

Cambridge AS & A Level · Biology 9700 · Notes

The mitotic cell cycle

AS

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Last checked 30 September 2026

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What you need to know

By the end of this topic you should be able to:

1. **Describe the structure of a chromosome:** DNA, histones, sister chromatids, centromere and telomeres.
2. **Explain why mitosis matters:** genetically identical cells for growth, replacement of cells, repair of tissues and asexual reproduction.
3. **Outline the mitotic cell cycle:** interphase (G1, S, G2), mitosis, cytokinesis.
4. **Outline how telomeres stop genes being lost** when DNA is replicated.
5. **Outline how stem cells replace cells and repair tissues** by mitosis.
6. **Explain how uncontrolled cell division can form a tumour.**
7. **Describe what the chromosomes, nuclear envelope, cell surface membrane and spindle do** in each stage of mitosis, in plant and animal cells.
8. **Interpret photomicrographs, diagrams and slides** of dividing cells, and identify the stages of mitosis.

Meiosis, and the detailed chemistry of how DNA is copied, belong to other topics. You don't need the words kinetochore or centrosome.

Understand it

Why cells divide by mitosis

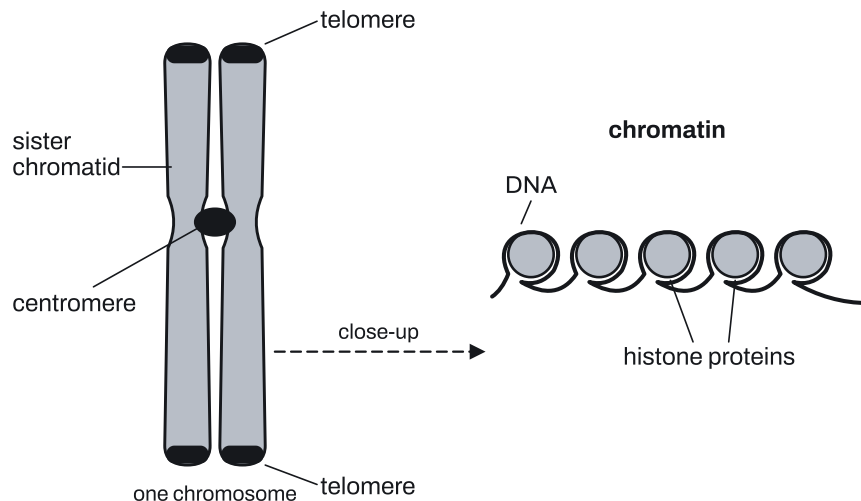
Mitosis is the division of the nucleus that gives two nuclei with **exactly the same genetic information** as each other and as the parent nucleus: the same number of chromosomes, carrying the same genes and alleles. Organisms need this whenever they want more cells of the same kind:

- **growth** of a multicellular organism: a zygote becomes billions of cells, and a root or shoot gets longer;
- **replacement** of cells that are damaged or die: skin cells, the lining of the gut, red blood cells;
- **repair of tissues** by making new cells to fill the damaged area, such as a cut in the skin or a broken bone;
- **asexual reproduction**: one parent makes genetically identical offspring (clones), for example a new plant growing from a runner.

The structure of a chromosome

Each chromosome is one very long DNA molecule. The DNA is wound around small proteins called **histones**, and the DNA and histones together are called **chromatin**. In interphase the chromatin is spread out through the nucleus, so separate chromosomes can't be seen.

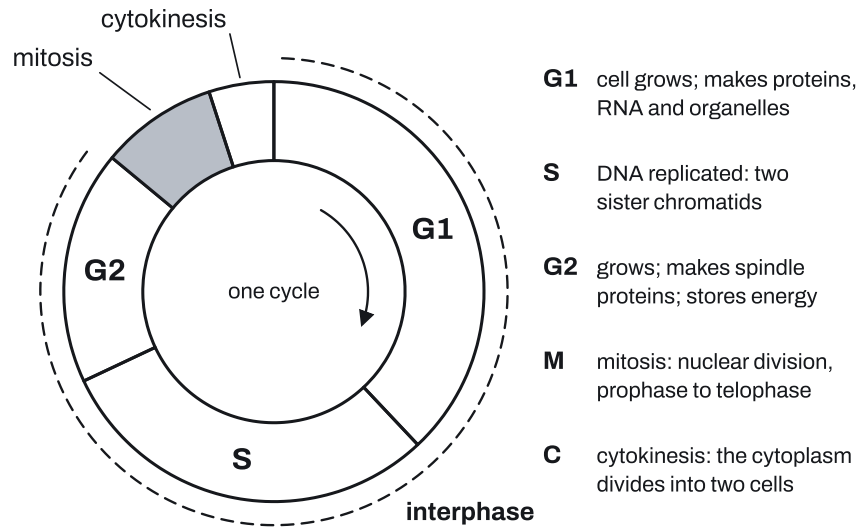
Before a nucleus divides, the chromatin **coils and condenses** into short, thick chromosomes that take up stain and are visible with a light microscope. By then each DNA molecule has been copied, so a chromosome at the start of mitosis is made of two identical **sister chromatids**, each one DNA molecule.



- **Sister chromatids:** the two identical copies made when the DNA was replicated. Each has one DNA molecule (a double helix, so two polynucleotide strands).
- **Centromere:** the narrow region that holds the sister chromatids together from S phase until anaphase. The spindle fibres attach to the chromosome here, and when it divides in anaphase one chromatid goes to each pole.
- **Telomeres:** long, repeated, non-coding DNA sequences at each **end** of each chromatid. A replicated chromosome has **4** telomeres; an unreplicated one (one chromatid) has **2**.

The cell cycle

The **mitotic cell cycle** runs from when a cell is made until it has divided into two.



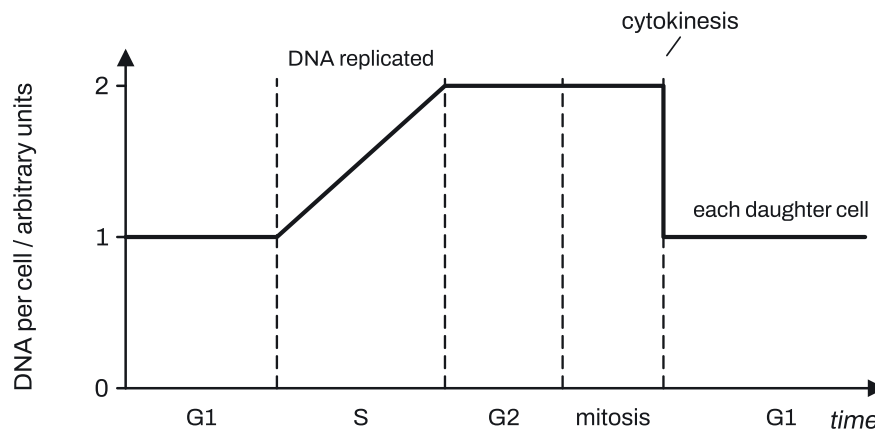
Interphase is most of the cycle. The cell is very active, but the nucleus is not dividing. All through interphase, G1 included, the cell respire and makes ATP for its growth and synthesis. How long interphase lasts varies: a cell can stay in interphase (usually G1) for a long time, even for the rest of its life, doing its normal job without dividing.

- **G1** (first growth phase): the cell grows. It transcribes genes (RNA polymerase) and makes proteins (including the enzymes it will need to copy its DNA) and organelles such as mitochondria, and does its normal job.
- **S** (synthesis phase): **the DNA is replicated**, semi-conservatively (DNA polymerase adds nucleotides; DNA ligase joins the fragments), so each chromosome now has two identical sister chromatids held together at the centromere. Histones are made to go with the new DNA. The telomeres get a little shorter here.
- **G2** (second growth phase): the cell grows more and gets ready to divide. It makes proteins for the spindle (tubulin, to build microtubules) and keeps making ATP for the division ahead. In animal cells the centrioles are copied during interphase.

Mitosis (M) is nuclear division: prophase, metaphase, anaphase and telophase. **Cytokinesis** is the division of the cytoplasm into two cells. Both are part of the cell cycle, but **only prophase to telophase are mitosis**. Interphase and cytokinesis are not.

The cell only moves on to the next phase when it is ready. Proteins check it at control points: before S (is the cell big enough, is the DNA undamaged?) and before mitosis (has all the DNA been copied?). Enzymes called cyclin-dependent kinases (CDKs) push the cell past these points. A question may tell you what a particular protein or inhibitor does; work out where the cell gets stuck, and so how many chromatids each chromosome has: stuck **before S** means one chromatid each; stuck **after S** (in G2) means two.

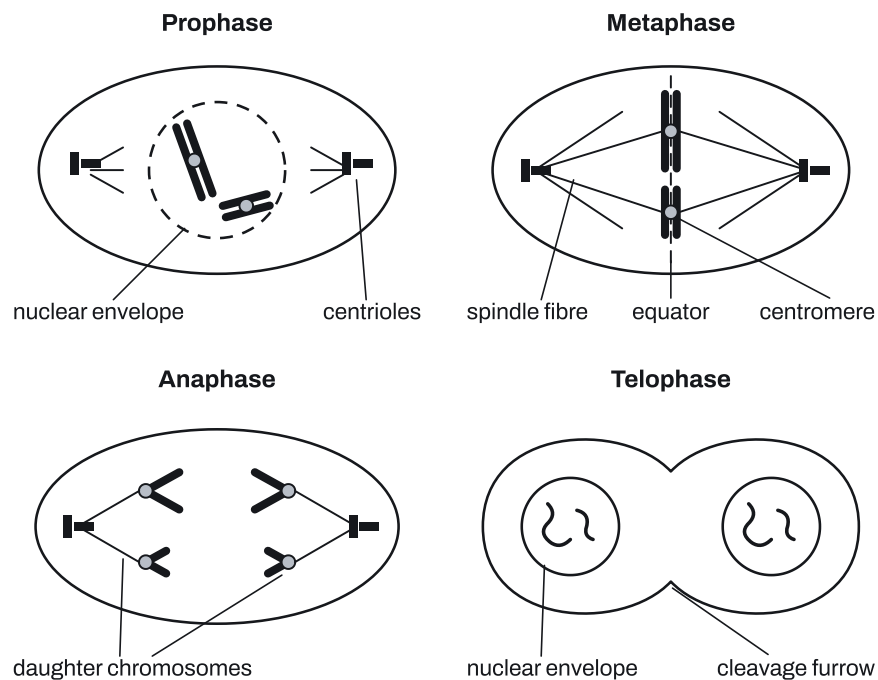
DNA content through the cycle



The **rise** is S phase: the DNA doubles. The **drop by half** is when one cell becomes two (per nucleus at telophase; per cell at cytokinesis). So a cell in G2 or in mitosis has twice the DNA of a cell in G1, and each daughter cell ends up with the same amount of DNA as the parent had in G1.

The stages of mitosis

These are the four named stages in an animal cell. Plant cells differ in a few ways, listed after.



Prophase

- The chromatin coils up and condenses: chromosomes become short, thick and visible, each as **two sister chromatids joined at the centromere**.
- The nucleolus disappears.

- In animal cells the two pairs of centrioles move to opposite ends (poles) of the cell; they organise the spindle's microtubules.
- The **spindle** starts to form: fibres made of **microtubules** grow out from each pole.
- At the end of prophase the **nuclear envelope breaks up** into small vesicles.

Metaphase

- The chromosomes line up on the **equator** of the spindle (the middle of the cell), one above another.
- Spindle fibres from **both** poles are attached to each **centromere**.
- The chromosomes are fully condensed and all in one plane, so this is the best stage for seeing and counting them.

Anaphase

- Each **centromere divides**, so the sister chromatids separate.
- The spindle fibres **shorten** and pull the chromatids to **opposite poles**, centromere first, so the arms trail behind in a V shape.
- Once separated, each chromatid is called a **daughter chromosome**: one chromatid, one DNA molecule, its own centromere.

Telophase

- A complete set of daughter chromosomes arrives at each pole.
- The chromosomes uncoil and become long and thin again (back to chromatin).
- A **nuclear envelope re-forms** round each group, from the vesicles; the nucleolus reappears.
- The spindle breaks down.

There are now two nuclei, each with the same number and kind of chromosomes as the parent nucleus.

The spindle's job: its microtubules attach to the centromeres, line the chromosomes up on the equator, then **shorten** to pull the sister chromatids apart to opposite poles. A drug that stops the spindle forming (such as colchicine) or stops its fibres shortening leaves cells stuck at metaphase: the chromosomes never separate, so no new cells are made.

On a graph of movement, starting at metaphase: the distance between the two sister chromatids of a chromosome stays near zero, then rises steeply in anaphase; the distance from each centromere to its pole (the length of the attached spindle fibres) stays steady, then falls in anaphase and levels off near zero when the chromatids arrive; the distance between the two poles changes little (it may rise slightly as the cell lengthens).

Cytokinesis follows. In an **animal cell** the **cell surface membrane pinches in** round the middle (a cleavage furrow) until the cell splits in two. The cell surface membrane stays intact through the whole of mitosis; it only changes shape at cytokinesis.

Plant cells divide in the same four stages, with these differences:

- **no centrioles:** the spindle still forms from microtubules, organised from the poles without centrioles;

- **no pinching in:** the cell wall is rigid, so at cytokinesis vesicles collect at the equator and fuse to form a **cell plate**, which grows outwards and becomes the new cell walls between the two cells;
- in plants, mitosis happens mainly in **meristems** (growing regions), such as the root tip.

Why the daughter cells are identical

1. In **S phase**, each DNA molecule is copied by **semi-conservative replication**, so the two sister chromatids have identical base sequences.
2. In **metaphase**, every chromosome lines up on the equator with spindle fibres from **both** poles attached to its centromere, so each pair of sister chromatids is ready to be split evenly.
3. In **anaphase**, the centromeres divide and **one chromatid of each chromosome goes to each pole**.
4. So each new nucleus gets one copy of every chromosome: the same number of chromosomes and the same quantity of DNA as the parent. The daughter cells carry the same genes and can make the same proteins and enzymes as the parent.

Replication is part of interphase, not of mitosis. "Identical" is what normally happens: a copying mistake (a mutation) can still change the DNA occasionally. Genetically identical is not the same as identical: just after cytokinesis the two daughter cells may differ in size and in how many mitochondria or other organelles they received, because the cytoplasm is not shared out exactly. They start smaller than the parent, then grow in G1.

Counting through the cycle

Many multiple-choice questions ask how many of something there are at a stage. Take a human body cell, with 46 chromosomes:

Stage	Chromosomes	Chromatids each	DNA molecules	Polynucleotide strands	Centromeres	Telomeres
G1	46	1	46	92	46	92
G2, prophase, metaphase	46	2	92	184	46	184
Anaphase (whole cell)	92	1	92	184	92	184
Telophase: each new nucleus	46	1	46	92	46	92
After cytokinesis: each cell	46	1	46	92	46	92

The rules behind the table:

- **DNA molecules = chromatids.** They double in S phase and stay doubled until the cell divides; a whole cell in telophase still has 92, shared between two nuclei.
- **Polynucleotide strands = $2 \times$ DNA molecules**, because each DNA molecule is a double helix.
- **Centromeres = chromosomes.** A replicated chromosome has one centromere until anaphase, when each centromere divides: 46 in prophase and metaphase, 92 in anaphase.
- **Telomeres = $2 \times$ chromatids**, one at each end.
- **Per chromosome, from most to fewest parts:** nucleotides (millions), then histones (thousands), then telomeres (4 once replicated), then DNA molecules (2), then the centromere (1).
- **Nothing is lost until the cell splits.** A whole cell in prophase, metaphase, anaphase or telophase still has all the DNA it had at the end of S (twice its G1 amount); only after cytokinesis does each cell hold the G1 amount again.

Telomeres

Each time a DNA molecule is replicated, the very end can't be copied, so the copy is a little shorter. Without protection, genes near the ends would soon be lost.

Telomeres are long stretches of a short, non-coding base sequence repeated many times. The piece lost at each replication comes out of the telomere, not a gene. So telomeres **prevent the loss of genes** during DNA replication and let a cell **divide many times**.

Telomeres get **shorter in each S phase**. When they become too short, the cell stops dividing, which is one reason most body cells can only divide a limited number of times.

The enzyme **telomerase** adds repeats back on to telomeres, so they don't shorten. It is active in cells that must keep dividing: **stem cells**, cells that make gametes, **activated lymphocytes** and most **cancer cells**. Most specialised body cells have little or none.

Only chromosomes with ends have telomeres: the linear chromosomes of eukaryotes (plants and animals). The circular DNA of bacteria, mitochondria and chloroplasts has none.

Stem cells

A **stem cell** is an unspecialised cell that can keep dividing by mitosis. Its daughter cells either stay as stem cells (**self-renewal**, so the supply is never used up) or **differentiate**: they become specialised for a particular job.

- **Bone marrow** stem cells divide all the time to make red blood cells, phagocytes and lymphocytes, replacing the blood cells that die each day.
- Stem cells in the **skin** and the **lining of the gut** replace cells that wear out; after an injury, stem cells in the tissue divide to **repair the tissue**.
- In plants, the **meristems** (for example the root tip and the cambium) are groups of stem cells whose daughter cells differentiate into xylem, phloem and other tissues.

Stem cells make **new cells**; they do not repair damaged cells. Adult stem cells can only form some cell types, not a whole new organism. A small pool of them is kept throughout life. They have the same genes as every other body cell; what keeps them dividing is active telomerase, not "extra" telomeres.

A **progenitor cell** is part-way to becoming specialised: it can still divide by mitosis, but it is not a stem cell, because it cannot make more cells like itself for ever (no self-renewal) and it can only form a narrower range of cell types.

When stem cells are put back into a tissue (for example into bone marrow after its own cells were destroyed by treatment), they settle, divide repeatedly by mitosis, and their daughter cells differentiate into all the cell types that tissue needs.

Uncontrolled division and tumours

Normally the cell cycle is tightly controlled. Some genes code for proteins that **stimulate** division when new cells are needed; others code for proteins that **stop** the cycle, for example if the DNA is damaged, so that it can be repaired before it is copied.

A **mutation** in these genes (caused, for example, by a carcinogen in tobacco smoke or by ionising radiation) can remove the control:

1. the cell divides by mitosis **again and again**, whether or not new cells are needed, with a shorter interphase;
2. damaged DNA is replicated instead of repaired, so more mutations build up;
3. the daughter cells inherit the mutation, divide without control and don't differentiate;
4. the result is a growing **mass of cells**: a **tumour**.

Other features of a tumour cell, compared with the specialised cell it came from: it **loses its specialised features** (does not differentiate), ignores signals from neighbouring cells, does not die when it should, often has **active telomerase** so its telomeres don't run out, and in a cancer may spread to other tissues. Its cycle is faster mainly because **interphase is shorter**.

Many anti-cancer drugs work by **stopping the cell cycle**: blocking DNA replication (cells can't pass S phase), blocking the enzymes that push cells into S or into mitosis, or stopping the spindle (cells stuck at metaphase). Dividing cells are hit hardest, so the tumour stops growing.

Looking at mitosis under the microscope

The usual slide is a **root tip squash**: the tip of a young root (a meristem) is stained and squashed so that cells lie in one layer. Most cells are in interphase, because interphase is the longest part of the cycle. The clues to each stage:

What you see	Stage
A clear nucleus, often a nucleolus, evenly stained chromatin, no separate chromosomes	Interphase
Separate thread-like chromosomes visible, often still inside a nucleus	Prophase

What you see	Stage
Chromosomes in a band across the middle of the cell, no nuclear envelope	Metaphase
Two groups of V-shaped chromosomes moving apart towards the ends	Anaphase
Two compact groups at the two ends, new nuclear envelopes, a cell plate or furrow between	Telophase

Plant tissue shows **cell walls**, cells packed in regular rows, and a **cell plate** rather than a cleavage furrow. Animal cells have no wall, are rounder, and show centrioles at the poles and a furrow at cytokinesis.

An **electron micrograph** of a dividing cell is a thin slice, so it may cut through only some of the chromosomes, and it is a still picture, so it can't show which way they are moving. That is why a late anaphase and an early telophase cell can be hard to tell apart.

The **mitotic index** is the percentage of cells in a sample that are in mitosis. It is highest where cells divide fastest, such as right behind a root tip.

Key facts and formulas

None of these is in the 9700 formula list (that list is for A Level statistics), so learn them all.

Formula	Status
Mitotic index = $\frac{\text{number of cells in mitosis}}{\text{total number of cells}} \times 100$	Learn it
Percentage in a stage = $\frac{\text{cells in that stage}}{\text{total cells}} \times 100$	Learn it
Number of cells after d divisions = starting number $\times 2^d$	Learn it
Actual size = $\frac{\text{image size}}{\text{magnification}}$, magnification = $\frac{\text{image size}}{\text{actual size}}$	Learn it
1 mm = 1000 μm = 1 000 000 nm	Learn it

The order to have ready: **G1** → **S** → **G2** (interphase) → **prophase** → **metaphase** → **anaphase** → **telophase** (mitosis) → **cytokinesis**.

How to do it

In the Paper 1 and Paper 2 questions we have tagged for this topic (150 questions, 2021–2025: 120 multiple choice and 30 structured), the types came up this often. 23 of the 150 questions mix types, so the counts add up to 191.

Question type	Questions
Identify or order the stages of mitosis from a photo, diagram or description	28
Describe what happens in a stage of mitosis	26

Question type	Questions
Place events in the cell cycle (G1, S, G2, mitosis, cytokinesis)	26
Count chromosomes, chromatids, DNA molecules, centromeres or telomeres	23
Roles of telomeres and telomerase	19
Roles of mitosis and why daughter cells are genetically identical	18
Roles and properties of stem cells	14
Describe or label chromosome structure	13
Tumours, cancer genes and anti-cancer drugs	8
Calculate from data: magnification, cell counts, mitotic index, cell numbers	7
Interpret a graph of DNA content, spindle fibre length or chromatid distance	5
Draw or complete a diagram of chromosomes in a stage	4

1. Identify or order the stages of mitosis (28 questions)

- 1. Look for the nuclear envelope.** Present with separate chromosomes inside: prophase (or, if the chromosomes are compact groups at two ends, telophase). Absent: metaphase or anaphase.
- 2. Look at where the chromosomes are,** using the table in "Looking at mitosis under the microscope": scattered, in a line, two groups moving apart, or two groups at the ends.
- 3. Check it is in mitosis at all.** An even, grainy nucleus with a nucleolus is interphase.
- 4. Order them:** interphase → prophase → metaphase → anaphase → telophase → cytokinesis.

Variations you will meet:

- **A description instead of a picture.** Turn each clue into a rule: two-chromatid chromosomes mean before anaphase; chromosomes on the equator mean metaphase; single chromatids heading to the poles mean anaphase; new envelopes mean telophase.
- **"What happens next?"** Name the next stage and give its main event, for example after metaphase the centromeres divide and chromatids move apart.
- **Which stage is missing** from a set of pictures: name each one first, then see which of the four names you have not used.
- **Plant or animal?** A cell wall, regular rows of cells and a cell plate mean plant; centrioles, no wall and a furrow mean animal.
- **Late anaphase or early telophase in an electron micrograph?** A still, thin slice can't show movement or every chromosome; the deciding clue is whether nuclear envelopes are forming.

2. Describe what happens in a stage of mitosis (26 questions)

- 1. Name the structures the question asks about:** chromosomes (or chromatids), centromeres, spindle, nuclear envelope, nucleolus, centrioles, cell surface membrane.

2. **Give one clear event for each**, using the lists in "Understand it". For a 2 or 3 mark part, give at least one more point than the marks.
3. **Use the right words: opposite poles, daughter chromosomes, centromere**, spindle fibres made of microtubules.

Variations you will meet:

- **"Describe telophase"**: chromosomes are at the poles; they uncoil; nuclear envelopes and nucleoli re-form; the spindle breaks down. "Chromosomes move to the poles" describes anaphase, and scores nothing here.
- **"What are spindle fibres made of, and what organises them?"** Microtubules; in animal cells the centrioles organise them.
- **"Role of the spindle or microtubules"**: attach to centromeres, line chromosomes up on the equator, shorten to pull sister chromatids to opposite poles.
- **"What happens to chromatin in prophase?"** It coils and condenses (supercoils) so the chromosomes become short, thick and visible.
- **"Why is metaphase best for counting chromosomes?"** They are fully condensed, so thick and dark, and lie in one plane.
- **A drug that acts on the spindle**: cells stop at metaphase, because chromatids can't be pulled apart.
- **True/false statements about a stage**: test each against the stage lists; watch for centrioles "attaching" chromosomes (it is the spindle fibres, at the centromere) and anything about the cell surface membrane breaking (it stays intact).

3. Place events in the cell cycle (26 questions)

1. **Write out the cycle** (the order under "Key facts").
2. **Match the event to the phase**:
 - growth, making proteins, RNA and organelles, transcription (RNA polymerase): G1 and G2;
 - DNA replication (DNA polymerase, DNA ligase), telomeres shortening, histones made: **S**;
 - making spindle proteins (tubulin), final growth: G2;
 - chromosomes condense, spindle forms, envelope breaks up: prophase; envelope re-forms: telophase;
 - the cytoplasm divides: cytokinesis.
3. **Check what the question includes**. "Part of the **cell cycle**" includes interphase, mitosis and cytokinesis. "Part of **mitosis**" is prophase to telophase only.

Variations you will meet:

- **G1 compared with G2** (a favourite structured part): S phase has come in between, so in G2 there is twice the DNA, and each chromosome is two sister chromatids (two DNA molecules) instead of one.
- **A mass of DNA given at one phase**. Apply the pattern: it doubles from G1 to the end of S, stays doubled through G2 and mitosis, and halves when the nucleus (telophase) or cell (cytokinesis) divides.

- **"Where would a drug or inhibitor act?"** Anything that stops DNA copying (polymerase, ligase, unwinding) acts in S; anything that stops the spindle holds cells in metaphase. If a protein stops the cell moving into S, its chromosomes have one chromatid each; if it stops the cell moving from G2 into mitosis, they have two, and the cell has had time to grow and make extra organelles such as mitochondria.
- **Points marked on a cycle diagram:** place each point, then ask what has and hasn't happened yet (for example a cell at the end of G2 has replicated its DNA, but its chromosomes haven't condensed).
- **Why daughter cells differ just after cytokinesis:** unequal share of cytoplasm and organelles, not of DNA.

4. Count chromosomes, chromatids, DNA molecules, centromeres or telomeres (23 questions)

1. **Write down the chromosome number N** of a body cell (in G1).
2. **Decide whether the DNA has been replicated.** From the end of S until the cell divides there are $2N$ DNA molecules in the cell.
3. **Use the rules** under "Counting through the cycle".
4. **Check the unit asked for:** the whole cell, one nucleus, one chromosome or one chromatid.

The commonest slip is stopping at DNA molecules when the question asks for polynucleotide strands (twice as many), or counting one nucleus when it asks for the whole cell.

Variations you will meet:

- **A single chromosome** at prophase or metaphase has 1 centromere, 2 chromatids, 2 DNA molecules, 4 strands and 4 telomeres; **a single daughter chromosome** in anaphase or telophase has 1 centromere, 1 DNA molecule, 2 strands and 2 telomeres.
- **Ranking the parts** of a chromosome from most to fewest: use the order under "Counting through the cycle".
- **Counting from a drawing:** count centromeres to get chromosomes, count arm ends to get telomeres; add up across the drawings if asked for a total.
- **As a percentage of the G1 amount:** a whole cell has 200% from the end of S until cytokinesis; each daughter cell has 100%.

5. Roles of telomeres and telomerase (19 questions)

1. **Say where and what they are:** repeated, non-coding base sequences at the ends of each chromatid (eukaryotic chromosomes only: plants and animals, not bacteria).
2. **Give the role:** some DNA is lost from the end at each replication, and it is lost from the telomere, so **genes are not lost**; this lets the cell replicate its DNA and divide **many times**; telomeres also stop chromosome ends sticking together.
3. **For telomerase:** it lengthens telomeres, so cells that have it (stem cells, gamete-making cells, activated lymphocytes, cancer cells) can keep dividing. Mature red blood cells (no nucleus) and most specialised cells don't need it.

Variations you will meet:

- **Telomere length data:** work out the loss per division from two points; the cell with the **shortest** telomeres has been through the most divisions, and cells with telomerase keep their length.
- **"Why is telomerase useful in stem cells?"** They must divide many times through life to replace cells, without losing genes.
- **"Why do tumour cells make a lot of telomerase?"** So their telomeres never become too short and they can go on dividing; blocking telomerase is a possible cancer treatment.
- **Long lifespan and high telomerase:** stem cells can keep replacing cells for longer.

6. Roles of mitosis and why daughter cells are genetically identical (18 questions)

1. **List the roles:** growth of multicellular organisms, replacement of cells, repair of tissues, asexual reproduction (for example a bud growing into a new individual). Cloning of lymphocytes in an immune response is mitosis too.
2. **Reject the traps:** repairing a damaged cell, growth of a unicellular organism, making genetically **different** cells, "replacing cancerous tissue", DNA being replicated "during mitosis".
3. **To explain identity,** give the steps under "Why the daughter cells are identical": replication in S, lining up in metaphase, one chromatid of each to each pole in anaphase.

Variations you will meet:

- **"Explain what is meant by repair of tissues":** damaged or dead cells are replaced by new, genetically identical cells made by mitosis, so the tissue's structure and function are restored.
- **"Which cells can divide by mitosis?"** Any eukaryotic cell with a nucleus that still divides: stem cells, cancer cells, lymphocytes. Not mature red blood cells (no nucleus) and not bacteria (they divide by binary fission).
- **Roles of mitosis in a healthy plant:** growth at meristems (root and shoot tips), replacing damaged cells, asexual reproduction (runners, tubers).

7. Roles and properties of stem cells (14 questions)

1. **Define:** an unspecialised cell that can divide repeatedly by mitosis and whose daughter cells can differentiate into specialised cells.
2. **Explain the role:** divide by mitosis to make many genetically identical cells; some stay as stem cells, the rest **differentiate** into the cell type the tissue needs; this replaces cells and repairs tissue.
3. **Link to the context:** bone marrow makes blood cells; gut or skin stem cells make lining cells; plant meristems (and procambium) make xylem and phloem.
4. **Processes in tissue repair:** DNA replication, transcription and protein synthesis, mitosis, cytokinesis, then differentiation.

Variations you will meet:

- **"Why is a progenitor cell not a stem cell?"** It can't self-renew and can only form a few cell types.

- **Stem cells returned after treatment** (for example to bone marrow): they divide repeatedly, keep a pool of stem cells, and differentiate to replace all the lost cell types.
- **True/false features**: true that daughter cells can stay as stem cells or specialise, and that a small pool is kept for life; false that stem cells have "more telomeres" or "more genes" than other body cells.
- **A diagram of several divisions**: the cell that keeps dividing and appears again is the stem cell; the cells at the ends that stop are differentiated.

8. Describe or label chromosome structure (13 questions)

1. **Label the parts**: sister chromatid, centromere, telomere (at the ends); inside, DNA wound round histones.
2. **Say what each does**: histones package the DNA; the centromere holds the chromatids together and is where the spindle attaches; telomeres prevent the loss of genes.
3. **Use a label line** that touches the right part.

Variations you will meet:

- **"How can you tell the DNA has already been replicated?"** Each chromosome is made of **two sister chromatids** joined at a centromere.
- **"Describe a chromosome at metaphase"**: two identical sister chromatids, joined at a centromere, telomeres at the ends, DNA with histones, tightly condensed, so short and thick.
- **"Explain the role of centromeres in the cell cycle"**: hold sister chromatids together after S; attach to the spindle; divide in anaphase so one chromatid goes to each pole; so each daughter cell gets one copy of every chromosome.
- **Name the term from a description**: repeated sequences at the ends (telomere); organises the spindle in animal cells (centriole); joins sister chromatids (centromere); proteins the DNA wraps round (histones).

9. Tumours, cancer genes and anti-cancer drugs (8 questions)

1. **Start with the mutation**: a change in a gene that controls the cell cycle.
2. **Say what control is lost**: the protein that stops division (for example when DNA is damaged) no longer works, or the protein that stimulates division is always active.
3. **Say what the cell does**: divides by mitosis repeatedly and without control, with a short interphase; the daughter cells inherit the mutation and don't differentiate.
4. **Finish with the tumour**: a mass of cells.

Variations you will meet:

- **Two genes that each hold division back**: a tumour is most likely when **both** have mutations, because either one working can still stop the cycle.
- **Features of tumour formation other than fast division**: see the list under "Uncontrolled division and tumours".

- **Drug data.** Describe with numbers, then explain by saying where in the cycle the cells are stopped. For example, a made-up drug that blocks DNA replication is added to dividing tumour cells: over the next 24 hours the percentage of cells in G1 rises from 40% to 85%, and the mitotic index falls from 8% to 0. Explanation: cells can't complete S phase, so they build up before it; cells that had already replicated their DNA finish mitosis, but no more follow, so no new cells form and the tumour stops growing.
- **Why a drug that blocks the cycle works on tumours:** tumour cells divide far more often than most body cells, so they are hit hardest.

10. Calculate from data (7 questions)

1. **Magnification or actual size:** measure the image in mm, convert to the unit of the answer ($\times 1000$ for μm , $\times 1\,000\,000$ for nm), then use $\text{actual} = \text{image} \div \text{magnification}$, or $\text{magnification} = \text{image} \div \text{actual}$. Write the formula if asked; it earns a mark. Round as asked.
2. **Stage counts:** add the stages that match the description, divide by the total and multiply by 100:
 - chromosomes made of two chromatids and visible: prophase + metaphase;
 - chromatids separated: anaphase + telophase;
 - in mitosis (the mitotic index): all four stages.
3. **Percentages to numbers:** $\text{number} = \text{percentage} \div 100 \times \text{total}$.
4. **Time spent in a stage:** in a tissue dividing steadily, the fraction of cells in a stage equals the fraction of the cycle spent in it, so $\text{time} = (\text{cells in stage} \div \text{total}) \times \text{length of cycle}$.
5. **Cell numbers after repeated division:** number of divisions $d = \text{time} \div \text{time per division}$; $\text{cells} = \text{start} \times 2^d$.
6. **Cells replaced per day:** $\text{total cells} \div \text{lifespan in days}$; as a percentage, divide by the total and multiply by 100.

Examples:

- **Scale bar:** a $2\,\mu\text{m}$ scale bar drawn 20 mm long gives magnification $\frac{20 \times 1000}{2} = \times 10\,000$; a chromosome measuring 48 mm on the same image is $\frac{48 \times 1000}{10\,000} = 4.8\,\mu\text{m}$ long.
- A garlic root tip squash of 640 cells: interphase 560, prophase 38, metaphase 18, anaphase 14, telophase 10. Mitotic index $= \frac{80}{640} \times 100 = 12.5\%$. Of the 80 dividing cells, $\frac{18}{80} \times 100 = 22.5\%$ are in metaphase.
- Working backwards: one cell dividing every 20 hours gives 1024 cells after $2^d = 1024$, so $d = 10$ divisions, which takes $10 \times 20 = 200$ hours.

Variation: mitotic index against distance from a root tip. It is highest in the meristem just behind the tip and falls further back, where cells elongate and differentiate instead of dividing.

11. Interpret a graph of DNA content, spindle fibre length or chromatid distance (5 questions)

1. **Read the axes:** DNA per cell or per nucleus? Distance between what?
2. **Match each part of the curve to a phase,** using "DNA content through the cycle" and "On a graph of movement":

- DNA: flat (G1), rising (S), flat and high (G2 and mitosis; the envelope breaks down at the start of mitosis, still on the high part), dropping by half (telophase for a nucleus, cytokinesis for a cell);
- sister chromatid separation: near zero, then rising in anaphase;
- centromere-to-pole distance and attached spindle fibre length: steady, then falling in anaphase;
- pole-to-pole distance: little change (perhaps a slight rise as the cell lengthens).

3. **Answer the exact event asked:** replication is the rise; the halving shows division; the fall in fibre length is anaphase, and when it stops the chromatids are at the poles.

12. Draw or complete a diagram of chromosomes in a stage (4 questions)

1. **Draw what the question says:** the number of chromosomes, the stage, and which cell.
2. **Metaphase:** chromosomes of two chromatids each, centromeres on the equator, spindle fibres from each pole (centrioles in an animal cell) to each centromere; label chromatid, centromere, spindle fibre, centriole.
3. **Anaphase:** separated chromatids, each **one** chromatid, V-shaped with the centromere leading, spindle fibres from the centromere to the pole.
4. **Daughter chromosomes in a new nucleus:** the same number and lengths as the parent's chromosomes, each one chromatid, the same set in both nuclei.
5. **One chromosome:** two chromatids, centromere, telomeres at the four ends, all labelled.

Worked examples

The bold codes show where marks are earned, as in Cambridge mark schemes. The number is how many marks.

- **M1** method mark: for a correct method, even if the numbers slip.
- **A1** accuracy mark: for a correct answer; it needs the M mark before it.
- **B1** mark for a correct result on its own, with no method needed.

Example 1

(a) A chromosome in a cell at metaphase has four telomeres. The same chromosome in G1 of that cycle had two. Explain this difference. **[2]**

(b) Cells taken from the lining of a sheep's artery were grown in culture, and the mean length of their telomeres was measured. After 10 divisions it was 9.0 kilobases (kb); after 40 divisions it was 7.2 kb. The cells stopped dividing when the mean length reached about 5.0 kb.

- (i) Calculate the mean length of telomere lost per division between division 10 and division 40. **[1]**
- (ii) Assuming the same rate of loss, estimate how many more divisions the cells could make after division 40. **[1]**

- (iii) Explain why the loss of DNA at each division does not remove any of the cells' genes. [2]

(a) The DNA was replicated in **S phase**, so by metaphase the chromosome is two **sister chromatids** (joined at the centromere); **B1** each chromatid is one linear DNA molecule with a telomere at **each end**, so $2 \times 2 = 4$. **B1**

(b)(i) $\frac{9.0 - 7.2}{40 - 10} = \frac{1.8}{30} = 0.06 \text{ kb (60 base pairs) per division. B1}$

(b)(ii) $\frac{7.2 - 5.0}{0.06} = 36.7$. After 36 more divisions the telomeres are $7.2 - 36 \times 0.06 = 5.04 \text{ kb}$; a 37th would take them to 4.98 kb, below the limit, so about **36** more whole divisions. **B1** (Since the limit is only "about" 5.0 kb, 37 would also be accepted; 36.7 is not, as a cell can't make part of a division.)

(b)(iii) The end of each DNA molecule can't be copied, so some DNA is lost from the end at every replication (S phase); **B1** the DNA lost comes from the repeated, **non-coding** telomere, so **no genes are lost. B1**

Example 2

A bean plant has 24 chromosomes in each body cell.

(a) State the number of:

- polynucleotide strands of DNA in the whole cell at metaphase;
- telomeres in the whole cell in anaphase. [2]

(b) A student counted the cells in each stage in a root tip squash of this plant.

Stage	Interphase	Prophase	Metaphase	Anaphase	Telophase
Number of cells	1032	96	30	24	18

Calculate the mitotic index. Show your working. [2]

(c) One complete cell cycle in this root tip takes 20 hours. Assuming the cells are dividing steadily, calculate the time spent in mitosis. [1]

(a) Metaphase: 24 chromosomes of two chromatids, so 48 DNA molecules, each two strands: $2 \times 48 = 96$ strands. **B1** Anaphase: 48 separated chromatids, each with a telomere at both ends: $2 \times 48 = 96$ telomeres. **B1**

(b) Total = $1032 + 96 + 30 + 24 + 18 = 1200$ cells; in mitosis = $96 + 30 + 24 + 18 = 168$. **M1**

Mitotic index = $\frac{168}{1200} \times 100 = 14\%$. **A1**

(c) The fraction of cells in mitosis is the fraction of the cycle spent there: $\frac{168}{1200} \times 20 = 2.8$ hours (168 minutes). **B1**

Example 3

(a) Describe the behaviour of the chromosomes, the nuclear envelope and the spindle in an animal cell from the start of prophase to the end of telophase. [6]

(b) State two ways in which the division of a plant cell differs from this. [2]

(a) Any six:

- **prophase**: chromosomes condense and become visible as two sister chromatids joined at a centromere; **B1**
- centrioles move to opposite poles and the spindle (microtubules) forms; **B1**
- the nuclear envelope breaks up (into vesicles); **B1**
- **metaphase**: chromosomes line up on the equator, with spindle fibres attached to each centromere; **B1**
- **anaphase**: centromeres divide and sister chromatids separate; **B1**
- spindle fibres shorten and pull the chromatids (daughter chromosomes) to opposite poles, centromere first; **B1**
- **telophase**: chromosomes reach the poles and uncoil; **B1**
- nuclear envelopes re-form around each group, and the spindle breaks down. **B1**

(b) Any two: plant cells have **no centrioles**; **B1** cytokinesis is by a **cell plate** forming across the middle instead of the cell surface membrane pinching in; **B1** mitosis happens mainly in meristems. **B1**

Example 4

The clear surface layer of the cornea of the eye is constantly worn away and replaced by stem cells at its rim. In one small patch there are 16 stem cells. Each divides once a day: one daughter stays a stem cell, and the other divides 4 more times by mitosis, all of its descendants becoming surface cells.

(a) Calculate how many new surface cells this patch makes each day. [2]

(b) Explain how the stem cells keep the number of surface cells steady. [3]

(c) A mutation in one stem cell makes a protein that tells the cell to divide stay switched on all the time. Explain how this could lead to a tumour. [3]

(a) Each non-stem daughter gives $2^4 = 16$ surface cells; **M1** $16 \times 16 = 256$ surface cells a day. **A1**

(b) Any three:

- stem cells divide repeatedly by **mitosis**; **B1**
- making large numbers of **genetically identical** cells; **B1**
- some daughter cells stay as stem cells (self-renewal), so the supply is not used up; **B1**
- the others **differentiate** into surface cells to replace those that are worn away. **B1**

(c) Any three:

- the cell is told to divide even when no new cells are needed, so it divides by mitosis **repeatedly / without control**; **B1**
- interphase is shortened, so cycles follow each other quickly; **B1**
- the daughter cells inherit the mutation, so they also divide without control; **B1**
- they don't differentiate, and further mutations build up, forming a **mass of cells (tumour)**. **B1**

Common mistakes

- **Putting DNA replication in mitosis, or in G1 or G2.** It happens in **S phase** of interphase. Examiners reject "replicates in G1", and "semi-conservative replication is part of mitosis" is a favourite wrong statement.
- **Calling interphase or cytokinesis part of mitosis.** They are part of the cell cycle; mitosis is only prophase to telophase.
- **Saying mitosis or stem cells "repair cells".** They make new cells, which replace cells and repair **tissues**. A damaged cell is not mended by mitosis.
- **Mixing up centromere, centriole and centrosome.** Spindle fibres attach at the **centromere**; centrioles sit at the poles in animal cells. Writing centrosome for centromere loses the mark.
- **Forgetting DNA is double-stranded.** Polynucleotide strands are twice the number of DNA molecules; many candidates stop at the number of molecules.
- **Drawing two chromatids in anaphase or after.** Once the centromere divides, each daughter chromosome is one chromatid.
- **Vague direction words.** Chromatids go to **opposite poles**, not to the sides or ends of the cell.
- **"Telomeres prevent loss of DNA / genetic material."** Telomeres are genetic material themselves and they do get shorter. Say they prevent the loss of **genes**, and add that more divisions can then happen.
- **Describing stem cells as dividing into specialised cells.** Division comes first, then the daughter cells differentiate, and some stay as stem cells.
- **Talking about pairs of homologous chromosomes in mitosis.** In mitosis talk about sister chromatids, then daughter chromosomes.
- **Describing a graph without numbers**, or explaining drug data without saying which stage the cells are stuck in.

How to get the marks

- **"Name" or "state"** needs one word or phrase: "microtubules", "telophase", "S phase". Only one stage name counts; words like "early" or "late" are ignored.
- **"Describe" a stage** means say what happens to each structure, one clear point per mark. Check the question's list (chromosomes, nuclear envelope, spindle, membrane) and cover each.
- **"Explain"** needs the reason too, not just the outcome.
- **"Suggest"** means apply what you know to a new situation; any sensible, biologically correct idea tied to the context can score.

- **Answer in the question's context.** If it is about gut lining stem cells, say they make gut lining cells, not blood cells.
- **Calculations:** write the formula when asked, show the numbers, give the unit and round as asked.
- **Data questions:** describe with numbers from the table or graph (and units), then explain with biology.
- **Drawings:** sharp continuous lines, the right number of chromosomes, the right number of chromatids, and label lines that touch the part.
- **Multiple choice with numbered statements:** test each statement separately and write ✓ or ✗ beside it before looking at the options.

Quick check

1. A body cell in G1 has 60 telomeres. How many chromosomes does it have, and how many telomeres are in the whole cell at metaphase?
2. Name the phase of the cell cycle in which each happens: (a) histones for the new DNA are made; (b) tubulin for the spindle is made; (c) nucleoli reappear; (d) a cleavage furrow forms.
3. On a photograph of chromosomes, a 5 μm scale bar is 40 mm long. One chromosome measures 30 mm. Calculate the magnification and the chromosome's actual length.
4. Explain why a cutting taken from a shoot grows into a plant that is genetically identical to its parent.
5. A cell starts with telomeres 8000 base pairs long, loses 50 base pairs at each division, and stops dividing when they reach 4000 base pairs. How many times can it divide? What would telomerase change?

Answers

1. In G1 each chromosome is one chromatid with 2 telomeres, so $60 \div 2 = 30$ chromosomes. By metaphase each is two chromatids, so $30 \times 2 \times 2 = 120$ telomeres.
2. (a) S phase; (b) G2; (c) telophase; (d) cytokinesis.
3. Magnification = $\frac{40 \times 1000}{5} = \times 8000$. Actual length = $\frac{30 \times 1000}{8000} = 3.75 \mu\text{m}$.
4. New cells in the cutting are made by mitosis in its meristems. Before each division the DNA is copied exactly by semi-conservative replication in S phase, and in anaphase one chromatid of each chromosome goes to each pole, so every new cell has the same chromosomes and genes as the parent plant. No gametes or fertilisation are involved.
5. $\frac{8000 - 4000}{50} = 80$ divisions. Telomerase adds repeats back on to the telomeres, so they would not shorten to the limit and the cell could keep dividing without losing genes.

Past questions to try

- [9700/11/M/J/23 Q18](#): stage counts from a root tip, as a percentage.
- [9700/22/O/N/23 Q1](#): how chromosomes change through interphase and mitosis, with a drawing.
- [9700/23/M/J/25 Q5](#): the role of telomeres.
- [9700/21/O/N/22 Q6](#): roles of mitosis in a plant, and the effect of an anti-cancer drug on the stages of mitosis.