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The Biology of Influenza and Vaccination

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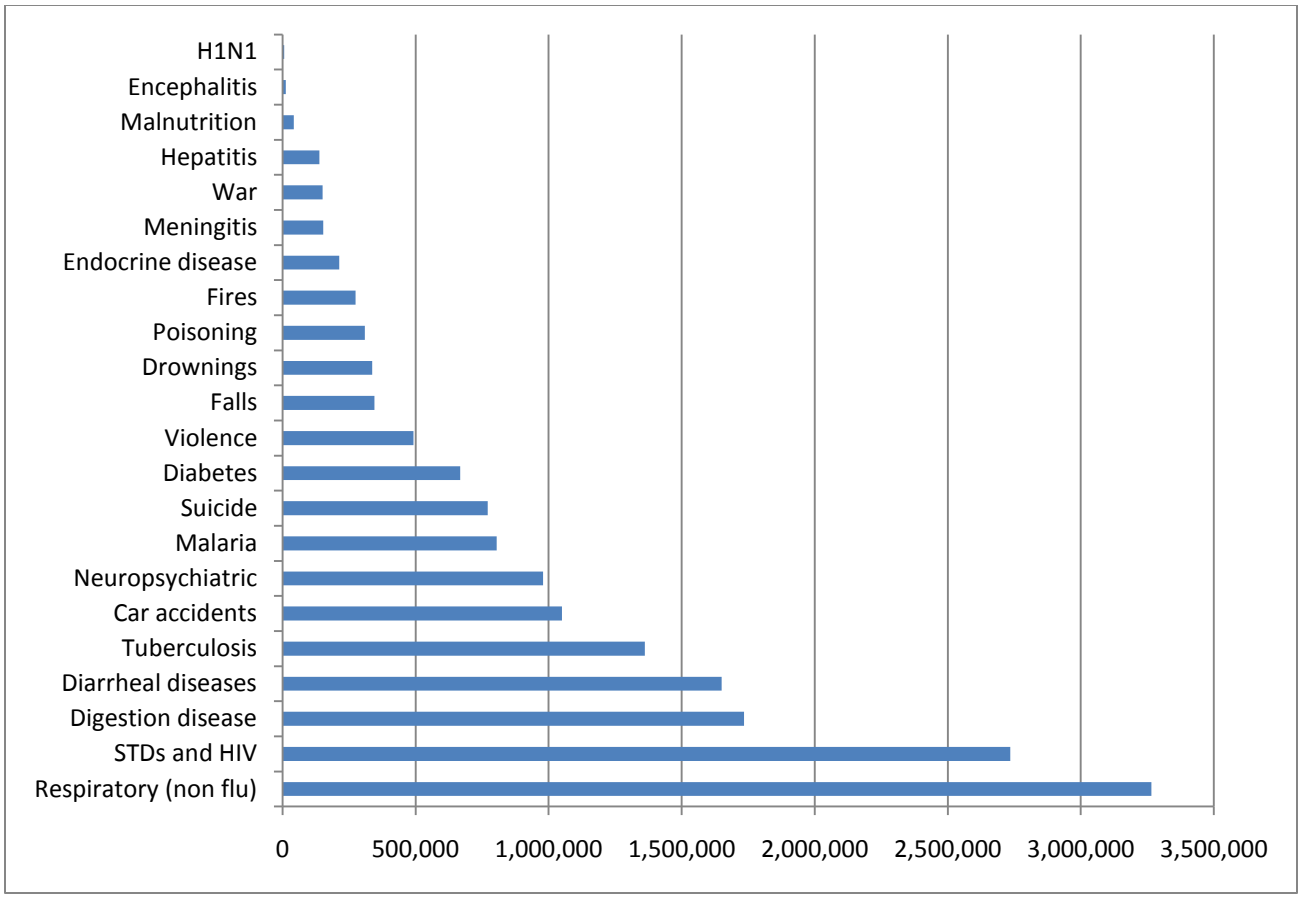
There is a lot of conflicting information circulating regarding the H1N1 pandemic and there is a lot of pressure to get vaccinated. It is very important to have some biology knowledge in order to make an educated decision about whether or not you will decide to vaccinate yourself or your children.

Yes, H1N1 is a different virus compared with the regular seasonal influenza virus. Seasonal influenza viruses are type B viruses; they only infect humans and usually cause mild disease in young healthy people. H1N1 is a type A virus, which can infect other animals, such as pigs and birds, as well as humans. When viruses infect multiple species, they have a higher mutation rate and therefore, they are not as easily recognized by our immune memory cells (from previous exposure to similar viruses) and can cause a more severe infection.

How would you know if you had the flu? The symptoms of influenza usually include fever, sore throat, muscle aches, headache, coughing, and fatigue, and sometimes vomiting. There are also at least 100 different 'common cold' viruses that can cause similar symptoms, but generally, symptoms of the flu occur more suddenly, and are associated with a higher fever, chills, more fatigue and muscle aches compared to a common cold. If you have these symptoms then you will need to stay home from work or school, drink a lot of fluids, take vitamins and Tylenol, and rest. There is nothing a doctor can do for you unless you are experiencing difficulty breathing. Your immune system will fight the infection as long as you are healthy. If you have severe symptoms or underlying health conditions, then you may need to see your doctor.

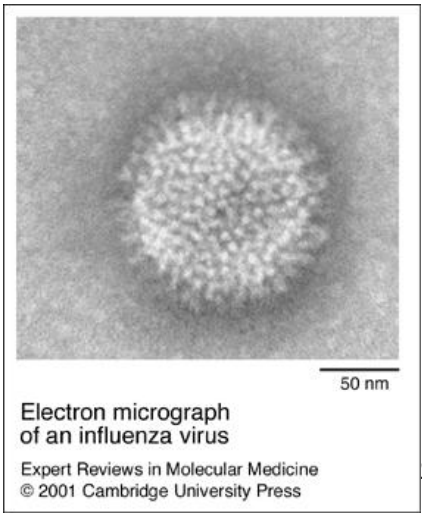
How many people die from the flu? Although people can die from H1N1 and from the yearly seasonal flu virus, most people have regular flu symptoms and recover within 5 – 7 days. Seasonal influenza kills approximately 36,000 people per year in the US, and about 2500 in Canada, and those people are generally very young or elderly or have underlying health conditions [1]. If we look at overall death rates in the world from H1N1 compared to other causes of death, we will see that although H1N1 is a "pandemic" it is not causing enormous fatalities and should not be cause to panic. Every year, approximately 50 million people die worldwide; approximately 30 million of those deaths are due to non-communicable diseases, 5 million people die from injury, and approximately 8 million people die from infectious diseases. Worldwide, approximately 5800 people have died from H1N1 since the pandemic began in the spring of 2009, 80 of those in Canada, 31 in Ontario.

The following graph shows the proportion of some causes of death worldwide from January – October 2009. **Note**: cardiovascular disease (14.7 million) and cancer (6.5 million) are not included on the graph because the number of deaths is so high that it skews the rest of the data.



What is happening in our body when we have the flu? Influenza is a virus made of the nucleic acid, RNA, and a protein capsule. When influenza infects our cells, it changes its RNA into DNA, then replicates itself and makes many new virus particles. Viruses cannot live for very long outside of an animal cell. Influenza infects our respiratory tract cells in our nose, throat, and lungs, and it can sometimes infect cells in the digestive system. Because influenza has to copy its RNA into DNA first, and then replicate new virus particles, it will not always make new viruses that are exactly the same. These RNA mutations are what lead to changes in the proteins in the virus (proteins that help it to infect cells, replicate, etc). This is also why every season there are different influenza viruses circulating in the population. This is also why H1N1 is quite different from seasonal influenza because as it moves from animals to humans, these mutations are increased.

How does influenza infect our cells? Influenza viruses bind through Hemagglutinin, a protein on the virus capsule, which binds to receptors on our respiratory cells. Our cells engulf the virus through phagocytosis, and then the virus can replicate itself, killing our cells in the process. Neuraminidase enzymes in the virus help the new virus particles to be released from our cells and then the replicated virus particles can spread and infect other cells. H1N1 is named because of the sequences of the Hemagglutinin and Neuraminidase genes.



Electron micrograph of an influenza virus

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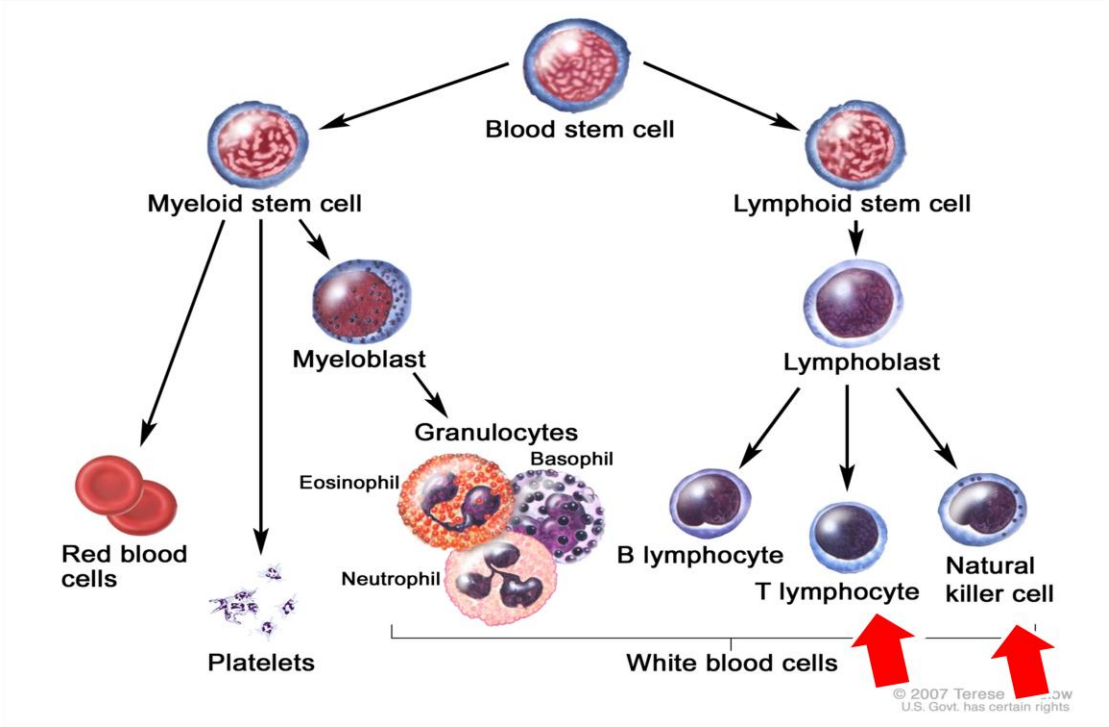
How does our immune system fight viral infections? We have evolved from a long line of ancestors that survived many very severe infections, such as plague, smallpox, cholera, typhus, etc. People, particularly children, could not have survived if their immune systems could not handle infections. Because of this, we have very strong immune systems that are capable of fighting off many bacterial, parasitic, fungal, and viral infections. Our immune cells are generally very good at keeping microorganisms under control. I personally believe that a certain amount of infection is actually required for our immune systems to stay strong and healthy. If we are not continually exposed to the microorganisms in our environment, eventually we would not be able to fight off simple infections (living in a 'bubble' makes us less healthy). This is also evident when young children start daycare or school, or people change from working at home to working in an office. The new exposure to microorganisms usually leads to an unhappy season of 'catching' everything that is going around, however, the following years; they are much less likely to have as many infections. This is due to memory cells, which I will talk more about shortly.

When we are infected with a flu virus, then our immune cells will recognize the proteins on the surface of that virus as "foreign". The lymphocytes that reside in our lymphatic tissue are all different; each one can recognize one specific foreign protein, we make all of these lymphocytes during embryonic development and early childhood. As virus proteins (carried by antigen-presenting cells) circulate through our lymphatic system, eventually a lymphocyte will recognize and bind to that protein….this is why it takes longer to recover from a new infection if there are no previous memory cells. Once a lymphocyte (T cell) has recognized a protein, it will proliferate and make millions of other T cells that also recognize that specific protein, they circulate throughout the body and attack viruses and infected cell that match that protein. (This will happen many times for several viral proteins that are recognized by the immune cells). We also have natural killer cells that kill virus-infected cells.



What are memory cells? Once the viral infection is under control (5 – 7 days, maybe longer depending on how new the virus is to your body and how healthy you are), the T cells will form memory cells….this process is crucial for preventing future infections from that exact same virus. Memory cells are the very reason why we are not continually bombarded with infections. Once we have made memory cells to a specific pathogen, then a second encounter with that pathogen will be promptly controlled because the memory cells can react very quickly, and you would likely not even realize that your immune system was fighting anything. We get sick when we encounter new pathogens. The symptoms of a cold or flu are primarily due to our immune system responding to the infection.

Because influenza viruses mutate, the proteins on the virus that are recognized by our immune cells are always slightly different every year, triggering a new primary immune response in our bodies. But with seasonal influenza, there are always some similar proteins that our immune system will recognize, and some that it won't. The more similar the virus proteins are to the previous year, the less sick you will feel when infected again. This is why people getting infected with H1N1 feel quite a bit worse than a normal seasonal flu, because it is a type A virus, the proteins that our immune system would recognize are much different than our immune cells have seen before. However, the good news is that if you are infected with H1N1 and you recover (which most people do), then you will have long-lasting memory cells that will help you fight off any recurring or slightly mutated version in the future. This is precisely why older people are not as affected by H1N1 compared to younger people.

Why is all of this information so important to understand when deciding whether or not to get vaccinated? When people get a seasonal influenza vaccine, the immune system does not react to the vaccine in the same way that it does to an actual infection. Vaccines are typically made from a killed virus along with other ingredients mentioned in more detail shortly. Our immune system does not mount the same intensity of a response to killed virus particles, and therefore, only a short-term immune response occurs. A killed-virus vaccine does not stimulate long-term memory cell production. So how would that affect your ability to naturally fight the slightly altered viruses the following year? You will not have memory cells to the previous antigens (proteins recognized by the immune cells) so new viruses will be less recognizable by your immune cells and you have more severe symptoms.

Vaccines. Vaccines are generally made in 2 different ways, live-attenuated, or killed virus. Live-attenuated viruses are grown in cells until a non-virulent form is produced but still stimulate the immune system to react, the idea is to have some common antigens so that memory cells will be produced and will recognize at least some of the antigens when exposed to the circulating virus. Influenza vaccines made this way tend to cause influenza symptoms, long-term memory cells would be produced (good) but people often get sick, which defeats the purpose of being vaccinated. The most common method used for influenza vaccines is to use killed viruses, that way they can't infect our cells but the proteins would still be there for our immune cells to recognize, but no long-term memory cells are produced. This is why the new vaccines are now containing adjuvant, which stimulates a much stronger immune response in order to induce long-term memory cells.

This year's vaccine, information from the Center for Disease Control website:

"The flu shot is an inactivated vaccine (containing killed virus) that is given with a needle, usually in the arm. The flu shot is approved for use in people older than 6 months, including healthy people and people with chronic medical conditions."

"The nasal-spray flu vaccine is a vaccine made with live, weakened flu viruses that do not cause the flu (sometimes called LAIV for "live attenuated influenza vaccine" or FluMist®). LAIV (FluMist®) is approved for use in healthy* people 2-49 years of age who are not pregnant."

Possible reactions to influenza vaccination (from CD website)

"The nasal spray (also called LAIV or FluMist®): The viruses in the nasal-spray vaccine are weakened and do not cause severe symptoms often associated with influenza illness. (In clinical studies, transmission of vaccine viruses to close contacts has occurred only rarely.)

In children, side effects from LAIV (FluMist®) can include: runny nose, wheezing, headache, vomiting, muscle aches, and fever. In adults, side effects from LAIV (FluMist®) can include: runny nose, headache, sore throat, and cough.

The flu shot: The viruses in the flu shot are killed (inactivated), so you cannot get the flu from a flu shot. Some minor side effects that could occur include: Soreness, redness, or swelling where the shot was given, fever (low grade), aches. If these problems occur, they begin soon after the shot and usually last 1 to 2 days. Almost all people who receive influenza vaccine have no serious problems from it. However, on rare occasions, flu vaccination can cause serious problems, such as severe allergic reactions."

Note: You cannot sue for damages if you are one of the unlucky people that have a serious adverse reaction.

What is in the vaccine? Because the killed viruses are usually ignored by our immune cells, other ingredients are added to help boost the immune response.

The following information is from the GlaxoSmithKline website (a Canadian company that makes influenza vaccines).

Seasonal vaccine contains:

- killed influenza virus particles (usually trivalent, so 3 of the most prevalent viruses from the previous season)
- Aluminum salts – to increase immune cell activity
- Formaldehyde – to kill the virus
- Sodium deoxycholate – detergent used to emulsify the vaccine into tiny particles that will be taken up by immune cells
- Tween 20 – fat-type molecule also used to emulsify vaccine (also used to make ice-cream)
- 5µg Thimerosal USP (mercury) per 0.5mL dose - preservative

H1N1 Vaccine contains:

- Arepanrix™ H1N1 (AS03-adjuvanted H1N1 pandemic influenza vaccine) is a two-component vaccine consisting of an H1N1 immunizing antigen (as a suspension), and an AS03 adjuvant (as an oil-in-water emulsion).
- The H1N1 antigen is prepared from virus grown in the allantoic cavity of embryonated hen's eggs. The virus is inactivated with ultraviolet light treatment followed by formaldehyde treatment, purified by centrifugation and disrupted with sodium deoxycholate (detergent).
- The AS03 adjuvant system is a sterile, homogenized, emulsion composed of DL-α-tocopherol (vit E), squalene and polysorbate 80 (type of oil to make vaccine thicker) in a 3mL vial, and 5µg Thimerosal USP per 0.5mL dose (mercury, used as preservative)
- The adjuvant is required to induce a strong enough immune response to produce memory cells

What is Squalene? Squalene is actually a naturally occurring fat-type hydrocarbon molecule that is produced normally in many cells, including human cells. We make squalene is some cells as a precursor to cholesterol and steroid hormones. However, when injected into humans, the immune system reacts to this substance (which is why it is used in the vaccine because it will induce a strong immune reaction). Some research in this area has shown that oil-water suspensions, including squalene were associated with the ability to induce lupus autoantibodies in mice [3] and another study showed that endogenous squalene was linked to autoimmune arthritis in rats [4].

The World Health Organization and US Dept of Defense both published extensive reports that emphasize that squalene is a chemical naturally occurring in the human body, present even in oils of human fingerprints. WHO also states that squalene has been present in over 22 million flu vaccines given to patients in Europe since 1997 and there have never been significant vaccine-related adverse events.

The US Dept of Defense concluded that there are still many doubts to whether or not squalene-containing vaccines are safe at all. There are no long-term studies to determine this yet.

What are the possible serious adverse reactions? Serious adverse reactions occurred in 1.6% of adults injected with a H5N1-adjuvant vaccine in a study in Germany (9873 people were assessed for 6 months). It is interesting to note that the investigators stated that the reactions were not likely due to the vaccine. (GlaxoSmithKline website)

Possible reactions include:

- Anaphylactic shock (1)
- Bell's Palsy (4)
- Convulsions (1)
- Immune-mediated diseases (11)

There are many other news articles and internet blogs and stories that discuss how so many people have suffered from Guillan Barre syndrome (GBS) and other paralytic reactions. I have only stated in this article the research that is published in scientific arenas. Even though a much higher number of people experienced GBS after the large-scale vaccination campaign in 1976, and post-vaccination encephalitis is discussed in microbiology textbooks, the current scientific database only states that it has never been proven that GSB is caused from vaccination. Autism is another very highly controversial area that I am not addressing in this article.

Concluding thoughts (my personal opinion based several years of research in autoimmunity). Yearly vaccinations could lead to more frequent serious reactions over time – especially in children that are already receiving so many childhood illness vaccinations and very young children are still developing their immune cell repertoire. Continual exposure to vaccines may have a long-term cumulative effect that we are not aware of yet. There are no long term studies yet that determine the safety or possible long-term ramifications of vaccination.

Three Cochrane reviews that compared all published scientific research involving vaccination of children, adults and the elderly stated that there are no fewer sick days or hospital visits, and the death rate from seasonal influenza has not decreased since widespread vaccinations have begun. All reports concluded that more information is required to determine if vaccination is beneficial. Yet, everywhere we hear that "vaccination is your best protection against the flu".

I think it is normal and healthy for our immune cells to be exposed to mild infections, if we avoid infections our immune system is not as strong, then any exposure would be worse, unless we got vaccinated every year against more and more microorganisms; consider then the effects if a predicted influenza virus was inaccurate (seasonal vaccines are based on the previous year's circulating viruses and some years the vaccine does not contain the correct antigens).

Antibiotics and hand sanitizers increase the rate of evolution of microorganisms, making them less effective when they are really needed. Both of these also kill our very important normal bacteria that act as a significant part of our first line of defense against pathogenic organisms. Use of hand sanitizers, outside of hospitals, will decrease infection in the short-term but will have a negative effect on the rate of mutations over time, causing us to be exposed to very different organisms faster than would naturally occur.

Vaccines without adjuvant do not induce the immune system to produce long-term memory cells and therefore, each year as viruses mutate, people will have decreased natural ability to fight infections over time.

Vaccines without adjuvant have been known to cause paralytic conditions and other serious adverse reactions, we do not know yet what vaccines with adjuvant will do.

Adjuvant is used in autoimmune research labs to induce paralysis and other autoimmune diseases such arthritis, MS, and lupus, it is now being used in vaccines to increase the immune response. What will this do to our immune systems over time? Consider the long-term possibilities when deciding to get vaccinated.

More information

1. http://www.cmaj.ca/cgi/reprint/168/6/761-a
2. GlaxoSmithKline website – vaccine ingredients http://www.gsk.ca/english/html/our-products/docs-pdf/Arepanrix_PIL_CAPA01v01.pdf
3. M. Satoh et.al.: Induction of lupus autoantibodies by adjuvants. *J Autoimmun.* 2003 Aug;21(1):1-9.
4. The Endogenous Adjuvant Squalene Can Induce a Chronic T-Cell-Mediated Arthritis in Rats – American Journal of Pathology
5. New horizons in adjuvants for vaccine development - Steven G. Reed1, Sylvie Bertholet, Rhea N. Coler and Martin Friede
6. Infectious Disease Research Institute - http://ajp.amjpathol.org/cgi/content/full/156/6/2057
7. WHO - http://www.who.int/vaccine_safety/topics/adjuvants/squalene/Jun_2006/en/index.html
8. http://www.cochrane.org/reviews/en/ab004879.html (vaccination in healthy children)
9. http://www.cochrane.org/reviews/en/ab004876.html (vaccination in the elderly)
10. http://www.cochrane.org/reviews/en/ab001269.html (vaccination in healthy adults)