

# Questions on Ewald (2005) & Bird Flu Blogs

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1. The blog at one point makes the assertion that the H5N1 virus will become milder because dead or very sick birds don't fly. What steps have been taken within the chicken industry to stop the spread of H5N1? If chicken houses continue to be a reservoir for H5N1, how could the virus evolve to be less virulent?
2. Ewald talks about "a gradual evolutionary approach toward optimum transmissibility" when discussing host-jumping. My understanding is that gradualism far less accepted in evolutionary theory compared with stasis-change models (e.g., punctuated equilibrium theory in macroevolution).
3. Is the low transmissibility of SARS enough to say with confidence that other EIDs will not enter the scene with immediate high transmission rates (or that high transmission couldn't arise rapidly post-emergence of the pathogen)?
4. Ewald talks about many diseases being associated with other diseases, disease symptoms, and/or neurological symptoms. Isn't it possible that having one disease increases the likelihood of having others (i.e., could immune system 'preoccupation' with the first condition lead to increased problems elsewhere in the body)?

5. If the 1918 flu only became a pandemic because it had many hosts in close quarters, and the H5N1 avian flu does best in packed chicken farms, can we assume that only densely populated areas are really at risk of a highly transmissible form of H5N1?
6. If efforts to control a flu pandemic are basically futile, then is there any reason to talk about preventative measures?
7. Poultry farms probably do play a large part in amplifying H5N1, but poultry farms are not unlike beef and other types of livestock farms...they provide an ideal setting for many different disease organisms to reproduce. Since these farms are producing the meat that so many of us love to eat, why are they being attacked for producing a supply to meet the demand? A bad strain of flu as a byproduct of a poultry farm could be compared to the many deaths and the constant environmental degradation caused by our need to drive automobiles.

If "local customs" in Asia are preventing autopsies from occurring to investigate the human cases of H5N1 (Gibbs and Soares), how will virologists be able to learn enough information about this influenza to prevent it from continuing to jump into humans, and preventing the "inevitable" spread from person to person?

How can we say that commercial poultry farming is entirely responsible for increasing virulence of bird diseases? In both farming and migration practices in many wild bird species, birds are usually in close contact for extended periods of time.

With regards to schizophrenia, are you stating that *T. gondii* is the ONLY way of acquiring the disease, or is just another contributing factor? Also, is it possible that those with a genetic disposition to mental illness are just at higher risk if exposed to the pathogen, instead of it actually being a causative agent?

8. Ebola, Nipah, H5N1 Influenza, West Nile and SARS viruses are widely publicized

examples of zoonotic transmission into humans. But none of them are so deadly as compared to HIV in terms of the human mortality index. What makes HIV different?

9. It's a known fact that pathogens that have recently been transmitted to humans are generally not well adapted for transmission between humans. Is there a way via modeling or otherwise, to estimate the point of time when the pathogen can start transmitting actively and thus trigger an outbreak?
10. What are your thoughts on reassortment with human and 'avian' influenza A subtypes in a swine intermediate and its relation to high-path H5N1 in humans? Possibly a reverse direction of the 1998 H3N2 human subtype that caused so much disease in the swine population?
11. What are your thoughts on combining the evolutionary medicine approach with the more 'traditional' medicine/epidemiology/etc approaches? Is the only way to find out which characteristics in either approach are right or wrong to wait and see what happens (e.g. in respect to the potential of a H5N1 pandemic)? Is there no safer compromise?
12. Ducks that have been found to be infected with H5N1 are now said to be shedding more virus for longer periods of time without showing symptoms of illness. With its implication for the role of ducks in transmitting disease to other birds and possibly to humans, do you find this as a concern with regards to a possible pandemic? What about the findings of H5N1 in pigs in China and infection in felines (experimental infection in housecats in the Netherlands and H5N1 isolation in Thai leopards and tigers)?
13. How extensive are the surveillance programs on wild birds in Asia, and would improvements on these programs increase our chances of preventing an epidemic?

14. What is the current state of our knowledge on the physiological effects of H5N1 virus on a wild bird?
15. As far as potential treatments for H5N1, one of the papers stated that the virus that has infected most humans is resistant to some antiviral drugs because they had been previously used on poultry in Asia. Should we stop (I really didn't even know they did) treating poultry and other carriers of viruses with drugs that could possibly be used to treat human strains of the virus in the future?
16. H5N1 evolves in 2 ways:
  - (a) random mutation
  - (b) gene swapping between different strains inside a single animal/person

I know that there were a few cases of less-virulent strains of avian influenza discovered during the past year in the U.S. Do the other strains evolve in similar ways? Should we be concerned that these less-virulent strains are evident in birds migrating through the U.S. in fear that they may evolve into more-virulent strains?

17. Now those scientists have been able to 'resurrect' the 1918 influenza virus, should we be worried? The world is a lot different than in 1918 with the ability of people to travel long distances in short amounts of time?
18. Is the worry over influenza pandemic justified considering the possibility of these viruses being used as biowarfare agents? In such a scenario the virus would be released in key environments to maximize transmission.
19. Is Ebola currently evolving into a less virulent virus? If not why?
20. I think the moderator in the blog raises a good point. He states, ' . . . might it not be a mistake to focus too exclusively on mortality as a measure of how devastating a

flu pandemic could be?’ Less infected people are only put out of commission for a few weeks. How would this affect a country economically? Is this the real threat we should be worried about?

Revere brings up two good points

- (a) Natural selection acts on chance mutations in the virus. What is to stop the H5N1 virus from suddenly acquiring a gene that would make it more transmissible?
- (b) Ewald uses the qualifier ‘trustworthy’ when referring to evidence supporting his work. What does he mean by trustworthy? What are examples of untrustworthy evidence?

21. Is assuming that chronic diseases are spurred on by infectious causes a dangerous concept? Could we be wasting time looking for nonexistent microorganisms? Shouldn’t we base such investigations on scientific evidence that an infectious agent exists?
22. Why dengue and plasmodium species fail to maintain their life cycles in the United States? Is it because of mosquito-proof dwellings?
23. Why the occurrence of transmission of *Toxoplasma gondii* from person to person outside of pregnancy is limited?
24. Is there any reason why the control of protozoal diseases has been less successful than the control of bacterial or viral diseases?
25. The H5N1 strain is widespread in Southeast Asia and is lethal to many wild birds. These articles focus on the disease as it pertains to humans, but I am curious as to what research is being conducted on the wild bird populations. Thailand is one of the world’s ”hot spots” with high biodiversity. Is anything being done to protect this area and its birds?

26. I was surprised to read in the Gibbs and Soares article that "local custom prohibited autopsies" on the three family members who died from H5N1 influenza. It seems like this virus has the potential to become a world issue, and local customs, although very valid, would be overlooked and/or overruled. Is it possible that local customs will always be honored in the case of an epidemic?
27. I would like to hear more about "the tendency for mental illnesses to be increasingly linked to infectious agents." Ewald p 460. I would have issues with a vaccine for *T. gondii* being marketed as a vaccine for Schizophrenia...much like the new vaccine for cervical cancer. It is not a vaccine for cervical cancer. It is, in fact, a vaccine for HPV, a sexually transmitted disease, of which certain strains have been shown to cause cervical cancer. It should not be marketed as a cancer vaccine but rather a vaccine for an STD which it really is.
28. In the chapter from Emerging Neurological Infections, Ewald states 'Any general framework for evaluating the relative threats of emerging diseases must therefore be able to explain why HIV emerged to cause a severe pandemic while other pathogens have not.' In regards to HIV's emergence, I would argue that HIV's emergence was caused by a change in the host's culture - not the agent. The 1960's free love movement preceded the emergence of HIV, this change in the attitudes of the susceptible population allowed HIV to spread much more rapidly and widely than it might have, had this change in attitude not occurred.
29. Since some cervical cancers have been shown to be caused by the Human Papilloma Virus (HPV), is it socially and morally right to require vaccination of all girls of a certain age, even though it doesn't prevent all forms of cervical cancer and may give young women a false sense of security?
30. What role do poultry mites/fleas play in the transmission/recombination of flu virus

between fellow poultry and between humans?

31. If autism is caused by a pathogen, why do more male children have autism?
32. Would treating a portion of the population at high risk for pandemic flu (like healthcare workers treating flu patients) with antivirals put selective pressure on the virus to evolve resistance to these drugs?
33. Normally viruses mutate because of a mistake produced by the polymerase enzyme or by recombination. For influenza to become pandemic, which mechanism will it use to mutate into something so dangerous?
34. Most people get vaccinations against different viral strains every year inducing our immunological system to produce antibodies against several epitopes. That could be the reason that we have not yet had an influenza pandemic?
35. Which characteristics of HIV-1 subtype M make it more pathogenic than the other strains? Has it been recognized which gene(s) are involved with it?