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Avian Flu: What Should Be Done

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Executive Summary

To combat a possible avian flu pandemic, we should consider the following:

1**.** The single most important thing we can do for a pandemic—whether avian flu or not—is to have well-prepared local health care systems. We should prepare for pandemics in ways that are politically sustainable and remain useful even if an avian flu pandemic does not occur.

2. Prepare social norms and emergency procedures which would limit or delay the spread of a pandemic. Regular hand washing, and other beneficial public customs, may save more lives than a Tamiflu stockpile.

3. Decentralize our supplies of anti-virals and treat timely distribution as more important than simply creating a stockpile.

4. Institute prizes for effective vaccines and relax liability laws for vaccine makers. Our government has been discouraging what it should be encouraging.

5. Respect intellectual property by buying the relevant drugs and vaccines at fair prices. Confiscating property rights would reduce the incentive for innovation the next time around.

6. Make economic preparations to ensure the continuity of food and power supplies. The relevant "choke points" may include the check clearing system and the use of mass transit to deliver food supply workers to their jobs.

7. Realize that the federal government will be largely powerless in the worst stages of a pandemic and make appropriate local plans.

8. Encourage the formation of prediction markets in an avian flu pandemic. This will give us a better idea of the probability of widespread human-to-human transmission.

9. Provide incentives for Asian countries to improve their surveillance. Tie foreign aid to the receipt of useful information about the progress of avian flu.

10. Reform the World Health Organization and give it greater autonomy from its government funders.

We **should not** do the following:

1. Tamiflu and vaccine stockpiling have their roles but they should not form the centerpiece of a plan. In addition to the medical limitations of these investments,

institutional factors will restrict our ability to allocate these supplies promptly to their proper uses.

2. We should not rely on quarantines and mass isolations. Both tend to be counterproductive and could spread rather than limit a pandemic.

3. We should not expect the Army or Armed Forces to be part of a useful response plan.

4. We should not expect to choke off a pandemic in its country of origin. Once a pandemic has started abroad, we should shut schools and many public places immediately.

5. We should not obsess over avian flu at the expense of other medical issues. The next pandemic or public health crisis could come from any number of sources. By focusing on local preparedness and decentralized responses, this plan is robust to surprise and will also prove useful for responding to terrorism or natural catastrophes.

Introduction

The current outbreak of H5N1 avian flu has been spreading to a variety of bird species, including ducks, chickens, magpies, crows, pigeons, and gulls. Today more birds have dangerous forms of avian flu than at any time in recorded history. H5N1 also has jumped to many species of mammals, including mice, tigers, cats and dogs. Recent events in Indonesia suggest the flu has mutated to jump from birds to humans with greater ease. Humans have picked up the flu—and died—simply from visiting birds in the zoo, most likely through pulverized feces in the air. As of early November, over sixty individuals have died of avian flu, all in Southeast Asia and mostly in Vietnam. The remaining question is whether the flu will evolve to allow for easy human-to-human transmission. Some family-based case clusters in Indonesia suggest that human-to-human transmission may be occurring, although not with great ease.

This "reservoir" of avian flu in birds and other animals is not going away soon. Most likely it will be with us for at least ten years and it will continue to spread. We will face the ongoing possibility of a dangerous mutation, allowing for easy human-to-human transmission and thus a pandemic.

History gives reason to worry. It is now believed that the 1918 "Spanish flu" pandemic may have killed fifty to one hundred million individuals.[1] This disease came from an avian flu, and from one surprisingly close to current strains. A relatively small number of mutations would be needed to transform current strains of avian flu into a large scale killer of humans.

It is commonly opined that a modern pandemic would kill fewer people, due to modern medicine. Perhaps modern flu immunities are stronger, due to greater urbanization, or antibiotics will limit the number of secondary respiratory infections. These features may prove significant, but in general our defenses against a killer strain are not strong. In 1918, most of the deaths occurred within the time span of a few months, followed by later cyclical waves. Today the flu has more potential victims, it would spread more rapidly, much of the world has poor medical care, and most of our potential solutions—even in the wealthy countries—would take many years or months to mobilize. We should not assume that a future onset of avian flu will be largely benign. Furthermore no country in the world—no matter what it claims—has adequate preparation. We do not currently have a good vaccine against avian flu, and any vaccine would be difficult to produce in large numbers very quickly. The relevant anti-virals are limited in supply and require timely application.

There is no built-up human immunity to current strains of avian flu. Some sources suggest a fatality rate of up to fifty percent, but this is unlikely. It is the case that over fifty percent of the patients reported as "avian flu cases" have died. But we can expect selection effects. Most of the patients who get to a doctor, and who receive a proper diagnosis, have the most obvious symptoms. Most current avian flu sufferers probably

[1] John M. Barry, *The Great Influenza: The Epic Story of the Deadliest Plague in History* (New York: Viking Press, 2004).

never receive such a diagnosis in the first place; we are talking about Vietnam, Thailand, Cambodia, and Indonesia. But avian flu does not need a high fatality rate to do serious damage. Some analysts have suggested that the 1918 pandemic had a fatality rate of only two percent. Yet fifty to one hundred million people died because the flu spread so widely.

The World Health Organization (WHO) has estimated that a pandemic strain of avian flu could kill between two and 7.4 million people worldwide. Some WHO sources have cited numbers as high as 150 million, although there was subsequent pressure to retract this estimate. The truth is, these are guesses and nobody knows how bad a pandemic would be.

Even in the absence of human-to-human transmission, avian flu is doing significant damage. Farmers have been killing chicken and duck stocks across Southeast Asia. Working with chickens and ducks, especially slaughtering them, has become a hazardous occupation. For many communities, this represents a significant loss of economic value. Even if we see no pandemic, poultry industries in Europe and North America could be hit with disaster. In addition, many people have backed away from eating chicken, whether rationally or not.

Recently Congress has been considering multi-billion dollar preparations for a pandemic. But if a pandemic came in 2006, American efforts would be statistically indistinguishable from zero preparation. Given the disaster of Hurricane Katrina, we can ill-afford to make another round of mistakes. This time the stakes are higher.

That being said, we should not dismiss the avian flu skeptics. Bird flu does not mutate to human-to-human transmission very readily. We cannot be sure that a pandemic is coming, or even that the probability of a pandemic in the near future is very high. We only know that the probability is much higher than before. Many other diseases and maladies threaten human life, including a rising risk of bioterror. Our preparations therefore should not be aimed at avian flu alone. We should prepare for pandemics in ways that are politically sustainable and remain useful even if a pandemic does not occur.

For an overview of the scientific issues surrounding avian flu, I recommend **FluWiki**, which is edited by health care professionals. For daily updates I recommend our blog, **Avian Flu: What You Need to Know** (http://avianflu.typepad.com/), and the other blogs and resources on its blogroll. **Effect Measure** (http://effectmeasure.blogspot.com/) often has the best public health information, and Henry Niman's **Recombinomics** (http://www.recombinomics.com/) has a running account of recent rumors, especially about mutations and recombinations. No static policy study can replicate the virtues of these more flexible media, so I will not try. I will focus on methods of thinking about avian flu problems, and for thinking about disaster preparedness more generally. This study is intended as a complement to on-line and other media, not a substitute for them. Blogs, however, are not always well suited for longer, conceptual pieces, thus the role for this study.

I will analyze the problems faced by a possible avian flu pandemic. This study will be divided into parts. First, I offer a list and analysis of what we should do. Second, I offer a list and analysis of what we should *not* do. Third, I offer some concluding remarks on how to think about the politics of these recommendations and whether they are robust across alternative disasters.

Our experience with pandemics is fragmentary and often set in the distant past. Estimating the effects of a pandemic today, or what we should do, has an ineradicably speculative component. Nonetheless, the time has come to ask difficult questions and address them as best we can.

This analysis has two common themes. First, a good response to a pandemic or crisis must allow for effective decentralized action. Detecting a pandemic, instituting protective measures, and applying treatment all require the effective cooperation of many different individuals and institutions. A strict top-down approach will not work. If a pandemic arrives, as a matter of practical fact we are likely to be "on our own" with respect to the federal government. There will not be close to enough centralized response capacity. Local health care institutions therefore must be both free and able to respond to crises.

Second, policy proposals must be consistent with realistic assumptions about human behavior and human self-interest. We should not assume that in a crisis all people will behave like angels and that all plans will go well. Systems will be gamed, black markets will arise, and many allocation mechanisms will break down. We will encounter unforeseen kinks in supply chains. A plan should consider unintended consequences; it does not suffice to have good intentions and a plan on paper.

Part I. What Should We Do?

We can classify response plans into two broad categories. The first kind of plan relies on centralized production and distribution of anti-virals (e.g., Tamiflu) and vaccines. The second kind of plan places greater emphasis on decentralized local responses and effective local public health care systems. Action in both directions in warranted, but the local plans are likely to have greater efficacy. **The single most important thing we can do for a pandemic—whether avian flu or not—is to have well-prepared local health care systems.**

1. Emphasize local preparedness

Local public health systems must be of high enough quality to handle an onslaught of pandemic cases without collapsing. Furthermore those health systems must give us adequate notice so we can close schools and many other public places before a pandemic is in full swing. We require greater investments in local, decentralized knowledge about how to handle a crisis.

Local preparedness should include a combination of the following measures:

a) Emergency room preparedness

Emergency rooms should have plans to handle the crush of arrivals, whether real cases or panicked individuals, during a pandemic. This should involve anti-viral and mask protection for essential staff, as well as alternative emergency room procedures for non-flu patients. Large numbers of non-flu patients will be afraid to come to emergency rooms, for fear of contracting flu. "Flu-safe" medical sites should be planned, designated and publicized. One of the biggest problems in a pandemic will be treating non-flu-infected individuals. On average over 300,000 Americans use the emergency room every day, often for reasons of life and death. We do not want our entire medical emergency infrastructure to shut down for months at a time or longer.[2]

If a pandemic arrives, public service announcements should tell people that only life-threatening illnesses should be brought to emergency rooms. Hotels, convention centers, schools, indoor stadiums, and other public facilities may be converted into emergency medical facilities. We should not focus our planning on flu victims alone. It may be the case that non-pandemic deaths will prove easier to reduce than pandemic deaths.

b) Testing kits and early warning systems

Singapore recently has developed an easy to use testing kit for avian flu. The United States should order or manufacture kits for local hospitals. If a cluster of avian flu cases arrives in the U.S., we wish to be informed as soon as possible. Furthermore the successful use of Tamiflu requires prompt knowledge that the victim is suffering from avian flu.

Currently we can say, in principle, within 40 hours of hospitalization whether a patient has H5N1. It takes another six hours to analyze the sequence of the gene. It takes another two days to reveal whether the virus is resistant to anti-virals such as Tamiflu and Relenza. But often the binding constraint is whether the hospitals in question know to apply these tests in a timely manner, know to ask for external help, and know to report and share results immediately. Local institutions should be prepared in this regard.[3]

c) Upon notice of a global pandemic, shut the schools immediately

A pandemic is most likely to start in Southeast Asia, or at the very least, outside the United States. We therefore can expect some advance warning of its arrival on our shores. It will come in a matter of months or weeks, no matter how hard we try to stop it (see the discussion below in section II). Once a pandemic breaks out abroad, we should shut the schools immediately. This will limit the ability of children to pass the flu to each

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[2] An ongoing study of Pennsylvania communities suggests that local preparedness and health care infrastructure was a good predictor of how well different communities coped with the flu pandemic of 1918. -See http://www.sciencedaily.com/releases/2005/10/051026085414.htm for more detail.

[3] On timing, see W. Waut Gibbs and Christine Soares, "Preparing for a Pandemic," *Scientific American*, November 2005, pp.45-54.

other in close, regular settings. We should assume that the flu is coming to the United States or has arrived, rather than remaining in denial, or believing that a quarantine will keep it out. We should not wait for the first wave of U.S. human cases to close the schools and day care centers. So far it appears that children are a group especially vulnerable to current H5N1 strains. If need be, some of the schoolwork could be posted on-line and taught in a virtual manner.

Difficult questions arise when both parents must work for reasons of income or because they supply essential medical or economic services. The need to care for children will produce high rates of workplace absenteeism. When both parents work in the supply of essential medical services, they should be offered a tax credit to pay for a babysitter. Most generally, we should expect childcare to be one of the major problems arising from a pandemic. Nonetheless these significant inconveniences are not worth the potential loss of thousands of children's lives through the school system. Children, of course, also pick up flu strains at school and bring the diseases back home. They are potential spreaders nonpareil, and we should limit this transmission mechanism before it gets well underway.

d) Prepare to treat secondary infections

During the 1918 pandemic millions of people died, not directly from the flu, but rather from resulting secondary infections and weaknesses. Many of these deaths could have been prevented with antibiotics, oxygen supply, IV fluids, respirators, dialysis, and other now-standard medical technologies. A priority is to make sure we have sufficient health care capacity to respond to an emergency event. Quite possibly this is how we can save the greatest number of lives.

We should not let modern technologies make us complacent about an avian flu pandemic. Currently, we would not be prepared to meet a crush of demand for these services. For instance, avian flu attacks the lungs and can infect the cells far down the respiratory passages. If a pandemic came, many individuals would require the use of ventilators. Yet the U.S. has only 105,000 ventilators, 95,000 of which are currently in use.[4] Current standards for assigning priority to these ventilators should be extended to cover avian flu cases.

Statin drugs are widely used to fight cholesterol, but they also can serve an anti-inflammatory function. Some evidence suggests that statins might help alleviate the secondary consequences of severe flu infection.[5] Many statins are off-patent, cheap, and available in significant quantities. For these reasons, U.S. medical research—including federally funded research –should pursue the relevance of statins with special vigor. Statins stand a chance of being especially important in poorer countries, given the problems associated with Tamiflu and vaccines (see below). We also should focus on

[4] The source is Tommy Thompson, former HHS secretary, cited in "The Avian Flu: How Scared Should We Be?", *Time* magazine, October 17, 2005, pp.30-34.

[5] See, for instance, Martin Enserink, "Old Drugs Losing Effectiveness Against Flu; Could Statins Fill Gap?", at http://www.sciencemag.org/cgi/content/full/309/5743/1976a.

whether extant anti-virals—some of which are lingering in obscurity—might prove effective against avian flu.

Currently the U.S. federal government is investing about $119 million a year in influenza-related research. Contrast this with the $10 billion we spend to research and develop anti-ballistic missile defense. One simple, budget-neutral piece of advice is to switch most of this money to the greater threat of influenza.

More generally, we should investigate which secondary health services could be expanded most readily and at lowest cost. We should then invest in these areas. While we cannot expect to be able to give every avian flu patient full treatment, we could be much better prepared than we are today. Note that such preparations need not be geared toward avian flu *per se*. They also would be useful in responding to terrorist attacks, natural climactic disasters, or other unforeseen catastrophic events.

Most of all, we are under-investing in surge capacity. The economic rationale for this institutional failure is simple. When surge capacity is most needed, it is then hardest to charge for the market value of that capacity. For instance, if we imagine a crush of demand for emergency room services, price is not an effective means of rationing. Hospitals are obliged by law to meet that demand and serve all comers. This unpriced resource implies that our normal, everyday institutions will underinvest in surge capacity.

e) Prepare databases of potential volunteers

Many doctors, nurses, or retired professionals will be willing to help out in a pandemic. This was the case in 1918. Local authorities should prepare relevant lists of potential volunteers and develop plans for how they might be used. Such plans need not be restricted to the medical sector but also could be used for critical "choke points," as would involve food and water supplies, or perhaps care given to the elderly in their homes.

f) Preparedness for deaths

Lack of mortuaries, coffins, and associated sanitary facilities was a major problem during the pandemic of 1918. Facilities for processing the dead should be encouraged to develop better plans for natural catastrophes.

g) Encourage local planning

The federal government does not have the resources or the competence to much help if a pandemic breaks out. Decentralized planning at the state, county, city and corporate levels will likely have the greatest positive impact.

Many unforeseen local problems will hinder an effective response to a pandemic. Supply lines may collapse, some individuals may panic, and unforeseen glitches in services will arise. Not all of these problems can be worked through in advance (for instance, when

individuals fled Hurricane Rita in Texas, it was not foreseen how many cars would run out of gas). The problem is not that we cannot imagine what might go wrong, but rather we can imagine too many potential scenarios.

We do not know in advance which scenarios will be most relevant. Having high-quality institutions is the most effective means of addressing this problem. Such institutions are the result of years of good policy and cannot be created overnight by fiat or by a list of short-term recommendations. If there is one overall lesson, it is that the quality of local health care, and local health care institutions, matters more than we used to think.

2. Hand-washing programs

Washing your hands regularly is one of the most effective protections against flu, including avian flu. Dr. Peter Sandman, a risk communication expert, writes: "Then there's hand hygiene—which isn't really "medical" because you don't need a doctor to do it right. Infection control experts agree, with solid evidence to support them, that the single best available precaution against the spread of influenza is washing your hands as often as you can. They also have evidence to support their advice to avoid touching your eyes, nose, and mouth."[6]

The federal government should hire professional marketing consultants to provide advice on how to distribute this message. It does not suffice if the government simply warns people that frequent hand-washing is in their best interest. As we know from Hurricane Katrina and numerous other episodes, people do not always trust their governments. People often will ignore fully sound advice, even when following that advice costs very little. So advice should be presented in the most persuasive form possible; one question is whether the marketing campaign should emphasize the benefits of compliance ("health"), or the dangers of non-compliance ("sickness"). Churches should be an important part of this transmission mechanism. Not only do they have credibility, but many churches encourage mass hand-holding behavior on a regular basis.

More restrooms should be built so that individuals can wash their hands without having to touch the droplets left by previous individuals. It should be easy to open and close restroom doors without having physical contact with droplets from other individuals. When possible, existing restrooms should be retrofitted to meet these standards or disposable gloves should be provided. Even many of the restrooms in health care institutions, such as the U.S. Department of Health and Human Services (HHS) or WHO, do not meet these elementary safety standards. Related questions involve how we can increase the safety of commonly touched public "hotspots," such as elevator buttons, public light switches, doorknobs, and gas pump handles, among other examples.[7]

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[6] http://www.psandman.com/col/panflu3.htm. For a more formal look at influenza transmission, see Stephanie A. Boone and Charles P. Gerba, "The Occurrence of Influenza A Virus on Household and Day Care Center Fomites," *Journal of Infection* 51 (2005): 103-109.

[7] In economic terms the problem is twofold. First, individuals have been underestimating pandemic risk in their facilities construction decisions. Second, facilities suppliers will not internalize the relevant externalities if their customers cannot easily observe the safety of their facilities.

In the case of a pandemic, the demand for handiwipes and disposable gloves would likely skyrocket, leading to a run on the market. Local police and other vital services should stockpile at least some handiwipes and disposable gloves for future protection.

We also should invest more in stockpiling high-quality masks, to protect against the spread of disease. In the case of a pandemic, there will be a run on masks, especially of the high-quality kind. We wish to make sure that police and other essential local services—including the chain of food and water supply—have access to mask protection. Note that unlike Tamiflu and vaccines, a mask stockpile will last for a long time without losing effectiveness.

If a pandemic arrives, we should encourage public norms against coughing, sneezing, and shaking hands in public places. During the 1918 pandemic governments passed (and sometimes enforced) laws against coughing and sneezing in the presence of others. At the very least, public service announcements should make it clear that everyone—not just individuals who show symptoms—is a potential spreader of the flu virus.

3. Develop better plans for the distribution of anti-virals

Problems of distribution are paramount in a pandemic. We should not equate "having a vaccine" or "having a Tamiflu stockpile" with solving the problem or saving the lives. Yes, we should invest in drugs and vaccines, but this constitutes only part of a good preparation.

The first question is where the relevant anti-viral drugs and vaccines would be kept, and under whose authority they would fall. Currently the Centers for Disease Control and Prevention (CDC) controls the stockpiles, but we should prefer as local a distribution and allocation system as possible (the exact means of allocation will depend in part upon the region under consideration, especially its population density). This will encourage speed of use, which is of essential importance in a pandemic; as noted above Tamiflu is effective only if applied within the first two days of symptoms. Allocation decisions should be under the control of local authorities, often at the level of the individual hospital or medical center. There should be as few links between drug and vaccine stockpiles and allocation as possible. Even if this lack of oversight leads to some unfairness (imagine a local hospital favoring local clients, friends, or family members of staff), the priority is making sure that the drugs and vaccine can be used at all. If local authorities must wait for broader clearance from higher levels of government, this will lead to many unnecessary deaths and of course further spread of the virus.

Once a given stockpile is produced and distributed, federal involvement (apart from periodic replenishment) should be limited to outlining broad principles for distribution. Regulations should specify an order of priority for drug or vaccine access. That being said, distribution should not require prior clearance from higher authorities; this will only delay health care institutions. Furthermore penalties should not be structured so as to paralyze immediate allocation for fear of eventual legal consequences.

The most important priority is to allocate available drugs and vaccines to medical personnel and medical volunteers, and then to police and fire personnel. To the extent that laws cannot be enforced and discretionary allocation occurs, a hospital is likely to follow these priorities of its own account, if only for reasons of self-interest. Furthermore it is acceptable (if a bit unfair) if hospital allocation leads to favorable treatment for family members of hospital staff and hospital volunteers. In fact this may provide a central motivation for individuals to continue working in hospitals. All of these factors militate in favor of local allocation at the level of the individual hospital or medical center.

The Bush/HHS plan would give priority to medical personnel, and then to individuals making the vaccine or anti-flu drugs, or otherwise involved in the supply chain. So far, so good, but then the priorities shift to the elderly, the severely ill, pregnant women, transplant and AIDS patients, and parents of infants. Then come policemen and firefighters.[8]

Choosing an order of priority does not admit of easy solution. Nonetheless we should consider revising the Bush list. After medical personnel are taken care of, we should give priority to healthy individuals, not individuals ailing from non-flu maladies. Healthy individuals, and the relatively young, tend to be relatively mobile and to have larger active circles of friends. For these reasons, they have the greatest likelihood of spreading flu to others. Furthermore healthy individuals are also most likely to play critical roles in supply chains for food, water, electricity, and the like. This suggests moving up healthy individuals in the queue. In addition, teenagers are the most likely to "hang out" in groups, and they are also the most likely to disregard instructions to avoid social groups. Treating and vaccinating teenagers therefore may yield a larger return in terms of number of lives saved. Furthermore the lives saved will last longer on average; we should think of ourselves as maximizing "life years" saved. It sounds heartless to "let old people die," but if a pandemic arrives many people will die in any case, both from the flu and from other causes. In fact, if the young are the most potent spreaders, we may save more of the elderly by targeting the young for greater protection. So we should alter our allocational priorities in the direction of younger individuals and healthier individuals.[9]

4. Reform our public policy treatment of vaccines

Current American policy toward vaccines brings us the worst of both worlds. Government discourages what it should be encouraging. U.S. firms have been leaving the business in droves, and we are unprotected against many regular flu strains and childhood

[8] See Gardiner Harris, "Bush Plan Shows U.S. Is Not Ready for Deadly Flu," *The New York Times*, October 5, 2005, pp.A1, A12. The plan itself can be found at http://www.hhs.gov/pandemicflu/plan/.

[9] Note that in the 1918 pandemic, individuals in the 20 to 40 year old age range were most vulnerable, largely because of cytokine storms. Many of these individuals died, not from the flu itself, but from the effects of massive inflammation or from the overreaction of their body's immune system. Healthier individuals were often more at risk than sick individuals. We cannot be sure whether this pattern will repeat itself, but this provides another potential reason to give greater priority to healthy individuals.

diseases, much less against a pandemic. If the U.S. needs more flu vaccine in a hurry, it is almost fully dependent on foreign producers.

We should focus on two reforms:

a) Institute prizes for effective pandemic vaccines

Currently many companies do not see the profit opportunity in developing vaccines that may never be used. The liability issues are significant and future demand is uncertain. Potential vaccine producers fear that the government will use its dominant-buyer position to negotiate very low prices.

Currently only four major American companies make vaccines and two of these four have significantly cut back on their vaccine research programs. For purposes of contrast, in 1957, twenty-six different companies were making vaccines. Vaccine shortages are now a matter of course. This has led to problems with tetanus, pneumonia, bloodstream infections, and meningitis in children. A flu epidemic in 2003-2004 killed 36,000 Americans, including 152 children. The next year there were 30 million doses fewer of the relevant vaccines; no surge capacity was available to make up for contamination problems in a foreign plant. Since 1998, nine of the twelve vaccines given routinely to young children have been in severe shortage; this includes measles, mumps, and rubella.[10]

Paul A. Offit writes: "For the four companies that still make vaccines, gross annual revenues from vaccines are less than 10 percent of total revenues; internationally vaccines account for about 1.5 percent of total revenues. Pharmaceutical companies are businesses, not public health agencies; they could stop making vaccines tomorrow without much of an impact on their bottom line."[11]

The federal government could alter these incentives by offering prizes for vaccines that meet the FDA's "fast track" designation for development. This would include prizes to protect against an avian flu pandemic. The federal government already buys a large percentage of the vaccines used for children, but typically it pays low prices, which has caused the market to shrink. Note that paying higher prices for vaccines would be similar in its effects to offering prizes. We could offer a super-prize if an easily scalable "DNA vaccine" technology is developed to protect us against avian flu and other possible pandemics.

The economic argument for such prizes is twofold. First, vaccines can protect against infectious diseases. These diseases involve "negative externalities," since the sickness of one person can make many other people sick as well. This is the classic argument for state action, and it is difficult to see how a pure market setting will take these external costs into account. Individuals are not willing to pay as much for a vaccine as would

[10] See Paul A. Offit, *The Cutter Incident: How America's First Polio Vaccine Led to the Growing Vaccine Crisis* (New Haven: Yale University Press, 2005), pp.xi, xii, and also pp.181-191.
[11] Ibid., p.189.

reflect the social costs of their infection; for this reason a subsidy is in order. Second, if a pandemic arrives, the property rights in vaccines and anti-viral drugs will—for better or worse—be confiscated or otherwise partially abrogated. We do not have the option of pure market incentives, and for this reason we must offer some rewards for innovation upfront.

b) Reform liability law for flu vaccines

Liability law is partly to blame for the increasing scarcity of vaccines. A vaccine which is very beneficial on net may still kill or disable some number of victims. These victims or their families can then sue the companies and receive large awards.

In 1986 Congress passed the National Childhood Vaccine Injury Act, which was designed to protect companies against frivolous lawsuits. But this legislation has not been fully effective. Most importantly, plaintiffs can opt out of the provisions of the Act. Furthermore lawyers still have the option of taking their chances before a jury, as they have done in the case against thimerosal in vaccines. Our legal system has driven thimerosal out of vaccines, even though the scientific evidence suggests that the compound makes vaccines safer rather than more dangerous. Furthermore the 1986 Act covers only vaccines used routinely for children (this rules out many vaccines, such as that for Lyme disease), and it does not cover unborn children. Investing in vaccines remains a liability disaster.

We should rewrite this legislation to eliminate the loopholes. Notice that the legislation does not eliminate the possibility of a damage reward, but rather makes rewards from a government fund, derived from an excise tax on vaccines. We need to encourage vaccine production, and we can best do this by limiting liability. The courts are a poor forum for guaranteeing good health care outcomes in this context. We also should consider funding governmental liability payments out of general revenues rather than taxing vaccines. We stand at dangerous margins where vaccines are on the verge of disappearing altogether. Liability law does serve the important function of protecting consumers, but the risk of pandemic has elevated the importance of encouraging innovation.

We also should reform FDA policies to encourage the production of new vaccines. Currently FDA regulations significantly raise the cost of both vaccine factories and vaccines. On average our regulations are tougher than those of Western Europe. Recognizing that medical innovations are now more important than we had thought, we should relax these regulations with the aim of encouraging more domestic vaccine production.

When it comes to an avian flu pandemic, we cannot rely on vaccines manufactured in Europe or elsewhere in the world. Countries are unlikely to export any effective vaccine until they have covered their own populations, at which point it may be too late. So it is important that our laws allow for a viable, ongoing domestic vaccine industry.[12]

[12] It has also been suggested that pharmaceutical companies be allowed to book revenue from vaccines when orders are placed, rather than when the vaccine is delivered. This may encourage vaccine production

We cannot expect that vaccines will necessarily protect us against avian flu, for reasons discussed further below. But these reforms are worth doing in their own right, whether or not they are required to protect us from a forthcoming pandemic.

5. Take intellectual property rights seriously

Tamiflu is produced by Roche, a Swiss pharmaceutical company. Recently Kofi Annan has questioned whether this property right should be respected. Compulsory licensing of the drug has been raised as one alternative policy. Some countries claim they know how to make Tamiflu, but they wonder how much they should respect current patent rights. India and Taiwan have announced plans to proceed with manufacture of a generic. Roche has denied that other suppliers have the competence to engage in large-scale manufacturing, but this is probably more rhetoric than reality. We can expect similar issues to arise with Relenza, an anti-influenza spray; for purposes of simplicity I will refer to Tamiflu but the arguments are more general.

An outright confiscation of drug property rights would set a dangerous precedent. Avian flu is not the only pandemic risk we will face. If drug companies expect their property rights to be confiscated, the next time there may be no Tamiflu, or its equivalent, in the first place. Who, for instance, would put much trouble into developing an HIV vaccine? When it came to Bayer's anti-anthrax medicine Cipro, we failed to send a clear signal of respecting property rights. Yet it is no longer obvious that anthrax is a major danger. If we continue down this path of failing to protect property rights in important ideas, we will become increasingly vulnerable to negative health care events.

The gains to an outright confiscation of intellectual property rights may be more limited than is commonly supposed. Individuals who favor breaking intellectual property (IP) rights often have an AIDS-like scenario in mind. In that case we have a slowly-building disease which infects and kills people over the course of more than twenty years. Many poor people have AIDS but cannot afford the basic drugs to extend their lives.

No matter what our views on IP policies for AIDS, an avian flu scenario is unlikely to fit this general description. Avian flu probably will come and go relatively quickly, over a period of one to two years, with most of the casualties up front. Distribution and availability of drugs (or protective devices more generally) likely will be a greater problem than price *per se*. Even if Roche agreed to make and sell more Tamiflu at zero price, most people still would not get it in time. The first problem is building up a stockpile in the first place. The second problem is ensuring that stockpile is distributed effectively and in a timely manner.

A further complication results from the nation-specific nature of Tamiflu production (the same applies for many other pandemic-linked drugs as well). Right now Tamiflu is produced abroad. Yet it is unlikely that the drug will continue to be exported if a true

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although the net effect is difficult to estimate. See "Death by Accounting?" by John Berlan, *The Wall Street Journal*, Friday, October 21, 2005.

pandemic arrives or becomes much more likely. Perhaps the Swiss will nationalize the supply or otherwise give preference to Swiss nationals. We are not dealing with pure market incentives. In the event of a pandemic, some other government may confiscate the relevant property rights anyway.

The best policy on the IP front is probably the following. First, offer Roche the option of licensing production in the United States, but at generous prices relative to the status quo. The U.S. government should subsidize the license price if necessary. Offer Roche favorable regulatory treatment and facility clearances (help with zoning, regulations, etc.) as well. This gives Roche an incentive to spread production, but without confiscating the underlying property right. President Bush has pushed for domestic production of Tamiflu, but success on this front is as much as two years away or more. Roche already has shown a (partially coerced) willingness to license the drug, but to encourage future innovation we should ensure this is on favorable terms.

If a pandemic does arrive, the U.S. federal government should buy the relevant license at a high value. Part of the deal will oblige the pharmaceutical firm to produce the drug at high levels. Ex post, the government can then distribute the drug to local hospitals and medical centers without regard for price. At the same time, Roche and other companies will retain the incentive for producing future anti-pandemic drugs. This will ensure maximum possible distribution for the Tamiflu drug and related options, as well as helping prepare for other future medical needs.

This policy will likely prove expensive, but it is one of the very best investments we can make. Note that most of the expense (i.e., the drug purchases) come only if a pandemic arrives; that is precisely the case when the expense is most worth bearing.

One problem is estimating how much a government should pay for the rights to an effective pandemic drug. We cannot simply look to replicate "market value," even if we had clear information about such value. The would-be market price, of course, will depend on how much of the drug is produced. The government need not offer the returns from the highest-profit, strongest-monopoly outcome. Right now our government might announce some prices for buying the rights to the drug, with the price contingent on the severity of the pandemic. The price also might be contingent on the probabilities shown in prediction markets for a pandemic (more on this below). As a good rule of thumb, if those announcements cause Roche stock (and other pharmaceutical companies) to fall in value, we probably have picked numbers which are too low. We should then revise the offer upwards. Governments often have a difficult time making credible commitments, but announcing such a future policy is better than not trying to make a commitment at all.

Other countries, especially poor countries, will in any case start producing generic versions of Tamiflu on their own. Such actions will be especially widespread if a pandemic arrives. Whether these infringements are desirable or not, we should take them as given. No one will listen to foreign pressures in such a crisis. But note that this **strengthens** the case for respecting intellectual property rights in the United States. **Someone** must pay for Tamiflu (or related drugs and vaccines) rather than just copying it,

if we wish to ensure more drugs for the next generation. By buying drug rights, rather than confiscating them, the United States would be providing a significant public good for the rest of the world. This will sound unfair to U.S. citizens if explained in these terms, but pragmatically speaking it is in our national self-interest as well. It is a much worse world for us if other countries, in the future, end up devastated through pandemics. Either those pandemics will spread to us, or they will endanger global stability and prosperity.

Critics of the pharmaceutical companies raise many issues. They point out that much research is funded by the National Institutes of Health (NIH), or is done in universities. Roche did not invent Tamiflu, but rather bought the rights from a smaller company, Gilead. The major drug companies are portrayed as greedy, super-rich, and withholding vital medicines from a global public. Even if we accept this portrait without revision, such criticisms do not address the basic point. Moralizing aside, the future supply of anti-virals and other drugs still will depend on expected profits. Gilead invented Tamiflu in part because it thought it could sell the rights to a wealthier company, namely Roche. If we eliminate or reduce such profits, we can expect less innovation in the future.

6. Make economic preparations

It remains an open question how badly a pandemic would damage the global, U.S., and Southeast Asian economies. We do know that SARS, which killed only about 800 people, shut down a good deal of Asian trade, business travel, and tourism. It was a noticeable blip in the gdp statistics and psyche of the region.

Looking back to 1918 gives us only a partial idea of the economic consequences. After the deaths themselves, the most serious economic problems stemmed from the large number of people who did not show up for work. Some estimates suggest that during the peak of the pandemic up to one-third of the work force was absent. Some of these people were sick, and of course many others stayed home for fear of catching the virus. Today absenteeism would be compounded by the frequency of two-income family and the resulting child care needs if the schools close.

It is an open question whether today the economic consequences of a pandemic would be more or less severe today. On the pessimistic side, at least four factors can be cited. First, a pandemic can spread more quickly than before, due to the greater use of air travel. Our cities are larger than before and we do our shopping in larger crowds. These factors will limit our response time. Second, fewer Americans live near farms than ever before. If the pandemic runs on for a long period of time, this could create problems with food supply. Third, long distance trade and “just-in-time” inventory methods are more widely used than in the past. This makes the economy more dependent upon ongoing transportation. Yet the transportation sector would be hit hard. Fourth, individuals have a less fatalistic attitude about death today. In 1918 individuals did not expect government to protect them from premature death. Life expectancy was much lower, rates of infant and childhood mortality were much higher, welfare states were much smaller, and we had nothing like Medicare and Medicaid. As individuals started dying from a pandemic, the pressures on

the federal government were weak, at least relative to what we expect today. Panicked pressures to "do something, do anything" are not necessarily helpful.

On the optimistic side, it is easier to speak and trade at a distance than before. The telephone and the Internet limit the necessity for direct interpersonal contact. The modern world has more diverse channels of production and distribution than ever before; this increases our ability to respond to bottlenecks or supply problems. Our medical technologies and response capabilities are more advanced. In general we have a far wealthier and safer society.

In terms of economic preparations, we should do the following:

a) Consider possible weak points in our chains of food and water supply. What will happen, for instance, if mass transit shuts down or is avoided, and many food workers do not arrive at their jobs? We should look toward general robustness and redundancy in our systems, rather than believing we can micro-manage every problem into a solution in advance. Keeping some mass transit going, but at an acceptable level of safety, should be one priority. We should expect that supplies of fresh meat, fruit, and vegetables would disappear quickly or be hard to come by. Food durables, such as protein-rich canned goods, will increase in importance. Inventory facilities for such goods will be especially valuable. As we found during Hurricane Katrina, we should expect temporary local reversions to barter in some instances.

b) The Federal Reserve should stand prepared to supply the appropriate liquidity to the nation's financial markets. This will help prevent bankruptcy of financial institutions, especially given that default rates would likely rise significantly. The macroeconomic crisis is unlikely to be one of inadequate aggregate demand *per se*. The major problems will be workplace absenteeism and disruption of supply chains, not unemployment of the traditional sort. We should not expect monetary policy to much alleviate high rates of unemployment. The Fed should be geared toward preventing bank runs, bank closures, and a shutdown of the nation's check-clearing system.

c) Prepare emergency legislation for mortgages. Sickness and workplace absenteeism will likely lead to high rates of mortgage default. Such defaults should be treated more leniently than under current law, especially if a connection to the pandemic can be shown.

d) Prepare for bankruptcy of the airline industry. Air travel would most likely shut down altogether for a while. The federal government should draw up policies to ensure that it gets restarted as soon as possible, or to keep some essential flights going.

e) Draw up port plans so we can continue to receive shipments of oil and natural gas. Getting those shipments to refineries should be another priority. We should

expect many other segments of international trade to shut down. Personnel will be overstretched, immigration will be extremely restricted, credit quality will decline, and countries may impose trade barriers on each others' goods. Many of the countries we trade with, especially in population-dense Asia, will have more severe pandemic problems than would the United States.

f) Repeal price-gouging laws, or declare their inapplicability during a pandemic. Many states have price-gouging laws which apply during natural emergencies. For instance, during a black-out, it is often against the law to dramatically raise the price of flashlights. During a snowstorm it is often against the law to raise the price of snow shovels, and so on. Not surprisingly, the results are significant shortages. At the lower price, demand far outstrips supply.

A pandemic, through supply disruptions, would create many more instances of this kind. Many prices would be much higher than what we are accustomed to. This change will be especially pronounced for durable goods, canned goods, and anything which might protect against the flu, such as face masks and disposable gloves.

The resulting high prices will be unpopular but in most cases the high price is a better alternative than a shortage. Keep in mind that shortages do not in fact make prices low. The excess demands are absorbed through black market activity, or favoritism in the allocation of goods. Individuals will pay the higher prices one way or another. But allowing for higher nominal prices in legal markets gives us the best chance of making sure that essential supplies flow to their most highly valued uses.

We should not obsess over whether "the rich" or "the poor" are obtaining a greater share of treatment or prevention. When the disease is contagious, the priority is mobilizing care and prevention in the first place. A higher *ex ante* level of care and preparation, no matter what its initial distribution, will rebound to the benefit of many citizens.

g) Holding elections. It is unlikely that a national election could or would be held while a pandemic is raging. If a delay arises, the Supreme Court should consider an appropriate proclamation to ensure that national elections are held as soon as possible. In general incumbents should not be allowed to overstay their legal welcome. A "small numbers" election held through the Senate or other means would be preferable to no elections at all.

7. Who should be in charge?

The ultimate authority for an avian flu crisis should rest in the hands of the Federal government. Protection against a major pandemic is truly a national (and international) public good. It relates to providing for the "general welfare" of the citizenry, as specified in the United States Constitution.

Whatever its pluses and minuses, federal control in the nominal sense is inevitable. No governmental response to a pandemic will be found satisfactory by the general citizenry. There will be numerous deaths and significant disruptions of supply chains. Even if state or local governments had initial responsibility, outcries would quickly lead to the federal government moving in and asserting control. This switch in accountability and command would likely prove disruptive and hinder an effective response. So it is better to start with federal authority in the first place.[13]

That being said, federal authority should not mean literal federal control over most variables of importance. If a pandemic arrives, the federal government will not have the resources to enforce most, if any, of its emergency mandates. Federal authority should be used to ensure a high degree of local autonomy, as discussed above. While it is good for the federal government to take a leadership role, it should not give local authorities the impression that they will be taken care of, or that they need not develop their own plans.

Within the federal government, the chain of accountability should be as unitary as possible. Currently both the Department of Homeland Security (DHS) and HHS have competing claims to leadership in a pandemic. The Department of Agriculture (USDA) appears to have authority on the veterinary response. The Department of State takes the lead on international issues. Coordination will not occur easily in a pandemic, and we should impose a structure with fewer linkages and less distribution of authority at the federal level.

8. Encourage the formation of "prediction markets" in an avian flu pandemic

We do not have a good handle on the probability of an avian flu pandemic. This makes it difficult to know how much to invest, or where we should be investing our resources. Furthermore if a pandemic started, we are not assured prompt notice. Human cases, even fatalities, are now being evaluated with lags of up to two weeks. Scientists on the scene are often involved with politics, rivalries, and competing claims for credit. Information is not always shared on the spot and it is not a simple matter to judge when a pandemic has started. We should look toward prediction markets—sometimes called "idea futures"—to get a better sense of the chance of a pandemic.

Prediction markets are now used on a widespread basis to forecast political and sporting events. A specified contract will pay a dollar, or some other sum, if a specified event (e.g., an election result) comes to pass before a certain date. In the meantime those contracts trade at some price, which reflects the probability of the defined event. If the contract pays off a dollar if Hillary Clinton is the next President of the United States, and if the current value of the contract is now 0.23, we can estimate (roughly) that Hillary has a 0.23 chance of being the next President. To cite one such set of markets, www.tradesports.com allows individuals to "bet" on a wide range of global, sporting, and political outcomes. Since this electronic market is located in Ireland, it does not violate

[13] A related question is who should be in control in Europe. Here I would favor immediate national authority, in the belief that EU dictates will not be followed in any case.

U.S. anti-gambling laws, or fall under the regulatory jurisdiction of the Commodity Futures Trading Commission (CFTC).

Currently tradesports.com does have a market (started in October 2005) for the likelihood that avian flu—as it infects birds—arrives in the United States. This is a good start, but it would be more useful to have a market in the chance of a pandemic for human beings.

A wide range of evidence suggests that prediction markets are the best predictors available for a wide class of events.[14] If some better predictor were available, this predictor would itself be used by bettors. The information contained in those other predictors would then come to be reflected in market prices. The use of a prediction market requires only that we have some objective standard of settling "bets" after they are made. This should not be difficult in the case of a flu pandemic; for instance individuals could wager on whether a flu strain is cited by WHO as killing so many people, or whether it is designated by the CDC as a pandemic, and so on.

To many people it sounds ghoulish to wager on the deaths of other human beings. Yet a prediction market in avian flu could be a critical tool in assessing risk. If a pandemic does get underway, the first inklings of knowledge are likely to be decentralized. A prediction market would help ferret out this information; individuals who know what is going on have an incentive to trade. A prediction market also would make it harder for governments or multilateral institutions to cover up the truth. The involved individuals, or their acquaintances, could make bets on the Internet, even if their free speech rights are stifled or if official agencies are not fully forthcoming.

Given current law, it is easiest to run such markets in overseas venues. The United States government therefore has few policy instruments as its disposal. The CFTC could announce that American citizens betting in such markets would not be punished. The CFTC also could promise not to otherwise retaliate against any offshore exchange offering such contracts. The U.S. government might take the bolder step of announcing that such contracts would be welcome on overseas venues. In the longer run, we might deregulate securities markets so as to make such contracts easier to set up in the United States.

9. Improve international surveillance

The flow of information across borders is extremely important in identifying and then limiting a pandemic. If we know the exact nature of avian flu strains, it is much easier to design an effective vaccine. Information from Asia also can give us a better sense of how the virus transmits, what makes human-to-human transmission more or less likely, and how to best protect against the secondary consequences of infection.

International surveillance of avian flu is currently in a poor state. Many victims or possible victims do not have their flu strains sequenced and recorded. It is believed that

[14] See, for instance, Wolfers, J., & Zitzewitz, E. (2004). "Prediction Markets," *Journal of Economic Perspectives*, 18 (2), 107-126.

current Indonesian tests, as applied, yield many false negatives. Many Southeast Asian countries, including China, Vietnam, and Indonesia, are secretive about what goes on within their borders. Their governments wish to control the flow of information during a crisis. For instance it appears that Indonesia has been engaged in a bird flu cover-up for the last two years. Furthermore those governments are sensitive to having foreigners—even medical officials—"snooping around" their country and reporting to outsiders. To cite one example, autopsies on human victims of avian flu are not generally available. None of these features are conducive to the free flow of information and the exchange of scientific knowledge.

In an ideal world, all governments would encourage the free flow information and would be fully transparent in exposing what they know. This is unlikely, but in the meantime the question is what the United States could do to encourage greater transparency. We could encourage further WHO agreements to ensure information flows. This is better than nothing, but the likely benefits are slight. Many such international agreements are simply ignored, most of all in crises. More significantly, we should deliver credible diplomatic messages that the future distribution of aid—including pandemic aid—will be linked tightly to *ex ante* transparency on major health care issues, including an avian flu pandemic.

10. Reform the World Health Organization

The World Health Organization (WHO) has many excellent staff members, and its 112 national influenza center laboratories, in 83 countries, are invaluable. But the organization as a whole tends to be timid. In recent times it has warned about the dangers of avian flu, but earlier it had sought to calm fears. Too often WHO parroted the line of a Southeast Asian government that the problem either was being taken care of, or that the problem did not exist in the first place. Arguably WHO has as much incentive to suppress information as to spread information.

The fundamental problem springs from the nature of WHO and its budget. WHO is funded by its member states on a biennial basis. If it offends those member states—even a single member—it can lose resources and face a political fight. WHO thus takes care to see that its pronouncements are non-controversial and unlikely to offend; the resulting WHO is poorly suited to speak unpleasant truths. In recent times one WHO official suggested that a pandemic could kill up to 150 million individuals; the organization as a whole quickly had to backtrack and distance itself from that comment.

An effective WHO would be more independent. This could involve longer funding cycles and perhaps a partial endowment in the form of a fund. The watchdog segment of WHO should feel free to speak out and offend the sensibility of member countries, when required. WHO should, ideally, be more like an independent central bank and less like a directly accountable bureaucracy. National governments, of course, are reluctant to give up control over the WHO for precisely these reasons. Nonetheless we might all be safer with a less politically-oriented, less politically-hampered WHO.

Summary Remarks: The Illusion of Control

To some extent these recommendations go against the U.S. national character. They will not strike an intuitive chord of approval from all quarters.

America typically responds to challenges by refusing to admit it can fail. We have a "can-do" mentality. We built the first atomic bomb, we put a man on the moon, we revitalized the American economy in the 1980s and 1990s, and so on. This trait is highly admirable and it has been responsible for much of our national greatness. Nonetheless it may hinder our progress in fighting avian flu. We tend to seek out paths which offer some option, however unlikely, of apparent invulnerability. Our approach should be different. We should be admitting that at this point we cannot stop a terrible event but we can only make it somewhat less bad.

For an example of our national tendency, consider the response to Hurricane Katrina. It was immediately decided that we should rebuild New Orleans as much as possible. I am not questioning whether this is a wise decision; maybe yes, maybe no. The point is we made this decision for reasons of emotion and temperament, rather than analysis and reflection. We refused to admit that a major American city would be wiped out by a mere act of nature. So we engaged in a large macro response, designed to overturn or reverse the initial calamity altogether. This way we do not have to admit defeat, at least not yet. We seek to control problems when we cannot. All human beings have this tendency, but it is perhaps strongest in the United States, due to our long record of exceptional achievement.

Such a tendency could influence avian flu policy in damaging ways. For instance systematic stockpiles, centrally directed, and military-directed quarantines both give the impression that we can control the course of the pandemic. We would be making a highly symbolic and visual stand of "We won't just let this happen." Nonetheless these are not the most effective measures. Preparing emergency rooms or instructing people to wash their hands is, in effect, admitting that the disease would spread and kill people. It is a partial admission of "defeat." Yet we might need some national modesty to address the problem in a relatively effective manner.

With those words in mind, let us now consider what we should not do.

Part II: What We Should Not Do

Most of the advice on what not to do follows from the analysis and recommendations above. Most directly, we should not assume that mere scientific advances, or centralized stockpiles, suffice to protect us from a pandemic. We should be suspicious of command and control approaches, and for the most part violating our civil liberties will not prove effective in saving human lives.

Let us consider a few concrete issues:

1. Do not expect vaccines to solve the problem

Contrary to some press reports, we do not (yet?) have effective vaccines for fighting avian flu. Many such vaccines are being tested around the world as you read this. As of October 2005, the Bush Administration is talking about having vaccines ready within six months. Any assessment of particular vaccine claims will be rapidly out of date, so consider these general principles:

a) No vaccine can ensure protection against the particular flu strain which ends up causing the pandemic. And by the time a pandemic comes, it takes a good deal of time to produce enough doses to protect against that strain. It could take over six months to have any doses at all, and it would take much longer to produce and distribute millions of doses. Growing viruses in chicken eggs is a key element of many vaccines. It is extremely difficult to speed up this process on a large scale, no matter how dire the emergency.

Because H5N1 is new to our immune system, citizens might require two vaccinations a few weeks apart; in principle the use of booster adjuvants might eliminate the need for a second shot, but we cannot count on this. Under most plausible vaccines, even if the vaccine were immediately available in large numbers of doses, people will not develop immunity to avian flu until seven or eight months after the first dose.[15]

b) Even if we had enough vaccine, adequate and timely distribution would remain an extremely difficult issue. Unless we address this issue in advance, we will waste much of our vaccine capacity. Here it is worth repeating some more general recommendations made above: we should use decentralized channels of distribution, relax liability law when necessary, and give priority to the young and healthy.

c) Most of the world's vaccine capacity is in Europe, not the United States. Some estimates place European capacity at seventy percent of the total. Only two plants are up and running in the United States. The next new facility is likely to come on line in 2009, four years from now.[16] In the event of a pandemic, European nations will not allow this capacity to be exported, at least not until their domestic populations are covered.

d) Vaccines expire within a few years' time. We might stockpile an effective vaccine for an avian flu pandemic. But if that pandemic came five years later,

[15] See "Bird flu: Kick-start vaccination or Face the Consequences," at http://www.newscientist.com/article.ns?id=mg18825215.900.

[16] See "Bird flu: Kick-start vaccination or Face the Consequences," at http://www.newscientist.com/article.ns?id=mg18825215.900, and also W. Waut Gibbs and Christine Soares, "Preparing for a Pandemic," *Scientific American*, November 2005, pp.45-54, see p.48.

rather than in two years, we would be left with little protection. At some point we will lose the political will to continue replenishing the stockpiles.

e) Without addressing the vaccine problem more generally, gearing up vaccine production for avian flu would involve high secondary costs. First, testing standards would be much lower. Second, vaccines commonly kill some of their recipients, and a design mistake could lead to many deaths. Third, we would have to forego producing normal flu season vaccines.

As discussed above, the United States should take significant steps to improve its vaccine capabilities. But we should not be overjoyed at media reports of successful vaccines. The world could have, on the scientific level, a good vaccine but still lose millions of lives from a pandemic.

2. Do not rely on quarantines or mass isolations

Smaller and relatively isolated countries, such as New Zealand, are considering quarantines in the case of a pandemic. This would involve closing their airports, preventing visitors from entering the country (or subjecting them to delay), and possibly restricting movement within the country. Such a plan stands some chance of working. Even if it only delays a wider onset of avian flu, it may save lives by increasing the time to implement a response plan. American Samoa successfully applied quarantines during the 1918 pandemic and never encountered Spanish flu deaths during this time.

Nonetheless quarantine is unlikely to be effective in the United States. We have three hundred million people, porous borders, areas of great population density, and many more transportation nodes connecting a given area. In the American Northeast, for instance, how would the quarantine proceed? Given the density of population, and our inability to measure and identify all flu cases, how would we draw the lines between a "safe side" and an "unsafe side"? Furthermore the quarantine, even if it could be enforced, would exacerbate food supply problems; keep in mind how much of the nation's food supply is trucked across many states, often from California, the Midwest, or Florida.

Quarantines involve many other problems. Few people live close to their food supplies and we are highly dependent on transportation. Most importantly, the avian flu virus is self-reproducing. Only a very small amount of the virus has to "get through" a quarantine to spread to a new area. Only one infecting carrier is needed. More likely than not, the individuals traveling to enforce the quarantine will themselves be spreaders. The very act of enforcing the quarantine will be self-defeating and might make the problem worse.

An alternative vision of quarantine—properly called isolation—would round up sick individuals and remove them from broader society. To be sure, we should isolate individual flu patients in hospitals and homes as much as we can. But we would be unwise to pursue broader isolation policies of putting individuals into large groups of the infected.

It is difficult to decide which individuals should be handled in this fashion; exactly how sick does a person need to be? Would we round up individuals who had non-avian flus or simply the symptoms of a common cold? We would have to test individuals at hospitals for avian flu. Even if we had such capacity, most likely these plans would discourage many individuals from seeking the proper medical care, for fear they will be isolated and taken away. Furthermore testing and transporting the individuals might spread infection more than simply leaving them at home.

Grouping sick individuals together could lead to more infection. Keep in mind that the 1918 pandemic had mortality rates of about two percent; we should not think of isolation as rounding up doomed individuals, all about to meet their death. Avian flu may well come in different strains, thereby enabling cross-infections. Grouping the individuals also will facilitate more gene shuffling and exchange and perhaps lead to new and deadlier flu strains. A large collection of sick individuals could itself alter the evolution of the virus and encourage a more virulent strain. Amongst healthy individuals, the flu virus cannot incapacitate its victims so thoroughly that no spreading is possible; such strains quickly become extinct. But when so many sick individuals are put in close proximity, this constraint is relaxed and more virulent strains may evolve. The isolation may prove self-defeating by making the virus worse.

Civil liberties issues arise as well. How should the authorities treat the many individuals who resist evacuation from their homes? Should we physically drag these individuals out, or perhaps threaten them with a later jail sentence? Would the patients threaten to cough or sneeze on law enforcement authorities in response? How hard would the local authorities try to track down such patients? Most likely we would be setting the stage for frequent and unpleasant confrontations, or the law would end up not being enforced at all.

Finally, isolation is unlikely to stop the spread of the virus. We simply do not have the infrastructure to find, identify, isolate and transport any significant percentage of the flu spreaders. Most of the victims we would identify would be found too late, after they had spread it to many others. Note also that many flu carriers can have sub-clinical infections and serve as spreaders, without ever looking or feeling sick.

Quarantines and isolations also tend to induce panic. When individuals hear that an area will be quarantined, many leave that area preemptively, whether such behavior is rational or not. Rumors of quarantine in Beijing, during the SARS epidemic, led 250,000 individuals to leave the city overnight. These adjustments only spread the disease further. Furthermore the people who leave may be less likely to report to the proper medical authorities, for fear of the legal consequences.

SARS is sometimes cited as an example of successful quarantine or isolation policy. But thirty different nations confronted the SARS epidemic. Some tried quarantine and others did not. SARS went away in each case. It appears that the properties of SARS itself—in particular its ability to immediately knock out its sufferers—is what prevented further spread of the disease. Furthermore SARS spreads less easily than most strains of flu; it

takes a SARS patient up to ten days to transmit the disease.[17] Many flu patients spread the virus before they know they are sick or, as noted above, never develop symptoms at all.

In some cases quarantine can serve a useful function of delay. In extreme cases it can stop the spread of a disease altogether. But in the modern United States, quarantine is probably counterproductive. At the very least, an avian flu response plan which relies on quarantine is a bad plan.

3. Do not rely too much on the Army or Armed Forces

In October President Bush cited the possible need to call in the Army to deal with avian flu and its repercussions. He also mentioned the possibility of bringing the National Guard under federal rather than state control. Such policies might constitute a revision of the "posse comitatus" act (1878), which limits the use of U.S. Armed Forces for domestic law enforcement purposes.[18]

I will not offer a systematic across the board assessment of whether such a legal revision would be a good idea. Many civil libertarians are skeptical of such changes and I share their concerns. But focusing only on avian flu, such a policy is unlikely to prove effective. The U. S. Armed Forces have little or no training in combating a pandemic. Their roles in enforcing a quarantine or isolation would be ill-advised, for reasons discussed above. One possible role for the armed forces might be to distribute Tamiflu from central stockpiles. But as discussed above, it would be better to store and allocate the Tamiflu from decentralized locations, such as hospitals and medical centers, in the first place.

4. Do not equate a Tamiflu stockpile with safety

Tamiflu can protect against avian flu (and many other flus) in most cases if a course of treatment is applied promptly and correctly. To date (November 2005) the U.S. government has acquired 4.3 million courses of Tamiflu; the plan is to have a national stockpile of 133 million courses available.

A stockpile of Tamiflu is a worthwhile investment. Nonetheless we should not equate such a stockpile—even if very large—with avian flu protection. Relying too heavily on a Tamiflu stockpile involves the following problems:

> a) The drug cannot be taken preventively with ease. A course for treatment of flu involves two tablets a day for five days. Ongoing tablets would provide advance protection, but there are not nearly enough tablets to go around. Medical health professionals could take the drug preemptively, but most individuals will not have

[17] W. Waut Gibbs and Christine Soares, "Preparing for a Pandemic," *Scientific American*, November 2005, pp.45-54, see p.50.

[18] It can be debated how much pandemic activity would count as "law enforcement." Some activities, such as delivering drugs and vaccines, would appear not to count.

this option. Keep in mind that a current course costs about $100. Significant increases in production will not, even in the medium-run, significantly alter these facts. There are simply not enough courses to go around for extensive preemptive use.

b) Preemption aside, Tamiflu is effective only if taken during the first two days after avian flu symptoms appear. We can expect that large numbers of people, with or without the flu, will be showing up at emergency rooms demanding Tamiflu treatments. Many people who have hoarded Tamiflu will exhaust their supplies fighting off the common cold and other false alarms. Many Tamiflu doses will be expended on inessential cases.

c) It is unclear whether medical institutions will be able to handle the flow of Tamiflu demand, given the necessity of rendering rapid evaluation and treatment. Even in a high-quality emergency room, under normal conditions, processing a patient can take many hours. In the case of a pandemic, hospitals will be overloaded and some professionals or support staff may refuse to show up for work, fearing contamination. A further delay may arise from judging where a patient fits on the priority list for Tamiflu or related medicines.

d) The allocation of Tamiflu will be a political football. We can expect political pressures, lawsuits, and interventions. This may hinder effective use of a Tamiflu stockpile, especially if that stockpile is held and controlled centrally. Let us say the pandemic came first to California. Would supplies in Kansas be shipped out west? Would they ever come back? In any case we can expect time-consuming fights.

e) Tamiflu does not remain potent forever. Most Tamiflu samples have expiration dates, typically within a few years time. The drug can still work after these dates but it does not last forever. So at some point in the relatively near future, a Tamiflu stockpile will lose its value. It is probably politically infeasible to expect this stockpile to be replenished repeatedly, at least if a pandemic does not come along soon. The stockpile would come to be seen as a boondoggle of sorts, and over time it would fall into disrepair or experience other maintenance problems. Yes, we should buy and stockpile Tamiflu, but the drug will not necessarily protect us in a longer run or against a more diverse series of risks.

5. Do not rely on blanket targeting in countries of origin

Several analysts have suggested that we can attack human-to-human avian flu by an intense targeting of the area of origin. A number of simulations suggest that such a sufficiently aggressive program, if applied within the first few weeks, could stop avian flu from spreading.

Sadly, such a program is unlikely to succeed in stopping a pandemic. The simulation models rest upon unrealistic assumptions. Most of all, they underestimate the difficulties of formulating and implementing policy in poor countries with weak institutions.

The most likely countries for an initial outbreak are Vietnam, Thailand, Indonesia, Cambodia, and China. These countries are allergic to scrutiny from the outside world. They also are jealous of their sovereignty and suspicious of interference by outsiders. China, for instance, took months to admit the existence of SARS, and later played a "shell game" with SARS patients, hiding them from WHO. It is also speculated that there may be H5N1 avian flu in Burma, one of the most secretive and xenophobic countries in the world. Migratory birds also may be bringing avian flu strains to East Africa, which includes some of the worst governed countries in the world.[19]

An attempt to wipe out human-to-human avian flu at the source likely would encounter denial or stonewalling from local officials, lack of transparency with flu samples, and corruption and hold up of Tamiflu (and other) supplies. Note that most of these same countries have yet to allow autopsies of human avian flu victims, even though this would aid in understanding the disease. Currently it is taking up to twenty days to confirm human avian flu cases, yet the entire targeting program has a time window of no more than a month.[20] Furthermore local farmers would resist the requisite killing of chickens, which are an important food source and a means of saving wealth in poor communities. In Indonesia, 30 million families keep 200 million chickens in their front or backyards.[21] We could not expect the necessary widespread culling to take place in a few weeks' time if ever. Would local citizens, many of whom trust in folk medicines, follow the precise instructions for taking Tamiflu or accepting a vaccine? Most generally, local institutions, whether legal or of civil society, are weak in these countries.

The implementation of such a plan would likely involve WHO and the United Nations. Both of these institutions, which are supposed to operate on a consensus basis, can be slow and bureaucratic. It could take weeks just to get the necessary approval for action at the multilateral level, much less to mobilize a plan.

Tamiflu targeting in poor countries of origin should be evaluated in humanitarian terms. Many of these countries have very little Tamiflu, or they have no effective means of distributing medical aid. But in making the calculation, we need to consider that sub-optimal dosing may simply encourage a more rapid onset of immunity to the drug. We might be making the ultimate pandemic better rather than worse. It is hard to imagine the UN withholding anti-viral drugs from poor countries, but a purely utilitarian analysis could possibly suggest this conclusion. In any case coordinated intervention is unlikely to

[19] On the SARS episode, see *Microbe: Are We Ready for the Next Plague?*, by Alan P. Zelicoff and Michael Bellomo, New York: American Management Association, 2005, chapter two.
[20] W. Waut Gibbs and Christine Soares, "Preparing for a Pandemic," *Scientific American*, November 2005, pp.45-54.
[21] See "Don't Fear or Panic: An Economist's View of Pandemic Flu," Dr. Sherry Cooper, Nesbitt Burns, p.6.

halt the spread of a pandemic. We should not treat it as a substitute for good domestic preparation, most of all at local and decentralized levels.

Summary remarks

This study does not address the core question of how much should be spent to prepare for an avian flu pandemic. Instead the focus is on how to spend a specified allocation, no matter how large or small that allocation may be. Our recipe is simple: for any given sum, spend more on local health infrastructure, emergency rooms, and general disaster preparation. Spend less on centralized command-and-control approaches, including quarantine, isolation, and use of the military. Stockpiling vaccines and drugs has a real rationale, but make sure some of the money goes toward a good distribution plan. In addition to being prudent, these recommendations point to relative cost-effective means of protecting against avian flu. Such recommendations should be welcome in an age of fiscal constraint.

While this study has focused on avian flu, we should not lose sight of the broader issues. The question is not just how to fight a pandemic in the near future, but also how to prepare for pandemics more generally. Just as SARS and AIDS were unexpected when they arrived, so might the next pandemic be a complete surprise. We should not fixate on protecting against avian flu at the expense of alternative possible pandemics. It is also widely recognized that bioterror will only become easier as the years pass.

No one knows the current probability of an avian flu pandemic. No one knows the likelihood of easy human-to-human transmission. No one knows how severe such a pandemic might be. We only know that the danger is especially high and the risk especially severe at the current moment. But we must live with these risks for a long time, not just for the next few years. Even if an avian flu pandemic does not arrive soon, the world still has a long-term "reservoir" of the virus in bird communities.

We must resist the tendency to "cry wolf" and focus on only a single warning for a single disease. The true dangers are diverse. If the case for fighting avian flu is made in the wrong way, it will be that much harder to convince politicians to take action the next time around. The "swine flu" debacle of the mid-1970s still remains an obstacle for mobilizing support to combat an avian flu pandemic. Unfortunately, we need plans not just for the here and now but also for a longer-term series of risks. We should not "spend all our political chips" preparing for a single catastrophe at a single point in time. That is yet another reason why these recommendations have focused on effective health care institutions at the micro-level. Following such advice will protect us against many different kinds of future catastrophic events.