CHAPTER

9 Cell cycle

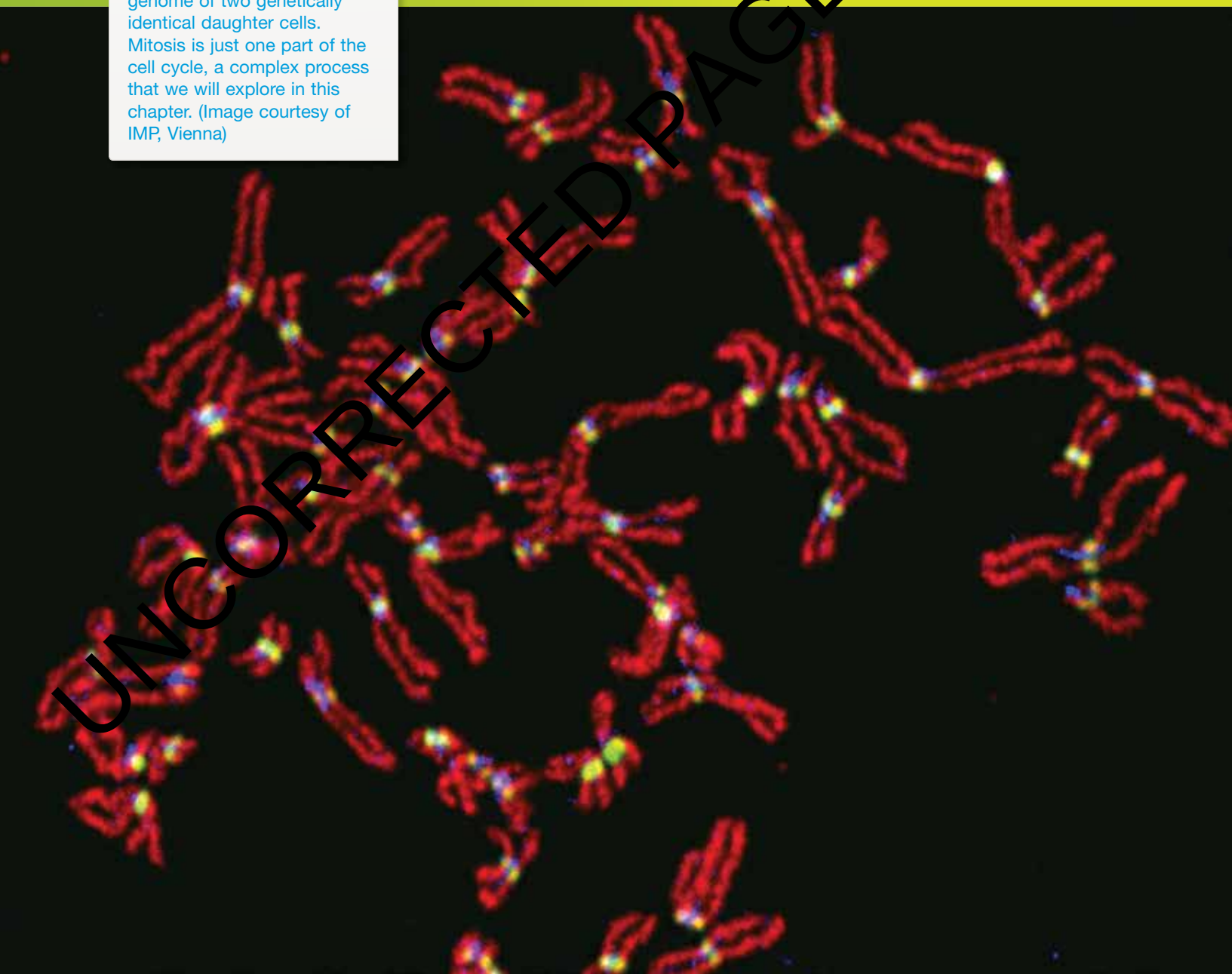

FIGURE 9.1 The duplicated chromosomes (stained red) of a HeLa cell. Each chromosome consists of two sister chromatids, with each chromatid having identical genetic information. When these sister chromatids separate during anaphase of mitosis, they will form the genome of two genetically identical daughter cells. Mitosis is just one part of the cell cycle, a complex process that we will explore in this chapter. (Image courtesy of IMP, Vienna)

KEY KNOWLEDGE

This chapter is designed to enable students to:

- gain understanding of the importance of the mitotic cell cycle in cell production for growth and repair in eukaryotes
- recognise that the cell cycle produces daughter cells that are identical to each other and are clones of the parent cell
- become familiar with the stages of the cell cycle and the chromosomal events that occur at each stage.

Saving burns victims

When Professor Fiona Wood (see figure 9.2) of the Royal Perth Hospital was made 2005 Australian of the Year, it was in recognition of her work related to the treatment of people with severe burns. For about 10 years prior to March 2003 Professor Wood had been developing improved methods for growing replacement skin. When 28 Australians were badly wounded and burnt as a result of a terrorist bombing in Bali, Indonesia, it was decided that they should be returned to Australia as soon as possible for treatment. They were sent to Professor Wood and Australians followed their progress through the daily press. 'Spray-on skin', known commercially as CellSpray, and Professor Wood became famous.

FIGURE 9.2 Professor Fiona Wood AM was awarded 2005 Australian of the Year for her work on developing an improved method of skin-cell regeneration, leading to improved and more rapid treatment for people with skin burns.

Skin: the outer layer

Normal intact skin provides a covering for the human body. The skin is composed of an outer **epidermis** and an underlying **dermis**. The epidermis and the dermis are held together by a non-cellular basement membrane.

Basement membranes occur throughout the human body. They consist of glycoproteins and provide structural support for tissues.

The epidermis consists of several cell layers (see figure 9.3):

- an outermost region consisting of layers of flattened dead cells, called the stratum corneum (*strata* = layer, coat; *corneum* = horny). These cells are constantly being shed from the skin surface. This layer is thickest on the soles of the feet and the palms of the hands.
- several layers of living cells called **keratinocytes** that are gradually pushed upwards, becoming flattened and eventually forming part of the outermost region of dead cells. The keratinocytes form the bulk of the epidermis.
- a basal layer which includes stem cells that are constantly dividing. For each two cells produced by division of a stem cell, one becomes a new keratinocyte and the other replaces the stem cell. The continual division of stem cells in the basal layer pushes the overlying keratinocytes towards the skin surface. Another group of cells present in the basal layer are the pigment-producing cells, or **melanocytes**.

ODD FACT

It has been estimated that each person replaces, on average, about 1 kg of skin cells during a lifetime. Dandruff, skin cells from our scalps, represents just a fraction of the skin cells we must replace.

The dermis lies below the epidermis. The dermis contains blood vessels, hair follicles, sweat glands, touch-sensitive and pain-sensitive cells, muscle fibres and collagen fibres.

The severity of burn damage to human skin may vary from first-degree burns, such as sunburn, that involve the epidermis only, to second-degree burns, such as scalds, that involve the epidermis and the upper section of the dermis, to severe third-degree or full thickness burns that destroy the epidermis and all or part of the dermis. Burns of this type were those seen in the seriously burnt victims of the Bali bombing and those who are badly burnt in bushfires in this country.

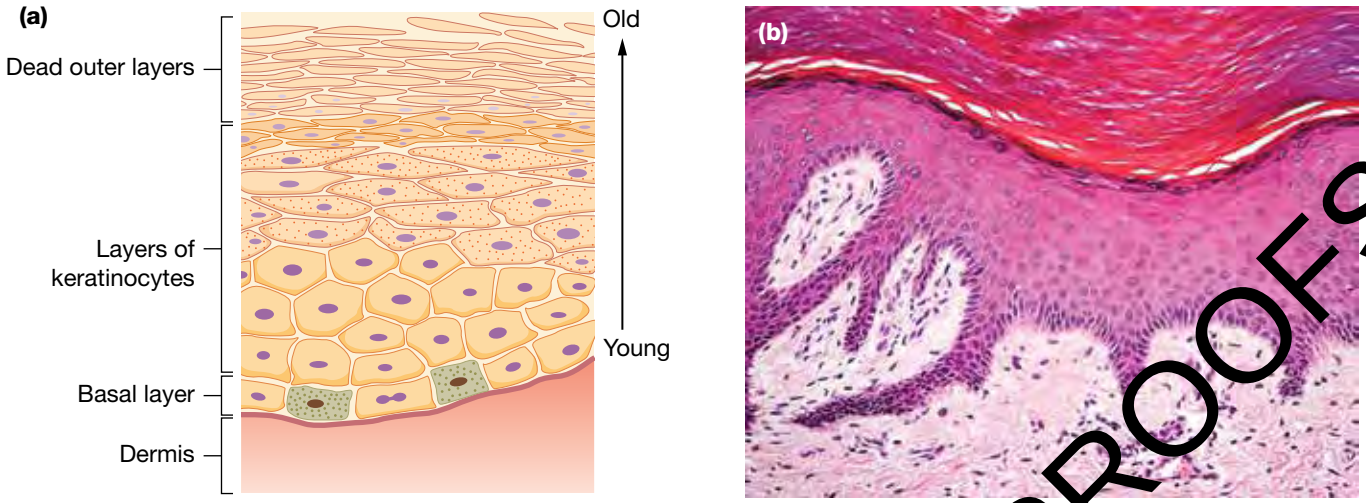

FIGURE 9.3 Section through human skin **(a)** Diagram showing the epidermis that overlays the dermis. The basal layer of epidermal cells includes stem cells that are capable of cell division. As keratinocytes are pushed towards the skin surface, they flatten and eventually become part of the dead outermost layers of skin cells. **(b)** Photomicrograph of stained epidermis of human skin. Note the change in shape of the keratinocytes as they become older and move closer to the outer surface of the skin. What is the origin of the keratinocytes that form the bulk of the epidermal tissue?

When areas of skin are severely damaged by fire, acid or some other trauma, the challenge is to get new skin to grow over the damaged area. In the past, the treatments available for persons suffering third-degree burns included the use of skin grafts taken from an uninjured part of the victim's body. Such a graft is called an **autograft** (*auto* = self) because it is a transplant of healthy skin from one area of a person to a damaged area of the same person. However, a problem with autografts is that the area of the graft must be as large as the area of the burned skin. So, for patients with severe burns over a large area of their skin surface, say 50 per cent or more, there is insufficient unburned skin to be used for grafting. In some urgent cases, skin from another person may be grafted onto the burned area of the victim; such a graft is an **allograft**. A skin allograft is a temporary measure because this graft will be rejected.

Another treatment involved covering a burn area with a thin sheet of skin cells grown in plastic dishes in a laboratory. This procedure used cells harvested from a small area of skin from the patient. A problem with skin grown in plastic dishes is that this procedure takes considerable time, with up to 21 days being needed to produce sheets of skin cells sufficiently large to cover severely burned areas. In addition, the sheets of skin cells are thin and very fragile. Another problem is that the sheets begin to act like skin and the surface cells form keratin and die so that they are less active growers when the transplant is carried out. Scarring tends to be more severe the longer the patient waits to be treated and the longer wait also increases the chance of infection and other complications with the wounds.

Alternatively, synthetic skin can be used for skin grafts. One example is Integra® Template. The outer layer of this artificial skin is a thin film of silicone, and the second layer is made of cross-linked fibrous proteins (collagen) and a complex carbohydrate (glycosaminoglycan). Synthetic skin is used to cover the burnt area where it acts as a scaffold that enables the patient's own dermal cells to regenerate the skin dermis. Then the silicone film is removed and covered with a thin epidermal skin graft, thus replacing the skin epidermis.

Spray treatments for burns

Professor Wood's research first led to the development of a spray-on solution of skin cells, or CellSpray, that contained a suspension of various skin cells. The cells came from skin harvested from unburnt areas of a patient's skin. These cells were first cultured in the laboratory for a period of about 5 days, during which their numbers increased by cell division. Later, when sprayed over a burn area, the cells spread and continued to divide forming a layer of skin.

FIGURE 9.4 Regenerative Epithelial Suspension™ created using ReCell®, developed by Professor Fiona Wood. A small skin sample is processed into an Epithelial Suspension™ using the ReCell® device and is sprayed onto burnt areas where it will continue to grow and form a new skin.

A further development of this technology is ReCell® Spray on Skin® (see figure 9.4), which is marketed as a self-contained kit (see figure 9.5a). The time interval from taking cells from a patient to applying these cells to a burn area on that patient is about 30 minutes. A small area of healthy skin — about 2 cm by 2 cm, about 0.2 mm thick and close to the area of the burn — is taken from a burns patient. The skin sample includes basal stem cells, pigment-producing cells, keratinocytes and fibroblast cells from the epidermis, as well as some cells from the dermis. The skin tissue is treated through a series of steps (see figure 9.5b) that includes treatment with an enzyme which removes the extracellular matrix that holds the skin cells together. The final suspension of skin cells, plus growth factors to stimulate cell division, is delivered directly to the burn site with a special spray applicator.

ReCell Spray on Skin technology is used in conjunction with skin grafts for deep or third-degree burns. In cases of limited thickness or second-degree burns, the technology is used alone and can cover burn areas up to about 1900 cm^2. Once the cell suspension is applied to a burn area, the basal stem cells will multiply through repeated cell cycles and, over time, the skin lost by the burn damage will be replaced.

As well as being used in the treatment of acute burns where donor skin grafts cannot be taken, the ReCell technology can be used to treat other conditions, such as chronic skin ulcers.

The science involved in growing new skin cells is possible because living skin cells are able to regenerate. We continually shed our old skin cells and so we continually need to replace them. **Skin cells are continually being replaced by the cell cycle, a process that results in the production of two new cells, each identical to the parent cell that gave rise to them. Mitosis** is an important part of that cycle and involves the replication of the genetic material in the cell. The cytoplasm of a cell is shared between the two new cells at **cytokinesis**.

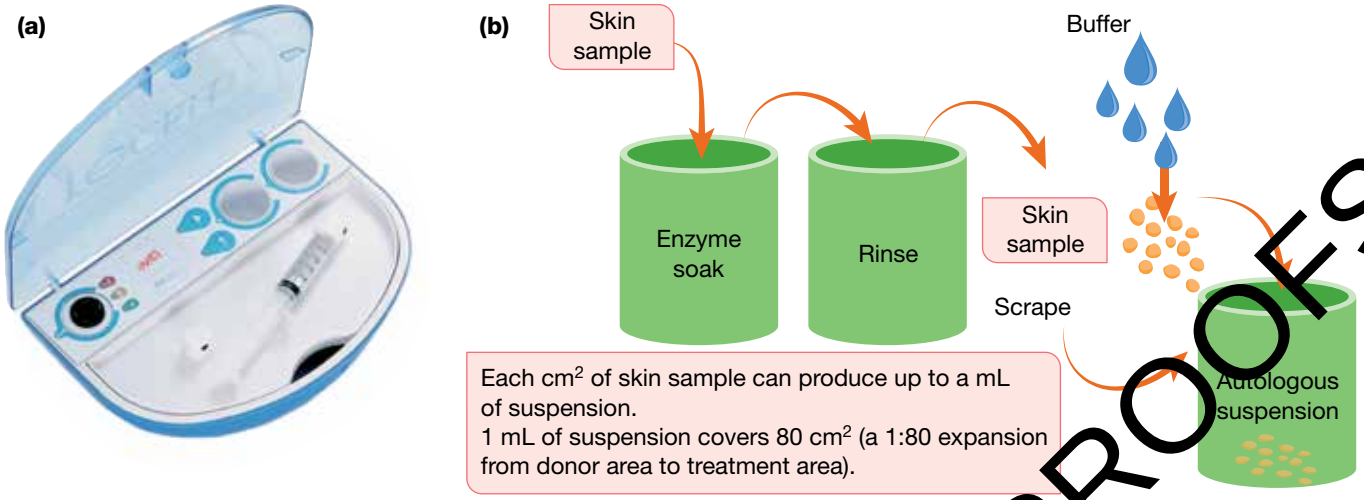

FIGURE 9.5 (a) The self-contained ReCell® Spray on Skin® kit. The sterile chambers and the tray are used for the various procedures involved in preparing a small sample of skin tissue for application to a burn site. What is the size of the patient's skin sample used in this procedure? (Image courtesy of Avita Medical Ltd) **(b)** Diagram showing the procedure that cells pass through with the ReCell kit. Each square centimetre of skin taken from a patient converts to 1 mL of cell suspension, and this can cover 80 cm^2 of burn area. (Image adapted from www.avitamedical.com/wp-content/uploads/2015/03/Avita-Corporate-Presentation-March-2015.pdf)

In this chapter, we consider in some depth the importance of mitosis and cytokinesis. We also explore where these processes occur in a range of animals and plants.

The cell cycle

Cells have evolved complex and exact mechanisms to ensure that genetic information can be passed without error from one cell to two daughter cells of the next generation. It is through the mechanisms of the **cell cycle** that somatic cells of eukaryotes can divide, producing two daughter cells from one parent cell. These daughter cells are genetically identical to each other and genetically identical to the parent cell: a process of natural cloning. To achieve this, eukaryotic cells must first replicate their DNA, then orient their chromosomes in a very precise way, and then separate the sister chromatids.

Key events in the cell cycle

The key events that occur during a cell cycle are summarised in simple terms in table 9.1. These events occur in three distinct phases of the cell cycle: interphase, mitosis and cytokinesis.

TABLE 9.1 A simplified summary of key events during the cell cycle

Cell cycle	What happens	Phase of cell cycle
step 1	replication of DNA of parent cell	interphase
step 2	organisation of chromosomes, followed by their separation into two identical groups at different poles of the parent cell	mitosis
step 3	division of parent cell into two cells	cytokinesis

Let's explore each of these steps in some detail.

Interphase: period of DNA replication

An essential process in the cell cycle is the replication of DNA, the genetic material. DNA replication occurs during a stage of the cell cycle known as the **interphase**. (This stage was once called the 'resting phase', but the cells are far from resting during interphase.) If you looked through a light microscope at cells during interphase, you would see the cell nucleus, but you would not see any discrete chromosomes. In interphase, the chromosomes are decondensed and distributed through the nucleus. However, if you could watch the uptake of the nucleic acids that are the building blocks of DNA, you would see that the cells were busily copying their DNA and performing many other biochemical activities.

In a mammalian cell, a complete cell cycle takes about 24 hours. The time spent by a cell in interphase is far longer than that spent in any other stage of the cell cycle. For example, in mammalian cells about 90 per cent of the time of a complete cell cycle is spent in interphase (see figure 9.6), that is about 22 hours. This highlights the importance of the activities occurring during interphase.

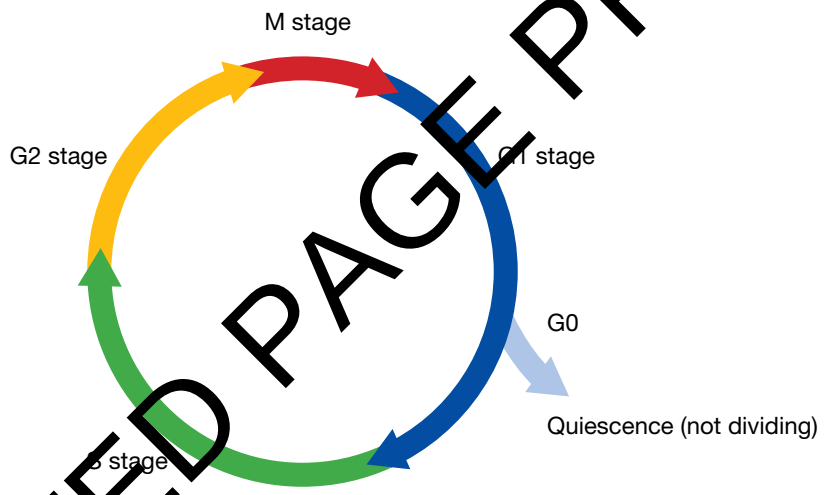

FIGURE 9.6 Stages of the cell cycle. Most of the cell cycle is taken up by the three stages of interphase (G1, S and G2). The M stage is the division stage that includes the division of the nucleus (mitosis) and the division of the remainder of the cell (cytokinesis). What key event takes place during the S stage of interphase?

Interphase is subdivided into three stages:

1. *The G1 or Gap 1 stage*. During the **G1 stage of interphase**, a cell undergoes growth, increasing the amount of cell cytosol. The cell also synthesises proteins that are needed for DNA replication. The mitochondria of the cell divide and, in the cases of photosynthetic plant cells, their chloroplasts also divide. It is near the end of this stage that the cell will either commit to continuing the cell cycle or will drop out and not divide. If the latter occurs, the cell enters a non-dividing quiescent G0 stage.
2. *The S or synthesis stage*. During the **S stage of interphase**, the parent cell synthesises or replicates its DNA, the genetic material of the cell. At the end of the S stage, the parent cell contains two identical copies of its original DNA.
3. *The G2 or Gap 2 stage*. During the **G2 stage of interphase**, further growth of the cell occurs in preparation for division. In addition, the synthesis of proteins occurs, including those that form the microtubules of the spindle. By the end of interphase, the cell has doubled its size.

For a typical human cell that requires 24 hours to complete one cell cycle, the time spent in the various stages might be: G1 stage about 11 hours, S stage about 8 hours, G2 stage about 4 hours and the remainder (mitosis and cytokinesis) about 1 hour. This is in contrast to the rapid process of **binary fission** in prokaryotes that produces two daughter cells within a period of 20 to 40 minutes.

Mitosis: organising and separating chromosomes

The appearance of chromosomes, initially thin and long, and the disappearance of the nuclear membrane mark the start of the part of the cell cycle known as mitosis, the M stage.

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Interactivity
Mitosis
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Mitosis includes a number of different stages:

- **Prophase**. Chromosomes gradually condense — becoming shorter and thicker — and become visible as double-stranded structures (see figure 9.7). The spindle forms and the nuclear membrane breaks down.
- **Metaphase**. The double-stranded chromosomes, also called **dyads**, line up around the equator of the cell.
- **Anaphase**. The sister chromatids separate and are pulled to opposite ends of the spindle by the contraction of spindle fibres (see figure 9.8).
- **Telophase**. A nuclear membrane forms around each separate group of single-stranded chromosomes and the chromosomes gradually decondense. Mitosis completes the division of the nucleus.

Figure 9.9 provides details of the different stages of mitosis.

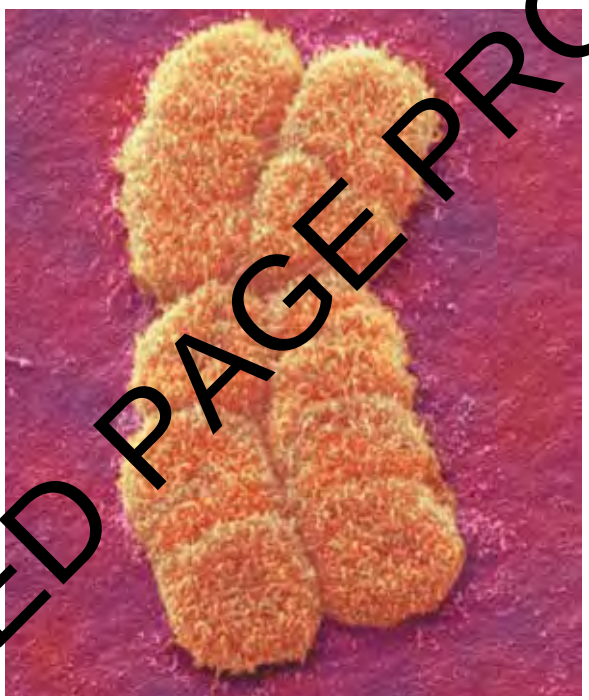


FIGURE 9.7 False coloured scanning electron microscope image of a human chromosome. At the metaphase stage of mitosis, the chromosome is double-stranded and can be called a dyad. In this image, the two sister chromatids of this chromosome are clearly visible. Each chromatid contains an identical copy of the same DNA molecule. At what stage of the cell cycle did the replication of this chromosome occur?

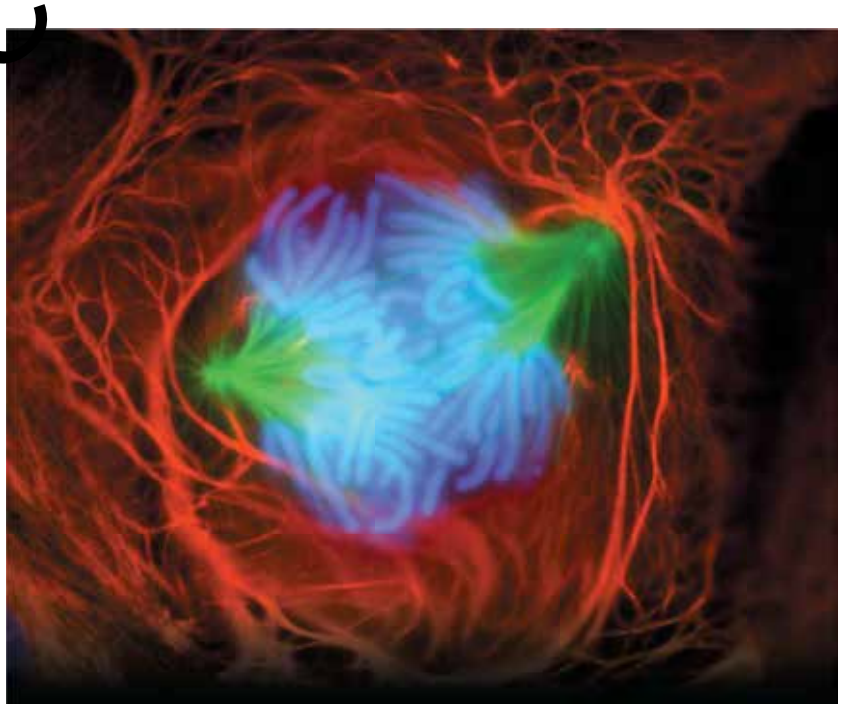
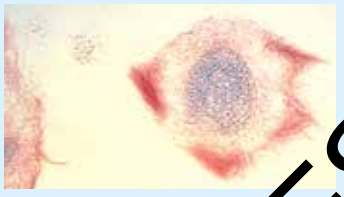


FIGURE 9.8 A dividing cell of a newt (*Notophthalamus* sp.) at anaphase of mitosis. The chromosomes (stained blue) are attached to the microtubules that form the spindle fibres (stained green). A duplicate set of chromosomes is being pulled to opposite poles of the spindle as fibres contract. Keratin fibres (stained red) surround the spindle.

STARTING POINT: One cell containing four single-stranded chromosomes

i. Nucleus is well defined at late interphase. Animal cells have a pair of centrioles in an aster of microtubules close to the nuclear envelope. Chromosomes are not visible but their DNA has already replicated.

Interphase

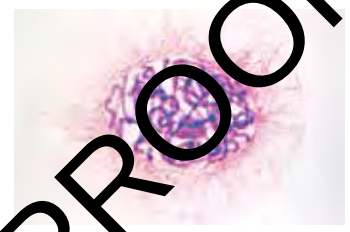


Interphase

MITOSIS

ii. Chromosomes become visible early in mitosis. At first they appear thin and long but gradually become thicker and shorter. Later, the chromosomes can be seen to be double stranded, held together at the centromere. The replicated centrioles move apart; microtubules of the mitotic spindle continue to extend from the centrioles.

Prophase



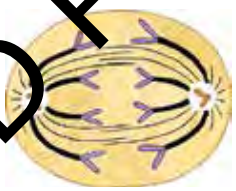
Prophase

iii. Mitotic spindle is fully formed between the pairs of centrioles at the two poles of the spindle. The double-stranded chromosomes (each strand is called a chromatid) line up around the equator of the cell. From the side, they form a line across the middle of the cell. The nuclear membrane has disappeared.

Metaphase

Metaphase

iv. Each centromere divides, so that the single-stranded copies of each chromosome move to opposite ends of the cell as the tubules shorten. This migration is orderly and results in one copy of each chromosome moving toward each end of the spindle.

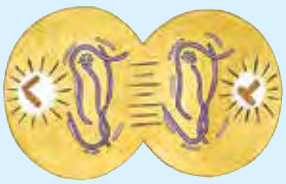


Anaphase

Anaphase

v. The chromosomes become thinner and less obvious. A new nuclear membrane begins to form around each group of chromosomes.

This completes the process of mitosis.

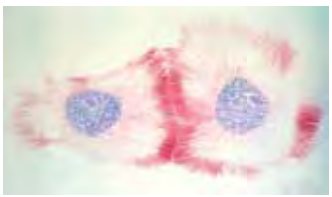


Telophase

Telophase

vi. Division of the cytoplasm by a process called cytokinesis is completed, new membranes form enclosing each of the two new cells (and cell walls in the case of plants), which become interphase cells.

Interphase



Interphase

END POINT: Two cells each containing four single-stranded chromosomes

FIGURE 9.9 Summary of mitosis and cytokinesis. The drawings (middle column) show a stylised version in an animal cell containing four chromosomes. The light micrographs (third column) show mitosis in the endosperm of the seed of an African blood lily, *Scadoxus katherinae* (18 chromosomes in each cell). Chromosomes are stained purple and microtubules are stained pink. Note the changes in chromosomes and the formation and distribution of microtubules and fibres as the cell moves through the cell cycle. Two daughter cells form from each cell by the completion of the cell cycle.

A protein called cohesin holds sister chromatids together. (It appears as a blue stained region in figure 9.1). Cohesin is removed at the metaphase–anaphase transition.

Individual chromosomes first become visible as double, thread-like structures held together in a constricted region. Each of these threads is called a **chromatid** and the position where they are held together is called a **centromere**. The fact that the chromosomes are double-stranded and therefore contain two molecules of DNA indicates that the genetic material in the parent cell has already been replicated.

The chromosomes continue to shorten and thicken and the nuclear membrane disintegrates. At the same time, the very fine protein fibres or microtubules in the cytosol move towards the nucleus. The function of the fibres is to guide the movement of the chromosomes in the cell. The fibres become arranged in the cell, rather like the lines of longitude on a globe, to form a structure called a **spindle**. **The chromosomes become attached by their centromeres around the 'equator' of the spindle.**

Two things then happen. The centromeres split, so that there are pairs of chromosomes, and the spindle fibres contract. The contraction of the spindle fibres is responsible for the movement of the chromosomes towards the poles of the spindle. The movement of the new chromosomes is very ordered. One of the new chromosomes from each pair moves to one end of the spindle; its identical pair moves towards the opposite pole. The end result is a set of chromosomes at each end of the spindle. Because the new chromosomes behave in an orderly way, **the set of chromosomes at one end of the spindle is identical to the set of chromosomes at the other end of the spindle.**

The chromosomes at each end of the spindle begin to lengthen and become less visible as distinct structures. At the same time, the protein fibres disperse back into the cytosol and a nuclear membrane develops around each group.

Remember that mitosis is a continuous process. The stages of mitosis identify key changes in the appearance and the position of chromosomes. Remember also that chromosomes are not routinely visible when viewing cells through a light microscope. Only cells that are capable of division will ever show chromosomes and this will be for only a short period during the cell cycle. The disappearance of discrete chromosomes does not mean that the genetic material has disappeared; rather, the DNA is present as chromatin granules dispersed throughout the nucleus.

WALTHER FLEMMING AND MITOSIS

Walther Flemming (1843–1905) was the German cytologist who discovered chromosomes and their role in cell division. Flemming used newly developed aniline dyes and improved microscopes to study nuclei in cells and found that scattered fragments in the nucleus became highly coloured. He named these fragments 'chromatin'. He found that, during cell division, the chromatin granules coalesced to form thread-like structures that were later called chromosomes (*chroma* = colour; *soma* = body). He showed that, during cell division, chromosomes split lengthwise and separate so that each daughter cell has as much genetic information as the original chromosome. Flemming called this process *mitosis*. The term mitosis comes from the Greek *mitos* = thread and *osis* = process.

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Unit 2
AOS 1
Topic 1
Concept 4

Cytokinesis
Concept summary and practice questions

Cytokinesis: one cell to two cells

At the end of mitosis, the division of the nucleus into two new identical nuclei is complete. However, the cell cycle is completed only after the cytosol and organelles in the cytosol distribute around the new nuclei and become enclosed within an entire plasma membrane. This final process of the cell cycle is called cytokinesis.

In January 2005, the journal *Trends in Cell Biology* (figure 9.10) announced a series of special articles on research into cytokinesis under the title 'Cytokinesis: the great divide'. In the first of these articles, Professor Jeremy Hyams of Massey University wrote:

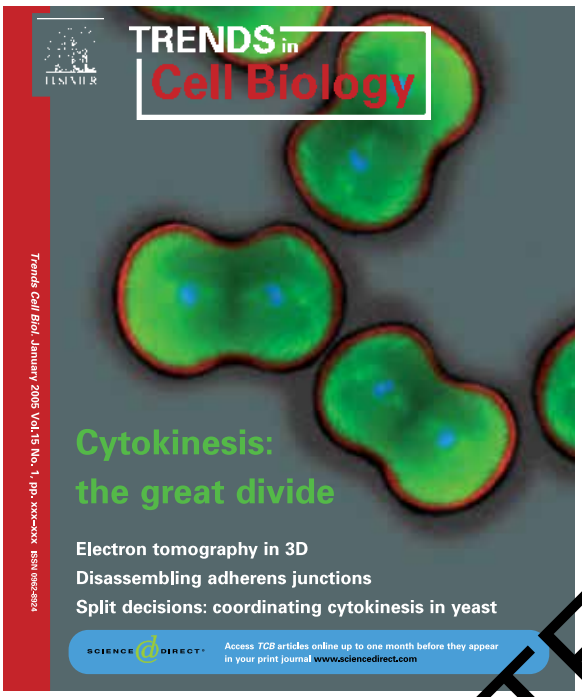

FIGURE 9.10 The front cover of the journal in which research into cytokinesis is discussed

> Cytokinesis brings the curtain down on the cell cycle; it is the final dramatic act in which one cell becomes two.

As the two new nuclei form at the end of mitosis, the cytosol and organelles, such as mitochondria and chloroplasts, surround each nucleus and cytokinesis occurs. Minor differences occur during cytokinesis in different organisms. Generally, in animals, the bridge of cytoplasm between the two new nuclei narrows as the plasma membrane pinches in to separate the nuclei and cytoplasm into two new cells (see figure 9.11a). In plant cells, a cell plate forms between the two groups of chromosomes and develops into a new cell wall for each of the newly produced cells (figure 9.11b).

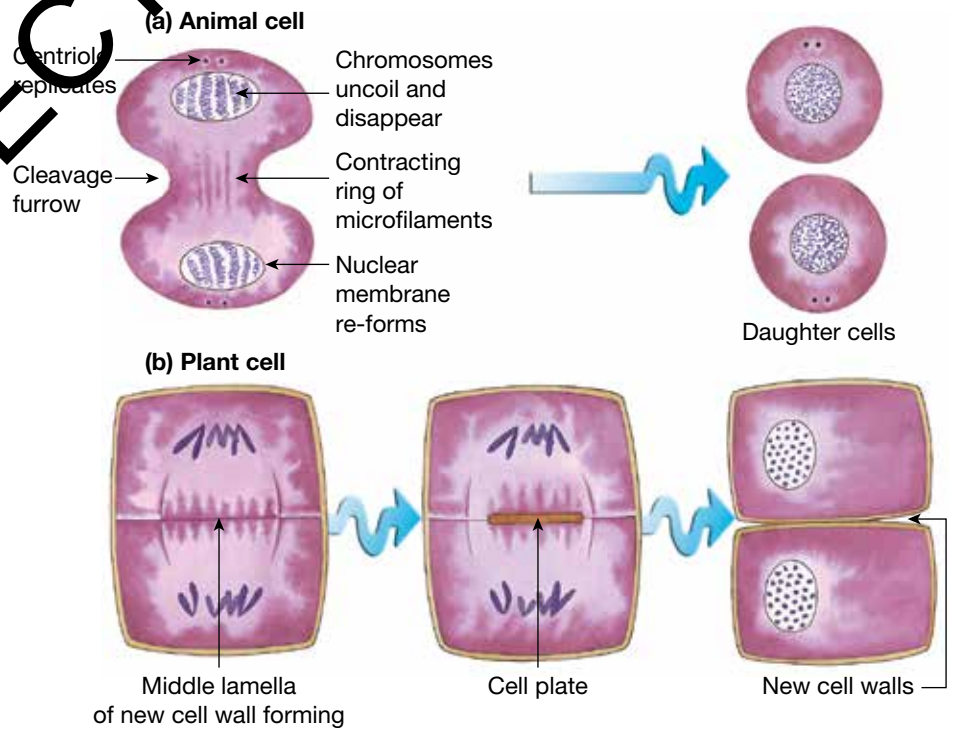

FIGURE 9.11 Minor differences are visible in plant and animal cells during mitosis and cytokinesis. **(a)** An animal cell has a pair of centrioles at each pole of the spindle and a ring of contracting filaments that separates the cytosol and organelles during cytokinesis. **(b)** In a newly replicating plant cell, a cell plate forms between the two groups of chromosomes and gives rise to a new cell wall for each new cell.

Mitosis is essentially the same in plant and animal cells. The small differences that do exist are not related to the genetic material, nor do they have an impact on the biological significance of the process.

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Unit 2 | AOS 1 | Topic 1 | Concept 1

Prokaryotic cell division
Concept summary and practice questions

Cell cycle in prokaryotes

Prokaryotes, such as bacteria and archaea, also have a cell cycle. This is a far less complex process than the cell cycle in eukaryotic cells. Note that bacteria and other microbes have a single circular DNA molecule in contrast to the many chromosomes of eukaryotic cells. The process in microbes is called binary fission and its essential components are shown in figure 9.12.

The process of asexual reproduction by binary fission in bacteria is simpler and faster than asexual reproduction in eukaryotic organisms. Asexual reproduction in eukaryotes involves the more complex process of mitosis followed by division of the cytoplasm (cytokinesis). This process typically takes many hours to complete. Binary fission in bacterial cells can be completed in about 20 minutes at room temperature. This means that, if resources are available, one bacterial cell, through successive binary fission over an 8-hour period, could produce 16 million descendants! This is an example of **exponential growth** (discussed further in chapter 8) and it reminds us why a bacterial infection, if not treated, can have serious outcomes. Figure 9.13 shows a cell of the bacterial species *Escherichia coli* dividing by binary fission.

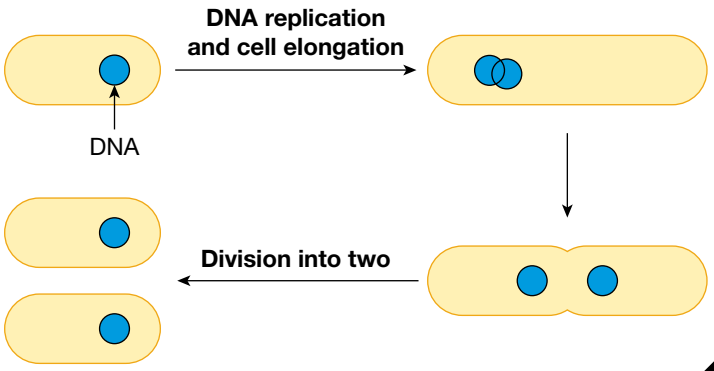


FIGURE 9.12 Diagram showing the essence of the cell cycle in a bacterial cell. The cell cycle in prokaryotes, such as the one shown, is far less complex and much faster than the cell cycle of eukaryotes. What elements of the prokaryotic cell cycle are also present in the cell cycle of eukaryotes?

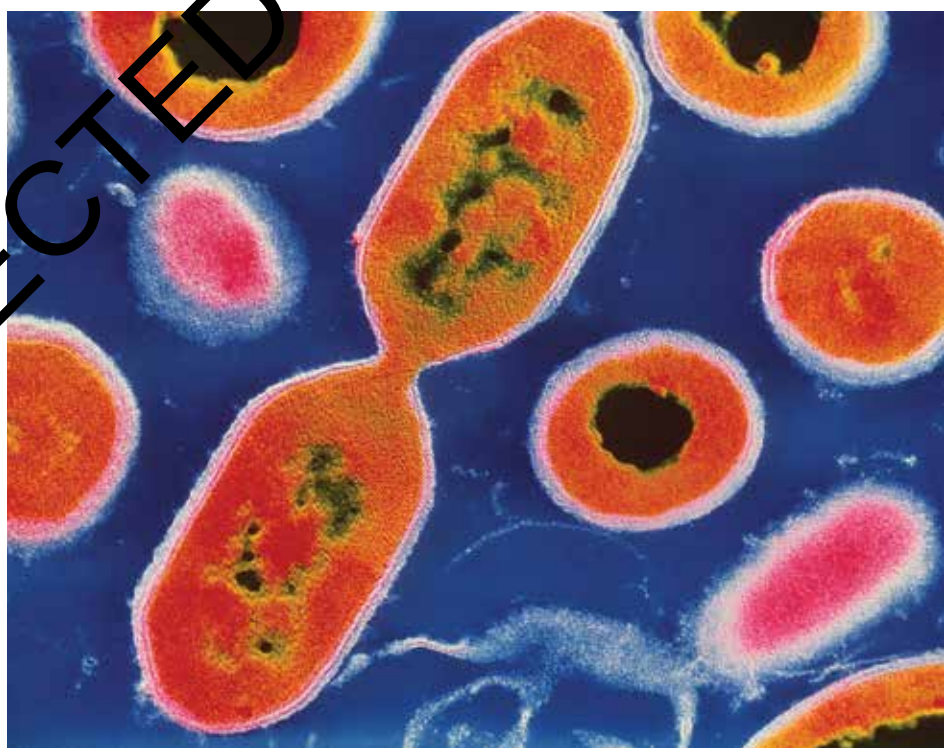


FIGURE 9.13 Cells of the bacterial species *Listeria* sp., one of which is dividing by binary fission. The circular outlines are cross-sections through bacterial cells. The DNA of the bacterial circular chromosome appears as darkly stained material.

KEY IDEAS

- Eukaryotic cells divide during the cell cycle giving rise to genetically identical daughter cells.
- An essential early process in the cell cycle is the replication of DNA.
- Carefully governed separation of sister chromatids is another essential step in cell division.
- Mitosis is followed by cytokinesis.
- Cell division in prokaryotes involves a relatively simple and rapid process of binary fission.

QUICK CHECK

1 What are the stages of interphase?
2 What is the key event of the S stage of interphase?
3 What is an average time for:
   a a complete cell cycle in a mammal
   b a complete cell cycle by binary fission in a microbe?
4 Identify whether each of the following statements is true or false.
   a Sister chromatids separate at metaphase.
   b During interphase, double-stranded chromosomes are visible.
   c Cytokinesis is the last step in the cell cycle.
   d In a cell cycle, more time is spent in interphase than any other stage.
   e Binary fission does not involve DNA replication.
   f The sequence of stages in interphase is G1 then G2 then S.

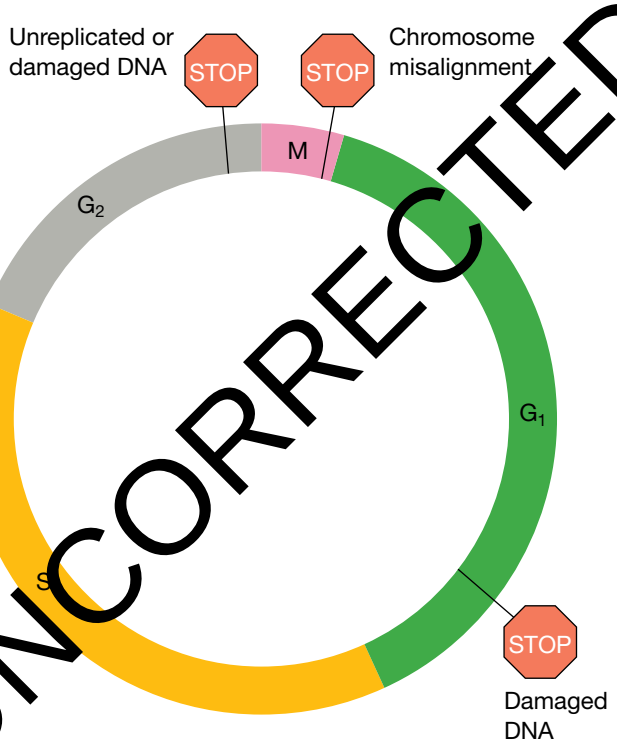


FIGURE 9.14 Checkpoints occur at various points in the cell cycle. The G1 and the G2 checkpoints check for the presence of unrepaired DNA or missing DNA. The M checkpoint checks a different feature. What is it?

Checkpoints in the cell cycle

The cell cycle is a complex series of events which, when operating without error, produces two daughter cells that are genetically identical to each other and to their original parent cell. In an error-free cell cycle the complete genome of the parent is accurately duplicated and then distributed to the two daughter cells.

During the cell cycle, there are several checkpoints that function to ensure that a complete and damage-free copy of the genome is transmitted to the two daughter cells. Each checkpoint can detect a particular kind of error. If an error is detected, depending on the type of error, the cell cycle is either aborted or delayed, allowing time for the error to be corrected.

Figure 9.14 shows the location of three checkpoints in the cell cycle.

The **G1 checkpoint** occurs at the G1 (Gap 1) stage of interphase. At this checkpoint, the cell is ready to undergo division so a check of the DNA of the cell occurs. If the DNA of the cell is found to be damaged or incomplete, the cell is stopped from continuing through the cell cycle. Instead, the cell may enter a non-dividing quiescent stage called G0, or it may be targeted for destruction. (The 'security guard' at the G1 checkpoint is a protein known as p53, a tumour-suppressor protein. What do you think might happen if a mutation occurred in the p53 protein so that it could not carry out its normal function?)

If the cell passes the G1 checkpoint, it proceeds into the cell cycle and enters the S stage of interphase. During the S stage, the cell replicates its DNA so that, by the end of the S stage, the cell should have double the amount of DNA and this DNA should be two complete and accurate copies of its genome. The cell now moves to the G2 stage of interphase where it must pass the **G2 checkpoint**.

At the G2 checkpoint, the replicated DNA of the cell is checked for completeness and lack of damage. If the cell passes this checkpoint, it can then advance to the mitosis stage of the cell cycle.

The **M checkpoint** (or spindle assembly checkpoint) occurs at the metaphase stage of mitosis. A check is carried out to ensure that the sister chromatids (i.e. the two strands of each double-stranded chromosome) are attached to the correct microtubules of the spindle. This check is to ensure that the sister chromatids are pulled in opposite directions to different poles of the spindle. If an error is detected, the cell cycle is delayed until the error is fixed.

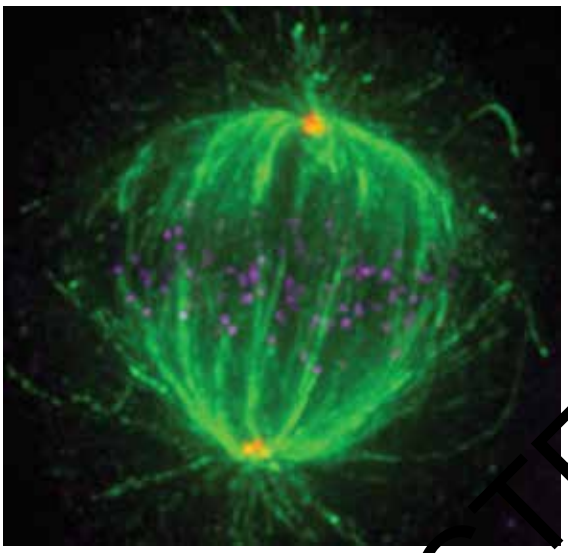


FIGURE 9.15 DeltaVision Widefield microscope image of a HeLa cell undergoing mitosis and treated with various stains. The pericentrin stain shows the centrioles (orange). The ACA stain shows the kinetochores (purple) that are protein complexes located at the centromere and bind each chromosome to the microtubules of the spindle. The A-tubulin stain shows the microtubules of the spindle (green). (Image courtesy A Loynton-Ferrand, IMCF, University of Basel)

The mitotic spindle

The focus in mitosis is typically on chromosomes. However, the positioning and the movement of the chromosomes depend on the presence of a microtubule framework, the spindle.

In animal cells, once mitosis starts, the paired **centrioles** move to opposite ends of the cell where they form the poles of the spindle. Clusters of microtubules grow out from the centrioles towards the middle of the cell. These microtubule clusters are called **spindle fibres**. At metaphase, these fibres anchor the double-stranded chromosomes around the equator of the cell. Each chromatid has a special attachment site called a **kinetochore** by which it links to a spindle fibre (see figure 9.15).

Spindle fibres from one pole attach to one sister chromatid and fibres from the opposite pole attach to its partner chromatid. (What would happen if the two sister chromatids of one chromosome became linked to fibres from the same pole of the spindle?) At the M checkpoint, the connection between chromatid and spindle fibres is checked and, if it is not correct, the cell cycle is delayed until the arrangement is corrected.

Spindle fibres are composed of actin, a contractile protein. At anaphase, the orderly migration of each pair of sister chromatids is achieved by contractions of the fibres that pull these now single-stranded chromosomes to the opposite poles of the spindle.

Mitochondria and chloroplasts also replicate

We have seen that mitosis is followed by cytokinesis. This is essential so that the two new nuclei formed can each be combined with cytosol to give two new cells. Obviously the **organelles such as mitochondria and chloroplasts within the cytosol must also be replicated during the cell cycle,** otherwise cells would contain an ever-decreasing number of these structures.

Just as a nucleus contains DNA that must replicate before two new nuclei are formed, mitochondria and chloroplasts contain DNA that must replicate before the organelles divide. The alga *Mallomonas splendens* (see figure 9.16a) has a single chloroplast composed of two lobes joined by a narrow connection. As a cell of *M. splendens* replicates, its chloroplast must also replicate. During replication of the chloroplast, the narrow connection breaks and each of the two lobes grows and constricts to give two, two-lobed chloroplasts (see figure 9.16b). Organelles such as chloroplasts and mitochondria can arise only from pre-existing organelles. Cells can arise only from pre-existing cells.

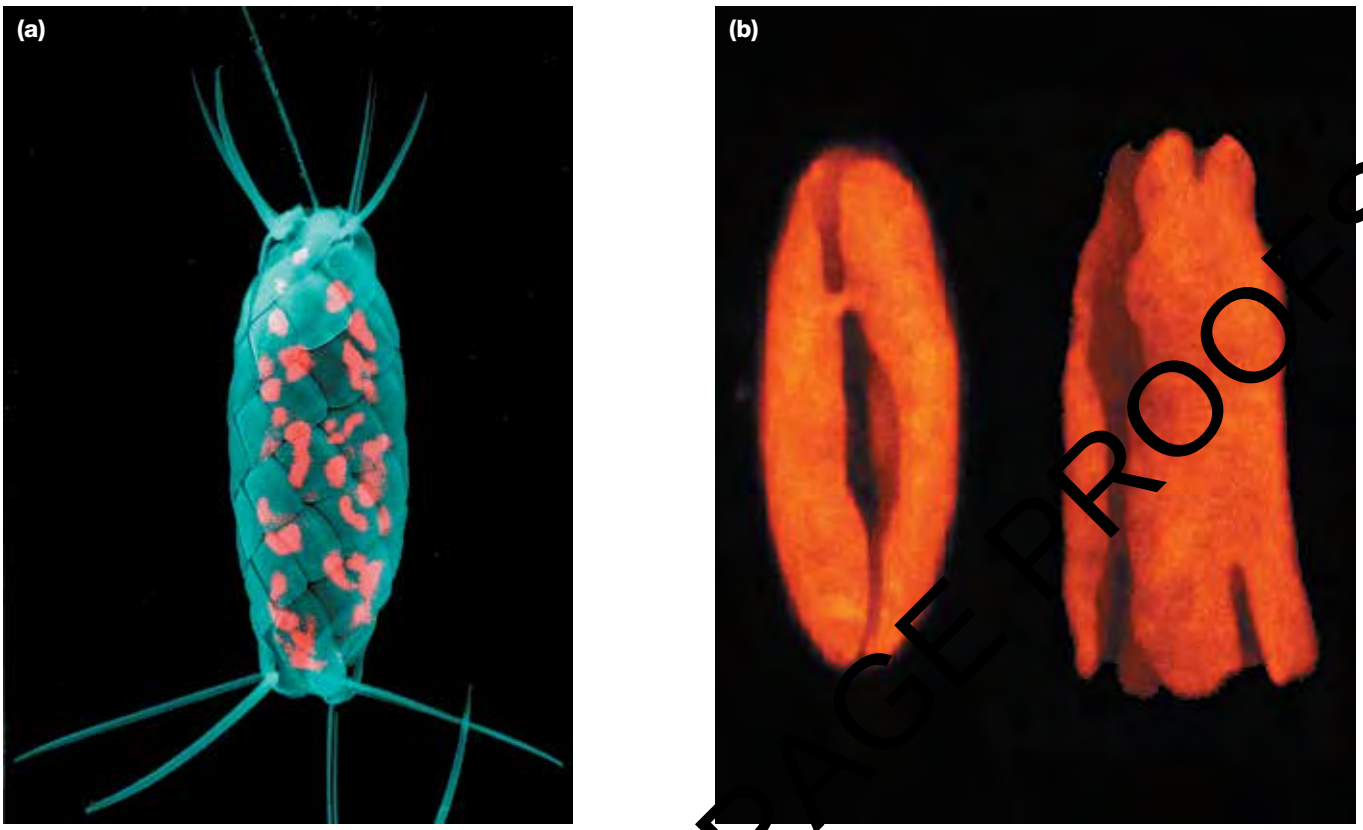


FIGURE 9.16 **(a)** *Mallomonas splendens*, a unicellular alga with scales and bristles, has a single large bilobed chloroplast. **(b)** Confocal microscope image showing autofluorescence of chloroplasts from two cells of *M. splendens*. On the left is a single chloroplast that is composed of two lobes joined by a narrow connection. On the right is a replicating chloroplast. Note that the connection has been broken and the each lobe is replicating to produce two double-lobed chloroplasts.

KEY IDEAS

- Checkpoints occur at various points in the cell cycle.
- Some checkpoints identify damaged or missing DNA and delay or stop the cell cycle.
- The spindle is essential for chromosome arrangement and precise movement during mitosis.
- Sister chromatids must become linked to spindle fibres from opposite poles of the spindle to pass the M checkpoint.

QUICK CHECK

5 What is the role of the M checkpoint?

6 Identify whether each of the following statements is true or false.

- **a** One sister chromatid has just half the DNA of a chromosome.
- **b** Chromosomes move of their own accord because they are made of contractile proteins.
- **c** Mitosis can proceed in the absence of a spindle.
- **d** The spindle is composed of microtubules.
- **e** An accurate separation of sister chromatids during mitosis depends on their being linked to fibres from opposite poles of the spindle.

Cell cycle in action

The cell cycle is a critical process in:

- growth, where the cell cycle produces new cells, resulting in an increase in cell number. This is most prominent during embryonic development of a multicellular organism. Early embryonic cell division is exponential, with one cell dividing to form two cells, these two form four cells, these four form eight cells, and so on. The power of the cell cycle is seen in the fact that a typical human is composed of 37 trillion cells that came originally from a single fertilised egg cell.
- repair and maintenance (regeneration), where the cell cycle produces new cells to replace dead or damaged cells
- reproduction, where the cell cycle produces identical cells, such as spores, that give rise to the next generation.

Not all cells of a multicellular organism are capable of dividing. For example, in the human body, nerve cells generally cannot regenerate. Cells from other organs, such as kidney and liver, may divide occasionally to replace cells lost through injury or death, but, for most of the time, these cells are in the G0 quiescent stage. However, cells of some human tissues produce new cells at a staggering rate. Let's meet some of them.

Cell cycle in mammals

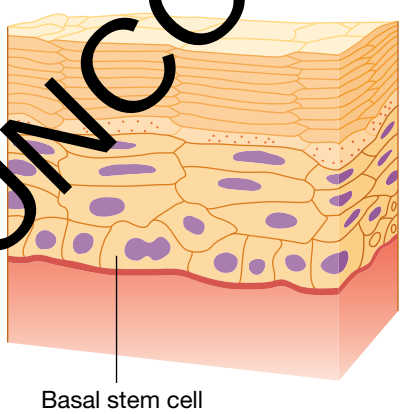
In mammals, such as a human adult, actively dividing cells are found in several tissues, such as the epidermis of the skin, the epithelial lining of the gut and the bone marrow. Cell division normally occurs at a tightly regulated rate, so that the production of new cells matches or balances the rate of cell loss. Tissues with a population of actively dividing stem cells are tissues that have a high and continual level of cell loss or cell death.

Basal stem cells of the epidermis

In human skin, surface cells are constantly being shed and are being replaced by daughter cells produced by division of basal stem cells. Each basal stem cell that undergoes cell division produces two daughter cells. Of these two daughter cells, one becomes a keratinocyte and the other remains in the basal layer as a basal stem cell, replacing the original parent cell. The other daughter cell progressively moves upwards through the epidermis, differentiates into a keratinocyte and is shed from the skin surface (see figure 9.17). Within a period of about 28 days, the entire epidermis is replaced by new cells. This means that the skin that you have, say, today is made of completely different cells from the skin that you had 2 months earlier.

For a newly produced cell to move from the base of the epidermis where it is formed to the base of the dead layer of cells takes about 2 weeks. To move through the layer of dead cells and be shed takes a further 4 weeks. An estimate of the rate of loss of dead skin cells from an adult person is 30 to 40 thousand per hour. This makes the cell cycle activity of basal stem cells of the epidermis very important.

The ability of the skin to heal after considerable damage, as exemplified by the recovery of burns patients, is due to the presence of stem cells in the basal layer of the epidermis and the stem cells in the dermis.



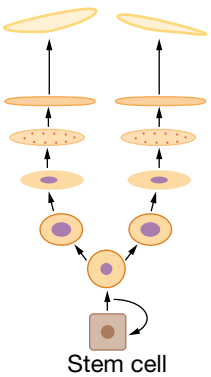


FIGURE 9.17 Cell division in the epidermis of the skin. The basal stem cells divide to produce two cells, one of which replaces the parent stem cell, while the other will differentiate and progressively move to the skin surface and be lost. The cells at the surface become filled with keratin and die.

Intestinal stem cells of the gut

The epithelial lining of the small intestine is regenerated every 4 to 5 days. This means that a person aged 18 years will have experienced more than 1000 replacement cycles of the lining of the small intestine.

As intestinal cells die, they are replaced by new cells produced by intestinal stem cells. These stem cells are located at the base of infoldings, known as **crypts**, that are located between intestinal villi (singular: villus) (see figure 9.18). The replacement cells formed by division of the stem cells take from 2 to 7 days to move from the crypts to the tip of the villi from where they are lost.

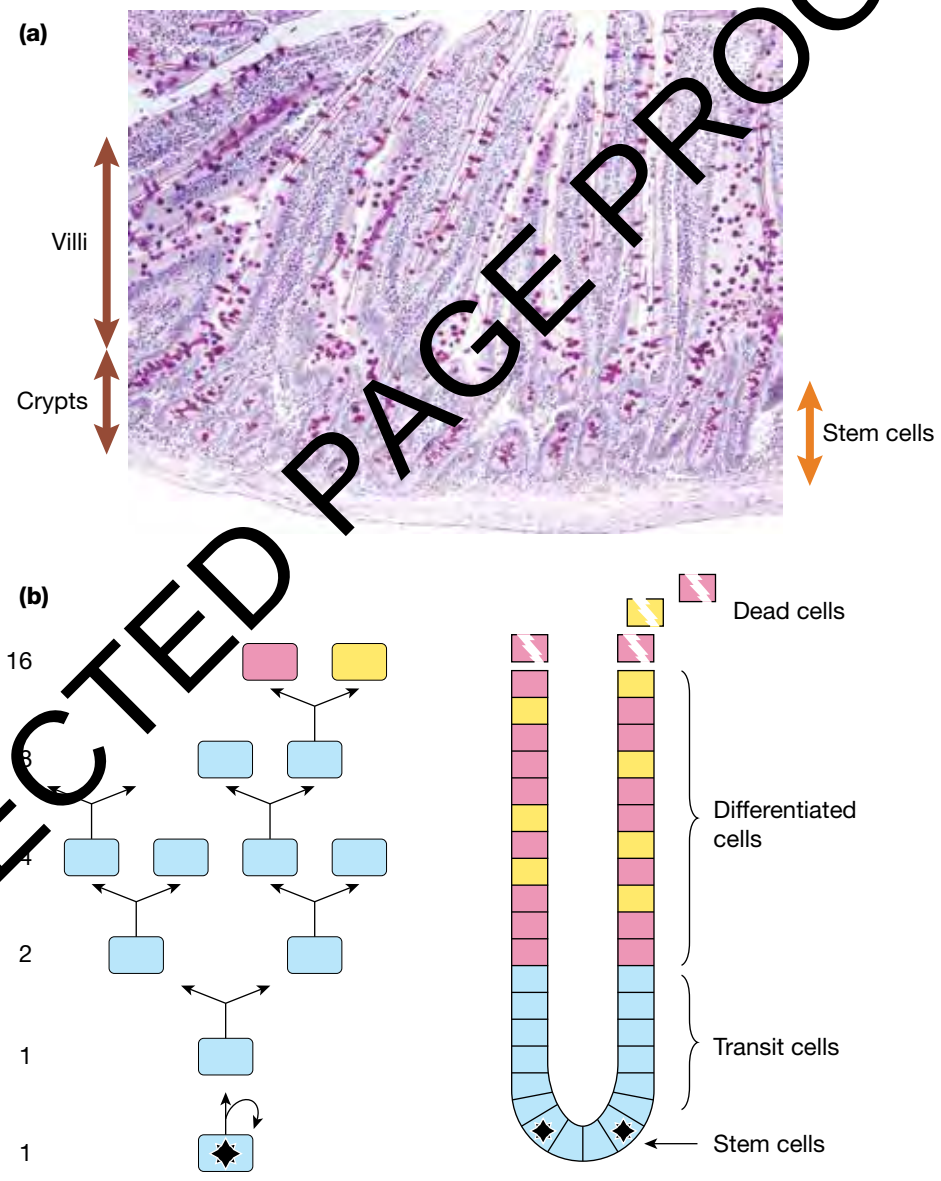


FIGURE 9.18 **(a)** Longitudinal section through the small intestine showing the upward projecting villi with the downward projecting crypts. Intestinal stem cells that are responsible for the regeneration of the intestinal lining are located in these crypts. **(b)** Diagram showing the progression of the cells produced by the intestinal stem cells. Note that of the two cells produced by a stem cell, one will differentiate into a cell on the villus and the other replaces the stem cell.

Haematopoietic stem cells

Haematopoietic stem cells, located in the bone marrow, divide to give rise to cells that subsequently differentiate into the various types of blood cells, including red blood cells, white blood cells of various kinds and platelets (refer to figure 4.17, p. 151). Bone marrow is a spongy tissue found in the core of most bones, including the ribs, hips and spine. Most blood cells are short lived and must be constantly replaced.

NOBEL LAUREATE IN PHYSIOLOGY OR MEDICINE

Dr Elizabeth H Blackburn

Dr Elizabeth Blackburn received her Nobel Prize from His Majesty King Carl XVI Gustaf of Sweden in Stockholm in December 2009 (figure 9.19) for her work on telomeres (figure 9.20) and telomerase. Telomeres are found at the ends of all eukaryotic chromosomes and comprise repetitive DNA strands that get shorter each time a cell divides. This shortening of the telomeres eventually leads to the death of a cell. However, telomerase is an enzyme that prevents shortening in some cells and so extends the life of those cells.

FIGURE 9.19 Dr Elizabeth Blackburn receiving her Nobel Prize from His Majesty King Carl XVI Gustaf of Sweden at the Stockholm Concert Hall, 10 December 2009

Elizabeth Blackburn was born in Tasmania in 1948, one of seven children. After moving to Melbourne, she completed secondary school at the University High School. This was followed by Honours (1971) and Masters degrees (1972) in Biochemistry from the University of Melbourne. Elizabeth then travelled to Cambridge University in England where she was admitted as a PhD student in the Medical Research Council's Laboratory of Molecular Biology. After completing her PhD, Dr Blackburn did postdoctoral training at Yale in the USA, and then worked in the Department of Microbiology and Immunology at the University of California, San Francisco (UCSF) (figure 9.21). She is currently the Morris Herzstein Professor of Biology and Physiology at UCSF and a non-resident fellow of the Salk Institute.

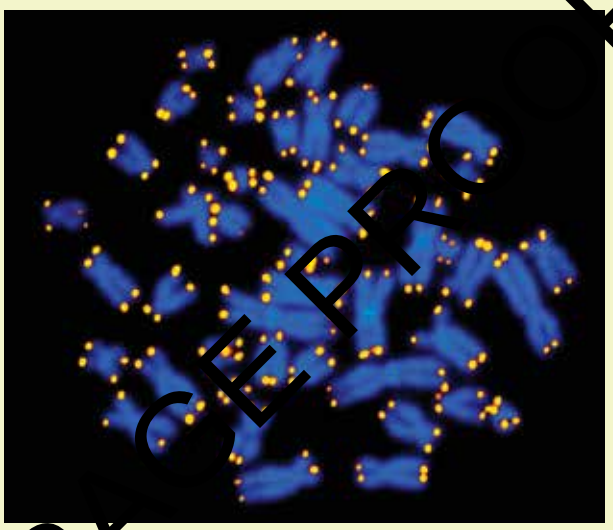


FIGURE 9.20 Mitotic chromosomes (blue) with telomeres (yellow) at the tips of each chromatid

FIGURE 9.21 Dr Elizabeth Blackburn in her lab at the University of California, San Francisco

Dr Blackburn has received many notable awards and honours. They include California Scientist of the Year (1999), American Cancer Society Medal of Honor (2000), L'Oreal–UNESCO Award for Women in Science (2008) and, of course, a Nobel Prize (2009). In 2007, Dr Blackburn was listed by *Time* magazine as one of the '100 most influential people in the world.'

FIGURE 9.22 If a starfish is cut into two, each half can regenerate into a whole.

Cell cycle in other animals

Planaria, phylum Platyhelminthes, are flatworms that live in water. They are one of the few animals that can reproduce asexually by regeneration. The parent breaks into two or more pieces and each piece grows into a new planarian. The new parts are produced by mitosis of cells and each new planarian is an exact copy of the parent.

If a starfish loses some of its 'arms', new ones are regenerated by mitosis (see figure 9.23).

FIGURE 9.23 If a starfish loses some of its 'arms', they regrow. Here you can see six new arms on a damaged starfish.

KEY IDEAS

- The cell cycle is important for the growth, repair and maintenance of eukaryotes.
- In some organisms, the cell cycle plays a role in producing cells involved in reproduction.
- Actively dividing human tissues include the epidermis of the skin, the epithelium of the gut and the bone marrow.
- Stem cells carry out the cell divisions that are responsible for tissue regeneration.

QUICK CHECK

7 Identify where you would find the following.
- **a** Skin stem cells
- **b** A red blood cell precursor
- **c** Keratinocytes
- **d** Haematopoietic stem cells

8 Identify whether each of the following statements is true or false.
- **a** All human cells regularly undergo cell division.
- **b** Haematopoietic stem cells are responsible for skin regeneration.
- **c** The intestinal crypts are where intestinal stem cells are located.
- **d** Tissues composed of short-lived cells would be expected to show a high rate of cell division.

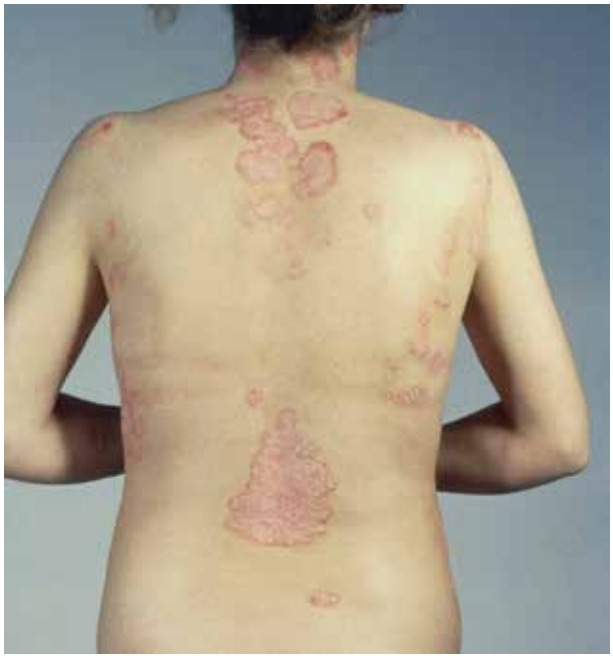


FIGURE 9.24 Psoriasis on the skin of a person's back. This condition is a result of the overproduction of skin cells.

When the cell cycle goes wrong

As identified earlier in this chapter, the cell cycle in various tissues is normally regulated so that, in a mature organism, the rate of production of new cells balances the rate of loss of cells.

If the rate of cell production exceeds that of cell loss, a build up of cells results. This may be seen in the skin condition **psoriasis** (see figure 9.24). Psoriasis is a chronic autoimmune condition in which skin cells are overproduced, resulting in raised patches of red inflamed skin, often covered in a crust of small silvery scales.

More serious consequences of errors in the regulation of the cell cycle in a tissue are cancers.

Cancer: control of cell cycle gone awry

Cancers may result from a breakdown of the normal regulation of the cell cycle, when the cell cycle becomes uncontrolled. In cancerous tissue, cells reproduce at a rate far in excess of the normal regulated rate of the cell cycle and produce masses of cells called tumours. Some tumours are malignant, such as **melanomas** that are cancers derived from the pigment-producing cells, or melanocytes, of the skin epidermis. In malignant tumours individual cells can break free from the primary tumour and migrate throughout the body, establishing sites of secondary cancers.

ODD FACT

The most common cancer diagnosed in Australians aged 15 to 29 years are melanomas, which account for just over 25 per cent of cancers diagnosed in this age group. Most deaths from skin cancers are due to melanomas because of their tendency to spread (metastasise) to other parts of the body.

A clue to what goes wrong in cancer comes from studying cells growing in culture in a Petri dish in a laboratory. In culture, normal (non-cancerous) cell numbers increase through regulated cell divisions and form a single, orderly layer attached to the base of plastic dishes. These cells do not crowd; they are said to show contact inhibition. In addition, normal non-cancerous cells typically undergo a limited number of cell cycles.

In contrast, cancerous cells in culture continue to divide in an unregulated manner. These cells show no contact inhibition, become crowded and form masses of cells in disorganised multiple layers. In addition, the number of cell cycles that cancerous cells can undergo is unlimited.

What causes the breakdown in the control of the cell cycle in cancerous cells? In normal cells, the rate of cell division is regulated so that, in a mature organism, cell production matches cell loss. In addition, checkpoints exist in normal cells to ensure that the DNA that is to be transmitted to daughter cells is complete and error free (refer to pp. 400–1). In cancerous cells, however, the genes that normally control the progress of a cell through the cell cycle are changed by mutation. These various mutations mean that the cell cycle occurs in an unregulated manner and that checkpoints are overridden. No error detection or error correction takes place. Cancerous cells continue to divide even in the presence of significant DNA damage. When this happens, abnormal cells with errors in their DNA continue through the cell cycle, passing these errors onto their daughter cells, and these cells in turn will pass the errors onto their daughter cells.

As mentioned on page 400 the 'security guard' that operates the G2 checkpoint is a protein called p53. The normal p53 protein binds to DNA and this sets up a sequence of events that stops cells from continuing through the cell cycle and enables checks to be carried out. However, when a mutation of the controlling gene occurs, the abnormal p53 protein cannot bind to DNA so that the cell cycle cannot be stopped. As a result, cells can divide in an uncontrolled manner and form tumours.

KEY IDEAS

- The cell cycle is normally regulated so that, in a mature organism, the rate of production of new cells balances the rate of loss of cells.
- Cancers may result from the breakdown of the normal control of the cell cycle.
- Cancerous cells are characterised by unregulated rates of cell division.

QUICK CHECK

9 Identify whether each of the following statements is true or false.
- **a** Cancerous cells divide at rates in excess of the normal regulated rate.
- **b** Cell production and cell loss are kept in balance by genes that regulate the cell cycle.
- **c** Normal non-cancerous cells in culture show contact inhibition.

Cell cycle in plants

In vascular plants, only the cells in meristematic tissues can complete cell cycles and divide to produce identical daughter cells. The cells in permanent plant tissues cannot divide (refer to chapter 4, p. 180). Meristematic tissue is present in several locations including root tips (see figure 9.25) and stems.

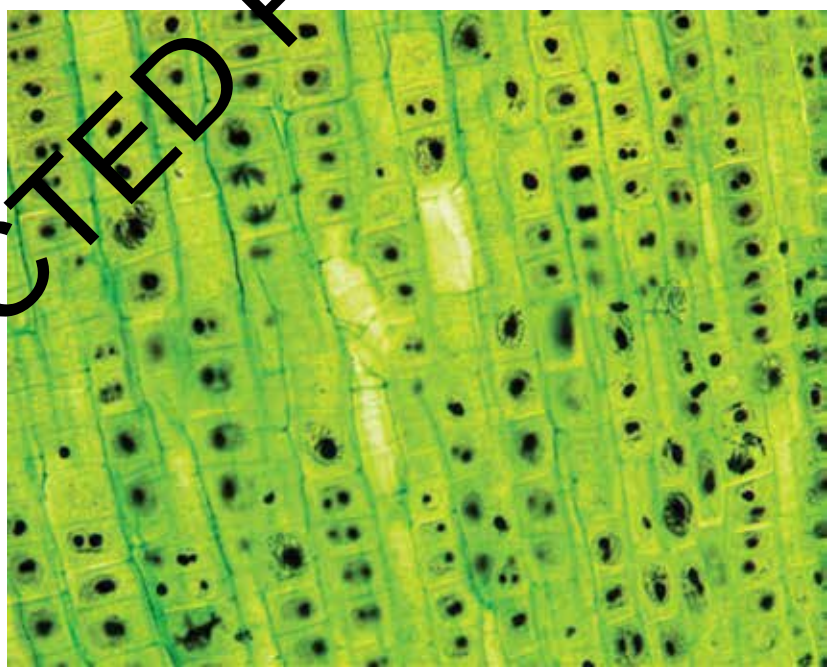


FIGURE 9.25 Light microscope image of a longitudinal section through the meristematic tissue of root tip. This is a region of active cell division and many rows of cells can be seen. Examine this image and see if you can identify some cells that are in the mitosis stage of the cell cycle.

Other examples of the cell cycle in plants include those discussed below.

Epicormic shoots after a bushfire

Bushfires are common in many areas of Australia. Although trees may appear to be burnt to a point that one might think they are dead, a picture such as the one in figure 9.26 (taken just 6 weeks after the area was devastated by bushfire) shows this is not the case. It is clear from the photograph that the fire has completely destroyed the undergrowth of grasses, shrubs and

FIGURE 9.26 The new shoots from the trunk of a burnt eucalypt tree develop as a result of mitosis in buds present beneath the bark. The buds do not develop unless the canopy is destroyed, as has happened in this case.

herbs. Fire-blackened trees with their scorched dead canopy of leaves are in the background, while in the foreground the burnt trunks of rough-barked eucalypt trees are visible. One tree is already showing signs of regrowth; it is a thick-barked eucalypt whose thick outer layer of protective bark has insulated the underlying living tissues from the effects of the fire.

The trunk of a eucalypt does not usually show growing shoots. However, if the normal leaf canopy is destroyed, as happened in this fire, buds that are present beneath the bark grow and reproduce new green leafy shoots, known as **epicormic shoots**. The growth of epicormic shoots involves the production of new cells. The buds below the bark contain tissue called **meristem**, which is made of cells that are able to reproduce to give rise to new cells. These new cells are identical to each other and to the parent cell.

New liverworts from cells in a cup

Liverworts, class Hepatica, are small plants that have a flat, fleshy, leaf-like structure from which **rhizoids** extend into the soil. The name *liverwort* is derived from the shape of the organism — rather like that of a liver — and the Anglo-Saxon word for herb — wort. As you might predict from the name, it was once thought that this plant might be useful in the treatment of liver diseases. In addition to reproducing sexually, liverworts reproduce asexually by means of fragmentation of parts of the plant. Also, liverworts produce gemmae, small multicellular bodies produced in special cuplike structures called gemma cups (see figure 9.27). When rain falls, the gemmae are splashed out of the cup. Gemmae are produced from cells of the parent plant by mitosis. When they grow into new plants they do so by mitosis. The new liverwort plants produced by growth of the gemmae are genetically identical to the parent plant from which they were derived.

FIGURE 9.27 A new plant develops from each of the small bodies that splash out of the gemma cups on a liverwort plant. The new plants are genetically identical to the parent plant.

Cell cycle in fungi

The cell cycle plays an important role in the reproduction of fungi.

The fungus or mould you see on bread or fruit grows by mitosis. A single cell, a fungal spore, lands on food and grows into a mass of threads called hyphae. Specialised stalks — each with a spore case at its tip — grow up from the mass of hyphae (see figure 9.28). Mitosis occurs within the spore case and thousands of black spores are formed. On maturing, the spore case splits open and the tiny, light spores are scattered. When conditions are favourable, each spore germinates and grows into a new hyphal mass.

FIGURE 9.28 The fungus on a rotting tomato **(a)** comprises a mass of white threads or hyphae. Asexual reproduction occurs at the tips of some hyphae and **(b)** large numbers of black spores are formed, each genetically identical with the parent.

KEY IDEAS

- The meristematic tissue of plants contains cells that can complete the cell cycle and produce identical daughter cells.
- In vascular plants, meristematic tissue is present in root tips, shoots and stems.
- Cell division in epicormic shoots is important in the recovery of trees damaged by bushfire.
- Some cells produced by the cell cycle have a reproductive function, but offspring from this process are genetically identical.

QUICK CHECK

10 In which plant tissues would you expect to find dividing cells?

11 Consider the gemmae of liverworts. Would the next generation of plants that are derived from the gemmae of one liverwort be genetically identical or genetically dissimilar?

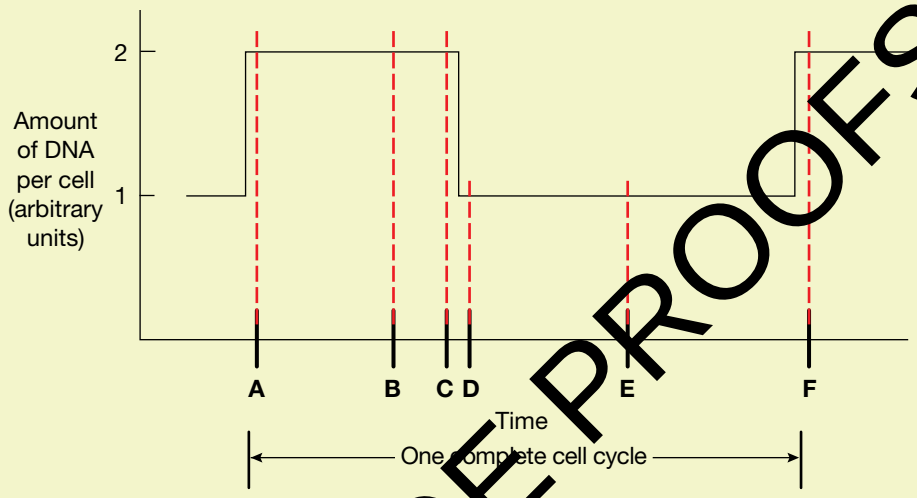
12 How do epicormic shoots contribute to the survival of fire-damaged trees in the Australian bush.

BIOCHALLENGE

1 A number of cells were monitored as they completed one cell cycle. The average amount of DNA per cell was measured and graphed over the time it took for the completion of one cycle. The graph obtained is shown on the right.

a The letters A to F in the graph represent different times in a cell cycle. What are the stages indicated?

b At the same time, sample cells were examined. The cells examined were as follows:



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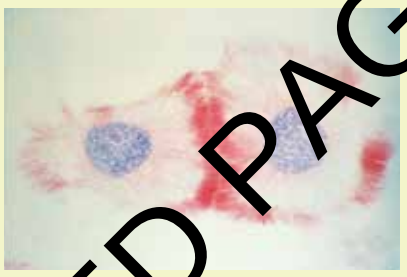

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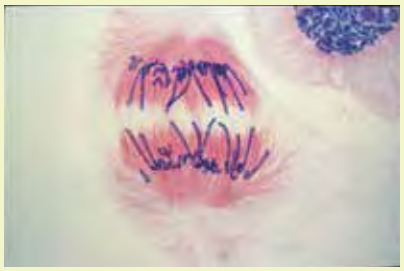

Match the cells 1, 2, 3, 4 and 5 with the appropriate points, A to F, in the cell cycle graph.

Chapter review

studyon
Unit 2 AOS 1 Topic 1
The cell cycle
Sit topic test

Key words

allograft
anaphase
autograft
binary fission
cell cycle
centrioles
centromere
chromatid
crypts
cytokinesis
dermis
dyad
epicormic shoots
epidermis
exponential growth
G1 checkpoint
G1 stage of interphase
G2 checkpoint
G2 stage of interphase
interphase
keratinocytes
kinetochore
M checkpoint
melanocytes
melanomas
meristem
metaphase
mitosis
prophase
psoriasis
rhizoids
S stage of interphase
spindle
spindle fibres
telophase

Questions

1 Making connections ➜ Use at least eight of the chapter key words to draw a concept map. You may use other words in drawing your map.

2 Applying understanding ➜ A cell containing 24 chromosomes reproduced by mitosis. A genetic accident occurred and one of the resulting cells had only 23 chromosomes.
- **a** How many chromosomes would you expect in the other cell produced? Explain why.
- **b** At what stage of cell reproduction do you think the genetic accident occurred?

3 Interpreting and applying understanding of a new concept ➜ Grafting is a technique used with some plants. In grafting, two pieces of living plant tissue are connected in such a way that they will unite and subsequently behave as one plant. For example, the shoot of one kind of plant can be grafted onto the root of another kind of plant (see figure 9.29). The shoot of a pear tree, *Pyrus communis*, was grafted onto the root of a quince tree, *Cydonia oblonga*, and then allowed to grow. The chromosome number of pear is 68 and the chromosome number of quince is 34.
- **a** After several years' growth, how many chromosomes would you expect in the leaves of the tree?
- **b** How many chromosomes would you expect in cells of a newly grown root? Explain.

4 Analysing and evaluating information ➜ Do you agree or disagree with each of the following claims about mitosis?
- **a** The nuclear envelope is visible throughout the process.
- **b** Mitosis would occur in the developing limb of a larval frog.
- **c** Mitosis in plants is significantly different from mitosis in animals.
- **d** Mitosis is accompanied by replication of cell organelles such as mitochondria and ribosomes.

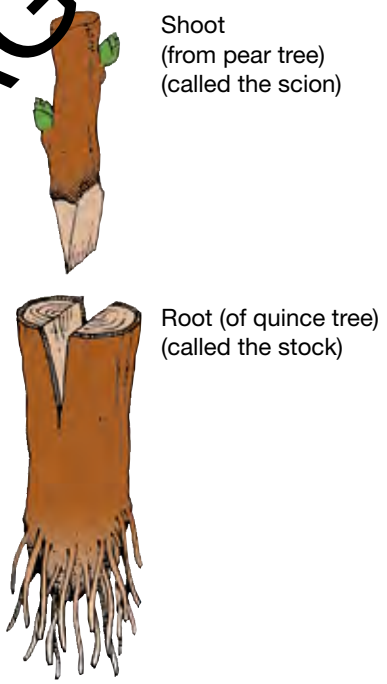

FIGURE 9.29 A slit is made in the bark of the stock and the bud graft with its own piece of bark is slipped inside. The graft is held in place with tape or twine and the wound covered with grease to exclude fungi and reduce evaporation.

5 Analysing and interpreting information ➜ Figure 9.30 shows a series of drawings, all of the same cell at some stage during mitosis.
- **a** Starting with cell A, place the drawings in the sequence that the stages would occur during mitosis.

b Draw what you would expect to see next in the sequence.

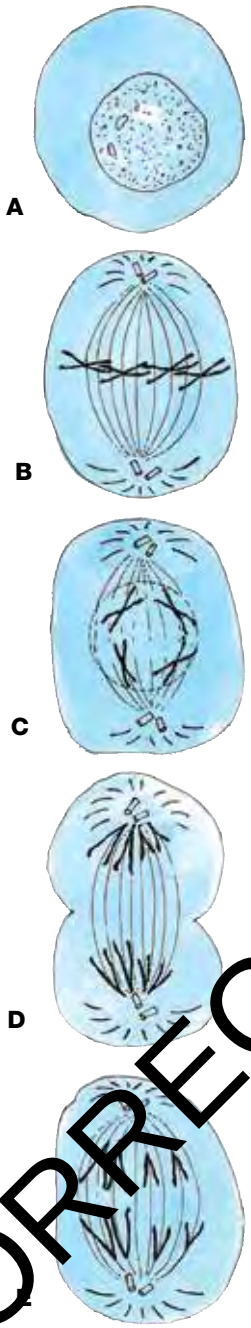

FIGURE 9.30

6 Applying understanding to new concepts ➜ Some drugs used in the treatment of some cancers act on microtubules. They act by interfering with the normal contraction and extension capabilities of microtubules. Explain the effect you would expect such drugs to have on mitosis and cell replication.

7 Applying knowledge ➜ Arrange the following events in animal cell replication in the correct order.

- **a** Alignment of chromosomes on the spindle equator
- **b** Attachment of microtubules to centromere region
- **c** Breakdown of nuclear envelope
- **d** Condensation of chromosomes
- **e** Decondensation of chromosomes
- **f** Duplication of centromere
- **g** Elongation of the spindle
- **h** Pinching of cell into two
- **i** Re-formation of nuclear envelope
- **j** Separation of centromeres
- **k** Separation of sister chromatids

8 Demonstrating skills of understanding and communication ➜ You are shown a video sequence of the entire cell cycle for one cell, but you are not told whether this cell is from an animal or a plant.

- **a** Is it possible to decide the identity of the cell as either animal or plant from the video?
- **b** If so, on what evidence would you base your decision? If not, give a reason for your choice.

9 Developing an explanation ➜ After a cell with 10 chromosomes completed the cell cycle, its daughter cells were examined. One daughter cell was found to contain 11 chromosomes and the other daughter cell had only 9 chromosomes. Suggest a possible explanation in biological terms for this observation.

10 Interpreting data and demonstrating understanding ➜ Cell A has four pairs of chromosomes with a total DNA content of 12 units. Cell A undergoes one cell cycle.

- **a** List, in order, the stages that cell A would proceed through, starting from the earliest.
- **b** At the end of this cell cycle, how many cells would be present: one, two or three?
- **c** How many units of DNA would be present in Cell A at the following point in the cell cycle?
  - i G2 stage of interphase
  - ii Anaphase of mitosis
  - iii G1 stage of interphase
- **d** How many units of DNA would be present in one daughter cell of cell A?
- **e** How many chromosomes would be present in this daughter cell?

11 Making predictions based on given information ➜ A particular gene mutation affects a protein that is a key part of the special attachment site, the kinetochore, that allows a chromatid to be linked to spindle fibres. This

mutation is present in cell B and it disables the function of the kinetochore.

a Would this mutation be expected to affect the progress of cell B through the cell cycle?

b If so, what effect would you predict? If not, give a reason for your decision.

12 **Applying skills of analysis and communication** ➜ Using a light microscope, you examine a longitudinal section of the meristematic tissue of a plant root. Consider each of the following statements in turn and identify whether or not you would expect to observe each in the particular cells you are viewing. Briefly explain your choice.

a The majority of the cells would be in one of the stages of mitosis.

b A cleavage furrow would be present in cells at telophase of mitosis.

c Sister chromatids at anaphase of mitosis would be moving away from the equator and towards opposite ends of the spindles.

d Double-stranded chromosomes would be visible in cells at the S stage of interphase.

13 **Demonstrating understanding** ➜ The cell cycle in eukaryotes is highly regulated so that cell production in a tissue occurs at a rate that balances cell loss.

a What is a possible outcome if a breakdown in the regulation of the cell cycle occurs?

b A disorder known as polycythemia vera is a result of the overactivity of the bone marrow, resulting in the production of too many red blood cells. This condition results in a thickening of the blood and the common treatment is the regular removal of a fixed amount of blood. The cause of polycythemia vera is a mutation in the **JAK2** gene. What is the probable function of the normal **JAK2** gene?

14 **Evaluating visual information** ➜ Figure 9.31 shows the winner of the 2012 Healthcare Cell Imaging Competition Microscopy Category; various fluorescent stains have been used to highlight different components of a cell that is progressing through the cell cycle.

a Suggest a possible identity for each of the following.

i The blue-stained structures

ii The green-stained structures

iii The red-stained structures

b At what stage of the cell cycle was this image taken?

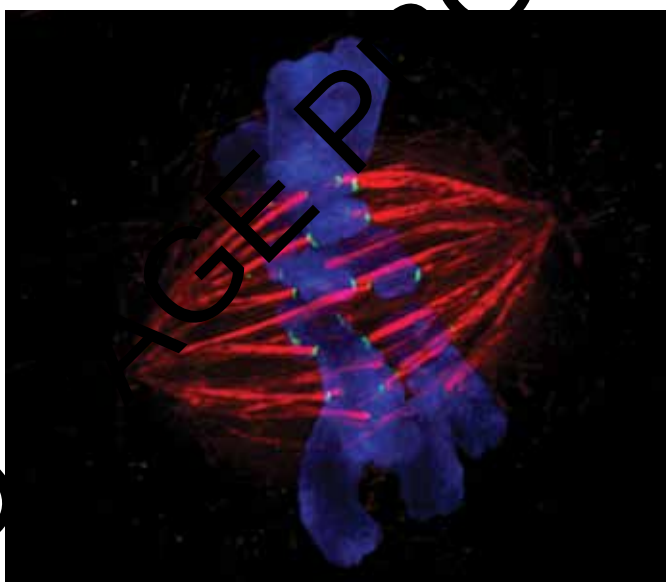

FIGURE 9.31 A cell stained for various components. This prize-winning image was displayed on the big screen at Times Square in New York City. (Image courtesy of Jane Stout, Research Associate, Walczak Laboratory, Indiana University)