Biology Units 3 & 4

Chapter 7 — The body's immune defences

This work is licensed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view a copy of this license, visit http://creativecommons.org/licenses/by-nc-nd/4.0/ or send a letter to Creative Commons, PO Box 1866, Mountain View, CA 94042, USA.

Attribution: Classbasics Pty Ltd, vwx.au

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

Theory

An animal or plant is surrounded by pathogens — bacteria, viruses, fungi and other agents that can cause disease. To stay healthy, an organism must stop most of these pathogens getting in, and deal with any that do. The defences that make this possible are organised into **lines of defence**. This subtopic deals with the **first line of defence**: the set of **surface barriers** that **prevent pathogens entering** the body in the first place. Because they work at the surface, before a pathogen has entered the tissues, the first line is a **preventative** defence.

Two features define the first line of defence:

- **It is non-specific.** The barriers act against **all** pathogens in the **same general way**. They are not tailored to any particular pathogen — a physical barrier such as skin blocks a virus, a bacterium and a fungal spore alike. (This is different from the specific responses of later subtopics, which are directed at one particular pathogen.)
- **It is innate (always present).** These barriers are in place **from birth**, are **ready at all times**, and do not need the body to have met the pathogen before. They give **immediate** protection.

The study design groups the first-line barriers into **three types — physical, chemical and microbiota barriers** — and requires the first line of defence in **both animals and plants**.

Physical barriers (animals). A physical (or mechanical) barrier is a **structure** that physically **blocks or removes** pathogens.

- **Skin.** Intact skin is the body's largest physical barrier. Its outer layer is made of tightly packed, flattened, dead cells filled with the tough protein **keratin**. This layer is **dry** and continuous, so it is difficult for pathogens to penetrate or to grow on. As long as the skin is **unbroken**, it keeps pathogens out of the tissues beneath.
- **Mucous membranes and mucus.** The body openings and tracts that are exposed to the environment — the respiratory (airway), digestive, urinary and reproductive tracts — are lined not by skin but by **mucous membranes**. These membranes secrete **mucus**, a sticky fluid that **traps** pathogens and particles before they can reach and attach to the underlying cells.
- **Cilia.** The cells lining the airways also carry **cilia** — tiny hair-like projections that beat in a coordinated, wave-like way. They **sweep the mucus (with its trapped pathogens) upwards and out** of the airways towards the throat, where it is swallowed or coughed out. Mucus and cilia therefore work as a team: the mucus traps, the cilia remove.
- **Flushing actions.** The steady flow of fluids physically **washes pathogens off surfaces** before they can establish. **Tears** flush the surface of the eye, **saliva** washes the mouth, and the flow of **urine** flushes the urinary tract.

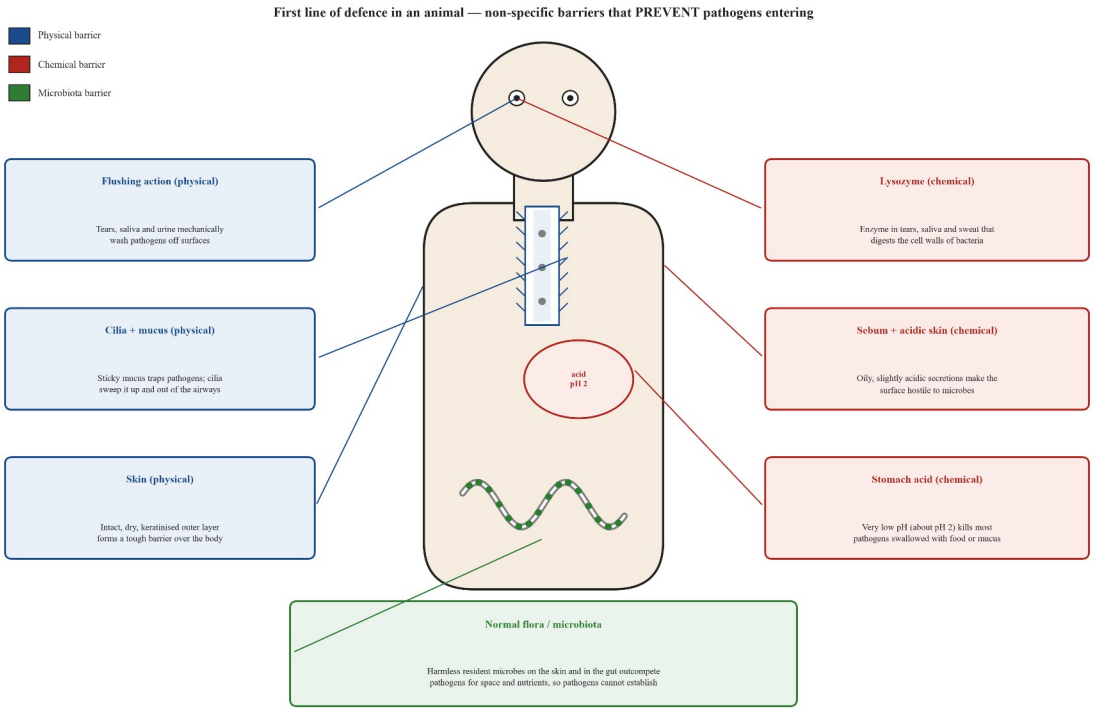
Chemical barriers (animals). A chemical barrier is a **secretion or substance** that **kills or inhibits** pathogens, usually by creating conditions in which they cannot survive.

- **Stomach acid.** The stomach produces gastric juice containing hydrochloric acid, giving it a **very low pH (around pH 2)**. This strongly acidic environment **kills most pathogens** that are swallowed with food or in mucus, by denaturing their proteins and enzymes.
- **Lysozyme.** This is an **enzyme** found in **tears, saliva and sweat** (and in mucus). It **breaks down the cell walls of many bacteria**, causing them to burst and die.
- **Sebum and acidic secretions.** Glands in the skin secrete **sebum**, an oily substance that, together with sweat, makes the skin surface **slightly acidic** (around pH 5) and contains fatty acids. These conditions **inhibit the growth** of many bacteria and fungi on the skin.

Microbiota barriers. The surfaces of a healthy body — the skin, the gut, the mouth and other tracts — are home to enormous numbers of **harmless resident microbes**. These make up the body's **normal flora** (also called the **microbiota** or normal microbial flora). Although they are microbes, they do **not** cause disease; instead they **help defend** the body against pathogens by **competitive exclusion**:

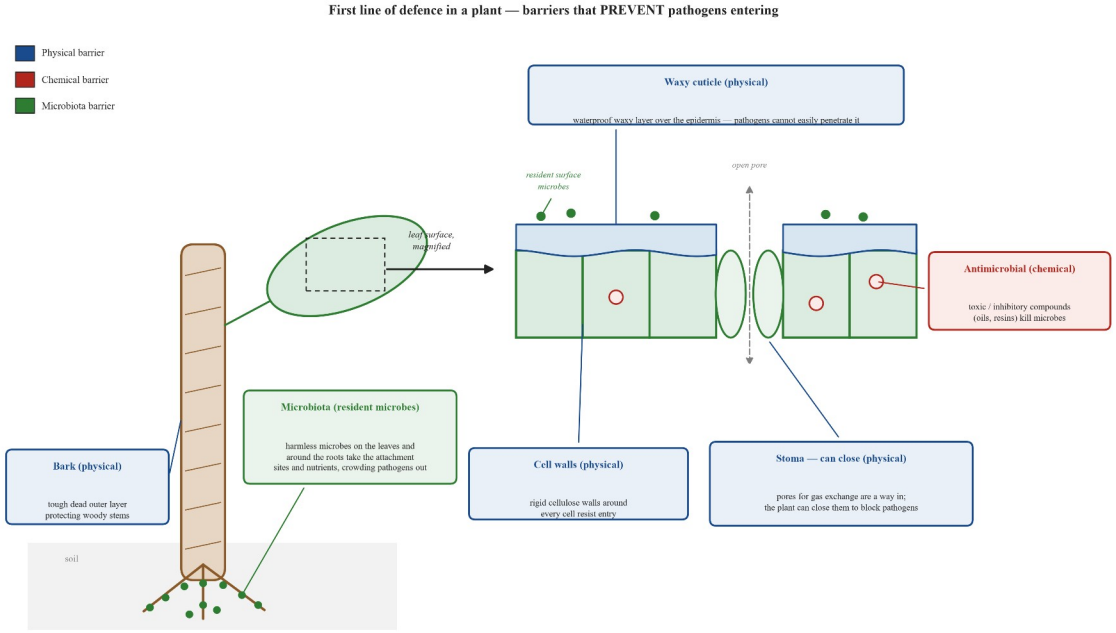
- **Competition for space.** The normal flora already **occupies the attachment sites** on the body's surfaces, leaving few places for an incoming pathogen to attach and settle.
- **Competition for nutrients.** The normal flora **uses up the available nutrients**, so an incoming pathogen cannot obtain enough food to grow and multiply.

By crowding out and starving pathogens (and by keeping the local environment acidic), the normal flora **prevents pathogens from establishing**. This is why disturbing the normal flora — for example, when a course of broad-spectrum **antibiotics** kills off much of the gut microbiota — can allow a pathogen to **overgrow** and cause infection.



Barriers in plants. Plants have no mobile defensive cells and no specific immune response, so the first line of defence is essentially the whole of a plant's protection. Plants are nevertheless well defended, because they have **all three of the same types of barrier as an animal — physical, chemical and microbiota** — with the physical barriers the most obvious.

- **The waxy cuticle (physical).** The outer surface of leaves and young stems is covered by a **waterproof waxy layer**, the **cuticle**, lying over the epidermis. It is a physical barrier that pathogens **cannot easily penetrate**, and it keeps the surface dry.
- **Cell walls (physical).** Every plant cell is surrounded by a **rigid cell wall** made largely of **cellulose**. These walls form a physical barrier around and between cells that **resists the entry** and spread of pathogens.
- **Bark (physical).** The woody stems and roots of many plants are covered by **bark** — a tough, mostly dead outer layer that acts as a physical barrier, much as skin does in an animal.
- **Closing of stomata (physical). Stomata** are small pores in the leaf surface used for gas exchange. Because some pathogens enter a leaf **through open stomata**, plants can **close their stomata** to block this route of entry.
- **Chemical defences.** Plants produce a range of **antimicrobial chemicals** — for example oils, resins and other toxic or inhibitory compounds — that **kill or inhibit** microbes at the surface and in the tissues, adding a chemical barrier to the physical ones.
- **Microbiota (resident microbes).** Like an animal, a plant carries **harmless resident microbes** on its surfaces — on the **leaves**, and most densely on and around the **roots** in the soil. These microbes are the plant's **microbiota**, and they defend it by the same **competitive exclusion**: they already **occupy the attachment sites** and **use up the nutrients** at the plant's surface, so a pathogen arriving from the air or the soil finds **nowhere to attach and too little food** to establish.



Where the first line fits. The first line of defence is the body's **outer wall**: a non-specific, always-ready set of physical, chemical and microbiota barriers that stop most pathogens **before** they ever enter the tissues. No single barrier is perfect, but together they block, remove, poison or crowd out the great majority of pathogens. If a pathogen **does breach** these surface barriers and enters the body's tissues, the **internal** responses of the later lines of defence take over — and those are the subject of the following subtopics.

The table summarises the first line of defence.

Barrier	Type	Found in	How it prevents infection
Skin	Physical	Animal	Dry, keratinised, unbroken layer blocks entry
Mucous membranes + mucus	Physical	Animal	Sticky mucus traps pathogens
Cilia	Physical	Animal	Sweep trapped mucus out of the airways
Flushing (tears, saliva, urine)	Physical	Animal	Wash pathogens off surfaces
Stomach acid	Chemical	Animal	Low pH (about pH 2) kills swallowed pathogens
Lysozyme	Chemical	Animal	Enzyme digests bacterial cell walls
Sebum / acidic skin	Chemical	Animal	Oily, acidic surface inhibits microbes
Normal flora (microbiota)	Microbiota	Animal	Outcompetes pathogens for space and nutrients
Waxy cuticle	Physical	Plant	Waterproof layer pathogens cannot penetrate
Cell walls	Physical	Plant	Rigid cellulose walls resist entry
Bark	Physical	Plant	Tough outer layer over woody stems
Closing of stomata	Physical	Plant	Blocks entry through leaf pores
Antimicrobial chemicals	Chemical	Plant	Toxic compounds kill or

Barrier	Type	Found in	How it prevents infection
			inhibit microbes
Leaf-surface and root microbes	Microbiota	Plant	Outcompete pathogens on leaves and around roots

Worked examples

Example 1 — scaffolded

A microbiologist lists three of the body's first-line defences: the **skin**, the **acid in the stomach**, and the **harmless bacteria that normally live in the large intestine**. (a) Classify each of the three as a physical, chemical or microbiota barrier. (b) Explain how the skin prevents pathogens from causing infection. (c) Explain how the harmless gut bacteria help prevent infection.

Working	Comment
(a) Skin = **physical** barrier; stomach acid = **chemical** barrier; harmless gut bacteria (normal flora) = **microbiota** barrier.	One of each type — match the barrier to what it *is*: a structure (physical), a substance (chemical), or resident microbes (microbiota).
(b) Intact skin is a **dry, tough, keratinised** outer layer that is **continuous over the body**, so pathogens **cannot penetrate** it to reach the tissues beneath.	Name the property (dry/keratinised/unbroken) *and* the consequence (blocks entry).
(c) The gut normal flora **occupies the attachment sites** and **uses up the nutrients** in the intestine, so an incoming pathogen has **nowhere to attach and not enough food** to grow — it is outcompeted.	Microbiota work by **competition** for space and nutrients (competitive exclusion), not by attacking the pathogen.
∴ the three barriers prevent infection in three different ways — by blocking, by killing, and by crowding out pathogens.	A one-line synthesis links the three mechanisms.

Example 2 — scaffolded

Long-term smoking damages the cilia lining the airways and thickens the mucus. (a) State the barrier type of cilia and mucus. (b) Describe how cilia and mucus normally protect the airways. (c) Predict, with a reason, how damaged cilia would affect a smoker's risk of respiratory infection.

Working	Comment
(a) Cilia and mucus are both **physical** barriers.	Structures that trap and remove pathogens are physical, not chemical.
(b) The **mucus traps** pathogens and particles that are breathed in; the **cilia beat to sweep the mucus (and trapped pathogens) up and out** of the airways, where it is swallowed or coughed out.	Give both jobs and their order: trap, then remove.
(c) With the cilia **damaged**, the trapped mucus and pathogens are **no longer swept out** and instead **stay in the airways**, so pathogens are more likely to reach and infect the lung cells — the risk of respiratory infection **increases**.	A prediction must state the effect (risk rises) *and* the reason (pathogens are not removed).
∴ damaging this physical barrier removes the airway's "cleaning" mechanism, so infections become more frequent.	Ties the damaged-barrier reasoning together.

Example 3 — unscaffolded

Explain why the first line of defence is described as **non-specific** and as acting **before** infection.

The first line of defence is **non-specific** because its barriers act against **all pathogens in the same general way**, rather than being aimed at one particular pathogen: intact skin, stomach acid and the normal flora block, kill or crowd out any bacterium, virus or fungus alike, without "recognising" which pathogen it is. It acts **before infection** because these barriers work at the body's **surfaces** — the skin and the linings of the tracts open to the environment — and their job is to stop pathogens **entering the tissues in the first place**. A pathogen only causes infection once it has got past these barriers into the body, so the first line is a **preventative** defence that operates at the boundary, not inside the tissues. ∴ the first line is non-specific (the same for every pathogen) and preventative (acting at the surface, before entry).

Example 4 — unscaffolded

A fungal spore lands on the surface of a healthy leaf. Describe the first-line barriers the spore must overcome before it could infect the plant.

To reach the living cells inside the leaf, the fungal spore must first get past the leaf's surface **barriers**. The outermost is the **waxy cuticle**, a **waterproof layer** covering the epidermis that the spore **cannot easily penetrate**, and which keeps the surface dry so the spore is less likely to germinate. If the spore tries to enter through a **stoma** (a leaf pore), the plant can **close its stomata** to block that route. Even if it reaches the cells, each plant cell is surrounded by a **rigid cellulose cell wall** that physically **resists entry**. On top of these physical barriers, the plant also produces **antimicrobial chemicals** (such as toxic oils and other compounds) that can **kill or inhibit** the fungus. The leaf surface is not bare either: it carries the plant's own **microbiota** of **harmless resident microbes**, which have already taken the attachment sites and surface nutrients, so the spore is **crowded out**. ∴ the spore faces a waxy cuticle, closable stomata and rigid cell walls (physical barriers), antimicrobial chemicals (a chemical barrier) and the resident leaf-surface microbes (a microbiota barrier) — all three types of non-specific first-line defence — before it could establish an infection.

Practice questions

Scaffolded

Q1. Define each of the following terms: (a) the first line of defence; (b) keratin; (c) a mucous membrane.

Q2. Skin, mucus and cilia are physical barriers of an animal. (a) State how intact skin acts as a physical barrier. (b) Describe how mucus and cilia work together to remove pathogens from the airways. (c) State one example of a flushing action and what it removes.

Q3. The body has several chemical barriers. (a) Name the chemical barrier found in the stomach and state the property that makes it effective. (b) State where lysozyme is found and what it does to bacteria. (c) Describe how sebum helps to prevent infection of the skin.

Q4. The normal flora is the body's microbiota barrier. (a) State what the normal flora is. (b) Describe two ways the normal flora prevents pathogens from establishing. (c) Predict what could happen if a course of antibiotics killed much of the gut normal flora.

Q5. Plants have their own first-line barriers. (a) Name two physical barriers found in a plant. (b) Explain how the waxy cuticle helps prevent infection. (c) Describe how a plant can use its stomata as a defence against pathogens.

Q6. The first line of defence has some general features. (a) State whether the first line of defence acts before or after a pathogen enters the body's tissues. (b) Explain what is meant by describing these barriers as non-specific. (c) Classify each of the following as a physical, chemical or microbiota barrier: skin; lysozyme; the harmless bacteria living on the skin.

Unscaffolded

Q7. Distinguish between a physical barrier and a chemical barrier, giving one example of each in an animal. *(2 marks)*

Q8. A hospital worker washes their hands many times each day with a harsh detergent that strips the natural oils from the skin. Explain, with reference to sebum and the acidic skin surface, why this could make a bacterial skin infection more likely. *(3 marks)*

Q9. Bark is sometimes described as a plant's equivalent of skin. Describe how bark acts as a first-line barrier in a plant, and state one similarity and one difference between bark and the waxy cuticle. *(3 marks)*

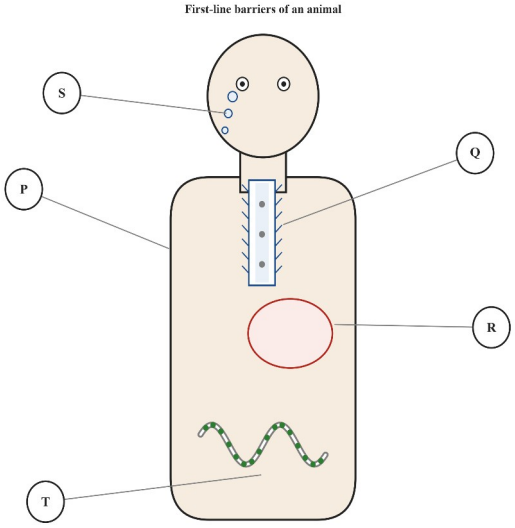
Q10. The first line of defence is described as **innate**. Explain what this means, and explain why an innate barrier can protect a person against a pathogen they have never met before. *(3 marks)*

Q11. Air breathed in is not sterile. Mucus in the airways traps the pathogens it carries, and that mucus is then swept up to the throat and **swallowed**. Explain what happens to a trapped pathogen at each of these two stages, and state the **type** of barrier acting at each stage. *(3 marks)*

Q12. A hailstorm makes a small break in the **waxy cuticle** of a leaf and also knocks a shallow chip out of the **bark** on the trunk of the same plant. Explain why the break in the cuticle is the more serious breach of the plant's first line of defence. *(3 marks)*

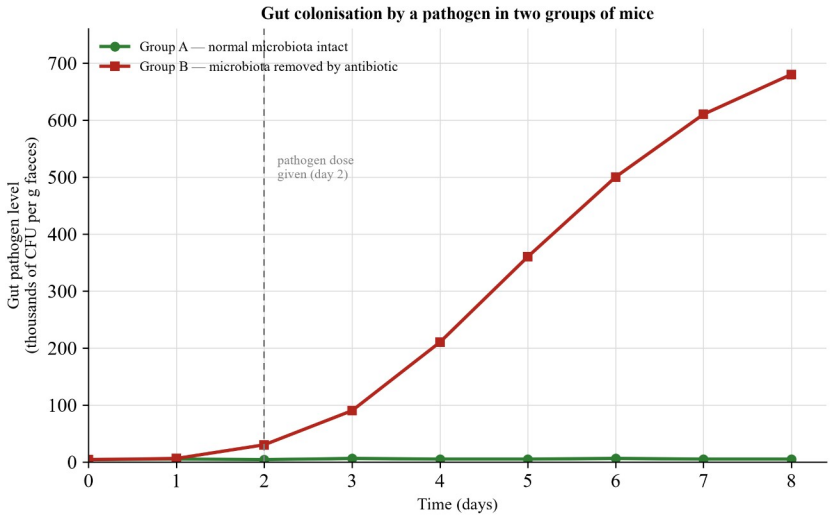
Q13. A person suffers a deep burn that destroys a large area of skin. Explain why this greatly increases their risk of infection, with reference to the first line of defence. *(3 marks)*

Q14. *(Stimulus.)* The diagram shows first-line barriers of an animal, labelled P, Q, R, S and T.



(a) Identify the barrier shown at each of P, Q, R, S and T.
(b) State the barrier type (physical, chemical or microbiota) of P, R and T.
(c) Explain how the barrier at Q prevents pathogens from entering the body. *(5 marks)*

Q15. *(Data interpretation.)* Two groups of mice were each given the same dose of a gut pathogen on day 2. Group A had a normal gut microbiota; Group B had earlier been given a broad-spectrum antibiotic that removed most of its gut microbiota. The level of the pathogen in the faeces was measured over eight days.



(a) Describe the difference between the two groups in the gut pathogen level over the eight days.

(b) Identify the independent variable, and state one variable that should have been kept the same (controlled) in both groups.

(c) Using the idea of competition, explain why the pathogen reached a high level in Group B but not in Group A. *(5 marks)*

Q16. *(Research vignette.)* A hospital study followed patients fitted with a urinary catheter — a thin tube passed through the urethra into the bladder so that urine drains continuously into a bag. The proportion of patients with bacteria growing in the bladder rose with every extra day the catheter was left in place, and almost all patients were affected by four weeks. (a) Name the first-line barrier that normally keeps bacteria out of the urinary tract, and state its type. (b) Describe how this barrier works in a person who does not have a catheter. (c) Explain why bacteria are far more likely to reach and multiply in the bladder of a patient whose catheter has been in place for several weeks. *(5 marks)*

Q17. Tears are said to provide both a physical and a chemical barrier. Explain how tears act in each of these two ways. *(3 marks)*

Q18. Compare the first-line barriers of animals and of plants, giving one similarity and two differences. *(3 marks)*

Q19. *(Stimulus.)* The table lists five first-line defences.

Feature	Description
1	A waxy layer covering the leaves of a plant
2	Low-pH fluid in the human stomach
3	Harmless bacteria that normally live on human skin
4	Hair-like structures that sweep mucus out of the airways
5	An enzyme in saliva that breaks down bacterial cell walls

(a) For each of features 1–5, state whether it is a physical, chemical or microbiota barrier.

(b) State which feature is found in a plant rather than an animal.

(c) State how feature 3 helps to prevent infection. *(5 marks)*

Q20. *(Synthesis.)* While bushwalking, a person grazes their knee on a rock, breaking the skin. Beside the track, a soil-borne bacterium in the wet soil reaches the root surface of a shrub. (a) Explain how intact skin normally prevents infection, and why the graze increases the risk of infection. (b) Later the person drinks water containing bacteria. Explain how first-line barriers act to prevent these swallowed bacteria from causing infection (refer to at least one chemical barrier and the microbiota barrier). (c) For the shrub, describe how its microbiota barrier and one physical

barrier protect the root from the soil-borne bacterium. (d) State the feature shared by all of these defences that makes them non-specific. *(8 marks)*

Answers

Q1. (a) The surface barriers that prevent pathogens entering the body; non-specific and always present. (b) The tough protein filling the flattened dead cells of the skin's outer layer, making it hard to penetrate. (c) The moist lining of the body tracts open to the environment, which secretes mucus. **Q2.** (a) A dry, tough, keratinised, unbroken layer that pathogens cannot penetrate. (b) Mucus traps pathogens; cilia sweep the mucus and trapped pathogens up and out of the airways. (c) e.g. tears flush the eye surface / urine flushes the urinary tract, washing pathogens away. **Q3.** (a) Stomach acid; its very low pH (about pH 2) kills pathogens. (b) In tears, saliva and sweat; it breaks down the cell walls of bacteria. (c) Sebum makes the skin oily and slightly acidic, inhibiting the growth of microbes. **Q4.** (a) The harmless resident microbes living on the body's surfaces. (b) Competes for space (occupies attachment sites) and for nutrients (uses up the food). (c) Pathogens could overgrow and cause an infection because the microbiota that normally outcompetes them has been removed. **Q5.** (a) Any two of: waxy cuticle, cell walls, bark. (b) It is a waterproof waxy layer over the epidermis that pathogens cannot easily penetrate. (c) The plant can close its stomata to block pathogens that would otherwise enter through these leaf pores. **Q6.** (a) Before. (b) The barriers act against all pathogens in the same way, not tailored to a particular one. (c) Skin = physical; lysozyme = chemical; harmless skin bacteria = microbiota. **Q7.** A physical barrier is a structure that blocks or removes pathogens (e.g. skin); a chemical barrier is a substance that kills or inhibits pathogens (e.g. stomach acid / lysozyme). **Q8.** Sebum (with sweat) keeps the skin surface oily and slightly acidic (about pH 5) — a chemical barrier that inhibits the growth of bacteria and fungi; stripping the oils away removes this barrier, so bacteria can grow and multiply on the skin and are more likely to establish an infection. **Q9.** Bark is a tough, mostly dead outer layer covering woody stems and roots; it is a physical barrier that pathogens cannot penetrate, so they are blocked from the living tissues beneath. Similarity: both bark and the cuticle are non-specific physical barriers forming a continuous outer covering. Difference: bark is a thick, tough, mostly dead layer on woody stems and roots, whereas the cuticle is a thin, waterproof waxy layer over the epidermis of leaves and young stems. **Q10.** Innate = present from birth and always in place, not made in response to a pathogen; so it acts immediately, and needs no previous exposure, so a pathogen new to the person meets a complete barrier. **Q11.** Airways: mucus traps the pathogen and cilia sweep it out — a physical barrier (removed, not killed). Stomach: acid at about pH 2 kills it — a chemical barrier. **Q12.** The cuticle is thin and lies directly over living epidermal cells, so a break exposes living tissue at once; bark is thick and mostly dead, so a shallow chip removes dead tissue only and living tissue is still covered. **Q13.** The skin is a physical barrier; destroying a large area removes that barrier, so pathogens can enter the tissues directly through the wound, greatly raising infection risk. **Q14.** (a) P = skin; Q = cilia + mucus (airway); R = stomach acid; S = tears (with lysozyme); T = normal flora (gut microbiota). (b) P = physical; R = chemical; T = microbiota. (c) Mucus traps pathogens and cilia sweep them up and out of the airways. **Q15.** (a) Group A stays low throughout; Group B rises steeply from day 2 to a high level. (b) IV = whether the gut microbiota is present (normal vs removed by antibiotic); controlled = e.g. same pathogen dose / same mouse strain / same diet / same age. (c) In A the normal flora outcompetes the pathogen for space and nutrients; in B the flora is gone, so the pathogen has space and nutrients and multiplies. **Q16.** (a) The flushing action of urine; physical. (b) Urine flows steadily out through the urethra, washing bacteria out before they can attach and multiply. (c) The catheter carries bacteria from the outside straight into the bladder and gives them a surface to grow along that the urine flow does not wash clean, so bacteria are not flushed out and have weeks in which to multiply. **Q17.** Physically, tears flush/wash pathogens off the eye surface; chemically, tears contain lysozyme, which breaks down bacterial cell walls. **Q18.** Similarity: both have all three types of non-specific barrier — physical, chemical and microbiota — preventing entry. Differences (any two): the structures differ (waxy cuticle, cell walls, bark, stomata in plants vs skin, mucus, cilia, flushing in animals); plants have no mobile defensive cells and no specific immune response, so the first line is essentially their whole defence, whereas animals have further internal lines behind it. **Q19.** (a) 1 physical; 2 chemical; 3 microbiota; 4 physical; 5 chemical. (b) Feature 1. (c) The harmless skin bacteria outcompete pathogens for space and nutrients, so pathogens cannot establish. **Q20.** (a) Intact skin is a physical barrier blocking entry; the graze breaks it, letting pathogens enter the tissues. (b) Lysozyme in saliva and stomach acid (low pH) kill many swallowed bacteria, and the gut normal flora outcompetes the rest. (c) The root microbiota has already taken the attachment sites and nutrients at the root surface, so the soil bacterium cannot establish; the rigid cellulose cell walls (or bark on woody roots) physically resist entry. (d) They all act against any pathogen the same way, not aimed at a particular one.

Fully-worked solutions

Q1. (a) The **first line of defence** is the set of **surface barriers** — physical, chemical and microbiota — that **prevent pathogens from entering** the body; it is non-specific and always present. (b) **Keratin** is the **tough, fibrous protein**

that **fills the flattened, dead cells** of the skin's outer layer; it makes that layer **tough, dry and hard-wearing**, so pathogens cannot easily penetrate it. (c) A **mucous membrane** is the **moist lining** of the body tracts that are **open to the environment** — the respiratory, digestive, urinary and reproductive tracts — which, unlike skin, **secretes mucus** to trap pathogens.

Q2. (a) Intact skin is a **dry, tough, keratinised** outer layer that is **continuous and unbroken** over the body, so pathogens **cannot penetrate** it to reach the tissues beneath. (b) The **mucus** produced by the mucous membranes **traps** pathogens breathed into the airways; the **cilia** then **beat to sweep the mucus and its trapped pathogens up and out** of the airways, where it is swallowed or coughed out. (c) Any one flushing action, e.g. **tears flush the surface of the eye** (or urine flushes the urinary tract), physically **washing pathogens away** before they can establish.

Q3. (a) The chemical barrier is **stomach acid**; its **very low pH (around pH 2)** kills most pathogens swallowed with food or mucus by denaturing their proteins. (b) **Lysozyme** is found in **tears, saliva and sweat**; it is an enzyme that **breaks down the cell walls of bacteria**, killing them. (c) **Sebum** is an oily secretion that makes the skin surface **oily and slightly acidic** (about pH 5), creating conditions that **inhibit the growth** of many bacteria and fungi.

Q4. (a) The **normal flora** is the population of **harmless resident microbes** that normally live on the body's surfaces (skin, gut, mouth, etc.). (b) It prevents pathogens establishing by **competing for space** (occupying the attachment sites so pathogens cannot attach) and **competing for nutrients** (using up the available food so pathogens cannot grow). (c) If antibiotics killed much of the gut normal flora, the **space and nutrients** it was using would become **available**, so a **pathogen could overgrow** and cause an infection that the intact flora would normally have prevented.

Q5. (a) Any two of: the **waxy cuticle**, the **cell walls**, and the **bark**. (b) The **waxy cuticle** is a **waterproof waxy layer** over the epidermis of leaves and stems that pathogens **cannot easily penetrate** (and it keeps the surface dry). (c) **Stomata** are pores in the leaf used for gas exchange and are a route some pathogens use to enter; the plant can **close its stomata** to **block this entry route**.

Q6. (a) The first line of defence acts **before** a pathogen enters the body's tissues (it is preventative). (b) **Non-specific** means the barriers act against **all pathogens in the same general way**, not tailored to any one particular pathogen. (c) **Skin = physical** barrier; **lysozyme = chemical** barrier; **harmless skin bacteria = microbiota** barrier.

Q7. A **physical barrier** is a **structure** that **physically blocks or removes** pathogens — for example, the **skin**, which blocks entry. A **chemical barrier** is a **substance (secretion)** that **kills or inhibits** pathogens — for example, **stomach acid** (low pH) or **lysozyme**. *(1 mark: physical = structure that blocks/removes + example; 1 mark: chemical = substance that kills/inhibits + example.)*

Q8. Glands in the skin secrete **sebum**, an oily substance which, together with sweat, keeps the skin surface **oily and slightly acidic** (around **pH 5**) and supplies fatty acids. This is a **chemical barrier**: those conditions **inhibit the growth** of many bacteria and fungi, so few can multiply on the skin. Washing repeatedly with a harsh detergent **strips this sebum away**, so the surface is **no longer oily or acidic** and the chemical barrier is **weakened or removed**. Bacteria landing on the skin can then **grow and multiply** freely, so they are far more likely to **establish an infection**. *(1 mark: sebum and sweat make the skin surface oily and slightly acidic — a chemical barrier; 1 mark: these conditions inhibit the growth of bacteria/fungi; 1 mark: stripping the sebum removes the barrier, so bacteria multiply and infection becomes more likely.)*

Q9. Bark is the **tough, mostly dead outer layer** covering the **woody stems and roots** of many plants. It acts as a **physical barrier**: pathogens **cannot penetrate it**, so they are **blocked from reaching the living tissues beneath**, much as intact skin protects an animal. **Similarity:** like the **waxy cuticle**, bark is a **non-specific physical barrier** that forms a **continuous covering over the plant's outer surface**, blocking any pathogen alike. **Difference:** bark is a **thick, tough, mostly dead** layer found on **woody stems and roots**, whereas the cuticle is a **thin, waterproof waxy layer** lying over the **epidermis of leaves and young stems** (and keeping that surface dry). *(1 mark: bark is a tough outer physical barrier blocking entry to the tissues beneath; 1 mark: a valid similarity; 1 mark: a valid difference.)*

Q10. Innate means the barriers are **present from birth** and **in place at all times** — they are built into the body's structure and secretions, rather than being produced in response to a particular pathogen. Because they are **already complete** when a pathogen arrives, they act **immediately**, with **no delay** while the body prepares a response. They also need **no previous exposure**: unlike a defence that must first meet a pathogen before it can act against it, the skin, mucus, acid and normal flora are **fully working before the first encounter**, so a person is protected on their **very first contact** with a pathogen that is new to them. *(1 mark: innate = present from birth / always in place, not made in*

response to a pathogen; 1 mark: therefore acts immediately, with no delay; 1 mark: no prior exposure is needed, so a pathogen met for the first time still meets a complete barrier.)

Q11. At the **first stage**, in the airways, the pathogen meets a **physical** barrier: the **mucus traps** it and the **cilia sweep the mucus up and out** to the throat, so the pathogen is **removed from the airways** — but at this stage it has only been **moved, not killed**. Swallowing then carries it to the **stomach**, where it meets a **chemical** barrier: the **gastric acid**, at about **pH 2**, **denatures its proteins and enzymes and kills it**. The pathogen is therefore **handed on from one barrier to the next** along the route it takes, and is destroyed without ever entering the tissues. *(1 mark: airway stage — mucus traps and cilia sweep it out; a physical barrier; 1 mark: stomach stage — acid at about pH 2 kills it; a chemical barrier; 1 mark: the pathogen is removed by the first barrier and then destroyed by the second, i.e. the barriers act in sequence along the route.)*

Q12. The **waxy cuticle** is a **thin layer lying directly on top of the epidermis**, so once it is broken there is **nothing left between the outside and the living epidermal cells** — a pathogen landing in the break reaches **living tissue straight away**. **Bark**, by contrast, is a **thick, mostly dead outer layer**, so a shallow chip removes **only dead tissue** and **more dead bark still lies between the pathogen and the living tissue** beneath. How serious a breach is therefore depends on **how much barrier is left** between the pathogen and the living cells: the same-sized injury breaches a thin barrier completely but barely dents a thick one. *(1 mark: the cuticle is thin and lies directly over living epidermal cells, so a break exposes living tissue at once; 1 mark: bark is thick and mostly dead, so a shallow chip removes dead tissue only and the living tissue is still covered; 1 mark: the seriousness of a breach depends on how much barrier remains between the pathogen and the living cells.)*

Q13. The **skin** is the body's main **physical barrier**: while intact, its dry, keratinised, unbroken layer **blocks pathogens** from reaching the tissues. A deep burn that **destroys a large area of skin removes this barrier**, leaving the underlying tissues **directly exposed** to the environment. Pathogens can now **enter the body straight through the wound**, without having to get past any physical barrier, so the **risk of infection is greatly increased**. *(1 mark: skin is a physical barrier that blocks entry; 1 mark: the burn destroys/removes this barrier; 1 mark: pathogens enter through the exposed area, so infection risk rises.)*

Q14. (a) **P = skin**; **Q = cilia and mucus** (of the airway); **R = stomach acid**; **S = tears** (which flush the eye and contain lysozyme); **T = the normal flora / microbiota** of the gut. (b) **P is a physical barrier**; **R is a chemical barrier**; **T is a microbiota barrier**. (c) At **Q**, the **mucus traps** pathogens breathed into the airways and the **cilia sweep the mucus and trapped pathogens up and out** of the airways, so they are **removed before** they can infect the lungs. *(a: 2 marks — five correct identifications, 1 mark for three or four correct; b: 1 mark for all three types correct; c: 2 marks — mucus traps + cilia sweep out.)*

Q15. (a) In **Group A** the gut pathogen level **stays low** across the whole eight days; in **Group B** the level **rises steeply** from day 2 onwards, reaching a **much higher level** (around 680 thousand CFU per gram by day 8). So the pathogen reaches high numbers only when the microbiota has been removed. (b) The **independent variable** is **whether the gut microbiota is present** (normal in A versus removed by antibiotic in B). A **controlled variable** could be any one of: the **dose of pathogen given**, the **strain/age of the mice**, or their **diet** — kept the same for both groups. (c) In **Group A** the **normal flora outcompetes the pathogen** for **space (attachment sites)** and **nutrients**, so the pathogen **cannot establish** and stays at a low level. In **Group B** the antibiotic has **removed the flora**, so there is now **spare space and spare nutrients**; the pathogen faces **no competition** and **multiplies to a high level**. *(a: 1 mark — A low, B rises steeply to a high level; b: 1 mark IV, 1 mark a valid controlled variable; c: 2 marks — flora outcompetes in A / no competition in B.)*

Q16. (a) The barrier is the **flushing action of urine**, a **physical** barrier. (b) Urine is produced continuously and **flows steadily out through the urethra**, so it **washes bacteria out of the urinary tract** before they can attach to the lining and multiply. (c) A catheter **bypasses this barrier**. The tube is pushed in from the outside, **carrying bacteria from the skin around the opening directly into the bladder**, past the flushing that would normally have removed them. It also gives bacteria a **surface to attach to and grow along that the urine flow does not wash clean**, and urine now drains straight down the tube instead of flushing the tract. Bacteria that reach the bladder are therefore **not removed**, and over several weeks they have **ample time to multiply** and establish an infection — which is why the proportion of affected patients rose with every extra day. *(a: 1 mark — flushing action of urine, physical; b: 1 mark — steady flow washes bacteria out before they can attach; c: 3 marks — 1 the catheter carries bacteria past the barrier into the bladder, 1 it provides a surface the urine flow does not clean / urine no longer flushes the tract, 1 bacteria are therefore not removed and multiply over time, so risk rises with each extra day.)*

Q17. Tears act as a **physical barrier** because they **flush (wash) across the surface of the eye**, mechanically **removing pathogens and particles** before they can settle and infect. Tears also act as a **chemical barrier** because they **contain the enzyme lysozyme**, which **breaks down the cell walls of bacteria** in the tear fluid, killing them. So the same secretion defends in **two different ways** — by washing pathogens away and by chemically destroying bacteria. *(1 mark: physical — flushing/washing the eye; 1 mark: chemical — contains lysozyme; 1 mark: lysozyme digests bacterial cell walls.)*

Q18. Similarity: both animals and plants have **all three types of non-specific first-line barrier** — **physical, chemical and microbiota** — working at their surfaces to **prevent pathogens entering**. **Differences (any two): (1)** the structures themselves differ — animals have **skin, mucous membranes, cilia and flushing actions**, whereas plants have a **waxy cuticle, cellulose cell walls, bark and closable stomata**; **(2)** plants have **no mobile defensive cells and no specific (adaptive) immune response**, so the first line is **essentially the whole of their defence**, whereas in animals it is backed by further internal lines of defence. *(1 mark: valid similarity; 1 mark + 1 mark: two valid differences.)*

Q19. (a) **1 = physical** (waxy cuticle); **2 = chemical** (stomach acid, low pH); **3 = microbiota** (harmless resident skin bacteria); **4 = physical** (cilia); **5 = chemical** (lysozyme, an enzyme). (b) **Feature 1** (the waxy cuticle) is found in a **plant** rather than an animal. (c) **Feature 3** — the harmless skin bacteria (normal flora) — helps prevent infection by **outcompeting pathogens for space and nutrients** on the skin, so a pathogen **cannot attach or obtain enough food** to establish. *(a: 3 marks — all five correct; deduct 1 mark per error, minimum 0; b: 1 mark; c: 1 mark.)*

Q20. (a) **Intact skin** is a **physical barrier**: its dry, tough, keratinised, unbroken layer **blocks pathogens** from reaching the tissues beneath. The **graze breaks the skin**, removing the barrier over that area, so pathogens can **enter the tissues directly through the wound**, increasing the risk of infection. (b) The swallowed bacteria meet several first-line barriers: **lysozyme in the saliva** (a chemical barrier) begins to **break down bacterial cell walls**; in the stomach, the **acid (about pH 2)** — a chemical barrier — **kills most** of the bacteria; and any that reach the intestine meet the **gut normal flora (microbiota)**, which **outcompetes them for space and nutrients** so they **cannot establish**. (c) At the root surface the shrub's **microbiota** — the dense community of **harmless resident microbes** living on and around its roots — has already **taken the attachment sites and used up the nutrients** released there, so the soil bacterium **cannot attach or obtain enough food** and is **crowded out**. Should it reach the root itself, it still meets a **physical** barrier: the **rigid cellulose cell walls** of the root cells (or, on older woody roots, the **bark**), which **resist entry** to the living tissue. (d) All of these defences act against **any pathogen in the same general way** — blocking, removing, killing or crowding out bacteria, viruses and fungi alike — rather than being aimed at one particular pathogen. ∴ the person and the shrub are each protected by **all three types of barrier — physical, chemical and microbiota** — every one of them working non-specifically at the surface to prevent infection. *(a: 2 marks — skin blocks entry + graze removes the barrier; b: 3 marks — lysozyme in saliva, stomach acid, gut flora; c: 2 marks — root microbiota outcompetes the bacterium + one plant physical barrier; d: 1 mark — acts against any pathogen the same way.)*

Theory

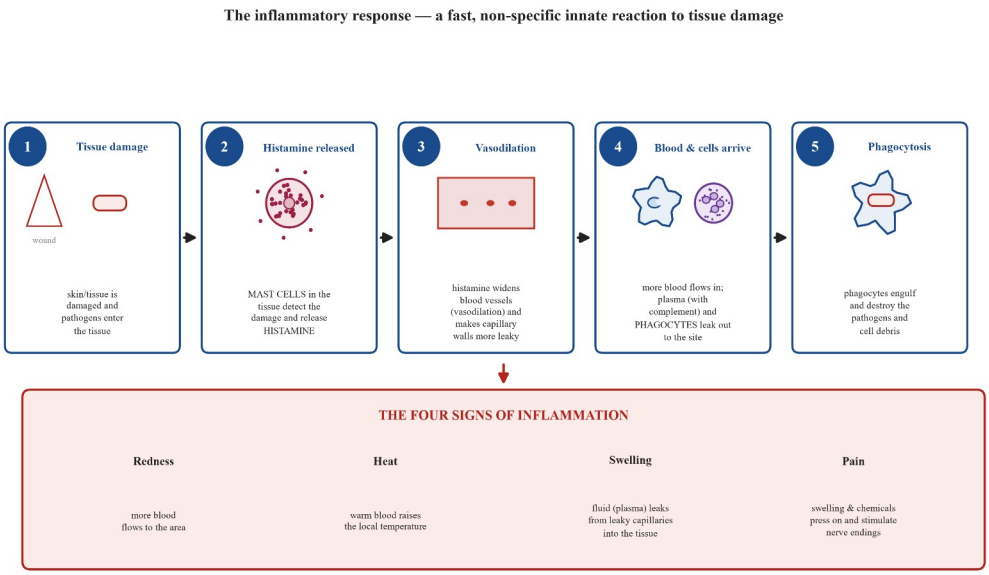
The body defends itself against pathogens using three "lines of defence". The **first line** is a set of surface **barriers** (such as the skin and the mucous membranes) that try to keep pathogens out of the body altogether. If a pathogen breaks through the first line and reaches the tissues, the **second line of defence** takes over. The second line is the **innate immune response** — a set of internal defences that act quickly against any invader that gets in. This subtopic covers the second line: the **inflammatory response** and the innate cells and molecules that carry it out.

Three features define the second line of defence and set it apart from the third line (covered later):

- **Fast.** It begins within minutes to hours of an infection, because the cells and molecules that carry it out are already present in the tissues and blood, ready to act.
- **Non-specific.** It responds in the **same way to every pathogen** — it does not target one particular microbe. The same inflammatory response and the same phagocytes act against a bacterium, a fungus or a virus alike.
- **No memory.** It does **not** "remember" a pathogen. A second exposure to the same microbe produces the same response, at the same speed and strength, as the first — the second line never becomes faster or stronger with repeated exposure.

(These three features are the opposite of the third line of defence, which is specific and does have memory.)

The inflammatory response. Inflammation is the innate response to tissue damage or infection. It is triggered whenever tissue is injured or a pathogen enters the tissue, and it follows an ordered sequence of events.



The steps, in order, are:

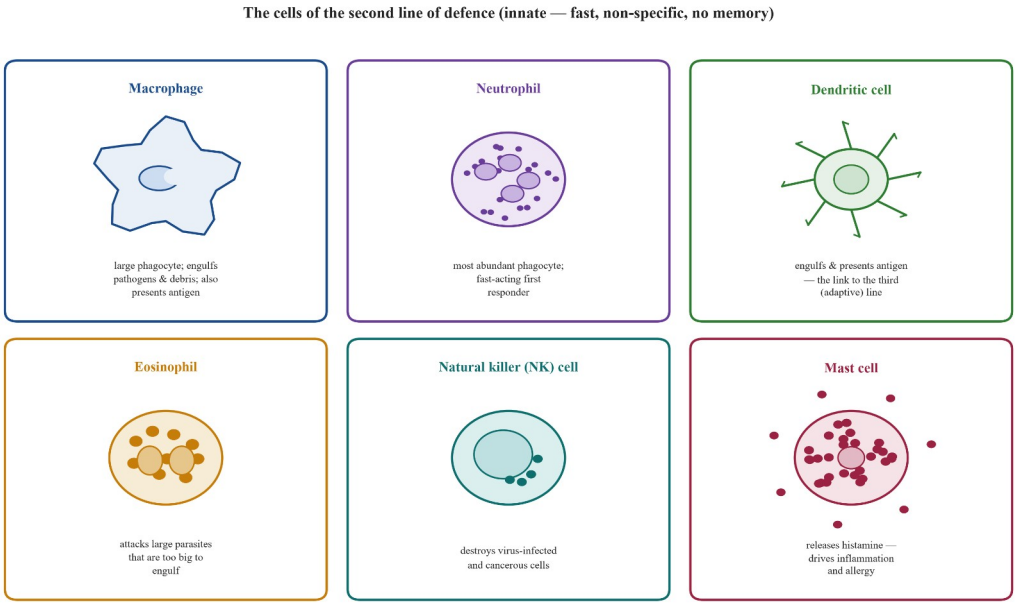
1. **Tissue damage / infection.** Tissue is damaged (for example, by a cut) and pathogens enter the tissue.
2. **Mast cells release histamine. Mast cells** already present in the damaged tissue detect the injury and release the chemical **histamine** (along with other signalling molecules).
3. **Vasodilation and increased permeability.** Histamine makes the local blood vessels **widen (vasodilation)** and makes the walls of the nearby capillaries **more permeable (leaky)**.
4. **More blood, plasma and phagocytes reach the site.** Vasodilation increases the **blood flow** to the area, and the leaky capillaries allow **plasma** (which carries complement proteins) and **phagocytes** to pass out of the blood and into the tissue.
5. **Phagocytosis.** The **phagocytes engulf and destroy** the pathogens and any damaged cell debris.

The visible **signs** of inflammation follow directly from these changes:

- **Redness** and **heat** — because more warm blood flows to the area (a result of vasodilation).
- **Swelling** — because fluid (plasma) leaks out of the permeable capillaries and collects in the tissue.
- **Pain** — because the swelling and the chemicals released press on and stimulate the local nerve endings.

Inflammation helps to contain the infection, remove pathogens and debris, and begin the healing of the tissue. It is fast and non-specific — the same response occurs whatever the pathogen.

The innate cells. Several kinds of white blood cell carry out the second line of defence. Each has its own role, but all of them act non-specifically.



- **Macrophages** are **large phagocytes** found throughout the tissues (they develop from monocytes that leave the blood). They **engulf and digest** pathogens, dead cells and debris. Macrophages are long-lived, and they also act as **antigen-presenting cells** — after engulfing a pathogen they display its antigens on their surface, which helps to activate the third line of defence.
- **Neutrophils** are the **most abundant** white blood cell and are **fast-acting phagocytes**. They are usually the **first cells to arrive in large numbers** at a site of infection, where they engulf and destroy pathogens. They are short-lived; dead neutrophils and pathogens make up much of the pus at an infected site.
- **Dendritic cells** sit in the tissues that meet the outside world — the skin, and the linings of the airways and the gut — and have many **long, branched projections** that spread out through the tissue, giving them a large surface area for trapping pathogens. They phagocytose pathogens and are especially effective at **presenting antigens**; they also **secrete interferons**. By carrying antigens from the site of infection and presenting them to lymphocytes, dendritic cells form the **key link between the innate (second) line and the adaptive (third) line** of defence. (The adaptive response itself is covered in a later subtopic.)
- **Eosinophils** target **large parasites** — such as parasitic worms — that are far too big for a single cell to engulf. They gather around the parasite and release toxic chemicals from their granules onto its surface.
- **Natural killer (NK) cells** destroy the body's own cells when those cells have become **infected by a virus** or have turned **cancerous**. They release chemicals that make the abnormal cell die. Note carefully that an NK cell kills the **infected body cell**, not the virus particles themselves — destroying the cell removes the place in which new virus is being made. NK cells recognise cells that are stressed or abnormal, and they act **non-specifically** — they do not target one particular virus.
- **Mast cells** are found in connective tissue throughout the body. They release **histamine** (and other chemicals) that **drive the inflammatory response** (and also drive allergic reactions).

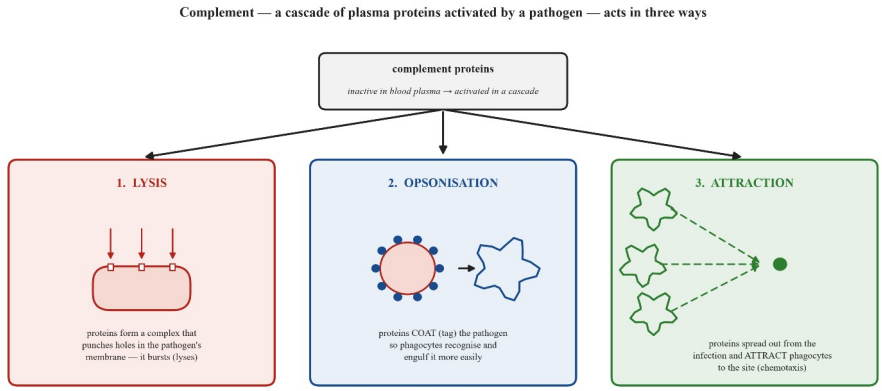
Phagocytosis. Macrophages, neutrophils and dendritic cells are all **phagocytes** — cells that destroy pathogens by **phagocytosis**. In phagocytosis the phagocyte:

1. is attracted to the pathogen (for example, by complement proteins) and binds to it;

2. **engulfs** the pathogen by wrapping its membrane around it, enclosing it in a vesicle inside the cell;
3. **digests** the pathogen when the vesicle fuses with a lysosome, releasing enzymes that break the pathogen down.

Note the distinction between the innate cells: phagocytes engulf small pathogens whole; eosinophils attack **large** parasites from the outside (because they are too big to engulf); and NK cells kill the body's **own** infected or cancerous cells rather than engulfing microbes.

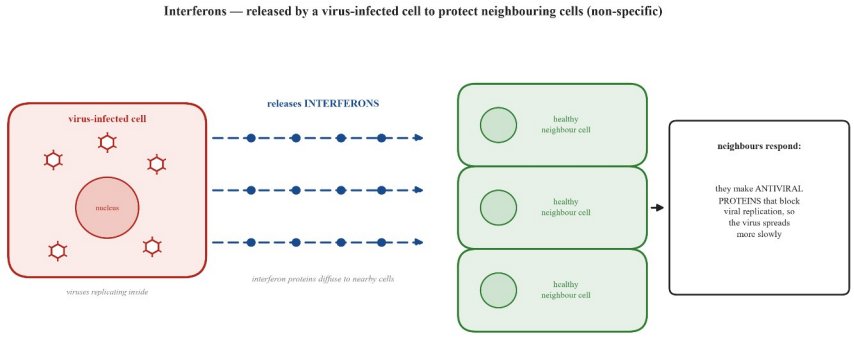
Complement proteins. Complement is a group of about twenty or more proteins that circulate **inactive in the blood plasma**. When they encounter a pathogen they are switched on in a **cascade** (one protein activates the next). Activated complement proteins act in **three ways**:



- **Lysis.** Some complement proteins join together to form a complex that **punches holes in the pathogen's membrane**, so that the pathogen bursts (lyses).
- **Opsonisation.** Complement proteins **coat (tag) the surface of the pathogen**, making it easier for phagocytes to recognise and engulf it.
- **Attraction (chemotaxis).** Complement proteins spread out from the infection and **attract phagocytes** towards the site.

(Complement proteins also help to promote inflammation.)

Interferons. Interferons are **signalling proteins** — they carry a chemical warning from one cell to another, and do **not** kill the virus themselves. They are released by cells which have become **infected by a virus** (dendritic cells also secrete interferons). They diffuse to the **neighbouring, uninfected cells** and cause those cells to produce **antiviral proteins**. These antiviral proteins interfere with viral replication, so the virus spreads more slowly through the tissue. Interferons cannot rescue the infected cell that released them — that cell is already making new virus — but they prepare its neighbours **before** the virus reaches them.



Interferons are **non-specific** — they protect cells against viruses in general, not against one particular virus — and they have **no memory**, which is why they are part of the second line of defence. (Some interferons also help to activate other immune cells, such as macrophages and NK cells.)

Innate versus adaptive — two contrasts to keep clear. Two components of the second line are easily confused with parts of the third (adaptive) line:

- **NK cells versus cytotoxic T cells.** Both can kill virus-infected and cancerous cells, but an **NK cell** is part of the **innate** second line — it is non-specific and has no memory — whereas a **cytotoxic T cell** belongs to the **adaptive** third line (it is specific and forms memory).
- **Interferons versus antibodies.** Both are proteins that help to fight infection, but **interferons** are **non-specific** innate proteins released by virus-infected cells, whereas **antibodies** are **specific** adaptive proteins made against one particular antigen.

In both cases the second-line component is **fast and non-specific with no memory**, while the third-line component is **specific and has memory**.

Worked examples

Example 1 — scaffolded

A gardener pricks their thumb on a rose thorn, pushing bacteria into the tissue. Within an hour the thumb is red, warm, swollen and sore. Outline the inflammatory response, in order, and explain why the thumb becomes red, warm and swollen.

Working	Comment
The damaged tissue and the bacteria trigger inflammation. Mast cells already in the tissue detect the damage and release **histamine**.	Start with the trigger, then name the cell (mast cell) and the chemical (histamine) it releases — these are the first steps.
Histamine causes **vasodilation** (the blood vessels widen) and makes the capillaries **more permeable**.	Give both effects of histamine on the blood vessels; both are needed to explain the signs.
More blood flows to the thumb, and plasma and phagocytes leak from the permeable capillaries into the tissue. The phagocytes then engulf the bacteria.	Link vasodilation to increased blood flow, and permeability to fluid and cells leaving the blood; end with phagocytosis.
The thumb is **red and warm** because more warm blood flows to the area; it is **swollen** because plasma has leaked out of the capillaries into the tissue.	Match each sign to its cause — redness and heat come from increased blood flow, swelling comes from fluid leaking into the tissue.

Example 2 — scaffolded

Complement proteins contribute to the second line of defence in three ways. Name and describe each way.

Working	Comment
Complement proteins are plasma proteins that circulate inactive until a pathogen switches them on in a cascade.	Set the scene: they are inactive in plasma until a pathogen activates them.
Lysis — some complement proteins form a complex that makes holes in the pathogen's membrane, so the pathogen bursts.	"Lysis" means bursting the cell; describe the mechanism (holes in the membrane).
Opsonisation — complement proteins coat the surface of the pathogen, so that phagocytes recognise and engulf it more easily.	Opsonisation is a coating (tagging) that promotes phagocytosis.
Attraction — complement proteins attract phagocytes to the site of infection (chemotaxis).	The third role draws phagocytes towards the pathogen.

Example 3 — unscaffolded

A cell in the lining of the nose is infected by a cold virus. Explain how this cell can help to protect the surrounding uninfected cells, and explain why interferons differ from antibodies.

The infected cell releases **interferons** — signalling proteins made by virus-infected cells. The interferons diffuse to the neighbouring, uninfected cells and cause them to produce **antiviral proteins**. These antiviral proteins block viral replication inside those cells, so that if the virus reaches them it spreads more slowly. Interferons differ from antibodies because interferons are **non-specific** (they act against viruses in general) and are part of the innate second line of defence, with no memory, whereas antibodies are **specific** to one antigen and belong to the adaptive third line. ∴ the infected cell protects its neighbours non-specifically by releasing interferons, which — unlike antibodies — are not targeted at one particular virus.

Example 4 — unscaffolded

Both natural killer (NK) cells and cytotoxic T cells can destroy a virus-infected body cell. Explain why an NK cell is considered part of the second line of defence, while a cytotoxic T cell is not.

An NK cell is part of the second line because it acts **non-specifically** — it destroys any virus-infected or cancerous cell it detects, without targeting one particular pathogen — it acts **quickly**, and it has **no memory** (it responds the same way on every exposure). These are the defining features of the innate second line of defence. A cytotoxic T cell, although it can also kill infected cells, is **specific** to one antigen and forms **memory**, and these are features of the adaptive third line of defence, not the innate second line. ∴ it is the NK cell's fast, non-specific and memory-free action that makes it a second-line (innate) cell, whereas the cytotoxic T cell's specificity and memory place it in the third line.

Practice questions

Scaffolded

Q1. Define each of the following: (a) the innate immune response; (b) inflammation; (c) phagocytosis.

Q2. The second line of defence is described as fast, non-specific and having no memory. (a) State what "non-specific" means in this context. (b) State what "no memory" means in this context. (c) Explain why the second line of defence is able to respond quickly to an infection.

Q3. The inflammatory response follows an ordered sequence. (a) Name the cell that releases histamine. (b) State the two effects that histamine has on the blood vessels. (c) Explain why the injured area becomes swollen.

Q4. Several of the innate cells are phagocytes. (a) Name the most abundant phagocyte, which is usually the first to arrive in large numbers at an infection. (b) State one role of a macrophage in addition to phagocytosis. (c) Explain why a dendritic cell is described as a link to the third line of defence.

Q5. Complement proteins are part of the second line of defence. (a) State where complement proteins are found before they are activated. (b) Name the three roles of complement proteins. (c) Explain how opsonisation helps phagocytes.

Q6. Interferons and natural killer (NK) cells both help to defend against viruses. (a) State what causes a body cell to release interferons. (b) Describe what interferons cause neighbouring cells to do. (c) State what an NK cell does to a virus-infected cell.

Unscaffolded

Q7. The steps of the inflammatory response are listed below in the wrong order.

- phagocytes engulf the pathogens
- mast cells release histamine
- tissue is damaged and pathogens enter
- blood vessels dilate and capillaries become more permeable
- plasma and phagocytes leave the blood and reach the site

Write the steps in the correct order. *(2 marks)*

Q8. A netball player twists an ankle. No skin is broken and no pathogen enters the tissue, yet within an hour the joint is swollen and painful. Explain why an inflammatory response occurs at the ankle even though no pathogen has entered, and explain what causes the joint to become **painful**. *(4 marks)*

Q9. Distinguish between the roles of neutrophils and macrophages in the second line of defence. *(3 marks)*

Q10. Describe the process of phagocytosis, from the phagocyte meeting a pathogen through to the pathogen being destroyed. *(3 marks)*

Q11. Natural killer (NK) cells are often said to "kill viruses", but this is not what they actually do. State what an NK cell actually destroys, explain how destroying it slows a viral infection, and name **one** other kind of body cell that NK cells destroy. *(3 marks)*

Q12. Complement proteins circulate in the blood plasma, but the bacteria they act on are in the tissue outside the blood vessels. Explain how the increased capillary permeability produced during inflammation allows complement to act on those bacteria, and explain what would happen to the body's complement defence at a wound if the capillaries did **not** become more permeable. *(3 marks)*

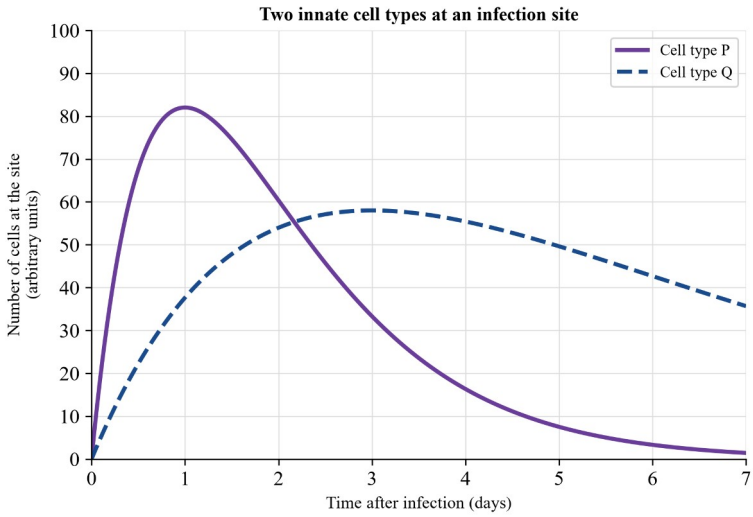
Q13. Interferons are sometimes wrongly described as chemicals that "kill viruses". State what kind of molecule an interferon actually is, explain why interferons cannot save the cell that released them, and name one other type of cell (besides a virus-infected cell) that secretes interferons. *(3 marks)*

Q14. *(Research vignette.)* A child suffers repeated bacterial infections of the skin and gums. The infected sites produce very little pus and are slow to clear. Tests show that the child has normal numbers of neutrophils in the blood, and that these neutrophils engulf and digest bacteria normally in a test tube — but they do not move towards the chemical signals released at a site of infection. (a) Explain why the child's infected sites produce very little pus. (b) Explain why the child's infections are slow to clear, even though their neutrophils carry out phagocytosis normally. (c) Suggest why the child is not completely defenceless against bacteria in the tissues. *(4 marks)*

Q15. Dendritic cells sit in the tissues that meet the outside world, such as the skin and the lining of the airways. Describe **two** characteristics of a dendritic cell that suit it to trapping pathogens at these sites. *(2 marks)*

Q16. A person is infected with a parasitic worm in the gut. The worm is far too large for a single white blood cell to engulf. Name the innate cell that responds to large parasites, and describe how it deals with the parasite. *(3 marks)*

Q17. *(Data interpretation.)* The graph shows the numbers of two innate cell types, P and Q, present at an infection site over seven days.



(a) State which cell type reaches its peak first and reaches the higher peak. Suggest which named innate cell type P is most likely to be, and give one reason for your choice.

(b) Suggest which named innate cell type Q is most likely to be, and state one role it performs at the site.

(c) Using the graph, estimate the day on which the two cell types are present in roughly equal numbers. *(5 marks)*

Q18. *(Research.)* A pharmaceutical team tests an antihistamine cream. On each of 40 volunteers they apply the antihistamine cream to an insect bite on one arm and an inactive (placebo) cream to a matching bite on the other arm, then measure the diameter of the red, swollen area after 30 minutes. The mean results are shown below.

Cream applied	Mean diameter of red, swollen area (mm)
Antihistamine cream	8
Placebo cream	21

(a) Identify the independent variable and the dependent variable in this experiment.

(b) Using your knowledge of the inflammatory response, explain why the antihistamine cream reduced the redness and swelling.

(c) Suggest one reason the researchers applied a placebo cream to the other arm rather than leaving it untreated. *(5 marks)*

Q19. *(Stimulus.)* The table describes four people, each of whom has a different fault in one part of the second line of defence. For each of W, X, Y and Z, predict **one** consequence of the fault for that person's defence against pathogens.

Person	Fault
W	macrophages engulf pathogens, but the vesicle cannot fuse with a lysosome
X	virus-infected cells cannot release interferons
Y	eosinophils cannot release the contents of their granules
Z	complement proteins are made, but can never be activated

(4 marks)

Q20. *(Synthesis.)* A quoll in a wildlife hospital is bitten by another animal, and bacteria enter the deep tissue of its shoulder. Six days later, while the shoulder is still healing, the quoll also becomes infected with a virus that replicates inside the cells lining its gut. (a) The bacteria in the shoulder are cleared by the second line of defence alone. Name **three** components of the second line that act against these bacteria, and for each state the action it performs. (b) Explain how the second line of defence can still act against the gut virus, which replicates inside the quoll's own cells where phagocytes cannot reach it. Refer to **two** different components. (c) The veterinarian remarks that the quoll's second line of defence "worked in exactly the same way for both infections". State what this tells you about the second line, and give one limitation this places on the protection the quoll receives. *(8 marks)*

Answers

Q1. (a) The body's fast, non-specific internal defence against any pathogen, with no memory. (b) The non-specific response of tissue to damage or infection, producing redness, heat, swelling and pain. (c) The process by which a cell engulfs and digests a pathogen or debris. **Q2.** (a) It responds the same way to every pathogen, not to one particular microbe. (b) It does not remember a pathogen; a repeat exposure gives the same response, at the same speed and strength. (c) The cells and molecules are already present and ready, so no time is needed to select or make specific cells. **Q3.** (a) Mast cells. (b) Vasodilation (vessels widen) and increased permeability of the capillaries. (c) Fluid (plasma) leaks from the permeable capillaries into the tissue. **Q4.** (a) Neutrophils. (b) Antigen presentation (displaying a pathogen's antigens). (c) It presents antigen to lymphocytes, activating the specific third line. **Q5.** (a) In the blood plasma (inactive). (b) Lysis, opsonisation and attraction (chemotaxis). (c) They coat/tag the pathogen so phagocytes recognise and engulf it more easily. **Q6.** (a) Becoming infected by a virus. (b) Make antiviral proteins that block viral replication. (c) Destroys it (releases chemicals that make the infected cell die). **Q7.** Tissue damaged / pathogens enter → mast cells release histamine → vessels dilate and capillaries become permeable → plasma and phagocytes reach the site → phagocytes engulf the pathogens. **Q8.** Inflammation responds to tissue damage as well as to infection: mast cells in the damaged tissue detect the injury itself and release histamine. Pain = leaked fluid and released chemicals build up and stimulate the local nerve endings. **Q9.** Neutrophils = the most abundant, fast, short-lived phagocytes that arrive first; macrophages = larger, long-lived phagocytes that also present antigen. **Q10.** The phagocyte binds the pathogen, engulfs it into a vesicle, then the vesicle fuses with a lysosome whose enzymes digest the pathogen. **Q11.** It destroys the body's own infected cell, not the virus particles; this removes the cell in which new virus is being made, so fewer new viruses are released. Also destroys cancerous cells. **Q12.** Leaky capillaries let plasma — which carries the complement proteins — pass into the tissue, so complement reaches the bacteria. Without this, complement would stay in the blood and could not act on them. **Q13.** A signalling (messenger) protein, not a killing chemical. The releasing cell is already infected and making virus, so antiviral proteins there come too late; interferons protect uninfected neighbours instead. Dendritic cells also secrete interferons. **Q14.** (a) Pus is mostly dead neutrophils (and pathogens); few neutrophils reach the site, so little forms. (b) A phagocyte can only destroy pathogens it reaches, and these neutrophils never arrive in numbers. (c) Macrophages are long-lived phagocytes already resident in the tissues, so they need no recruitment. **Q15.** Any two: many long, branched projections spread through the tissue give a large surface area for trapping pathogens; it is a phagocyte, so it engulfs and digests what it traps; it is positioned in the tissues that meet the outside world, where pathogens first break through. **Q16.** Eosinophil; it gathers around the large parasite and releases toxic chemicals from its granules onto the parasite's surface. **Q17.** (a) P peaks first and highest (day 1) — likely neutrophils, because they are the most abundant, fast-acting first responders. (b) Q likely macrophages; they engulf remaining pathogens and debris (and present antigen) and are long-lived. (c) About day 2 (roughly day 2–2.5). **Q18.** (a) IV = the type of cream (antihistamine vs placebo); DV = the diameter of the red, swollen area. (b) The antihistamine blocks histamine, so there is less vasodilation and less increased permeability, giving less blood flow (redness/heat) and less fluid leaking out (swelling). (c) So the only difference between the arms is the active ingredient (a controlled comparison / fair test). **Q19.** W = the pathogen is engulfed but never digested, so it is not destroyed. X = neighbouring cells are not warned and make no antiviral proteins, so the virus spreads faster. Y = large parasites cannot be attacked from the outside, so they survive. Z = pathogens are not lysed or opsonised and phagocytes are not attracted, so clearance is much slower. **Q20.** (a) Any three, with an action: mast cells (release histamine, starting inflammation); neutrophils/macrophages (phagocytosis); complement (lysis, opsonisation, attraction). (b) Infected gut cells release interferons, so neighbours make antiviral proteins and the virus spreads more slowly; NK cells destroy the infected cells themselves. (c) It is non-specific — the same components acted against both a bacterium and a virus; limitation: it is not tailored to either pathogen and never becomes faster or stronger (no memory).

Fully-worked solutions

Q1. (a) The **innate immune response** is the body's **fast, non-specific** internal defence that acts against **any** pathogen that enters the tissues, and which has **no memory**. (b) **Inflammation** is the **non-specific response of tissue to damage or infection**, producing the signs of redness, heat, swelling and pain. (c) **Phagocytosis** is the process in which a cell **engulfs and digests** a pathogen (or cell debris).

Q2. (a) **Non-specific** means the second line responds in the **same way to every pathogen** — it is not directed at one particular microbe. (b) **No memory** means it does **not remember** a pathogen: a second exposure to the same microbe

produces the **same response, at the same speed and strength**, as the first. (c) The second line can respond quickly because the cells (such as phagocytes and mast cells) and molecules (such as complement) are **already present and ready** in the tissues and blood — no time is needed to select or produce cells that match a particular pathogen.

Q3. (a) **Mast cells** release histamine. (b) Histamine causes **vasodilation** (the blood vessels widen) and makes the capillaries **more permeable (leaky)**. (c) The injured area becomes swollen because the **increased permeability** lets **plasma (fluid) leak out of the capillaries** and collect in the surrounding tissue.

Q4. (a) **Neutrophils** are the most abundant phagocyte and are usually first to arrive in large numbers. (b) A macrophage also acts as an **antigen-presenting cell** (it displays a pathogen's antigens). (c) A dendritic cell **presents antigen to lymphocytes**, which activates the **specific third line of defence**, so it links the innate second line to the adaptive third line.

Q5. (a) Complement proteins are found **inactive in the blood plasma**. (b) The three roles are **lysis, opsonisation and attraction (chemotaxis)**. (c) In **opsonisation** the complement proteins **coat (tag) the surface of the pathogen**, so that phagocytes can **recognise and engulf it more easily**.

Q6. (a) A body cell releases interferons when it becomes **infected by a virus**. (b) They cause neighbouring cells to **produce antiviral proteins** that block viral replication. (c) An NK cell **destroys** the virus-infected cell (it releases chemicals that make the infected cell die).

Q7. In the correct order: **(1)** tissue is damaged and pathogens enter → **(2)** mast cells release histamine → **(3)** blood vessels dilate and capillaries become more permeable → **(4)** plasma and phagocytes leave the blood and reach the site → **(5)** phagocytes engulf the pathogens. *(2 marks: 2 for the fully correct order; 1 mark if only one step is out of place.)*

Q8. Inflammation is the innate response to **tissue damage** as well as to infection, so it does not need a pathogen to trigger it. The **mast cells already present in the damaged tissue** detect the injury itself and release **histamine**, which begins the response in the twisted ankle exactly as it would at an infected wound. The joint becomes **painful** because the fluid that has leaked into the tissue, and the chemicals released there, **build up** in and around the joint; this pressure, and the chemicals themselves, **stimulate the local nerve endings**, which the brain interprets as pain. *(1 mark: inflammation responds to tissue damage, not only to infection; 1 mark: mast cells in the damaged tissue detect the injury and release histamine, so no pathogen is needed; 1 mark: leaked fluid and released chemicals build up in the tissue; 1 mark: these stimulate the local nerve endings, felt as pain.)*

Q9. Neutrophils are the **most abundant** white blood cell and **fast-acting** phagocytes that are usually the **first to arrive in large numbers**, but they are **short-lived**. **Macrophages** are **larger, longer-lived** phagocytes that engulf pathogens and debris and **also present antigen** to help activate the third line. Both are phagocytes, but they differ in abundance, speed, lifespan and the macrophage's extra antigen-presenting role. *(1 mark: neutrophil most abundant / fast / first; 1 mark: macrophage large / long-lived; 1 mark: macrophage also presents antigen.)*

Q10. In **phagocytosis**, the phagocyte is first **attracted to and binds** the pathogen. It then **engulfs** the pathogen by wrapping its membrane around it, enclosing it in a **vesicle** inside the cell. The vesicle **fuses with a lysosome**, whose **enzymes digest and destroy** the pathogen. *(1 mark: bind the pathogen; 1 mark: engulf it into a vesicle; 1 mark: lysosome enzymes digest it.)*

Q11. An NK cell does not destroy the virus particles themselves; it destroys **the body's own cell that the virus has infected**. Killing that cell **removes the place in which new virus is being made**, so the infected cell cannot go on producing and releasing new virus particles into the tissue, and the infection spreads more slowly. NK cells also destroy the body's own cells that have turned **cancerous**. *(1 mark: it destroys the body's own infected cell, not the virus; 1 mark: this removes the cell in which new virus is made, so fewer new viruses are released; 1 mark: cancerous / abnormal body cells.)*

Q12. During inflammation the capillaries near the wound become **more permeable (leaky)**, which lets **plasma pass out of the blood and into the infected tissue**. The complement proteins are carried **dissolved in that plasma**, so making the capillaries leaky **delivers the complement to the tissue where the bacteria are**, and it can be activated there, at the site of infection. If the capillaries did not become more permeable, the complement proteins would **remain inside the bloodstream**: they could not reach bacteria sitting in the tissue, so those bacteria would not be lysed or opsonised and phagocytes would not be drawn to them, and the infection would be cleared far more slowly. *(1 mark: leaky capillaries let plasma pass out of the blood into the tissue; 1 mark: complement is carried in the*

plasma, so it is delivered to the bacteria and activated there; 1 mark: without this, complement stays in the blood and cannot act on bacteria in the tissue.)

Q13. An interferon is a **signalling (messenger) protein** — a chemical warning sent from one cell to another — **not** a chemical that kills viruses. Interferons cannot save the cell that released them because that cell is **already infected** and is already making new virus; the antiviral proteins that interferons trigger act by **blocking viral replication before the virus arrives**, so producing them in an already-infected cell is too late. Interferons are useful instead because they reach the **neighbouring, uninfected** cells in time. Besides virus-infected cells, **dendritic cells** also secrete interferons. *(1 mark: a signalling protein, not a killing chemical; 1 mark: the releasing cell is already infected / already making virus, so the antiviral response comes too late for it — the neighbours are protected instead; 1 mark: dendritic cells.)*

Q14. (a) Most of the pus at an infected site is made of **dead neutrophils** together with dead pathogens and debris. This child's neutrophils **cannot follow the chemical signals** to the site, so very few of them ever arrive there and very little pus can form. (b) A phagocyte can only destroy the pathogens it actually **reaches**. Normally neutrophils leave the blood during inflammation and follow chemical signals (such as those released by complement) to the bacteria. Because these neutrophils cannot do that, they stay in the bloodstream while the bacteria multiply in the tissue — so a normal ability to engulf and digest is of little use, and the infection clears slowly. (c) **Macrophages** are long-lived phagocytes that are **already resident in the tissues**, so they do not have to be recruited from the blood; they can engulf and digest bacteria at the site straight away. *(a: 1 mark — pus is largely dead neutrophils, and few neutrophils reach the site. b: 2 marks — neutrophils must be attracted to and reach the site to act; they remain in the blood while the bacteria multiply. c: 1 mark — macrophages are long-lived phagocytes already present in the tissues.)*

Q15. Any **two** of: a dendritic cell has **many long, branched projections** that spread out through the surrounding tissue, giving it a **large surface area** over which it can sample and trap passing pathogens; it is a **phagocyte**, so it can **engulf and digest** the pathogens it traps; and it is **positioned in the tissues that meet the outside world** (skin, airway and gut linings), which is exactly where pathogens first break through the first line of defence. *(1 mark each for any two valid characteristics, linked to trapping pathogens.)*

Q16. The innate cell that responds to large parasites is the **eosinophil**. Because the parasite is **far too large to be engulfed** by phagocytosis, eosinophils instead **gather around the parasite** and **release toxic chemicals from their granules onto its surface**, damaging and killing it from the outside. *(1 mark: eosinophil; 1 mark: too large to engulf; 1 mark: releases toxic chemicals onto the parasite's surface.)*

Q17. (a) Cell type **P** reaches its peak **first** (at about day 1) and reaches the **higher peak** (about 80 units on the graph's scale). P is most likely to be **neutrophils**, because neutrophils are the **most abundant** white blood cells and are **fast-acting first responders** that arrive at an infection in the largest numbers early on. (b) Cell type **Q** is most likely to be **macrophages**; the graph shows Q peaking later (about day 3) and still present at day 7, which matches a **long-lived** cell, and at the site macrophages **engulf remaining pathogens and cell debris** (and present antigen). (c) The two curves cross at about **day 2** (roughly day 2 to 2.5), when the two cell types are present in roughly equal numbers. *(a: 1 mark P peaks first and highest, 1 mark neutrophils + a valid reason; b: 1 mark macrophages, 1 mark a valid role; c: 1 mark about day 2.)*

Q18. (a) The **independent variable** is the **type of cream applied** (antihistamine versus placebo); the **dependent variable** is the **diameter of the red, swollen area** (mm). (b) In inflammation, **histamine** causes **vasodilation** and **increased capillary permeability**. The antihistamine **blocks the action of histamine**, so there is **less vasodilation** (less blood flow, so less redness and heat) and **less leakage of plasma** into the tissue (so less swelling) — giving the smaller diameter. (c) Applying a **placebo cream** to the other arm means the **only difference** between the two arms is the **active antihistamine ingredient**, so any effect can be attributed to that ingredient rather than to the act of applying a cream (a controlled comparison / fair test). *(a: 1 mark IV, 1 mark DV; b: 2 marks — antihistamine blocks histamine, so less vasodilation/permeability reduces redness and swelling; c: 1 mark — controls for the effect of applying any cream.)*

Q19. W — the pathogen is engulfed into a vesicle but the **digestive enzymes never reach it**, so it is **not destroyed**; it may even survive inside the macrophage, so phagocytosis fails to clear the infection. **X** — the neighbouring uninfected cells are **never warned** and so do not make antiviral proteins in advance; the virus therefore **spreads through the tissue more quickly**. **Y** — the toxic chemicals never reach the parasite's surface, so **large parasites** (which are far too big to be engulfed) **cannot be attacked** and survive in the body. **Z** — pathogens are **not lysed**, are

not coated (opsonised) for the phagocytes, and phagocytes are **not attracted** to the site, so pathogens are cleared much more slowly. *(1 mark each for a valid consequence at W, X, Y and Z.)*

Q20. (a) Any **three** components, each with its action. **Mast cells** in the damaged shoulder tissue release **histamine**, which starts the inflammatory response. **Neutrophils** (and **macrophages**) are **phagocytes**: they engulf the bacteria and digest them. **Complement proteins** are activated by the bacteria and **lyse** them, **coat (opsonise)** them for the phagocytes and **attract** phagocytes to the shoulder. (b) The virus is out of reach of the phagocytes, but two other components still act. First, the **infected gut-lining cells release interferons**, which diffuse to the **neighbouring uninfected cells** and cause them to make **antiviral proteins**, so the virus replicates and spreads more slowly through the gut lining. Second, **natural killer (NK) cells** destroy the quoll's **own infected cells**, removing the cells in which new virus is being made. (c) It tells you that the second line is **non-specific**: the same cells and molecules were used against a bacterium and a virus alike, because they are not directed at any one pathogen. The limitation is that this untailored response is the **only** one the second line can give and it has **no memory** — it never becomes faster or stronger, so a pathogen it cannot clear (like the gut virus) will keep spreading until the specific third line takes over. ∴ the innate second line acts quickly and against anything, but at the cost of being untargeted and unable to improve. *(a: 3 marks — 1 mark each for any three named second-line components, each with a correct action. b: 3 marks — interferons released by the infected cells; neighbours make antiviral proteins so the virus spreads more slowly; NK cells destroy the infected cells. c: 2 marks — non-specific, the same response to both pathogens; a valid limitation, e.g. untargeted and with no memory, so it never improves.)*

Theory

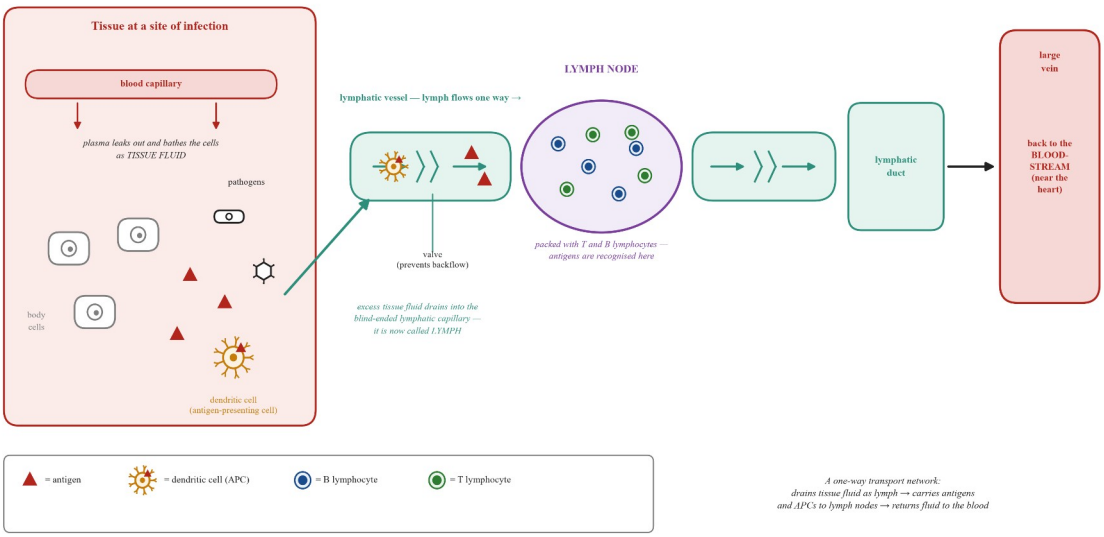
The body's defences depend on getting the right cells and the right information to the right place. The **lymphatic system** is the network that makes this possible. It is a system of vessels and small organs that runs alongside the blood circulation, and in the immune response it acts as a **transport network**: it collects fluid that has leaked out of the blood, and it carries foreign material and defensive cells to the places where an immune response can be organised. This subtopic follows that fluid — and the antigens it carries — from a site of infection to a **lymph node**, where **T and B lymphocytes** meet and recognise the antigen.

Tissue fluid and lymph. Blood travels through the body in blood vessels, but the liquid part of blood does not stay inside them completely. As blood passes through the tiny **blood capillaries**, some of the **plasma** (the watery part of blood) is forced out through the capillary wall into the spaces between the cells. This escaped fluid is called **tissue fluid** (also called interstitial fluid). Tissue fluid **bathes the body cells**, supplying them with oxygen and nutrients and carrying away wastes.

Most of the tissue fluid seeps back into the blood capillaries, but not all of it. The **excess tissue fluid** drains instead into a separate set of vessels — the **lymphatic vessels**. Once tissue fluid has drained into a lymphatic vessel, it is given a new name: it is called **lymph**. So lymph and tissue fluid are essentially the **same fluid** at different stages — tissue fluid is the fluid **bathing the cells**, and lymph is that fluid **once it has entered the lymphatic vessels**.

Lymphatic vessels and one-way flow. The lymphatic vessels begin in the tissues as fine, **blind-ended lymphatic capillaries** (closed at one end, so fluid can enter but the system does not form a loop). These join into larger and larger lymphatic vessels. Unlike blood, which is pumped around a closed circuit by the heart, lymph is **not** circulated in a loop and there is **no central pump**. Instead, lymph is moved along mainly by the **squeezing action of nearby skeletal muscles** as the body moves. To keep it moving in one direction, the larger lymphatic vessels contain **valves** that **prevent the lymph flowing backwards**. The result is a **one-way flow**: lymph always travels **from the tissues towards the bloodstream**.

The lymphatic vessels eventually join into large **lymphatic ducts**, which empty the lymph into **large veins near the heart**. In this way the fluid that leaked out of the blood is **returned to the bloodstream**. Returning this fluid keeps the volume of blood and tissue fluid balanced — but for immunity the important point is what the lymph carries on the way.



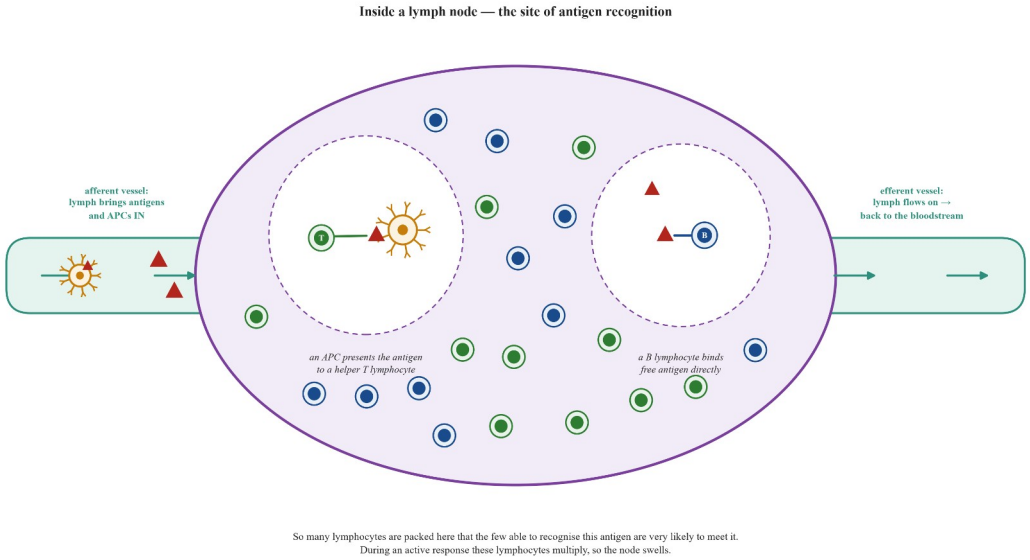
The transport role in the immune response. At a **site of infection**, pathogens and their **antigens** (the foreign molecules the body can recognise as non-self) end up in the tissue fluid. Certain defensive cells, especially **dendritic cells**, act as **antigen-presenting cells (APCs)**: at the infection site they take up antigen and then travel into the lymphatic vessels. When the tissue fluid drains into the lymphatic capillaries as lymph, it therefore carries with it both

free antigens and **antigen-presenting cells that are carrying antigen**. The one-way flow of lymph then transports this cargo **away from the infection site and along the lymphatic vessels to the nearest lymph node**. This is the heart of the lymphatic system's job in immunity: it is the **transport network** that delivers antigen — and the cells displaying it — from wherever an infection is, to the place where lymphocytes are waiting.

Lymph nodes — the sites of antigen recognition. Spaced along the lymphatic vessels are hundreds of small, bean-shaped organs called **lymph nodes** (clusters of them lie in places such as the neck, the armpits and the groin). Lymph is delivered into a node by incoming (**afferent**) vessels, filters slowly through it, and leaves by an outgoing (**efferent**) vessel to continue on its way. What makes a lymph node special is that it is **packed with lymphocytes** — huge numbers of both **T lymphocytes** and **B lymphocytes** are concentrated inside it.

Because **all of the lymph draining from a region must pass through its lymph nodes**, and because the node is crowded with lymphocytes, the node brings the incoming **antigen** into contact with an enormous sample of lymphocytes in a very small space. A lymph node is therefore the **site where an antigen is recognised by T and B lymphocytes**: the particular lymphocyte that carries the **receptor matching that antigen** is able to encounter it here. This recognition event is what **starts and coordinates the adaptive (specific) immune response**. (Exactly how the T and B lymphocytes then respond — making antibodies, activating other cells and forming memory — is dealt with in the next subtopic; here the key idea is simply that the lymph node is **where** recognition happens.)

Two ways an antigen is recognised in a node. The two kinds of lymphocyte do not recognise antigen in the same way, which is why it matters that the lymph delivers antigen in **two forms**. A **B lymphocyte** recognises antigen **directly**: it binds the **free antigen** carried in the lymph using its own membrane-bound receptor. A **T lymphocyte** cannot do this — it recognises an antigen only when that antigen is **displayed on the surface of another cell**. Providing that display is the job of the **antigen-presenting cells** that travelled here in the lymph: an APC **presents** the antigen it took up at the infection site to the **helper T lymphocytes** waiting in the node. So a node can be the site of antigen recognition **by T and by B lymphocytes** precisely because the lymph delivers both the **free antigen** the B lymphocytes bind and the **antigen-presenting cells** the T lymphocytes need.



Why concentrating lymphocytes works. Each lymphocyte carries receptors of **one kind only**, so any one antigen can be recognised by only the **few** lymphocytes whose receptors happen to **match** it. If those few were spread thinly throughout the whole body, the chance of the right lymphocyte meeting the antigen would be tiny. By concentrating vast numbers of lymphocytes in lymph nodes, and by channelling all the antigen-bearing lymph through those nodes, the lymphatic system makes it **very likely** that an antigen will meet a lymphocyte that can recognise it. The node is, in effect, a **meeting point** engineered to bring antigen and lymphocytes together efficiently.

Swollen lymph nodes signal an active response. When lymphocytes in a node recognise an antigen, those lymphocytes **multiply rapidly**, and the node fills with dividing and responding cells. As a result the node **enlarges** and can become **swollen and tender** — the familiar "swollen glands" felt in the neck during a throat infection. A swollen lymph node is therefore a useful **sign that an immune response is actively underway** in the region that node drains.

Linking the innate and adaptive responses. The lymphatic system also acts as the **bridge** between the body's two kinds of internal defence. The early, non-specific response happens at the site of infection; antigen-presenting cells such as dendritic cells there capture antigen and then **travel through the lymphatic vessels** to a lymph node, where they **present that antigen to the helper T lymphocytes**, while the free antigen that drained there is bound by the **B lymphocytes** whose receptors match it. In this way the lymphatic system physically **connects** the response at the wound to the specific response organised in the node — antigen collected at the front line is transported back to where the adaptive response can be launched.

The essentials to remember.

- **Lymph** = tissue fluid that has drained into the **lymphatic vessels**; it flows **one way**, from the tissues back to the **bloodstream**.
- The lymphatic system is a **transport network** that carries **antigens** and **antigen-presenting cells** from a **site of infection** to a **lymph node**.
- **Lymph nodes** are packed with **T and B lymphocytes** and are the **sites where antigens are recognised**, initiating the adaptive immune response. **B lymphocytes** bind the **free antigen** directly; **antigen-presenting cells** present antigen to the **helper T lymphocytes**.
- **Swollen** lymph nodes are a sign of an **active immune response**.

Worked examples

Example 1 — scaffolded

A person cuts their finger and bacteria enter the wound. Describe how the bacterial antigens are transported from the wound to a lymph node in the armpit.

Working	Comment
At the wound, the bacteria and their **antigens** enter the **tissue fluid** that bathes the cells; some antigen is also taken up by **dendritic cells (antigen-presenting cells)**.	Start where the antigen actually is — in the tissue fluid at the site of infection.
The excess tissue fluid, carrying the free antigens and the antigen-presenting cells, **drains into the blind-ended lymphatic capillaries** and is now called **lymph**.	Name the change: tissue fluid becomes lymph once it enters the lymphatic vessels.
The lymph flows **one way along the lymphatic vessels**, moved by muscle action and kept flowing forward by **valves**, towards the lymph nodes in the armpit.	The transport step — emphasise the one-way flow away from the wound.
The lymph is delivered into the **lymph node**, so the antigens and the antigen-presenting cells are brought to the lymphocytes concentrated there.	Finish at the destination: the antigen has reached the node.

Example 2 — scaffolded

Explain why a lymph node is described as a site of antigen recognition by T and B lymphocytes.

Working	Comment
A lymph node is **packed with large numbers of both T lymphocytes and B lymphocytes**.	The node concentrates the cells that do the recognising.
All of the lymph draining from a region — carrying antigens and antigen-presenting cells — **must pass through** the node.	The transport network delivers the antigen to this exact spot.
Inside the node the antigen is brought into contact with a huge sample of lymphocytes, so the lymphocyte whose **receptor matches** that antigen is able to **encounter and recognise** it.	Recognition depends on a matching receptor; crowding raises the chance of a match.
This recognition **initiates the adaptive immune**	Link the recognition event to its consequence.

response, which is why the node is called the site of antigen recognition.

Example 3 — unscaffolded

Explain why the lymph nodes near a site of infection often become swollen and tender.

Lymph draining from the infected region carries **antigens** and **antigen-presenting cells** into the nearby lymph nodes. Inside a node, the **T and B lymphocytes** that **recognise** the antigen begin to **multiply rapidly**, and the node fills with these dividing and responding cells. Because the node now contains far more cells than usual, it **enlarges** and becomes **swollen and tender**. ∴ the swelling is a direct sign that an **immune response is actively underway** in the area that node drains.

Example 4 — unscaffolded

A student states: "The lymphatic system circulates lymph around the body in a loop, just like blood." Explain why this statement is incorrect.

The statement is incorrect because the lymphatic system does **not** form a circulating loop. Lymph begins as **tissue fluid** that drains into **blind-ended lymphatic capillaries** in the tissues, so fluid can only **enter** at one end. From there the lymph flows in **one direction only** — from the tissues, through the lymphatic vessels and lymph nodes, into large ducts that **empty into veins near the heart**. There is **no central pump** and **valves prevent any backflow**, so the lymph is not driven around and around a circuit. Blood, by contrast, is pumped by the heart around a **closed circuit**. ∴ the lymphatic system is a **one-way drainage and transport network** that returns fluid to the blood, not a circulating loop.

Practice questions

Scaffolded

Q1. Define each of the following terms: (a) tissue fluid; (b) lymph; (c) lymph node.

Q2. The lymphatic system carries fluid from the tissues back to the blood. (a) State where tissue fluid comes from. (b) State what the fluid is called once it has drained into a lymphatic vessel. (c) State where the lymph is finally returned to the bloodstream.

Q3. During an infection the lymphatic system transports material to a lymph node. (a) Name **two** things that lymph carries from a site of infection to a lymph node. (b) Name the type of antigen-presenting cell that carries antigen from an infection site to a node. (c) State what happens to the lymph after it leaves the last lymph node.

Q4. Lymph nodes are the sites of antigen recognition. (a) Name the two types of lymphocyte that are concentrated in a lymph node. (b) State which of these two types an antigen-presenting cell presents its antigen to. (c) Explain why only a small number of the lymphocytes in a node are able to recognise any one antigen.

Q5. Swollen lymph nodes can be a sign of infection. (a) State one observable change in a lymph node that is responding to an infection. (b) Explain why the node changes in this way. (c) State what a doctor might infer from finding swollen lymph nodes in a patient's neck.

Q6. The flow of lymph is carefully controlled. (a) State the function of the valves in the lymphatic vessels. (b) Explain how lymph is moved along the vessels, given that there is no central pump. (c) Explain why the flow of lymph must be one-way, rather than to and fro, if the lymphatic system is to do its job in the immune response.

Unscaffolded

Q7. Describe the role of the lymphatic system as a transport network in the immune response. *(3 marks)*

Q8. Distinguish between tissue fluid and lymph. *(2 marks)*

Q9. The lymph arriving at a node carries antigen in two forms: **free antigen**, and antigen that has already been taken up by an **antigen-presenting cell**. Explain why both forms must be delivered if the node is to be a site of antigen recognition by **both** T and B lymphocytes. *(3 marks)*

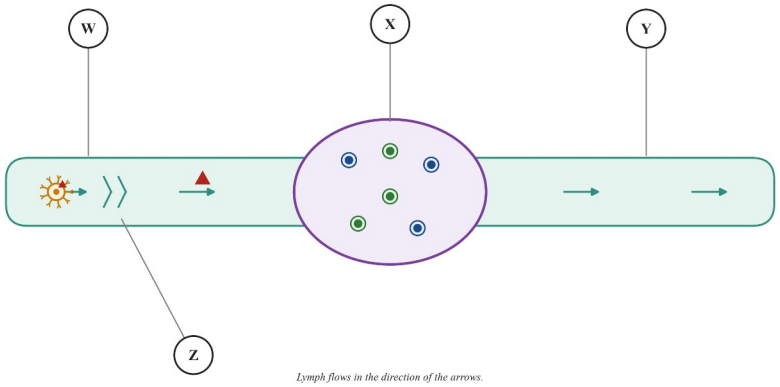
Q10. In the tissues, the lymphatic system begins as fine, **blind-ended** lymphatic capillaries. Explain how this structure suits them to collecting the excess tissue fluid, referring to where that excess fluid comes from. *(3 marks)*

Q11. *(Scenario.)* After an operation a patient must stay in bed and cannot move their legs for several weeks. Suggest why the flow of lymph from the legs would slow, and predict one consequence for the tissues of the legs. *(2 marks)*

Q12. The flow of lymph is one-way. Describe the path taken by lymph from the tissues back to the bloodstream, and explain how the one-way flow is maintained. *(3 marks)*

Q13. Explain how the lymphatic system links the innate (non-specific) response with the adaptive (specific) response. *(3 marks)*

Q14. *(Stimulus.)* The diagram shows a length of a lymphatic vessel with a lymph node. Lymph flows in the direction of the arrows.



(a) Name the structures labelled **W**, **X**, **Y** and **Z**.

(b) State what happens to the antigens carried in the lymph as it passes through structure **X**. *(5 marks)*

Q15. *(Scenario.)* A person develops a bacterial infection in a cut on the sole of their foot. A few days later, the lymph nodes behind their knee and in their groin become swollen, even though these nodes are some distance from the foot. Explain, in terms of the lymphatic system, why nodes at a distance from the infection are the ones that swell. *(4 marks)*

Q16. *(Data interpretation.)* A lymph node draining an infected wound was measured over several days. The table shows the diameter of the node.

Day of infection	Lymph-node diameter (mm)
0	6
2	9
4	15
6	21
9	14
13	7

(a) Describe the trend in lymph-node diameter over the 13 days.

(b) Explain, in terms of the lymphocytes in the node, why the diameter changes as it does between day 0 and day 6.

(c) Suggest why the diameter falls again after day 6. *(4 marks)*

Q17. After surgery, the lymphatic vessels that drain a patient's right arm are damaged and no longer carry lymph away effectively. Suggest why the patient might mount a **slower or weaker** immune response to an infection in that arm. *(3 marks)*

Q18. Any one antigen can be recognised by only a small number of lymphocytes. Explain why concentrating B and T lymphocytes in lymph nodes, rather than spreading them evenly through the tissues, makes antigen recognition more effective. *(3 marks)*

Q19. *(Experimental design.)* To find out how quickly a vaccine antigen reaches a lymph node, researchers injected the same dose of a harmless labelled antigen into the upper-arm muscle of each of 60 adult volunteers. A scanner was then used to measure the amount of label in the volunteer's armpit lymph nodes. A different group of 10 volunteers was scanned at each of 1, 2, 4, 8, 12 and 24 hours after the injection. (a) Identify the independent variable in this investigation. (b) Identify the dependent variable. (c) State **one** variable the researchers kept constant, and explain why doing so was important. *(3 marks)*

Q20. *(Synthesis.)* A child has a throat infection. The lymph nodes in the child's neck become swollen and tender. (a) Trace the path taken by antigens and antigen-presenting cells from the infected throat tissue to the lymphocytes that recognise them. (b) Explain the role of the lymph node in the immune response. (c) Explain why the neck lymph nodes swell, and state what this sign indicates. *(7 marks)*

Answers

Q1. (a) Fluid (from blood plasma) that has leaked out of blood capillaries and bathes the body cells. (b) Tissue fluid once it has drained into a lymphatic vessel. (c) A small bean-shaped organ along a lymphatic vessel, packed with lymphocytes, where antigens are recognised. **Q2.** (a) Plasma forced out of blood capillaries. (b) Lymph. (c) It empties (via lymphatic ducts) into large veins near the heart. **Q3.** (a) Antigens and antigen-presenting cells (e.g. dendritic cells). (b) Dendritic cells. (c) It flows on through further vessels and is eventually returned to the bloodstream. **Q4.** (a) T lymphocytes and B lymphocytes. (b) T lymphocytes (helper T cells). (c) Each lymphocyte carries receptors of one kind only, so only those whose receptor matches that antigen's shape can bind and recognise it. **Q5.** (a) It becomes swollen (enlarged)/tender. (b) The lymphocytes that recognise the antigen multiply, filling the node. (c) That an immune response is active in the region drained by those nodes (an infection nearby). **Q6.** (a) They prevent lymph flowing backwards, keeping flow one-way. (b) By the squeezing action of surrounding skeletal muscles as the body moves. (c) One-way flow always carries antigen away from the tissues and on to the lymph nodes (and then the blood), instead of washing it back into the tissue it came from, so antigen collected at an infection is reliably delivered to the lymphocytes. **Q7.** It drains tissue fluid as lymph, carries antigens and antigen-presenting cells from a site of infection to lymph nodes, and returns the fluid to the bloodstream. **Q8.** Tissue fluid bathes the body cells; lymph is that same fluid once it has drained into the lymphatic vessels. **Q9.** A B lymphocyte binds free antigen directly with its own receptor, so free antigen must arrive; a T lymphocyte can only recognise antigen displayed on another cell, so an antigen-presenting cell must bring it and present it. Delivering both forms lets both types of lymphocyte recognise the antigen in the node. **Q10.** Some plasma is forced out of the blood capillaries as tissue fluid and most, but not all, seeps back in — the excess is left in the spaces between the cells. The lymphatic capillaries begin among those spaces and are closed at one end, so fluid can only enter them; they therefore act as a one-way drain that takes up the excess fluid and carries it away (as lymph) towards the bloodstream. **Q11.** There is no central pump for lymph — it is pushed along mainly by the squeezing action of nearby skeletal muscles as the body moves, so with the legs still there is little to drive it forward (valves only prevent backflow). Excess tissue fluid is therefore drained away more slowly, so fluid builds up in the leg tissues and they swell. **Q12.** Tissues → lymphatic capillaries → lymphatic vessels → lymph nodes → lymphatic ducts → large veins (bloodstream); one-way flow is maintained by valves that prevent backflow. **Q13.** Antigen-presenting cells (e.g. dendritic cells) act at the infection site, then travel through the lymphatic vessels to a node and present antigen to the helper T lymphocytes there, so the lymphatic system bridges the non-specific response and the specific response. **Q14.** (a) W = afferent lymphatic vessel; X = lymph node; Y = efferent lymphatic vessel; Z = valve. (b) They are recognised by the T and B lymphocytes (those with the matching receptor). **Q15.** Antigens/APCs from the foot enter the lymph and are carried one-way along the lymphatic vessels draining the leg, which pass through the nodes behind the knee and in the groin; recognition there makes lymphocytes multiply, so those (distant) nodes swell. **Q16.** (a) Diameter rises from 6 mm to a peak of 21 mm at day 6, then falls back to near normal (7 mm) by day 13. (b) Antigen arriving in the lymph is recognised, and the responding lymphocytes multiply, filling and enlarging the node. (c) The infection is cleared, the response winds down and lymphocyte numbers fall, so the node shrinks back. **Q17.** Antigens/APCs from an infection in that arm cannot be carried efficiently to the lymph nodes, so fewer reach the concentrated lymphocytes and recognition is delayed/reduced, slowing or weakening the response. **Q18.** Only a few lymphocytes match any one antigen; spread through the tissues they would rarely meet it, but concentrating them in nodes that all lymph passes through makes a meeting very likely. **Q19.** (a) The time since the injection. (b) The amount of label measured in the armpit lymph nodes. (c) E.g. the dose of antigen injected (or the injection site) — kept the same so that any difference in the amount of label was due to the time elapsed and not to some other factor. **Q20.** (a) Antigens/APCs from the throat enter the tissue fluid, drain into lymphatic vessels as lymph and flow to the neck lymph nodes. (b) The node concentrates T and B lymphocytes and delivers the antigen to them, so the antigen is recognised and the adaptive response begins. (c) The responding lymphocytes multiply and fill the node, so it swells — a sign of an active immune response.

Fully-worked solutions

Q1. (a) **Tissue fluid** is fluid derived from **blood plasma** that has been forced out through the walls of the **blood capillaries** and collects in the spaces between cells, where it **bathes the body cells**. (b) **Lymph** is that tissue fluid **after it has drained into the lymphatic vessels** — the same fluid, given a new name once it is inside the lymphatic system. (c) A **lymph node** is a small, bean-shaped organ positioned along a lymphatic vessel; it is **packed with T and B lymphocytes** and is the site where **antigens carried in the lymph are recognised**.

Q2. (a) Tissue fluid comes from **blood plasma** that is forced out of the **blood capillaries** as blood flows through them. (b) Once it has drained into a lymphatic vessel it is called **lymph**. (c) The lymph is returned to the bloodstream where the large **lymphatic ducts empty into large veins near the heart**.

Q3. (a) Lymph carries **antigens** (free foreign material from the pathogens) and **antigen-presenting cells** such as dendritic cells (which are carrying antigen). (b) **Dendritic cells** (antigen-presenting cells). (c) After leaving the last node the lymph **continues along further lymphatic vessels and is eventually returned to the bloodstream** (via the lymphatic ducts into large veins).

Q4. (a) **T lymphocytes** and **B lymphocytes**. (b) An antigen-presenting cell presents the antigen it is carrying to the **T lymphocytes** (specifically the **helper T cells**). A **B** lymphocyte is not presented to — it binds the **free antigen** in the lymph directly, using its own membrane-bound receptor. (c) Every lymphocyte carries membrane receptors of **one kind only**, so a lymphocyte can recognise **one** antigen. Only those few lymphocytes whose receptor shape is **complementary to that particular antigen** can bind it, so the vast majority of the lymphocytes packed into the node cannot recognise it at all.

Q5. (a) The node becomes **swollen (enlarged)** and often tender. (b) When lymphocytes in the node **recognise the antigen** they **multiply rapidly**, so the node **fills with dividing and responding cells** and enlarges. (c) The doctor can infer that an **immune response is active** in the region those neck nodes drain — that is, that there is (or recently was) an **infection** nearby.

Q6. (a) The **valves** allow lymph to move forward but **close to prevent it flowing backwards**, keeping the flow **one-way**. (b) There is no central pump, so lymph is pushed along mainly by the **squeezing (massaging) action of nearby skeletal muscles** as the body moves. (c) The system's immune job is to **collect** antigen in the tissues and **deliver** it to the lymphocytes in a lymph node. A **one-way** flow guarantees that direction of travel: everything that drains in at an infection site is carried **away from the tissues, through the nodes and on to the bloodstream**, and cannot wash back into the tissue it came from. A to-and-fro flow would simply move the antigen back and forth near the wound, so it would not reliably reach a node.

Q7. As a transport network the lymphatic system does three things in the immune response. First, it **drains excess tissue fluid** from the tissues into the lymphatic vessels, where it becomes **lymph**. Second, this lymph **carries antigens and antigen-presenting cells** (such as dendritic cells) from a **site of infection along the vessels to the lymph nodes**. Third, after passing through the nodes the lymph is **returned to the bloodstream**. In this way it delivers foreign material to the place where it can be recognised. *(1 mark: drains tissue fluid as lymph; 1 mark: carries antigens/APCs to lymph nodes; 1 mark: returns fluid to the bloodstream.)*

Q8. Tissue fluid and **lymph** are the **same fluid at different stages**. **Tissue fluid** is the fluid, derived from blood plasma, that has leaked out of the blood capillaries and **bathes the body cells** in the tissues. **Lymph** is that fluid **once it has drained into the lymphatic vessels**. *(1 mark: tissue fluid bathes the cells / from plasma; 1 mark: lymph is the same fluid once inside the lymphatic vessels.)*

Q9. The two types of lymphocyte recognise antigen in **different ways**, so each needs the antigen delivered in a different form. A **B lymphocyte** recognises antigen **directly**: its membrane-bound receptor binds the **free antigen** floating in the lymph, so free antigen must reach the node for the B lymphocytes to have anything to bind. A **T lymphocyte** cannot bind free antigen; it recognises antigen only when that antigen is **displayed on the surface of another cell**, which is why the **antigen-presenting cells** that took up antigen at the infection site must travel in the lymph and **present** it to the **helper T lymphocytes** in the node. If the lymph delivered only one form, only one type of lymphocyte could recognise the antigen; delivering **both** is what makes the node a site of antigen recognition by **T and B lymphocytes**. *(1 mark: B lymphocytes bind free antigen directly with their own receptor; 1 mark: T lymphocytes recognise antigen only when it is presented on an APC's surface; 1 mark: so both forms must arrive for both types of lymphocyte to recognise the antigen.)*

Q10. Tissue fluid forms because some **plasma is forced out through the walls of the blood capillaries** into the spaces between the cells. **Most** of it seeps back into the blood capillaries, but **not all** — the **excess** is left in the tissue spaces and must be collected. The lymphatic capillaries are well suited to this job: they are **fine vessels that begin among the tissue spaces themselves**, and they are **blind-ended (closed at one end)**, so fluid can **only enter** them — it cannot pass straight through from another vessel, and the closed end means it cannot simply drain back out the way it came. They therefore act as a **one-way drain**: the excess fluid is **taken up from the tissues** and, once inside, is

carried away as **lymph** towards the bloodstream. *(1 mark: the excess comes from plasma forced out of the blood capillaries, not all of which seeps back; 1 mark: the capillaries begin in the tissue spaces and are closed at one end, so fluid can only enter; 1 mark: so they act as a one-way drain that takes up the excess fluid and carries it away as lymph.)*

Q11. Unlike blood, lymph has **no central pump** to drive it: it is moved along mainly by the **squeezing (massaging) action of nearby skeletal muscles** as the body moves, while the **valves** only stop it flowing **backwards**. If the patient cannot move their legs, the leg muscles are **not contracting and squeezing the lymphatic vessels**, so there is little to push the lymph forward and the **flow slows**. As a result the **excess tissue fluid is drained away more slowly than it forms**, so fluid **accumulates in the tissue spaces** and the legs **swell**. *(1 mark: there is no central pump — lymph is moved by skeletal muscle contraction, which is absent when the legs are still; 1 mark: the excess tissue fluid is drained more slowly, so fluid builds up in the leg tissues and they swell.)*

Q12. Lymph travels: from the **tissues** → into the **blind-ended lymphatic capillaries** → along larger **lymphatic vessels** → through the **lymph nodes** → into the large **lymphatic ducts** → which empty into **large veins near the heart** (the bloodstream). The flow is kept **one-way** by **valves** along the vessels that **close to prevent lymph flowing backwards** (helped by the squeezing of nearby muscles pushing the lymph forward). *(1 mark: correct ordered path from tissues to vessels/nodes; 1 mark: ends by emptying into veins/bloodstream; 1 mark: valves prevent backflow to keep flow one-way.)*

Q13. The lymphatic system acts as the **bridge** between the two internal responses. The early, **non-specific** response occurs at the **site of infection**, where **antigen-presenting cells** such as dendritic cells **capture antigen**. These cells then **travel through the lymphatic vessels** to a **lymph node**, where they **present the antigen to the helper T lymphocytes** (while the free antigen carried in the same lymph is bound directly by the matching **B lymphocytes**). This encounter starts the **specific (adaptive) response**. So by **transporting antigen and antigen-presenting cells** from the front line to the lymphocytes, the lymphatic system **connects** the non-specific and specific responses. *(1 mark: APCs capture antigen at the infection site; 1 mark: they travel via lymphatic vessels to a node; 1 mark: they present antigen to the helper T lymphocytes there, starting the adaptive response / linking the two.)*

Q14. (a) **W** = the **afferent lymphatic vessel** (bringing lymph into the node); **X** = the **lymph node**; **Y** = the **efferent lymphatic vessel** (carrying lymph out of the node); **Z** = a **valve**. (b) As the lymph passes through the node (**X**), the antigens it carries are **recognised by the T and B lymphocytes** concentrated there — specifically by the lymphocytes with the **matching receptor** — which begins the adaptive immune response. *(1 mark each for W, X, Y and Z correctly named = 4 marks; 1 mark: antigens are recognised by the T and B lymphocytes in the node.)*

Q15. The infection is in the **foot**, so the antigens (and antigen-presenting cells carrying them) enter the **tissue fluid** there and **drain into the lymphatic vessels** as lymph. Lymph flows **one way** along the vessels that **drain the leg**, and these vessels **pass through the lymph nodes behind the knee and in the groin** on the way back towards the bloodstream. The antigen is therefore delivered to **those** nodes, where it is **recognised** and the lymphocytes **multiply**, so it is those distant nodes — not the foot itself — that **swell**. *(1 mark: antigens/APCs from the foot enter the lymph; 1 mark: lymph flows one-way along the vessels draining the leg; 1 mark: those vessels pass through the knee/groin nodes; 1 mark: recognition there makes lymphocytes multiply, so those nodes swell.)*

Q16. (a) The diameter **increases** from 6 mm at day 0 to a **peak of 21 mm at day 6**, then **decreases** back to near its starting size (7 mm) by day 13. (b) During days 0–6, antigen arriving in the lymph is **recognised** by lymphocytes in the node, and those lymphocytes **multiply rapidly**; the node **fills with these cells and enlarges**, so its diameter rises. (c) After day 6 the **infection is being cleared**, so less antigen arrives, the **response winds down**, the extra lymphocytes are no longer produced in such numbers and the node **shrinks back** towards its normal size. *(1 mark: describes the rise to a peak then fall, with figures; 2 marks: rise explained by antigen recognition and lymphocyte multiplication filling the node; 1 mark: fall explained by the infection clearing / response winding down.)*

Q17. An infection in that arm produces antigens (and antigen-presenting cells) in the tissue fluid, but if the **lymphatic vessels draining the arm are damaged**, this material **cannot be carried away efficiently** as lymph. As a result, **fewer antigens and APCs reach the lymph nodes** where the lymphocytes are concentrated, so the antigen is **recognised more slowly and by fewer lymphocytes**. Since recognition in the node is what **triggers** the adaptive response, that response is **delayed or weaker**. *(1 mark: damaged vessels can't carry antigens/APCs away efficiently; 1 mark: fewer reach the lymph nodes / lymphocytes; 1 mark: so recognition is reduced/delayed, slowing or weakening the response.)*

Q18. Any one antigen can be recognised only by the **few lymphocytes whose receptors match it**. If all the lymphocytes were **spread thinly and evenly through the tissues**, the chance of the antigen happening to meet one of those few matching lymphocytes would be **extremely low**. By **concentrating** enormous numbers of B and T lymphocytes in **lymph nodes**, and by **channelling all the antigen-carrying lymph through those nodes**, the system brings the antigen and a huge sample of lymphocytes together in a small space — making it **very likely** that a matching lymphocyte will be present and recognise the antigen. Recognition is therefore **far more efficient** than it would be with lymphocytes spread out. *(1 mark: spread evenly through the tissues, the antigen would be very unlikely to meet one of the few lymphocytes that match it; 1 mark: a node concentrates enormous numbers of B and T lymphocytes in a small space and channels all the antigen-carrying lymph through them; 1 mark: the antigen is therefore brought into contact with a huge sample of lymphocytes, so a matching one is very likely to be present and recognition is far more efficient.)*

Q19. (a) The **independent variable** is the **time between the injection and the scan** — the variable the researchers deliberately changed. (Note that 1, 2, 4, 8, 12 and 24 hours are the *levels* of this variable, not the variable itself.) (b) The **dependent variable** is the **amount of label measured in the armpit lymph nodes** — the quantity measured to see the effect of the time elapsed. (c) Any one suitable controlled variable, with a reason. For example, every volunteer was given the **same dose of labelled antigen** (alternatively: the same injection site, the same muscle, the same scanner and settings). This must be held constant so that any difference in the amount of label found in the nodes can be attributed to the **time elapsed** alone; if some volunteers received a larger dose, more label would be detected for that reason rather than because more time had passed. *(1 mark: IV = time since injection; 1 mark: DV = amount of label in the armpit lymph nodes; 1 mark: one valid controlled variable with the reason that differences can then be attributed to the IV.)*

Q20. (a) In the infected throat, antigens from the pathogens enter the **tissue fluid**, and **antigen-presenting cells** (such as dendritic cells) also **take up antigen**. This tissue fluid drains into the **lymphatic capillaries** and becomes **lymph**, which flows **one way along the lymphatic vessels** to the **lymph nodes in the neck**, delivering the antigens and APCs to the lymphocytes there. (b) The **lymph node** concentrates huge numbers of **T and B lymphocytes** and channels all the antigen-carrying lymph through them, so it is the **site where the antigen is recognised** by the lymphocyte with the matching receptor; this recognition **initiates and coordinates the adaptive immune response**. (c) Once the antigen is recognised, the responding **lymphocytes multiply rapidly** and the node **fills with these cells and enlarges**, so the neck nodes become **swollen and tender**; this swelling is a **sign that an immune response is actively underway**. ∴ the lymphatic system transports the antigen from the throat to the neck nodes, where recognition begins the response and the resulting swelling signals that response. *(a: 3 marks — antigens/APCs enter tissue fluid, drain as lymph, carried to the neck nodes; b: 2 marks — node concentrates T and B lymphocytes and is where the antigen is recognised / response begins; c: 2 marks — lymphocytes multiply and fill the node so it swells, a sign of an active response.)*

Theory

The first two lines of defence act quickly but in the **same way against every invader** — they are non-specific. If a pathogen gets past them, or if body cells become infected or abnormal, the body calls on its **third line of defence**: the **adaptive immune response** (also called the **specific immune response**). This subtopic is about how that response works.

The adaptive immune response has two features that set it apart from the earlier lines of defence:

- It is **specific** — each response is targeted at **one particular antigen**, using cells whose receptors have a shape complementary to that antigen.
- It has **memory** — after the first encounter it leaves behind long-lived **memory cells**, so a second encounter with the same antigen produces a **faster and stronger** response.

Because it must first find and multiply the few cells that match a new antigen, the adaptive response is **slower to get going** the first time (it takes several days), whereas the earlier lines act within minutes to hours.

The two arms of the adaptive response. The third line of defence has two branches that work at the same time and deal with two different kinds of threat:

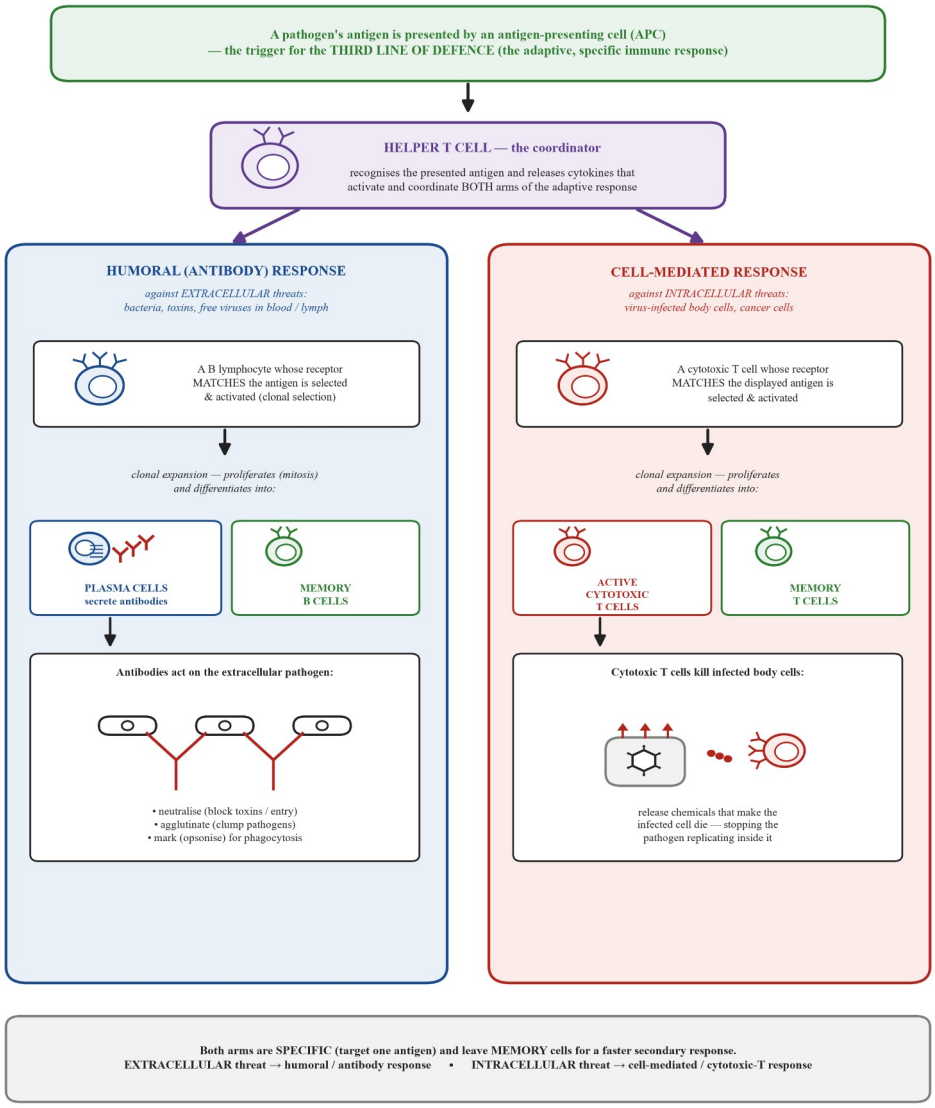
- The **humoral (antibody-mediated) response** deals with **extracellular threats** — pathogens and their products that are **outside** body cells, such as **bacteria, toxins and free viruses** travelling in the blood or lymph. It is carried out by **B lymphocytes**, which give rise to **antibodies**.
- The **cell-mediated response** deals with **intracellular threats** — antigens **hidden inside** the body's own cells, such as **virus-infected cells** and **cancer (abnormal) cells**. It is carried out by **T lymphocytes**, in particular **cytotoxic T cells**.

The trigger. Both arms begin only after a pathogen's **antigen is presented** to the lymphocytes by an **antigen-presenting cell (APC)** such as a macrophage or dendritic cell (the capturing and presenting of antigen is part of the earlier defences). Presentation of a non-self antigen is what **initiates** the third line of defence.

The lymphocytes. The cells of the adaptive response are **lymphocytes**, a type of white blood cell. Each lymphocyte carries membrane receptors of a **single specificity** — it can recognise **only one** antigen. There are two families:

- **B lymphocytes (B cells)** mature in the **bone marrow**. Their surface receptors are membrane-bound antibodies. When activated they form **plasma cells** and **memory B cells**.
- **T lymphocytes (T cells)** mature in the **thymus**. Two types are important here: **helper T cells**, which **coordinate** the whole response, and **cytotoxic T cells** (also called killer T cells), which **destroy infected body cells**.

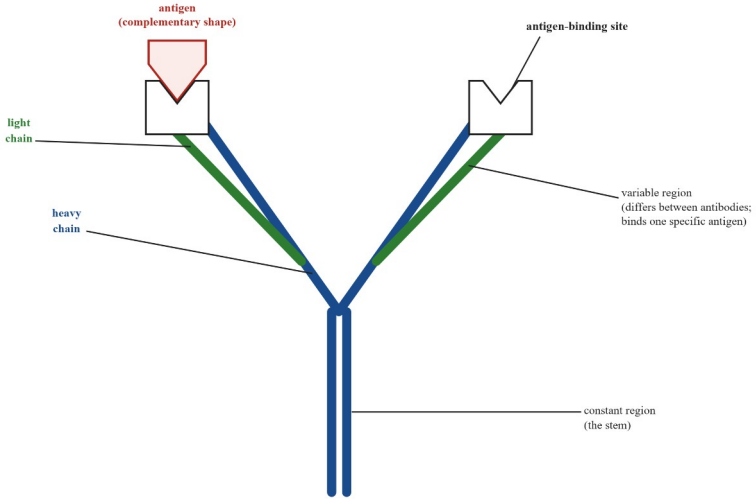
Clonal selection and clonal expansion. The body carries an enormous variety of lymphocytes, each matching a different antigen. When an antigen is presented, the few lymphocytes whose receptors have a **complementary shape** to that antigen are **selected and activated** — this is **clonal selection**. Each selected cell then **proliferates** (divides repeatedly by mitosis) to form a large **clone** of identical cells — this is **clonal expansion**. The clone differentiates into **effector cells**, which fight the current infection, and **memory cells**, which remain in the body long afterwards. Because only the cell that matches the antigen is selected, the response is **specific** to that antigen.



The humoral response — B cells and antibodies (extracellular threats). When an extracellular pathogen is met, the humoral arm produces antibodies against it:

1. A **B cell** whose surface receptor **matches** the antigen binds to it and is **selected**.
2. A **helper T cell** that has recognised the same presented antigen releases **cytokines** (chemical messengers) that fully **activate** the B cell.
3. The activated B cell undergoes **clonal expansion**, proliferating and **differentiating** into:
    - **Plasma cells** — effector cells that **secrete large numbers of antibodies** specific to the antigen. A plasma cell is essentially an antibody factory.
    - **Memory B cells** — long-lived cells that provide a rapid response if the same antigen returns.
4. The secreted **antibodies** travel in the blood and lymph and act on the extracellular pathogen.

Antibody structure. An **antibody** (also called an immunoglobulin) is a **Y-shaped protein**. It is built from four polypeptide chains — two longer **heavy chains** and two shorter **light chains** — held together in a Y. The two tips of the Y are the **antigen-binding sites**: an antibody has **two identical binding sites**, one at the end of each arm. These sites lie in the **variable region**, whose shape **differs from one antibody to another**, so each antibody binds **only the one antigen** whose shape is **complementary** to its binding sites (a lock-and-key fit). The stem is the **constant region**, which is **the same from one antibody to the next**.



An antibody is a Y-shaped protein with TWO identical antigen-binding sites.

How antibodies act. Antibodies do **not** usually destroy a pathogen by themselves; instead they bind its antigens and disable or tag it in three main ways:

- **Neutralisation.** Antibodies bind to a **toxin**, or to the surface molecules a virus or bacterium uses to enter cells, **blocking** them. The toxin can no longer act and the pathogen can no longer attach to or enter host cells.
- **Agglutination.** Because each antibody has **two** binding sites, one antibody can bind **two** pathogens at once, cross-linking many of them into **clumps**. Clumped pathogens cannot spread easily and are simpler to remove.
- **Marking (opsonisation).** Antibodies **coat** a pathogen, flagging it so that **phagocytes recognise and engulf it more readily**. The antibody acts as a label that says "destroy this".

The cell-mediated response — cytotoxic T cells (intracellular threats). Antibodies circulate in the body's fluids and so **cannot reach a pathogen that is hidden inside a cell**. A virus that has entered a body cell, or a cell that has become **cancerous** and begun to divide uncontrollably, is dealt with by the **cell-mediated** arm:

1. An infected or abnormal cell **displays fragments of the foreign or abnormal antigen on its surface markers (MHC markers)**, advertising that something is wrong inside it.
2. A **cytotoxic T cell** whose receptor **matches** the displayed antigen is **selected and activated** (helped by cytokines from helper T cells) and undergoes clonal expansion.
3. The active cytotoxic T cells **bind to the infected cells** and **release chemicals that make each infected cell die**. Destroying the host cell **stops the pathogen inside it from replicating and spreading** to other cells.
4. **Memory T cells** also form, ready for a future encounter.

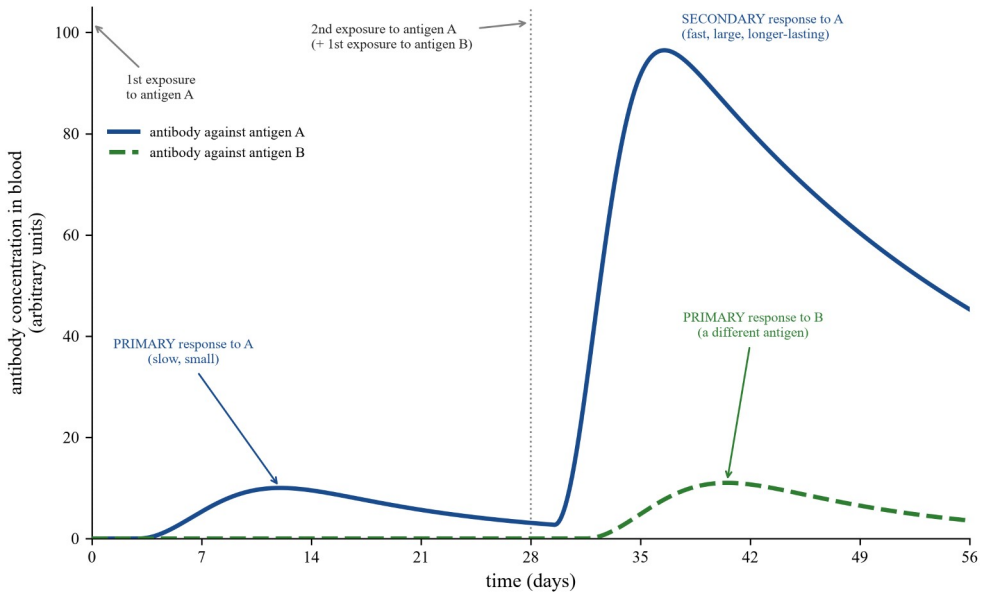
The helper T cell — the coordinator. The **helper T cell** is the central organiser of the whole adaptive response. After recognising a presented antigen, it releases **cytokines** that **activate and coordinate both arms**: they help activate the **B cells** of the humoral response and the **cytotoxic T cells** of the cell-mediated response. Because both arms depend on this help, the helper T cell is described as the **coordinator** — if helper T cells are lost, the entire adaptive response is crippled.

Matching the threat to the response. The key link to remember is:

- **EXTRACELLULAR** threat (bacteria, toxins, free viruses) → **humoral** response → **B cells** → **plasma cells** → **antibodies**.
- **INTRACELLULAR** threat (virus-infected cells, cancer cells) → **cell-mediated** response → **cytotoxic T cells kill the affected cells**.

Memory, and the primary versus secondary response. The **first** time the body meets a particular antigen it mounts a **primary response**. Clonal selection and expansion take time, so there is a **lag of several days** before antibody levels rise, and the response is **relatively slow and small**. During this response, **memory cells** are formed and remain in the body.

If the **same** antigen is met **again**, the **memory cells** recognise it immediately and rapidly proliferate into effector cells. This **secondary response** is **faster** (shorter lag), reaches a **higher** antibody level, and **lasts longer** than the primary response. This is why recovering from an infection often protects a person against becoming ill from the **same** pathogen a second time. Importantly, memory is **specific**: memory cells formed against one antigen give **no** head start against a **different** antigen, which still produces only a slow, small primary response.



Worked examples

Example 1 — scaffolded

A species of bacterium enters the bloodstream, where it multiplies. Outline how the humoral arm of the third line of defence produces antibodies against this bacterium.

Working	Comment
The bacterium is an **extracellular** threat, so the **humoral (antibody) response** deals with it.	Identify the arm first — extracellular threats are handled by antibodies.
A **B lymphocyte** whose surface receptor **matches** the bacterium's antigen binds it and is **selected** (clonal selection).	Only the B cell with a complementary receptor is chosen — this makes the response specific.
A **helper T cell** releases **cytokines** that **activate** the selected B cell.	Name the helper T cell's role — it coordinates/activates the B cell.
The B cell undergoes **clonal expansion**, dividing and differentiating into **plasma cells** and **memory B cells**.	Two products: effector plasma cells now, memory cells for later.
The **plasma cells secrete large numbers of antibodies** that circulate and act on the bacterium.	The plasma cell is the antibody-producing effector cell.

Example 2 — scaffolded

A virus infects several of a person's body cells. Describe how the cell-mediated response deals with the infected cells.

Working	Comment
Once the virus is **inside** a body cell it is an **intracellular** threat, which antibodies cannot reach; the **cell-mediated response** is needed.	Explain why the humoral arm cannot do the job here.
The **infected cells display fragments of viral antigen on their surface markers**.	This is how the immune system "sees" that a cell is infected.
A **cytotoxic T cell** with a **matching receptor** is **selected**	Clonal selection and expansion of the correct cytotoxic

Working	Comment
and activated (with help from helper T cells) and multiplies.	T cell.
The active cytotoxic T cells **bind the infected cells and release chemicals that kill them**.	State the killing action clearly.
Destroying the infected cells **stops the virus replicating and spreading**; **memory T cells** also form.	Give the purpose of the killing, plus the memory outcome.

Example 3 — unscaffolded

Explain how the structure of an antibody suits its function, referring both to how it recognises an antigen and to one way it helps remove a pathogen.

An antibody is a **Y-shaped protein** with **two identical antigen-binding sites**, one at the tip of each arm. These sites lie in the **variable region**, whose shape differs between antibodies, so a binding site is **complementary** to just one antigen — this lets the antibody **recognise and bind only that specific antigen** (a lock-and-key fit). Having **two** binding sites also suits its function: one antibody can bind **two** pathogens at once and cross-link many of them into **clumps** (**agglutination**), which stops the pathogens spreading and makes them easier for phagocytes to engulf. ∴ the antibody's specific binding sites let it target one antigen, and its two-armed shape lets it clump pathogens together for removal.

Example 4 — unscaffolded

After recovering from an infection with a particular virus, a person is exposed to the **same** virus a year later but does not become ill. However, when exposed to a **different** virus they do become ill. Explain these observations.

During the first infection the adaptive response mounted a **primary response** and formed **memory cells** specific to that virus's antigen. When the **same** virus is met again, these **memory cells** recognise the antigen immediately and rapidly produce effector cells, giving a **secondary response** that is **faster and stronger** than the first. The pathogen is cleared **before it can cause illness**. The protection is **specific**, however: the memory cells match only the **first** virus's antigen. A **different** virus carries a **different** antigen for which the person has **no matching memory cells**, so it produces only a **slow, small primary response**, and the person can become ill while that response develops. ∴ memory gives fast, strong protection against the same antigen, but not against a new one.

Practice questions

Scaffolded

Q1. Define each of the following terms: (a) clonal selection; (b) plasma cell; (c) memory cell.

Q2. The adaptive immune response has two arms. (a) Name the arm that defends against extracellular threats. (b) Name the arm that defends against intracellular threats. (c) State two features that characterise the third line of defence (adaptive response).

Q3. Antibodies are produced during the humoral response. (a) Name the cell that secretes antibodies. (b) Describe the overall shape of an antibody and state how many antigen-binding sites it has. (c) Explain what determines which antigen a particular antibody can bind.

Q4. Helper T cells and cytotoxic T cells have different roles. (a) State the role of a helper T cell. (b) State the role of a cytotoxic T cell. (c) Explain why a cytotoxic T cell, rather than an antibody, is needed once a virus is inside a body cell.

Q5. A B lymphocyte is activated by an antigen. (a) State what is meant by clonal expansion. (b) Name the two types of cell that an activated B lymphocyte differentiates into. (c) State the function of each of these two cell types.

Q6. The cells of the third line of defence are lymphocytes. (a) Name the two families of lymphocyte and state where each matures. (b) State what is meant by saying that each lymphocyte carries receptors of a single specificity. (c)

Explain why a pathogen's antigen must be presented by an antigen-presenting cell before the adaptive response can begin.

Unscaffolded

Q7. Distinguish between the humoral response and the cell-mediated response, referring to the type of threat each deals with and the main type of cell that carries it out. *(4 marks)*

Q8. An antibody is built from four polypeptide chains and contains a variable region and a constant region. Name the two types of polypeptide chain, describe where the variable region and the constant region lie in the Y-shaped molecule, and state which of the two regions is the same from one antibody to the next. *(3 marks)*

Q9. Antibodies do not usually destroy a pathogen directly. Describe **three** ways in which antibodies help the body deal with an extracellular pathogen. *(3 marks)*

Q10. Explain the role of the helper T cell in the adaptive immune response, and why it is described as the coordinator of the response. *(3 marks)*

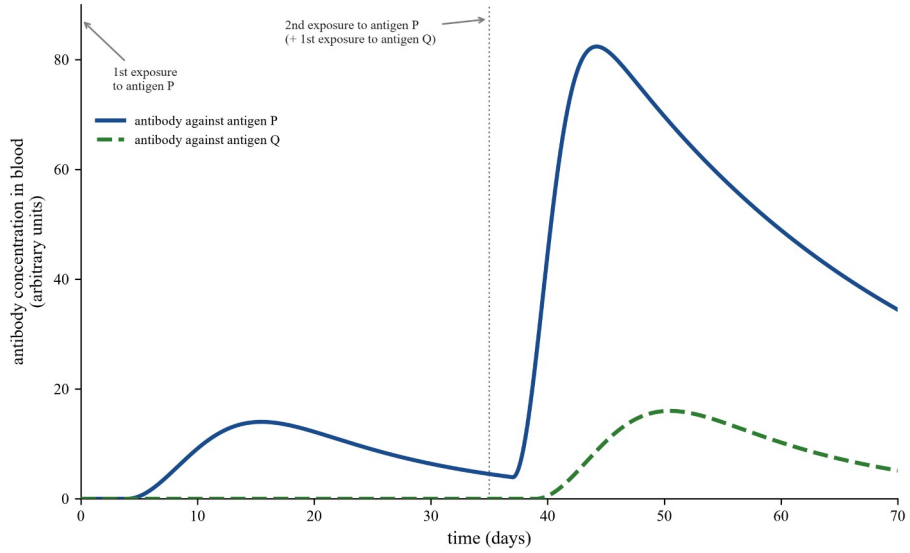
Q11. A body cell becomes cancerous and begins to display abnormal proteins on its surface. Explain how the cell-mediated response recognises and destroys this cell, and state what would happen to the abnormal cell if it were not destroyed. *(4 marks)*

Q12. In a rare condition, a person's lymphocytes are selected and activated normally but are then unable to undergo clonal expansion. Predict the effect this would have on the person's response to a first infection, and on their response if the same pathogen returned years later. Explain your predictions. *(4 marks)*

Q13. For each of the following threats, name the arm of the adaptive response that would deal with it, and justify your choice: (i) a bacterial toxin circulating in the blood; (ii) a body cell infected with a virus; (iii) a cancerous body cell. *(3 marks)*

Q14. Explain what is meant by clonal selection, and how it makes the adaptive immune response specific to a particular antigen. *(3 marks)*

Q15. *(Stimulus.)* The graph below shows the concentration of antibodies against two antigens, P and Q, over 70 days. Antigen P was introduced on day 0 and again on day 35; antigen Q was introduced for the first time on day 35.



Compare the antibody response to antigen P after day 35 with the response to antigen Q, and explain what the difference between them shows about the adaptive immune system. *(4 marks)*

Q16. *(Data interpretation.)* The table shows the concentration of antibodies (arbitrary units) measured after a first, and then a second, exposure to the **same** antigen.

Days after exposure	After 1st exposure	After 2nd exposure
0	0	0

Days after exposure	After 1st exposure	After 2nd exposure
3	0	15
6	2	60
9	6	90
12	9	78

(a) State the antibody concentration on day 9 after each exposure, and calculate the difference between them.

(b) Using the data, describe **two** ways in which the response to the second exposure differed from the response to the first.

(c) Explain, in terms of memory cells, why the second exposure produced this different response. *(4 marks)*

Q17. The first and second lines of defence act within minutes to hours, but the third line of defence takes several days to become effective the first time a particular antigen is met. Explain why the third line is so much slower to act. *(3 marks)*

Q18. *(Application.)* A person has a condition in which their helper T cells are absent. Predict the effect this would have on **both** the humoral and the cell-mediated responses, and explain your prediction. *(4 marks)*

Q19. Distinguish between a memory B cell and a memory T cell in terms of the arm of the adaptive response each belongs to and the cells each gives rise to when the same antigen is met again. *(2 marks)*

Q20. *(Research.)* Researchers grew identical samples of virus-infected tissue in the laboratory. To **Group 1** they added cytotoxic T cells that matched the virus; from **Group 2** these cytotoxic T cells were left out. They then measured the amount of virus (the viral load) in each sample over six days. The viral load rose steadily in Group 2 but fell in Group 1. (a) Identify the independent variable and the dependent variable in this experiment. (b) Using your knowledge of the cell-mediated response, explain the difference in viral load between the two groups. (c) State one variable that should have been kept the same between the two groups. *(4 marks)*

Q21. *(Synthesis.)* A new respiratory virus, provisionally named **Virus K**, spreads through a population. When it infects a person, some virus particles travel free in the blood while other particles enter and infect the person's airway cells. An antigen-presenting cell presents Virus K antigen to the person's lymphocytes. (a) Describe how the body produces antibodies against the free Virus K particles, and describe **one** way those antibodies act on the virus. *(4 marks)* (b) Explain how the body destroys the airway cells that Virus K has already infected. *(2 marks)* (c) Explain why, if the same person is infected with Virus K again some years later, they are likely to recover more quickly. *(2 marks) (8 marks)*

Answers

Q1. (a) The selection and activation of the lymphocyte(s) whose receptor matches a presented antigen. (b) An effector B cell that secretes large numbers of antibodies. (c) A long-lived lymphocyte that remains after an infection and gives a fast, strong secondary response to the same antigen. **Q2.** (a) The humoral (antibody-mediated) response. (b) The cell-mediated response. (c) Any two of: it is specific (targets one antigen); it has memory; (it is slower to develop on first exposure). **Q3.** (a) A plasma cell. (b) Y-shaped; two antigen-binding sites. (c) The shape of its binding sites (variable region), which must be complementary to the antigen. **Q4.** (a) Recognises presented antigen and releases cytokines that activate and coordinate both arms (B cells and cytotoxic T cells). (b) Recognises and kills infected/abnormal body cells. (c) Antibodies cannot reach inside a cell; a cytotoxic T cell can recognise the antigen displayed on the infected cell and destroy it. **Q5.** (a) The activated lymphocyte proliferates (divides by mitosis) to form a clone of identical cells. (b) Plasma cells and memory B cells. (c) Plasma cells secrete antibodies; memory B cells give a fast secondary response later. **Q6.** (a) B lymphocytes, which mature in the bone marrow; T lymphocytes, which mature in the thymus. (b) All of its receptors have the same shape, so it can recognise only one antigen. (c) Presentation displays the antigen where lymphocytes can meet it, so the few whose receptors are complementary to it can be selected and activated; without this the specific response is never initiated. **Q7.** Humoral: deals with extracellular threats; carried out by B cells → plasma cells → antibodies. Cell-mediated: deals with intracellular threats; carried out by cytotoxic T cells that kill infected cells. **Q8.** Two longer heavy chains and two shorter light chains. The variable region forms the two tips of the arms (where the antigen-binding sites are); the constant region forms the stem. The constant region is the one that is the same from one antibody to the next. **Q9.** Neutralisation (block toxins/entry); agglutination (clump pathogens); marking/opsonisation (tag for phagocytosis). **Q10.** It recognises presented antigen and releases cytokines that activate both B cells (humoral) and cytotoxic T cells (cell-mediated); it is the coordinator because both arms depend on its help. **Q11.** The abnormal proteins are displayed as non-self antigen on the cell's surface markers; a cytotoxic T cell with a matching receptor is selected, activated and multiplies; it binds the abnormal cell and releases chemicals that make it die; otherwise the abnormal cell would keep dividing to produce more abnormal cells. **Q12.** The matching lymphocyte would still be selected and activated, but could not multiply into a clone, so only a handful of effector cells (and very little antibody) would be produced — far too few to control a first infection. Almost no memory cells would form either, so a later encounter with the same pathogen would again produce only a weak, slow response. **Q13.** (i) Humoral — the toxin is extracellular, so antibodies neutralise it. (ii) Cell-mediated — the virus is now intracellular, so cytotoxic T cells kill the infected cell. (iii) Cell-mediated — the cancer cell is an abnormal body cell, killed by cytotoxic T cells. **Q14.** The lymphocyte whose receptor is complementary to the antigen is selected and activated from the many present; only that matching cell responds, so the response targets that specific antigen. **Q15.** After day 35 the response to P is fast and large (a secondary response); the response to Q is slow and small (a primary response). This shows memory (the body had met P before) and specificity (memory to P gives no head start against the different antigen Q). **Q16.** (a) Day 9: 6 (first) and 90 (second); difference = 84. (b) Faster (antibodies detectable by day 3, whereas none were detectable until day 6 after the first exposure) and much higher (a peak of 90 units on day 9, whereas the first response had reached only 9 units by day 12 and was still rising). (c) Memory cells from the first exposure respond rapidly to the second exposure. **Q17.** The first two lines act the same way against every invader, so nothing has to be matched to the pathogen and they act at once. The third line must first have the antigen presented, then select the few lymphocytes whose receptors match it, then multiply those few into effector cells — which takes days. **Q18.** Both arms would be severely impaired: without helper T cells, B cells are poorly activated (few antibodies, weak humoral response) and cytotoxic T cells are poorly activated (weak cell-mediated response), leaving the person vulnerable to infection. **Q19.** A memory B cell belongs to the humoral arm and gives rise to plasma cells that secrete antibodies; a memory T cell belongs to the cell-mediated arm and gives rise to active cytotoxic T cells that kill infected or abnormal body cells. **Q20.** (a) IV = presence/absence of matching cytotoxic T cells; DV = viral load. (b) In Group 1 the cytotoxic T cells killed the infected cells, stopping viral replication, so viral load fell; in Group 2, with no cytotoxic T cells, the virus kept replicating and viral load rose. (c) Any one of: type/amount of tissue, virus type and starting amount, temperature, time period. **Q21.** (a) A B cell with a matching receptor is selected and activated (helper-T help), undergoes clonal expansion and forms plasma cells that secrete antibodies; the antibodies neutralise / agglutinate / mark the free virus. (b) A cytotoxic T cell recognises viral antigen displayed on the infected airway cells and kills them, stopping viral replication. (c) Memory cells formed in the first infection give a faster, stronger secondary response.

Fully-worked solutions

Q1. (a) **Clonal selection** is the **selection and activation of the lymphocyte(s) whose receptor matches (is complementary to) a presented antigen** — out of the huge variety of lymphocytes, only the matching one is chosen. (b) A **plasma cell** is an **effector B cell** that **secretes large numbers of antibodies** specific to the antigen. (c) A **memory cell** is a **long-lived lymphocyte** that remains in the body after an infection and enables a **fast, strong secondary response** if the **same** antigen is met again.

Q2. (a) The **humoral (antibody-mediated) response**. (b) The **cell-mediated response**. (c) Any **two** of: it is **specific** (each response targets one particular antigen); it has **memory** (it leaves memory cells for a faster secondary response); it is **slower to develop on first exposure** (it must first select and multiply the matching cells).

Q3. (a) A **plasma cell** secretes antibodies. (b) An antibody is **Y-shaped** and has **two** antigen-binding sites. (c) The antigen a particular antibody can bind is determined by the **shape of its antigen-binding sites** (in the **variable region**): only an antigen whose shape is **complementary** to those sites will bind, so each antibody is specific to one antigen.

Q4. (a) A **helper T cell** recognises the **presented antigen** and releases **cytokines** that **activate and coordinate both arms** of the response (both B cells and cytotoxic T cells). (b) A **cytotoxic T cell recognises and kills infected or abnormal body cells**. (c) An **antibody circulates in body fluids and cannot enter a cell**, so once a virus is **inside** a body cell an antibody cannot reach it. A **cytotoxic T cell**, however, can recognise the **viral antigen displayed on the infected cell's surface** and **destroy the whole cell**, dealing with the intracellular threat.

Q5. (a) **Clonal expansion** is the **proliferation** of the activated lymphocyte — it **divides repeatedly by mitosis** to form a large **clone of identical cells**. (b) An activated B lymphocyte differentiates into **plasma cells** and **memory B cells**. (c) **Plasma cells secrete antibodies** against the antigen (the effector cells of the current response); **memory B cells** persist long-term and provide a **rapid secondary response** if the same antigen returns.

Q6. (a) The two families are **B lymphocytes (B cells)**, which mature in the **bone marrow**, and **T lymphocytes (T cells)**, which mature in the **thymus**. (b) Every receptor on a given lymphocyte has the **same shape**, so that one cell can **recognise only one antigen**; the body copes with the range of antigens it meets by carrying an enormous **variety** of lymphocytes rather than by giving any one cell a range of receptors. (c) An **antigen-presenting cell** (such as a macrophage or dendritic cell) **displays fragments of the pathogen's antigen on its own surface**, where circulating lymphocytes can encounter it. Only then can the few lymphocytes whose receptors are **complementary** to that antigen bind it and be **selected and activated**. Presentation of a **non-self antigen** is therefore the **trigger** — without it the third line of defence is never initiated.

Q7. The **humoral response** deals with **extracellular threats** (pathogens and toxins outside cells, such as bacteria and free viruses) and is carried out by **B lymphocytes**, which form **plasma cells** that secrete **antibodies**. The **cell-mediated response** deals with **intracellular threats** (antigens inside the body's own cells, such as virus-infected or cancer cells) and is carried out by **cytotoxic T cells**, which **kill the affected body cells**. So the two arms differ both in the **kind of threat** (outside versus inside cells) and in the **main cell** (B cells/antibodies versus cytotoxic T cells). *(1 mark: humoral targets extracellular threats; 1 mark: humoral uses B cells → antibodies; 1 mark: cell-mediated targets intracellular threats; 1 mark: cell-mediated uses cytotoxic T cells that kill infected cells.)*

Q8. An antibody is built from **two longer heavy chains** and **two shorter light chains**, held together in a Y. The **variable region** lies at the **two tips of the arms**, where the two **antigen-binding sites** are; the **constant region** forms the **stem** of the Y. Of the two, it is the **constant region** that is **the same from one antibody to the next** — the variable region is the part that differs between antibodies, which is why different antibodies bind different antigens. *(1 mark: two heavy chains and two light chains; 1 mark: variable region at the arm tips, constant region as the stem; 1 mark: the constant region is the one that is the same in different antibodies.)*

Q9. Antibodies help deal with an extracellular pathogen in three main ways. **(1) Neutralisation** — they bind to a **toxin** or to the molecules a pathogen uses to enter cells, **blocking** them so the pathogen or toxin can no longer act. **(2) Agglutination** — because each antibody has two binding sites, antibodies **cross-link pathogens into clumps**, which stops them spreading and makes them easier to remove. **(3) Marking (opsonisation)** — antibodies **coat the pathogen**, tagging it so that **phagocytes recognise and engulf it more readily**. *(1 mark each for neutralisation, agglutination and marking/opsonisation, correctly described.)*

Q10. The **helper T cell** recognises the **antigen presented** by an antigen-presenting cell and then releases **cytokines** — chemical messengers that **activate and coordinate both arms** of the adaptive response. Its cytokines help **activate the B cells** of the **humoral** response and the **cytotoxic T cells** of the **cell-mediated** response. It is described as the **coordinator** because **both arms depend on this help**: without helper T cells neither the antibody response nor the killing of infected cells proceeds properly. *(1 mark: recognises presented antigen / releases cytokines; 1 mark: activates both B cells and cytotoxic T cells; 1 mark: it is the coordinator because both arms depend on it.)*

Q11. The **abnormal proteins** on the cancerous cell act as **non-self antigen displayed on the cell's surface markers (MHC markers)**, advertising that the cell is abnormal. A **cytotoxic T cell whose receptor is complementary** to that antigen is **selected and activated** (helped by cytokines from a helper T cell) and undergoes **clonal expansion**. The active cytotoxic T cells then **bind the abnormal cell and release chemicals that make it die**. If the cell were **not destroyed** it would **go on dividing uncontrollably**, producing **more and more abnormal cells**. *(1 mark: the abnormal proteins are displayed as non-self antigen on the cell's surface markers; 1 mark: a cytotoxic T cell with a matching receptor is selected, activated and multiplies; 1 mark: it binds the abnormal cell and releases chemicals that kill it; 1 mark: otherwise the abnormal cell keeps dividing to produce more abnormal cells.)*

Q12. Clonal selection would still work normally: the few lymphocytes whose receptors are **complementary** to the antigen would still be **selected and activated**. What they could not do is **clonal expansion** — **divide repeatedly by mitosis** into a large **clone of identical cells**. Only a **handful of effector cells** would therefore ever exist, so the person would secrete **far too little antibody**, and make **far too few active cytotoxic T cells**, to bring a **first infection** under control; the infection would be severe and slow to clear. The clone is also the source of **memory cells**, so **almost no memory cells** would be left behind. If the **same pathogen returned years later**, there would be **no fast, strong secondary response** — the person would again mount only the same weak, slow response, and would be **just as vulnerable** as the first time. *(1 mark: clonal selection is unaffected — the matching lymphocyte is still selected and activated; 1 mark: without clonal expansion only a handful of effector cells forms; 1 mark: too little antibody / too few cytotoxic T cells to control the first infection; 1 mark: almost no memory cells form, so a later encounter with the same pathogen produces no faster or stronger response.)*

Q13. (i) A **bacterial toxin in the blood** is an **extracellular** threat, so the **humoral response** deals with it — **antibodies neutralise** the toxin. **(ii)** A **virus-infected body cell** is an **intracellular** threat, so the **cell-mediated response** deals with it — **cytotoxic T cells kill the infected cell**. **(iii)** A **cancerous body cell** is an **abnormal body cell** (an intracellular-type threat), so the **cell-mediated response** deals with it — **cytotoxic T cells kill the abnormal cell**. *(1 mark each: (i) humoral/antibodies for the extracellular toxin; (ii) cell-mediated/cytotoxic T for the infected cell; (iii) cell-mediated/cytotoxic T for the cancer cell.)*

Q14. Clonal selection means that, from the enormous variety of lymphocytes present, only the lymphocyte whose **receptor is complementary to the presented antigen** is **selected and activated**. Because **only that matching cell responds** (and then multiplies to form a clone), the response is directed at **that one antigen** and no other — this is what makes the adaptive response **specific**. *(1 mark: only the lymphocyte with a matching/complementary receptor is selected; 1 mark: that selected cell is activated and proliferates; 1 mark: so the response targets that specific antigen — specificity.)*

Q15. After **day 35**, the antibody response to **antigen P rises quickly to a high level** — a **secondary response** — because antigen P had been met before (on day 0) and **memory cells** were formed. The response to **antigen Q**, met for the first time on day 35, is **slow and reaches only a low level** — a **primary response**. The difference shows two things about the adaptive immune system: it has **memory** (the strong, fast response to P occurs because the body remembers P), and it is **specific** (the memory cells for P give **no advantage** against the different antigen Q, which still produces only a primary response). *(1 mark: P after day 35 is fast and large / secondary; 1 mark: Q is slow and small / primary; 1 mark: this demonstrates memory; 1 mark: this demonstrates specificity.)*

Q16. (a) On **day 9** the antibody concentration was **6** units after the first exposure and **90** units after the second exposure; the difference is **90 − 6 = 84 units**. (b) The response to the second exposure was **faster** (antibodies were already detectable by **day 3**, whereas after the first exposure none were detectable until **day 6**) and reached a **far higher antibody concentration** (it **peaked at 90 units on day 9**, whereas after the first exposure the concentration had reached only **9 units by day 12** and was **still rising**). (c) During the first exposure, **memory cells** specific to the antigen were formed. On the second exposure these **memory cells recognised the antigen at once and proliferated rapidly** into antibody-secreting cells, producing antibodies **sooner and in far greater amounts**. *(1 mark: day-9 values 6 and 90, difference 84; 2 marks: two valid differences — an earlier/faster rise and a far higher antibody*

concentration — each supported with data; 1 mark: memory cells from the first exposure give the rapid, larger second response.)

Q17. The **first and second lines of defence are non-specific** — they act in the **same way against every invader**, so nothing has to be matched to the particular pathogen and they can act **immediately**. The **third line is specific**, and that costs time. The antigen must first be **presented**; then the **few lymphocytes whose receptors are complementary to that one antigen** have to be found and **selected** from the enormous variety present (**clonal selection**); and those few cells must then **proliferate by mitosis** into a large clone and **differentiate into effector cells** (**clonal expansion**) before enough plasma cells or cytotoxic T cells exist to control the infection. Building the response from a handful of matching cells is what **takes several days**. *(1 mark: the first two lines are non-specific, so they need no matching step and act at once; 1 mark: the third line must have the antigen presented and select the few lymphocytes with a complementary receptor; 1 mark: those few cells must then proliferate and differentiate into effector cells, which takes days.)*

Q18. Without functioning **helper T cells**, **both arms** of the adaptive response would be **severely impaired**, because the helper T cell is the **coordinator** that activates them. In the **humoral** response, the **B cells would be poorly activated**, so few plasma cells and **few antibodies** would be produced. In the **cell-mediated** response, the **cytotoxic T cells would be poorly activated**, so infected and abnormal body cells would **not be efficiently killed**. As a result, the person's adaptive immunity would be **greatly weakened** and they would be **highly vulnerable to infection**. *(1 mark: helper T cell coordinates/activates both arms, so both are affected; 1 mark: humoral impaired — B cells poorly activated, few antibodies; 1 mark: cell-mediated impaired — cytotoxic T cells poorly activated; 1 mark: overall adaptive response severely weakened / person vulnerable.)*

Q19. A **memory B cell** belongs to the **humoral (antibody-mediated) arm**: when the same antigen is met again it proliferates rapidly and gives rise to **plasma cells**, which **secrete antibodies** against the extracellular pathogen. A **memory T cell** belongs to the **cell-mediated arm**: on re-exposure it gives rise to **active cytotoxic T cells**, which **kill body cells that are infected or abnormal**. *(1 mark: memory B cell — humoral arm, gives plasma cells that secrete antibodies; 1 mark: memory T cell — cell-mediated arm, gives cytotoxic T cells that kill infected/abnormal cells.)*

Q20. (a) The **independent variable** is the **presence or absence of matching cytotoxic T cells** (added to Group 1, left out of Group 2); the **dependent variable** is the **viral load** measured over six days. (b) In **Group 1**, the **cytotoxic T cells recognised and killed the infected cells**, which **stopped the virus replicating**, so the **viral load fell**. In **Group 2**, with **no cytotoxic T cells**, the infected cells were not killed and the **virus continued to replicate and spread**, so the **viral load rose**. This shows the cell-mediated response controls an intracellular infection. (c) Any **one** of: the **type and amount of tissue**, the **type and starting amount of virus**, the **temperature**, or the **time period over which viral load was measured**. *(1 mark: correct IV and DV; 2 marks: cytotoxic T cells killed infected cells and lowered viral load in Group 1, virus replicated unchecked in Group 2; 1 mark: a valid controlled variable.)*

Q21. (a) An **antigen-presenting cell presents Virus K antigen**, and a **B lymphocyte whose receptor matches** that antigen is **selected and activated** (with cytokines from a **helper T cell**). The B cell undergoes **clonal expansion** and differentiates into **plasma cells**, which **secrete antibodies** specific to Virus K. These antibodies act on the **free virus particles** — for example by **neutralising** them (binding the virus so it can no longer enter host cells), or by **agglutinating** (clumping) them, or by **marking** them for phagocytosis. *(1 mark: matching B cell selected and activated; 1 mark: clonal expansion into plasma cells; 1 mark: plasma cells secrete antibodies against Virus K; 1 mark: one correct antibody action described.)* (b) The **infected airway cells display Virus K antigen on their surface markers**. A **cytotoxic T cell with a matching receptor** recognises this, **binds the infected cell and releases chemicals that kill it**, which **stops the virus replicating** inside those cells. *(1 mark: cytotoxic T cell recognises viral antigen on the infected cell; 1 mark: kills the infected cell, halting viral replication.)* (c) During the first infection, **memory cells** specific to Virus K were formed. On a later infection with the **same virus**, these memory cells produce a **faster and stronger secondary response**, clearing the virus more quickly, so the person recovers sooner. ∴ immunological memory gives faster recovery on re-infection. *(1 mark: memory cells formed in the first infection; 1 mark: they give a faster/stronger secondary response on re-infection.)*

Theory

When a pathogen breaks through the innate defences (7A–7B), the **adaptive immune response** (7D) fights it using **antibodies** and produces **memory cells**. That response is what gives a person **immunity** — the ability to resist a particular pathogen. But immunity does not always have to be built by the person themselves, and it is not always gained by chance. This subtopic sorts out the different ways immunity is **acquired**, classifying each along **two independent axes**:

- **active vs passive** — *whose* antibodies are protecting the person, and whether memory forms;
- **natural vs artificial** — *how* the immunity was acquired (through ordinary life, or through a deliberate medical intervention).

Active immunity — the body makes its own defences. In **active immunity**, the person's **own** adaptive immune system meets the antigen and mounts its own response: it makes its **own antibodies** and forms its **own memory cells**. Because the body has to build this response from scratch, active immunity is **slow to develop** — it takes **days to weeks** for antibody levels to rise after the first exposure. In return, it is **long-lasting**: the memory cells persist (often for years, sometimes for life), so that if the same antigen is met again the response is **faster and larger** and the person usually does not become ill. Active immunity is protection the person has **earned** and can **maintain**.

Passive immunity — ready-made antibodies are handed over. In **passive immunity**, the person does **not** make the antibodies. Instead, **ready-made antibodies** produced by someone (or something) else are introduced into their body. Because working antibodies are present the moment they arrive, protection is **immediate**. But it is **short-term**: the borrowed antibodies are gradually **broken down** and are **not replaced**, because the person's own adaptive system was never activated and **no memory cells form**. Once the antibodies are gone (typically after a few **weeks to months**), the protection is gone, and re-exposure produces no faster response. Passive immunity is protection that is **borrowed** — fast, but temporary.

Natural vs artificial — how the immunity was acquired. This second axis is about the *route*:

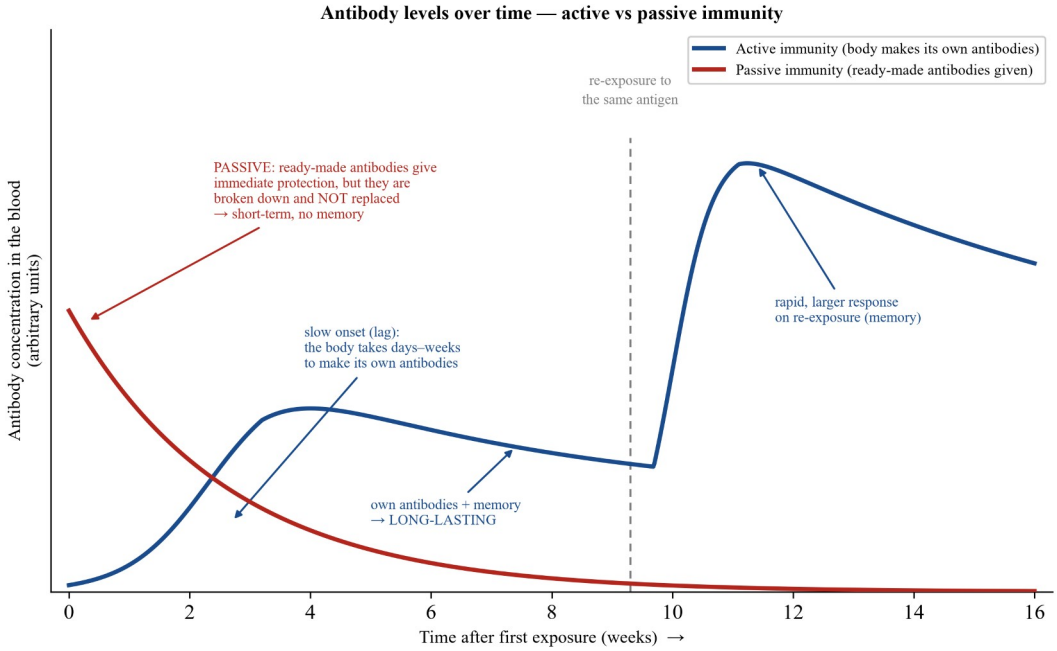
- **Natural** immunity is acquired through **ordinary living**, with **no medical intervention** — by catching an infection, or by antibodies passing naturally from a mother to her baby.
- **Artificial** immunity is acquired **deliberately, through a medical intervention** — by being vaccinated, or by being injected with ready-made antibodies.

Combining the two axes gives **four types** of acquired immunity:

- **Natural active** — immunity gained by **catching the infection**. The body meets the live pathogen, makes its own antibodies and memory cells, and is left with lasting protection (e.g. lifelong immunity after recovering from chickenpox).
- **Artificial active** — immunity gained by **vaccination**. A vaccine contains a **harmless form of the antigen** (such as a weakened or dead pathogen, or one of its molecules), which triggers the body's **own** antibody production and memory — **without** the person having to suffer the disease (e.g. a tetanus or measles vaccine).
- **Natural passive** — **ready-made antibodies transferred from mother to baby**. Antibodies cross the **placenta** to the foetus before birth, and pass in **breast milk and colostrum** after birth, protecting the baby while its own adaptive system is still developing.
- **Artificial passive** — **ready-made antibodies injected** as an **antiserum** (or immunoglobulin). These give instant protection in an emergency (e.g. antivenom after a snake bite, or anti-tetanus immunoglobulin after a deep wound).

Notice that the **active/passive** axis and the **natural/artificial** axis are independent: the two active types both build the body's own memory (they differ only in *how* the antigen was met), and the two passive types both hand over ready-made antibodies (they differ only in *how* those antibodies were delivered).

Speed of onset and duration. The clearest way to see the difference between active and passive immunity is to follow the **level of antibody in the blood over time**:



- **Active immunity (blue)** starts from nothing: there is a **lag** while the body mounts its response, then antibody levels rise. Even as they fall, **memory cells remain**, so protection is **long-lasting**; on **re-exposure** the memory produces a **rapid, larger** rise in antibodies.
- **Passive immunity (red)** starts **high and immediately** — the antibodies are already there — but then **only declines**, because they are broken down and not replaced. There is **no memory**, so a later exposure produces no boost.

The essential contrast is a trade-off:

Feature	Active immunity	Passive immunity
Source of antibodies	the person's **own** immune system makes them	**ready-made**, from another source
Memory cells formed?	**yes**	**no**
Speed of onset	**slow** (days–weeks to develop)	**immediate** (antibodies already present)
Duration of protection	**long-lasting** (often years)	**short-term** (weeks–months)
Response on re-exposure	faster and larger (memory)	none (must be given again)
Examples	infection (natural); vaccination (artificial)	mother→baby (natural); injected antiserum (artificial)

Choosing a strategy. The two-sided nature of the trade-off decides which is useful when. If someone faces an **immediate threat** and has no time to build their own defence — a snake bite, a possible rabies exposure, a deep wound risking tetanus — **passive** immunity (injected antibodies) buys time by protecting them **now**. If the goal is **lasting protection** against a disease they may meet in the future, **active** immunity (usually vaccination) is used, accepting the slow start in exchange for **durable** protection. Sometimes both are given together: the injected antibodies cover the person immediately, while their own vaccine-triggered response develops over the following weeks.

> This subtopic classifies *how immunity is acquired*. The cellular detail of *how* B and T cells and antibodies actually work is covered in 7D (apply it here, do not re-describe it); the design and roll-out of **vaccination programs** and the idea of **herd immunity** belong to Chapter 8 — here, vaccination matters only as the **artificial active** category.

Worked examples

Example 1 — scaffolded

In its first months of life, a breastfed baby is protected against some gut infections by antibodies present in its mother's breast milk. Classify this immunity along **both** axes (active/passive and natural/artificial) and justify your classification.

Working	Comment
The antibodies are **not made by the baby** — they are ready-made antibodies from the **mother**, handed to the baby in the milk. So on the first axis this is **passive** immunity.	Ask "whose antibodies?": if they come from another source, it is passive.
No medical intervention is involved — the antibodies pass naturally through **breastfeeding**. So on the second axis this is **natural** immunity.	Ask "how acquired?": through ordinary life = natural; through a medical procedure = artificial.
Therefore this is **natural passive** immunity.	State both axes together for the full classification.
It gives **immediate** protection (the antibodies are already active) but is **short-term** — the antibodies are broken down and not replaced, and the baby forms **no memory cells** from them.	Passive immunity always has this onset/duration signature; note it to justify fully.

Example 2 — scaffolded

After stepping on a rusty nail, a patient is given (i) an injection of ready-made anti-tetanus antibodies and, in the other arm, (ii) a tetanus vaccine. Compare the **speed of onset** and the **duration** of the protection each one provides.

Working	Comment
The **injected antibodies (i)** are ready-made, so they protect the patient **immediately** — important because tetanus toxin could act within days.	This is artificial **passive** immunity: immediate onset.
But (i) is **short-term**: those antibodies are broken down over the following weeks and are not replaced, so the protection fades.	Passive = no memory → short duration.
The **vaccine (ii)** is a harmless form of the antigen; the body must mount its **own** response, so its protection is **slow to start** (antibody levels take days–weeks to rise).	This is artificial **active** immunity: slow onset.
But (ii) is **long-lasting**: the body forms **memory cells**, giving durable protection and a rapid, larger response if the toxin is met again.	Active = memory → long duration. Giving both covers the patient now *and* into the future.

Example 3 — unscaffolded

Explain why passive immunity provides **immediate but short-lived** protection.

Passive immunity works immediately because the person is given **ready-made antibodies** that are **already active** and able to bind the pathogen or toxin the moment they enter the body — no time is needed to build a response. However, the protection is **short-lived** because these antibodies are **gradually broken down** by the body and are **not replaced**: the person's **own** adaptive immune system was never triggered by the antigen, so it makes **no antibodies of its own** and forms **no memory cells**. Once the borrowed antibodies have degraded, protection ends, and a later exposure produces no faster response. ∴ passive immunity trades **long duration** for **immediate onset** — it protects at once, but only temporarily.

Example 4 — unscaffolded

A person catches measles as a child, recovers, and is immune to measles for the rest of their life. Years later, before travelling overseas, the same person is injected with ready-made antibodies to protect them against hepatitis A during the trip. Identify the type of immunity in **each** case and explain the difference in how long each one lasts.

Recovering from the measles **infection** gave **natural active** immunity: the person's **own** immune system met the live pathogen, made its own antibodies and, importantly, formed **memory cells**. Because those memory cells **persist**, the protection is **long-lasting** — here, lifelong. The hepatitis A injection gave **artificial passive** immunity: **ready-made** antibodies were delivered by a medical procedure, giving **immediate** protection but forming **no memory cells**. Those antibodies are broken down and not replaced, so this protection lasts only **weeks to months**. ∴ the measles immunity lasts because the body maintains its own memory, whereas the hepatitis A protection fades because the borrowed antibodies are used up with nothing to replace them.

Practice questions

Scaffolded

Q1. Define each of the following: (a) active immunity; (b) passive immunity; (c) what the terms *natural* and *artificial* refer to when describing immunity.

Q2. For each situation, state whether the immunity is **active or passive**, and **natural or artificial**: (a) a child develops immunity after having whooping cough; (b) a person is vaccinated against influenza; (c) a newborn receives antibodies across the placenta before birth.

Q3. Active and passive immunity differ in where the antibodies come from. (a) In active immunity, where are the antibodies made? (b) In passive immunity, where do the antibodies come from? (c) State which type forms memory cells, and what this means for how long protection lasts.

Q4. Active and passive immunity differ in onset and duration. (a) State which type gives more immediate protection. (b) State which type gives longer-lasting protection. (c) Explain why passive immunity does not last long.

Q5. A newborn baby receives antibodies from its mother. (a) Name **two** ways antibodies can pass from a mother to her baby. (b) State whether this is active or passive immunity, and give a reason. (c) Explain why this protection lasts only a few months.

Q6. A vaccine is used to produce immunity against a disease. (a) State what a vaccine contains. (b) Explain why vaccination gives **active** immunity even though the person does not become ill. (c) State whether the protection is short- or long-term, and why.

Unscaffolded

Q7. *(Classify.)* A veterinary nurse is scratched by a stray dog that may be carrying rabies. She is immediately given an injection of ready-made anti-rabies antibodies. Classify this immunity along both axes (active/passive and natural/artificial) and justify each choice. *(2 marks)*

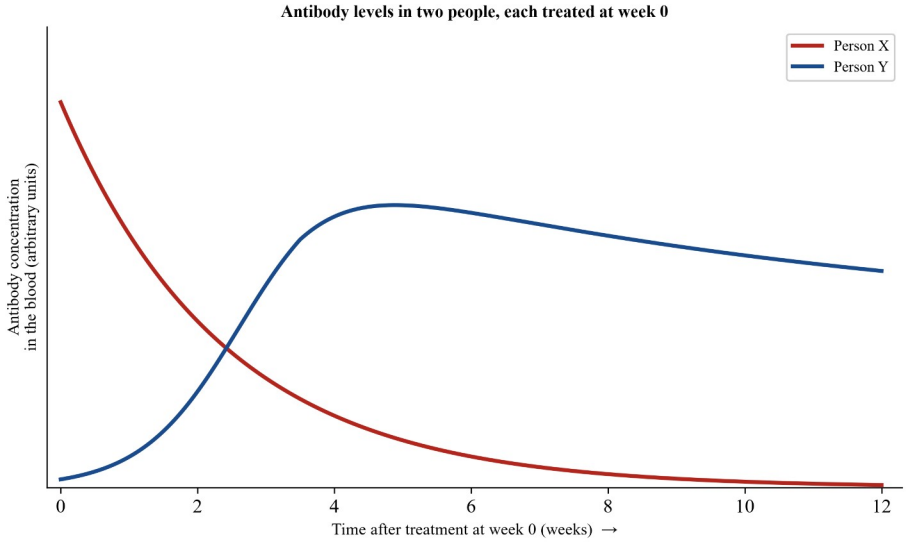
Q8. Distinguish between **active** and **passive** immunity, with reference to the **source of the antibodies** and whether **memory cells** form. *(3 marks)*

Q9. Distinguish between **natural** and **artificial** immunity, giving one example of each. *(2 marks)*

Q10. Compare the **speed of onset** and the **duration of protection** provided by active and passive immunity. *(4 marks)*

Q11. A newborn is protected against a disease by antibodies that crossed the placenta before birth. Her older brother is protected against the same disease because he caught it as a toddler. Both children acquired their immunity **naturally**, yet only one of them is **actively** immune. State which child has active immunity and which has passive immunity, and explain what this pair of cases shows about how the two classification axes are related. *(3 marks)*

Q12. *(Data interpretation.)* Two people who work at the same animal shelter are **at risk** of meeting a pathogen that neither has encountered before. At week 0, Person X is given an injection of ready-made antibodies against that pathogen and Person Y is given a vaccine against it. Neither actually meets the pathogen during the study. The graph shows the antibody level in the blood of each person over the following weeks.



(a) State which person, X or Y, has **active** immunity and which has **passive** immunity, justifying your answer from the **onset** and the **shape** of each curve.

(b) Predict what would happen to each person's antibody level if they **did** meet that pathogen several months later, and explain the difference. *(5 marks)*

Q13. *(Scenario.)* A traveller must fly tomorrow to a region where there is an outbreak of a serious disease, and will also travel there again in future years. A public-health nurse can offer either an injection of ready-made antibodies or a course of vaccination. (a) Which option gives protection in time for **tomorrow's** flight? Justify your answer. (b) Which option gives lasting protection for **future** trips? Justify your answer. (c) State one limitation of the immediate-protection option. *(5 marks)*

Q14. Explain how antibodies passed from a mother to her baby protect the baby, and why this natural passive immunity is **important in the first months** of life yet **does not last**. *(4 marks)*

Q15. *(Data — classification.)* The table describes how four different individuals acquired immunity to a disease. Copy the table and classify each one as *natural active*, *artificial active*, *natural passive* or *artificial passive*.

Individual	How immunity was acquired
P	Recovered from a bout of mumps as a child
Q	Received an injection of antivenom after a spider bite
R	Was vaccinated against measles at 12 months of age
S	Received antibodies through the placenta before birth

(4 marks)

Q16. Vaccination gives artificial active immunity. Explain, with reference to what a vaccine does in the body, why the immunity produced is **(i) active** and **(ii) long-lasting**. *(3 marks)*

Q17. *(Evaluate.)* A student states: "Passive immunity is better than active immunity, because it works straight away." Evaluate this statement. *(3 marks)*

Q18. Explain why active immunity is **slow to develop** but provides **long-lasting** protection. *(3 marks)*

Q19. *(Synthesis.)* A hospital cleaner is jabbed by a used needle while emptying a bin. The needle had been used on a patient infected with the hepatitis B virus, and the cleaner has never been vaccinated against hepatitis B. Within hours the cleaner is given an injection of **hepatitis B immunoglobulin** (ready-made anti-hepatitis-B antibodies) and, at the same visit, the **first dose of the hepatitis B vaccine**. (a) State which treatment gives **passive** immunity and which gives **active** immunity, giving the full classification (both axes) in each case. (b) Explain why the cleaner is given the

immunoglobulin as well as the vaccine, with reference to the time each takes to protect. (c) Eight weeks later the cleaner's blood still contains antibodies against hepatitis B. Explain how repeating the antibody measurement over the next few months would show whether these antibodies came from the injected immunoglobulin or from the cleaner's own response to the vaccine. (d) State which of the two treatments would still be protecting the cleaner five years later, and why. *(7 marks)*

Answers

Q1. (a) Immunity in which the body makes its **own** antibodies and memory cells in response to an antigen. (b) Immunity in which **ready-made** antibodies from another source are introduced into the body. (c) *Natural* = acquired through ordinary life (no medical intervention); *artificial* = acquired deliberately through a medical intervention. **Q2.** (a) Active, natural. (b) Active, artificial. (c) Passive, natural. **Q3.** (a) Made by the person's own immune system. (b) From another source (ready-made). (c) Active immunity forms memory cells, so it is long-lasting; passive does not, so it is short-term. **Q4.** (a) Passive. (b) Active. (c) The ready-made antibodies are broken down and not replaced, and no memory cells form. **Q5.** (a) Across the placenta, and in breast milk/colostrum. (b) Passive — the antibodies come from the mother, not the baby. (c) The antibodies are broken down and not replaced, and no memory cells form, so protection fades in a few months. **Q6.** (a) A harmless form of the antigen (e.g. a weakened/dead pathogen or one of its molecules). (b) The body mounts its **own** response and makes its own antibodies and memory cells — the antigen is harmless, so no disease results. (c) Long-term, because memory cells persist. **Q7.** Passive (ready-made antibodies given, not made by her) and artificial (delivered by injection — a medical intervention); i.e. artificial passive immunity. **Q8.** Active = the body makes its **own** antibodies and forms memory cells; passive = **ready-made** antibodies from another source, with no memory cells formed. **Q9.** Natural = acquired through ordinary life (e.g. catching an infection); artificial = acquired through a medical intervention (e.g. vaccination). **Q10.** Onset: active is slow (days–weeks); passive is immediate. Duration: active is long-lasting (memory); passive is short-term (antibodies not replaced). **Q11.** The brother = active (his own immune system met the pathogen and formed memory cells); the newborn = passive (ready-made maternal antibodies). Both are natural, so the natural/artificial axis (how the immunity was acquired) is independent of the active/passive axis (whose antibodies protect the person, and whether memory forms). **Q12.** (a) Person X = passive, i.e. artificial passive (antibody already high at week 0, then only declines); Person Y = active, i.e. artificial active (starts near zero, rises steeply from about week 1 to a peak at about week 5, then falls only slowly while staying well above X, as the body makes and maintains its own antibodies). (b) On meeting the pathogen months later, Y (active) shows a rapid, larger rise (memory cells); X (passive) shows no such response and would need another injection. **Q13.** (a) The antibody injection (passive) — it gives immediate protection. (b) Vaccination (active) — it forms memory cells for lasting protection. (c) The injected antibodies are short-term (they fade in weeks–months, with no memory). **Q14.** Ready-made maternal antibodies (via placenta and breast milk) protect the baby immediately while its own adaptive system is immature; but they are broken down and not replaced and form no memory, so protection lasts only months. **Q15.** P = natural active; Q = artificial passive; R = artificial active; S = natural passive. **Q16.** (i) Active because the body makes its own antibodies and memory cells in response to the vaccine's antigen. (ii) Long-lasting because the memory cells persist, giving a rapid, larger response on re-exposure. **Q17.** Partly right (passive does act immediately) but wrong overall: passive is short-term and forms no memory, whereas active is long-lasting; neither is simply "better" — it depends on whether immediate or lasting protection is needed. **Q18.** Slow because the body must build its own adaptive response (days–weeks); long-lasting because it forms memory cells that persist and respond rapidly on re-exposure. **Q19.** (a) The immunoglobulin = passive, and artificial passive in full; the vaccine = active, and artificial active in full. (b) The immunoglobulin's ready-made antibodies act immediately, covering the cleaner now, while the vaccine's own response takes days–weeks to develop — the passive cover bridges that lag. (c) Injected antibodies are broken down and not replaced, so their level would keep falling towards zero; the cleaner's own antibodies would instead be maintained (or rise further), so a level that is maintained/rising shows they are the cleaner's own. (d) The vaccine (artificial active), because its memory cells persist, whereas the injected antibodies were gone within weeks–months.

Fully-worked solutions

Q1. (a) **Active immunity** is immunity in which the person's **own** immune system responds to an antigen by making its **own antibodies** and forming its **own memory cells**. (b) **Passive immunity** is immunity in which **ready-made antibodies** produced by another source are introduced into the person's body, rather than being made by the person. (c) **Natural** means the immunity is acquired through **ordinary living, without any medical intervention** (catching an infection, or antibodies passing from mother to baby); **artificial** means it is acquired **deliberately through a medical intervention** (vaccination, or an injection of antibodies).

Q2. (a) Developing immunity after **having** whooping cough is **active** (the child made its own response) and **natural** (through catching the infection). (b) A **vaccination** is **active** (the body makes its own response to the vaccine antigen)

and **artificial** (a deliberate medical procedure). (c) Antibodies received **across the placenta** are **passive** (ready-made, from the mother) and **natural** (no medical intervention).

Q3. (a) In active immunity the antibodies are **made by the person's own immune system** in response to the antigen. (b) In passive immunity the antibodies are **ready-made and come from another source** (e.g. the mother, or an injected antiserum). (c) **Active** immunity forms **memory cells**, so it gives **long-lasting** protection; **passive** immunity forms **no** memory cells, so it is **short-term**.

Q4. (a) **Passive** immunity gives more immediate protection, because the antibodies are already present and active. (b) **Active** immunity gives longer-lasting protection. (c) Passive immunity does not last long because the **ready-made antibodies are gradually broken down and are not replaced**, and because **no memory cells form** (the person's own immune system was not activated), so no lasting protection is built.

Q5. (a) Antibodies pass **across the placenta** (before birth) and in **breast milk and colostrum** (after birth). (b) This is **passive** immunity, because the antibodies are **ready-made and come from the mother**, not from the baby's own immune system. (c) The protection lasts only a few months because the maternal antibodies are **broken down and not replaced**, and the baby forms **no memory cells** from them, so once they are gone the protection ends.

Q6. (a) A vaccine contains a **harmless form of the antigen** — for example a weakened or dead pathogen, or one of its molecules (such as an inactivated toxin). (b) Vaccination gives **active** immunity because the person's **own** immune system responds to the vaccine's antigen, making its **own antibodies and memory cells**; because the antigen is harmless, this happens **without** the person developing the disease. (c) The protection is **long-term**, because the **memory cells persist** and give a rapid, larger response if the real pathogen is later encountered.

Q7. The nurse is given **ready-made antibodies** that she did not make herself, so this is **passive** immunity *(1 mark)*. They are delivered by an **injection — a deliberate medical intervention** — so it is **artificial** *(1 mark)*. Stating both axes together, this is **artificial passive** immunity.

Q8. In **active** immunity the antibodies are **made by the person's own immune system** in response to an antigen *(1 mark)*, and the body forms **memory cells** *(1 mark, active side)*. In **passive** immunity the antibodies are **ready-made and supplied from another source**, and **no memory cells form** *(1 mark, passive side)*. So the key distinction is *own antibodies + memory* (active) versus *borrowed antibodies + no memory* (passive).

Q9. Natural immunity is acquired through **ordinary life, with no medical intervention** — for example, becoming immune after **catching an infection** such as chickenpox *(1 mark)*. **Artificial** immunity is acquired **deliberately through a medical intervention** — for example, through **vaccination** *(1 mark)*.

Q10. Speed of onset: active immunity is **slow** — the body needs **days to weeks** to build its own response *(1 mark)* — whereas passive immunity is **immediate**, because the antibodies are already present and active *(1 mark)*. **Duration:** active immunity is **long-lasting** (often years), because **memory cells persist** *(1 mark)*, whereas passive immunity is **short-term** (weeks to months), because the borrowed antibodies are broken down and not replaced and no memory forms *(1 mark)*.

Q11. The **brother** has **active** immunity: catching the disease meant that **his own** immune system met the pathogen, made its **own antibodies** and formed **memory cells** *(1 mark)*. The **newborn** has **passive** immunity: the antibodies that crossed the placenta were **ready-made by her mother**, so the baby's own adaptive system was never activated by the antigen and formed **no memory cells** *(1 mark)*. Both children acquired their immunity **naturally** — through ordinary living, with no medical intervention — and yet one is active and the other passive. This shows that the two axes are **independent**: *natural/artificial* records only **how** the immunity was acquired, whereas *active/passive* records **whose antibodies** are doing the protecting and whether memory forms. Knowing that immunity was acquired naturally therefore tells you nothing about whether it is active or passive *(1 mark)*.

Q12. (a) **Person X has passive immunity** (artificial passive) and **Person Y has active immunity** (artificial active) *(1 mark)*. Person X's curve is **already high at week 0** and then **only declines** towards zero — the signature of **ready-made antibodies** that are active the moment they are injected but are broken down and **not replaced** *(1 mark)*. Person Y's curve starts **near zero**; after a short lag of about a **week** it **rises steeply through weeks 1–4** to a peak at about **week 5**, and then falls only **slowly**, staying well above X's — the signature of the body having to **build its own** response to the vaccine antigen given at week 0, and then **maintaining** it *(1 mark)*. (b) If they met the pathogen several months later, **Person Y (active)** would show a **rapid and larger** rise in antibodies, because their **memory**

cells respond quickly to the same antigen *(1 mark)*. **Person X (passive)** would show **no such response** — they formed no memory, so they would gain no faster protection and would need **another injection** of antibodies to be protected *(1 mark)*.

Q13. (a) The **injection of ready-made antibodies (passive immunity)** gives protection in time for tomorrow's flight, because it works **immediately** — the antibodies are already active and do not need time to develop *(2 marks)*. (b) **Vaccination (active immunity)** gives lasting protection for future trips, because the body makes its **own** antibodies and **memory cells**, which persist and respond rapidly on later exposure *(2 marks)*. (c) A limitation of the antibody injection is that it is **short-term** — the antibodies fade within weeks to months and form no memory, so it would not protect the traveller on future trips *(1 mark)*.

Q14. A mother's **ready-made antibodies** pass to her baby **across the placenta** before birth and in **breast milk and colostrum** after birth *(1 mark)*. These antibodies are **already active** and can bind pathogens immediately, protecting the baby at a time when its **own adaptive immune system is still immature** and cannot yet respond well *(1 mark)* — which is why this protection is so important in the **first months** of life *(1 mark)*. However, it **does not last**: the maternal antibodies are **broken down and not replaced**, and the baby forms **no memory cells** from them, so the protection fades over a few months as the baby's own immune system matures *(1 mark)*.

Q15. P — natural active: immunity built by the child's **own** response to **catching** mumps (no medical intervention) *(1 mark)*. **Q — artificial passive: ready-made antibodies (antivenom)** given by **injection** *(1 mark)*. **R — artificial active:** a **vaccine** (medical intervention) triggers the child's **own** response *(1 mark)*. **S — natural passive: ready-made maternal antibodies** received **across the placenta**, naturally *(1 mark)*.

Q16. (i) The immunity is **active** because the vaccine's antigen makes the person's **own** immune system respond, producing its **own antibodies and memory cells** — the antibodies are not supplied ready-made *(1 mark for active + own response)*. **(ii)** It is **long-lasting** because the response includes **memory cells that persist** long after the vaccine *(1 mark)*; if the real pathogen is later encountered, these give a **rapid, larger** response that stops illness *(1 mark)*.

Q17. The statement is **partly correct**: passive immunity **does** act straight away, because ready-made antibodies are given, which is a genuine strength when protection is needed urgently *(1 mark)*. But it is **misleading overall**: passive immunity is **short-term and forms no memory**, so it gives no lasting protection, whereas active immunity is **long-lasting** because it builds the body's own memory *(1 mark)*. So **neither is simply "better"** — the best choice **depends on the situation**: passive for immediate protection, active for durable protection *(1 mark)*.

Q18. Active immunity is **slow to develop** because the body must **build its own adaptive response** from scratch — recognising the antigen and making antibodies takes **days to weeks** *(1 mark)*. It is **long-lasting** because, as part of that response, the body forms **memory cells that persist** *(1 mark)*; these remain ready long after the antigen has gone, so that on **re-exposure** they mount a **rapid, larger** response that prevents illness *(1 mark)*.

Q19. (a) The **injection of hepatitis B immunoglobulin** gives **passive** immunity — the antibodies are **ready-made** (produced by someone else, not by the cleaner) — and, because it is delivered by a deliberate medical procedure, it is **artificial passive** immunity *(1 mark)*. The **hepatitis B vaccine** gives **active** immunity — it contains a **harmless form of the antigen**, so the cleaner's **own** immune system makes its **own antibodies and memory cells** — and, being a medical intervention, it is **artificial active** immunity *(1 mark)*. (b) The virus may already be in the cleaner's body, so protection is needed **now**: the immunoglobulin's antibodies are **already active** and can bind the virus **the moment they are injected**, giving **immediate** protection *(1 mark)*. The vaccine cannot do this, because **active** immunity is **slow to develop** — the cleaner's own antibody level takes **days to weeks** to rise — so the injected antibodies **bridge that lag** until the cleaner's own response takes over *(1 mark)*. (c) The injected (passive) antibodies are **not replaced**: they are steadily **broken down**, so on repeat testing their level would **keep falling**, towards zero within weeks to months *(1 mark)*. Antibodies made by the cleaner's **own** response to the vaccine would instead be **maintained, or rise further**, because the cleaner's immune system is still producing them. So a **falling** level means the antibodies are the remains of the immunoglobulin, whereas a **maintained or rising** level means they are the cleaner's own *(1 mark)*. (d) Only the **vaccine** (artificial active) would still be protecting the cleaner five years later, because the response it triggered formed **memory cells that persist**, whereas the injected antibodies were broken down and not replaced within weeks to months *(1 mark)*.