

Cambridge AS & A Level · Biology 9700 · Notes

Immunity

AS

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Read first: [Biological molecules](#), [Cell structure](#), [Cell membranes and transport](#)

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What you need to know

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

1. **Describe how phagocytes work:** how macrophages and neutrophils find, engulf and digest pathogens.
2. **Explain what an antigen is**, and the difference between **self antigens** (on your own cells) and **non-self antigens** (foreign ones).
3. **Describe the primary immune response** in order, with the roles of macrophages, B-lymphocytes and the plasma cells they become, and two kinds of T-lymphocyte: T-helper cells and T-killer cells.
4. **Explain the role of memory cells** in the secondary immune response and in long-term immunity.
5. **Relate the structure of an antibody to its functions.**
6. **Outline the hybridoma method** for making monoclonal antibodies.
7. **Outline how monoclonal antibodies are used** to diagnose disease and to treat disease.
8. **Describe the differences between active and passive immunity, and between natural and artificial immunity.**
9. **Explain that vaccines contain antigens** that stimulate an immune response and give long-term immunity.
10. **Explain how vaccination programmes help control the spread of infectious diseases.**

Questions often link this topic to others: protein structure (antibodies), cell structure (plasma cells, lysosomes), endocytosis and exocytosis, and the diseases in "Infectious diseases" (HIV destroying T-helper cells, TB, cholera, measles).

Understand it

Two kinds of defence

Your body defends itself against pathogens in two ways.

- **Non-specific defence:** phagocytes engulf and destroy **any** pathogen or foreign particle they meet. They act at once and work the same way every time.

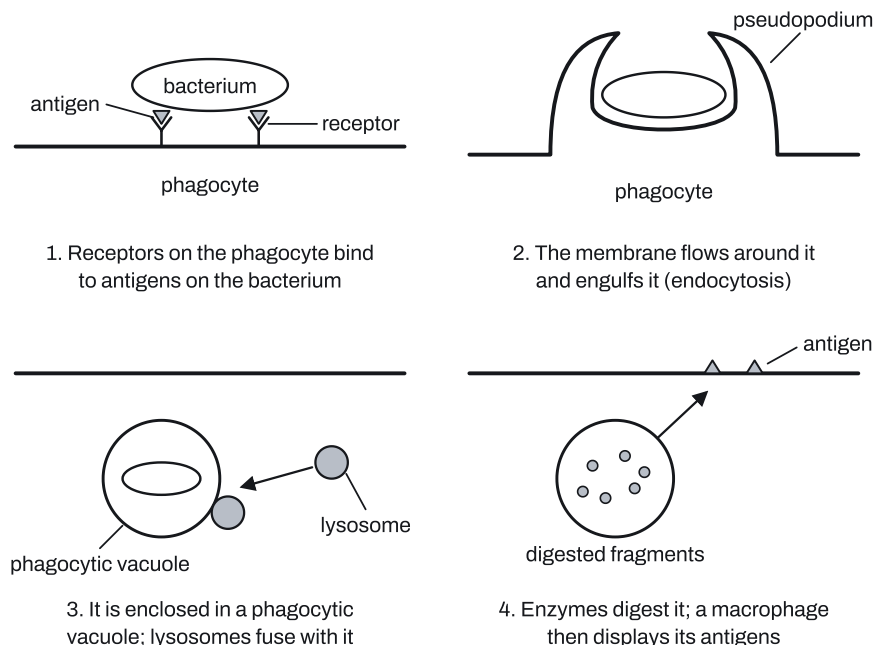
- **Specific defence:** lymphocytes respond to **one particular antigen**. The first time they meet it they are slow, but they remember it, so the next response is much faster.

All white blood cells are made from stem cells in the **bone marrow**.

Cell	How to recognise it	What it does
Neutrophil	lobed nucleus, granular cytoplasm	phagocyte; most common white cell; first to arrive at an infection; short-lived
Monocyte	large cell, bean-shaped (kidney-shaped) nucleus	phagocyte; leaves the blood and becomes a macrophage in the tissues
Macrophage	large; found in organs such as the lungs, liver, spleen and lymph nodes	phagocyte; long-lived; presents antigens to lymphocytes
Lymphocyte (B or T)	small; large round nucleus filling most of the cell, little cytoplasm	specific immune response; not phagocytic

Phagocytes

A **phagocyte** is a cell that engulfs and digests pathogens. Neutrophils and macrophages are phagocytes. Chemicals released by pathogens and by damaged body cells attract them to the site of an infection; neutrophils squeeze out through the walls of capillaries to reach it.



The steps, in order:

1. **Receptors** on the phagocyte's cell surface membrane **bind** to molecules (antigens) on the pathogen. They bind even more easily if antibodies are already stuck to the pathogen, because phagocytes have receptors for the antibodies' constant region.

2. The membrane flows around the pathogen as **pseudopodia** and engulfs it: this is **endocytosis**, and it uses ATP.
3. The pathogen is enclosed in a **phagocytic vacuole** (a phagosome).
4. **Lysosomes** move to the vacuole and **fuse** with it, releasing **hydrolytic enzymes** (proteases, lipases, lysozyme and others) into it.
5. The enzymes **hydrolyse** the pathogen. Useful products are absorbed; waste leaves the cell by **exocytosis**.

A **macrophage** does one more thing: it keeps some of the pathogen's antigens and puts them on its own cell surface membrane. It is now an **antigen-presenting cell**, and this is how the specific response starts. (Macrophages are the main antigen-presenting cells. One Cambridge question also treats a neutrophil as displaying antigens it has ingested, [9700/11/M/J/25 Q39](#), so don't reject that idea if it appears.)

Lysozyme, one of the enzymes, hydrolyses bonds in the **peptidoglycan** of bacterial cell walls. The wall is weakened, water enters by osmosis and the bacterium bursts.

Phagocytosis is **non-specific**: the same cell engulfs any bacterium, virus, dead cell or dust particle, and phagocytes do not make memory cells or divide to form clones.

Antigens: self and non-self

An **antigen** is a molecule that is recognised by the immune system and can **stimulate an immune response**, such as the production of antibodies. Antigens are usually **proteins or glycoproteins** (sometimes polysaccharides) on the surface of cells and viruses; toxins released by bacteria are antigens too. The immune system recognises an antigen by its **shape**: lymphocyte receptors and antibodies have a **complementary** shape that fits it.

- **Self antigens** are on your own cells, for example the glycoproteins on your macrophages ([9700/12/O/N/25 Q39](#)). They do not normally cause a response. While lymphocytes develop, any whose receptors fit self antigens are destroyed.
- **Non-self antigens** are foreign: on pathogens (the protein coat of a virus, the wall or flagella of a bacterium), on the cells of another person (a transplanted kidney, transfused blood), toxins, and the changed antigens on cancer cells. They stimulate an immune response.

A non-self antigen is a **molecule**, not a whole virus or bacterium; one bacterium carries many different antigens.

Autoimmune diseases happen when the immune system fails to tell self from non-self and attacks self antigens. In myasthenia gravis, for example, antibodies are made against the receptors on muscle cells at neuromuscular junctions.

Blood groups apply the same idea. Red blood cells carry antigen A, antigen B, both (group AB) or neither (group O), and the plasma contains antibodies against the antigens the person lacks. A transfusion is safe when the **recipient's plasma has no antibodies against the donor's antigens**:

Recipient	Antibodies in plasma	Can receive
A	anti-B	A, O
B	anti-A	B, O
AB	none	A, B, AB, O
O	anti-A and anti-B	O

Lymphocytes

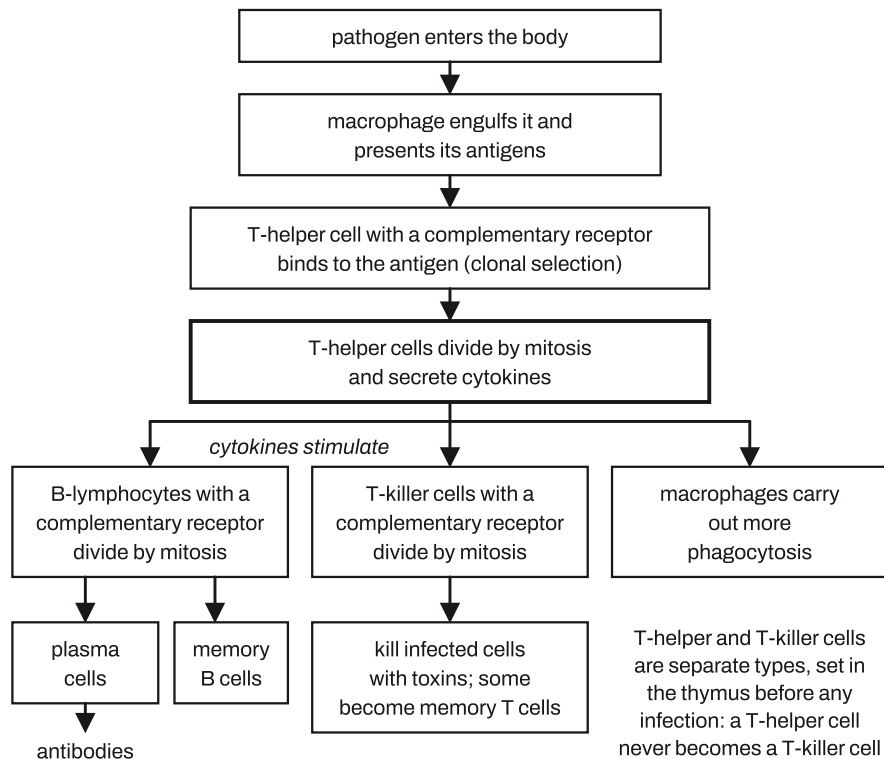
Lymphocytes are made in the bone marrow. **B-lymphocytes** mature there; **T-lymphocytes** move to the **thymus** to mature. While they mature in the thymus, T-lymphocytes **differentiate into two separate types: T-helper cells and T-killer cells**. So each T cell is already a helper or a killer before it ever meets an antigen; activation later only selects it and makes it divide, it doesn't decide its type. Mature lymphocytes circulate in the blood and lymph and wait in the lymph nodes and spleen; they can also leave the blood and gather at sites of infection.

Each lymphocyte has receptors of **one shape only**, so it can respond to only one antigen. There are millions of different lymphocytes, but before an infection there are only **a few** of each kind. A B-lymphocyte's receptors are antibody molecules held in its cell surface membrane.

	B-lymphocytes	T-lymphocytes
Mature in	bone marrow	thymus
Activated by	an antigen binding to their receptor (and cytokines from T-helper cells)	an antigen presented on another cell's surface
Types before any infection	one kind	two separate kinds, fixed in the thymus: T-helper cells and T-killer cells
When activated, divide to give	plasma cells , which secrete antibodies, and memory B cells	more cells of the same type: active T-helper cells, which secrete cytokines, or active T-killer cells, which kill infected cells; plus memory T cells

The primary immune response

The **primary immune response** is what happens the first time the body meets a particular antigen.



1. **Antigen presentation.** A macrophage engulfs the pathogen and displays its antigens on its cell surface membrane.
2. **Clonal selection.** Among the millions of T-helper cells, the few with receptors **complementary** to that antigen bind to it. T-killer cells and B-lymphocytes with complementary receptors bind the same antigen. Only these cells are "selected"; the rest do nothing.
3. **Clonal expansion.** The selected cells divide again and again by **mitosis**, making a clone of identical cells with the same receptor. A T-helper cell's clone is all T-helper cells and a T-killer cell's clone is all T-killer cells: helpers never turn into killers.
4. **T-helper cells** secrete **cytokines**, signalling molecules that:
 - stimulate the selected **B-lymphocytes** to divide and to become **plasma cells**;
 - stimulate the selected **T-killer cells** to divide;
 - stimulate **macrophages** to carry out more phagocytosis.
5. **Plasma cells** secrete large amounts of one **antibody**, specific to that antigen, into the blood and lymph by exocytosis. They are packed with rough endoplasmic reticulum (to make the protein), Golgi bodies (to package it) and mitochondria (for ATP). They live only a short time and **do not divide**.
6. **T-killer cells** bind to body cells that display the antigen, such as cells infected with a virus, cancer cells or cells of a transplanted organ. They release **toxins**, such as perforin (which makes holes in the cell surface membrane), hydrogen peroxide and enzymes, that kill the cell. They do **not** engulf anything and do not make antibodies.
7. Some of the B and T cells in each clone become **memory cells**, which stay in the body for years.

It takes several days before antibodies appear, because there are so few cells of the right kind at the start and clonal selection and expansion take time. Meanwhile the pathogen multiplies, so the person becomes ill.

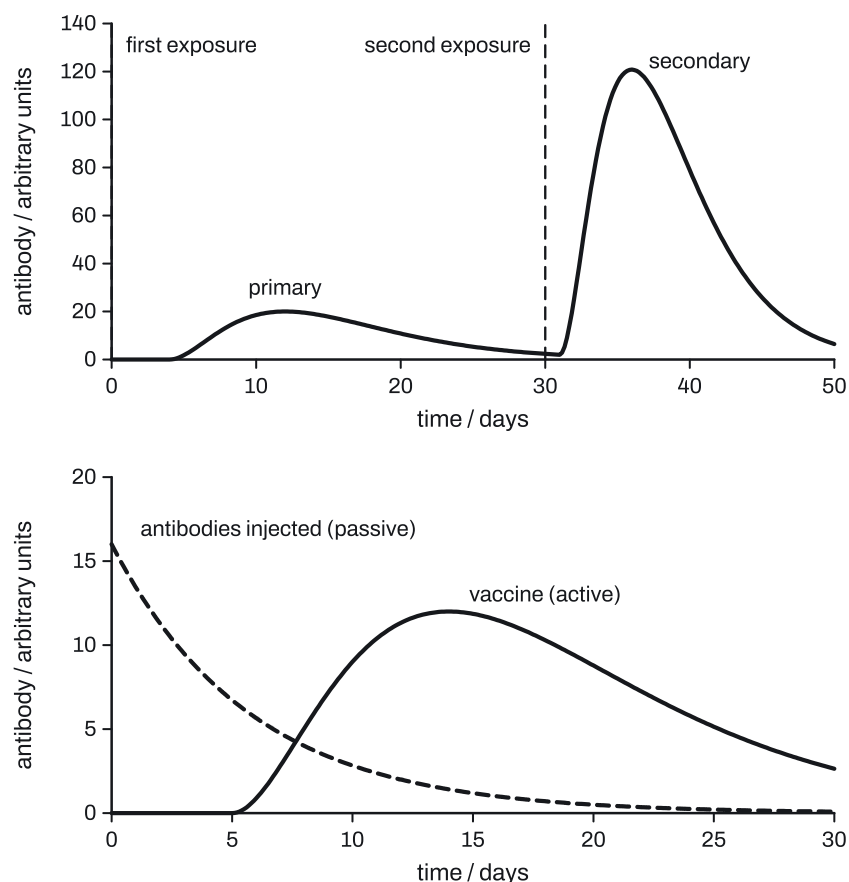
Why losing T-helper cells matters: HIV destroys T-helper cells. With fewer cytokines, fewer B-lymphocytes are activated, so fewer plasma cells, fewer antibodies and fewer memory cells are made; fewer T-killer cells divide; macrophages are less stimulated ([9700/11/M/J/25 Q40](#)).

Memory cells and the secondary response

Memory cells are long-lived B and T cells with receptors for the antigen. They stay in the blood, lymph nodes and spleen after the pathogen has gone, and there are **many more** of them than there were cells of that kind before the first infection.

If the same antigen enters the body again, the **secondary immune response** follows:

- memory cells meet the antigen sooner, because there are so many of them;
- memory B cells divide by mitosis at once and become **plasma cells** (and more memory cells); memory T-helper cells divide into more active T-helper cells, and memory T-killer cells into more active T-killer cells;
- so antibodies appear within a day or two, reach a **much higher** concentration and stay high for longer;
- the pathogen is destroyed **before it can cause symptoms**. The person is **immune**.

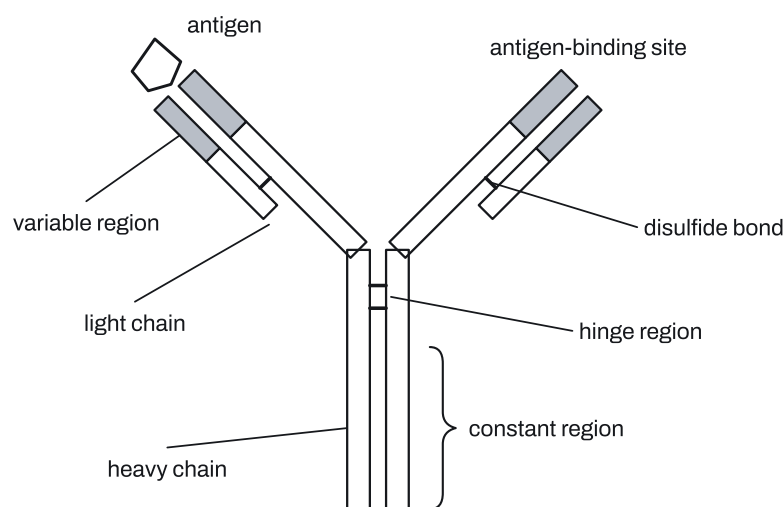


The top graph shows the difference: in the primary response the peak comes 12 days after exposure; in the secondary response it comes 6 days after, and it is 6 times higher.

Long-term immunity depends on memory cells. The antibodies made in the first response are broken down within weeks, so they are not what stays in the blood for years; the memory cells remain, ready to divide into plasma cells that quickly make new antibodies when the pathogen returns. Antibodies still do the protecting on re-infection: they are just new ones, made fast.

Antibodies

Antibodies (immunoglobulins) are glycoproteins secreted by plasma cells. Each antibody is made of **four polypeptide chains**: two identical **heavy chains** and two identical **light chains**. Having more than one polypeptide gives it **quaternary structure**. The chains are held together by **disulfide bonds**; peptide bonds join the amino acids, and hydrogen, ionic and disulfide bonds hold each chain's tertiary structure.



Part	Structure	Function
Variable region	tip of each arm, on both the heavy and the light chain; its amino acid sequence differs from one antibody to another	forms the antigen-binding site
Antigen-binding site	two per antibody, identical , each made by one heavy and one light chain	its specific amino acid sequence gives a specific shape, complementary to one antigen, so the antibody is specific
Hinge region	where the arms meet the stem, held by disulfide bonds	flexibility : the arms can move to bind two antigens different distances apart
Constant region	the stem (and lower arms); the same in all antibodies of one class	binds to receptors on cells of the immune system, such as phagocytes (and B-lymphocytes)

Why the binding site is specific: its **sequence of amino acids** (primary structure) decides how the chain folds, and the R groups of those amino acids decide its **shape** and charges. Only an antigen with a complementary shape fits.

How antibodies help destroy pathogens:

- **Agglutination:** with two binding sites, one antibody can bind two pathogens, so antibodies clump pathogens together; the clumps can't spread and are easy for phagocytes to engulf.
- **Neutralising toxins:** antibodies that bind toxins (antitoxins) block them so they can't act.
- **Blocking entry:** antibodies bound to a pathogen's surface stop it attaching to and entering host cells.
- **Marking for phagocytes:** phagocytes' receptors bind the constant region of antibodies attached to a pathogen, so it is engulfed more quickly.

Antibodies do not "kill antigens" and are not enzymes: they have antigen-binding sites, not active sites.

Monoclonal antibodies

A **monoclonal antibody** is one kind of antibody, made by a **clone** of identical cells, so every molecule is identical and binds the same antigen. Plasma cells can't be grown for long outside the body because they do not divide, so they are fused with cancer cells.

The hybridoma method:

1. **Inject the antigen** (not the whole pathogen) into a small mammal such as a mouse.
2. **Wait** a few weeks while it makes an immune response; booster injections may be given.
3. **Remove the spleen** and extract its B-lymphocytes (plasma cells).
4. **Fuse** them with **myeloma cells** (cancer cells), using a chemical such as polyethylene glycol. Each fused cell is a **hybridoma**.
5. Grow the cells in a medium in which only hybridomas survive, and put single hybridomas into separate wells.
6. **Screen** each clone and **select** the one making the wanted antibody.
7. **Clone** it: culture it on a large scale and collect the antibody it secretes.

Why fuse? The B-lymphocyte (plasma cell) makes the **specific antibody** but can't divide or survive in culture. The myeloma cell can **divide indefinitely** by mitosis. The hybridoma does both ([9700/12/F/M/21 Q40](#)).

Traps: T-lymphocytes are never used; antibodies are not fused with anything; a hybridoma clone makes **one** antibody, not a variety; what is grown in culture is **clones** of hybridoma cells.

Using monoclonal antibodies in diagnosis. Because one monoclonal antibody binds only one antigen, it can show whether that antigen (and so the disease or hormone) is present:

- **Test strips** (pregnancy tests, and tests for malaria, TB and cholera). The sample moves along the strip:
 1. it passes **mobile antibodies** attached to a coloured marker (tiny gold particles, or a dye), which bind the antigen if it is there;
 2. at the **test line**, **immobilised antibodies** (fixed to the strip) bind a different part of the same antigen, so the antigen–antibody–marker complex is held there and a coloured line appears;

3. at the **control line**, other immobilised antibodies bind the mobile antibodies themselves, so a line appears whether or not the antigen is present, showing the test has worked.

Test strips are quick, cheap, portable and need no laboratory or training, so treatment can start sooner and drugs are not used "just in case".

- **Finding where cells are:** monoclonal antibodies labelled with a radioactive or fluorescent marker are injected and bind to, for example, cancer cells or a blood clot, which a scanner can then detect.

Using monoclonal antibodies in treatment. Cancer cells have antigens that normal cells lack, so an antibody can target them. A monoclonal antibody can:

- **bind to antigens on cancer cells** and mark them, so the patient's immune system (T-killer cells, phagocytes) destroys them;
- **block receptors** on cancer cells that receive signals to divide (trastuzumab binds to a receptor on some breast cancer cells);
- **block the molecules that switch T-cells off**, so the patient's T-cells can kill the cancer cells ([9700/11/M/J/22 Q38](#));
- **carry a drug, toxin or radioactive substance** straight to the target cells, so healthy cells are not harmed;
- in autoimmune diseases such as rheumatoid arthritis, **block the receptors or cytokines that trigger the immune response**; this treats autoimmunity, not cancer ([9700/13/M/J/22 Q38](#), [9700/14/M/J/25 Q40](#));
- give **passive immunity** against an infection, including viral infections, or neutralise a toxin.

Mouse antibodies are themselves non-self antigens in a human. They are **humanised** (most of the protein changed to the human sequence) so the patient doesn't make antibodies against them. Monoclonal antibodies don't divide or make copies of themselves, and they don't give active immunity: they are broken down, so treatment is repeated.

Types of immunity

Active immunity: your own lymphocytes respond to an antigen, so **you make the antibodies and memory cells**. It takes time to develop but lasts a long time.

Passive immunity: you are **given antibodies** made by another person or animal. It works **at once**, but there is no immune response of your own and **no memory cells**. The antibodies are **broken down** within weeks, so the protection is short-lived; on a later infection you get only a primary response.

Natural means it happens in normal life; **artificial** means it comes from a medical treatment.

	Natural	Artificial
Active	having the infection (for example repeated malaria infections)	a vaccine (antigens injected or swallowed)

Natural	Artificial
Passive antibodies passing from mother to fetus across the placenta , or to a baby in breast milk (colostrum): so a baby at birth has natural passive immunity	an injection of antibodies : antitoxin or antiserum (for example against snake venom, rabies or tetanus toxin), or monoclonal antibodies

The bottom graph in the diagram above shows the difference: injected antibodies are at their highest immediately and then fall; a vaccine gives nothing for several days, then a rise. Passive immunity is useful when protection is needed **now**: after a snake bite, after exposure to rabies or tetanus, or for someone whose immune system can't respond.

Vaccines

A **vaccine** contains **antigens** that stimulate a primary immune response without causing the disease. Clonal selection and expansion happen as usual, and **memory cells** are made, giving long-term (artificial active) immunity. When the real pathogen arrives, the secondary response destroys it before it causes illness.

Vaccines can contain:

- **live, weakened (attenuated)** pathogens, such as the BCG vaccine for TB or the measles vaccine; they reproduce a little, so they give a strong response and may need no boosters;
- **dead (inactivated)** pathogens;
- **toxoids**: toxins made harmless (for example with formaldehyde) that still have the toxin's antigens (tetanus);
- **pieces** of the pathogen, such as surface proteins;
- **mRNA** coding for an antigen: the body's cells take it up, ribosomes translate it into the antigen protein, the cell displays the protein on its surface, lymphocytes with complementary receptors bind it and memory cells form ([9700/13/O/N/23 Q40](#)).

Points that questions test:

- Immunity is **not immediate** after a vaccine, because memory cells haven't been made yet ([9700/14/O/N/25 Q38](#)). A **booster** dose produces a secondary response and many more memory cells.
- Two weeks after a vaccine, it is the number of **plasma cells** in the blood that has gone up ([9700/13/O/N/25 Q39](#)).
- Most vaccines are **injected**, because protein antigens would be **digested** in the stomach and small intestine ([9700/11/O/N/22 Q39](#)).
- A new influenza vaccine is needed most years because the virus **mutates**, so its **antigens change shape**; the old memory cells' receptors and antibodies are no longer complementary. This is **antigenic variation**. It is the antigens that change: never say the virus "becomes resistant" to antibodies.
- A vaccine can protect against a related pathogen if its antigens are **similar in shape** ([9700/12/M/J/21 Q40](#)).

- A vaccine works less well in someone with few T-helper cells (HIV) or a weak immune system, who may make few memory cells.

Vaccination programmes

A vaccine protects a person. A **vaccination programme** vaccinates a large part of a **population** to control a disease.

Herd immunity: when a high enough proportion of the population is immune, the pathogen can't find enough people to infect, so **transmission** is broken. An unvaccinated person is then unlikely to meet an **infected** person, so even people who can't be vaccinated (young babies, people who are ill) are protected (9700/11/O/N/23 Q40). The more infectious the disease, the higher the proportion that must be immune.

What a successful programme needs:

- a vaccine that is effective, safe, cheap (or free) and easy to give, with plentiful supply;
- a pathogen whose **antigens don't change**, so one vaccine works everywhere for years;
- reaching the **whole population**, including rural and remote areas; vaccinating children early enough; giving boosters;
- keeping vaccines cold (a **cold chain**) unless they are heat-stable (freeze-dried);
- trained staff, funding and good records of who has been vaccinated;
- **surveillance:** finding every new case, then **contact tracing** and **ring vaccination** (vaccinating everyone around a case);
- education to counter misinformation, so people agree to be vaccinated.

Smallpox was eradicated because its virus hardly changed (one vaccine worked for everyone for life), the vaccine was a live, closely related virus that gave strong, long-lasting immunity, it was freeze-dried and easy to store and give, and cases were easy to spot so ring vaccination could stop outbreaks.

Measles is harder: it is very infectious, so almost everyone must be immune; babies can't be vaccinated in the first months because antibodies from their mother (natural passive immunity) bind the vaccine's antigens before it can work; two doses are needed and many children miss the second; war, poverty and remote areas stop programmes; some people refuse the vaccine.

Things that make a programme **less** successful: a pathogen that mutates often, a pathogen that infects T-cells, and the need for frequent boosters (9700/12/M/J/23 Q40).

Key facts and formulas

Nothing in this topic is in the syllabus's list of given formulae, so learn all of it.

Formula	Status
How many times higher = $\frac{\text{larger value}}{\text{smaller value}}$ (for example peak antibody concentrations)	Learn it

Formula	Status
Percentage = $\frac{\text{part}}{\text{whole}} \times 100$ (for example vaccination coverage, correct test results)	Learn it
Phagocytosis: receptors bind → endocytosis → phagocytic vacuole → lysosomes fuse → hydrolytic enzymes digest → (macrophage) presents antigens	Learn it
Primary response: antigen presentation → clonal selection → clonal expansion (mitosis) → cytokines → plasma cells (antibodies), T-killer cells, memory cells	Learn it
Secondary response: memory cells → plasma cells → faster, more, longer-lasting antibody	Learn it
Antibody: 2 heavy + 2 light chains, disulfide bonds, 2 identical antigen-binding sites (variable regions), hinge, constant region	Learn it
Hybridoma: B-lymphocyte (plasma cell) + myeloma cell	Learn it
Vaccine = artificial active; injected antibodies = artificial passive; placenta and breast milk = natural passive; infection = natural active	Learn it
Transfusion is safe if the recipient has no antibodies against the donor's antigens	Learn it

How to do it

We have tagged 112 questions on this topic from 2021–2025 (82 multiple-choice, 30 structured). 18 of them mix more than one type, so the counts add up to 135.

Question type	Questions
Vaccines, memory cells and the secondary response	21
Identify immune cells and match them to their roles	18
Describe or order the primary immune response	15
Outline the hybridoma method	15
Classify immunity and explain its features	14
Describe phagocytosis	13
Uses of monoclonal antibodies in diagnosis and treatment	12
Relate antibody structure to function	11
How vaccination programmes control disease	9
Antigens: self and non-self	7

1. Vaccines, memory cells and the secondary response (21 questions)

1. **Say what the vaccine contains:** antigens (weakened or dead pathogen, toxoid, surface proteins, or mRNA that cells use to make the antigen). Never antibodies.
2. **Primary response to the vaccine:** lymphocytes with complementary receptors are selected and divide; plasma cells make antibodies; **memory cells** are made.
3. **On infection:** memory cells are already present in large numbers, so they meet the antigen quickly and divide by mitosis into **plasma cells**, which secrete antibodies sooner, in larger amounts and for longer. The pathogen is destroyed before symptoms appear.

Variations you will meet:

- **A graph of two injections or two exposures (9700/22/F/M/25 Q4):** the second peak is higher and earlier because memory cells from the first response are present, there are more lymphocytes with complementary receptors, more plasma cells are made, and antibodies are made faster. Quote the peaks and times from the graph.
- **Why immunity is delayed after a vaccine:** memory cells have not been made yet, not "not enough antibodies" (9700/14/O/N/25 Q38).
- **What memory cells become:** plasma cells, never macrophages, neutrophils or monocytes (9700/11/O/N/24 Q39). Plasma cells do not become memory cells.
- **Memory T cells** (BCG vaccine, 9700/21/O/N/24 Q3): memory T cells bind the antigen quickly, T-helper cells release cytokines, which increase phagocytosis, the B-lymphocyte response and the T-killer response.
- **Getting a disease twice** (influenza): antigens change by mutation, so memory cells no longer fit; also a weak immune system making few memory cells, or HIV lowering T-helper cells (9700/13/M/J/24 Q40).
- **Oral versus injected vaccines:** protein antigens are digested in the gut, so most vaccines are injected.
- **Antibodies and future protection: two statements that look alike.** "Vaccination leads to the production of antibodies that protect against future infections" is **true**: the vaccine stimulates antibody production and memory cells, and the memory cells let antibodies be made quickly when the pathogen arrives (9700/12/O/N/22 Q39). "The antibodies made in response to the vaccine remain in the blood to give long-term immunity" is **false**: those antibody molecules are broken down within weeks, and long-term immunity comes from the memory cells (9700/11/M/J/25 Q39).
- **A vaccine against one virus protecting against others:** the antibodies bind antigens that closely resemble its own; antibodies never bind "any antigen".

2. Identify immune cells and match them to their roles (18 questions)

Use the tables in "Understand it". In tick tables, fill **every** box.

- **From a description or micrograph:** lobed nucleus → neutrophil; bean-shaped nucleus → monocyte (becomes a macrophage); large round nucleus with little cytoplasm → lymphocyte (9700/22/F/M/24 Q2). A cell full of rough ER, Golgi and mitochondria → plasma cell, which makes a lot of protein (9700/11/M/J/24 Q38).

- **Which cells divide in clonal expansion?** B-lymphocytes, T-helper and T-killer cells; **not** plasma cells, and not phagocytes.
- **Which cells secrete cytokines as their main role?** T-helper cells only.
- **Which secrete antibodies?** Plasma cells. Because plasma cells are activated B-lymphocytes, an option saying "B-lymphocytes secrete antibodies" counts as correct when plasma cells are not offered ([9700/11/O/N/23 Q38](#)); T-lymphocytes never make antibodies.
- **Which kill infected cells?** T-killer cells, with toxins. They do not engulf ([9700/11/M/J/23 Q39](#)).
- **"Involved in phagocytosis"** can mean T-lymphocytes when all the options are lymphocytes: T-helper cells' cytokines stimulate macrophages ([9700/13/O/N/24 Q39](#)).
- **Which make memory cells?** Both B- and T-lymphocytes.
- **Where are antibodies found?** In the blood plasma, and on the surface of B-lymphocytes and memory B cells as receptors ([9700/11/O/N/21 Q39](#)).
- **More white cells in a blood sample** during an infection: clonal expansion of lymphocytes and more phagocytes. With HIV/AIDS, fewer (T-helper cells destroyed).
- **Organelles of a plasma cell** ([9700/21/M/J/22 Q2](#)): nucleolus (makes ribosomes), rough ER (makes the antibody polypeptides), Golgi body (modifies and packages antibodies into vesicles), mitochondria (ATP), exocytosis at the membrane.

3. Describe or order the primary immune response (15 questions)

1. Macrophage **engulfs** the pathogen and **presents** its antigens.
2. T-helper cells with **complementary receptors** bind (**clonal selection**).
3. They **divide by mitosis** (**clonal expansion**) and secrete **cytokines**.
4. Cytokines stimulate selected **B-lymphocytes** to divide and become **plasma cells**, which secrete **antibodies**; they also stimulate **T-killer cells** to divide and **macrophages** to be more active.
5. T-killer cells bind infected cells and release **toxins** that kill them.
6. **Memory cells** form.

For an "order these steps" MCQ, find the first step (phagocytosis or presentation) and the last (antibodies secreted or memory cells), then fill in the middle. For example, T-helper cells meet a macrophage, then activate other lymphocytes, then B-lymphocytes divide, then plasma cells secrete antibodies ([9700/13/O/N/24 Q40](#)).

Variations you will meet:

- **Cancer cells or a transplanted organ** ([9700/12/O/N/23 Q39](#), [9700/21/M/J/25 Q4](#)): the same steps, with the cancer cell's or donor's antigens as the non-self antigens. T-helper cells secrete cytokines, T-killer cells multiply, bind the cells and release toxins (perforin, hydrogen peroxide, enzymes). If cytokines are released (for example by a drug), they stimulate clonal expansion and macrophages; the antigens trigger clonal selection.

- **Roles of T-helper and T-killer cells (9700/23/O/N/24 Q5):** helper → secretes cytokines that stimulate B-lymphocytes to divide into plasma cells and stimulate macrophages; killer → secretes chemicals such as perforin that kill infected cells.
- **Losing T-helper cells (HIV):** fewer cytokines, so fewer plasma cells and antibodies, fewer memory cells, fewer T-killer cells, less active macrophages. A T-helper cell never destroys infected cells itself.
- **Why is mitosis important?** It lets B-lymphocytes produce many plasma cells (clonal expansion). Mitosis does not "let them make antibodies".
- **A response to a non-disease antigen** (such as a food protein): antigen presentation, clonal selection, clonal expansion, cytokines, plasma cells, antibodies. The steps are the same.

4. Outline the hybridoma method (15 questions)

1. Inject the **antigen** into a mouse (or other small mammal).
2. Wait a few weeks for an immune response.
3. Remove **B-lymphocytes (plasma cells)** from the **spleen**.
4. **Fuse** them with **myeloma (cancer) cells** to make **hybridomas**.
5. **Screen and select** the hybridoma making the wanted antibody.
6. **Clone** it (divides by mitosis) and collect the antibody.

For 5 marks, give all six steps; extra detail (a fusing chemical, separating cells into wells, a medium in which only hybridomas survive, humanising the antibody) can earn a mark too.

Variations you will meet:

- **"Why fuse the cells?":** the B-lymphocyte makes the specific antibody but can't divide or survive in culture; the myeloma cell divides indefinitely (9700/22/O/N/25 Q2).
- **MCQs on the two cells:** a tumour (myeloma) cell and a B-lymphocyte (or plasma cell). Wrong options: T-lymphocytes, stem cells, macrophages, antigens, antibodies, clones.
- **What is removed from the spleen?** Lymphocytes. **What is cultured?** Clones of hybridoma cells.
- **Statements to judge:** "the antigen triggers mitosis of specific B-lymphocytes" is correct; "antibodies are collected and fused with myeloma cells" is wrong; "a hybridoma makes a variety of antibodies" is wrong (9700/12/O/N/24 Q36).
- **Fill the gaps in a flow chart:** B-lymphocytes, fuse, hybridoma.

5. Classify immunity and explain its features (14 questions)

1. **Who makes the antibodies?** The person's own lymphocytes → **active**. Antibodies given ready-made → **passive**.
2. **How did it happen?** In normal life (infection, placenta, breast milk) → **natural**. A medical treatment (vaccine, injection of antibodies) → **artificial**.
3. Write **both words**: "artificial passive", not just "passive".

Features to list for passive immunity (usually for 2–4 marks): acts **immediately**; **short-term**, because the antibodies are **broken down**; **no immune response** of your own, so **no memory cells** and no new antibodies; no protection on re-infection. For active immunity: takes time, memory cells made, long-lasting.

Variations you will meet:

- **A table comparing a vaccine and injected antibodies** (9700/22/O/N/25 Q2): the component that causes the effect is the antigen (vaccine) or antibody; memory lymphocytes yes (vaccine) or no; time to have an effect longer (vaccine) or shorter; duration longer (vaccine) or shorter.
- **A graph**: a curve that is highest at once and then falls is passive; a curve that starts at zero, rises after a lag and peaks later is active (9700/12/M/J/25 Q40).
- **What happens if the passively protected person meets the pathogen later?** No memory cells, so only a slow primary response: their antibody peaks well after infection (9700/13/O/N/21 Q40).
- **Scenarios**: horse antiserum after a snake bite, rabies antibodies → artificial passive; repeated malaria → natural active; a baby at birth → natural passive; TB infection or a vaccine injection → active.
- **Why passive immunity is short**: antibodies are broken down; don't say they "die".

6. Describe phagocytosis (13 questions)

1. Pathogen's antigens **bind** to **receptors** on the phagocyte's cell surface membrane.
2. The membrane surrounds it (pseudopodia): **endocytosis**.
3. A **phagocytic vacuole** forms.
4. **Lysosomes fuse** with the vacuole and release **hydrolytic enzymes**.
5. The pathogen is **hydrolysed** (digested); a macrophage then presents its antigens.

Variations you will meet:

- **Put the steps in order** (9700/12/M/J/25 Q39): bind → engulf into a vacuole → lysosome fuses → digest → display antigens.
- **Which processes are part of phagocytosis?** Receptor binding, endocytosis, hydrolysis and exocytosis (of waste); antibody production is not (9700/12/F/M/23 Q40).
- **Which responses are true for phagocytes?** They recognise pathogens and secrete enzymes; they don't divide by mitosis to respond, or make memory cells.
- **Non-specific**: a neutrophil ingesting a bacterium is the non-specific response (9700/11/O/N/25 Q40); anything involving clones or particular antigens is specific.
- **Lysozyme**: hydrolyses peptidoglycan, so the wall is weakened and the bacterium bursts by osmosis (9700/21/O/N/25 Q6).
- **Macrophages in organs**: in the liver they engulf and digest old red blood cells in the same way (9700/22/O/N/23 Q3); in the lungs, alveolar macrophages engulf inhaled bacteria. Lysosomes also digest worn-out organelles.
- **TB granulomas** (9700/22/M/J/25 Q4): macrophages that have engulfed *Mycobacterium tuberculosis* but not killed it are walled off by many immune cells. This confines the bacteria so they don't reach the bloodstream, but it takes up lung tissue, reducing the surface area for gas exchange.

7. Uses of monoclonal antibodies in diagnosis and treatment (12 questions)

Test strips (2–4 marks):

1. The antibody is **specific**: its antigen-binding site has a shape **complementary** to one antigen, because of its specific sequence of amino acids.
2. **Mobile** antibodies with gold particles bind the antigen; the complex moves to the **test line**, where **immobilised** antibodies bind it too, so a line appears only if the antigen is present.
3. The **control line** shows that the mobile antibodies have flowed along the strip, so the result is valid. No control line means the test failed.
4. The immobilised antibodies in the control area differ in the **shape of their variable regions** (primary and tertiary structure), because they bind the mobile antibodies rather than the antigen (9700/21/O/N/24 Q3).

Variations you will meet:

- **Read a result**: a band in the test area for one strain and the control band means that strain is present; a control band alone means negative (9700/22/M/J/22 Q2).
- **Percentage correctly detected**: $\text{correct positive results} \div \text{all people who really had the disease} \times 100$.
For example 97 of 102: $\frac{97}{102} \times 100 = 95.1\%$.
- **Advantages**: quick, cheap, no trained staff or laboratory, portable, so treatment starts sooner and drugs aren't used "just in case".

Treatment:

- Explain why they suit treatment: **specific** to one antigen, and can be **humanised** so they don't act as antigens themselves (9700/12/F/M/24 Q39). They do not divide by mitosis.
- **Which types treat cancer?** Those that mark cancer cells for the immune system, block the molecules that inactivate T-cells, or block receptors that trigger cell division; not those that block receptors that trigger the immune response (9700/14/M/J/25 Q40).
- **What can be concluded from trial data** (9700/11/M/J/22 Q38): only what the information shows. A drug that blocks a receptor so T-lymphocytes stay active lets the patient's own immune system kill the cancer cells; the antibody does not kill them itself.
- **Smaller antibodies** (from sharks, or single chains): pass more easily through capillary walls into the tissue fluid around a tumour and reach more cells.
- Monoclonal antibodies give **passive** immunity, never active; they can treat viral infections.

8. Relate antibody structure to function (11 questions)

1. **Four polypeptides**: 2 heavy, 2 light; **quaternary** structure; held by **disulfide bonds**.
2. **Variable regions** at the tips form **two identical antigen-binding sites**, each from one heavy and one light chain.
3. Each binding site has a **specific amino acid sequence**, so a specific shape **complementary** to one antigen.
4. **Hinge** gives flexibility; **constant region** binds receptors on phagocytes and other immune cells.

Variations you will meet:

- **Label a diagram (9700/12/O/N/25 Q40)**: the binding site is the tip of a heavy chain plus the tip of the light chain beside it; the two heavy chains are identical to each other, and so are the two light chains.
- **Statements to judge**: four polypeptides but only **two** binding sites (9700/12/O/N/22 Q40); the binding site is **complementary**, not "similar", in shape to the antigen; the binding sites are on both chains, not "light chains only"; the hinge is held by disulfide bonds (9700/13/M/J/25 Q36).
- **Bonds in an antibody**: peptide, hydrogen and disulfide bonds (and ionic bonds).
- **Why antibodies binding to macrophage receptors helps**: the macrophage engulfs the antibody-coated pathogen more easily (9700/21/M/J/24 Q6).
- **How antibodies protect against a pathogen (9700/23/O/N/23 Q1)**: bind its antigens (complementary shape), stop it entering host cells, mark it for phagocytes, agglutinate it.
- **How millions of different antibodies can be made** is about splicing the primary transcripts of antibody genes in different combinations: see "Nucleic acids and protein synthesis".

9. How vaccination programmes control disease (9 questions)

1. Vaccinate a **large proportion** of the population, so most people have memory cells and don't become ill or pass the pathogen on.
2. **Herd immunity**: the transmission cycle is broken, so unvaccinated people are unlikely to meet an **infected** person.
3. Give practical steps (for "discuss" questions, each with a reason): free, available everywhere (towns and remote areas), vaccinate children early, boosters, records to find the unvaccinated, surveillance and contact tracing, **ring vaccination** around new cases, enough supply, trained staff, funding, cold chain or heat-stable vaccine, education and countering misinformation.

Variations you will meet:

- **Eradicating polio worldwide (9700/23/O/N/24 Q5)**: the list above, for 4 marks.
- **Why smallpox was eradicated (9700/23/M/J/21 Q2)**: the virus didn't mutate, so one vaccine protected for life everywhere; a live, closely related virus gave a strong immune response and memory cells; freeze-dried, so easy to store and transport.
- **Why measles persists (9700/23/O/N/21 Q5)**: very infectious; babies can't be vaccinated soon after birth because of maternal antibodies; coverage doesn't reach herd immunity; boosters missed; war, remote areas, too few staff; refusal.
- **What affects success (9700/12/M/J/23 Q40)**: frequent mutation, infecting T-cells and frequent boosters all matter; vaccinating from eight weeks old does not.
- **A graph of cases falling after a vaccine was introduced**: vaccines give artificial active immunity, and fewer people can act as hosts (9700/12/F/M/24 Q40).
- **Advantages of a live, freeze-dried vaccine** such as BCG: a strong primary response (it replicates, lots of antigen), memory cells, no boosters, doesn't cause disease, easy to transport and store.

10. Antigens: self and non-self (7 questions)

- **Features of a non-self antigen** (3 marks, 9700/22/M/J/23 Q3): a molecule, usually a protein, glycoprotein or polysaccharide; foreign (on pathogens, infected cells, cancer cells, another person's cells, or a toxin); recognised by lymphocytes, so it stimulates an immune response; binds to antibodies with a complementary binding site.
- **Which could be a self antigen?** One on your own cells: a glycoprotein on your macrophage, not a viral protein, a viral envelope lipid or a toxin.
- **Molecules that bind an antibody's binding site** are called antigens (9700/22/M/J/25 Q5).
- **Blood group MCQs**: use the table in "Understand it". The recipient must not have antibodies to the donor's antigens.
- **Autoimmunity** (9700/22/M/J/21 Q6): an autoimmune disease is one where the immune system fails to distinguish self from non-self and makes antibodies against self antigens (in myasthenia gravis, the receptors at neuromuscular junctions).

Worked examples

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

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

Example 1

A neutrophil is a white blood cell with a lobed nucleus.

(a) Describe how a neutrophil destroys a bacterium. **[4]**

(b) Explain why the destruction of bacteria by neutrophils is described as non-specific. **[1]**

(c) State one role of macrophages in the immune response that neutrophils do not usually carry out. **[1]**

(a) Receptors on the neutrophil's cell surface membrane bind to molecules (antigens) on the bacterium. **B1**
The membrane surrounds the bacterium and engulfs it by endocytosis, forming a phagocytic vacuole. **B1**
Lysosomes fuse with the vacuole **B1** and release hydrolytic enzymes, which digest the bacterium. **B1**

(b) A neutrophil engulfs any bacterium or foreign particle, not only one with a particular antigen. **B1**

(c) Macrophages present the bacterium's antigens on their cell surface membrane to T-helper cells (antigen presentation). **B1**

Example 2

A person was infected with a virus on day 0 and recovered. On day 60 the same person was exposed to the same virus again but had no symptoms. The antibody against the virus peaked at 35 arbitrary units on day 14, and at 560 arbitrary units on day 66.

(a) Calculate how many times higher the second peak was than the first. **[1]**

(b) Explain the differences between the two responses. **[4]**

(c) Explain why the person had no symptoms after the second exposure. **[2]**

(a)

$$\frac{560}{35} = 16 \text{ times higher}$$

B1

(b) The first response took 14 days to peak and the second only 6 days (day 60 to day 66). **B1** During the first response only a few B-lymphocytes had receptors complementary to the viral antigen, and clonal selection and expansion took time. **B1** The first response left many memory cells. **B1** On the second exposure the memory cells quickly met the antigen and divided by mitosis into many plasma cells, so more antibody was made, sooner. **B1**

(c) Antibodies were made so quickly and in such large amounts **B1** that the virus was destroyed before it could multiply enough to cause symptoms: the person was immune. **B1**

Example 3

A company wants to make a monoclonal antibody against a protein found only on the surface of one type of cancer cell.

(a) Outline how the hybridoma method could be used to make this antibody. **[5]**

(b) Explain why the B-lymphocytes are fused with myeloma cells. **[2]**

(c) Suggest two ways in which this antibody could be used to treat the cancer. **[2]**

(a) Inject the cancer-cell protein (the antigen) into a mouse. **B1** Wait several weeks for an immune response. **B1** Remove the spleen and extract the B-lymphocytes (plasma cells). **B1** Fuse them with myeloma cells to form hybridoma cells. **B1** Screen the hybridomas, select the one making the antibody against the protein, and clone it to make large amounts of antibody. **B1**

(b) The B-lymphocytes make the specific antibody but cannot divide in culture. **B1** Myeloma cells divide indefinitely, so the hybridoma both makes the antibody and keeps dividing. **B1**

(c) Any two, for example: the antibody binds to the protein and marks the cancer cells for destruction by the immune system; a drug or toxin attached to the antibody is carried only to the cancer cells; it blocks a receptor the cancer cells need for signals to divide. **B1 B1**

Example 4

In one region there are 250 000 children, and 205 000 of them have been vaccinated against measles.

(a) Calculate the percentage of children who have been vaccinated. **[1]**

(b) Health officials say that 95% of children must be vaccinated to give herd immunity. Calculate how many more children must be vaccinated. **[2]**

(c) Explain how herd immunity protects babies who are too young to be vaccinated. **[2]**

(d) Suggest why the measles vaccine is not given to newborn babies. **[2]**

(a)

$$\frac{205\,000}{250\,000} \times 100 = 82\%$$

B1

(b) $0.95 \times 250\,000 = 237\,500$ children must be vaccinated. **M1** $237\,500 - 205\,000 = 32\,500$ more children.

A1

(c) When most people are immune, the virus cannot pass from person to person, so the transmission cycle is broken. **B1** An unvaccinated baby is then unlikely to meet an infected person. **B1**

(d) A newborn has antibodies from its mother that crossed the placenta or came in breast milk (natural passive immunity). **B1** These antibodies bind to the vaccine's antigens, so the baby's own lymphocytes are not stimulated and no memory cells are made. **B1**

Common mistakes

- **Antibody, antibiotic, antigen.** Examiners report the mix-up every year. Antigens are the molecules recognised; antibodies are proteins made by plasma cells that bind them; antibiotics are drugs against bacteria.
- **Calling the antigen-binding site a "receptor" or an "active site".** Antibodies are not enzymes. Say "antigen-binding site" (or "variable region"), with a shape **complementary** to the antigen.
- **Saying T-lymphocytes turn into T-helper or T-killer cells when an immune response starts.** Examiners report this often. The two types are already separate: they differentiate while the T-lymphocytes mature in the thymus. Activation selects the cells whose receptors fit the antigen and makes them divide into more of the same type.
- **Saying T-lymphocytes make antibodies.** Only plasma cells (from B-lymphocytes) do. Nearly half of candidates in one session didn't know that T-killer cells release toxins.
- **Saying plasma cells divide** in clonal expansion. B-lymphocytes divide; plasma cells secrete antibody and don't divide.
- **"Antibodies kill antigens" or "kill the pathogen".** They bind to antigens; they agglutinate, neutralise and mark pathogens so phagocytes can destroy them.

- **Treating a non-self antigen as a whole virus or bacterium**, or putting "receptors on antigens". The antigen is a molecule on the pathogen; the receptors are on the lymphocytes.
- **Hybridoma errors**: injecting the pathogen instead of the antigen, or fusing antibodies (rather than B-lymphocytes) with myeloma cells.
- **Passive immunity**: antibodies are **broken down**; they don't "die". No immune response and no memory cells happen.
- **Mixing up the four types of immunity**. A vaccine gives artificial **active** immunity, not passive; natural immunity after an infection is still active.
- **"The virus became resistant to the vaccine."** Its antigens changed by mutation, so the memory cells and antibodies no longer fit. Resistance is a word for bacteria and antibiotics.
- **Vaccine versus vaccination programme**. A question on programmes wants the population: herd immunity, coverage, surveillance, ring vaccination, not only how a vaccine works in one person.
- **Saying the antibodies from a vaccine or infection remain in the blood to give long-term immunity**. Those antibody molecules are broken down within weeks; what lasts is the **memory cells**, which divide into plasma cells that make new antibodies quickly on re-infection. Vaccination producing antibodies that help protect against future infection is still correct.

How to get the marks

- **"Describe"** a sequence (phagocytosis, the primary response, the hybridoma method): give the steps **in order**, one mark-worthy idea per step, with the right terms: receptors, endocytosis, phagocytic vacuole, lysosomes, hydrolytic enzymes; clonal selection, clonal expansion, mitosis, cytokines, plasma cells.
- **"Explain"**: link each point with "so" or "because". "Memory cells are present, **so** they divide into plasma cells quickly, **so** antibodies are made sooner."
- **Specificity** questions: use "complementary shape", "specific sequence of amino acids" and "antigen-binding site" (or "variable region") together.
- **Type of immunity**: always two words (artificial passive, natural active). Then give features for the marks: immediate or delayed, memory cells or none, long or short.
- **Graphs**: quote values with units and days: time to the peak, the peak height, the lag, how long it stays high. Compare with a calculation such as "16 times higher".
- **Tick tables**: fill every box; a table with blanks can lose whole rows or columns.
- **"Suggest"** (unfamiliar drugs, vaccines, test strips): apply the ideas here: complementary shapes, antigen presentation, clonal selection, memory cells.
- **"Discuss"** for programmes: several different steps, each with a reason; marks are for range.
- **Spell precisely**: lymphocyte, phagocyte, myeloma, hybridoma, cytokine, disulfide.

Quick check

1. A white blood cell has a large round nucleus that fills most of the cell. Name the type of cell, and state whether it carries out phagocytosis.

2. Name the type of immunity in each case: (a) a baby feeding on breast milk; (b) recovering from chickenpox; (c) an injection of tetanus antitoxin; (d) a tetanus toxoid vaccine.
3. Explain why a plasma cell contains a lot of rough endoplasmic reticulum and many Golgi bodies.
4. A child's antibody concentration reached a peak of 40 arbitrary units 21 days after a first dose of vaccine, and 480 arbitrary units 5 days after a booster dose. How many times higher was the second peak, and why was it reached so much sooner?
5. Explain why a person may need a new influenza vaccine in most years.

Answers

1. A lymphocyte. It does not carry out phagocytosis; it takes part in the specific immune response.
2. (a) Natural passive. (b) Natural active. (c) Artificial passive. (d) Artificial active.
3. Plasma cells secrete large amounts of antibody, which is a protein. Its polypeptides are made on the ribosomes of the rough ER; the Golgi bodies modify the antibody and package it into vesicles, which release it by exocytosis.
4. $\frac{480}{40} = 12$ times higher. The first dose left many memory cells, so after the booster they met the antigen straight away and divided into plasma cells, without the wait for clonal selection and expansion: the peak came after 5 days instead of 21.
5. The influenza virus mutates, so its antigens change shape. Memory cells and antibodies from earlier vaccines or infections are no longer complementary to the new antigens, so a vaccine containing the new antigens is needed.

Past questions to try

- **9700/23/M/J/25 Q6:** the hybridoma method, then the parts of a monoclonal antibody drug.
- **9700/23/O/N/24 Q5:** the roles of T-helper and T-killer cells, and eradicating polio.
- **9700/21/M/J/22 Q2:** a plasma cell's organelles, the hybridoma method and why injected antibodies don't give lasting protection.
- **9700/21/O/N/24 Q3:** a monoclonal antibody test strip for TB, and memory T cells after the BCG vaccine.