C3.2 Defence against disease

Interaction and interdependence—Organisms

Standard level and higher level: 5 hours

Guiding questions

• How do body systems recognize pathogens and fight infections?

• What factors influence the incidence of disease in populations?

C3.2.1–Pathogens as the cause of infectious diseases

Students should understand that a broad range of disease-causing organisms can infect humans. A disease-causing organism is known as a pathogen, although typically the term is reserved for viruses, bacteria, fungi and protists. Archaea are not known to cause any diseases in humans.

Humans coexist with billions of microorganisms, as they provide nutrient-rich, warm, and moist environments for small organisms – the normal flora of humans.

Pathogens are diverse agents and microorganisms that cause disease in their **host** (the organism being infected). They include bacteria, fungi, viruses, protists, and prions. Regardless of whether they are living organisms or not, all pathogens share the same characteristics (**CRANS**):

- ability to **c**olonize the host
- use host resources to **r**eplicate
- circumvent, **a**void, or subvert the host's immune responses
- find a **n**iche that is nutritionally compatible in the host
- **s**pread to a new host

Archaea are a domain of unicellular organisms, and are (so far) not known to cause any disease in humans. While they do possess some characteristics of a pathogen like toxic genes, it is thought that humans do not contain compatible nutritional sources for them.

NOS: Students should be aware that **careful observation** can lead to important progress. For example, careful observations during 19th-century epidemics of childbed fever (due to an infection after childbirth) in Vienna and cholera in London led to breakthroughs in the control of infectious disease.

Rapid industrialization during the 19th century and the development of flushing toilets and sewers led to the outbreak of water-borne diseases like cholera in London. John Snow, considered the founding father of epidemiology, carefully observed the frequency of cholera incidence and areas of the city where contaminated water was distributed to homes. His **observation** led to preventive measures, like preventing citizens from accessing a water pump sourced from contaminated water. The city also became the first to use chlorine as a water disinfectant in 1897, greatly improving methods of controlling infectious disease.

Ignaz Semmelweis, a Hungarian physician, **observed** that physicians who examined cadavers and then immediately after assisted in the birth of a child had higher frequences of childbed fever fatalities compared to midwives, who did not examine cadavers. He then suggested using chlorinated lime as a disinfectant after examining cadavers, greatly reducing incidences of death.

Main idea: both scientists observed data about where fatality rates are highest and identified potential causes, enabling the development of infection control methods.

C3.2.4—Differences between the innate immune system and the adaptive immune system

Include the idea that the innate system responds to broad categories of pathogen and does not change during an organism's life whereas the adaptive system responds in a specific way to particular pathogens and builds up a memory of pathogens encountered, so the immune response becomes more effective. Students are not required to know any components of the innate immune system other than phagocytes.

The **immune system** is an intricate collection of cells and organs that destroys or reduces the effects of pathogens that would otherwise damage or kill the host organism. It is comprised of the innate and adaptive immune systems.

The **innate immune system** is composed of the first and second lines of defence, with the **adaptive immune system** being the third line of defence.

Innate immunity		**Adaptive immunity**
First line of defence	**Second** line of defence	**Third** line of defence
Physical barriers (skin, saliva, mucosal membranes, gastric acid, cilia, urine)	**Non-specific** cellular and chemical barriers (phagocytotic cells)	**Specific** cellular and chemical barriers (lymphocytes)

Innate	**Adaptive**
Instantaneous or quick reaction to pathogens	Slow reaction during the first infection
Targets a broad range of pathogens (non-specific)	Specific to particular pathogens
Does not change during an organism's lifetime	Builds up a memory of encountered pathogens
Primarily controlled by physical barriers and phagocytotic cells	Controlled by lymphocytes

C3.2.2—Skin and mucous membranes as a primary defence

The skin acts as both a physical and chemical barrier to pathogens. Students are not required to draw or label diagrams of skin.

The skin and mucous membranes are the primary defence of humans. While gastric acid and cilia are also part of the first line of defence, the skin and its mucosal membranes are the *first* physical barrier the pathogens come across. In the case where the pathogen is able to make its way into the human body, further physical barriers, like acid and cilia, are present to defend the body.

The skin and mucous membranes act as a primary defence due to (**TACID**):

- tears and mucous **t**rap and rinse pathogens away
- skin's **a**cidity increases difficulty of pathogen survival
- **c**ompetition of pathogen with normal flora reduces its survivability
- acting as a continuous, **i**mpermeable barrier to pathogens
- killing or deactivating pathogens by **d**esiccation (drying out)

C3.2.3—Sealing of cuts in skin by blood clotting

Include release of clotting factors from platelets and the subsequent cascade pathway that results in rapid conversion of fibrinogen to fibrin by thrombin and trapping of erythrocytes to form a clot. No further details are required.

Abrasions or punctures to the skin (physical barrier) may allow pathogens to enter into the body. To rapidly respond to such injuries, a cascade pathway is initiated, leading to:

1. release of clotting factors from platelets and damaged cells
2. conversion of prothrombin (inactive) to thrombin (active form)
3. conversion of fibrinogen (soluble) into fibrin (insoluble) by thrombin

Insoluble fibrin forms a mesh around the site of injury, trapping erythrocytes (red blood cells) to form a clot. This helps to restore a temporary physical barrier until the skin and surrounding tissue heal.

C3.2.5—Infection control by phagocytes

Include amoeboid movement from blood to sites of infection, where phagocytes recognize pathogens, engulf them by endocytosis and digest them using enzymes from lysosomes.

If a pathogen is able to surpass physical barriers and start attacking host cells, the second line of defence (still part of the innate immune system) is put to work, and is comprised mainly of phagocyte cells.

A **phagocyte** (also called **macrophage**) is a white blood cell (leukocyte) that performs **phagocytosis**. The phagocyte takes in the pathogen inside itself via endocytosis into a vesicle, subsequently fusing with a lysosome and the digestive enzymes it contains in order to destroy the pathogen.

To reach the site of infection, phagocytes are characterized by movement that resembles that of amoeba (**amoeboid movement**). This specific movement allows phagocytes to rapidly move through small pores within capillaries to reach sites of injury quickly, as seen below.

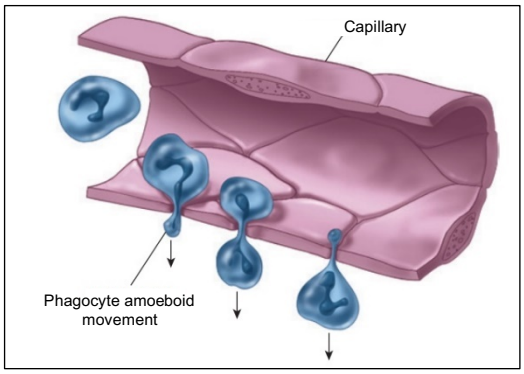

Figure 1: amoeboid movement of phagocytes (Leukocytes…).

C3.2.6—Lymphocytes as cells in the adaptive immune system that cooperate to produce antibodies

Students should understand that lymphocytes both circulate in the blood and are contained in lymph nodes. They should appreciate that an individual has a very large number of B-lymphocytes that each make a specific type of antibody.

Lymphocytes are part of the adaptive immune system and are majorly composed of **T-** ("T" because it is produced in the **t**hymus) and **B-** ("B" because it is produced in the **b**one marrow) **lymphocytes**.

There are around 2×10^{12} lymphocytes in the human body, comparable in cell mass to the brain or liver. They are present in both the blood and **lymph** (interstitial fluid that has entered lymphatic vessels) in large quantities to rapidly and effectively defend the body against disease.

Each B-lymphocyte produces a specific **antibody** (immunoglobin), which is any group of proteins that binds to an antigen. The variable region of the antibody, as seen below, is what determines the specificity of the antibody, similar to how the shape of the active site of an enzyme determines its substrate specificity.

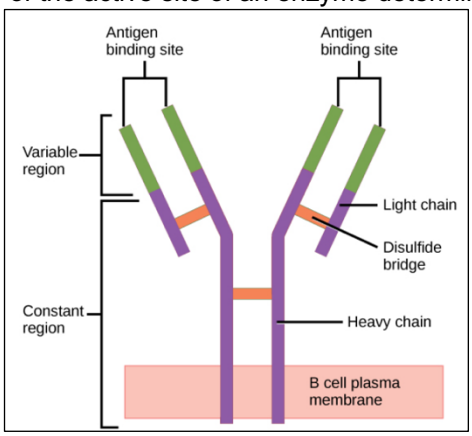

Figure 2: antibody structure (Ann Clark).

Antibodies defend the body against disease through three major mechanisms (CON):

- **Complement activation**: the complement system is a large number of proteins that work to fight off disease by opsonization and cell lysis – it 'complements' the work of antibodies.
- **Opsonization**: the antibody binds to the pathogen's antigens to promote phagocytosis and make it easier for phagocytes to identify and engulf the pathogen.
- **Neutralization**: the antibody prevents the pathogen from adhering to host cells, reducing its ability to cause damage. It also 'neutralizes' pathogenic toxins by binding to them to prevent host cell damage.

C3.2.7—Antigens as recognition molecules that trigger antibody production

Students should appreciate that most antigens are glycoproteins or other proteins and that they are usually located on the outer surfaces of pathogens. Antigens on the surface of erythrocytes may stimulate antibody production if transfused into a person with a different blood group.

Antigens are mostly (glycol)proteins that can bind to an antibody, usually found on the surface of pathogens and host cells. They are called as such due to their ability to **gen**erate **anti**bodies.

Heteroantigens are any antigen derived from one *species* (pathogen) that is able to stimulate an immune response in another species (host). **Self-antigens** (autoantigens) are normal constituents of an *individual* and have the capacity of producing an immune response in that individual and in specific circumstances (i.e. tumor cells).

The ABO blood group system is the classification of human blood based on absence or presence of antigens A or B. All blood types have the same basic structure on the surface molecule that identifies them, but those with antigens A and B have extra unique additions while people with blood type O have no extra addition to the basic structure.

An individual with antigen A has antibodies for antigen B (anti-B), and a person with antigen B has antibodies for antigen A (anti-A). A person with blood type O has antibodies for both A and B. This is particularly important during blood transfusions, as the donated blood must contain the same antigen of the recipient otherwise an immune response will occur in which the donor blood cells break down (hemolysis) and an uncontrollable clotting cascade initiates (agglutination).

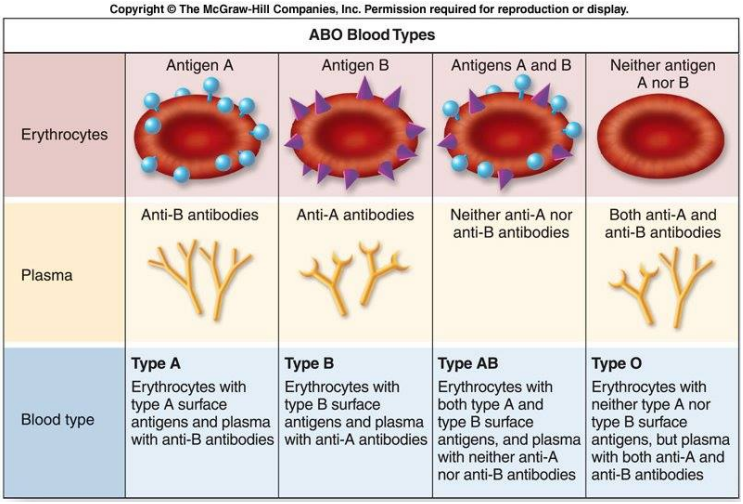

Figure 3: ABO blood types and antibodies (McGraw-Hill).

C3.2.8—Activation of B-lymphocytes by helper T-lymphocytes

Students should understand that there are antigen-specific B-cells and helper T-cells. B-cells produce antibodies and become memory cells only when they have been activated. Activation requires both direct interaction with the specific antigen and contact with a helper T-cell that has also become activated by the same type of antigen.

After phagocytes engulf a pathogen, they present its antigens on their surface, which T-cells detect. B-cell activation occurs only when both contact with helper T-cells and direct interaction with the specific antigen take place.

C3.2.9—Multiplication of activated B-lymphocytes to form clones of antibody-secreting plasma cells

There are relatively small numbers of B-cells that respond to a specific antigen. To produce sufficient quantities of antibody, activated B-cells first divide by mitosis to produce large numbers of plasma B-cells that are capable of producing the same type of antibody.

Activation of B-cells results in **clonal expansion** – which is the process by which activated B-cells first divide by mitosis into large amounts of plasma cells.

Plasma cells are differentiated B-cells capable of producing one type of antibody that is specific to the antigen presented by T-cells.

C3.2.10—Immunity as a consequence of retaining memory cells

Students should understand that immunity is the ability to eliminate an infectious disease from the body. It is due to the long-term survival of lymphocytes that are capable of making the specific antibodies needed to fight the infection. These are memory cells.

Some of the T- and B-cells do not differentiate into plasma cells – instead they become **memory cells**. These cells do not produce antibodies during the first exposure, but can immediately start producing upon a second infection or exposure. Lymphocytes involved in the first infection undergo apoptosis (death) after the pathogen is cleared, but memory cells persist. The length of time memory cells persist varies, which is why booster shots for certain diseases are sometimes needed, but these cells can last many years.

C3.2.11—Transmission of HIV in body fluids

Include examples of the mechanisms of HIV (human immunodeficiency virus) transmission.

Immunodeficiency is the acquired or inherited delay, insufficiency, or failure of the immune system to defend against disease.

The **Human Immunodeficiency Virus** (**HIV**) is a major global health issue, transmitted by:

- bodily fluids of an infected person, including breast milk, blood, vaginal fluids, and semen
- a pregnant woman to her baby
- contaminated needles and other injecting equipment for drugs
- unsafe blood transfusions, injections, tissue transplantation, and unsterile medical procedures

HIV is **not** transmitted through ordinary contacts such as sharing a glass, coughing, sneezing, or kissing.

C3.2.12—Infection of lymphocytes by HIV with AIDS as a consequence

Students should understand that only certain types of lymphocyte are infected and killed, but that a reduction in these lymphocytes limits the ability to produce antibodies and fight opportunistic infections.

HIV weakens the immune system by destroying and depleting helper T-cells, reducing the efficacy of the adaptive immune system. Although the body does produce antibodies against the virus, helper T-cell levels eventually drop to an extent where the body is no longer able to (a) fight off the virus (b) defend itself against other pathogens that would normally not cause infection in people with healthy immune systems.

Acquired Immunodeficiency Syndrome (**AIDS**) is the last and most serious stage of an infection with HIV, and occurs when the individual's immunity is so weak that other pathogens start causing illnesses that would normally not occur in a healthy person. There is currently no cure for HIV, but patients are usually treated with antiretroviral drugs which slows down the spread of the virus in the body.

C3.2.13—Antibiotics as chemicals that block processes occurring in bacteria but not in eukaryotic cells

Include reasons that antibiotics fail to control infection with viruses.

Antibiotics are chemicals that block processes (usually DNA replication, transcription, and translation) occurring in bacteria but not in eukaryotic cells, which is why they are toxic to bacteria but not humans.

Since viruses are not considered 'living,' antibiotics are **not** an option for controlling viral infections.

C3.2.14—Evolution of resistance to several antibiotics in strains of pathogenic bacteria

Students should understand that careful use of antibiotics is necessary to slow the emergence of multiresistant bacteria.

There are several reasons as to why the emergence of multiresistant bacteria has significantly increased:

- inappropriate prescription of antibiotics to patients
- overuse in hospitals and agriculture
- reduced availability of new antibiotics due to high research expenses

This is alarming because the world could return to the 'pre-antibiotic era' of high mortality rates.

NOS: Students should recognize that the development of new techniques can lead to new avenues of research; for example, the recent technique of searching chemical libraries is yielding new antibiotics.

Chemical or compound libraries are collections of compounds that are designed to interact with specific and related targets. They are used to screen against therapeutic targets in order to discover new compounds that have the potential to be further developed into drugs. This improves the efficiency of the drug discovery process, reducing costs and hopefully encouraging investment into new antibiotics.

C3.2.15—Zoonoses as infectious diseases that can transfer from other species to humans

Illustrate the prevalence of zoonoses as infectious diseases in humans and their varied modes of infection with several examples including tuberculosis, rabies and Japanese encephalitis. Include COVID-19 as an infectious disease that has recently transferred from another species, with profound consequences for humans.

Zoonoses (*zoon* for animals and *noson* for disease) are, as defined by the WHO in 1951, "diseases and infections that are naturally transmitted between vertebrate animals and (humans)." Examples include:

- **Tuberculosis** (TB) is a bacterium mainly transmitted by **cattle** to humans by drinking their contaminated milk or inhaling their sneeze or cough droplets.
- **Rabies** is a viral disease mainly transmitted by **dog bites** and affects the central nervous system.
- **Japanese encephalitis** is a viral disease transmitted through **mosquito bites**.
- **COVID-19** is a viral disease that is accepted to have been transmitted from **bats**, causing a world-wide pandemic and lockdown for more than a year.

C3.2.16—Vaccines and immunization

Students should understand that vaccines contain antigens, or nucleic acids (DNA or RNA) with sequences that code for antigens, and that they stimulate the development of immunity to a specific pathogen without causing the disease.

Immunization stimulates the development of immunity to a specific pathogen by producing memory cells through various methods, such as:

- an attenuated version of the pathogen
- a killed version of the pathogen
- fragments of the pathogens (i.e. its antigens)
- mRNA that codes for the pathogen's antigens, stimulating antibody production in the vaccinated person

C3.2.17—Herd immunity and the prevention of epidemics

Students should understand how members of a population are interdependent in building herd immunity. If a sufficient percentage of a population is immune to a disease, transmission is greatly impeded.

Herd immunity occurs when a large portion of the population has been infected with a disease or vaccinated against it – greatly impeding its spread. The percentage of the population needed to be vaccinated in order to reach herd immunity can be calculated using the following formula:

$$(1 - \frac{1}{R0}) \times 100$$

Where $R0$ is the average number of people infected by one person.

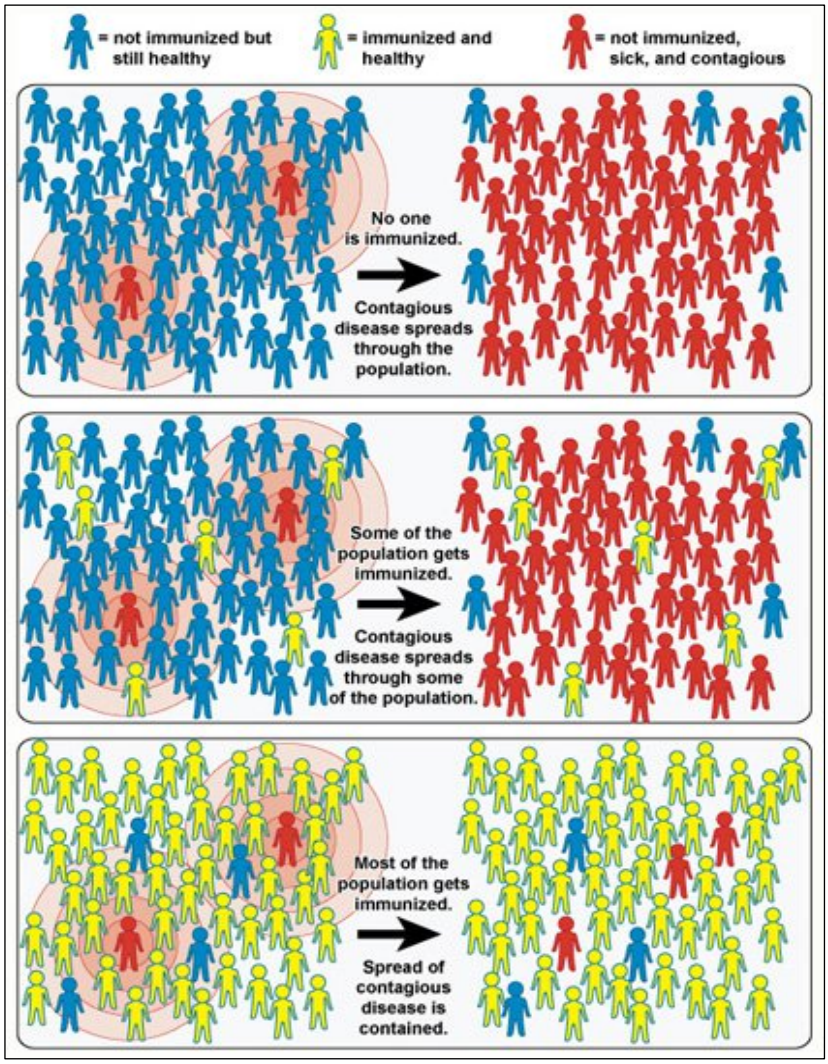

Figure 4: herd immunity (Helft).

NOS: Scientists publish their research so that other scientists can evaluate it. The media often report on the research while evaluation is still happening, and consumers need to be aware of this. Vaccines are tested rigorously and the risks of side effects are minimal but not nil. The distinction between pragmatic truths and certainty is poorly understood.

Peer review takes time, and media reports do not always cover the full picture of a new research endeavor. Misinformation on new scientific phenomena can become widespread, so critical evaluation of sources is needed by the public in order to validate pragmatic truths.

C3.2.18—Evaluation of data related to the COVID-19 pandemic
Application of skills: Students should have the opportunity to calculate both percentage difference and percentage change.
In order to evaluate a set of data numerically, percentage difference and change should be calculated. $$\text{Percentage difference} = \frac{\text{numerical value 1}}{\text{numerical value 2}} \times 100$$ $$\text{Percentage change} = \frac{\text{final value} - \text{initial value}}{\text{initial value}} \times 100$$ This is helpful in epidemiological analysis, for example when analyzing the spread and control of the COVID-19 pandemic in different continents and countries.

Note: There is no additional higher level content in C3.2.

Linking questions

• How do animals protect themselves from threats?

• How can false-positive and false-negative results be avoided in diagnostic tests?

Review questions

- Define a pathogen. [1]
- Define herd immunity. [1]
- Distinguish between HIV and AIDS. [1]
- Outline the role of chemical libraries in discovering new antibiotics. [2]
- Outline the reasons for the rapid emergence of antibiotic resistance. [2]
- Distinguish between plasma and memory cells. [2]
- Outline why antibiotics are not a viable option for eliminating HIV. [2]
- Describe the functions of antibodies. [3]
- Distinguish between antibodies and antigens. [4]
- Distinguish between the innate and adaptive immune systems. [4]
- Describe the processes that take place when skin cuts occur. [4]
- Using two examples, explain the role of observations in advancing understanding of infectious disease. [4]
- Explain how phagocytes control infection. [4]
- Describe the role of lymphocytes in controlling diseases. [4]
- Using examples, explain the various modes of zoonotic transmission. [5]
- Explain how the skin and mucous membranes act as a primary defence against pathogens. [4]
- Explain the organization of the immune system in humans. [7]
- As Eula Biss once said, “Imagine the action of a vaccine not just in terms of how it affects a single body, but also in terms of how it affects the collective body of a community.” Explain how vaccines work, including their role in herd immunity. [7]
- Enzymes bind to substrates in an “induced fit model,” whereas antibodies fit like “a lock and key” with specific antigens. Explain the difference between each model, outlining any implication. [7]
- Antibodies produced by mammalian adaptive immune systems are extraordinarily diverse. Explain the functions that result from such diversity, and how this diversity is achieved. [7]
- Discuss how a virus that enters the airways of an individual is combatted by the body. [7]
- Distinguish between the different types of cells involved in the human immune response. [7]
- Explain how the body detects and fights off infections. [8]

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