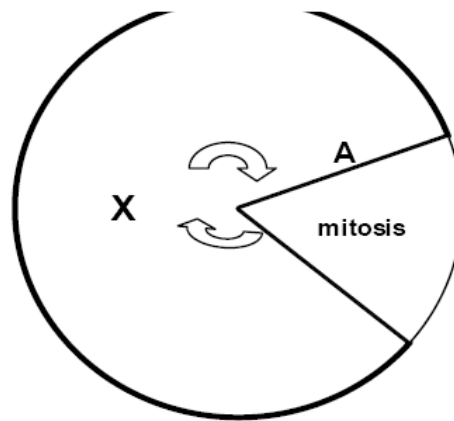
B. _____

(d) What is the function of mitosis in single-celled organisms?

(e) Give one function of mitosis in multicellular organisms.

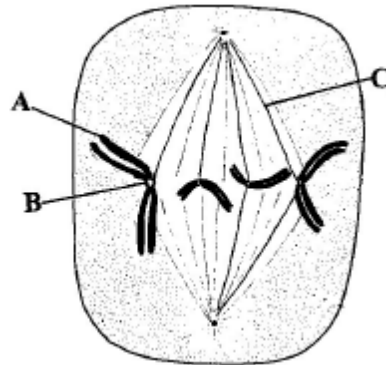
(f) Give one location where mitosis occurs in flowering plants.

2008 Q2



- (a) What stage of the cycle is represented by X?
- (b) Give the names of the two processes involving DNA which take place during stage X.
1..... 2
- (c) For convenience of study, mitosis is divided into four stages. List these in order starting at A.
.....
- (d) In which of the stages of mitosis that you have listed in (c) would you expect to see the spindle fibres contracting?
- (e) Explain the term diploid number
.....
- (f) What term is used to describe a group of disorders of the body in which cells lose the normal regulation of mitosis?

2007 Q3



(a) Name A, B and C.

A..... B C

(b) What stage of mitosis is shown?

Give a reason for your answer.

(c) What is the diploid number of this nucleus which is undergoing mitosis?

(d) Give a role of structure A.

(e) Some cells in the human body undergo meiosis. Give one function of meiosis.....

2005 Q5

(a) In the space below draw a diagram of a nucleus during metaphase of mitosis where $2n = 6$.

Label the spindle and a centromere in your diagram.

(b) State a function of mitosis in a single-celled organism.

.....

(c) State a function of mitosis in a multicellular organism

.....

(d) State one way in which mitosis differs from meiosis.

.....

(e) When the normal control of mitosis in a cell is lost, cancer may result. Suggest two possible causes of cancer.

1.....2.



Examcraft 2014

The diagram shows a diploid cell undergoing **anaphase** during mitosis.

- (a) Label clearly on the diagram the location of the equator of the cell.



- (b) Explain why the chromosomes are being pulled to opposite ends of the cell.

- (c) Explain what is meant by the term *diploid*.

- (d) In what group of organisms does mitosis normally result in growth?

- (e) Explain under what circumstances mitosis can result in cancer developing.

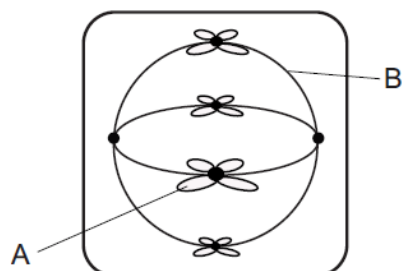
- (f) Some organisms also use a second type of cell division called meiosis. Give **two** functions of meiosis in such organisms.

- (i)

- (ii)

DEB 2017

The diagram shows a stage of mitosis.



- (a) Identify the stage of mitosis shown in the diagram.

- (b) Name the parts labelled A and B.

A _____

B _____

- (c) Explain the significance of mitosis in single-celled organisms.

- (d) Once mitosis is complete, the cell divides. What is this process called in the case of animal cells?

- (e) What does the term *cancer* mean in relation to cells?

- (f) Suggest **two** possible causes of cancer.

(i) _____

(ii) _____

DEB 2014

Study the diagrams which show the stages of mitosis in plants and answer the following questions.
(The stages are not in the correct order.)



- (a) List the stages of mitosis shown in the diagrams above in the correct order, starting with interphase.

- (b) Name stage E and describe what is happening to the chromosomes in this stage.

E _____ What is happening _____

- (c) In bees, females are diploid and males are haploid. This means females produce gametes by meiosis but males produce gametes by mitosis. Distinguish between:

1. Diploid and haploid _____

2. Meiosis and mitosis _____

- (d) Give one function of mitosis in multi-cellular organisms.

Examcraft 2016

- (a) Explain what is meant by the term *cell continuity*.

- (b) What is the main function of mitosis in multicellular organisms?

- (c) Name the stage of mitosis during which the chromatin begins to condense.

- (d) What name is given to the part of the cell cycle during which no cell division is taking place?

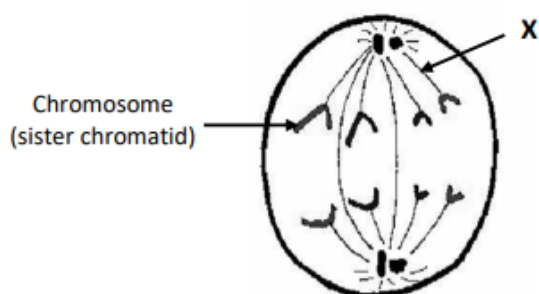
- (e) Towards the end of mitosis, in what type of cell does a cleavage furrow form?

- (f) Name the group of disorders that arise if normal regulation of mitosis is lost.



2021 Q3

3. The diagram shows a nucleus of a diploid cell undergoing one stage of mitosis. Answer the following in relation to mitosis.



- (a) Name the stage of mitosis shown in the diagram.

- (b) Justify your answer at part (a) above.

- (c) Identify the part labelled X in the diagram.

- (d) Explain the term *diploid*.

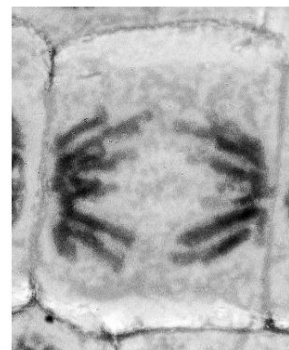
- (e) What is the diploid number of this cell?

- (f) Outline **one** function of mitosis in humans.

- (g) Give **one** example of a human cell not produced by mitosis.

2024 Q17 (d)

- (d) The image shows a stage of mitosis in an onion cell.
Mitosis is a stage of the cell cycle.



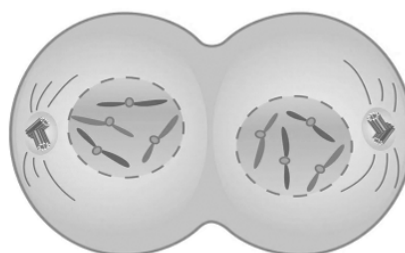
- (i) What name is given to the stage of the cell cycle when the cell is in a state of non-division?
- (ii) Give any **two** cell activities that occur during the state of non-division.
- (iii)
 1. What name is given to the stage of mitosis shown in the image?
 2. Explain how you know it is this stage.
- (iv) What stage of mitosis occurs immediately before the stage you named in (d) (iii) 1. above?
- (v) Sketch a diagram of a cell with a diploid number of 4 (i.e. $2n = 4$) that is at the stage of mitosis you named at part (d) (iv) above.
- (vi) What is the function of mitosis in multicellular organisms such as the onion?
- (vii) What name is given to the group of disorders where a cell loses control of mitosis and the number of cell divisions?

2025 16 (c)

- (c) The cell cycle involves interphase and mitosis.

- (i) What is interphase?
- (ii) Name a cell activity that occurs during interphase.
- (iii) The diagram shows a stage of mitosis.

1. Name the stage shown.
2. What is the diploid number of this cell?
3. Draw a series of labelled diagrams of this cell as it would appear during the **other three** stages of mitosis.



- (iv) Meiosis is another type of cell division.
Give **two** ways in which meiosis is different to mitosis.