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Kayce Boggess

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By Kayce Boggess

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ABSTRACT

The influenza virus has plagued humans for centuries. Recently antiviral medications, which shorten the duration of the flu, have been introduced into society. These medications along with vaccinations, which try to give the body immunity before the virus strikes, help to stop the flu before it attacks the host. The virus, however, replicates using host cells and can slightly change itself with each replication, which over time could lead to a strain immune to the current antiviral medication and vaccines. However, using more preventative measures could help slow the changing strains of the flu virus. Using vaccines to stop the virus at the host before it mutates and using antiviral medication before the flu starts replicating inside patients are both examples of preventative measures. In the future, research must be focused on creating vaccines to limit the need for antiviral medication to slow the evolution process of the influenza virus overall.

KEYWORDS: Influenza, Virus, Vaccine, Antiviral, Evolution

INTRODUCTION

Viruses are tiny pathogenic agents that can infect organisms. Though not living themselves, a virus can use living cells' nuclei and cytoplasm in order to replicate itself and change its genetic structure.[1] This creates viral proteins that become resistant to medicines used to fight them. Thus, to fight this resistance, different drugs are needed to fight the virus. However, this plan of attack allows the virus to build up an immunity to the specific drugs used. This means many viruses have the potential to become deadlier as humans run out of medicines that the virus is not resistant to.

One such virus is influenza. Influenza, or the flu, is a dangerous virus that can cause symptoms ranging from mild cough and fever to death depending on the person and

severity of the strain. Influenza emerges from other animals, making the problem not only a human one but also a veterinary one.[2] This causes influenza to have many forms due to the sheer number of hosts, ranging from humans to birds to pigs. Due to a large number of hosts influenza can spread not only from person to person but also animal to person. This rapid spreading will cause about 250,000 deaths every year around the world, and thus about 16 out of 100 people who contract this virus will die (see figure 1).[3]

Antiviral medication can be used on patients who contract the flu. For example, Oseltamivir, or Tamiflu is an antiviral used to control the flu by stopping surface proteins which stops the replication process of influenza.[3] However, after the 2007-2008 outbreak of influenza, an antiviral-resistant strain was discovered.[3] This means as influenza continues to plague humankind, the flu may become much more life-threatening. This review will analyze the medication available for influenza as well as its evolution. The review will then look at prevention and future measures that could be taken to ensure influenza will remain a treatable disease.

INFLUENZA

Influenza is a common disease in the world. This virus strikes usually in colder, more humid climates. In a study of the months where the flu was most prominent, the occurrences of influenza in the Southern Hemisphere were most common in the colder months.[4] Even though the flu could strike throughout the year, it often strikes in the wetter months. Using Australia as an example of different climates, influenza depends on a seasonal approach with very few cases outside the season.[5] However, in tropical regions with a more constant climate, the flu is more present throughout the year.[5] This is due to the always constant humidity in the environment. Additionally, influenza's persistence can be related to weather patterns. In a study in Cote d'Ivoire in Africa, there is a correlation between a few weeks before a rainstorm or high levels of humidity and an increase in the influenza virus in humans.[6] The flu spikes right before a lot of moisture either due to precipitation or humidity. Thus, it would be reasonable to assume that snow in colder months also correlates with the flu season.

Once a person catches the flu there is little to be done until the virus runs its course. Having another chronic disease or being pregnant increases the likelihood of getting the virus.[7] More vulnerable people, such as pregnant women and the elderly, catch the flu more often than young adults. The reasoning for these certain subgroups of people

getting the flu more often than the average human is due to their immune system already being somewhat weakened due to age or carrying a baby.

ANTIVIRAL MEDICATION

Antiviral medications can be administered to shorten the duration of the flu, which could help save lives. According to models of flu outbreaks, antiviral medicines that work most effectively in the beginning stages of the virus infection, before replication has begun to occur.[8] Using antivirals after replication is still effective, but there is a greater chance of a mutant strain appearing that happens to be resistant to the medication the person is currently taking. This scenario will make the virus much harder for the body to fight off in the long run.[8] Overall, antiviral medication is a good start to fighting influenza but could cause mutations to begin in the virus itself. Usually, the best way to fight the virus is by using a few different antiviral drugs together. This technique is called combination therapy. Combination therapy seems to be one of the best methods in using antiviral medication to prevent evolution in a drug-resistant strain.[9] Overall, all antiviral medication will help unless a strain of influenza is resistant against a certain one, which is why combination therapy is the most popular method for combatting influenza. For example, in treating mice infected with influenza no matter when the antiviral drug was administered, all of the drugs helped if given early in the infection period.[10] However, as the infection went on the medication's effectiveness tapered off.[10] For example, when giving oseltamivir within 2 hours after the infection took place, 60% of the mice survived, while after 24 hours the antiviral medication did very little to prevent death in mice.[10] Antiviral medications are helpful in the short-term, yet must be taken in a short window of time when the infection begins in order to ensure their effectiveness. This limited use of antiviral medication is the reason why a future direction should be taken in another way.

EVOLUTION OF THE FLU

Viruses experience a form of evolution. This evolution comes from the replication process they undergo, which causes changes in the strain. Usually, from year to year viruses change minimally on a genetic level. For example, one study analyzed the flu seasons between 2007-2008 and 2008-2009 and there was not a significant difference.[11] However, the flu strain present in the 2008-2009 season caused more deaths.[11] Even though a change in the genetic structure between the strains was very minute, the strain in the 2008-2009 seasons had more complications in the public than

the earlier year. This minor difference shows that even a small evolution can cause a much deadlier strain in influenza. This evolution also leads to certain antiviral-resistant strains. There is 4 types of influenza, A, B, C, and D respectively.[12] A and B are the seasonal outbreaks and what this review is focused on while C is a mild form of the flu and D only affects cattle.[12] In influenza A, subtypes are formed based on two surface proteins nicknamed H and N.[12] This leads to the naming of certain flu types like H1N1. In Japan, H1N1 influenza strains in the 2010-2011 season showed genetic differences but were closely related to the next season's H1N1.[13] However, almost all were resistant to an antiviral drug.[13] These seasons show a drug-resistant future for influenza. If this resistance continues more vulnerable people such as children, elderly, and pregnant women will contract more lethal strains of influenza resulting in more death worldwide.

VACCINES

The main defense in today's world against the flu is vaccines. Vaccines are usually effective against influenza during seasonal outbreaks. In Thailand, of the 200 children in 2013-2014 flu season and 290 children in 2014-2015 season only about 4% received a vaccine leading to about 50% of the children falling ill with flu.[14] Vaccines reduce the need for treatment, however, they have to selectively target certain strains that might change.[15] If the present strain is not covered by the vaccine, then more infections could occur.[15] In Spain, for example, the vaccines used in 2010 and in 2016 both worked well for their flu season.[16] However, the other seasons in that time frame were affected by the H3N2 strain of influenza, which was not covered by the vaccine given that year.[16] Vaccines need to cover a wider set of strains in order to account for the variability of the virus. However, scientists have discovered that vaccines might not be a one size fits all type of deal. Depending on the age, gender, and any previous illnesses some different prevention methods such as intranasal might be better for the person in question.[17] However, this does not change the fact that the immune system will do better if some form of the virus, whether dead or weakened, has previously been introduced to the body. This makes vaccine the go-to way to prevent influenza infections because some prevention is better than no prevention.

PREVENTION/FUTURE MEASURES

No matter the direction that will be taken with influenza prevention, the flu will continue to evolve and change to be harder to prevent due to the nature of the virus. Transfer can occur between animal hosts and human hosts.[18] This transfer allows the

virus to change in animal hosts to become deadly when it moves to human hosts. However, this fact could help stop influenza in an earlier stage in its animal host than in its human host. For example, in the swine industry a watch program called USDA IAV-S has been founded that could watch for strains of influenza in pigs that could be transferable to humans.[19] Vaccines are created and given to the pigs in order to avoid the influenza virus from killing the animals and spreading to human hosts.[19] This could further prevent changing strains as the influenza virus due to the prevention of that virus in the host animal. Thus, stopping the virus in the animal could stop the virus from ever spreading to humans.

Another method for stronger prevention of the flu would be creating a vaccine that could fight against all strains of the virus. A universal vaccine for influenza is in the works by targeting NP, a common viral protein in influenza A, but the dose must be further tested for human use since it has only been tested on mice.[20] These tests were relatively successful in providing protection from a few lethal strains from past outbreaks in infected mice.[20] With the creation of a vaccine that could provide protection from any strains, vaccines will stop falling short on some seasons by not providing any immunity to the host during that current flu season. This would stop seasons that have high amounts of infections due to a faulty vaccine made for the wrong strain of influenza.

CONCLUSION

Influenza is one of the deadliest pathogens. It has caused numerous outbreaks and deaths annually. Its lethal nature comes from its ability to replicate and change itself within its host. This means the flu often comes with resistance to specific antiviral medications. This puts prevention via vaccinations against influenza at step one. Future research should be focused on creating a universal vaccine. By having a universal vaccine, the flu could be a lot less dangerous since the unpredictable nature of the virus could be factored out. This universal vaccine could be achieved by focusing on host animals such as pigs to prevent the spread to human hosts. Overall, the influenza virus should be a concern to the science community due to its highly versatile nature that will continue to plague humans each flu season.

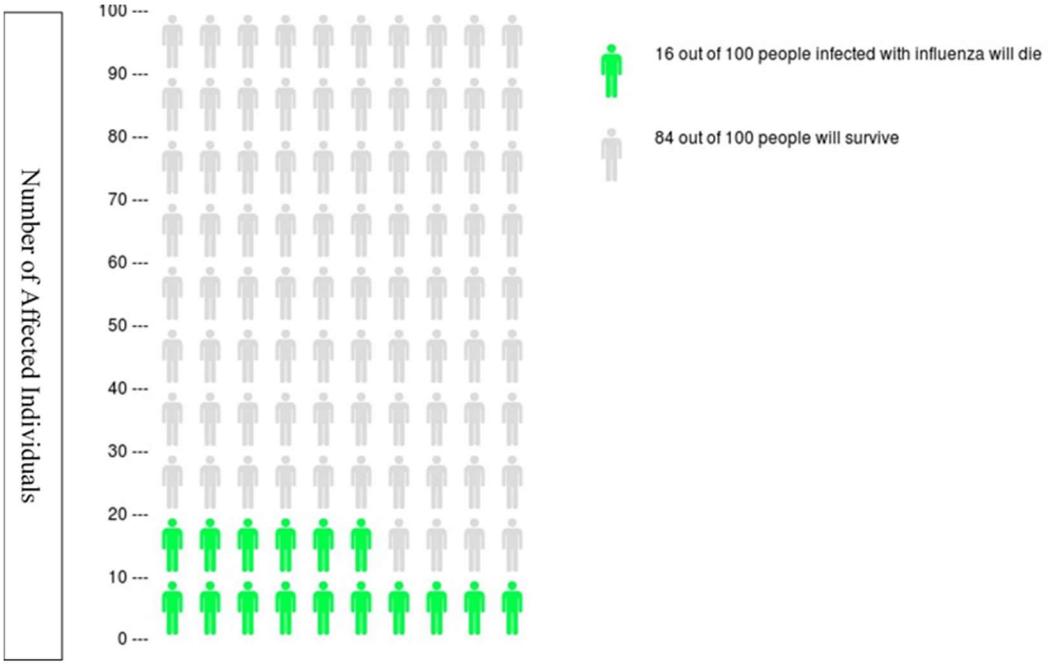

Figure 1. Lethality of the Influenza Virus. Out of all the people who catch the flu 16 out of 100 people will die.[3] This information was found due to annual collection of data from WHO (World Health Organization). Complications from influenza usually arise from respiratory issues in more vulnerable types of people. Image altered from http://www.iconarray.com/.

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