What is immunology? Immunology is study of the immune system. So then the question is:

**What is the immune system?**
The immune system is one of the most complex group of cells and organs that keeps us alive. Every minute of every day, with every breath, with every meal, our body is exposed to thousands of „non-self“ particles; particles that don't belong to our own body. These can be anything from proteins or metal atoms to bacteria and viruses. Most of these particles are harmless, but bacteria and viruses are possibly the best examples of particles which are harmful, and, if left uncontrolled could kill us within days. Click [here](#) to see a brief overview of what an immune response involves.

**Cells of the immune system, innate or adaptive?**
The immune system consists of lots of different types of cells, each specialised to do a very specific task. They all work together very well, they all communicate together constantly either by direct contact or by sending protein signals to each other (cytokines). In this way, the threat to the body is removed in an extremely efficient way.

The immune system itself can be divided into two categories, the innate immune system and the adaptive immune system. Both are as important as each other and they overlap in their function.

**Innate immune system**
*The innate immune system* is aptly named since it is the system we are born with. It consists of cells such as neutrophils or macrophages which have one primary function which is to eat or *phagocytose* the invading threat. These cells kick into action extremely quickly from queues given to them by the invading threat. It’s a mechanism which has developed over millions of years and some aspects of this system can even be identified in plants. It’s a crude way of tackling the problem and it’s extremely fast; just what you want on your front line defenses.

**Did you know?**
Although the immune system is best known to protect us against „non-self“, a healthy immune system can also protect us from ourselves! Scientists have calculated that immune cells can remove up to 200 potential cancerous cells a day. Cancerous cells are „self“ but they are recognised as not normal and therefore are killed. When this recognition does not occur, potentially malignant cancers can develop uncontrolled.
Adaptive immune system
The adaptive immune system is far more complex. It’s one which responds over a period of days rather than seconds. The reason for this is that during those days, a carefully targeted and highly orchestrated immune response is being developed by the immune cells. Highly specialised cells that will respond only to the specific threat are bulked up in numbers. This is done by trial and error and therefore takes time, days. It may be slow, but it is effective, far more effective than the innate immune system. The crowning jewel of the adaptive immune system is that it also remembers what we were infected with for life, the underlying basis for vaccination.

Neutrophils
Neutrophils are the most abundant cell of the innate immune system. They circulate in the blood stream and are very sensitive to any stimulus. They are loaded with potent enzymes which allow them to plough through the blood vessels (extravasation) and underlying tissues to reach the sites of danger or infection. Once there, the neutrophils’ main function is to eat or phagocytose non-self particles. They are therefore a member of the phagocyte family (cells that eat). Neutrophils are capable of sensing what is self and what is not. Once non-self is identified, the intruder is engulfed by the neutrophil within seconds. Once inside the neutrophil, the invading particle is digested by enzymes in an acid bath within 1 minute. Pretty fast and pretty gruesome!

Macrophages
Macrophages get their name from being big (Greek:makro) and by eating a lot (Greek:phagein). They too are part of the phagocyte family because they eat a lot. Macrophages also belong to the innate immune system but the function of macrophages is determined by the adaptive immune system. As the name states, macrophages also eat invading particles such as bacteria and they do so fairly rapidly, although not as fast as neutrophils until the adaptive immune system tells them to act. So the main difference between neutrophils and macrophages is that macrophages listen to what the adaptive immune systems says and also directly interacts with cells of the adaptive system.

Dendritic cells
Dendritic cells are also phagocytes, but in comparison with the neutrophil and even the macrophage, they pale in comparison on the eating or phagocytosis capabilities. Their main function is to bridge both the innate and adaptive immune systems. When ‘immature’ dendritic cells are stimulated, they will eat some particles and then immediately migrate from where they were sitting (for instance, the skin) to one of hundreds of special organs called the lymph node. There, they change their function from phagocyte to antigen presenting cell (APC) or fully mature dendritic cell. In the process of phagocytosing a few particles, the dendritic cell also killed the invading pathogen within a few minutes, but the true function of the dendritic cell now starts: dendritic cells show the remains of the particle (usually protein segments or peptides, commonly called antigens) to the rest of the

Did you know?
Dendritic cells were first described by Ralph Steinman in 1973 in the Journal of Experimental Medicine. In 2011, Steinman’s pioneering work with dendritic cells earned him the Nobel Prize for Physiology or Medicine. Sadly, Ralph Steinman passed away 3 days before he was due to receive his prize.
immune system, essentially 'advertising' what has been caught and killed. Now the adaptive immune system can 'see' what the danger is and can mount its response to the invading pathogen.

**T cells**

T cells are so called because they are selected in the thymus (although originating from the bone marrow), a specialised organ that sits above the heart. These cells are at the heart of the adaptive immune system and instruct other immune cells how to behave in order to eradicate the unwanted invasion.

T cells are made in such a way that for each single possible combination of amino acid sequence in the antigen, there exists at least one T cell that will recognise it. This is done by a process of DNA recombination, mutations and trial and error. Of course this would mean some may turn out to recognise self, but this is where the thymus comes in. The thymus' function is to select only T cells which recognise non-self antigens by processes called **positive and negative selection**.

Thymus-selected T cells travel through the body, blood and lymph and percolate through lymph nodes checking to see if there are dendritic cells advertising the specific sequence that it will recognise. If during its travels it doesn't find this antigen, it just keeps on circulating. However, if the T cell encounters the antigen that it was designed to recognise, then very quickly the T cell begins to proliferate or duplicate itself. This happens over the space of hours and is a rapid process where every 6 hours the cells duplicate.

This rapid proliferation occurs in the **lymph nodes**, which are distributed throughout the body, namely around the neck, the armpits and the groin. When you have a sore throat, often you can feel large lumps on the side of your throat, these are lymph nodes swollen because they contain millions and millions of T cells. Tonsils are also lymph nodes.

There are many different types of T cells but the main categories are called **CD4 helper T cells** and **CD8 cytotoxic T cells**. Within each category, these can be subdivided even more depending on the types of functions they have.

**B cells**

B cells are so called because the originate from the bone marrow. The main function of B cells is to produce **antibodies**. Antibodies are Y-shaped molecules that are used to neutralise an invading pathogen. Antibodies fix themselves to specific proteins of the intruder and don’t let go. They do this by recognising specific shapes that are foreign. B cells start producing antibodies that are not particularly specific to the foreign antigen at first. However T cells communicate with B cells in the lymph node and give them signals to recombine and mutate their DNA in a trial and error fashion to make more specific antibodies. The more specific the antibody gets, the more encouragement the T cells provide the B cells by providing cytokines such as interleukin-4. The B cells that rearrange their DNA to make specific antibodies then proliferate massively and produce millions upon millions of antibody molecules that travel through the body, capturing the foreign proteins that they were designed to recognise.
Once the specific antibody latches onto the foreign particle, other cells of the immune system such as phagocytes can capture it and eat it by the process of phagocytosis.

How does it work?
The best way to explain the immune system is to take examples. Below are a few simple examples of how the immune system works.

Bacterial infections
Suppose you fall over while running and as a result you cut your hand open on the ground. Your skin is usually the first layer of protection against the millions of bacteria you have on your skin, but this time this first barrier has been breached, and bacteria have entered the skin. The first line of defense is the innate immune system and in particular, neutrophils. Neutrophils phagocytose the bacteria furiously, but they are indiscriminate, they secrete enzymes that destroy not only the bacteria but also the skin tissue. Millions and millions of neutrophils are flooding into the area of skin that has been breached, this causes the affected area to feel warm, swollen and sore. Blood vessels around the cut become more permeable, allowing more immune cells to go from the blood into the skin by a process called extravasation.

In the skin, there are also specialised immature dendritic cells, these have eaten only a few bacteria and subsequently left the infected area to go to the closest lymph node (in the case of the hand, this will be in the armpit). While they migrate from the skin to the lymph node via the lymphatic system, they process the bacteria they phagocytosed and present hundreds of foreign antigens or protein fragments on their surface using a molecule called MHC class II. This cell surface molecule presents antigen that has been acquired via phagocytosis.

Meanwhile back at the infection site, macrophages have arrived near the breached skin and are also phagocytosing the bacteria but not as fast as neutrophils.

In the lymph node, some antigens being presented by the now mature dendritic cells have been recognised as foreign by a few T cells and this causes the T cells to proliferate furiously. Some T cells leave the lymph node and enter the bloodstream. Eventually these T cells will also extravasate into the site of infection where the breach to the skin took place. Here, they will secrete cytokines, soluble messenger proteins which instruct other cells in the body. For instance, interferon gamma (IFN-γ) secreted by T cells will boost the macrophages into phagocytosis overdrive.

While macrophages have been stimulated to phagocytose as many bacteria as possible, antibody production has begun back in the lymph node, where T cells have been instructing B cells into making specific antibodies to some bacterial surface antigens. These antibodies circulate in the blood and bind the surface of the bacteria in a process called opsonization. Bacteria remaining in the
Did you know?
When infected with the flu, other than feeling generally bad, your throat will be sore and itchy. This is because your CD8 T cells are killing virally infected epithelial cells in your throat. A rise in body temperature commonly known as fever is also beneficial to the immune system but hinders bacterial and viral proliferation, giving the edge to your own body’s defenses. Therefore signs of illness such as sore throats, swollen lymph nodes and fever are all indications that your body is fighting the infection.

Complement system
The complement system is seen as an innate immune response, it is extremely rapid and efficient. Activation of the complement system occurs on surfaces, such as the surface of a bacterium. The activation of complement is initiated by antibodies that bind to bacterial cell surface antigens. The complement cascade is then initiated whereby proteins secreted by the host bind to the antibodies and the surface of the bacterium with multiple enzyme reactions occurring at the surface of the bacterium. The result is that potent chemoattractants are produced, attracting more neutrophils and macrophages to the site of infection and large pores are punched into the bacterial membrane which leads to the death of the bacteria.

Viral infection
Viral infections differ considerably in terms of the immune response. Viruses do not contain the necessary machinery within them to reproduce by themselves and therefore viruses need a host cell in order to replicate. This means that the large majority of the time, viruses are hijacking host cells and are intra-cellular. Cells which are infected by virus particles present viral antigens on MHC class I cell surface molecules, and these are recognised by Natural Killer T cells and CD8 cytotoxic T cells, not CD4 T helper cells as in bacterial infections (which interact with MHC class II molecules).

Natural Killer T cells are essentially innate T cells which recognise certain distress signals shown by virally infected cells. These killer immune cells kill virally infected host cells. They are however rather crude in their specificity and create a lot of collateral damage when they are activated.

The more specific and adaptive immune CD8 T cells differ greatly from CD4 in that their main function is to seek and lyse (permeabilise and thus kill) cells which are infected with virus. In addition to CD8 T cell activation, B cells are also stimulated to produce specific antibodies to viral coat proteins in order to neutralise free floating viruses. This has the effect of disabling the virus from infecting other cells and also causing phagocytes (macrophages and neutrophils) to phagocytose antibody covered viral particles. The immune system has therefore adopted a mechanism of destroying infected cells as a primary defense strategy against viral infections.
Immune memory and vaccinations

The immune system has just been described as a highly complex set of specialised cells which all work together in harmony during an infection. The majority of the time, we are not even aware that we have been infected by bacteria or viruses. However, the most interesting and important aspect of the immune system is „immune memory“. Once we have been infected with a bacteria or a virus, the immune system „remembers“ the infection by keeping some immune cells (CD4, CD8 and B cells) specific to that infection for many years. This means that the entire process of T cell selection and B cell antibody maturation and affinity does not need to occur again if the host is infected by the same type of bacterium/virus.

It is this principle of immune memory that medicine has taken advantage of in the process of vaccination. Vaccines are typically proteins or „attenuated“ versions of the bacteria or viruses for which we are being vaccinated against. This gives the body the chance to experience exposure to the bacterial or viral proteins without the real risk of infection. Specific T cells are selected, specific antibodies are generated without any illness or symptoms of infection. The host will maintain a pool of specific cells throughout the lifetime of the host and thus when a real infection occurs for which the host has been vaccinated, the immune cells are primed and ready to fight, thus giving the host the upper hand during the immune response.

What happens to the immune system in Space?

Effects of microgravity

Back in 1983, during the Spacelab 1 Mission, it was observed that T cell activation was hampered in microgravity. Further investigations using clinostat machines used to approximate microgravity conditions on earth, showed that T cells lose their capability to become activated after encountering their specific antigen. Studies in animals also showed that Killer cells were unable to behave normally under microgravity conditions and unable to effectively fight off viral infections.

Subsequent studies have shown that cells have mechano-receptors which are sensitive to gravity. These receptors are closely associated with the „skeleton“ of cells (cytoskeleton) which is responsible for maintaining the shape of the cells but also distributing organelles and enzymes within the cells. Some important intracellular enzymes which trigger signalling cascades within immune cells simply do not function in microgravity conditions.

Cosmic radiation

Cosmic radiation is everywhere in space. When combined with other factors such as microgravity, it is highly likely that radiation can have an aggravates effect on the immune system.

When on extended mission, astronauts will be exposed to stronger and more varied types of radiation than that experienced normally. For more information on types of radiation please see the radiation lesson. These radiation types primarily consist of solar energetic particles, protons and highly charged energetic particles of galactic cosmic rays. The degree of exposure to solar energetic particles will increase during interplanetary missions as the partial shielding from the Earth’s magnetic field is no longer protective when leaving Earth’s orbit.

Did you know

The term „vaccination“ comes from „vaccinia virus“ (which causes cow pox) which was first used to demonstrate the principle of immunological memory when Edward Jenner found cowpox virus protected humans from small pox infection (a slightly different variant of the cow pox virus).
Although little is known about the consequence of cosmic radiation on immune cells, many publications confirm the impact of other forms of radiation on immune cells. Such radiation can kill cells, cause mutations, cause inflammation and malignancies and otherwise weaken the immune system. This damage however, can take years to become apparent. So only time will tell whether astronauts are at higher risk of developing immune related diseases.

Mission related stress
Preparation for a mission is an intensive period of time for an astronaut, strict schedules of countless hours of work, training and travel all amount to an increased level of stress to the astronaut. The stress associated with mission preparation and during the actual mission is known to affect how the body responds to infection. During stressful periods, the body produces high levels of cortisol, the stress hormone, which increases blood pressure, blood sugar levels and suppresses the immune response. Indeed, when under strain, humans are more likely to get sick. In studies of medical students during the highly stressful time of exams, tests showed increased stress hormones and suppressed immune cell activities, which lead to reactivation of dormant viruses such as HSV1 which leads to cold sores and EBV which leads to glandular fever.

Much in the same way that students succumb to reactivation of dormant viruses, astronauts also fall victim. Elevated cortisol levels suppress the immune system at both the innate and adaptive levels. Blood taken from astronauts before and after flight shows impaired ability post flight in macrophages to produce adequate levels of H2O2 (which is used to kill phagocytosed bacteria). Similarly, the adaptive immune response is affected as T cells seem unable to respond effectively when encountering their antigen.

Dangerous space bacteria
Research on the ISS has shown that bacteria are also subject to change in microgravity. However, unlike the immune system of the astronaut which is rendered less functional, the bacteria tend to become more dangerous. The bacteria tested in these studies were Salmonella typhimurium (which cause food poisoning) and when grown in the ISS, they showed increased ability to infect due to changed genetic expression profiles.

Therefore the combination of radiation, defective cellular response, the downregulating effect of stress hormones on the immune system and the increased virulence of certain pathogens all add up to the simple conclusion that if man wants to conquer space, we need to do more research on the immune system.