Biology Units 3 & 4

Chapter 6 — Antigens and pathogens: self versus non-self

Aboriginal and Torres Strait Islander content has been excluded as accuracy cannot be guaranteed, and it is better to be respectful than cover the entire curriculum inaccurately.

Significant effort has been made to ensure this content is legal. Please send any areas of concern to admin@vwx.au with appropriate document/legal references so errors can be verified and changes be made.

Contents

Chapter 6 Antigens and pathogens: self versus non-self — 6A Recognising self from non-self

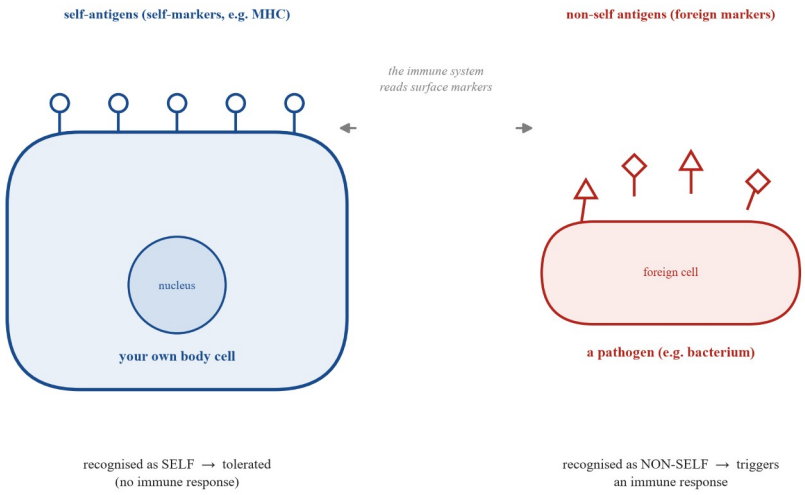
Theory

Your body is made of trillions of cells, and it is constantly exposed to microorganisms and other foreign material. Before the immune system can defend the body, it must answer one question about anything it meets: is this part of **me** (self), or is it **foreign** (non-self)? Getting this answer right is the starting point of every immune response — the immune system responds to what is foreign while leaving the body's own cells unharmed. This subtopic is about how that recognition works, and about the kinds of foreign agents the immune system has to recognise.

Antigens — the molecules the immune system reads. An **antigen** is a molecule that the immune system can recognise and that may trigger an immune response. Antigens are usually large molecules — most often **proteins or glycoproteins** (a protein with a carbohydrate group attached) — found on the **surface** of cells and particles. Because different cells and organisms carry different surface molecules, antigens act like identity tags: the immune system identifies a cell by the antigens displayed on its surface. It is the **antigen**, not the whole organism, that is actually recognised.

Self-antigens versus non-self antigens. Every cell in your body displays **self-antigens** — surface markers that are unique to you. An important group of these are the **MHC (major histocompatibility complex) markers**, also called self-markers. Because they are your own molecules, the immune system treats them as "self" and does **not** attack the cells that carry them.

A **non-self antigen** is a foreign molecule that the body does not recognise as its own. Non-self antigens are found on the surface of **pathogens** (disease-causing agents such as bacteria and viruses), on the cells of a **transplanted organ** from another person, and on other foreign material that enters the body. When the immune system detects a non-self antigen, it treats it as a threat and mounts an **immune response** against it.



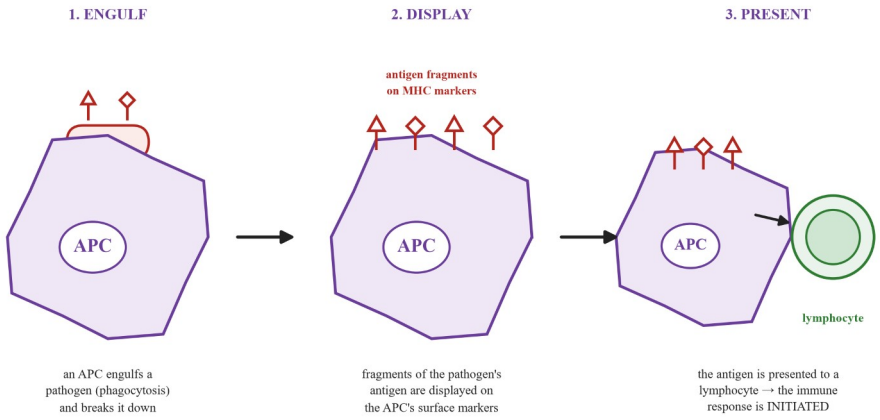
Distinguishing self from non-self — tolerance. As the immune system develops, its cells "learn" the body's own self-antigens. Immune cells that would react against self-antigens are removed or switched off, so the mature immune system becomes **tolerant** of self — it does not attack the body's own tissues. This is called **self-tolerance**. The immune cells that remain respond only to antigens they were **not** taught to accept — that is, to **non-self**. In short: **tolerate self, respond to non-self**.

When recognition fails — autoimmunity (briefly). Occasionally self-tolerance breaks down and the immune system mistakenly treats a self-antigen as foreign, attacking the body's own cells. This is an **autoimmune** condition (examples include type 1 diabetes and rheumatoid arthritis). Autoimmunity shows just how important correct recognition is: it is a **failure to recognise self**.

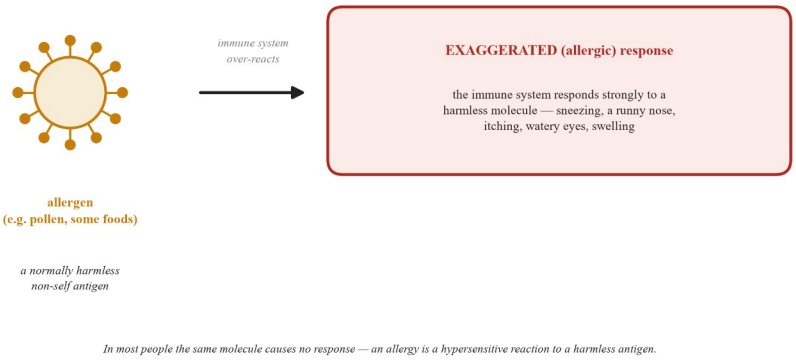
Antigen presentation — initiating the immune response. Detecting a non-self antigen has to *start* a response. This is the job of **antigen-presenting cells (APCs)** — cells such as macrophages and dendritic cells. The process, called **antigen presentation**, is the **initiation** step of the immune response and works like this:

1. An APC **engulfs** a pathogen (takes it inside the cell by phagocytosis) and breaks it down.
2. It **displays fragments** of the pathogen's antigen on **MHC markers** on its own surface.
3. It **presents** this displayed antigen to a **lymphocyte** (a white blood cell of the specific immune system), which **activates** the lymphocyte and so **initiates** the immune response against that antigen.

In this way the APC acts as a messenger: it captures a sample of the invader and shows it to the cells that will organise the specific response. (What the activated lymphocytes then go on to do is covered in a later subtopic.)



Allergens — an over-reaction to a harmless antigen. Not every non-self antigen is dangerous. An **allergen** is a **normally harmless** non-self antigen — one that poses no serious threat to the body — such as pollen, dust-mite droppings, or a food protein, that triggers an **exaggerated** immune response in some people. The molecule itself does no direct harm; the symptoms (sneezing, a runny nose, itching, watery eyes, swelling) come from the immune system **over-reacting** to it. This kind of exaggerated response to a harmless antigen is called a **hypersensitivity** or **allergic** reaction. In most people the same molecule causes no response at all — which is why an allergy is described as an *exaggerated* or *inappropriate* immune response rather than a normal defensive one.

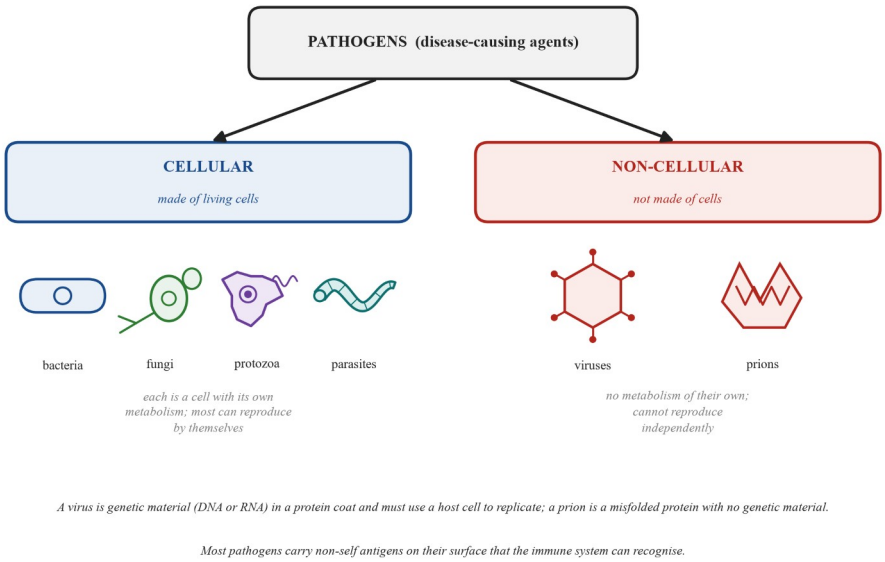


In most people the same molecule causes no response — an allergy is a hypersensitive reaction to a harmless antigen.

Cellular and non-cellular pathogens. The non-self antigens that most often trigger an immune response belong to **pathogens** — agents that cause disease. Pathogens fall into two broad groups based on whether they are made of cells:

- **Cellular pathogens** are **made of one or more living cells**. They include **bacteria, fungi, protozoa** and **parasites** (such as parasitic worms). Each is a cell — or cells — with its own cell membrane, its own metabolism, and, for most, the ability to reproduce by itself.
- **Non-cellular pathogens** are **not made of cells**. They carry out **no metabolism of their own** and **cannot reproduce independently**. They include **viruses** (genetic material — DNA or RNA — inside a protein coat, which must use a **host cell** to replicate) and **prions** (misfolded proteins that carry no genetic material at all).

This distinction matters because the two groups differ in structure and in how they cause disease, which in turn affects how the immune system deals with them. The detailed biology of each group is examined in the next two subtopics; here you need only place a pathogen in the correct category and give examples.



A virus is genetic material (DNA or RNA) in a protein coat and must use a host cell to replicate; a prion is a misfolded protein with no genetic material.

Most pathogens carry non-self antigens on their surface that the immune system can recognise.

Worked examples

Example 1 — scaffolded

A splinter carrying soil bacteria enters a person's finger. Using the ideas of self-antigens and non-self antigens, explain why the immune system responds to the bacteria but leaves the surrounding skin cells unharmed.

Working	Comment
Every one of the person's own cells displays **self-antigens** — surface markers (such as **MHC** markers) that the body itself makes.	Start with what the body's own cells carry.
The immune system has become **tolerant** of these self-antigens, so the skin cells around the splinter are recognised as **self** and are not attacked.	Tolerance accounts for the "no response" half of the question.
The bacteria carry **surface antigens the person's body does not make**, so to the immune system these are **non-self** (foreign).	The foreign half: it is the antigen that is read, not the organism as a whole.
Recognising these non-self antigens, the immune system mounts an **immune response** against the bacteria only.	Name the outcome and tie it back to the self/non-self distinction.

Example 2 — scaffolded

Describe how an antigen-presenting cell initiates an immune response against a bacterium.

Working	Comment
An **antigen-presenting cell (APC)**, such as a **macrophage**, **engulfs** the bacterium by phagocytosis and **breaks it down**.	Step 1 — the APC takes in and digests the pathogen.
The APC **displays fragments** of the bacterium's antigen on **MHC markers** on its surface.	Step 2 — the captured antigen is put on display.
It **presents** the displayed antigen to a **lymphocyte**.	Step 3 — the sample is shown to a cell of the specific immune system.
This **activates the lymphocyte**, which **initiates** the	The outcome — antigen presentation is the initiation

Working	Comment
immune response against that antigen.	step.

Example 3 — unscaffolded

Hay fever is caused by pollen. Explain why pollen is described as an allergen, and how the response to pollen in a person with hay fever differs from a normal immune response to a pathogen.

Pollen is an **allergen** because it is a **normally harmless non-self antigen** — it does not itself damage the body — yet it triggers an immune response in some people. In a person with hay fever, the immune system **over-reacts** to the pollen, producing an **exaggerated (hypersensitive) response** with symptoms such as sneezing, a runny nose and watery eyes. This differs from a normal immune response in two ways: the trigger is **harmless** rather than a genuine threat, and the response is **excessive** relative to any danger posed. A normal immune response, by contrast, is directed at a **harmful pathogen** and is **proportionate** to the threat it poses. ∴ pollen is an allergen because a harmless antigen provokes an exaggerated response, unlike the proportionate response mounted against a true pathogen.

Example 4 — unscaffolded

Classify each of the following as a cellular or a non-cellular pathogen, and justify each classification: (i) an influenza virus; (ii) the bacterium that causes tuberculosis; (iii) a prion that causes a brain disease.

A pathogen is **cellular** if it is made of one or more living cells, and **non-cellular** if it is not made of cells and cannot reproduce independently. (i) An influenza **virus** is **non-cellular** — it is genetic material (RNA) inside a protein coat, not a cell, and can only reproduce inside a host cell. (ii) The **bacterium** that causes tuberculosis is **cellular** — it is a single living cell with its own membrane and metabolism that can reproduce by itself. (iii) A **prion** is **non-cellular** — it is a misfolded protein with no cell structure and no genetic material. ∴ only the tuberculosis bacterium is a cellular pathogen; the virus and the prion are both non-cellular.

Practice questions

Scaffolded

Q1. Define each of the following terms: (a) antigen; (b) self-antigen; (c) non-self antigen.

Q2. The immune system normally tells the body's own cells apart from foreign cells. (a) State what is meant by self-tolerance. (b) Name the general term for a condition in which the immune system attacks the body's own cells. (c) Name the group of surface self-antigens that act as the body's main self-markers.

Q3. Antigen presentation is the first step in responding to a pathogen. (a) Name one type of cell that acts as an antigen-presenting cell. (b) Describe what an antigen-presenting cell does with a pathogen it has engulfed. (c) State the outcome of antigen presentation (why it is called the initiation step).

Q4. An allergen triggers an allergic response. (a) Define the term *allergen*. (b) Give one example of an allergen. (c) Explain how an allergic response differs from a normal immune response to a pathogen.

Q5. Pathogens are classified as cellular or non-cellular. (a) State what a pathogen is. (b) List two types of cellular pathogen. (c) Name the two types of non-cellular pathogen.

Q6. *(Stimulus.)* Two cells are examined inside a patient. **Cell J** displays surface markers identical to those on the patient's own body cells. **Cell K** displays surface markers that the patient's body does not produce. (a) Which cell carries self-antigens? (b) Which cell would trigger an immune response in the patient? (c) Explain your answer to part (b).

Unscaffolded

Q7. Define the term *antigen* and explain why an antigen can trigger an immune response. *(2 marks)*

Q8. Distinguish between a self-antigen and a non-self antigen. *(2 marks)*

Q9. Explain how the immune system is able to distinguish the body's own cells from foreign cells. *(3 marks)*

Q10. Autoimmune conditions such as type 1 diabetes involve the immune system attacking the body's own cells. Explain what this shows about self/non-self recognition. *(2 marks)*

Q11. *(Application.)* A protozoan parasite that lives in a person's bloodstream coats its outer surface with molecules that it strips from the person's own red blood cells. Using the idea of self and non-self antigens, explain why this coating helps the parasite avoid an immune response, and predict what would happen to the parasite if the coating were lost. *(4 marks)*

Q12. In a laboratory culture, antigen-presenting cells engulfed bacteria and broke them down normally, but were kept physically separated from all lymphocytes. No specific immune response developed against the bacteria. Explain this result, and use it to justify describing antigen presentation as the *initiation* of an immune response. *(4 marks)*

Q13. A person with a peanut allergy is told that their symptoms are produced by their own immune system rather than by the peanut protein itself. Explain why this statement is correct. *(3 marks)*

Q14. Distinguish between cellular and non-cellular pathogens, giving **two** examples of each. *(4 marks)*

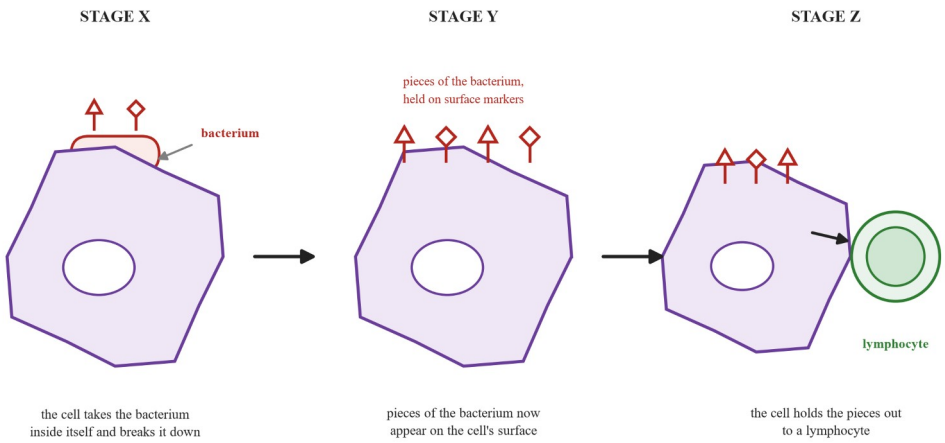
Q15. *(Data / classification.)* A pathology laboratory recorded four disease-causing agents isolated from different patients.

Agent	Description
P	a single cell with a nucleus and a cell wall; reproduces by budding off daughter cells
Q	a multicellular organism with a gut and a nervous system; lives attached to the intestine wall
R	genetic material (RNA) inside a protein coat; no membrane and no metabolism of its own
S	a misfolded protein; contains no genetic material and no cell structure

(a) Classify each agent (P, Q, R, S) as a cellular or a non-cellular pathogen.

(b) Agent R can only be copied inside a host cell, whereas agent P can increase in number on its own. Explain this difference. *(4 marks)*

Q16. *(Stimulus.)* The diagram shows three stages by which a cell of the immune system responds to a bacterium.



In **stage X** the cell engulfs the bacterium; in **stage Y** it displays part of the bacterium on markers on its surface; in **stage Z** it shows this to a lymphocyte. (a) Name the type of cell carrying out stages X–Z. (b) Name the overall process shown. (c) Explain the importance of stage Z for the immune response. *(4 marks)*

Q17. Both viruses and prions are non-cellular pathogens. Describe **one** way in which a virus differs from a prion. *(2 marks)*

Q18. A body cell is infected by a virus and begins to display fragments of viral protein on the MHC markers on its own surface. Explain why the immune system may now respond against this cell, even though it is one of the body's own cells. *(3 marks)*

Q19. *(Research.)* Immunologists cultured lymphocytes taken from a human volunteer with three different protein samples and recorded the percentage of lymphocytes activated after 48 hours.

Sample	Protein added to the culture	Lymphocytes activated (%)
1	a liver protein taken from the volunteer	2
2	the equivalent liver protein taken from a horse	47
3	a surface protein taken from a bacterium	56

(a) Identify the trend shown by the data.

(b) Using the ideas of self-antigens and non-self antigens, explain why Sample 1 activated so few lymphocytes compared with Samples 2 and 3.

(c) The whole experiment was repeated using lymphocytes from a second volunteer and gave very similar results. Explain why this strengthens the researchers' conclusion. *(4 marks)*

Q20. *(Synthesis.)* A child is stung by a bee. The bee venom contains proteins that are foreign to the child's body. After the sting, an antigen-presenting cell processes the venom proteins and initiates an immune response. In a small number of people, a later exposure to bee venom instead causes a severe, exaggerated allergic reaction. (a) Explain why the venom proteins are described as non-self antigens. *(2 marks)* (b) Describe how an antigen-presenting cell would initiate an immune response to the venom proteins. *(3 marks)* (c) Explain why, in some people, bee venom acts as an allergen, and how this differs from the immune system's normal response to a foreign antigen. *(2 marks) (7 marks)*

Answers

Q1. (a) A molecule (usually a surface protein/glycoprotein) that the immune system can recognise and that may trigger an immune response. (b) A surface marker (e.g. MHC) unique to an individual, recognised as the body's own and tolerated. (c) A foreign molecule not recognised as the body's own, which triggers an immune response. **Q2.** (a) The immune system does not attack the body's own (self) antigens. (b) An autoimmune condition (autoimmunity). (c) The MHC (major histocompatibility complex) markers. **Q3.** (a) A macrophage (or dendritic cell). (b) Breaks it down and displays fragments of its antigen on MHC markers on the APC surface. (c) The antigen is presented to a lymphocyte, activating it and starting (initiating) the immune response. **Q4.** (a) A normally harmless non-self antigen that triggers an exaggerated immune response. (b) Pollen (or dust-mite droppings, a food protein, etc.). (c) It is an exaggerated response to a harmless antigen, whereas a normal response targets a harmful pathogen and is proportionate. **Q5.** (a) A disease-causing agent. (b) Any two of: bacteria, fungi, protozoa, parasites. (c) Viruses and prions. **Q6.** (a) Cell J. (b) Cell K. (c) Cell K carries non-self antigens (markers not made by the patient), which the immune system recognises as foreign and responds to. **Q7.** An antigen is a molecule the immune system can recognise; it can trigger a response when it is recognised as non-self (foreign). **Q8.** Self-antigen = the body's own surface marker, tolerated; non-self antigen = a foreign molecule, which triggers a response. **Q9.** Immune cells learn the body's self-antigens during development; cells that react to self are removed/switched off (self-tolerance), so the immune system responds only to non-self. **Q10.** It shows that self/non-self recognition has failed — the immune system has wrongly treated a self-antigen as non-self (a breakdown of self-tolerance). **Q11.** The coat is made of the person's own molecules, so the parasite's surface presents self-antigens; the immune system is tolerant of these and does not recognise the parasite as foreign, so no response is mounted. Lose the coat and its own non-self antigens are exposed, so it would be recognised as foreign and attacked. **Q12.** Digesting the bacteria is not enough — the APC must present the displayed antigen to a lymphocyte. With no lymphocyte contact none is activated, so the specific response never starts. This shows antigen presentation is the step that initiates the response. **Q13.** A peanut protein is a normally harmless non-self antigen that does no direct damage; it is recognised as non-self and the immune system over-reacts, and the symptoms (swelling, itching, breathing difficulty) are produced by that exaggerated response, not by the protein. **Q14.** Cellular = made of living cells, each with its own metabolism and most able to reproduce themselves (e.g. bacteria, fungi/protozoa/parasites); non-cellular = not made of cells, no metabolism of their own and cannot reproduce independently (e.g. viruses, prions). **Q15.** (a) P = cellular; Q = cellular; R = non-cellular; S = non-cellular. (b) P is a cell with its own membrane, metabolism and machinery, so it can copy itself unaided; R is not a cell and has no metabolism or machinery of its own, so copies can only be made using a host cell's machinery. **Q16.** (a) An antigen-presenting cell (e.g. macrophage/dendritic cell). (b) Antigen presentation. (c) Presenting the antigen to a lymphocyte activates it and initiates the specific immune response. **Q17.** A virus contains genetic material (DNA or RNA) in a protein coat, whereas a prion is a misfolded protein with no genetic material. **Q18.** The infected cell now displays viral protein fragments — non-self antigens — on its MHC markers alongside its own self-antigens; the immune system reads the antigens displayed on a cell's surface, recognises the non-self antigen as foreign, and responds against the cell. **Q19.** (a) Very few lymphocytes were activated by the volunteer's own protein (2%), while the horse protein (47%) and the bacterial protein (56%) activated many. (b) The volunteer's own liver protein is a self-antigen the immune system is tolerant of, so lymphocytes are not activated; the horse and bacterial proteins are not made by the volunteer's body, so they are non-self antigens and are recognised as foreign. (c) The same pattern in a second volunteer shows the result is reproducible and not peculiar to one person. **Q20.** (a) They are foreign molecules not made by the child's body, so are recognised as non-self. (b) An APC engulfs the venom proteins, displays fragments on MHC markers, and presents them to a lymphocyte, initiating the response. (c) The venom itself causes only minor local pain and swelling, and in most people the response to it is proportionate; in some people the immune system instead over-reacts, producing a severe, exaggerated (hypersensitive) allergic response far greater than the harm the venom does.

Fully-worked solutions

Q1. (a) An **antigen** is a **molecule** — usually a surface **protein or glycoprotein** — that the immune system can **recognise** and that may **trigger an immune response**. (b) A **self-antigen** is a surface marker (such as an **MHC** molecule) that is **unique to the individual**; the immune system recognises it as the body's **own** and is **tolerant** of it. (c) A **non-self antigen** is a **foreign** molecule that the body does **not** recognise as its own (for example, an antigen on the surface of a pathogen), and which **triggers an immune response**.

Q2. (a) **Self-tolerance** means the immune system **does not attack the body's own (self) antigens** — it recognises them as "self" and leaves those cells unharmed. (b) An **autoimmune** condition (autoimmunity). (c) The main self-markers on a body cell's surface are the **MHC (major histocompatibility complex) markers**. Because the body makes them itself, the immune system reads them as **self** and tolerates the cells that carry them.

Q3. (a) A **macrophage** (a dendritic cell is also acceptable). (b) The APC **breaks the pathogen down** and **displays fragments of its antigen on MHC markers** on the APC's own surface. (c) It then **presents the displayed antigen to a lymphocyte**, which **activates** the lymphocyte and **starts (initiates) the immune response** — which is why antigen presentation is called the initiation step.

Q4. (a) An **allergen** is a **normally harmless non-self antigen** that triggers an **exaggerated immune response** in some people. (b) Any one of: **pollen**, dust-mite droppings, a food protein (e.g. peanut), bee venom, animal dander. (c) An **allergic response** is an **exaggerated (hypersensitive) response to a harmless antigen**, whereas a **normal immune response** is directed at a **genuinely harmful pathogen** and is **proportionate** to the threat.

Q5. (a) A **pathogen** is a **disease-causing agent**. (b) Any **two** of: **bacteria, fungi, protozoa, parasites**. (c) **Viruses** and **prions**.

Q6. (a) **Cell J** carries self-antigens — its surface markers are **identical to the patient's own**. (b) **Cell K** would trigger an immune response. (c) Cell K displays **surface markers the patient's body does not produce**, so they are **non-self antigens**. The immune system **recognises these as foreign** and mounts an **immune response** against Cell K, whereas Cell J's markers are recognised as **self** and tolerated.

Q7. An **antigen** is a **molecule** (usually a surface protein or glycoprotein) that the immune system can **recognise**. An antigen can **trigger an immune response** when it is recognised as **non-self** — that is, as foreign rather than part of the body — because the immune system responds to non-self antigens. *(1 mark: definition of antigen; 1 mark: triggers a response because recognised as non-self/foreign.)*

Q8. A **self-antigen** is a surface marker that is **part of the body's own cells** (e.g. an MHC self-marker) and is **tolerated** — the immune system does **not** attack it. A **non-self antigen** is a **foreign** molecule (e.g. on the surface of a pathogen) that the body does **not** recognise as its own and which **triggers an immune response**. *(1 mark each side, congruent: own/tolerated versus foreign/triggers a response.)*

Q9. As the immune system **develops**, its cells **"learn" the body's own self-antigens**. Immune cells that would react against these self-antigens are **removed or switched off**, so the mature immune system is **tolerant of self**. The cells that remain therefore respond **only to antigens they were not taught to accept** — that is, to **non-self** antigens. In this way the immune system can tell the body's own cells (self, tolerated) from foreign cells (non-self, attacked). *(1 mark: cells learn/become tolerant of self-antigens; 1 mark: self-reactive cells removed/switched off; 1 mark: system then responds only to non-self.)*

Q10. In an autoimmune condition the immune system **attacks the body's own cells**, which means it has **treated a self-antigen as if it were non-self (foreign)**. This shows that self/non-self recognition has **failed** — specifically a **breakdown of self-tolerance**, the normal mechanism by which the immune system avoids attacking self. *(1 mark: the immune system has mistaken self for non-self; 1 mark: this is a failure/breakdown of self-tolerance.)*

Q11. The immune system decides whether to respond by reading the **antigens displayed on an agent's surface**. Because the parasite has coated itself in molecules **taken from the person's own red blood cells**, the molecules on its outside are the person's own — that is, **self-antigens**. The immune system is **tolerant** of these, so it does not recognise the coated parasite as foreign and **no immune response is mounted against it**. If the coating were lost, the parasite's **own surface antigens** would be exposed; these are molecules the person's body does not make, so they would be read as **non-self** and the immune system would **recognise the parasite as foreign and respond against it**. *(1 mark: recognition depends on the antigens displayed on the surface; 1 mark: the borrowed coat presents the person's own self-antigens; 1 mark: self-antigens are tolerated, so no response while coated; 1 mark: without the coat its own non-self antigens are exposed and a response is triggered.)*

Q12. Engulfing the bacteria and breaking them down is only the **first part** of antigen presentation: the antigen-presenting cell must then **display fragments of the bacterial antigen on its MHC markers** and **present them to a lymphocyte**. In this culture the APCs were kept away from all lymphocytes, so **no lymphocyte ever met the displayed antigen and none was activated**. Because the specific immune response begins with the **activation of a**

lymphocyte, blocking that contact means **the response cannot start at all**, even though the pathogen was detected and digested. This is precisely why antigen presentation is called the **initiation** of an immune response: it is the step that converts detection of a non-self antigen into an actual response, and removing it stops the response before it begins. *(1 mark: digestion alone is not enough — the antigen must be displayed and presented to a lymphocyte; 1 mark: with no contact, no lymphocyte is activated; 1 mark: without an activated lymphocyte the specific response cannot begin; 1 mark: therefore antigen presentation is the step that initiates the response.)*

Q13. A peanut protein is a **normally harmless non-self antigen** — the molecule itself does the body's tissues **no direct damage**. It is nevertheless recognised as **non-self**, and in a person with the allergy the immune system mounts an **exaggerated (hypersensitive) response** against it. The swelling, itching, hives and difficulty breathing are the effects of **that immune response**, not of the peanut protein acting on the tissues. The statement is therefore correct: in an allergy the harm comes from the **body's own over-reaction**, which is why an allergic response is described as inappropriate rather than defensive. *(1 mark: the allergen itself is harmless and does no direct damage; 1 mark: it is recognised as non-self and provokes an exaggerated/hypersensitive response; 1 mark: the symptoms are produced by that immune response, not by the molecule.)*

Q14. Cellular pathogens are **made of one or more living cells**: each has its own cell membrane and metabolism, and most can **reproduce by themselves**. Examples: **bacteria** and **fungi** (protozoa and parasites are also acceptable). **Non-cellular pathogens** are **not made of cells**: they carry out **no metabolism of their own** and **cannot reproduce independently**. Examples: **viruses** (which must use a host cell to replicate) and **prions**. *(1 mark: cellular = made of cells / reproduces itself; 1 mark: two cellular examples; 1 mark: non-cellular = not cells / no metabolism of its own and cannot reproduce independently; 1 mark: two non-cellular examples.)*

Q15. (a) **P = cellular** (a single cell, with a nucleus and a cell wall, that reproduces itself); **Q = cellular** (a multicellular organism, so it is built of cells); **R = non-cellular** (genetic material in a protein coat, with no membrane and no metabolism); **S = non-cellular** (a misfolded protein with no cell structure and no genetic material). (b) **P is a cell**: it has its own membrane, its own **metabolism** and all the machinery (ribosomes, enzymes) needed to copy itself, so it can **increase in number unaided**. **R is not a cell**: it is genetic material in a protein coat with **no metabolism and no machinery of its own**, so the only way copies of it can be made is by **entering a host cell and using that cell's machinery**. *(2 marks: all four agents correctly classified — 1 mark if exactly one is wrong; 2 marks: P is a cell with its own metabolism and machinery so it copies itself, and R is not a cell and has neither, so it needs a host cell's machinery.)*

Q16. (a) The cell is an **antigen-presenting cell (APC)** — for example a **macrophage** or dendritic cell. (b) The overall process is **antigen presentation**. (c) In **stage Z** the APC **presents the antigen to a lymphocyte**. This is important because it **activates the lymphocyte and initiates the specific immune response** — without this presentation step the lymphocytes would not be activated against the pathogen, so the response could not begin. *(1 mark: APC; 1 mark: antigen presentation; 2 marks: stage Z presents to a lymphocyte, activating it and initiating the immune response.)*

Q17. A **virus** consists of **genetic material (DNA or RNA) enclosed in a protein coat**, whereas a **prion** is a **misfolded protein that contains no genetic material** at all. (Accept also: a virus carries the instructions for making more of itself as nucleic acid; a prion does not.) *(1 mark: virus has genetic material in a protein coat; 1 mark: prion is a misfolded protein with no genetic material.)*

Q18. An uninfected body cell displays only **self-antigens** — its own MHC markers — and the immune system is **tolerant** of these, so the cell is left alone. Once the cell is infected, it also displays **fragments of viral protein** on those MHC markers, and these fragments are **not molecules the body makes**: they are **non-self antigens**. The immune system responds to the **antigens displayed on a cell's surface**, so a body cell that is now showing a non-self antigen is **recognised as foreign** and a response is mounted against it, even though the cell itself is the body's own. *(1 mark: an uninfected body cell displays only tolerated self-antigens; 1 mark: the infected cell now displays viral fragments, which are non-self antigens; 1 mark: recognition is based on the antigens displayed, so the cell is treated as foreign.)*

Q19. (a) Lymphocyte activation was **very low with the volunteer's own protein (2%)** but **high with both foreign proteins** — 47% with the horse protein and 56% with the bacterial protein. (b) The liver protein taken from the volunteer is one the volunteer's **own body makes**, so it is a **self-antigen**: the immune system is **tolerant** of it, and the lymphocytes that could have reacted against it were removed or switched off during development, so almost none were activated. The horse protein and the bacterial protein are **not made by the volunteer's body**, so they are **non-**

self antigens; the lymphocytes **recognise them as foreign** and are activated. (c) Repeating the whole experiment on a **second volunteer** and obtaining the **same pattern** shows the result is **reproducible** and not a peculiarity of one person's immune system, so the conclusion can be applied with more confidence. *(1 mark: trend — low activation by the volunteer's own protein, high by both foreign proteins, with figures; 2 marks: the volunteer's own protein is a self-antigen and is tolerated, and the horse/bacterial proteins are non-self antigens recognised as foreign; 1 mark: repetition shows the result is reproducible rather than specific to one individual.)*

Q20. (a) The venom proteins are **not made by the child's own body** — they are **foreign molecules** introduced by the sting. Because the immune system does **not recognise them as self**, they are **non-self antigens**. *(1 mark: foreign, not made by the body; 1 mark: therefore recognised as non-self.)* (b) An **antigen-presenting cell** would **engulf the venom proteins** and **break them down**, then **display fragments of them on MHC markers** on its surface, and **present** this antigen to a **lymphocyte**. This **activates the lymphocyte and initiates the immune response** against the venom. *(1 mark: APC engulfs/processes the venom; 1 mark: displays antigen on MHC markers; 1 mark: presents to a lymphocyte, initiating the response.)* (c) Bee venom does cause **minor local harm** — the pain and swelling at the sting site — but it is **not a serious threat** to the body, and in most people the immune response to it is **proportionate** to that small threat. In some people the immune system instead **over-reacts to the venom proteins**, producing a **severe, exaggerated (hypersensitive) allergic response** that is far more damaging than the venom itself. This differs from the immune system's **normal response to a foreign antigen**, which is **proportionate** to the actual threat rather than excessive. ∴ in those people the venom acts as an **allergen**, provoking a response far larger than the danger it poses. *(1 mark: exaggerated/hypersensitive over-reaction to the venom antigen; 1 mark: contrast with a proportionate normal response.)*

Theory

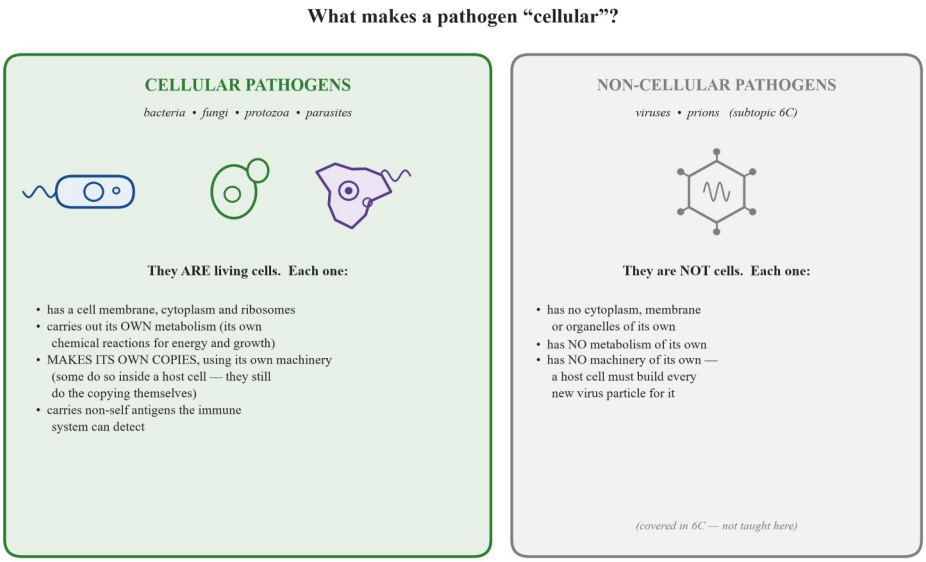
A **pathogen** is any agent that can cause disease in a host. Pathogens fall into two broad groups according to whether or not they are living cells: **cellular pathogens** and **non-cellular pathogens** (viruses and prions, covered in subtopic 6C). This subtopic looks at the cellular pathogens — what they are, how they enter the body and cause disease, and why the immune system is able to recognise them as foreign.

What makes a pathogen "cellular". A cellular pathogen **is a living cell** — or, in the case of a parasitic worm, a whole many-celled organism built from living cells. Like all cells it has a **cell membrane**, **cytoplasm** and **ribosomes**, and it can do two things a non-living agent cannot:

- it carries out its **own metabolism** — its own chemical reactions to obtain energy and to build the molecules it needs; and
- it **makes its own copies** — it reproduces using its **own machinery** (its own ribosomes, enzymes and DNA), rather than handing the job of building the copies to a host cell.

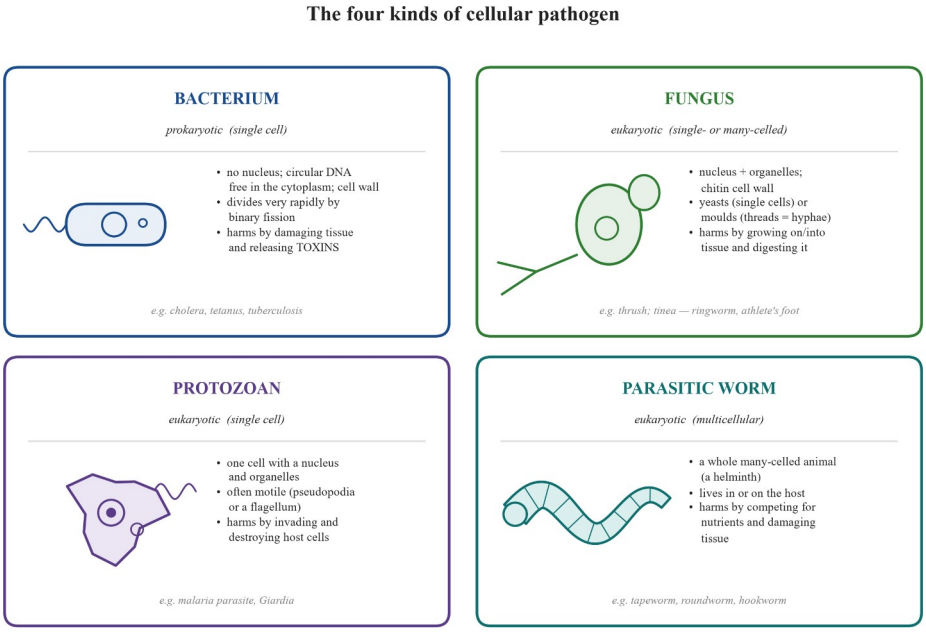
This is the key contrast with the non-cellular pathogens of subtopic 6C: a **virus** is not a cell and **cannot reproduce on its own** (it has no machinery, so it must hijack a host cell's machinery), and a **prion** is merely a misfolded protein. So the defining feature of every cellular pathogen is simply that **it is a cell that lives, metabolises and reproduces in its own right**.

Careful: what matters is *whose* machinery does the copying, not whether a host cell is involved. Several cellular pathogens live and multiply **inside** the host's cells — the malaria parasite, for example, multiplies inside red blood cells — yet each one is still a complete cell that divides *itself*, using its own ribosomes and enzymes. A virus is different in kind: it has no machinery of its own at all, so the host cell must manufacture every new virus particle for it. "Needs to be inside a host cell" therefore does **not** make a pathogen non-cellular; "has no machinery of its own" does.



Non-self antigens. Every cellular pathogen is built from molecules that are foreign to the host — for example the components of a bacterial cell wall, a fungal cell wall, or the surface proteins of a protozoan or a worm. A molecule that the immune system can recognise is called an **antigen**, and an antigen that is **foreign to the host** is a **non-self antigen**. (How the body distinguishes its own "self" molecules from "non-self" is the subject of subtopic 6A.) Because each cellular pathogen carries non-self antigens, the immune system is able to detect it as an invader and mount a response against it (the immune response itself is covered in Chapter 7).

The four kinds of cellular pathogen. Cellular pathogens are usually grouped into bacteria, fungi, protozoa and multicellular parasites such as parasitic worms.



- **Bacteria.** Bacteria are **prokaryotic** cells: small (roughly 1–5 μm), with **no membrane-bound nucleus** and no membrane-bound organelles. Their DNA is usually a single **circular chromosome** free in the cytoplasm (often with small extra rings called plasmids), and they have a **cell wall**. Given warmth and nutrients they **reproduce very rapidly** by binary fission — one cell simply splits into two — so a small infection can grow enormously within hours. Bacteria cause disease in two main ways: by **damaging tissue** as they multiply within it, and by releasing **toxins** (poisonous chemicals) that harm cells near the infection or, if they reach the blood, around the whole body. Bacterial diseases include cholera, tetanus, tuberculosis and strep throat.
- **Fungi.** Fungi are **eukaryotic** — their cells have a nucleus and organelles — and they have a cell wall containing chitin. Some are single-celled **yeasts**; others are **moulds** that grow as branching threads called **hyphae**. Fungi that infect humans usually cause disease by **growing on or into tissue and digesting it**: they release enzymes that break the tissue down and absorb the released nutrients, and some also produce toxins. Most human fungal infections affect the skin, nails or moist surfaces — for example **tinea**, the dermatophyte infection of the skin that is called ringworm (tinea corporis) on the body and athlete's foot (tinea pedis) on the feet, and **thrush** (a *Candida* yeast infection).
- **Protozoa.** Protozoa are **single-celled eukaryotes** — one cell, complete with a nucleus and organelles — and many can move actively (for example using pseudopodia or a flagellum). They usually enter through contaminated food or water, or are injected by a **vector** such as a biting insect. They cause disease by **invading and destroying host cells or tissues**. The best-known example is malaria: the malaria parasite (*Plasmodium*) is carried by mosquitoes and multiplies inside, and destroys, the host's red blood cells. Another is *Giardia*, a gut protozoan that causes diarrhoea.
- **Parasites, including parasitic worms.** A **parasite** is an organism that lives on or in a host and benefits at the host's expense. Many protozoa live this way, but the term also covers larger, **multicellular** parasites — most importantly the **parasitic worms**, or **helminths**, such as tapeworms, roundworms and hookworms. A parasitic worm is a whole many-celled animal that lives inside the host, often in the gut or the blood. It causes disease mainly by **competing with the host for nutrients**, by **physically damaging or blocking** tissues and vessels, and by **feeding on** the host's tissue or blood. Because it is made of many cells, a worm shows most clearly that a cellular pathogen can be a complete organism, not just a single cell.

How cellular pathogens enter the body. Before it can cause disease, a cellular pathogen must get past the body's outer barriers. Common routes of entry are:

- **ingestion** of contaminated food or water (many bacteria, protozoa and worms);
- **inhalation** of droplets or spores (for example tuberculosis bacteria, or the spores of some fungi);

- through **breaks in the skin** such as cuts, wounds or bites (for example tetanus bacteria entering a dirty wound);
- by **direct contact** (for example the skin fungi that cause tinea); and
- by a **vector** — an animal, often a biting insect, that carries a pathogen from one host to another (for example a mosquito carrying the malaria protozoan).

Summary. The table below draws the four types together. In every case the pathogen is a **cell** (or an organism built of cells) that metabolises and reproduces in its own right, and that carries non-self antigens the immune system can detect.

Cellular pathogen	Cell type	Key cell features	Typical way it causes disease
Bacterium	Prokaryotic (single cell)	No nucleus; circular DNA; cell wall; divides rapidly by binary fission	Damages tissue as it multiplies; releases toxins
Fungus (yeast or mould)	Eukaryotic (single- or multicellular)	Nucleus + organelles; chitin cell wall; yeasts or hyphae	Grows on/into tissue and digests it; some release toxins
Protozoan	Eukaryotic (single cell)	One cell with a nucleus and organelles; often motile	Invades and destroys host cells / tissue
Parasitic worm (helminth)	Eukaryotic (multicellular)	A whole many-celled animal; lives in or on the host	Competes for nutrients; damages/blocks tissue; feeds on host

Worked examples

Example 1 — scaffolded

A disease is caused by a rod-shaped organism about 3 μm long. It has no nucleus; its DNA is a single circular chromosome lying free in the cytoplasm; it has a cell wall; and it divides in two roughly every 30 minutes. State whether this organism is a cellular or a non-cellular pathogen, name the group it belongs to, and justify your answer.

Working	Comment
The organism has a cell membrane, cytoplasm and its own DNA, and it divides on its own — so it **is a cell**. It is therefore a **cellular pathogen**.	First decide the cellular/non-cellular question by asking whether the agent is a cell that reproduces itself.
It has **no nucleus** and its DNA is a **single circular chromosome** free in the cytoplasm, with a **cell wall** — these are the features of a **prokaryotic** cell.	Match the described features to a cell type; "no nucleus + circular DNA" signals a prokaryote.
A prokaryotic cellular pathogen that divides by splitting in two (binary fission) is a **bacterium**.	Name the specific group, not just "a cell".
∴ it is a **cellular pathogen — a bacterium**, because it is a living (prokaryotic) cell that carries out its own metabolism and reproduces independently by binary fission.	Justify by naming the defining feature of a cellular pathogen.

Example 2 — scaffolded

A person is bitten by a mosquito that injects a single-celled organism into their blood. The organism has a nucleus and organelles, and it multiplies inside and destroys the person's red blood cells. (a) State the type of cellular pathogen. (b) Explain how it causes disease. (c) State why the immune system is able to detect it.

Working	Comment
(a) It is a **single-celled eukaryote** (one cell, with a	"Single cell + nucleus + organelles" = eukaryote; a

Working	Comment
nucleus and organelles) that is a parasite carried by a vector — this is a **protozoan** (here, the malaria parasite).	single-celled eukaryotic parasite is a protozoan.
(b) It causes disease by **invading and destroying host cells**: it multiplies inside the **red blood cells** and destroys them, so the person has fewer working red blood cells.	Give the mechanism (invade + destroy host cells), tied to the described red blood cells.
(c) The protozoan is built from molecules that are **foreign (non-self)** to the host; it carries **non-self antigens** that the immune system can recognise.	Link detection to the non-self antigens it carries.

Example 3 — unscaffolded

Bacteria, fungi, protozoa and parasitic worms are all classified as **cellular** pathogens. Explain what this classification means and why all four are placed in this group.

Classifying a pathogen as **cellular** means that the pathogen **is a living cell**, or — as with a parasitic worm — a whole organism built from living cells. All four groups belong here because each is made of one or more cells that have a **cell membrane, cytoplasm and ribosomes**, that carry out their **own metabolism**, and that **make their own copies** using their own machinery rather than leaving a host cell to build them. A **bacterium** is a single prokaryotic cell; a **fungus** is one or many eukaryotic cells; a **protozoan** is a single eukaryotic cell; and a **parasitic worm** is a multicellular eukaryotic animal. This is the feature that separates them from the non-cellular pathogens (viruses and prions), which are not cells and cannot metabolise or reproduce on their own. ∴ all four are cellular pathogens because each is (or is built from) living cells that metabolise and reproduce in their own right.

Example 4 — unscaffolded

Compare the way a **bacterium** and a **parasitic worm** cause disease in a host.

Both a bacterium and a parasitic worm are cellular pathogens that harm the host, but they do so in different ways. A **bacterium** is a single prokaryotic cell that **multiplies rapidly within the tissue**, **damaging it directly** as its numbers grow, and it also releases **toxins** — poisonous chemicals that harm the host's cells nearby or, once carried in the blood, elsewhere in the body. A **parasitic worm** is a large multicellular animal living inside the host (often in the gut); rather than releasing toxins, it harms the host mainly by **competing for nutrients** — absorbing the host's digested food so the host is left short — and by **physically damaging or blocking** tissues and vessels as it feeds and grows. ∴ a bacterium harms chiefly by rapid multiplication and toxins, whereas a worm harms chiefly by taking the host's nutrients and by physical damage.

Practice questions

Scaffolded

Q1. Define each of the following terms: (a) pathogen; (b) cellular pathogen; (c) non-self antigen.

Q2. Bacteria are prokaryotic cellular pathogens. (a) State two structural features of a bacterial cell. (b) Describe how bacteria reproduce. (c) Describe two ways in which bacteria cause disease.

Q3. Fungi and protozoa are both eukaryotic cellular pathogens. (a) State one difference between a yeast and a mould. (b) Describe how a protozoan such as the malaria parasite causes disease. (c) State the cell type shared by fungi and protozoa.

Q4. Parasitic worms are cellular pathogens. (a) State what is meant by a parasite. (b) Explain why a tapeworm is described as a *cellular* pathogen. (c) Describe one way in which a parasitic worm causes disease.

Q5. Cellular pathogens carry non-self antigens. (a) Define the term antigen. (b) State why a pathogen's antigens are described as "non-self". (c) State why the presence of these antigens is important for the host.

Q6. Cellular pathogens must enter the body before they can cause disease. (a) State two different routes by which a cellular pathogen can enter the body. (b) Define the term vector. (c) Give one example of a cellular pathogen that is spread by a vector.

Unscaffolded

Q7. A single bacterium enters a wound, where it divides by binary fission about every 20 minutes. Explain why this feature allows the infection to damage the wound tissue within a day. *(2 marks)*

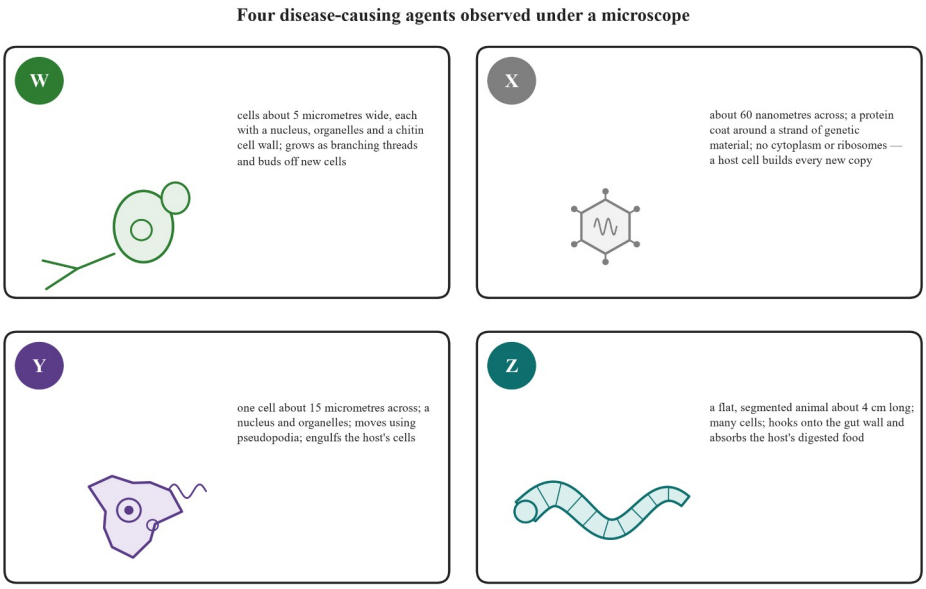
Q8. A skin scraping from one patient shows branching threads growing into the tissue; a mouth swab from a second patient shows single oval cells budding off daughter cells. Both infections are fungal. Name the growth form seen in each patient, and state **two** features of fungal cells that are present in both. *(3 marks)*

Q9. A bacterium can cause disease by releasing a toxin. Explain how a toxin released at a small site of infection can cause harm elsewhere in the body. *(2 marks)*

Q10. Compare the cell structure of a bacterium with that of a protozoan. *(3 marks)*

Q11. Tuberculosis bacteria reach the lungs when droplets carrying them are breathed in, while the protozoan *Giardia* reaches the gut when contaminated water is swallowed. Name the route of entry in each case, explain why each route delivers the pathogen to the part of the body it infects, and name **one** further route by which a cellular pathogen can enter the body. *(3 marks)*

Q12. *(Stimulus.)* Four disease-causing agents were observed under a microscope. Their features are shown below.



(a) State, for each of W, X, Y and Z, whether it is a cellular or a non-cellular pathogen.
(b) For each of the cellular pathogens, name the type of cellular pathogen it is.
(c) Justify your classification of agent **X**. *(5 marks)*

Q13. *(Data interpretation.)* The table gives four features of three pathogens, P, Q and R.

Pathogen	Is it a single cell or many cells?	Has a nucleus?	How are new copies made?	Main way it harms the host
P	one cell	no	it divides in two, using its own ribosomes and enzymes	multiplies in tissue; releases a toxin
Q	many cells	yes	it produces eggs,	absorbs the host's

Pathogen	Is it a single cell or many cells?	Has a nucleus?	How are new copies made?	Main way it harms the host
			using its own cells	digested food in the gut
R	not a cell	no	it has no machinery of its own; a host cell is made to build the copies	destroys the host cell as the new copies are released

(a) Identify which of P, Q and R are cellular pathogens, and justify your answer using the table.

(b) Explain why R cannot be classified as any of the four kinds of cellular pathogen, and name the group to which it belongs instead.

(c) Identify which pathogen harms the host mainly by competing for nutrients, and name that type of pathogen. *(4 marks)*

Q14. Explain why a parasitic worm shows that a cellular pathogen does not have to be a single cell. *(2 marks)*

Q15. A person develops malaria after being bitten by a mosquito. A blood film shows the malaria parasite multiplying **inside** the person's red blood cells. Explain why the mosquito is described as a *vector* rather than as the pathogen, and explain why the malaria parasite is still classified as a *cellular* pathogen even though it multiplies inside the host's cells. *(3 marks)*

Q16. Bacteria and fungi both have a cell wall, yet only bacteria are prokaryotic. Explain why the presence of a cell wall does not show that a pathogen is a bacterium, and state the feature that does distinguish a bacterial cell from a fungal cell. *(2 marks)*

Q17. Compare how a **fungus** and a **bacterium** cause disease in the tissues they infect. *(3 marks)*

Q18. Athlete's foot is a fungal infection of the skin, while tetanus is a bacterial infection that can follow a deep wound. Using these two examples, describe **two** different routes by which cellular pathogens can enter the body. *(2 marks)*

Q19. Explain why a bacterium can make copies of itself but a virus cannot, and state what this difference means for how each is classified. *(3 marks)*

Q20. *(Synthesis.)* A rural clinic reports three patients on the same day.

- **Patient 1** has severe diarrhoea after drinking from a creek. A stool sample shows a single-celled organism that has a nucleus and two flagella and moves actively.
- **Patient 2** has a deep wound that has become infected. A swab shows rod-shaped organisms with no nucleus, dividing rapidly, and a toxin is detected in the surrounding tissue.
- **Patient 3** has been losing weight and feels constantly tired. A stool sample shows the eggs of a flat, segmented, multicellular animal that is living in the gut.

(a) For each patient, name the type of cellular pathogen responsible and state its cell type. *(3 marks)*

(b) Explain how the pathogen in Patient 2 can cause tissue damage both at the wound and at sites away from it. *(2 marks)*

(c) Explain how the pathogen in Patient 3 causes the patient's weight loss. *(1 mark)*

(d) State one feature shared by all three pathogens that places them in the group *cellular pathogens*. *(1 mark)*

(e) Explain why the immune system is able to respond to all three pathogens. *(1 mark)*

Answers

Q1. (a) Any agent that can cause disease in a host. (b) A pathogen that is a living cell (or an organism built of living cells). (c) A foreign molecule, carried by the pathogen, that the host's immune system can recognise. **Q2.** (a) Any two of: no nucleus; circular DNA (chromosome); cell wall; (plasmids; no membrane-bound organelles). (b) By binary fission — one cell splits into two — very rapidly. (c) Any two of: damaging tissue as they multiply; releasing toxins that harm host cells locally or around the body. **Q3.** (a) A yeast is a single cell; a mould grows as branching threads (hyphae) / is multicellular. (b) It invades and destroys host cells (e.g. the malaria parasite multiplies inside and destroys red blood cells). (c) Eukaryotic (eukaryotic cells). **Q4.** (a) An organism that lives on or in a host and benefits at the host's expense. (b) Because it is a whole organism made of living (eukaryotic) cells that metabolise and reproduce in their own right. (c) Any one of: competes with the host for nutrients; physically damages or blocks tissue; feeds on the host's tissue/blood. **Q5.** (a) A molecule that the immune system can recognise. (b) Because it is foreign to the host — not one of the host's own molecules. (c) It allows the immune system to detect the pathogen as an invader and respond to it. **Q6.** (a) Any two of: ingestion of food/water; inhalation of droplets/spores; through breaks in the skin; direct contact; via a vector. (b) An animal (often a biting insect) that carries a pathogen from one host to another. (c) The malaria parasite (protozoan), spread by mosquitoes. **Q7.** Each division doubles the number of bacteria, so in a day the numbers become enormous; that large population damages the tissue as it multiplies through it and releases far more toxin. **Q8.** Branching threads = a mould (hyphae); budding oval cells = a yeast. Both are made of eukaryotic cells — a nucleus and membrane-bound organelles — with a cell wall containing chitin. **Q9.** The toxin can be carried in the blood/body fluids from the infection site to other parts of the body, where it harms cells far from the original infection. **Q10.** Bacterium = prokaryotic: no nucleus, circular DNA free in the cytoplasm, has a cell wall. Protozoan = eukaryotic: has a nucleus and membrane-bound organelles (a much larger, more complex cell). **Q11.** Tuberculosis = inhalation; *Giardia* = ingestion. Breathed-in droplets are carried down the airways into the lungs, and swallowed water passes into the gut, so each route ends at the tissue the pathogen infects. One further route: a break in the skin (also acceptable: direct contact; a vector). **Q12.** (a) W cellular; X non-cellular; Y cellular; Z cellular. (b) W = fungus; Y = protozoan; Z = parasitic worm (helminth). (c) X is non-cellular because it is not a cell (a protein coat around genetic material, with no cytoplasm or ribosomes) and has no machinery of its own — a host cell has to build the copies. **Q13.** (a) P and Q are cellular pathogens — each is a cell (or built from cells) that makes its own copies using its own machinery; R is not (it is not a cell and has no machinery of its own). (b) R is not a cell at all, so it cannot be a bacterium, fungus, protozoan or worm; it is a non-cellular pathogen — a virus. (c) Q — a parasitic worm (helminth). **Q14.** A parasitic worm is a whole multicellular animal, yet it is still a cellular pathogen because it is built from living cells — so a cellular pathogen can be many-celled, not just a single cell. **Q15.** The mosquito only carries and transfers the parasite between hosts — the parasite, not the mosquito, causes the disease. The parasite is a complete living cell that copies itself with its own machinery; living inside a host cell does not make it non-cellular. **Q16.** Fungi are eukaryotes and also have a cell wall (one containing chitin), so a wall does not identify a bacterium. The distinguishing feature is the nucleus: a bacterium has none. **Q17.** Both damage the infected tissue. A fungus grows on/into the tissue and digests it (releasing enzymes, and sometimes toxins); a bacterium multiplies rapidly in the tissue, damaging it, and releases toxins. **Q18.** Athlete's foot enters by direct contact with the skin; tetanus enters through a break in the skin (a deep wound). **Q19.** A bacterium is a complete cell with its own machinery (ribosomes, enzymes), so it can copy itself by binary fission; a virus is not a cell and lacks this machinery, so it must use a host cell to reproduce. Therefore the bacterium is classified as cellular and the virus as non-cellular. **Q20.** (a) P1 protozoan (single-celled eukaryote); P2 bacterium (prokaryotic cell); P3 parasitic worm (multicellular eukaryote). (b) It multiplies and damages the wound tissue directly, and releases a toxin that is carried in the blood to harm cells elsewhere. (c) It absorbs/competes for the host's digested food, so the host is left short of nutrients. (d) Each is, or is built from, living cells (that metabolise and reproduce independently). (e) Each carries non-self antigens the immune system can recognise.

Fully-worked solutions

Q1. (a) A **pathogen** is any agent that can **cause disease** in a host. (b) A **cellular pathogen** is a pathogen that **is a living cell** — or a whole organism built from living cells — and so has its own membrane, cytoplasm and ribosomes, carries out its own metabolism and makes its own copies using its own machinery. (c) A **non-self antigen** is a **foreign molecule** (carried by the pathogen) that the host's **immune system can recognise** as not belonging to the host.

Q2. (a) Any **two** structural features of a bacterial (prokaryotic) cell: **no nucleus**; a single **circular chromosome** (DNA free in the cytoplasm); a **cell wall**; (also acceptable: plasmids; no membrane-bound organelles; a cell membrane). (b) Bacteria reproduce by **binary fission** — a single cell copies its DNA and **splits into two** identical cells — and they can do this **very rapidly** when warmth and nutrients allow. (c) **Two** ways bacteria cause disease: **(1)** by **damaging tissue** as they multiply within it; **(2)** by releasing **toxins** (poisonous chemicals) that harm the host's cells near the infection or, once in the blood, around the body. *(1 mark each way.)*

Q3. (a) A **yeast** is a **single-celled** fungus, whereas a **mould** grows as branching threads called **hyphae** (it is multicellular). (b) A protozoan such as the malaria parasite (*Plasmodium*) causes disease by **invading and destroying host cells** — it multiplies inside, and destroys, the host's **red blood cells**. (c) Both fungi and protozoa are **eukaryotic** — their cells have a nucleus and membrane-bound organelles.

Q4. (a) A **parasite** is an organism that **lives on or in a host** and **benefits at the host's expense** (taking nutrients or shelter while harming the host). (b) A tapeworm is a **cellular** pathogen because it is a **whole organism made of many living (eukaryotic) cells**, each with a membrane, cytoplasm and ribosomes, that carry out their own metabolism and (as an organism) reproduce using **its own cells**, not a host cell's machinery. (c) One way a parasitic worm causes disease: it **competes with the host for nutrients** (for example a tapeworm absorbs the host's digested food); *(also acceptable: it physically damages or blocks tissues/vessels, or feeds on the host's tissue or blood.)*

Q5. (a) An **antigen** is a **molecule that the immune system can recognise**. (b) A pathogen's antigens are described as **non-self** because they are **foreign to the host** — they are not among the host's own ("self") molecules. (c) Their presence is important because it allows the **immune system to detect the pathogen** as an invader and **mount a response** against it; without a recognisable non-self antigen, the pathogen could not be identified as foreign.

Q6. (a) Any **two** routes: **ingestion** of contaminated food or water; **inhalation** of droplets or spores; through **breaks in the skin** (cuts, wounds, bites); **direct contact**; via a **vector**. (b) A **vector** is an **animal (often a biting insect) that carries a pathogen from one host to another**. (c) The **malaria parasite** (a protozoan) is spread by **mosquitoes**. *(Any correct vector-borne example is acceptable.)*

Q7. In **binary fission** the bacterium copies its DNA and **splits into two**, so every division **doubles** the number of bacteria present. Dividing about every **20 minutes** means roughly three doublings an hour, so one cell becomes thousands within a few hours and an enormous population within a day. Because bacteria harm the host by **damaging the tissue they multiply within** and by **releasing toxins**, that rapidly growing population does correspondingly more damage — which is why a wound infection can become serious in a single day. *(1 mark: each division doubles the number, so numbers rise extremely rapidly; 1 mark: the large population damages the tissue and releases much more toxin.)*

Q8. The first patient's **branching threads** are **hyphae**, so that fungus is growing as a **mould**; the second patient's **single oval cells budding off daughter cells** are **yeast** cells, so that fungus is growing as a **yeast**. Despite the different growth forms, the cells themselves share the features of all fungi: they are **eukaryotic** — each cell has a **nucleus** and **membrane-bound organelles** — and each is surrounded by a **cell wall containing chitin**. *(1 mark: mould/hyphae and yeast both correctly named; 1 mark each for two shared fungal cell features, to a maximum of 2.)*

Q9. A **toxin** is a poisonous chemical released by the bacterium. Although the bacteria may be confined to a small site of infection, the toxin can be **carried away in the blood or body fluids** to other parts of the body, where it **harms cells far from the original infection**. In this way a localised infection can produce damage or symptoms throughout the body. *(1 mark: toxin carried in the blood/body fluids; 1 mark: harms cells at a distant site.)*

Q10. A **bacterium** is a **prokaryotic** cell: it has **no nucleus**, its DNA is a single **circular chromosome free in the cytoplasm**, and it has a **cell wall**; it has no membrane-bound organelles. A **protozoan** is a **eukaryotic** cell: it has a **true nucleus** enclosing its DNA and a range of **membrane-bound organelles**, and it is generally a much larger, more complex cell. *(1 mark: bacterium prokaryotic / no nucleus / circular DNA; 1 mark: protozoan eukaryotic / has nucleus; 1 mark: protozoan has membrane-bound organelles / bacterium does not.)*

Q11. The tuberculosis bacteria enter by **inhalation** and *Giardia* enters by **ingestion**. Each route matches the site of infection: droplets that are **breathed in** are carried along the airways **into the lungs**, which is exactly where the tuberculosis bacteria grow, while water that is **swallowed** passes down the digestive tract **into the gut**, where *Giardia* lives and causes diarrhoea. A cellular pathogen may also enter through a **break in the skin** (a cut, wound or bite). *(1*

mark: inhalation and ingestion both named; 1 mark: each route carries the pathogen to the organ it infects — airways to lungs, gut for swallowed water; 1 mark: one further valid route — break in the skin, direct contact, or a vector.)

Q12. (a) **W** is **cellular**; **X** is **non-cellular**; **Y** is **cellular**; **Z** is **cellular**. (b) **W** is a **fungus** (its cells have a nucleus and organelles and a chitin cell wall, and it grows as hyphae and buds off new cells — a eukaryote); **Y** is a **protozoan** (a single cell with a nucleus and organelles that moves by pseudopodia — a eukaryotic cell); **Z** is a **parasitic worm** / helminth (a flat, segmented, multicellular animal living in the gut). (c) **X is non-cellular** because it is **not a cell** — it is just a **protein coat around a strand of genetic material**, with **no cytoplasm or ribosomes** — so it has **no machinery of its own** and a **host cell has to build** every new copy of it. *(a: 2 marks for all four correct; b: 2 marks for all three types; c: 1 mark for a justified reason.)*

Q13. (a) **P and Q are cellular pathogens.** From the table, P is one cell and Q is many cells, and **each makes its own copies using its own machinery** (P divides in two using its own ribosomes and enzymes; Q produces eggs from its own cells) — so each is, or is built from, living cells. **R is not** a cellular pathogen: it is **not a cell** and it has **no machinery of its own**. (b) R **is not a cell at all**, so it cannot be a **bacterium, fungus, protozoan or parasitic worm** — every one of those is a cell or is built from cells. The third column of the table settles where R does belong: nothing in R does the copying — the host cell is made to do it — and that is the mark of a **non-cellular** pathogen. R is a **virus**. (c) **Q** harms the host mainly by **competing for nutrients** (it absorbs the host's digested food); Q is a **parasitic worm** (helminth). *(1 mark: P and Q cellular, justified; 1 mark: R not cellular; 1 mark: R is a virus/non-cellular; 1 mark: Q = worm.)*

Q14. A **parasitic worm** (such as a tapeworm) is a **whole multicellular animal**, made of many living cells — yet it is still a **cellular pathogen** because being a cellular pathogen only requires that the agent **is, or is built from, living cells** that metabolise and reproduce in their own right. This shows that a cellular pathogen **need not be a single cell**: it can be a complete many-celled organism. *(1 mark: a worm is multicellular yet cellular; 1 mark: cellular pathogen means made of living cells, so it can be many-celled.)*

Q15. The **mosquito** is a **vector**: it **carries the malaria parasite from one host to another** and **injects it into the blood** when it bites, but the mosquito itself does not cause the disease — the **parasite** is the agent that causes it, so the parasite is the pathogen. The parasite is still a **cellular** pathogen because it **is a complete living cell** (a single-celled eukaryote with its own membrane, cytoplasm, ribosomes and metabolism) that **makes its own copies using its own machinery**. Being **inside** a red blood cell does not change that: what makes a pathogen non-cellular is having **no machinery of its own** — as a virus does, so that the host cell must build the copies — not merely needing to be inside a host cell. *(1 mark: the mosquito transfers the parasite between hosts but is not the disease-causing agent; 1 mark: the parasite is a living cell that copies itself with its own machinery; 1 mark: living inside a host cell does not make it non-cellular / the test is whose machinery does the copying.)*

Q16. A **cell wall** is not unique to bacteria: **fungi also have a cell wall**, one containing **chitin**, and fungi are **eukaryotes**. So finding a cell wall shows only that the pathogen is a bacterium **or** a fungus, not which. The feature that does separate them is the **nucleus**: a bacterial cell is **prokaryotic** and has **no membrane-bound nucleus** (its DNA is a single circular chromosome lying free in the cytoplasm), whereas a fungal cell is **eukaryotic** and has a **true nucleus** and membrane-bound organelles. *(1 mark: fungi have a cell wall too, so a wall does not identify a bacterium; 1 mark: the nucleus — absent in a bacterium, present in a fungus — is the distinguishing feature.)*

Q17. Both a fungus and a bacterium damage the tissue they infect, but by different means. A **fungus** causes damage by **growing on or into the tissue and digesting it** — it releases **enzymes** that break the tissue down and absorbs the released nutrients (and some fungi also release toxins). A **bacterium** causes damage by **multiplying rapidly within the tissue** (harming it directly as numbers grow) and by releasing **toxins** that poison the host's cells. *(1 mark: fungus grows into and digests tissue; 1 mark: bacterium multiplies in / damages tissue; 1 mark: bacterium releases toxins / congruent comparison.)*

Q18. Cellular pathogens can enter the body by several routes. **Athlete's foot** shows entry by **direct contact**: the skin fungus is picked up by contact with an infected surface or skin. **Tetanus** shows entry through a **break in the skin**: the tetanus bacterium enters through a **deep wound** in the skin. *(1 mark each route, correctly matched to the example.)*

Q19. A **bacterium** is a **complete cell**: it has its own **ribosomes, enzymes and DNA**, so it can **copy itself independently** by **binary fission**. A **virus** is **not a cell** and lacks this machinery, so it **cannot reproduce on its own** — it must **enter a host cell and use that cell's machinery** to make new virus particles. Because **having the**

machinery to copy itself is a feature of a living cell, the bacterium (which has it) is classified as a **cellular** pathogen, while the virus (which has none) is classified as **non-cellular**. *(1 mark: bacterium has its own machinery / divides by binary fission; 1 mark: virus lacks machinery / needs a host cell; 1 mark: hence cellular vs non-cellular.)*

Q20. (a) **Patient 1:** a **protozoan** — a **single-celled eukaryote** (one cell with a nucleus and flagella that moves actively). **Patient 2:** a **bacterium** — a **prokaryotic cell** (rod-shaped, no nucleus, dividing rapidly). **Patient 3:** a **parasitic worm** (helminth) — a **multicellular eukaryote** (a flat, segmented, many-celled animal). *(1 mark each patient, type + cell type.)* (b) The bacterium in Patient 2 **multiplies rapidly in the wound**, **damaging that tissue directly**; it also releases a **toxin** which is **carried away in the blood** to harm the host's cells at sites **away from the wound**. *(1 mark: local tissue damage from multiplication; 1 mark: toxin carried in the blood to distant sites.)* (c) The worm in Patient 3 lives in the gut and **absorbs / competes for the host's digested food**, so the host takes in less nourishment and **loses weight**. *(1 mark.)* (d) One shared feature: each **is, or is built from, living cells** (with their own membrane, cytoplasm and ribosomes) that **carry out their own metabolism and reproduce independently**. *(1 mark for any one valid cellular feature.)* (e) The immune system can respond to all three because each carries **non-self (foreign) antigens** — molecules it can **recognise as not belonging to the host**. *(1 mark.)*

Chapter 6 Antigens and pathogens: self versus non-self — 6C Non-cellular pathogens

Theory

A **pathogen** is any agent that causes disease in a host. Pathogens fall into two broad groups according to whether or not they are made of cells. **Cellular pathogens** are living cells — for example bacteria, fungi and protozoa (dealt with in 6B) — each of which has its own cytoplasm, membranes and metabolism and can reproduce by itself. **Non-cellular pathogens** are the opposite: they are **not cells at all**. They have no cytoplasm, no organelles and no metabolism of their own, and they cannot reproduce independently. The two kinds of non-cellular pathogen you must know are **viruses** and **prions**.

What "non-cellular" means. A cell is the smallest unit that is alive: it is bounded by a plasma membrane, contains cytoplasm and the machinery (such as ribosomes and enzymes) needed to carry out **metabolism**, and can grow and reproduce on its own. A non-cellular pathogen has none of this. It is not built from cells, it carries out **no metabolism** of its own (it cannot make ATP or build its own proteins), and it **cannot reproduce by itself**. This single feature — no cell structure and no independent metabolism — is what separates viruses and prions from every cellular pathogen. Because of it, many biologists do not regard viruses and prions as truly "living".

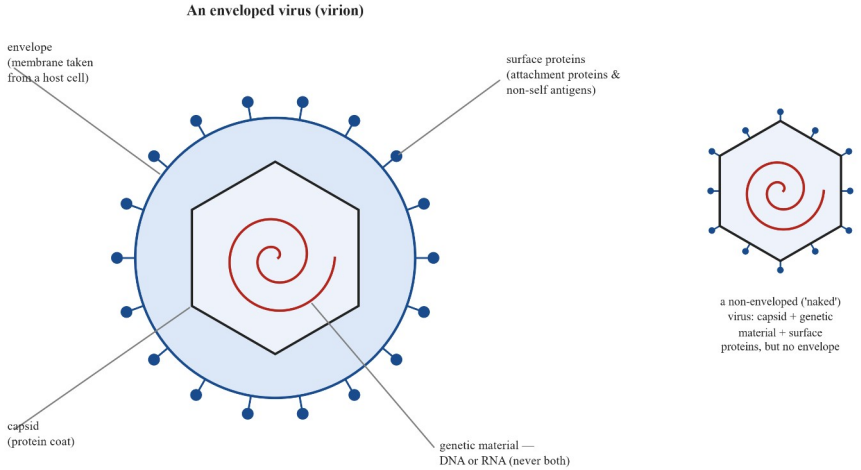
Viruses. A virus is an extremely small infectious particle — typically 20–300 nm across, far smaller than a bacterial cell (about 1–10 μm). A single complete virus particle is called a **virion**, and it has two essential parts:

- **Genetic material (the genome).** This is either **DNA or RNA** — a virus has one or the other, **never both**. It may be single- or double-stranded. The genome carries the instructions for making new copies of the virus.
- **A capsid.** This is a coat built from protein subunits that **surrounds and protects** the genetic material.

Some viruses have a third, outer layer as well:

- **An envelope.** This is a layer of membrane (lipids) that the virus **takes from a host cell's membrane** as it leaves that cell, with viral proteins embedded in it. The envelope **holds the viral surface proteins** and, because it is itself made of membrane, it can **fuse with a host cell's membrane** to deliver the genome inside. Viruses that have this layer are called **enveloped** (for example influenza virus, HIV and coronaviruses); those without it are **non-enveloped** (or "naked", such as many common-cold viruses).

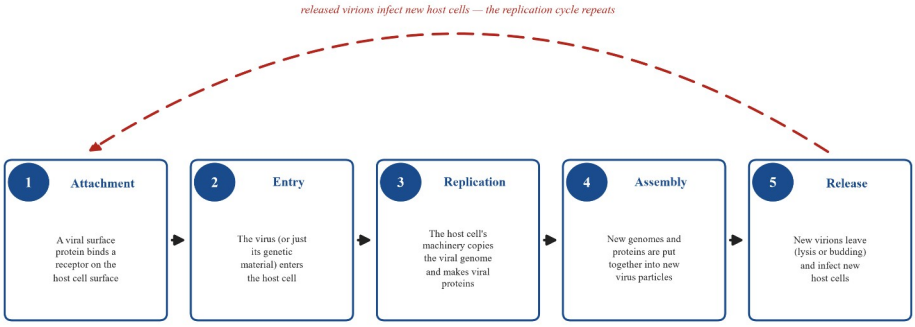
Projecting from the outer surface — the envelope where there is one, otherwise the capsid — are the **viral surface proteins**. These have two jobs: they let the virus **attach** to a specific host cell, and they act as **non-self antigens** — foreign surface markers by which the host can tell the virus apart from the body's own cells. (How the body recognises and then responds to these antigens is the work of later chapters; here we only note that a virus carries them.)



Why a virus is non-cellular and must have a host. A virus has no cytoplasm, no plasma membrane of its own (an envelope is only borrowed host membrane, not a working cell membrane), no ribosomes and no metabolism. It therefore cannot make its own proteins, cannot generate its own energy, and cannot copy its own genome unaided. To reproduce, a virus must get **inside a living host cell** and take over that cell's machinery — its ribosomes, enzymes, nucleotides, amino acids and ATP. For this reason a virus can only replicate **inside a host cell**: it is an **obligate intracellular** agent. Outside a host cell a virion is completely inert. Because attachment depends on a viral surface protein fitting a matching **receptor** on the host cell, each virus can usually infect only **certain host species and certain cell types** — its host range. A virus whose surface protein fits a receptor found only on human respiratory-tract cells, for instance, will infect only those cells.

How viruses cause disease — the viral replication cycle. Viruses cause disease by entering host cells and hijacking them to build many new viruses, damaging or killing the cells in the process. A simple replication cycle has five steps, in this order:

1. **Attachment.** A surface protein of the virus binds to a complementary **receptor** on the surface of a host cell. This binding is specific and decides which cells the virus can infect.
2. **Entry.** The virus — or just its genetic material — gets **inside** the host cell (the whole virion is taken in, or the envelope fuses with the host membrane and releases the genome). The genetic material is now within the cell.
3. **Replication (using host machinery).** The virus uses the **host cell's** ribosomes, enzymes, nucleotides, amino acids and ATP to **copy its genetic material** and **make viral proteins** (such as new capsid proteins). The host cell does the work, following the viral instructions.
4. **Assembly.** The newly made genomes and proteins are put together into **many new virions** inside the host cell.
5. **Release.** The new virions leave the cell to infect further host cells. Release may be by **lysis** (the cell bursts and dies) or by **budding** (enveloped viruses push out through the host membrane, wrapping a piece of it around themselves as their envelope).

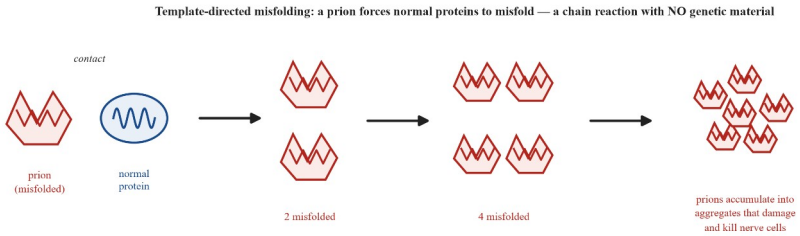


The harm done to the host's cells — cells killed by lysis, or their normal functions disrupted — is what produces the symptoms of a viral disease such as influenza, measles, hepatitis or the common cold. (Some viruses do not begin the cycle straight away; they can stay **dormant** inside a host cell for a long time before replicating.)

Prions. The second kind of non-cellular pathogen is stranger still. A **prion** is an infectious agent made **only of protein**, with **no genetic material at all** — no DNA and no RNA. A prion is a **misfolded** form of a protein that is normally present in the body (a protein found mainly in nervous tissue). The very same chain of amino acids can fold into a normal, working shape or into an abnormal, misfolded shape; the misfolded shape is the prion. Prions cause disease as follows:

- A misfolded prion acts as a **template**: when it comes into contact with a normal, correctly folded copy of the protein, it causes that normal protein to **misfold** into the abnormal shape as well.
- Each newly misfolded protein can then convert **more** normal proteins, so the misfolding spreads as a **chain reaction** and the number of prions grows — all without any genetic material and without the prion ever reproducing the way a cell does.

- The misfolded proteins are **resistant to being broken down** and steadily **accumulate**, clumping into **aggregates** that **damage and kill nerve cells**. In the brain this leaves sponge-like holes (a spongy, degenerated appearance), which is why prion diseases are called **spongiform**.
- The result is a slowly developing, **fatal neurodegenerative disease**. Examples include **Creutzfeldt–Jakob disease** and **kuru** in humans, **bovine spongiform encephalopathy** ("mad cow disease") in cattle, and **scrapie** in sheep.



Because a prion is simply a protein, it is **non-cellular** for the same reasons as a virus — no cell structure, no metabolism, and (unlike a virus) not even any genetic material. Prions are also remarkably hard to destroy: ordinary cooking and disinfection do not reliably inactivate them.

Non-cellular versus cellular pathogens. Because viruses and prions carry out no metabolism of their own and are not cells, **antibiotics have no effect on them** — antibiotics work by attacking structures or processes found in bacterial *cells* (such as the cell wall or bacterial ribosomes), which viruses and prions simply do not have. The table below sets the two non-cellular pathogens against a typical cellular pathogen so the defining differences are clear.

Feature	Cellular pathogen (e.g. a bacterium — see 6B)	Virus	Prion
A living cell?	Yes	No	No
Genetic material	DNA	DNA **or** RNA (never both)	None
Main structure	plasma membrane + cytoplasm + ribosomes	genetic material + protein capsid (± envelope)	a single misfolded protein
Own metabolism (makes its own ATP and proteins)?	Yes	No	No
How it increases in number	reproduces by itself (e.g. binary fission)	forces a host cell to make copies	templates normal proteins into more prions
Needs a host cell to multiply?	No	Yes	Converts the host's own proteins
Approximate size	~1–10 µm	~20–300 nm	a single protein molecule
Affected by antibiotics?	Often yes	No	No

Worked examples

Example 1 — scaffolded

A newly identified virus, "virus X", is found to have an outer layer of membrane carrying protein spikes, a protein coat beneath it, and a single molecule of RNA at its centre. (a) Name the part that stores the virus's instructions, and state whether virus X is a DNA or an RNA virus. (b) Name the protein coat and the outer membrane layer. (c) Explain why virus X cannot reproduce unless it is inside a host cell.

Working	Comment
(a) The instructions are stored in the **genetic material (genome)**. Virus X contains RNA, so it is an **RNA virus**.	A virus has DNA *or* RNA, never both — here it is RNA.
(b) The protein coat is the **capsid**; the outer membrane layer is the **envelope** (so virus X is an enveloped virus).	Naming the layers: capsid = protein coat, envelope = borrowed host membrane with viral proteins.
(c) A virus has **no ribosomes, no enzymes of its own and no metabolism**, so it cannot make proteins or copy its genome by itself. It must enter a **host cell** and use that cell's machinery (ribosomes, enzymes, ATP) to replicate.	The answer must give the *reason* (no machinery of its own) and the *consequence* (needs the host's machinery).
∴ virus X is **non-cellular** and can only replicate **inside a host cell** (it is an obligate intracellular agent).	A one-line conclusion ties the parts together.

Example 2 — scaffolded

The five stages of a viral replication cycle are listed here out of order: **assembly, attachment, release, entry, replication**. (a) Write the five stages in their correct order. (b) Describe what happens during the replication stage. (c) Explain why a particular virus can usually infect only certain types of cell.

Working	Comment
(a) Correct order: **attachment → entry → replication → assembly → release**.	The cycle must start with attachment and end with release; assembly comes before release.
(b) During **replication**, the virus uses the **host cell's** machinery — its ribosomes, enzymes, nucleotides and ATP — to **copy the viral genome** and **make viral proteins**.	"Replication" = copying the genome *and* making viral proteins, using the host's resources (not the virus's).
(c) Attachment depends on a **viral surface protein binding a specific receptor** on the host cell. Only cells that carry the matching receptor can be attached to and entered.	Specificity comes from the surface-protein/receptor fit — a complementary-shape idea.
∴ a virus can only infect cells that display the **receptor its surface protein fits**, which limits its host range.	The conclusion links receptor specificity to host range.

Example 3 — unscaffolded

A prion contains no DNA and no RNA, yet a single prion entering the brain can lead to millions of prions and to fatal disease. Explain how this is possible.

A prion is a **misfolded protein**, and it multiplies not by reproducing but by **template-directed misfolding**. When the misfolded prion contacts a **normal, correctly folded** copy of the same protein (a protein normally present in nervous tissue), it forces that normal protein to **refold into the abnormal, misfolded shape**. Each newly misfolded protein then acts as a template for more normal proteins, so the misfolding spreads as a **chain reaction** and the number of prions rises rapidly — without any genetic material and without the prion ever dividing like a cell. The misfolded proteins are **resistant to breakdown** and **accumulate as aggregates** that damage and kill nerve cells, leaving the brain with a sponge-like (spongiform) appearance. ∴ a prion increases in number by converting the body's own proteins, which is why no genetic material is needed to cause a progressive, fatal neurodegenerative disease.

Example 4 — unscaffolded

A microbiologist writes that a virus and a bacterium are "fundamentally different kinds of pathogen". Using the idea of non-cellular versus cellular pathogens, explain **two** ways in which a virus differs from a bacterium.

A **bacterium is a cellular pathogen** — a complete living cell — whereas a **virus is a non-cellular pathogen**, so the two differ in fundamental ways. **First, in structure and metabolism:** a bacterium is a cell with a plasma membrane, cytoplasm, ribosomes and its own metabolism, so it can make its own proteins and generate its own energy; a virus is only genetic material inside a protein capsid (sometimes with an envelope), has **no ribosomes, no metabolism** and is

not a cell at all. **Second, in how it multiplies:** a bacterium **reproduces on its own** by binary fission, whereas a virus **cannot reproduce by itself** — it must enter a **host cell** and hijack that cell's machinery to make new virions. ∴ the two are fundamentally different because a bacterium is a self-sufficient living cell while a virus is a non-cellular particle that depends completely on a host cell to replicate.

Practice questions

Scaffolded

Q1. Define each of the following terms: (a) non-cellular pathogen; (b) capsid; (c) prion.

Q2. A virus particle is examined and found to have a protein coat enclosing a single molecule of DNA, with no surrounding membrane. (a) State whether this is a DNA virus or an RNA virus. (b) Name the protein coat. (c) State whether the virus is enveloped or non-enveloped, and justify your answer.

Q3. A virus infects a host cell and completes a replication cycle. (a) Name the first step of the cycle. (b) Describe what happens during the assembly step. (c) State two ways in which new virions may be released from the host cell.

Q4. Viruses are described as non-cellular pathogens. (a) State two structures found in a living cell that a virus does not have. (b) Explain why a virus must enter a host cell in order to reproduce. (c) Name the part of a virus that acts as a **non-self antigen**, and state what "non-self" means here.

Q5. Prions are a type of non-cellular pathogen. (a) State what a prion is made of, and whether it contains any genetic material. (b) Describe how one prion leads to an increase in the number of prions. (c) Name the type of disease that prions cause.

Q6. Viruses and prions are both non-cellular, but they are not the same. (a) State one feature that viruses and prions have in common. (b) State the key difference between a virus and a prion in terms of genetic material. (c) State one way a virus differs from a bacterium.

Unscaffolded

Q7. Distinguish between a cellular pathogen and a non-cellular pathogen. *(2 marks)*

Q8. Describe the structure of an enveloped virus, naming **three** of its parts and stating the function of each. *(3 marks)*

Q9. Explain why a virus is described as **non-cellular** and why it must be an **intracellular** pathogen. *(3 marks)*

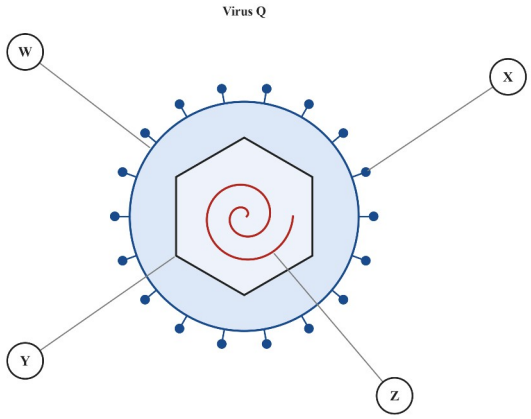
Q10. The steps of a viral replication cycle are: attachment, entry, replication, assembly, release. Describe what happens at **each** of these five steps, in order. *(5 marks)*

Q11. Instruments used in brain surgery are routinely decontaminated by a procedure that kills bacteria and destroys any DNA or RNA left on them. Explain why this procedure cannot be relied on to make the instruments safe after surgery on a patient with prion disease. *(4 marks)*

Q12. Compare a virus and a prion. In your answer give **three** differences between them. *(3 marks)*

Q13. A patient with a cold is told that "the virus has become resistant to antibiotics, so the antibiotics will not work". Explain why this statement is incorrect. *(2 marks)*

Q14. *(Stimulus.)* The diagram shows a virion, "virus Q", with four features labelled W, X, Y and Z.



(a) Identify the parts labelled W, X, Y and Z.
(b) Explain what is meant by the statement that a virus's genetic material is "DNA or RNA, but never both".
(c) State the two functions of the parts labelled X. *(5 marks)*

Q15. *(Data interpretation.)* A single animal cell in culture was infected with **one** virion. The number of new virions present inside the cell was counted at intervals:

Time after infection (hours)	New virions in the cell
0	0
2	0
4	8
6	95
8	640
10	3100

(a) Describe the trend in the number of new virions from 4 hours onwards.
(b) Account for the fact that **no new virions** were present during the first 2 hours, referring to the replication cycle.
(c) Predict what is likely to happen to the host cell soon after 10 hours, and give a reason. *(4 marks)*

Q16. *(Research vignette.)* On a deer farm, several animals develop a slowly progressing, ultimately fatal disease. Affected deer become uncoordinated and waste away over months. After death, their brain tissue is found to have a sponge-like appearance. Investigators can find **no bacterium, no virus and no nucleic acid** in the affected tissue, but they do detect large amounts of an **abnormally folded protein**. The disease spreads between deer that share feeding grounds. (a) Identify the most likely type of pathogen responsible, and justify your answer using **two** pieces of evidence from the vignette. (b) Explain how this pathogen causes the sponge-like damage seen in the brain. *(5 marks)*

Q17. A virus infects only cells of the human liver. In the laboratory, its surface protein is altered so that the protein now fits a receptor found only on human muscle cells. Predict which cells the altered virus will be able to infect, and explain your reasoning. *(3 marks)*

Q18. Viruses and prions are sometimes said to sit "on the border between living and non-living". Using **two** features of these agents, explain why. *(3 marks)*

Q19. *(Stimulus.)* Three disease-causing agents, P, Q and R, were described as follows:

Agent	Composition	Genetic material	Approx. size
P	a protein capsid enclosing RNA, with an outer envelope	RNA	110 nm
Q	a cell with a wall, membrane, cytoplasm and	DNA	2 µm

Agent	Composition	Genetic material	Approx. size
	ribosomes		
R	a single misfolded protein	none	protein molecule

(a) Classify each of P, Q and R as either a cellular or a non-cellular pathogen.

(b) State which agent is a virus and which is a prion, and justify each choice using the table.

(c) Which of the three agents could be treated with an antibiotic? Explain your answer. *(5 marks)*

Q20. *(Synthesis.)* Two disease-causing agents, **J** and **K**, were isolated from different patients and put through the same four tests.

Test	Agent J	Agent K
Kept 48 h in sterile nutrient broth (no living cells)	large increase in numbers	no increase
Kept 48 h with a culture of living human cells	large increase in numbers	large increase in numbers
Nucleic acid found in the purified agent	DNA	RNA
Passes through a filter with 200 nm pores	no	yes

(a) Classify J and K as cellular or non-cellular pathogens, justifying each choice with **one** result from the table.

(b) Account for the difference between agent K's result in the sterile broth and its result in the living-cell culture, and give the term used for an agent that behaves in this way.

(c) Explain how the filter result supports your classification of agent K.

(d) Agent K is later found to have an outer envelope. Explain why having an envelope does **not** make agent K a cell. *(8 marks)*

Answers

Q1. (a) A disease-causing agent that is not a cell (no cytoplasm, no metabolism, cannot reproduce by itself) — a virus or a prion. (b) The protein coat that surrounds and protects a virus's genetic material. (c) An infectious misfolded protein, with no genetic material, that causes normal proteins to misfold. **Q2.** (a) A DNA virus. (b) The capsid. (c) Non-enveloped ("naked") — it has no membrane layer around the capsid. **Q3.** (a) Attachment. (b) The newly made viral genomes and proteins are put together into many new virions inside the host cell. (c) By lysis (the cell bursts) and by budding. **Q4.** (a) Any two of: ribosomes, cytoplasm, its own plasma membrane, metabolic enzymes / metabolism. (b) It has no machinery or metabolism of its own, so it must use a host cell's machinery to replicate. (c) The viral surface proteins; "non-self" means they are foreign markers that are not found on the host's own cells, so the host can tell the virus apart from itself. **Q5.** (a) Protein only; it contains no genetic material (no DNA or RNA). (b) It acts as a template, making normal copies of the protein misfold into the prion shape — a chain reaction. (c) A (fatal) neurodegenerative / spongiform disease. **Q6.** (a) Both are non-cellular (not cells; no metabolism of their own). (b) A virus has genetic material (DNA or RNA); a prion has none. (c) A bacterium is a living cell that reproduces by itself, whereas a virus is non-cellular and needs a host cell to replicate (accept: virus much smaller; bacterium has ribosomes/metabolism). **Q7.** A cellular pathogen is a living cell (e.g. a bacterium) with its own metabolism that can reproduce by itself; a non-cellular pathogen (a virus or prion) is not a cell, has no metabolism of its own and cannot reproduce independently. **Q8.** Genetic material (DNA or RNA) — carries the instructions; capsid — a protein coat that protects the genome; envelope — an outer membrane layer taken from a host cell that holds the surface proteins and can fuse with a host cell's membrane to let the genome in; surface proteins — attachment and non-self antigens (any three parts + functions). **Q9.** Non-cellular = it is not a cell (no cytoplasm, ribosomes or metabolism); intracellular = it has no machinery of its own, so it must enter a host cell and use the host's machinery to replicate. **Q10.** Attachment: viral surface protein binds a host-cell receptor. Entry: the virus/its genome enters the cell. Replication: the host machinery copies the genome and makes viral proteins. Assembly: new genomes and proteins form new virions. Release: virions leave (lysis or budding) to infect new cells. **Q11.** A prion is not a cell and holds no DNA or RNA, so killing bacteria and destroying nucleic acid removes nothing it depends on; the infectious agent is the misfolded protein itself, which resists being broken down by ordinary sterilising treatments, so it stays on the instrument and can template a new patient's normal proteins into the misfolded form. **Q12.** A virus has genetic material (DNA or RNA) whereas a prion has none; a virus is genome + capsid (± envelope) whereas a prion is only protein; a virus replicates using host-cell machinery whereas a prion multiplies by templating normal proteins. **Q13.** Viruses were never affected by antibiotics in the first place, so they cannot "become" resistant to them: antibiotics act on structures/processes of bacterial cells (cell wall, bacterial ribosomes), and a non-cellular virus has none of these targets. **Q14.** (a) W = envelope; X = surface proteins (spikes); Y = capsid; Z = genetic material. (b) The virus has either DNA or RNA as its genome, but not both together. (c) X allows the virus to attach to a host cell, and acts as a non-self antigen. **Q15.** (a) The number of new virions rises rapidly (exponentially/steeply) with time. (b) During the first 2 hours the virus is attaching, entering and beginning replication, so no new virions have been assembled yet. (c) The cell is likely to burst (lyse) and die, because the many assembled virions are released, which typically destroys the host cell. **Q16.** (a) A prion, because there is an abnormally folded protein present but no nucleic acid / microbe, and it causes a fatal neurodegenerative disease with spongy brain tissue. (b) The misfolded prion templates the animal's normal proteins into the misfolded shape; these accumulate as aggregates that damage and kill nerve cells, leaving sponge-like holes. **Q17.** It will infect muscle cells but will no longer infect liver cells — infection begins with attachment, and only cells carrying a receptor the surface protein fits can be attached to and entered, so the host range shifts rather than widens. **Q18.** Any two features with reasoning: neither is a cell and neither has a metabolism of its own (non-living-like), yet a virus carries genetic material and can direct its own multiplication and evolve (life-like); a prion has no genetic material at all, yet it still multiplies, by templating the host's normal proteins; a virion is inert outside a host cell but replicates inside one. **Q19.** (a) P non-cellular; Q cellular; R non-cellular. (b) P is a virus (genome + capsid ± envelope, nm-sized); R is a prion (protein only, no genetic material). (c) Only Q — it is a cell, so an antibiotic has cell structures/processes to attack; P and R are non-cellular. **Q20.** (a) J is cellular — it multiplied in sterile broth with no living cells present; K is non-cellular — it multiplied only when living cells were supplied. (b) Free nutrients are useless to K because it has no ribosomes and no metabolism of its own; it can multiply only by getting inside a living cell and using that cell's machinery — it is an obligate intracellular agent. (c) K passed through 200 nm pores, so it is under 200 nm across (viruses ~20–300 nm), far smaller than any cell (~1–10 μm). (d) The envelope is only membrane taken from a host cell, not a membrane K makes or maintains; a cell also needs cytoplasm, ribosomes and its own metabolism inside that membrane, and K has none of these.

Fully-worked solutions

Q1. (a) A **non-cellular pathogen** is a disease-causing agent that is **not a cell**: it has no cytoplasm, organelles or metabolism of its own and cannot reproduce independently. Viruses and prions are the two examples. (b) A **capsid** is the **protein coat** that **surrounds and protects** a virus's genetic material. (c) A **prion** is an infectious agent made **only of protein** — a **misfolded** version of a normal body protein, containing **no genetic material** — that causes normal copies of the protein to misfold.

Q2. (a) The genome is DNA, so this is a **DNA virus**. (b) The protein coat is the **capsid**. (c) It is **non-enveloped** ("naked"): the description says there is **no membrane** surrounding the capsid, and only enveloped viruses have that outer membrane layer.

Q3. (a) The first step is **attachment**. (b) During **assembly** the **newly made viral genomes and the newly made viral proteins** (such as capsid proteins) are **put together into many new virions** inside the host cell; this happens after replication and before release. (c) New virions may be released by **lysis** (the host cell bursts and dies) or by **budding** (enveloped viruses push out through the host membrane, taking a piece of it as their envelope).

Q4. (a) Any two of: **ribosomes**, **cytoplasm**, a **plasma membrane of its own**, or **metabolic enzymes / a metabolism**. (b) A virus has **no ribosomes, no metabolism and no way of making proteins or energy for itself**, so it cannot copy its genome or build new virus parts alone. It must enter a **host cell** and use that cell's machinery to replicate — it is an obligate intracellular agent. (c) The **viral surface proteins** act as non-self antigens. **"Non-self"** means they are **foreign surface markers** — molecules that are **not found on the host's own cells** — so the host is able to tell the virus apart from its own tissue and treat it as an invader.

Q5. (a) A prion is made **only of protein** and contains **no genetic material** (no DNA and no RNA). (b) A misfolded prion acts as a **template**: it makes **normal, correctly folded copies** of the protein **refold** into the misfolded prion shape, and each new prion converts more normal proteins — a **chain reaction** that raises prion numbers. (c) Prions cause a **fatal neurodegenerative (spongiform) disease**, such as Creutzfeldt–Jakob disease or bovine spongiform encephalopathy.

Q6. (a) Both are **non-cellular** — neither is a cell and neither has a metabolism of its own. (b) A **virus has genetic material** (either DNA or RNA); a **prion has none** (it is protein only). (c) A **bacterium is a living cell** with its own metabolism that **reproduces by itself**, whereas a **virus is non-cellular** and must use a **host cell** to replicate (also acceptable: a virus is far smaller; a bacterium has ribosomes and carries out metabolism).

Q7. A **cellular pathogen** is a **living cell** — for example a bacterium — that has its own cytoplasm, membranes and **metabolism** and can **reproduce by itself**. A **non-cellular pathogen** — a **virus or a prion** — is **not a cell**: it has no metabolism of its own and **cannot reproduce independently** (a virus needs a host cell; a prion templates existing proteins). *(1 mark each side, congruent treatment.)*

Q8. An enveloped virus has (naming any **three** parts with a function each): **genetic material** (**DNA or RNA**) that **carries the instructions** for making new viruses; a **capsid**, the **protein coat** that **surrounds and protects** the genome; an **envelope**, an outer membrane layer taken from a host cell, which **holds the surface proteins** and can **fuse with a host cell's membrane to let the genome enter**; and **surface proteins** projecting from the envelope that allow **attachment** to a host cell and act as **non-self antigens**. *(1 mark per correctly named part + function, to a maximum of 3; a part named without a function scores 0.)*

Q9. A virus is **non-cellular** because it is **not a cell**: it has **no cytoplasm, no ribosomes and no metabolism** of its own, so it cannot make proteins or generate energy for itself. Because it lacks this machinery, it can only reproduce by using a **host cell's** machinery, which means it must be **inside** a living cell to replicate — it is an **intracellular** (obligate intracellular) pathogen. *(1 mark: not a cell / no cytoplasm-ribosomes-metabolism; 1 mark: cannot make proteins/energy itself; 1 mark: must use a host cell's machinery from inside the cell.)*

Q10. Attachment: a **surface protein of the virus binds a specific receptor** on the host cell. **Entry:** the virus, or just its **genetic material**, gets **inside** the host cell. **Replication:** the **host cell's machinery** (ribosomes, enzymes, ATP) is used to **copy the viral genome and make viral proteins**. **Assembly:** the new genomes and proteins are **put together into many new virions**. **Release:** the new virions **leave the cell** (by **lysis** or **budding**) and go on to infect further host cells. *(1 mark for each correctly described step, in order.)*

Q11. The procedure is aimed at the wrong kind of target. A prion is **not a cell**, so killing bacteria removes nothing, and a prion contains **no DNA and no RNA**, so destroying nucleic acid destroys nothing the prion depends on — the infectious agent **is the misfolded protein itself**. Misfolded prion protein is also **resistant to being broken down**, and ordinary cooking, disinfection and sterilising treatments do **not reliably inactivate it**, so infectious prion protein can **remain on the instrument** after the procedure. If that protein is then introduced into another patient's nervous tissue it can act as a **template**, forcing that person's **normal copies of the protein to refold** into the abnormal shape in a **chain reaction**, which leads to a fatal neurodegenerative disease. *(1 mark: a prion is non-cellular and has no nucleic acid, so neither part of the procedure targets it; 1 mark: the infectious agent is the misfolded protein itself; 1 mark: misfolded prion protein resists breakdown by ordinary sterilising treatments, so it survives on the instrument; 1 mark: surviving prion protein can template a new patient's normal proteins and cause disease.)*

Q12. A virus and a prion are both non-cellular but differ in three important ways: **(1) Genetic material —** a **virus contains genetic material** (DNA or RNA), whereas a **prion has none** (it is protein only). **(2) Composition —** a **virus** is a **genome enclosed in a protein capsid** (sometimes with an envelope), whereas a **prion** is simply a **misfolded protein**. **(3) How it multiplies —** a **virus** forces a **host cell's machinery** to make new virions, whereas a **prion** multiplies by **templating the host's normal proteins** into the misfolded shape. *(1 mark per difference, each given as a congruent two-sided comparison — the same feature stated for both agents; a one-sided statement scores 0. Maximum 3.)*

Q13. The statement is wrong because it assumes the virus was **once affected by antibiotics** and has since changed. **Antibiotics** kill bacteria by attacking **structures or processes that are part of a bacterial cell** — for example the **cell wall** or the **bacterial ribosomes** used to make proteins. A **virus is non-cellular**: it has **no cell wall, no ribosomes and no metabolism of its own**, so an antibiotic **never had a target to act on** in the first place. A virus therefore cannot "become resistant" to antibiotics — it was **never susceptible** to them, and a cold would not be helped by antibiotics even if no virus had ever changed. *(1 mark: antibiotics target bacterial-cell structures/processes, which a non-cellular virus does not have; 1 mark: viruses were never susceptible, so "becoming resistant" to antibiotics does not apply to them.)*

Q14. (a) **W = the envelope** (outer membrane layer); **X = surface proteins** (the spikes); **Y = the capsid** (protein coat); **Z = the genetic material** (genome). (b) It means the virus's genome is made of **either DNA or RNA, but not both at the same time** — an individual virus carries only one type of nucleic acid. (c) The parts labelled X (surface proteins) let the virus **attach to a specific host cell** (by binding a receptor) and act as **non-self antigens** — foreign surface markers the host can recognise. *(a: 2 marks — 1 mark for two or three correct labels, 2 marks for all four; b: 1 mark; c: 2 marks, one per function.)*

Q15. (a) From 4 hours onwards the number of new virions **rises rapidly**, increasing more and more steeply over time (an approximately **exponential** increase: 8 → 95 → 640 → 3100). (b) In the **first 2 hours no new virions** are present because the virus is still going through the **early steps of the cycle** — **attachment, entry and the start of replication** — so the host cell has **not yet assembled** any new virus particles. (c) Soon after 10 hours the host cell is likely to **burst (lyse) and die**, because the very large number of assembled virions are **released** from the cell, and this release (lysis) typically destroys the host cell. *(1 mark: rapid/exponential rise; 1 mark: early cycle steps before assembly; 1 mark: cell lyses/dies; 1 mark: reason — release of many virions.)*

Q16. (a) The most likely pathogen is a **prion**. Two pieces of supporting evidence: **(1)** there is **no bacterium, virus or nucleic acid** in the tissue, but an **abnormally folded protein** is present — a prion is protein only, with no genetic material; and **(2)** the disease is a **slow, fatal neurodegenerative** one leaving **sponge-like (spongiform) brain tissue**, which is characteristic of prion disease. (b) The misfolded prion **templates the deer's own normal proteins**, forcing them to misfold; the misfolded proteins **accumulate as aggregates** that **damage and kill nerve cells** in the brain, and the loss of these cells leaves the **sponge-like holes** seen in the tissue. *(a: 1 mark prion + 2 marks for two justifications; b: 2 marks for templating → aggregates kill nerve cells.)*

Q17. Prediction: the altered virus will now be able to infect **muscle cells**, and it will **no longer be able to infect liver cells** — its host range has **shifted**, not widened. **Reasoning:** infection can only begin at the **attachment** step, where a **viral surface protein** must bind a **complementary receptor** on the host cell. The altered surface protein fits the receptor carried by muscle cells, so the virus can now attach to and enter them; it no longer fits the liver-cell receptor, so it can no longer attach to or enter liver cells, and a virus that cannot get inside a cell cannot replicate at all. *(1 mark: predicts it infects muscle cells; 1 mark: predicts it can no longer infect liver cells; 1 mark: reasoning — attachment*

requires the surface protein to fit a complementary receptor, so only cells carrying the matching receptor can be entered.)

Q18. Viruses and prions straddle the living/non-living boundary (any **two** features, each explained): **(1)** Neither is a cell and neither has a **metabolism** of its own — like non-living things they cannot grow or generate energy. **(2)** Yet a **virus carries genetic material and can direct its own multiplication** (and can evolve) once inside a host — a life-like property. **(3)** A **prion**, although it has **no genetic material at all**, still **increases in number**, by templating the host's normal proteins into the misfolded form — multiplication without any of the machinery of life. **(4)** A virion is **completely inert outside a host cell**, behaving like a non-living particle, but **becomes "active"** and replicates inside one. *(1 mark per feature with reasoning, to a maximum of 2; + 1 mark for the concluding link — because these agents combine non-living and life-like properties they sit on the border between living and non-living.)*

Q19. (a) **P — non-cellular**; **Q — cellular**; **R — non-cellular**. (b) **P is the virus**: it is a **genome (RNA) enclosed in a protein capsid with an envelope** and is **nm-sized** — the structure of a virion. **R is the prion**: it is a **single misfolded protein with no genetic material**, matching the definition of a prion. (Q is a cell — a bacterium-like cellular pathogen.) (c) Only **Q** could be treated with an **antibiotic**, because Q is a **cell** with structures and processes (such as a cell wall and ribosomes) that antibiotics attack. **P and R are non-cellular** and have no such targets, so antibiotics would not work on them. *(a: 1 mark all three correct; b: 2 marks, one each for P and R with justification; c: 2 marks — Q identified + reason that non-cellular P and R lack targets.)*

Q20. (a) **J is a cellular pathogen**: it increased in number in **sterile broth containing no living cells**, so it must be a complete cell able to take in nutrients and **reproduce by itself**. **K is a non-cellular pathogen**: it showed **no increase in the same broth** and increased **only when living cells were supplied**, so it cannot multiply on its own. (b) The broth supplied plenty of free nutrients, but K has **no ribosomes, no enzymes of its own and no metabolism**, so it can neither build proteins nor copy its genome from those nutrients and its numbers did not change. Once **living cells** were provided, K could get **inside a host cell** and use **that cell's machinery** — ribosomes, enzymes, nucleotides and ATP — to copy its genome and make its proteins, so many new particles were produced. An agent that can only multiply inside a living host cell in this way is described as an **obligate intracellular** agent. (c) K **passed through pores 200 nm across**, so K is **smaller than 200 nm** — within the ~20–300 nm size range of a **virion** — whereas a cell is **~1–10 µm** (about 5–50 times larger) and, like J, cannot pass such a filter. Being far too small to be a cell supports the classification of K as non-cellular. (d) An envelope is **only a piece of membrane taken from a host cell** as the virion left that cell — it is **not a plasma membrane K makes or maintains for itself**. Being wrapped in membrane is not what makes something a cell: a cell must also contain **cytoplasm, ribosomes and its own metabolism** inside that membrane, and K has **none of these** — it is genetic material in a capsid with a borrowed membrane around it. ∴ J is a cellular pathogen that reproduces by itself, while K is a non-cellular, obligate intracellular agent whose envelope does not change that. *(a: 2 marks — 1 mark for each agent correctly classified **with** a supporting result from the table; b: 3 marks — 1 mark: no ribosomes/metabolism of its own, so free nutrients are unusable; 1 mark: must enter a living cell and use its machinery; 1 mark: names it an obligate intracellular agent; c: 1 mark — under 200 nm, the size of a virion and far smaller than any cell; d: 2 marks — 1 mark: the envelope is borrowed host membrane, not the agent's own; 1 mark: a cell also needs cytoplasm, ribosomes and metabolism, which K lacks.)*