Avian Influenza, or "Bird Flu": What You Need to Know

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Influenza, or "the flu," is a viral infection distinct from the common cold, characterized by fever, muscle aches, malaise, cough, sore throat, runny nose, and, often, nausea and vomiting (see Appendix A for detailed information about how flu works at the cellular level and how various flu types physically differ). While it is no picnic for anyone, for the elderly, the very young, and others with weakened immune systems, influenza can be far more than an uncomfortable inconvenience: it can result in severe illness or death. Indeed, 30,000-40,000 Americans die annually from influenza.

Vaccination against influenza is the primary—although not foolproof—means of flu prevention. Vaccines must be given annually as influenza viruses change frequently, rendering last year's vaccine obsolete. Each year, scientists test the viral strains circulating globally in order to predict the strain that will predominate during the next flu season. The result is a vaccine containing pieces of a few different and carefully selected flu strains. To allow time for vaccine production, however, the strains to be included must be selected between January and April of each year. Occasionally, a new strain will emerge after the vaccine is formulated. In such cases, the annual flu vaccine may not be protective against all circulating flu viruses. Even with effective injectable and inhaled vaccines, however, many people who are at high-risk for influenza infection do not receive an annual vaccination: only two-thirds of Americans ages 65 and older, 28 percent of people with chronic illness, and 30 percent of children 6 to 23 months were vaccinated in 2002. On average, 12 to 13 million does of influenza vaccine are unused and discarded annually. Even during the vaccine shortage of the 2005 influenza season, close to 4 million doses went unused.

What is avian influenza?

Avian influenza, commonly called "bird flu," refers to a large group of influenza viruses that typically infect and are spread among birds, just as human influenza viruses are spread among people. While some avian flu strains cause only mild or asymptomatic forms of disease in infected birds, others cause illness severe enough to decimate flocks. To date, all avian influenza strains that have been severely disease-causing in birds have involved H5 and H7 subtypes. Worldwide, wild birds—particularly migrating aquatic birds like ducks or geese—often carry mild bird flu viruses and never become ill. However, if passed to domesticated birds—like chickens and turkeys—mild bird flu strains can spread rapidly through flocks where they sometimes change, or "mutate," to a more pathogenic form. If this occurs, entire flocks can be wiped out.

Why are health experts so concerned about H5N1 if it is a bird flu, not a human flu?

The current strain of bird flu infecting poultry flocks in Asia—H5N1—is highly contagious among birds and has resulted in the death or destruction of over 150 million birds. The outbreaks, which began in 1997, are the most severe on record and the most widespread; infected birds often die within two days and, as of early 2006, birds in at least 30 countries have been affected.

Historically speaking, most bird flus rarely infect humans. While bird flus are generally highly "species specific"—meaning they only infect birds—occasionally they cross the species barrier and infect mammals, such as pigs or humans. Research indicates that, due to natural changes, the current H5N1 is becoming more capable of causing disease in mammals than past bird flus. In fact, there have been reported cases of H5N1 in pigs and some feline species (wild and domestic), the latter of which had previously been considered resistant to natural (in non-laboratory settings) influenza infection. Though none have become ill, some canine species in Thailand have also tested positive for H5N1 antibodies, indicating infection by the virus. Currently, researchers believe the risk posed to humans by these infected animals is very low. Because such viruses rarely infect people, however, scientists fear we may have little or no immunity to them, making us particularly susceptible to illness should H5N1 undergo the changes necessary to spread among humans.

Since 2003, there have been over 170 cases of human infection with H5N1 among people working in close contact with infected domesticated birds in Asia. Direct bird-to-human transmission of any H5 avian influenza virus resulting in illness was unheard of before then. According to the World Health Organization, in the first 175 cases of bird-to-human transmission of H5N1, there were 96 deaths. In other words, more than half of those infected have died. This mortality rate of roughly 54 percent is one reason public health authorities worldwide are so concerned: it is over a hundred times that of common seasonal flus, and about twenty-fold higher than that of the great flu pandemic of 1918, which had a mortality rate of roughly 2.5 percent. It should be noted, however, that the high mortality rate associated with avian influenza in humans is likely to be an overestimation. This is a common phenomenon when a new disease emerges as new cases are typically found by observing those who are severely ill, many of whom will die. Those who are not as ill often go unobserved. It is important to note, though, that even if the mortality rate currently associated with avian influenza were to fall to 1 percent, upwards of one million deaths could be expected in the first pandemic wave, if it is not rapidly controlled.

Thus far, it seems difficult for humans to acquire the virus from birds and even more difficult for the virus to spread among people. In fact, no suspected cases of person-to-person transmission have been definitively confirmed thus far. This indicates that the species barrier is still fairly strong. However, given how devastating H5N1 has been both for birds and the small number of humans it has infected, health experts are concerned that further mutations of H5N1 could change the virus into a form easily transmitted from person to person, resulting in a worldwide outbreak of the disease, or "pandemic." The good news is that, if H5N1 does acquire the ability to routinely infect humans, it may have a far lower mortality rate than it currently does. Some researchers have even theorized that H5N1 infection in humans is far more common than reports indicate, but that these infections result only in mild illness and may go unreported as a result. This theory, however, is yet to be supported by serological (blood) data.

What exactly is a pandemic, and how serious is the risk of a bird flu pandemic?

The word "pandemic" is used to describe a disease that affects people on a worldwide scale. An "epidemic," on the other hand, is usually confined to a particular locale, and is a term used to describe a sudden, sharp rise in the incidence of a disease. Flu pandemics have occurred roughly every 20 to 30 years throughout history, the most serious being the misnamed "Spanish flu" of 1918, the "Asian" flu of 1957, and the "Hong Kong" flu of 1968.

Three conditions must be met to result in a pandemic: first, the emergence of a new flu strain; second, the ability of that strain to infect humans and cause serious illness; and third, the ability to spread easily among humans. Currently, H5N1 meets all but the third condition, and is still a disease of birds. The likelihood that this final condition will be met is unpredictable, but it will remain a possibility as long as opportunities for human infection occur, which in turn depends on how long the virus continues to afflict domesticated birds. For this reason, many researchers feel that the best way to prevent a pandemic is to destroy H5N1 at its source, the birds themselves.

Most experts agree that the question is not *if* another flu pandemic will occur but *when*. But while some scientists worry that the current H5N1 situation indicates a looming pandemic, others doubt that there is any immediate danger. Regardless of whether a pandemic occurs in the next year or the next 50 years, however, the consensus among public health officials is that we should prepare ourselves for this eventuality now. Worst-case scenarios rarely come to fruition, but we should be equipped for an emergency.

Where has H5N1 bird flu recently struck?

Since late 2003, birds in over a dozen nations in Asia and at least seven nations in Europe have been struck by H5N1. In early 2006, the virus reached Africa and recently has been detected throughout Europe, primarily in wild birds. Specifically, outbreaks or isolated incidents of H5N1 infection in birds have been seen in the following countries, in order of reporting: South Korea, Vietnam, Japan, Thailand, Cambodia, Laos, Indonesia, China, Malaysia, Russia, Kazakhstan, Mongolia, Turkey, Romania, Croatia, Ukraine, Iraq, Nigeria, Azerbaijan, Bulgaria, Greece, Italy, Slovenia, Iran, Austria, Germany, Egypt, India, France, Hungary, Bosnia-Herzegovina, Switzerland, Georgia, Niger, Slovakia, Poland, Sweden, and Serbia-Montenegro. Representatives from some of these countries claim that outbreaks are under control as a result of culling flocks and vaccinating poultry. Thus far, there has been no invasion of the virulent H5N1 strain in North or South America. Avian flu strains recently found in birds in North America have been mild and easily controlled.

How many people have been infected with bird flu so far, and where?

Since 2003, there have been 175 confirmed cases of H5N1 transmission from birds to humans in Cambodia, Indonesia, China, Thailand, Turkey, Iraq, and Vietnam. This is a very small number in the context of the large number of birds affected and the near-constant exposure of individuals in some countries to infected birds or their secretions. It is not understood why some people have contracted bird flu and others with similar exposure to infected birds have not. (Numbers throughout are from early March 2006. Updated figures can be found at www.who.int/csr/disease/avian_influenza/en/index.html)

How were people who were infected with bird flu exposed to it?

The current H5N1 virus is not easily transmitted from bird to human. So far, those who have contracted bird flu have been in direct and prolonged contact with infected poultry, or surfaces, areas, and materials (such as cages, water, feed, and dirt) contaminated with the birds' feces, saliva, or nasal secretions. Most human cases have occurred in rural areas where people own freely roaming poultry flocks and slaughter and clean the birds themselves. Often, these birds share the same living environments as and live in close quarters with farmers and their children, increasing the risk of virus exposure. Because many of these households depend on their poultry flocks for income and food, the birds are either sold upon signs of illness or are immediately killed and eaten. According to the World Health Organization (WHO), human exposure most likely occurs during slaughtering or during food preparation processes.

Do migratory birds carrying the H5N1 strain of bird flu pose a threat?

There is reason to believe that infected migratory birds may introduce the H5N1 strain that has killed so many birds in Asia to currently unaffected areas. This potentially includes the United States and Canada, as migratory birds—particularly waterfowl and shorebirds—often travel along “flyways” that cross the Bering Strait between Asia and Alaska. U.S. agencies plan to monitor 30 migratory bird species for the H5N1 virus this spring. Migration of infected wild birds is believed to be responsible for the most recent appearance of H5N1 in some European nations.

Has bird flu been transmitted person-to-person?

To date, transmission of H5N1 between people has proven extremely difficult, but may be possible given the appropriate circumstances. Reports of such person-to-person transmission of bird flu have been very rare. In these unconfirmed cases, it is possible that those infected with bird flu may actually have acquired the illness from poultry after all. Cases of person-to-person transmission would require extremely close contact with infected individuals. Health experts are concerned, however, that the virus may evolve into a form that is more easily transmissible among people. This kind of transmission could potentially initiate a pandemic.

If bird flu can one day be passed person-to-person, how will it be spread?

If one day, due to mutation, H5N1 can be passed among people, it will likely spread in much the same way that typical flu viruses spread, either in droplets from the nose and throat that are expelled from infected people when they cough, sneeze, or even talk, or by direct contact with respiratory secretions—for example, by shaking hands with an infected person—followed by touching one’s nose or mouth.

If bird flu is one day passed among people, can I protect myself by simply avoiding those who appear ill?

Unfortunately, the avoidance of individuals who seem ill with the flu is not a foolproof strategy and will only offer minimum protection. As with our annual flu strain, it is likely that symptoms will not become evident until two to five days after infection. Therefore, before an infected person even develops a cough or chills, they may unknowingly carry and spread the incubating virus to others. This is one reason why quarantines or those exposed or the isolation of disease-carriers are unlikely to prevent the spread of any kind of flu. Furthermore, influenza viruses may remain suspended in small particles in the air for short periods allowing transmission without close contact.

What is currently being done to prevent and prepare for a possible bird flu pandemic?

Efforts to prepare for a possible bird flu pandemic are an ongoing global endeavor, with the World Health Organization playing a pivotal role. Research into vaccine development and mass-production, new antiviral drugs—which disrupt a virus's ability to replicate—and ways to contain the virus to minimize spread are among the efforts being undertaken.

As noted above, the ideal means of preventing an H5N1 pandemic is to eliminate the virus from the bird population. Indeed, countries experiencing outbreaks are employing a variety of different measures to reduce the number of infected birds, including culling entire poultry flocks in which infection has been observed and even administering a series of vaccines to individual birds of currently uninfected flocks to immunize them against H5N1. For numerous reasons, most of which are organizational and logistical, many health experts say these may not be entirely effective techniques. Some even argue that poultry vaccination efforts, if not carefully executed, could accelerate the spread of disease as contaminated material is carried between flocks on the shoes and equipment of vaccination teams. In addition, the farms where H5N1 infected flocks are found and/or culled must be thoroughly disinfected since H5N1 can survive for long periods, particularly in very cold weather.

Research into the development of a vaccine to protect humans from H5N1 is underway in several countries. The United States government has proposed a plan to set aside several billion dollars in order to accelerate vaccine development, increase surge capacity (the amount of vaccine that can be developed within a certain timeframe), stockpile vaccines and antiviral drugs, increase global surveillance of H5N1 outbreaks, monitor migratory bird paths, and cre-

A Closer Look at Mutation: What has to happen for H5N1 to be more easily spread person-to-person, and is this likely?

All influenza viruses have the potential to evolve, or “mutate,” and frequently do. Flu viruses can mutate in two ways: by exchanging segments of genetic material with other flu viruses and/or as a result of small changes to their own genetic material. Both types of changes occur randomly. Data indicate that pandemics are most likely to occur when a flu virus acquires a new H or N type to which humans have never been exposed. (The flu strains responsible for the Hong Kong and Asian flu pandemics exhibited a novel H and N type, respectively.)

If a cell becomes infected with two different flu viruses simultaneously, the genes from these viruses can randomly mix and match to create new flu viruses. This process is known “genetic reassortment.” Sometimes these reassortment events are substantial enough to cause an “antigenic shift” which results in the emergence of a new H or N protein to which humans have no immunity. For example, if a poultry farmer who contracts H5N1 also happens to be infected with a typical human flu strain such as H3N2, genetic reassortment between these strains could result in a new flu type, like a hypothetical “H5N2.” This new virus may share characteristics of both original viruses, such as the ability to easily infect humans (a characteristic of H3N2) and, at the same time, the ability to cause severe illness (like H5N1). It may also be unrecognizable to the human immune system, since part of it comes from a virus that usually infects other species. For this reason, the recent infection of humans and other mammals with H5N1 is alarming, as it provides an opportunity for the virus to exchange genes with other virus strains and perhaps become more infectious to people. Antigenic shift may result in sustained person-to-person transmission of the illness and result in a pandemic. However, the likelihood of this “worst case scenario” shift occurring is unknown and may, in fact, never occur.

Another means by which H5N1 could change and perhaps become more easily transferred among people is through a process called “antigenic drift.” Each time a virus replicates, it accumulates small mutations in its genetic material. Over time, the accumulation of these minor changes—particularly to the virus’s hemagglutinin and/or neuraminidase proteins—may be significant enough to result in a previously unencountered form of the virus. These changes are what necessitate the annual updating of human flu vaccines and are the reason why we can get the flu multiple times, even if we were vaccinated or contracted the flu in a previous year. By contrast, as a result of their low mutation rates, a single infection with the viruses that cause chicken pox or measles (or immunization against them) confers near-lifetime immunity.

ate public education programs. In addition, the U.S. has announced international partnerships that will aid in reaching these goals. Protection of pharmaceutical companies from frivolous lawsuits has also been proposed both to encourage current vaccine manufacturers to participate in this important endeavor and to encourage companies who have not previously made vaccines to do so. In the last decade, fear of litigation has been an impediment to vaccine research and production and may, in part, be responsible for declining numbers of vaccine manufacturing companies. Profitability of vaccine sales and the time it takes to bring a vaccine to market after several levels of clinical trials are other barriers. If these situations continue, they will likely stand in the way of the production of new vaccines, particularly in the large quantities that may be required globally.

While many states have been monitoring poultry flocks for over twenty years, the United States National Chicken Council recently announced a plan to annually test 1.6 million birds in flocks nationwide in an effort to head off a domestic epidemic of avian influenza. According to the Council, poultry-processing companies controlling more than 90 percent of U.S. chicken production have joined the program. Through this initiative, chicken farmers, most of whom raise flocks under poultry industry contracts, will take blood or oral samples from 11 birds in each of their flocks. Suspect results will be sent to the United States Department of Agriculture for confirmation. If any H5 strains are found, the flock will be destroyed on-site and flocks within a two-mile radius will be detained for weekly testing.

Shouldn't it be easy to make a human vaccine for bird flu if we make seasonal flu vaccines every year?

Traditionally, the production technology of flu vaccines involves growing flu viruses in chicken eggs. This poses several problems. First, the H5N1virus against which we would like to develop a vaccine originates in birds and has been shown to kill chicken embryos. Also, this traditional process is also logistically complex and time-consuming. In order to manufacture enough vaccine for the entire world's population, estimates indicate that hundreds of millions of 11-day-old fertilized chicken eggs must be available daily. To solve these problems, scientists are trying to develop new technologies to produce vaccines that involve cell cultures or other processes instead of eggs. Currently, there are a few alternative techniques that various researchers and pharmaceutical companies are working with, including various genetic technologies and mammalian cell culture methods. A few companies are already testing potential vaccines for safety and efficacy in clinical trials. Recent reports indicate that mice immunized with an adenovirus (a common cold virus) genetically engineered to produce a component of H5N1 were protected from death upon subsequent infection with H5N1. Similar techniques may prove effective in humans. In the event that any of these vaccines prove both effective and safe in humans, the U.S. Food and Drug Administration (FDA) will be responsible for their approval, on an accelerated basis if necessary.

A bigger hurdle, and one beyond our ability to predict, involves changes in the virus that may render any vaccines developed today partially or totally ineffective, just as last year's flu vaccine is not particularly effective against this year's flu strain. Some experts are concerned that stockpiling vaccines now, that may prove useless if a pandemic arrives, is a waste of valuable resources. To counter this problem, scientists hope to create vaccines involving "constant" parts of the virus that tend not to undergo much mutation. Other researchers believe that even if H5N1 changes dramatically, the vaccines we will have created may still confer some protection and thus help save lives. Regardless of whether changes to H5N1 do render vaccines created today obsolete, scientists will have learned a great deal in the process that will aid them in producing updated vaccines more quickly.

Another problem inherent in creating an H5N1 vaccine is one of production capacity. Production of a vaccine that is effective against an H5N1 strain that readily infects people will require the ability to produce it in quantities large enough to protect the world's population, particularly given that people may need multiple vaccinations to acquire immunity. Currently, companies operating worldwide do not have this manufacturing capacity. Another concern, given the cost of new technologies utilizing the genetic material from viruses, is the ultimate cost to the public of the vaccine. This cost may inhibit production and reduce distribution to poor countries in Asia and the rest of the world. (For this reason, researchers are exploring the possibility of using an "adjuvant"—a substance added to vaccines to boost the immune response—in order to stretch the vaccine supply. One class of adjuvants under consideration—aluminum salts—has long been approved for such use by the FDA. Others are being considered and tested.)

If I get my annual flu shot, will it also protect me from bird flu?

Getting your annual flu shot will not protect you from H5N1. However, given that the virus has only been seen in birds in Asia and Europe and that it is not easily transmitted person-to-person, the risk of contracting bird flu in the near future is extremely low. However, you should still make sure you visit your doctor for a flu vaccination in order to reduce your risk of infection with a seasonal flu strain.

How is bird flu different from the regular flu?

Thus far, bird flu symptoms in humans initially look very much like those associated with the typical flu—such as cough, sore throat, fever, aches, fatigue, and chills—but these symptoms generally become more severe fairly rapidly. H5N1 seems to replicate more rapidly and attacks the lungs more aggressively than seasonal flu. People who have been infected with bird flu have developed eye infections, bleeding from the nose and gums, vomiting, diarrhea, high fever, viral pneumonia, Acute Respiratory Distress Syndrome, and multi-organ failure, among other life-threatening complications. Also, unlike the flu strains we combat annually, which have a mortality rate somewhere around 0.1 percent, bird flu appears to have resulted in the death of more than half of its human victims, an estimated mortality rate of 54 percent. As best as we can determine, the death rate associated with the 1918 flu epidemic was about one twentieth that. The incubation period for H5N1 may also be longer than that of seasonal influenza, although this has been difficult to determine. Bear in mind, however, that most of the tragic deaths so far from bird flu occurred in areas without the degree of medical care and expertise to which more developed areas are fortunate enough to have access. Remember, too, that as a flu virus acquires the means to spread more easily between species, its degree of severity may decrease.

How is bird flu detected in humans?

Specific laboratory tests conducted by public health authorities are required to confirm that a person has contracted bird flu. Conventional tests, such as blood and cell cultures, work but typically take time (two days to two weeks) to yield results. Other test-types are quick and simple, but cannot differentiate one flu subtype from another. Newer test methods have recently been developed that test potentially infected humans specifically for genes unique to H5 subtypes of influenza.

Is there a treatment or preventive for bird flu?

There are two drugs that, if administered early enough post-infection, have been shown to reduce symptoms of bird flu in some infected humans, thereby reducing mortality and morbidity (severity of illness). These drugs—Tamiflu (oseltamivir) and Relenza (zanamivir)—belong to a class of drugs known as “antivirals.” (For more details on how such drugs work, see Appendix B.)

Tamiflu is commonly prescribed upon a patient’s exposure to seasonal (human) flus or at the onset of seasonal flu symptoms in order to prevent full-blown illness. In this way, it acts both to prevent the flu and to treat the flu if a person is in the early stages of infection.[1] Tamiflu is available both in pill form (with a shelf life of 48 months) and in a drinkable liquid suspension (with a shelf life of 18 months). Relenza, on the other hand, has not been FDA approved for the prevention of flu viruses. Its labeled indication is to treat flu victims by reducing the severity of symptoms and duration of illness. Unlike Tamiflu, Relenza comes in an inhaler.

As for avian flu, we have no evidence that any currently available drug will prevent humans from being infected by H5N1, or have any effect on the course of the illness. However, because of the efficacy of these drugs in treating and preventing common seasonal flus, experts believe that they may work against avian flu. Further testing is ongoing.

Should people stock up on Tamiflu and Relenza immediately, and will taking them now provide protection?

No. Because the current supply of Tamiflu worldwide is inadequate to meet the demand that would arise in the event of an avian influenza pandemic, experts have urged individuals not to stock up on such antiviral medications and have urged doctors to exercise caution in prescribing them. Further, as we have already learned, misuse of these drugs could contribute to increasing viral resistance and render these important antivirals less useful in the event of an H5N1 pandemic. For these important reasons, you should not hoard or unnecessarily take Tamiflu or Relenza.

Will antibiotics or other types of vaccines protect against bird flu?

Neither vaccines that protect against bacterial infections (such as the pneumococcal polysaccharide vaccine, PPV) nor antibiotics will protect individuals from flu viruses of any kind. However, they are often useful against some of the secondary bacterial infections responsible for many cases of severe illness and death in those who contract seasonal flu viruses. Unfortunately, deaths that have resulted thus far from H5N1 infections in humans appear to be directly due to primary viral infections. In other words, it is the H5N1 virus that is making people sick, not the treatable bacterial infections that typically complicate seasonal flus. As a result, antibiotics and PPV may be poor defenses against the complications of bird flu. It is possible, however, that changes in H5N1 as it evolves might actually decrease the severe viral illness associated with H5N1 and cause the strain to behave more like our seasonal flu, leading to more secondary bacterial infections that can be treated with antibacterial agents. Regardless, antibacterial agents cannot be relied upon as a means of preparing for a bird flu outbreak.

1. It should be noted that these antiviral drugs are not a substitute for vaccination against annual influenza.

Will wearing some kind of mask or respirator protect humans from contracting bird flu?

Currently, the CDC does not recommend that the general public wear respirators or surgical masks to prevent exposure to or transmission of flu viruses, seasonal or otherwise, given a lack of epidemiological evidence that they will be effective. While the fitted N95 respirators used during the SARS outbreak overseas are recommended for use in healthcare settings to help prevent exposure to and spread of respiratory infections, such devices have not been tested for effectiveness in community settings such as schools, workplaces, and public gatherings. An August 2005 CDC posting states, "the use of surgical or procedure masks by infectious patients may help contain their respiratory secretions and limit exposure to others [but] no studies have definitively shown that mask use by either infectious patients or health-care personnel prevents influenza transmission."

In the event of an avian influenza pandemic, however, we should understand some important differences between respirators and surgical masks—the most important of which is intended use. Respirators, such as N95s, are designed to protect the wearer from exposure to infectious agents by filtering particulate contaminants from air as it is inhaled. They must be fit-tested to individuals to ensure they are properly sealed to wearers' faces. When properly fitted, most of the air inhaled by the wearer will pass through the filter into the wearer's lungs rather than through gaps between the device and the wearer's face. In order to be effective, they must be worn the entire time one is in a contaminated area. Even then, however, they cannot guarantee protection. The National Institute for Occupational Safety and Health (NIOSH) certifies a respirator only if it meets stringent test criteria, after which the device will receive a NIOSH seal of approval. N95 respirators meet this criteria and are relatively cheap.

Surgical masks, on the other hand, are designed to protect the people and environment around the wearer from large particles expelled by individuals—such as mucus or saliva—and from splatter. They do not adequately filter contaminants from the air, nor are they fitted to individuals' faces. During inhalation, air can enter through gaps between the wearer's face and the mask. As a result, they offer little respiratory protection to wearers. Instead, surgical masks are generally worn for specific procedures and can be taken on and off easily and frequently. Surgical masks are not tested and certified by NIOSH and must only meet certain minimum requirements set by the FDA.

Despite the current lack of epidemiological data, there is little downside to wearing a respirator or surgical mask in the event of an avian influenza pandemic except perhaps a false sense of security. Surgical masks should not be relied upon to prevent exposure to any influenza viruses. NIOSH-approved respirators, when fitted and used properly, will provide some reduction in exposure to airborne particles, including viruses. However, it is not known if this level of exposure reduction is sufficient to prevent disease. Be sure to read and follow all instructions on the fit, use, and warnings provided by the manufacturer before using any respirator. It is also important to note that masks and respirators do not kill the pathogens (viral or bacterial) that they entrap. Therefore, they must be removed and disposed of properly to prevent contamination. Hands should always be washed thoroughly after removing masks and respirators.

In the absence of masks and respirators, however, individuals can help protect themselves by practicing what the CDC refers to as “respiratory hygiene” and “cough etiquette.” These guidelines include: covering one’s nose and mouth when coughing or sneezing; using tissues to contain respiratory secretions (and discarding tissues after use); and frequent hand-washing with soap and water, alcohol-based hand-rubs, or antiseptic handwash. These procedures should reduce the concentration of infectious agents in the environment and, therefore, reduce the risk of transmission.

Will vitamin supplements and other Internet-advertised medicines and products that claim to offer protection against bird flu actually help?

No. In general, consumers should be wary of any products sold online that are touted to promote health, and in this situation to protect against bird flu. This includes vitamins, supplements, or masks sold by organizations that may be posing as legitimate medical resources but in fact are not. Doctors will know what, if any, medications or precautions should be taken in the event of a bird flu pandemic and from whom they should be obtained. Any products currently sold on the Internet that make such claims as “proven to prevent bird flu” are likely to be snake-oil treatments designed to capitalize on people’s fears and to bring in revenue from an anxious public. Remember too that respirators and surgical masks that are not certified by NIOSH or the FDA may not be effective at preventing exposure to influenza viruses.

Can humans contract bird flu from eating poultry or eggs?

There have been no reports of humans contracting bird flu from eating poultry. It is safe to continue eating poultry and poultry products—such as eggs and foods containing them—if proper cooking and hygiene guidelines are followed to avoid a variety of food-borne illnesses. First and foremost, there is currently no H5N1 in the United States and, should it appear, infected flocks would be destroyed and never enter the food chain. Further, a 2004 ban issued by the United States government on the importation of poultry from countries affected by bird flu viruses—including H5N1—is still in effect today. If, however, the unlikely circumstance arose in which H5N1-infected poultry did enter the food chain, proper cooking would kill the virus.

In countries currently experiencing outbreaks of H5N1, however, certain precautions must be taken when handling or preparing poultry for consumption. Individuals in or traveling to these areas should make sure that poultry and poultry products are cooked to at least 180 degrees Fahrenheit throughout, particularly for whole birds. There should be no pink parts or runny yolks. The H5N1 virus is not killed by refrigeration or freezing.

Consumers in affected areas should also be aware of cross-contamination. Surfaces upon which uncooked poultry products have been placed should be thoroughly cleansed to prevent any infectious agents (viral or otherwise) from contaminating other food items, particularly those that may not be cooked before consumption. Hands should also be thoroughly and frequently washed with soap and hot water after handling poultry. To date, there is no evidence of H5N1 infection resulting from the consumption of cooked poultry products, even when those products were found to carry the H5N1 virus.

Who is most at risk of catching bird flu if it becomes easily spread among people?

Generally, very young children and the elderly are most vulnerable to flu infections of any kind. While this remains true for bird flu, it is expected that people of all ages will be susceptible to catching bird flu if it changes in a way that allows it to spread among humans more easily. This is because humans do not typically encounter H5 viruses and, as a result, are unlikely to harbor any immunity to them. This was the case during the pandemic of 1918, when a significant fraction of deaths occurred among healthy middle-aged people. Most of the cases in Southeast Asia have occurred in children or young adults.

Is it safe to own chickens and other domestic poultry?

It is safe to keep poultry flocks in the United States, and there is no need to change standard procedures for taking care of them. The U.S. Department of Agriculture is monitoring any potential poultry infections by bird flu and other infectious agents.

What precautions should be taken by people traveling to countries with reported outbreaks?

People traveling in any countries that have reported cases of bird flu, either in birds or in people, should avoid poultry farms, avoid handling any animals in food markets, and completely avoid surfaces or terrain that may be contaminated with feces from birds or other farm animals. Travelers should wash their hands regularly with soap and hot water or use alcohol-based hand sanitizers. They should also make sure that *all* food—particularly poultry meat and eggs—is cooked thoroughly. They may want to contact their primary care physicians before such travel regarding what medications to bring. Medications easily obtained in the U.S. are often difficult to come by overseas.

People who have recently traveled to an area affected by bird flu and are experiencing respiratory symptoms and fever should be assured that there is no need to panic. Bird flu is not easily transmitted from birds to humans and is even less readily transmitted between people. Recent travelers exhibiting such symptoms should describe them to their primary care physicians.

Where can I get additional accurate information?

Further sound scientific information on bird flu can be found at the following websites:

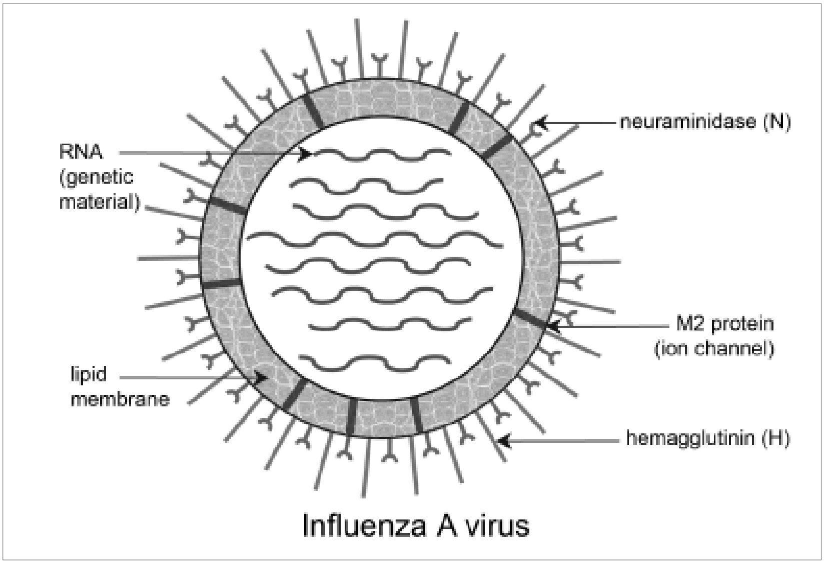
The Centers for Disease Control and Prevention (CDC) on Pandemic Influenza: Worldwide Preparedness:
www.cdc.gov/flu/pandemic/
The World Health Organization (WHO) on Avian Influenza:
www.who.int/csr/disease/avian_influenza/en/
United States Department of Health and Human Services:
www.os.dhhs.gov/
United States Agency for International Development (USAID):
www.usaid.org
PandemicFlu.gov:
www.pandemicflu.gov/
Nature Web Focus: on Warnings of a Flu Pandemic:
www.nature.com/nature/focus/avianflu/index.html

Appendix A. Flu at the cellular level: an overview

Influenza viruses can be separated into types A, B, and C. Influenza A viruses are responsible for regular flu outbreaks in humans, as well as in animals such as dogs, horses, ferrets, birds, and even whales. Influenza A viruses are roughly 100 nanometers (one ten-millionth of a meter) in diameter, and are surrounded by a lipid membrane, which encloses the viral "genome." The genome of an influenza A virus consists of eight RNA segments which, depending on the flu strain, carry a total of 10 or 11 genes. **(Figure 1)**. The genes on these RNA segments dictate which animal species the virus can infect and code for specific proteins, each of which have important roles to play in the viral lifecycle: some proteins aid the flu virus in infecting a host cell; some aid in viral replication within the host cell; and some mediate the ability of newly replicated viruses to burst out of infected host cells so that they may go on to infect neighboring cells.

Influenza A viruses can be further classified by two surface proteins—hemagglutinin (H) and neuraminidase (N)—which project from the viral membrane like studs on a snow tire. There are 16 different H and 9 different N subtypes that can combine to make a variety of different influenza A subtypes. Some of these occur commonly in humans (H1N1, H2N2, H3N2). Some tend to infect other species. Still others infect multiple species.

Figure 1: Influenza A



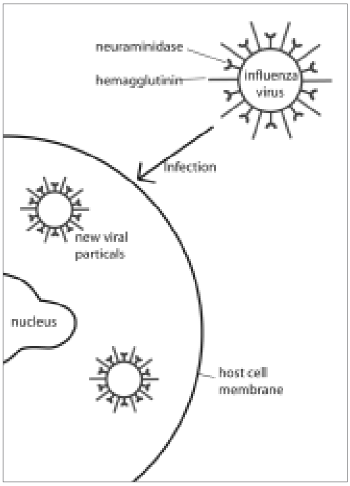
Appendix B. How do antiviral drugs for bird flu work?

Both Tamiflu and Relenza are known as “neuraminidase inhibitors.” Flu viruses always have an H component and an N component (as in **H**5**N**1). The N portion of a flu virus’s genetic material codes for a substance called “neuraminidase” that is crucial to the virus’ ability to replicate itself. When the flu virus infects a lung cell, it basically turns the cell into a factory to make more virus particles. These pieces are then put together into brand new viruses and released from the cell back into the body, where they can infect other cells. Simply put, neuraminidase inhibitors block the release of new viruses from the infected cells in which they are manufactured and keep the virus from spreading. Ultimately, this reduces the severity and duration of illness **(see Figure 2)**.

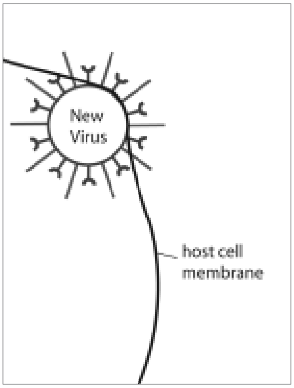
There are some concerns, however, about the use of Tamiflu and Relenza for avian influenza. First, in order to provide treatment, they must be administered within 48 hours of infection, after which their effectiveness decreases significantly. Administration within this short window of time will likely prove difficult: because symptoms often do not appear for a few days, people may not know they have been infected. Second, the use of Tamiflu for flu treatment or prevention is only approved for individuals over one year of age. Relenza is not licensed for flu prevention in anyone and is not approved for flu treatment in children under seven. These are problems given that children play a central role in the transmission of epidemic influenza.

There is also the chance that, over time, H5N1 will change in ways that make it resistant to Tamiflu and Relenza, particularly if these drugs are misused. Indeed, a December 2005 study showed that aspects of Tamiflu’s molecular structure could actually facilitate the development mutations in H5N1 that would render the virus resistant to the antiviral. Relenza’s chemical structure does not have this effect. Currently, H5N1 appears susceptible, or “sensitive,” to both Tamiflu and Relenza, although there have been reports of individuals infected with an H5N1 strain that failed to respond to Tamiflu. Some theorize that these cases may not reflect actual Tamiflu resistance, but instead indicate the rapid disease progression and deterioration of patients infected with H5N1. During the 1918 pandemic, many victims died from lung hemorrhage within 24-36 hours from the appearance of symptoms. In cases such as these, Tamiflu might simply have not had the chance to work. Thus far, there have been no cases of H5N1 in which resistance to Relenza was observed. In preparation for the emergence of Tamiflu-resistant H5N1 strains, scientists are researching new neuraminidase inhibitors (one such new drug is “peramivir”)

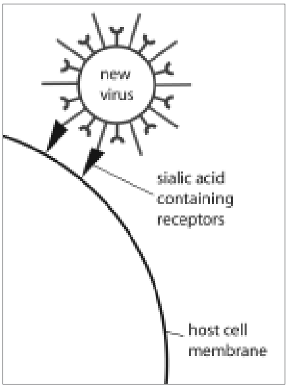
Figure 2



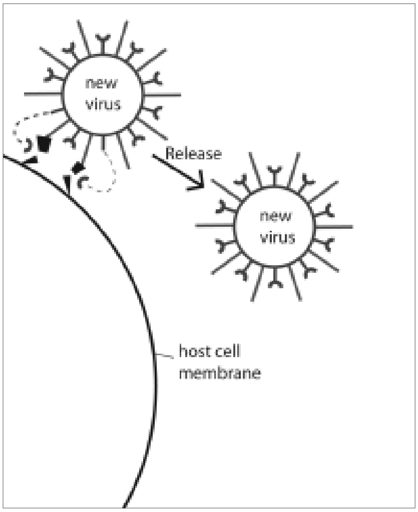
1. **Infection and Replication:** Influenza viruses take over the “machinery” of the cells they infect in order to replicate, or make more of themselves.



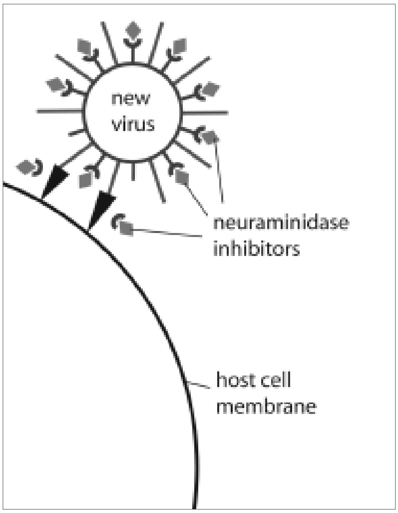
2. **Budding of New Viral Particles:** Each newly replicated virus escapes the host cell by “budding” out of the host cell membrane.



3. **Binding of Hemagglutinin to Sialic Acid-containing Receptors:** After budding, the host cell’s sialic acid-containing membrane receptors bind to the new virus’s hemagglutinin proteins, anchoring it to the host cell and preventing the infection of neighboring cells.



4a. **Release of New Viruses:** The release of the new virus from its anchored position on the host cell’s surface is mediated by the viral neuraminidase protein which breaks the bond between the viral hemagglutinin and the host cell’s sialic-acid containing receptors. The freed virus can now infect neighboring cells, thereby continuing the viral replication cycle and worsening the severity of infection.



4b. **Prevention of Viral Release by Neuraminidase Inhibitors (Tamiflu and Relenza):** Neuraminidase inhibitors, such as Tamiflu or Relenza, block the function of viral neuraminidase and allow the hemagglutinin-sialic acid receptor bond to stay intact. This prevents the release of new viruses from the host cell surface, and the subsequent infection of other host cells.

and are encouraging doctors and patients to appropriately prescribe current antivirals (see below).

Currently, there is a problem of limited production capacity for Tamiflu and Relenza, resulting in a very short supply. As of October 2005, the national stockpile contained 2.3 million treatment courses of Tamiflu and a mere 84,000 treatment courses of Relenza. Even though manufacturing capacity has quadrupled, it will take years to make enough Tamiflu to protect even 20 percent of the global population. To remedy this, the company that controls Tamiflu's patent (Roche) is creating partnerships with other companies in order to increase production rates. Regardless, Tamiflu's cost may still be prohibitively high for the countries that need it most.

An older class of antiviral drug known as M2 inhibitors ("adamatanes") may also confer some protection against a bird flu pandemic. These drugs, amantadine and rimantadine, block the function of a passageway called the "M2 channel" on the surface of a flu virus. When that passageway is blocked, certain particles lose their usual ability to enter the virus and trigger the disintegration of the virus's coating—which is the usual means of releasing viral material into infected cells. As a result, the virus cannot take over the host cell. A serious problem with M2 inhibitors, however, is that a flu virus's M2 region undergoes frequent changes. Consequently, flu viruses quickly become resistant to M2 inhibitors. The current strain of H5N1 is already resistant to amantadine and ramantadine, but, according to the WHO, as the virus randomly changes through "shift" and "drift," it may become susceptible to these M2 inhibitors once again. Amantadine is approved for both flu treatment and prevention in individuals over 1 year of age. Rimantadine is approved for flu prevention in individuals over 1 year of age, but is only approved for flu treatment in adults (18 years and over).

Recent studies geared towards elucidating differences between the genetic structures of human and avian flu viruses have revealed that avian versions of an influenza protein named "NS1" are unique compared to the NS1 protein produced by human influenzas. It has been theorized that this difference may contribute to the high mortality rate associated with H5N1 and that the NS1 protein may prove an excellent target for new vaccines or a new class of flu-fighting antiviral drugs to work in concert with neuraminidase and M2 inhibitors.