AVIAN FLU: THE NEXT PANDEMIC?

Overview

Infectious diseases have posed a threat to human health both on a regional level (epidemic) as well as on a global level (pandemic). Treatment of these diseases has also changed from time to time with the development of technology and scientific research.

Most trips to the doctor result in a written prescription for an antibiotic to be taken in order to combat and kill the source of the bacterial infection. These antibiotics have been successful in treating a variety of bacterial infections but not all the time. Diseases such as tuberculosis still exist today due to the development of a drug resistant strain of tuberculosis.

The development of vaccines helped to eradicate certain viral infections such as smallpox; however, a vaccine for HIV has yet to be developed and at the moment it is treated with various drug cocktails to inhibit the virus from spreading throughout the body. Another better-known type of virus that spreads quickly throughout the human population is influenza. Every year millions of people throughout the world get their flu shot in hopes of preventing the flu virus from infecting them. This infectious disease, depending upon the strain can be contained with vaccines; however, there is a new type of influenza threat to humans known as the avian flu. What this virus looks like and how it could mutate to infect and possibly kill humans is the purpose of this paper.

What is a virus?

Because a virus is neither alive nor dead, it must have a living, viable host cell in order to live and reproduce. The virus brings with it the ability to attach itself to a cell and the information that is needed to replicate, which are the DNA and the RNA. Viruses that contain DNA material do not mutate as often as the RNA material, which is unstable and mutates quickly. Hepatitis B is an example of a virus containing DNA information, while the avian flu virus contains only RNA information.
All viruses have the same structure although the shape of each may be different. Some viruses are in the shape of rods while others are spheres, or filaments. The outside of a viral cell possesses two types of antigens (proteins), known as hemagglutinin (HA) and neuraminidase (NA). Both types of antigens are spike like projections protruding from the capsid in order to attach themselves to a host cell. Within the capsid, there exists the necessary genetic material (DNA or RNA) to be released into the cell’s cytoplasm in order for replication to take place. Some viruses have an additional lipid coating called a lipid envelope on the capsid to protect the virus.

The purpose of the hemagglutinin (viral protein) is to find the right host cell in which to attach. To do this, the virion needs to match the HA to the receptors of the host cell. When this is complete, the virus is able to enter the cell’s membrane and into the cytoplasm where it will release the genetic information either in the form of DNA or
RNA. There are many different methods used by the virion to reproduce using the parts of the host cell. Once enough virion cells have been made by the host cell, the neuraminidase (protein enzyme) helps with the process of releasing the virions from the host cell to infect other healthy host cells.

**Influenza Pandemics**

The possibility of a pandemic is not new to the US. There have been several pandemics over the past 100 years with some having more deadly results than others. The first viral pandemic took place in 1918 and was known as the Spanish Flu. It spread quickly throughout the world with deadly results. The majority of the victims were young adults. Many virologists are not quite sure why this pandemic was so highly virulent, nor are they sure of its origin, but epidemiological evidence at the moment appears to support the fact that the influenza virus appeared in humans and moved into the swine population (Kilbourne, 2006). The second pandemic occurred in 1957 with the onset of the Asian flu. Scientific technology was more advanced and the US was quickly able to isolate and identify the virus as type A influenza H2N2, a new never previously seen virus in humans (Kilbourne, 2006). As a result, scientists were able to develop and administer a limited supply of vaccine to the population. The last pandemic was the 1968 Hong Kong flu, which compared to the other pandemics was considered to be the mildest. What is unique about this type A influenza was the difference in the hemagglutinin antigen from H1 to H3, while the neuraminidase antigen remained the same as N2. Today, the new possible pandemic is the avian flu virus or A(H5N1). What is unique about this virus is its ability to jump directly from poultry to humans. Most flu viruses move from poultry to swine to humans. This is the first known virus to jump directly to humans. With each pandemic, scientists and governments have become more efficient at handling the outbreaks due to increased scientific technology and worldwide communication. However, with the emergence of a possible new pandemic in the form of the avian flu with a present mortality rate of 50% (Webster et al. 2006), virologists are scrambling to identify and develop vaccines, medicines to prevent its worldwide spread.
What is the Avian Flu?

Orthomyxoviridae is the family name for viruses. Orthomyxoviridae influenza are classified into three groups: Influenza A, Influenza B, and Influenza C. Although all three types may affect humans in varying degrees, influenza A is by far the most studied due to its ability to infect both humans and domesticated animals. Influenza A type viruses may cross over into different species such as pig to human, or dog to human. As a result, this type of virus presents the most danger to humans. Influenza B is restricted to local outbreaks usually in schools and nursing homes. Type C is common among humans but is not serious.

Avian influenza has existed within the bird population since it was first discovered in Italy in 1878 (WHO, 2006). The main carriers of the low pathogenic virus have been the wild birds, particularly waterfowl such as ducks and geese. Poultry, such as chickens, become infected when they come in contact with the waterfowl, or with any surface that has come into contact with the virus. The virus is spread through several avenues such as feces, nasal fluids, and saliva. Although the wild birds may be the carrier, they rarely became ill with the virus until recently.

http://www.news-medical.net/images/Avian%20Influenza%20Virus.jpg

Avian Influenza Virus A(H5N1)
Bird Flu Virus

There are two forms of the avian influenza, the mildly pathogenic and the highly pathogenic. Most birds that have been infected with the mild type A(H5N1) influenza show no obvious symptoms. As a result, this may go undetected by humans and the disease could be passed on to other poultry living within close range. On the other extreme, one sees the devastating effects of the highly pathogenic A(H5N1) upon both the poultry population and the people who are the farmers. Once the highly pathogenic form of the virus infects the poultry, they all must be culled in order to stop the spread of the virus.

Until recently, it was thought that the wild birds, waterfowl were simply the carriers of the virus. However, in April of 2005, 6000 migratory birds were found dead from the highly pathogenic form of the avian flu virus in the Qinghai Lake nature preserve located in central China (WHO, 2006). Following the path these migratory birds traveled in China, demonstrated the spread of the virus within those areas. Migratory birds not only can carry the virus but now they can become infected by it, which may indicate that it is only a matter of time before it spreads throughout the world’s bird population including the poultry industry. Already parts of European countries are experiencing outbreaks of this highly pathogenic virus within the poultry industry. This fact supports the notion that the migratory birds that carry the virus may spread the virus to other bird populations throughout Europe and the world.

The avian influenza virus has not crossed the Atlantic Ocean as of this writing; however, it has made itself known throughout Asia and parts of Europe. Several Asian countries have begun to immunize their flocks for the avian flu virus with some degree of success. It is important to note that the vaccine has to be strong, effective, and appropriate to the correct strain of the virus that is infecting the population or else it is useless. One needs to keep in mind that the correct vaccine will only protect the poultry from becoming infected; it will not stop the spread of the virus through the wild bird population. Migratory birds whose path leads them across the Pacific or Atlantic oceans, and are infected with either the low or high pathogen form of A(H5N1) may easily spread
the virus to the bird population in North/South America. This would result in a pandemic that would greatly affect not only the bird population but the human population as well.

**How the Virus is Transmitted to Humans**

Many scientists are curious as to why the avian influenza virus has yet to become a pandemic among humans. Yes, there have been reported cases of infection among humans, which have resulted in fatalities but not so on a global scale. To find the answer to that question, scientists need to take a closer look at the virion itself and study how it is able to infect host cells.

Of the human cases reported, the virus was transmitted to humans through either the direct or indirect contact with infected poultry. Workers on poultry farms are the most susceptible to contracting this virus. Humans may contract the virus through inhaling the nasal secretions of infected birds or through the cleaning of the feces within the cages. The virus will then attach itself to the cells in the respiratory tract (nose, lungs, throat) of the human.

Virions of influenza A(H5N1) contain 10 proteins and 8 strands of RNA. The RNA carries the codes for making protein. The virion’s outer covering is a lipid envelope, which consists of a fat and a protein. Located on the lipid envelope are spike like projections called hemagglutinin and neuraminidase. These two structures are important in the binding of the virion to the receptor cell in order to reproduce. The avian flu virus (H5N1) identifies the number hemagglutinin and neuraminidase that connects with the receptor cell. The receptor cells of a chicken are more receptive to the A(H5N1) virus than that of a human due to the shape of the cell. Each species varies in the shape of the receptors located on the cell wall and as a result not all viruses will affect all species unless a mutation or a reassortment occurs that will allow the virus to mutate in such a way so that the virus will be able to bind itself to the receptor cell. This is the key in the lack of the avian flu virus to mutate to humans. The few cases of humans infected with the avian flu virus has virologists thinking that some type of immediate small mutation must have taken place for the antigen hemagglutinin of the viral cell to be able to attach itself to receptors on the epithelial cell located in the respiratory tract. What that
mutation was and how it was able to do that remains a mystery. What worries virologists is that the virus will be able to mutate to such a degree as to be easily transmissible from human to human. The virus A(H5N1) has not been able to achieve this mutation but many people in the field of science feel that it is only a matter of time before it is achieved and there could be a pandemic as a result.

**How Can the Virus Mutate?**

The main reason why this virus has not been able to spread readily to humans is because it does not quite fit the shape of our cells. In other words, the virus receptors of hemagglutinin and neuraminidase do not fit the receptors located on our cells. Much like having pants that do not fit, you either have to lose the weight or change the size, this is what the hemagglutinin of the virus must do. It needs to change its shape of receptors in order to fit our cell structure. The virus has not been able to completely do this and as a result there have not been many humans infected. But as virologists indicate it is only a matter of time before it happens, and the ways in which it could happen varies.

**Antigenic Drift**

This type of mutation is considered to be point mutation in that the RNA for the surface protein hemagglutinin of the virus is erroneously coded and as a result has mutated in a manner to accommodate the ciliated structure of the epithelial cells of the respiratory tract. This type of point mutation has resulted in the fatalities from the virus thus far.

**Antigenic Shift**

Antigenic shift occurs when the genomes of one virus are mixed with the genomes of a second virus in a host cell. The result is a mutated virus that is easily transmitted from one species or organism to another. Since the avian virus A(H5N1) is not so easily transmitted to humans, it will probably need an intermediate host where it can infect a cell, which may simultaneously be infected with another human influenza virus that is quite easily transmissible to humans. RNA information would thus be switched particularly the genome code for the hemagglutinin and the end result is a mutation of the avian virus that can easily be transmissible from human to human. This
is known as genetic reassortment and is quite a realistic path the virus could take. The most likely intermediate host where this could feasibly take place would be the pig. Since both human and avian viruses can infect the pig, it would be the ideal place for the two types of viruses to switch genetic information and thus form a new strain of virus. While forming the new strain, a receptor mutation could take place, which would allow the hemagglutinin of the avian virus to now have the capability of attaching itself to the ciliated epithelial cells in the respiratory tract of humans.

**Adaptive Mutation**

This mutation would occur over a period of time and require numerous infections to humans. This method would take some time to occur since the avian virus would have to infect small groups of humans at a time in order to mutate enough to infect a global population. If this were to be one of the paths that the virus takes, then the medical field would have time to develop vaccines and treatments to help prevent and stop the transmission of the virus.

**Current Research**

Presently the focus of the research has been on two areas, transmission and prevention. Whittaker and Chu (Steele, 2005) of Cornell University have found that the virus A(H5N1) cannot enter the cell by simply attaching the hemagglutinin receptor to the ciliated epithelial cell. There is another yet unidentifiable process, which must take place in order for the virion to enter the cell and release its RNA information for replication. What that second process is, researchers do not as of yet know but they are continually working on the mystery of transmission.

As for prevention in the form of a vaccine, there is controversy abound and several problems to overcome. One of the major problems for developing vaccines is the sheer number of mutations or strains of influenza that do or will exist. A vaccine developed for one particular strain will not be effective in preventing the infection of another strain. This has many researchers and scientists scrambling to figure out what type of vaccine would be the most effective against the most virulent strain. Another
avenue that scientists are looking at is DNA. Scientists are looking at the proteins within a virus in the hopes of developing a DNA vaccine that would replicate a protein to fight the virus (Mackenzie, 2006). This vaccine would not be administered like the other vaccines. It would be injected directly into the immune cells where it would activate the immune system. If researchers could develop a DNA vaccine, it would be easier and faster to manufacture than other vaccines. This would allow more people to be vaccinated and more lives to be saved. There is also some evidence that a DNA vaccine would offer cross protection to other strains of the flu virus. If this were the case, then the chances of any type of flu being transmitted human to human would decrease.

It is necessary for researchers to continue to be fully supported and funded to investigate how the avian influenza virus can be prevented from becoming a pandemic. It is only through the process of studying, investigating, and sharing information on a global scale that we will be able to successfully stop a global threat.
Abstract

Infectious diseases have occurred in humans both at a localized level as well as a global level. How and why these diseases develop and spread has been the subject of scientific research and discussion. One infectious disease that has scientists worried is that of the so-called avian flu virus. Within the last 6 years, millions of chickens have been culled and many humans have become infected and died as a result of this infection. Scientists are working on how this virus is able to spread throughout the bird population and how it can mutate to possibly infect humans and thus possibly become the next pandemic among humans.
REFERENCES


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Kathleen Tait
MISEP
Capstone
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