# Invasion and infection

## Our bodies are homes to millions of organisms

Millions of microbes have made your body their habitat and most of them will never do you any harm. However, some can be pathogenic, which means that they cause disease. Human pathogens include some bacteria, viruses and fungi, as well as parasites such as tapeworms and flukes, and protozoa like *Plasmodium*, which causes malaria.

Some microbes can be good for us. It's known that the gut microbiota, the bacteria in our gastrointestinal tract, exist in a mutualistic relationship with us – one where both parties benefit. But it's not clear how the immune system views these cells. Recent studies suggest that newly discovered populations of immune cells may help train the immune system to tolerate beneficial bacteria.

| | Organisms included | Number of cells | Presence of mitochondria | Type of immune system | Type of reproduction |
|---|---|---|---|---|---|
| **Eukaryotes** | Animals, plants, fungi | Often, but not always, multicellular | Cells use mitochondria to release energy | Some multicellular eukaryotes have sophisticated circulatory, nervous and immune systems | Sexual or asexual reproduction |
| **Prokaryotes** | Bacteria and cyanobacteria | Always single-celled | No mitochondria | Basic immune responses | Usually, but not always, asexual reproduction |
| **Viruses** | Viruses | No cells, just virus particles called virions (RNA or DNA inside a protein coat) | No mitochondria | No immune system | Viral replication by taking over a host cell |

## *Barriers help protect our insides from outside*

One organ acts as your largest and perhaps most important barrier against infection. Spread out on the ground, it would cover two square metres: your skin. It's tough – skin cells are packed full of strong structural proteins called keratins, which act as a barrier. As the cells grow outwards, they die. The stratum corneum – the outermost layer of the epidermis, which is the outermost layer of the skin – is completely dead. Viruses can't replicate in dead cells. Microbes are often outcompeted by bacteria that live on our skin in a mutualistic relationship with us.

Inside our bodies, sticky mucous membranes line our airways and guts, as well as the tracts in our urinary and reproductive systems. These need to be protected because they are constantly exposed to microbes – for example, in the air we breathe and the food we eat. Mucus traps and destroys microbes by deploying enzymes such as lysozyme, which breaks down bacterial cell walls. Cells in the stomach lining secrete hydrochloric acid, creating an acidic environment too inhospitable for many bacteria.

However some bacteria, such as *Helicobacter pylori*, which cause stomach ulcers, have adapted their defences. These bacteria produce an enzyme called urease, which uses urea from human tissues to make ammonia – an alkaline chemical that neutralises the acid.

If something goes wrong with these barriers, we become more susceptible to disease. For instance, some people have genetic mutations that affect a protein in the skin called filaggrin. Filaggrin plays an important role in strengthening the skin, by helping organise the keratin filaments in skin cells and also by moisturising the skin. Filaggrin mutations weaken the skin barrier, allowing allergens to enter through it. This leads to some cases of eczema, asthma and hay fever.

### *How diseases spread*

Disease spreads when the body's defensive barriers are breached. Bacteria or viruses might be transmitted directly through contact with infected bodily fluids such as blood, saliva or semen. Some viruses, like influenza, survive just long enough in saliva and nasal secretions that they can be transferred by a sneeze, whereas HIV can't, and is usually spread through sex or the sharing of needles used to inject drugs.

Infectious agents can also be transmitted indirectly by other organisms – so-called vectors like the female *Anopheles* mosquito that carries the malaria parasite. The death toll of malaria (over 620,000 people globally in 2012) has led to the mosquito being described as the world's most dangerous animal.

Not all diseases cause symptoms straight away, meaning that there may be a window for potentially spreading the infection without realising. This 'incubation period', the time between infection and symptoms starting to show, varies between infections: it is a few days for flu, but a few weeks, months or even longer for HIV.

## Some infections are with us for life

Some microorganisms can lie latent in our cells for months or years. Although they may not multiply and don't cause disease during this time, they remain undefeated by the immune system.

A common example is herpes simplex virus 1 (HSV-1), which causes cold sores. It persists in nerve cells in the peripheral nervous system (outside of the brain and spinal cord) and can be reactivated by factors like stress, illness or sunlight to cause new cold sores.

Another herpes-type virus is cytomegalovirus, which causes severe developmental abnormalities if contracted by an unborn baby. In children and adults, cytomegalovirus might cause only one bout of flulike disease, but it takes up lifelong residence in the body just like HSV-1. Cytomegalovirus can recur and cause more-serious problems in people with weakened immune systems, like those undergoing chemotherapy.

## Cold or flu?

*People sometimes confuse these very different viruses*

At the root of most runny noses are one of two different kinds of virus: orthomyxoviruses (influenza) or rhinoviruses (the common cold). There are many different strains of each, but influenza viruses generally cause much more severe symptoms.

Viruses evolve very quickly, meaning that under the selective pressure of our immune systems, new cold and flu strains can emerge within a single season. Viruses have only a few genes, which means that one mutation can make a big difference. It's this ability to adapt, known as antigenic variation, that produces viruses that can dodge our defences. The immune system might produce antibodies to deal with one strain, but when a new strain emerges, it isn't recognised.

Flu can be fatal – the 1918–19 pandemic killed more people than World War I – so it is the subject of intense research. Much of this research focuses on variation in H (haemagglutinin) and N (neuraminidase) proteins embedded in the virus's outer coat. Changes to these proteins make it harder for the host immune system to recognise the virus.

Rhinoviruses, though less deadly, are also remarkably adept at avoiding the human immune system. Some dampen immune responses by interfering with the signals that attract immune cells, while those that receive a strong immune response seem to evolve even more rapidly to escape it.

## Tuberculosis (TB) is a disease caused by *Mycobacterium tuberculosis*

Centuries ago, TB was known as 'consumption' and was thought to be incurable. Today, TB is treatable with antibiotics, but over a million people with the disease still die every year, mostly in poorer countries.

Not everyone who gets infected with the bacterium *M. tuberculosis* develops symptoms, which include coughing and weight loss. Worldwide, as many as 1 in 3 people may carry the bacterium. The bacteria are phagocytosed in the lungs by immune cells called macrophages. In most people, tuberculosis infection remains latent, kept in check by T cells. But in people with weakened immune systems, such as caused by HIV, it can reactivate to cause post-primary TB, usually affecting the lungs.

If the bacterium that causes TB gets into the brain through the bloodstream it can cause an infection called tuberculous meningitis. The live Bacille Calmette–Guérin (BCG) vaccine can prevent this in children, but it does not protect against lung disease in adolescents or adults. The BCG vaccination is no longer routinely given to teenagers in the UK because cases there are so rare, but it is used in the UK for at-risk babies.

Blood tests for TB measure the levels of an immune molecule called interferon-gamma, which is produced by an infected person's white blood cells when they are mixed with antigens from *M. tuberculosis*. Treatment for TB involves taking a combination of different drugs for several months, but this regimen must be strictly adhered to or the bacterium can become drug-resistant and harder to treat. Drug-resistant forms of TB are a serious health concern.

## Investigating immunotherapy

Immunotherapy is a treatment approach intended to ramp up the body's natural immune response in order to fight off disease. For example, a drug called ipilimumab effectively puts T cells into permanent destruction mode and is used to treat advanced skin cancer. The downside of this approach is that the immune system is very powerful, so although the T cells may kill the cancer cells, they can also attack healthy cells. These side-effects can themselves be fatal.

Immunotherapy is also used in allergic diseases to try to reduce allergy symptoms by gradually increasing the immune system's tolerance of an allergen. Patients receive tiny amounts of the offending antigens under the tongue or by injection, and the amount given is gradually increased. Benefits of immunotherapy have been shown for hay fever, rhinitis (inflammation of the inside of the nose), and allergies to insect bites or peanuts.