The Bird Flu – What's all the fuss about?

A health topic that has aroused considerable public interest in recent times is "the bird flu". Virtually every newspaper and magazine has carried an article on it. What is it all about? Is it really something so important, and if so, why? This article seeks to clarify some of these issues: it will explain what "flu" is, how they come about as epidemics and pandemics, connection to other animals including birds, what we can do to prevent such calamities, and where we stood with regard to the recent outbreak of Bird Flu.

The Flu: Spreads amongst man

The word *flu* is an abbreviation connected to the term *influenza.* Influenza is a disease caused due to an infection by a group of viruses called *influenza viruses*, which are transmitted from patients to others usually by spread through air borne particles of respiratory secretions (which are called *droplets*). Thus, patients who have the flu will, when coughing or sneezing, spread the virus particles with droplets into the environment around them.

People who are within about 2 meters from the patient may then get infected by the virus, because the droplets will enter through the nose, land on the eyes and mouth, and from there it will enter their respiratory tracts. This is called ***droplet spread.*** Alternatively, the virus may settle upon nearby surfaces, such as door handles or railings, which others touch frequently. The virus may remain viable for several hours on such surfaces while some viruses get easily destroyed by exposure to natural sunlight and dry environments. A person who touches such a surface may then get the virus onto his own hands – and if he then touches his own eyes or mouth, the virus will enter the body (even though he had never even met the original patient!). This is called ***contact spread.*** These facts are important because this knowledge is useful to prevent the spread of infection. Hence, steps that health care workers take to prevent the spread of infection within hospitals are called ***droplet precautions*** and ***contact precautions***, respectively.

It is interesting to note that the most effective techniques of preventing such spread, even in this "high-tech" 21st century, are still good old **basic hygiene measures** – such as hand washing and avoidance of touching one's eyes, nose and mouth with unwashed hands. A basic hygienic measure is the most important barrier for preventing almost all health problems caused by pathogens and other chemical agents that can enter in to the body. But not all types of influenza viruses can cause infections in humans. The virus needs special ***surface proteins*** to help them adhere to human cells, from whence they can then enter the cell. Influenza viruses that have the necessary 'tools' to infect human beings are termed ***human influenza viruses.*** **The vast majority of influenza viruses cannot infect humans and, in fact, they are mostly seen in nature amongst various species of water birds.** This is known as their ***natural reservoir***, and it is from this reservoir that other species of animal will get various different influenza viruses.

Our defences against the flu

We have our own natural defence against such infections. One of the most important defences is that our own cells are immune to infection unless the virus happened to have the necessary 'tools' for entering into cells, the relevant surface proteins. If it does, then it can infect human cells and cause human disease. But each infected human will then go on to develop his own cellular and molecular weapons against the virus: ***antibodies.*** We form antibodies against various surface structural proteins on the virus, and these antibodies then go on to make the virus incapable of surviving in our body – such specific antibodies are called ***neutralizing antibodies.***

Of course, there is one problem: we can form antibodies only after we have been exposed to the specific protein (which is called the *antigen*) of the virus, which happens in nature by becoming infected with the whole virus itself. In other words, we must first get the infection (and the disease) before we start producing effective specific neutralizing antibodies. And that is not very good news – because the flu is a very severe illness, and some of us actually die from it! But once we have survived, we will be all right – until a new influenza virus with fever specific proteins (against which the earlier specific neutralizing antibodies have no effect) comes along, when the cycle is repeated.

There is, of course, a way we can fortunately get a particular type of specific and effective neutralizing antibody without getting the disease: this is ***vaccination***. During vaccination, the surface protein of the virus that gives rise to the formation of the specific neutralizing antibody (the antigen) is given to humans who have never been infected by the virus. Since the whole virus particle is not given to the person, there will not be viral replication in his body, hence there is no illness. But the antigens will stimulate the formation of the relevant specific neutralizing antibody. When the person now comes across the relevant influenza virus in nature, he has already got the specific weapon against it: the specific neutralizing antibody. By this way, he will be ***immune*** from illness due to that particular virus.

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But there is one problem: there are so many different types of influenza viruses with different antigen proteins prevailing amongst us, that it is practically not possible to have a single vaccine against all of them.

To make matters worse, the influenza viruses are also capable of changing their genetic material so that new antigenic proteins are produced. This is because their genetic material (called the ***genome***) is stored in 8 separate segments. This makes it easy for it to exchange genetic material with other influenza viruses that it comes across (this is called ***re-assortment*** of genetic material), so that the virus then goes on to acquire new material from other influenza viruses. Also, it can form genetic codes for new proteins on its own, like any other organism, by the process called *mutation*, which is the process where its genetic material undergoes slight changes during replication of deoxyribonucleic acid (DNA), so that slightly new codes of genetic material is then manufactured. Whether by re-assortment or by mutation, when an influenza virus gets a new codes in the genome, it gets new surface proteins - and this means that we, as human beings, may not have a specific neutralizing antibody against it, so that this virus then has the ability to infect us multiply and cause disease.

Epidemics and pandemics

Our battle with the human influenza viruses and other pathogenic viruses also is, therefore, a never ending one. New human influenza viruses keep appearing form time to time, and when we come across a virus that we have not been exposed to earlier (or been vaccinated against earlier), we will get the illness. We will then either survive (with development of immunity to that particular virus type thereafter) or die.

Influenza viruses are classified into 3 major groups according to their surface proteins, called groups A,B and C. It is group A that causes most of the deadly disease in humans.

Two of the most important surface proteins on influenza viruses are called the ***haemagglutinins*** and the ***neuraminidases***. In fact, influenza viruses are classified according to these proteins. Hence, for example, the influenza virus of the group A that possess the haemagglutinin protein type 1 and the neuraminidase protein type 1 is called the influenza virus A/H1N1. Altogether there are about 15 haemagglutinins and 9 neuraminidases that help classify the influenza S virus in this way; most human epidemics in the past have been due to the subtypes, H1, H2 and H3. The haemagglutinin helps the virus to adhere new human cells before entering them, and the neuraminidase helps virus particles that have replication inside human cells to get released from the cell.

The influenza viruses keep changing their haemagglutinins and neuraminidases slightly, from year to year. When a slightly different type appears, it will come across a few persons in the community, who are not immune to it, and

therefore cause a small ***epidemic.*** The majority of the population would usually be immune to it (due to previous exposure), and hence the epidemic will involve only a minority of persons in the community. The genetic mechanism by which the virus achieves this small, continuous change is called ***antigenic drift.***

Some countries monitor the types of viruses that are in circulation, and are then able to predict the virus types that are likely to cause problems later on during the year (this usually happens during the winter season). They can therefore anticipate the problem and make a vaccine several months before the epidemic starts, so that the epidemic is curtailed in that country. This vaccine, which will have to be made anew every year, is called the ***annual influenza vaccine*** (or the flu vaccine).

But once in every few decades, the influenza virus gets modified in to something quite different and dangerous: it comes up with a new human influenza virus that has an antigenic make up that is entirely different to what is in circulation. This major shift is bad news to all of humanity, and not just to a country or two – because the whole human population is vulnerable to it, and everyone exposed to it will get the illness. This major natural modification in genetic make-up is said to occur by ***antigenic shift,*** and it gives rise to ***pandemics,*** which are massive epidemics involving several countries or continents.

The influenza virus caused several such pandemics in the past. It has probably caused them since Hellenic times (323 to 30 BC), and well-characterised pandemics have been recorded in history since the 15th century. In the 20th century itself, there have been 3 proven pandemics: in 1918, 1957 and 1968.

The 1918 pandemic itself was the largest ever recorded outbreak of an infectious disease: it affected one-third of the world's population and killed 2-3% of it and, according to German war historians, contributed to ending World War I than any other single reason!

From animal to man: The giant leap

Where do these new, deadly viruses come from? The most likely explanation is that they are viruses that have already existed in animals (especially the natural reservoir, the wild waterfowl), and they have recently succeeded in acquiring the surface proteins required to infect human cells. How these viruses acquire these proteins is itself not very clear: it would be either by re-assortment or by mutation of genetic material.

The process of a wild animal's virus becoming a human virus is a step-wise and gradual process, rather than a sudden one. In the first stages, human coming into close contact with animals (such as those working in the poultry industry) will be victims, because the virus is transmitted from those animals to man during close contact, The infected humans themselves may suffer or even die, but the virus has not yet 'learnt' how to 'jump' from one man to another – the infected human is therefore a 'dead-end' host, and each new human patient is the result of animal-to-man transmission through close animal-human contact. Such animal-to-man contact where the man is a dead-end host is known as ***zoonotic transmission,*** and the illness is called a ***zoonosis*** (meaning that it is essentially an animal disease that man has got 'accidentally'). Later on, the virus will learn how to 'jump' from one human to another- and this is when the virus becomes a truly 'human' virus. This marks the beginning of a new pandemic!

This is probably how it happened just before 1918, 1957 and 1968. The difference between then and now is simply that, now, we know all this – we are able to monitor the changes that are taking place, warn ourselves and be prepared.

All three of the 20th century pandemics started in Asia, then spread across Russia to Europe as they became pandemics. Each new virus would have initially caused a few zoonotic infections in people coming in close contact with animals, and suddenly, once the virus had become human, it would have flared up as a pandemic.

Current situation

What is the situation now? The World Health Organization (WHO) has been keeping a close eye on the emergence of new influenza viruses for several years now, knowing that another influenza pandemic is only a matter of time. It

appears that the most likely virus to cause the next pandemic is the type called influenza virus A/H5N1.

Influenza virus A/H5N1 first came to the world's notice in 1997, when it caused illness in 18 humans (killing 6 of them) in Hong Kong. The WHO immediately went into action, and within 2 years it had prepared a very comprehensive assessment of the risks involved, and came out with the ***Pandemic Preparedness Plan,*** which spells out in detail how we should prepare ourselves to face the threat and what to do at various stages of the outbreak. According to this plan, 6 phases are identified: stages 1 and 2 are the ***inter-pandemic periods*** where only animal cases are seen, phases 3 to 5 are the ***pandemic alert phases*** with cases and an increasing risk of the breakout of a pandemic, and phase 6 is when the pandemic is officially declared. It is already causing large outbreaks amongst birds, especially in the poultry industry. Over 100 humans coming in close contact with these birds have become infected, and nearly half have died. We are currently probably in phase 4 (defined as the occurrence of small clusters of human-to human transmission, each cluster involving less than 25 cases and lasting less than 2 weeks).

In other words, it is still a ***zoonosis,*** but it will only be a matter of time before it becomes a human virus. What we do not know yet is when, and where, it would turn into a human virus.

Are we prepared?

We are, as a world, better prepared than before. For instance, we are able to use modern scientific technology to monitor the situation and warn ourselves. We have tests to detect the disease in humans, some of them very rapidly. We also have effective medications, which can be used to treat patients as well as to prevent illness in those who have been recently exposed. It is even possible that we could make a vaccine to give protection to millions of people before they become infected.

But all this required international monitoring, surveillance and cooperation. The WHO is trying its best to achieve this cooperation so that the technology that humanity currently possesses is put to good use in good time – saving millions of lives, hopefully. Its recent success in controlling the spread of SARS (another respiratory illness due to a new, but unrelated virus) has given the health authorities much needed confidence that this task is achievable.

In Sri Lanka too, much work has already been done in this regard. Sri Lanka has stopped importing poultry (killed or alive) for several months now. Our state veterinary services are maintaining a close eye on our poultry. There is a small risk of the virus being brought in by migratory birds, and if this happens it will be noticed firstly amongst our poultry.

Of course, once the virus becomes a human virus and the pandemic starts, it will be very easy for the illness to come to Sri Lanka – as indeed to all countries of the world. All it takes then is for a person to travel to a country where the virus occurs, become infected with it (which is very easy!), and come back to Sri Lanka within a day or two... We have a small chance of escaping because we are an island – provided travel between our country and affected countries become severely restricted (as happened during the period when we talked about SARS). But in today's world of globalisation and air travel, this would be a very difficulty feat to achieve.

And even if it did arrive, there is still quite a lot we can do to limit the spread of the epidemic. Basic public health measures coupled with judicious use of medications may help us, and it is possible that a vaccine may also become available eventually. What the public must do is to keep confidence in the country's public health system, be aware of their latest advice, and follow it meticulously. The experts can only advice: its practice is in the hands of the people. A pandemic influenza virus will not have the mood to forgive a people who don't take good advice.

It is important to realise that an influenza epidemic going out of control is a disastrous experience for all of us. The patients who catch the disease will suffer badly, and some will die. Economic, educational and social activities will come to a standstill, greatly upsetting the lives of even those who are well. The hospital services (which in Sri Lanka are already overburdened, understaffed and under-equipped) will easily become overwhelmed. A full scale flu outbreak in Sri Lanka is not something that we can afford.

Perhaps more than ever before, **"prevention is better than cure!"**

Dr Panduka Senanayake
who serves as a Senior Lecturer,
Faculty of Medicine, University of Colombo,
is a Consultant Physician.