

A VIRAL HANDSHAKE

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We constantly interact with microbes of all sizes and shapes. But, only a very small number of these interactions lead to disease. So, how do disease-causing microbes enter our body? How does the human body defend itself against them? This article explores some of these questions in the context of common cold.

"I tried to picture myself as a virus or a cancer cell and tried to sense what it would be like." Jonas Salk
(Scientist and discoverer of the polio vaccine)

What do you do when you meet someone? If you are meeting for the first time, you greet them politely or shake hands with them. If you're meeting a friend, you give them a smile, or greet them with a hug. But what if it's someone you don't like or see as a threat? It's most likely that you'll try to ignore them; under some circumstances, you may even fight with them! We interact with a lot of people – friends, family, people we work/study with - every day of our lives. But did you know that your body is also constantly interacting, in some pretty similar ways, with thousands of living organisms every day? 'How, Where, and Why?' you may ask. To understand, let's take a look at some of these interactions – and

what better example can we choose for this than those resulting in the common cold!

Briefly, colds are caused by viruses. If the interactions of the human body with the cold causing virus were to be made into a movie, it would most likely be called 'Cell Wars: Attack of the Cold Virus'. Like any popular movie, this one would also have a Villain (the tiny but cunning cold virus), a Heroine (our body) whom the villain is out to hurt and the Heroes (the small but courageous immune cells).

A virus is a very tiny microorganism that is smaller than a speck of dust! A virus is typically made up of a nucleic acid within a protein coat, and can multiply only within another living cell/ host.

The cold virus

Allow me to introduce you to the villain of our story - the Virus. Many different viruses can cause colds, but up to 80% of all colds are caused by a viral species, known as Rhinovirus.

Humans have been getting colds since ancient times. Most adults get colds at least two times a year, while children can get colds 6-12 times a year!

What is a rhinovirus? It is a very small virus, so small in fact that it can only be seen using a very powerful microscope called an Electron Microscope. Its actual size is only 30 nanometers or 0.000003 millimeters (which is almost a billion times smaller than a rhinoceros!). A typical rhinovirus looks very much like a football, with pentagonal parts attached to each other to form a rounded structure. But while a football is smooth on the outside, the outer surface of the rhinovirus (let's just call it the cold virus) is anything but smooth - it's covered with lots of knob-like outgrowths (do remember these knobs, for they play an important role in our story!). There are around 115 different types of rhinoviruses, with very minor differences between them.

Before we go any further, I know what you are impatiently waiting to hear. If it does not look like a Rhinoceros, and is nowhere close to being the same size, why is this cold virus called a rhinovirus? The word 'rhinos' (pronounced rhy-noz) means 'nose' in Greek, which is where this virus likes living. How boring! But at least it will help you remember the name better!

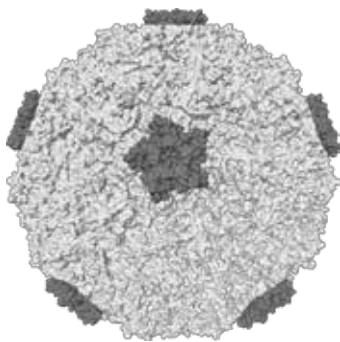


Figure 1. A rhinovirus looks like much like a football, except for protein spikes coloured in grey here. Source: Wikimedia Commons. URL: <https://upload.wikimedia.org/wikipedia/commons/e/ef/Rhinovirus.PNG>. GNU Free Documentation License.

THE COST OF THE COMMON COLD & INFLUENZA

Work it out like this.

On an average 2 days work are lost a year by each worker

Say there are 10 million people on vital war production

That means 20 million days lost each year—

The work of 50,000 men for one year.

★ IF one third of all the men and women who lost these days were making tanks, one third bombers, and one third rifles

Then in that time they could make



3,500 TANKS



1,000 BOMBERS



1,000,000 RIFLES

That is the cost to our war effort. We can all help to reduce that cost. Do your bit to prevent the spread of infection—by trapping the germs in a handkerchief when you cough or sneeze.

HELP TO KEEP THE NATION FIGHTING FIT

Figure 2. The cost of common cold (and influenza).

Source: U.S. National Library of Medicine: History of Medicine

The Cost Of The Common Cold & Influenza. Wikimedia Commons.

URL: https://en.wikipedia.org/wiki/File:The_Cost_Of_The_Common_Cold_%26_Influenza.jpg. Image in Public Domain.

Although not a very dangerous microbe, the cold-causing virus is very cunning and so successful that it attacks almost everybody - rich or poor, old or young, male or female - at some point in their lives. Who amongst us doesn't remember the unpleasantness of having a runny nose, sore throat, a feverish body, and in some cases, even the feeling that we may not

Rhinoviruses can infect only humans, gibbons and chimpanzees

survive this bout of infection! But don't we almost always recover from the cold, even when we haven't been to a doctor for medicines or had the homemade potion made by our grandmother?!

How does the cold virus come in contact with your body? The virus can only reach and infect you if you are in close contact with a person already suffering from cold. If we wanted to sound very knowledgeable, we'd call this 'contact transmission'. When a sick person touches an object (like door handle, books, water bottles or clothes), he leaves lakhs of cold viruses on it. Cold viruses can survive (stay alive) for 4-5 hours on contaminated objects (the colder the weather, the longer they live). When an unsuspecting healthy person touches their nose/mouth after shaking hands with a sick person or touching a surface contaminated with the virus, the virus enters this person's naso-pharynx (the cavity in the back of your throat which connects the nose and mouth). In some cases, you can also catch a cold when a sick person coughs or sneezes near you - the virus comes out in small droplets which hang in the air (much like the spray from perfume bottle) and can directly reach your nose. This is called aerosol infection.

If you (or your friend/family members) are suffering from a cold, then cover your nose and mouth while sneezing or coughing, and wash your hands with soap and water to prevent the virus from spreading.



Figure 3. Aerosol infections are caused by the viruses in droplets sneezed out by an infected person. Source: James Gathany - CDC Public Health Image library ID 11162. Wikimedia Commons. URL: <https://en.wikipedia.org/wiki/Sneeze#/media/File:Sneeze.JPG>. Image in Public Domain

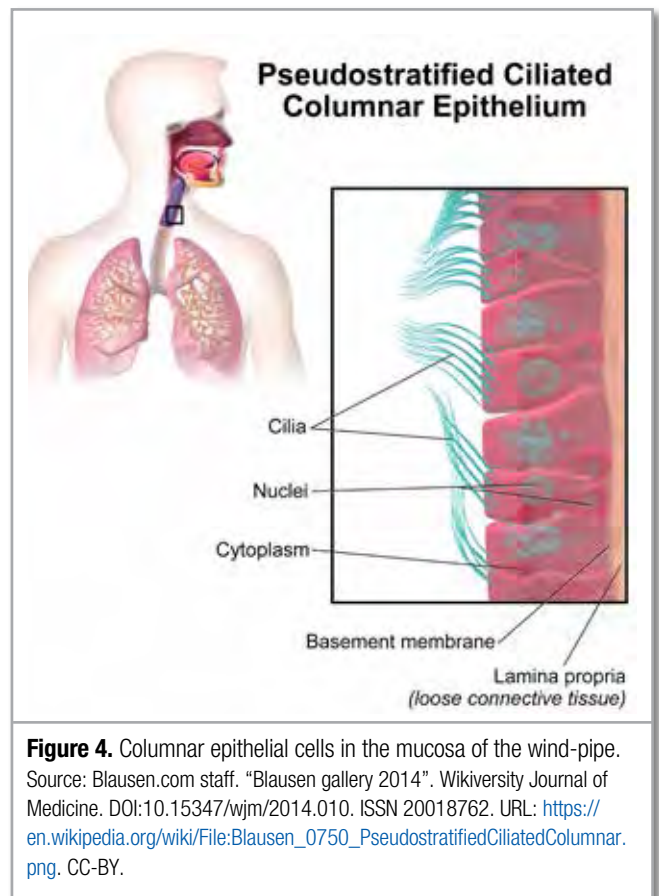


Figure 4. Columnar epithelial cells in the mucosa of the wind-pipe. Source: Blausen.com staff. "Blausen gallery 2014". Wikiversity Journal of Medicine. DOI:10.15347/wjm/2014.010. ISSN 20018762. URL: https://en.wikipedia.org/wiki/File:Blausen_0750_PseudostratifiedCiliatedColumnar.png. CC-BY.

We all know that the air we breathe in through our nostrils reaches the lungs through a hollow tube called the wind-pipe. The wind-pipe consists of four parts – the nasal cavity, pharynx, trachea and bronchi. The entire inner surface of the wind-pipe is lined with a membrane called the mucosa, which is made up of different types of cells arranged in many layers. The outermost layer is made up of epithelial cells (cells arranged in layer to form a tissue which covers the internal organs and the internal surfaces of the body) shaped like columns. Each of these columnar cells has various molecules, also known as receptors, on their surface that are known by exotic names, like ICAM-1 and LDL receptors. As soon as the virus reaches the nose of a healthy person, it starts its dirty work. Remember the knob-like outgrowths on the outer surface of the virus? Well, the virus uses these knob-like appendages (limbs) to hold onto the receptors on

A receptor is a structure on the surface of the cell (or sometimes within the cell) which can attach or hold on to specific substances or molecules.

All animals, including humans, reproduce/replicate using DNA (Deoxyribonucleic Acid) as their genetic material. All information, like the colour of our eyes, whether we have straight or curly hair etc., is contained within our DNA, which we get from our parents. In contrast, the genetic material in rhinoviruses is in the form of RNA, which performs roles similar to that of DNA within our body.

the cells of the nasal mucosa. **This is very similar to two people shaking hands when they meet, except that the virus is very rude and does not release the cell's hand!**

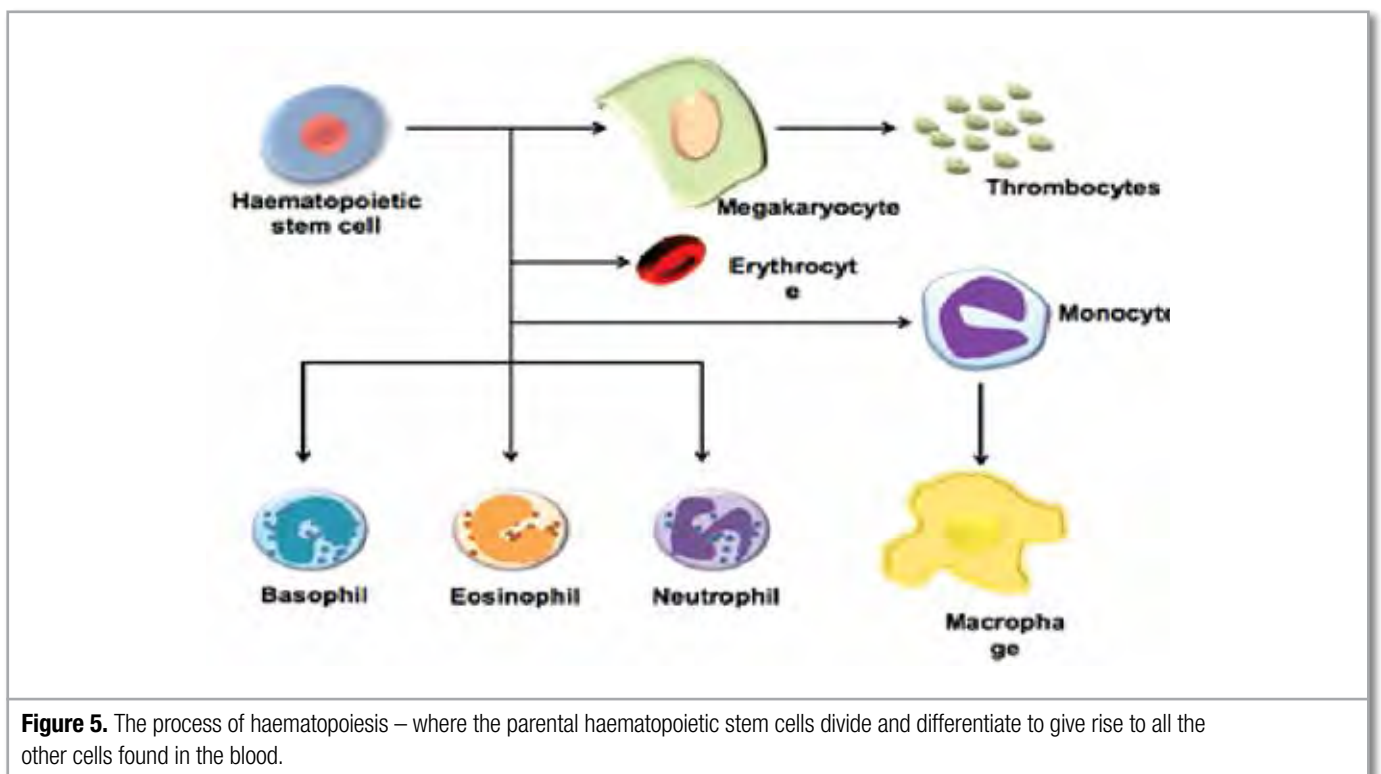
Once the virus has attached itself to one of these mucosal cells lining our respiratory tract, it does something very devious. It makes a hole in the wall of the cell and injects its genetic material (in the form of Ribonucleic Acid or RNA) into the cell. This is where the virus shows us that even though it is smaller than even a speck of dust, it is very, very smart. It tricks the cell into thinking that the viral RNA is part of the cell. Unable to see through this illusion, the poor host cell uses its own energy and resources to make hundreds of thousands of copies of the viral RNA. Each one of these RNA molecules, in turn, tricks the cell into making a football-like protein cover with knobs on it. Thus are born lakhs of new viruses. All

this is accomplished without the virus spending any energy or resources of its own.

By this time, the host cell has run out of its resources. The newly formed viruses break out from their host cell, killing it in the process, and quickly attack its neighbouring cells, continuing the infection. This is somewhat like a stranger entering your house, fooling you by pretending to be a family member and making you feed him, while he constantly makes copies of himself till you finally starve to death. You can fully appreciate the speed and efficiency of the cold virus when I tell you that one virus can produce lakhs of new viruses within 5-8 hours!

Now that you know how smart rhinoviruses are, and how they attack and kill cells in our body, I can hear you asking me “Why did you tell us that it is not a particularly dangerous microbe? More importantly, how is it that the virus does not kill all the cells in our nasal cavity, and kill us in the process?”

The thick nasal discharge or phlegm (pronounced flem) that we produce during illness contains cells killed by the virus, and lakhs and lakhs of the virus. The irritation in the throat and nose that are typical of a cold is because of the thousands of mucosal cells that are being killed by the virus, making these areas red and irritable.



The immune response

This is where the good guys come in. Ladies and gentlemen, a big round of applause for the courageous defenders of our body! Allow me to introduce the mighty 'Dendritic cell', the majestic 'Macrophage', the hard-working 'B cell' and finally the dependable 'T cell'. Before we get to the climax of our story and the fight between the forces of good and evil, let me quickly tell you about the cells of our immune system.

Our immune system is what protects us against attacks from the hundreds of thousands of microbes, which interact with our body every single minute of our lives. The life story of the cells of the immune system starts inside our bones, in the soft red portion known as the bone marrow. It is here that some very talented cells, called the haematopoietic stem cells, are born. These cells have the capacity to form all the different types of blood cells. Thus, erythrocytes (which carry oxygen and give blood its red colour), lymphocytes (T and B cells), basophils, neutrophils, eosinophils and monocytes (which give rise to macrophages and dendritic cells) are all formed in the bone marrow. From here, they travel in the blood to various parts of the body. Most monocytes, basophils, eosinophils, T cells and B cells stay in the blood, circulating the body continuously in search

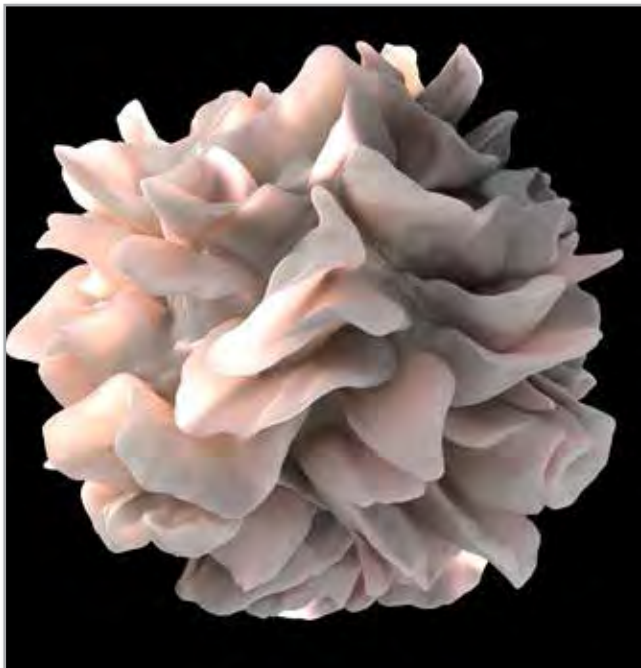


Figure 6. An artistic rendering of the surface of a dendritic cell. Source: National Institutes of Health (NIH), Wikimedia Commons. URL: https://upload.wikimedia.org/wikipedia/commons/f/fa/Dendritic_cell_revealed.jpg. Image in Public Domain.

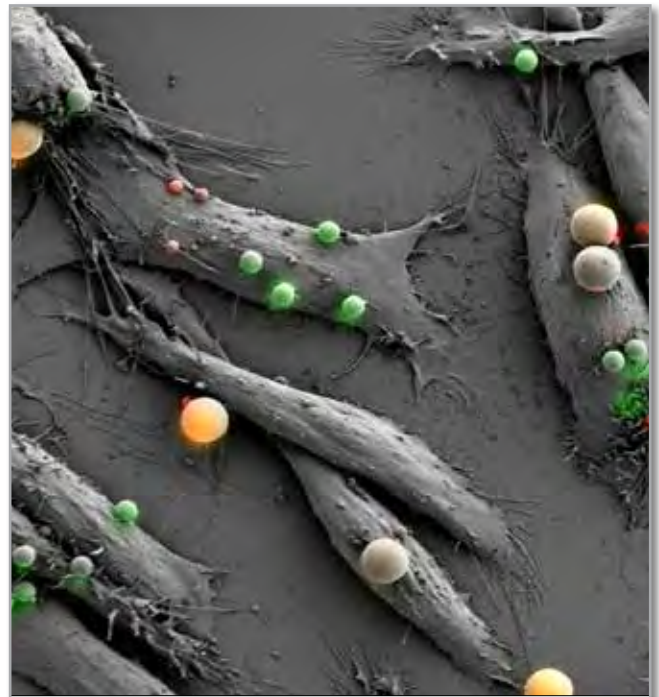


Figure 7. Macrophages (with fluorescent beads). Source: Sample by Jeffrey L. Caplan and Kirk J. Czymmek, Bioimaging Center, Delaware Biotechnology Institute. Imaging by ZEISS Microscopy Labs, Munich, Germany. URL: https://c1.staticflickr.com/9/8368/8574591304_66c9ae7e6e_b.jpg. CC-BY-NC-ND.

Stem cells are master cells in our body. They are capable of dividing throughout our lives, with the ability to grow into many different cell types. They act as the repair system of our body, constantly replacing dead or damaged cells. The haematopoietic stem cell can give rise to any of the different blood cells.

of invaders. Some monocytes migrate to the skin and mucous membranes of our nasal cavity, oesophagus (food pipe) and intestine, where they change into more mature forms, called dendritic cells. In contrast, monocytes that migrate to organs like the liver and lungs change into the more mature macrophages.

Coming back to our story; when the cold virus first enters our nose and attacks the cells of the nasal mucosa, the attacked cells send out a call for help by releasing chemicals called cytokines. Just like you would find hot samosas by letting your nose guide you to the place where this smell is strongest, the cytokines guide immune cells to the place of attack. The basophils in blood are the first to rush to the area. When the basophils reach the attacked cell, they at once sense the danger and release another very powerful

chemical calling for backup forces. This is similar to what happens when a ship sinks in the sea. The sailors at once send out a radio message saying “Mayday, Mayday, Mayday”. This is picked up by nearby boats, which rush to the area. On reaching the sinking ship, they help as many people as they can, but also fire bright flares to help rescue planes and ships find other survivors.

The chemical signals are picked up by the dendritic cells and macrophages in the mucosa. These cells immediately swing into action and start attacking the invaders. They not only swallow (eat up) any virus seen outside a host cell, but also swallow some of the infected mucosal cells itself. This process of eating up invaders is called

WHAT HAPPENS WHEN?

(a timeline of events during common cold infection)

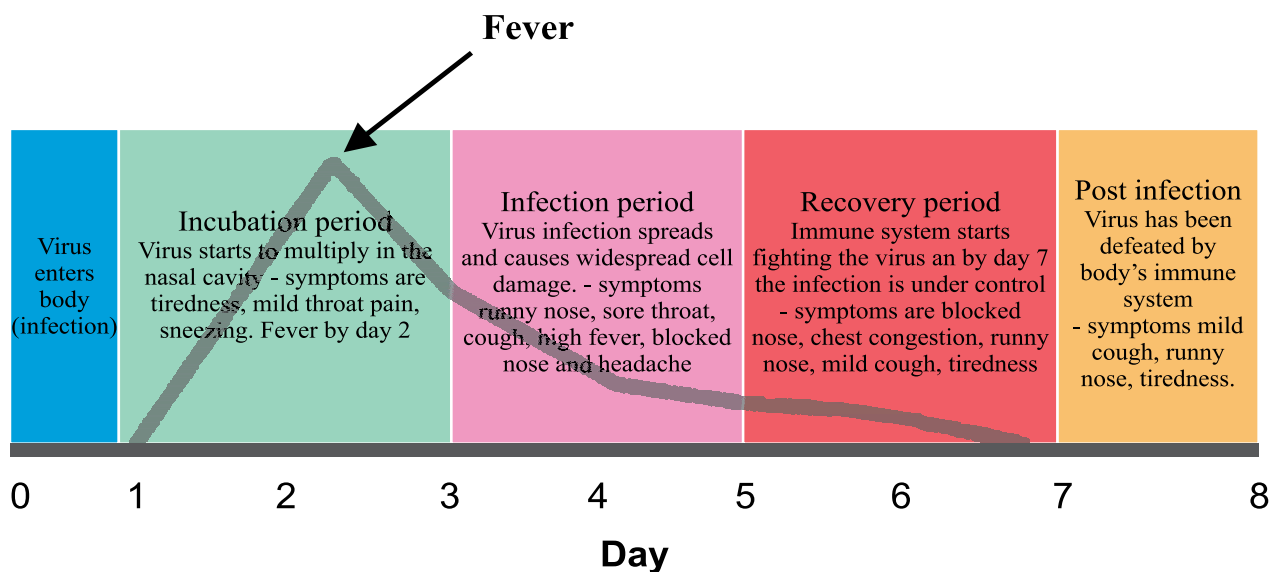


Figure 8. A timeline of events.

Related online resources:

The Human Immune System and Infectious Disease. In the History of Vaccines. Retrieved from <http://www.historyofvaccines.org/content/articles/human-immune-system-and-infectious-disease>

Understanding How Your Immune System Works (A Cartoon Story). Retrieved from <http://www.healthaliciousness.com/blog/How-Your-Immune-System-Works-A-Cartoon-Story.php>

Animation: The Immune Response. Retrieved from http://highered.mheducation.com/sites/0072507470/student_view0/chapter22/animation_the_immune_response.html

Rhinoviruses. In eMedicine. Retrieved from <http://web.archive.org/web/20080102183521/http://www.emedicine.com/med/topic2030.htm>.

'Phagocytosis' in scientific jargon. Once the virus or infected cell is swallowed, it is chewed up into tiny bits inside special sacs, called lysosomes, containing many enzymes and acids. This is very similar to how the food we eat is digested in our sack-like stomachs. What makes this interesting is the fate of the digested virus. Macrophages and dendritic cells display the chewed up bits of virus like flags on the outer surface of their membranes, almost as if they are saying "I have killed this virus and here is the proof".

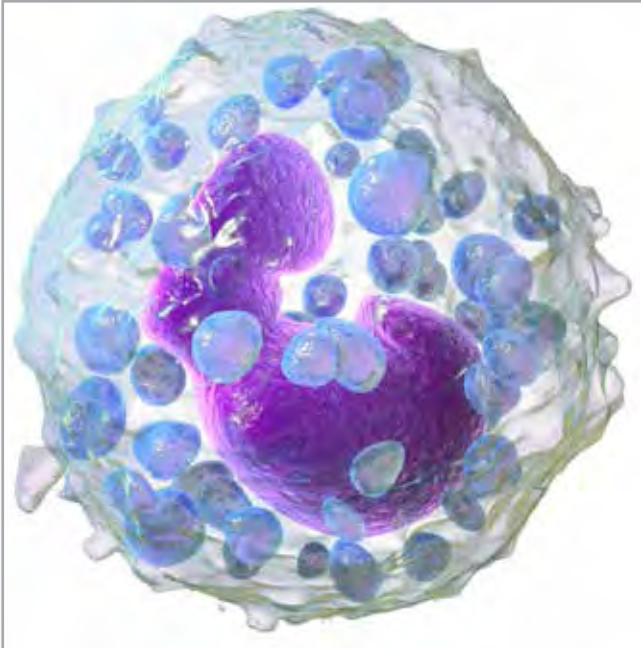


Figure 9. A 3-D rendering of a Basophil. Source: Blausen.com staff. "Blausen gallery 2014". Wikiversity Journal of Medicine. DOI:10.15347/wjm/2014.010. ISSN 20018762. URL: https://upload.wikimedia.org/wikipedia/commons/5/5d/Blausen_0077_Basophil.png. CC-BY-NC-ND.

These flag-carrying macrophages then travel throughout the body till they reach organs like the liver, contacting the lymphocytes (T cells and B cells) along the way. The lymphocytes notice the flags (virus particles) on the surface of the macrophage/dendritic cell. T and B cells have molecules (receptors) on their surface which can recognize and bind to these viral particles only when they are stuck on the macrophage cell surface. It is like when you go to a party and see a stranger there. You do not speak to the stranger till you are introduced to him/her by a mutual friend.

Once introduced to the virus properly, the T cells get 'activated' and are now capable of dealing with the virus themselves (no more introduction necessary). But first they start multiplying very rapidly to produce

Some of the activated T and B cells also store a picture of the virus in their database and can live for a very long time. This helps them recognize the same virus the next time it enters the body and they kill it immediately before it has the opportunity to cause the disease. These T and B cells are called 'Memory T and B cells' and they provide our body with long-term immunity to the virus.

thousands of 'activated' T cells. To understand this, imagine that you let a guard dog smell a bag of explosives. The guard dog remembers the smell and can sniff these out from anyone anywhere. If the guard dog could also produce many copies of itself, each of which retained this ability to sniff out explosives, they'd be very much like the newly produced copies of activated T cells. These activated T cells are the main

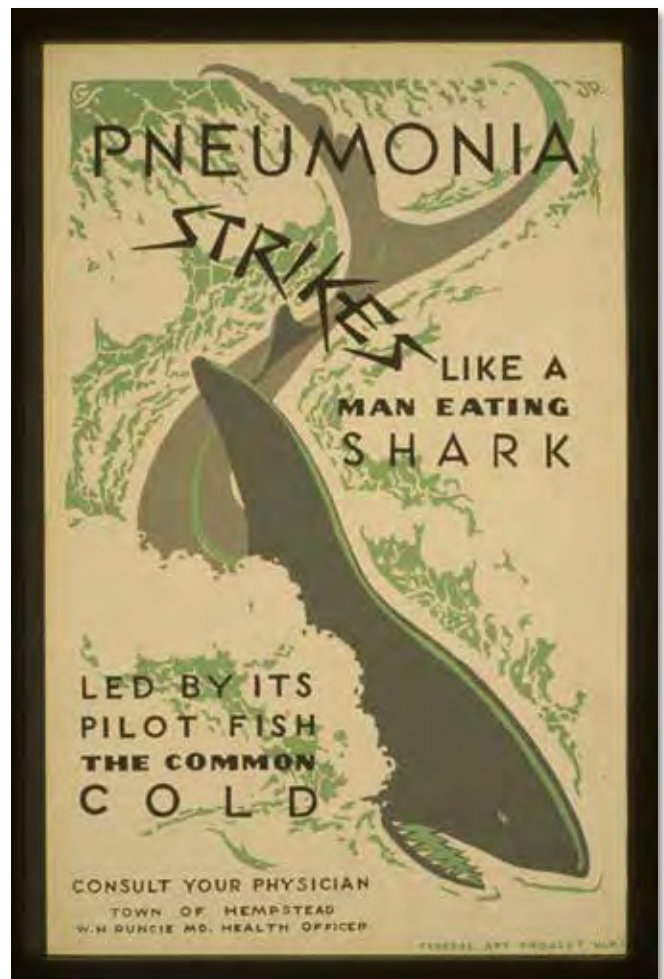


Figure 10. Poster encouraging citizens to "consult your physician" Source: Federal Art Project, Work Projects Administration Poster Collection (Library of Congress), 1937. URL: https://upload.wikimedia.org/wikipedia/commons/7/73/Pneumonia_strikes_like_a_man_eating_shark.jpg. Image in Public Domain.

army which help defeat the cold virus. They march rapidly to the battle site in the nasal cavity, where they 'sniff out' all the infected human cells, among the many other similar-looking normal body cells. They then attack all these virus-infected cells with powerful chemicals called toxins that kill them before the virus has a chance to multiply inside them. This effectively prevents the virus from multiplying and spreading, thus eliminating the virus from our body. Since these T cells kill infected body cells, they are called 'cytotoxic T cells' (cyto-cell; toxic-poisonous). Some activated T cells help activated B cells produce molecules called antibodies, which can bind to any exposed viruses and help inactivate them. Antibodies stay in our body for a long time and can help prevent attacks by the same virus again, thus protecting us in the future. Once again the forces of good have triumphed over the forces of evil and rid us of a menace, though we are a bit weak from the battle and will need some time to get back our energy and zest for life.

I hope you found that story fun. What? You have another question? Why do we keep catching colds (especially since I've said that we have immunity and memory to protect us)? That is a fantastic

There is NO known cure against the common cold. Antibiotics (which protect us against bacteria) are of no use against viruses, and only help in protecting us from bacteria which might see our weakened state as an opportunity to attack us. Other medicines, like paracetamol and aspirin, only help in relieving the symptoms. This is the basis of the common saying "An untreated cold lasts for 7 days and a treated cold for a week"!

question. Remember I told you that there are around 115 types of rhinoviruses. Each time we are infected with a particular type of rhinovirus, we get immunity to ONLY that particular type of virus and not to the others. Also, other viruses like influenza virus, picornavirus (with 99 types), coronavirus and adenovirus can also cause cold, thus making it very difficult for our body to develop immunity against cold.

The next time you catch a cold, Worry Not! Your own private army is alert and will defend you against this menace!



References

1. Geo F. Brooks, Karen C. Carroll, Janet S. Butel, Stephen A. Morse, Timothy A. Mietzner. (2012). Jawetz, Melnick, & Adelberg's Medical Microbiology. The McGraw-Hill Companies. 26th Edition.
2. Willey J, Sherwood L, Woolverton C. (2007). Prescott, Harley and Klein's Microbiology. McGraw-Hill Higher Education. 6th edition.

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