Bird Flu

The current news on bird flu is important because it is possible for very serious human flu viruses to develop from bird flu viruses. At this point, it appears that some people have been infected with the bird flu, and some have died from it. So far, the evidence is that transmission of the bird flu from human to human is very limited. This is only slightly reassuring; the real concern is that the virus will change (e.g., mutate) to allow efficient transmission between humans.

General points to consider in thinking about "bird flu"

In an effort to help the reader sort through the confusing news on this topic, here are some general points to consider. Most of the points here are probably fairly well accepted, though not necessarily completely firm. I hope that this dialog will give you a framework for exploring this topic further, and for following the news.

Current status in birds

There is a type of bird flu that is spreading around the world rapidly. This "bird flu" is of the H5N1 type. Note that H5N1 is a type of virus, not a specific virus. That is, simply knowing that a virus is H5N1 does not in itself tell us much about properties of interest.

- The current H5N1 bird flu is extremely virulent in a wide range of birds, including domestic poultry. Therefore, regardless of any other concerns about this virus, it has serious economic consequences, simply for its effect on the poultry industry.
- The current H5N1 bird flu is spreading around the world. At least one reason for its spread is that it infects migratory birds. Known migration routes are being used to predict the spread of bird flu.

Despite those generalities above, we should also note:
- The virulence of H5N1 flu viruses in birds varies widely. Some H5N1 strains grow in some birds with no apparent ill effect. This actually has an important implication... Healthy infected birds (i.e., asymptomatic birds) are perhaps more of a threat for transmission of the virus over large distances. After all, sick birds don't fly much.
- Although migratory birds are suspected as one major source of long distance transmission of the virus, the clear facts on the matter are usually minimal. Trade -- both legal and illegal -- is also suspect.
- "H5N1" is not really synonymous with "bird flu". Many types of flu virus grow in birds. The two terms are sometimes -- and perhaps carelessly -- used synonymously in the current context, where a particular bird flu virus, of the H5N1 type, is of concern.

**Current status in humans**

The current H5N1 bird flu can infect humans. However, it seems that very few humans have been infected by it; most who are infected have had very close contact with infected birds.

- The current virus is poorly (rarely) transmitted from one human to another.
- The mortality rate for humans who do get infected by it is very high -- perhaps well over 50%.
- With "common" flu, mortality is greatest among the elderly and others in weakened condition. For the bird flu, this is not the case; people who are young and healthy die from it. We should note that this characteristic was also true of the famed 1918 flu virus.
- Where is a caveat in the information about bird flu in humans. It is hard to know how many people might have been infected that we do not know about -- people with mild symptoms or perhaps no symptoms at all. It is possible that many many have been infected, but that we are only aware of the severe cases. There is a way to test for this (by testing many people in bird flu areas for antibodies to the virus); to my knowledge, there is no answer yet.


An update. 2007 has come and gone, without a major bird flu impact on humans. Reported cases of bird flu in humans were actually down a bit for the year -- though no one knows how much these reported numbers underestimate what actually happened. Does this mean that the bird flu problem is over? No, not at all. The virus is still out there in birds; the risk of it mutating to become a pandemic virus are probably not much different than before. Anyway, some flu virus will become a serious pandemic threat at some point, so the general attempt to become prepared is good. News story: A pandemic that wasn't but might be, January 22, 2008. [http://www.nytimes.com/2008/01/22/science/22flu.html](http://www.nytimes.com/2008/01/22/science/22flu.html).

Winter 2007-8 flu problem? You may be hearing about this being a bad winter for flu. Does this mean that the bird flu has arrived? No, it is another issue. This year's flu vaccine turns out to be not very good. Each year, a flu vaccine is designed based on a "best guess" as to which strains of flu will likely be prevalent. Usually these guesses are fairly close, but this year they missed on one. So, there will be probably be more flu this winter than expected -- but it will be the usual types of flu, not the feared bird flu.

**Summary: Current concerns**

Based on what is stated above, the current H5N1 bird flu is a serious problem for birds. It is also a problem for those
whose living is based on birds (economic impact). It is also somewhat of a health risk for those in close contact with infected birds. It does not seem to be of much risk to the general public -- those not in direct contact with birds that are likely to be infected.

So why is there is so much said about the health risk?

Influenza viruses change rapidly. To some extent this is a common property of viruses, but there are aspects of flu virus biology that make this case worse. We are aware of the rapid change in flu viruses simply from the need to design a new flu vaccine each year. The big concern is that the current bird flu virus will acquire the ability to transmit well to humans, and in particular to transmit well from one human to another. If this happens, the number of people infected with this flu virus could increase dramatically -- from "very few" (now) to "almost everyone". If the virus that adapted to humans had the same virulence we think the current bird flu virus does, that could be very serious.

How likely is it that the bird flu virus will change so that it efficiently infects humans?

The short answer is that we don't know. However, the more widespread the bird virus is, the more chance there is for the change to happen.

If the bird flu virus acquires the ability to efficiently infect humans, will it have the high mortality in humans that it now seems to have?

Again, the short answer is that we don't know.

So, if we don't know the answers to the previous two questions, why is there so much concern?

Because we don't know the answers. If we don't know, it is prudent to consider a range of possibilities, including "worst case" scenarios. It is plausible that the virus might mutate to efficiently infect humans, and with high mortality. We do know that new strains of the flu arise regularly (that's why we have a new vaccine each year), and we know that very serious new strains arise from time to time. There are some features of the current bird flu virus that make it a good candidate to develop into a serious challenge to humans. These include its widespread distribution and its current high mortality in humans. Further, it is a type of flu virus to which people have not been generally exposed, so there is little or no immunity among humans.

Do all those working on flu viruses agree that the current bird flu virus is a serious threat to humans?

No. But even those who are most skeptical agree that a serious flu virus will emerge again at some point. So they do
agree that the current effort, stimulated by the H5N1 bird flu, to better understand flu virus changes and virulence, and to plan how we would deal with a major flu pandemic, are worthwhile efforts -- even if this virus is not "the one".

What about predictions that fifty million people (choose your number) will die from the bird flu pandemic?

These numbers come from models of how a virus may spread and kill. Each number comes from a specific model, using a specific set of assumptions. That is, each number really means that, if such and such happens, then the following consequences will occur. The models are useful to public health officials, because it helps them to understand how a virus spreads, and therefore what are the most important places to try to intervene. That is, what is most important to the scientists is to see how the models make different predictions as the assumptions are varied. Making "worst case" scenarios is useful to those trying to understand what might happen and to those planning how we might respond. It is somewhat unfortunate that these numbers are quoted without the context of how they were estimated. One should not take any such number as a prediction in the sense that someone really thinks it will happen, and is "wrong" if it does not. What the numbers do is to illustrate the potential danger, if a pandemic happens and we do not respond well.

No one knows how many people died from the 1918 flu. Estimates are in the range 20-100 million. The current world population is 3-4 fold greater than then. Flu viruses are now able to travel around the world at speeds unknown in 1918 (on jet planes). Yes, we now have vaccines and drugs, but we are not sure how effective they would be against a novel flu strain that moves fast. These brief comments should show that we do not know how bad a new flu pandemic would be, but that it plausibly could kill not only 50 million, but far more.

What about vaccines and drugs?

Questionable. These are complex topics, and I don't want to spend much time on them now. However, neither helps much in the short term. Conventional flu vaccines are made for specific strains. So we can't make a (conventional) vaccine against a strain that has not yet emerged, and it takes several months to make a new vaccine. (There is some effort to make generic H5N1 vaccines, and this may prove to be useful experience. However, there can be no claim that any such vaccine prepared in advance would actually be useful against a new strain that emerges.) There are a few drugs that are of some use against flu virus. Oseltamivir is perhaps the best known -- by the Roche brand name Tamiflu. These drugs are quite expensive, and useful only in the very early stages of the infections. They may be useful in a local area to stop spread of the virus. One should not expect too much from them.

Drug notes

Tamiflu no longer works for dominant flu strain. This news story (February 7, 2009) is about an odd -- and discouraging--finding: One of the major strains circulating this season has become resistant to one of the major drugs used. No one knows why; it does not seem related to use -- or overuse -- of the drug. It just happened. Of course, most important is whether such resistance will spread to or emerge in other strains. Time will tell. The story is at http://articles.latimes.com/
Vaccine developments. There have been several recent announcements of progress with flu vaccines, including ones specifically intended for possible use in a pandemic. Some examples of these announcements follow. These are all "progress" -- and "good news". But it is also important to understand that the problems have not been "solved". All of these stories are incomplete, and many are untested or incompletely tested.

Antibodies Could Radically Alter Approach to Flu. This news story (February 23, 2009) discusses a new paper with a new approach to developing broad-range antibodies to influenza virus. In this work they develop monoclonal antibodies that target a highly conserved critical region of the H (hemagglutinin) protein, responsible for proper fusion of the virus with the membrane. They show that these antibodies are effective against a considerable range of flu viruses, and that they are effective both in preventing and treating flu in mice. They provide some evidence that the virus cannot easily mutate to avoid these antibodies, because of their critical function. The story is at [http://www.medpagetoday.com/InfectiousDisease/URItheFlu/12994](http://www.medpagetoday.com/InfectiousDisease/URItheFlu/12994). The bottom of the story identifies the paper and an accompanying news story in the journal (shown as "Primary source" and "Additional source"), with links. That news story is particularly good at putting the work in perspective, including dealing with its limitations.

GE, Novavax team up on pandemic flu vaccine. A press release from two companies, December 10, 2007. They propose use of a "generic" vaccine -- rather than one against a specific strain. They propose use of cell culture, rather than the traditional egg method for vaccine production. And they propose use of inexpensive disposable reactors for growing the vaccine-producing cells. There is much new here. That means it is potentially very interesting, and may lead to vaccine production that is both faster and cheaper. However, it is unproved. The press release is at [http://www.reuters.com/article/2007/12/10/idUSN1041110520071210](http://www.reuters.com/article/2007/12/10/idUSN1041110520071210).

New vaccine may give long-term defense against deadly bird flu and its variant forms. A press release from Purdue Univ, April 17, 2008. They have developed a vaccine with a couple of useful features. First, it is not made in eggs. Whatever the usual reservations are about the traditional system of making flu vaccine in eggs, it will be particularly problematic when growing a vaccine strain that is active in birds. Second, the vaccine appears to be active against a group of H5N1 viruses, not just a single strain. They thus suggest that this vaccine could be stockpiled in anticipation of an outbreak, even though a more specific vaccine might be developed when the outbreak occurs. So far, testing of this vaccine is only with mice. Nevertheless, this is an encouraging development, which will be followed up. The press release gives a good overview of the flu vaccine issues, and includes abstracts of a couple of recent papers on the work. The press release is at [http://news.uns.purdue.edu/x/2008a/080417MittalBirdflu.html](http://news.uns.purdue.edu/x/2008a/080417MittalBirdflu.html).

A new vaccine has been approved for possible emergency (but not routine) use in the US. As you read the news story, note that it is of rather limited effectiveness. News story: First Vaccine Against H5N1 Avian Flu Approved In The US, April 18, 2007. [http://www.medicalnewstoday.com/articles/68109.php](http://www.medicalnewstoday.com/articles/68109.php). There is a link at the end to more information from the FDA.

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Is it safe to eat poultry and poultry products (e.g., eggs)?

Probably. But it is good to understand the reasons behind that conclusion, so you can re-evaluate at some point if things change. There are three reasons why eating poultry should be safe. First, in terms of the American food supply, there is no H5N1 bird flu virus in the system at this point. Second, proper cooking will kill the flu virus. (Remember, there are...
other things you can get from poultry, such as Salmonella. So proper food hygiene is an issue anyway. We also know that not everyone follows "best practice".) Third, the flu virus probably does not infect humans by oral ingestion. Some have suggested that this is not known for sure, but so far there is no reason to believe it is infectious orally. On balance, I'm inclined to suggest that this is not a problem, at least now. One of the links below is on food safety issues regarding bird flu.

The new 2009 flu

This section started in April 2009, as a new flu strain emerged. It quickly became known as the swine flu, for better or worse. Things moved fast. I can't capture all that here, but the goal is to simply point to some resources.

Here is a short message that I received from ASM (American Society for Microbiology). It offers a key resource that I am sure will be kept quite up to date. It also offers a key piece of practical advice. (Links have been updated.)

"The ASM is closely following the swine flu outbreak and wants to make you aware of current information and educational resources that you may find helpful. For general information please go to CDC site on the new flu. The CDC site contains information in print, podcast and Spanish translation for your use. In all infectious disease outbreaks, handwashing is one of the first and most important lines of defense against disease spread. The ASM has long been a leader in increasing awareness of the importance of handwashing and also has public education resources on handwashing for download and distribution at Don't Get Caught Dirty Handed."

In general terms, much of what is discussed on this page for bird flu is similar for the new 2009 swine flu. In fact, the new flu was a chance to test some of the flu preparedness ideas that had developed in preparation for the bird flu.

More information (web resources, articles)

Added May 28, 2011. There are numerous Musings posts on various flu issues. Most are listed on the supplementary page: Musings: Influenza.

New, December 22, 2010. What makes a flu virus virulent? Comparison of the genes in various flu viruses, including the 1918 pandemic virus and the 2009 virus, allows one to ask which features are important for virulence in humans. The work offers clues, but not simple answers. This article is a readable overview, written for a general audience. It discusses the viruses and their genes, and the various experimental systems. Recommended. J A Belser & T M Tumpey, What We Learned from Reconstructing the 1918 Influenza Pandemic Virus. Microbe 5:477, 11/10. It is online, free access, at microbemagazine.org/index.php...pandemic-virus.

Why winter? It is common knowledge that flu is a disease of winter. Why this is so has been unclear, with various ideas being considered. Now, a new report shows that the virus transmits best at low absolute humidity (rather than relative humidity). The humidity effect may reflect the stability of the virus under various conditions. The paper is: J Shaman et
al, Absolute humidity and the seasonal onset of influenza in the continental United States. PLoS Biology 8:e1000316, 2/10. It is online, free access, at http://www.plosbiology.org/article/info%3Adoi%2F10.1371%2Fjournal.pbio.1000316. For a brief introduction to the work, see an announcement from the NIH: Dry air may spur flu outbreaks (3/8/10).

Google tracks the flu. You may have heard about this in the news. Google, in collaboration with the CDC, says they can track the flu by the frequency of searches on flu symptoms and such. The idea is not new, but their implementation of it is more advanced than prior efforts. The big advantage is the speed at which the information becomes available. See http://www.google.org/flutrends/. That page shows what is happening. The page also links to more information, which includes the paper published in the Feb 19 issue of Nature.

Antibodies from 1918. Researchers studied 32 survivors from the 1918 flu epidemic -- and found that all had antibodies to the 1918 flu strain. They were able to isolate antibody-producing memory cells from some of these survivors -- a testament to how long immunological memory can survive. They then used these cells to develop some potent monoclonal antibodies to the 1918 virus. This work has no direct impact on current issues, but is fascinating general information about our immune system. A news story about this work... 1918 Flu Antibodies Resurrected From Elderly Survivors, August 17, 2008: http://www.mc.vanderbilt.edu/news/releases.php?release=83. The paper is X Yu et al, Neutralizing antibodies derived from the B cells of 1918 influenza pandemic survivors. Nature 455:532, 9/25/08.

What determines virulence? We know that viruses differ in their ability to infect, and in the severity of disease (virulence) if they do infect. One difference between bird flu and human flu viruses is in the specific structure they recognize on the cell surface. Simply, the common H5N1 flu virus just doesn't do very well at getting into human cells, at least in the "usual" part of the respiratory tract. But if it does, then what? A recent paper compared two H5N1 bird flu strains, one of which was rather virulent to mice and the other of which was not. They were able to show that a specific amino acid change was responsible for this difference -- and that it probably acts through the host defense system. Implication? Well, for now, it is mainly one piece of information that helps us understand the picture better. It is possible that the protein involved would be a good target for anti-viral therapy. The paper is: P Jiao et al, A Single-Amino-Acid Substitution in the NS1 Protein Changes the Pathogenicity of H5N1 Avian Influenza Viruses in Mice. Journal of Virology 82:1146-1154, 2/08. It is online, with free access to at least the abstract, at http://jvi.asm.org/cgi/content/abstract/82/3/1146.

H5N1 overview. Article: R G Webster et al, H5N1 influenza continues to circulate and change. Microbe 1:559, 12/06. "As the H5N1 viruses continue to expand their range and behave in unexpected ways, they remain a serious threat to birds and humans." Microbe, the news magazine of the American Society for Microbiology, is free online; this item is at forms.asm.org/microbe/index.asp?bid=47152 (HTML) or forms.asm.org/ASM/files/ccLib...1206000559.pdf (PDF).

Avian Influenza (Bird Flu): Implications for Human Disease. http://www.cidrap.umn.edu/cidrap/content/influenza/avianflu/biofacts/avflu_human.html. Excellent. This is part of the CIDRAP site. Other flu pages here include "General Influenza and Flu Vaccine Information" and "Pandemic Influenza"; see the menu bar at the left of their page. I also list CIDRAP as a good general source of information on Emerging diseases.

Reassortment. The flu virus has a segmented genome -- rather analogous to the way humans have 23 separate chromosomes. (This is different from most viruses, which have only one "chromosome"). A concern is that an avian flu virus and a human flu virus infecting the same cell could "reassort" their segments, producing progeny with all sorts of
combinations of flu and human segments. In the worst case, one or more such "reassortants" might have the worst properties of each -- virulence of the avian virus and transmission characteristics of the human virus. It is thought that the virus for some recent flu pandemics did arise this way, at least in part. A recent report showed that many of the simple reassortants one might get do not have any particularly bad properties. It should be emphasized that this does not preclude that reassortment will be a problem; it simply excludes certain things they have tested. A news story in Science a couple years ago is a good discussion of the background for such work -- including concern about the ethics of doing an experiment which might well make a dangerous virus. M Enserink, Virology: Tiptoeing around Pandora's box. Science 305:594, 7/30/04.


The April 21, 2006, issue of Science contains a Feature section on Influenza. Topics include patterns of flu virus spread, issues of host specificity, drugs, and vaccines. Many of the articles should be readable by the general audience. The following link is to the introduction: http://www.sciencemag.org/content/312/5772/379.short. This introductory article briefly describes and links to the other articles of this Feature section, and also other materials that are available in Science. This reference is also listed on my page of Further reading: Medical topics.

Nature web sites on influenza:
www.nature.com/swineflu/ Swine Flu. (Spring 2009; Nature updates it.)
www.nature.com/avianflu/index.html Avian flu news. (Spring 2007 to February 2009.)
http://www.nature.com/nature/focus/a...flu/index.html Warnings of a Flu Pandemic. (2005-6.)
http://www.nature.com/nature/focus/1918flu/index.html 1918 influenza pandemic. (October 2005; Nature updates it.)

Access to Nature web sites may be incomplete, unless you have a subscription. If you use a UC library terminal, you will have full access. In any case, even partial access is probably "useful".

Avian flu: food safety issues, from the World Health Organization (WHO): www.who.int/foodsafety/micro/avian/en/. At this point, most transmission of the bird flu to humans is in cases where people are substantially exposed to infected flocks. Contact with an occasional infected dead chicken might, though is not likely to, transmit the flu. Ordinary cooking would inactivate the virus. Also available in French.

Vaccine development. A news story: FDA, producers moving toward mammalian cell-based flu vaccines. Microbe 1:54, 2/06. Microbe, the news magazine of the American Society for Microbiology, is free online; this item is at forms.asm.org/microbe/index.asp?bid=40620.

The 1918 influenza pandemic killed 20 million people over the course of a couple years. Can it happen again -- worse this time? Well, if a new strain emerges with high virulence and we have limited protection against it, sure. One of the problems with influenza is that new strains arise regularly, and move rapidly. The US government is making plans to deal with a new flu pandemic. The Pandemic Influenza Plan, from the US Dept of HHS, November 2005: www.hhs.gov/
pandemicflu/plan/. (This is part of a larger Pandemic Flu site, from the Dept HHS: http://www.pandemicflu.gov/.)

UC Berkeley Pandemic Flu Preparedness. www.uhs.berkeley.edu/pandemicflu/. In the event of a real problem, this site would provide useful local information. But beyond that, it is good general information, intended to be read and used by real people.

Also see the section on Vaccines (general). Although the page listed there about thimerosal is general, it of particular interest regarding the flu vaccine.

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