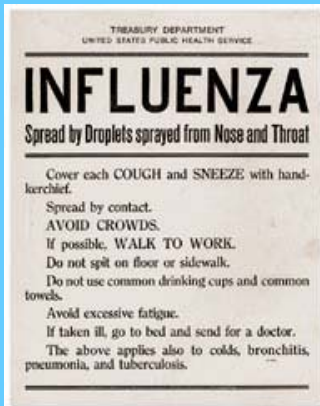
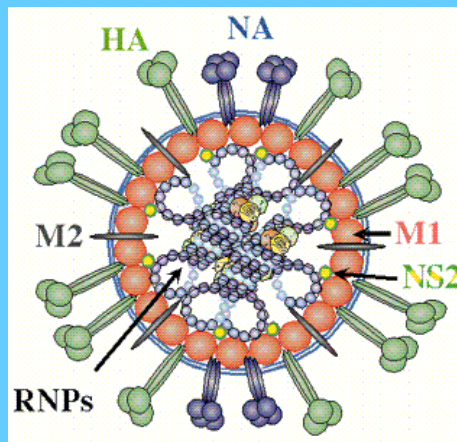


# Consumer Medication Stockpiles for Pandemic Influenza



A Foolish Idea or a Prudent Preparation for the Coming Influenza Pandemic?

By Grattan Woodson, MD, FACP  
Author of *The Bird Flu Preparedness Planner*  
and *The Bird Flu Manual*

This booklet contains series of recently updated essays written in 2005 and 2006 that have a bearing on whether or not physicians should support their patient's request to obtain a supply of drugs for use during an influenza pandemic. Some of this material was excerpted from *The Bird Flu Manual* published in September 2006.

This is a controversial issue and has been opposed by many in public health, ethics, and infectious disease. I have a different view and hope that physicians will find the time in their busy day to consider it.

To some extent, the material presented is redundant, a circumstance brought about because each essay was written as a stand-alone document. Since repetition is an important learning tool maybe this will feature of the booklet will not be as great disadvantage to the reader. This booklet and the essays are available as individual downloads from the [www.BirdFluManual.com](http://www.BirdFluManual.com) website on the Resources section in the Home Influenza Treatment folder.



Grattan Woodson, MD, FACP  
November 19, 2006

Copyright 2006 Grattan Woodson

This material may be freely copied and shared for educational use only.

The images and illustrations in the booklet are not the property of the author and not covered by the copyright. They are including in this booklet for educational purposes only.



# Druid Oaks Health Center

**2801 North Decatur Road, Suite 375 Decatur, Georgia, 30033**

**Grattan Woodson, MD, FACP**

November 19, 2006

Dear Colleague,

The last thing any of us needs is to be given something else to read by a well-meaning patient but this is an unusual circumstance for which I beg your pardon and forbearance. Among virologists and flu experts there is no debate; another influenza pandemic will occur. What is unknown is which avian flu strain will cause it, when it will occur and how bad it will be.<sup>1</sup> I think there are good reasons to think H5N1 “bird fu” will become pandemic and within a year or two. Its adaptation to humankind and the genetic material H5N1 is accumulating suggests that once pandemic, bird flu is likely to resemble the 1918 Spanish Flu in terms of its severity.<sup>2</sup>

It was enlightening to read what the US Department of Health and Human Services predicts will happen during the next pandemic.<sup>3</sup> They estimate the pandemic will last between 12 to 18-months and during that time 1 in 3 Americans will develop acute influenza. Half will have a mild to moderate case that they will manage on their own at home. The other half will have moderate to severe illness necessitating several office or ER visits. Of this group, 20% will be critically ill requiring hospitalization. The case fatality rate is projected at 2%. The numbers of excess ill patients this represents is rather astounding:

- 100 million people develop acute influenza

- 50 million patients self-treat at home
- 50 million patients will require 2 or 3 outpatient physician visits
- 10 million critically ill patients will require hospitalization
- 2 million influenza patients will die

The average US hospital today is running at 75% occupancy and most doctors I know are pretty busy too. We could always see a few more patients each day but not nearly enough to accommodate an increase in case burden of this magnitude since it would fall mainly upon the 40% of US doctors in primary care<sup>4</sup>. The limited hospital and office practice surge capacity available is likely to result in delayed treatment for many seriously ill patients. It is easy to predict that under these circumstances, health outcomes will not be optimum. An alternative approach I chose to use with my patients is to help them prepare for the pandemic by giving them information on home treatment of influenza and prescribing a select set of drugs useful for flu treatment, including the antiviral Tamiflu, to have on hand at home for use during the pandemic.

While not an ideal solution for use in every patient, it has the potential to provide responsible patients willing to learn how to properly use these drugs for treatment of flu an added measure of security. In many respects, this practice is similar to giving a patient traveling to Mexico a course of ciprofloxacin and promethazine to have on hand should they come down with traveler's diarrhea. Admittedly, there is controversy surrounding consumer drug stockpiles for the pandemic and there are valid arguments both pro and con. Weighing these carefully, it appears to me that the benefits of helping patients stockpile out weighs the risks or disadvantages. There were two factors that above all others that persuaded me to follow this course.

First, our offices and ERs will be overwhelmed with very sick patients. At times, we could even be trying to manage critically ill patients in an exam room or in their home because there are no available hospital beds. Even if we cancelled all routine follow-up visits, extended our hours,

and just treated flu patients all day long, it is unlikely that we could see all the extremely sick folks needing an appointment. To be clinically effective, Tamiflu must be started within 48 hours of the onset of flu symptoms.<sup>5</sup> Under these circumstances, how many of your patients with severe influenza do you think will be able to begin Tamiflu within its therapeutic window? The only way I see to finesse this problem is to have the patient obtain a supply of Tamiflu now for future use during the pandemic.

The second point has to do with the inevitable drug supply shortages that will occur during the pandemic. Even if your patient could get a timely office appointment and a Tamiflu prescription from you, what are his or her chances of getting it filled? The demand for OTC and prescription cough syrup, antihistamines, analgesics, antiemetics, and especially the antivirals will be so high; wholesalers will be required to ration supplies. It may be several days before a patient given prescriptions for any of these drugs but most particularly Tamiflu could get them filled. The conditions likely to be present during the pandemic make it unlikely that our patients will be able to benefit from Tamiflu if we wait to prescribe it to them then. Unfortunately, many of our colleagues are telling patients just this. They will not prescribe Tamiflu until the patient has acute influenza. Under normal circumstances, a policy like this makes sense but not under pandemic conditions.

While treatment of influenza mainly involves keeping the patient well hydrated until they are able to clear the infection, from experience most physicians agree that treatment of flu symptoms with a select few OTC and prescription drugs can certainly make a rocky road a lot smoother. This is why I am giving my patients prescriptions for cough syrup, analgesics, and anti-emetics. Because secondary bacterial infections commonly complicate flu, I am also including an antibiotic providing good coverage for the agents causing community acquired pneumonia for patients to add to their emergency stockpile.<sup>6</sup> One additional measure I've added is vaccinating all patients over age 2 with Pneumovax®. This is an effective measure against pneumococcal

associated diseases that are common post-influenza and increasingly resistant to antibiotics.

These days only a small number of patients are aware of pandemic influenza and even fewer are concerned enough to consider stockpiling. Those that are have impressed me by their understanding of influenza virology, epidemiology, and treatment. These are serious people who have studied the issues and plan to use the drugs carefully and appropriately.

For a more thorough discussion of this issue including the opinions of those opposing consumer stockpiling, visit the [www.BirdFluManual.com](http://www.BirdFluManual.com) website Resource section in the Medical Reference folder.<sup>7,8</sup> Thank you for giving this issue your attention. I welcome your comments, criticisms, and suggestions on this topic and on pandemic influenza. You can reach me by leaving a message in the Feedback section of the BirdFluManual.com website.

Sincerely,

A handwritten signature in black ink that reads "Grattan Woodson". The signature is written in a cursive, slightly slanted style.

Grattan Woodson, MD, FACP

## Table of Contents

Chapter 1: Enlisting Your Doctor's Help.....	9
These days being a doctor is not much fun.....	9
Put yourself in your doctor's shoes.....	10
An uphill battle.....	11
Don't be pushy.....	11
Be polite and respectful.....	11
Easy does it.....	11
Provide them with information but not too much.....	12
The bird flu is not going away so be persistent.....	12
Doctor's have their patient's best interests at heart.....	13
Canadian Internet Pharmacies.....	13
Chapter 2: Consumer Drug Stockpiling Pros and Cons.....	14
The unintended consequences of the present policy.....	20
Chapter 3: Stocking Up on Regular Medications.....	22
Stockpile rotation, expiration dates, and storage.....	22
Critical medications.....	23
Contraception critical for women of childbearing age.....	23
Patients with special medical problems.....	24
Non-critical medications.....	24
Rely on your doctor's advice and guidance.....	24
Chapter 4: Supporting Consumer Drug Stockpiling.....	26
What patients need and why.....	26
Stockpiling a 6-month supply of regular medications.....	26
Stockpiling drugs for treatment of pandemic influenza.....	27
Pandemic threats to the pharmaceutical supply.....	28
Risky business: Our dependence on disposable medical supplies.....	29
Medical first responder and healthcare worker absenteeism.....	30
First responders.....	30
Healthcare workers.....	31
The sacrifice of those who serve.....	32
Chapter 5: Obstetric care during the pandemic.....	34
So shall ye sow, so shall ye reap.....	35
Chapter 6: Tamiflu Treatment and Resistance.....	36

Questions about the current Tamiflu regimen .....	37
Probenecid, a Tamiflu dose multiplier .....	39
Chapter 7: Support for a Personal Tamiflu Stockpile .....	41
The Tamiflu shortage .....	41
The lack of a pandemic flu vaccine.....	44
Would personal stockpiles Tamiflu be properly used? .....	44
Bird flu resistance to Tamiflu.....	46
Chapter 8: Flu Treatment Kit Substitutes and Alternatives.....	49
The value of using drugs properly .....	50
Index FTK OTC Drug.....	51
References .....	53

# Chapter 1: Enlisting Your Doctor's Help

This essay is written to provide consumers with some ideas how to successfully enlist their doctors to secure a medication stockpile for use during the pandemic. Drugs that need to be stockpiled include those taken regularly for chronic medical disorders and those for treatment pandemic influenza.

## **These days being a doctor is not much fun**



Being a doctor today is hard, especially for Pediatricians, Family Practitioners and Internists, the disciplines that provide the bulk of primary care in the US. The demands placed upon them are rising while their pay is falling. Many are burned out, frustrated, and depressed. Not a few are leaving practice early due to stress and fewer of the best and brightest students graduating from college today choose a career in medicine. There are many reasons for why medical practice has changed so much in the past decade but they are not the subjects of this article. I mention them only to provide you with some insight into why the experience many patients have today with their doctors are not as satisfying as it was in the past.

Frankly, doctors are not in the mood to deal with the pandemic issue. At work they pressed for time. Patients today are very demanding and have access to considerably more information than ever before. Doctors are bombarded with patient requests for drugs seen advertised on TV or in magazines. Patients seeking to use an unproven alternative herbal or “natural” treatment for their serious medical disorders instead of the proven conventional drug treatment is a recurring headache. As they say, a little knowledge can be dangerous, especially when it comes to the

practice of medicine. These encounters have made doctors skeptical of anything brought to them by the patient.

The fact is most doctors simply don't appreciate the gravity of the risk we face from pandemic influenza. Almost all the doctors who practiced during the last important pandemic in 1957 have retired or are dead. The only people alive today who survived the 1918 pandemic were children at the time and not many of them recall much about the event. In medical school, little is taught about pandemics although there is a good bit of time given to seasonal flu and the value of annual flu vaccination.

Those of you who have really studied this issue probably know more about influenza history, virology and genetics than the average primary care doctor. While the seasoned doctor realizes that virtually everything they know about the practice of medicine is learned from the care of patients, few of us think that our patients are a reliable source of medical education. These factors are some of the reasons most patients have been frustrated in their efforts to obtain their doctor's help to prepare for the pandemic.

## **Put yourself in your doctor's shoes**

Having set the stage as above, imagine you are the doctor and know virtually nothing about the coming pandemic. You walk in the exam room to see a patient and to your surprise discover the reason for the visit is to secure a handful of prescription drugs for treatment of bird flu in the event it becomes pandemic. You think to yourself where did my patient get this crazy idea?

The logical thing for most to do is refuse to help you without further discussion. Some doctors may refuse based upon an editorial or position paper they scanned in the medical journals opposing personal stockpiling. Maybe they just don't want to write 6 prescriptions because of the time it takes to do it. They might object because it was not their idea to use these drugs for flu and they don't want to take the

responsibility for your misusing them. Maybe they think you are unnecessarily worried about bird flu and have been misled into seeking these drugs that you will never need. As you can see, helping your doctor to see the issue as we do is not going to be an easy task.

### **An uphill battle**

By understanding your doctor's frame of mind and the conditions he or she is working in today is an important first step in obtaining your goal. From this prospective, you will be better equipped to plan an effective strategy. It should be obvious from the foregoing that a direct frontal approach is not likely to succeed. Nor are you likely to have your request fulfilled quickly if your doctor is predisposed against stockpiling. It is going to take time, patience, and persistence to educate the doctor. Here's how.

### **Don't be pushy**

If you argue with the doctor about this you are sure to lose. Not because you are wrong but because most doctors are not able to admit that you could be right and them wrong about something medical. Their egos just will not permit it. So, don't go there.

### **Be polite and respectful**

Behaving in any other way will get you nowhere. It will also prevent the doctor from being able to give you a fair hearing when you are speaking to him or her about this issue.

### **Easy does it**

Go slow. Doctors are only able to absorb one or two pertinent facts at each encounter. Don't place the whole opus before them at once and expect he or she to get it. You won't get very far along in the 5 minutes they give you these drugs anyway for an office visit. Write down your arguments for why helping you establish a stockpile is reasonable. Boil it down to the core elements of the argument. When given the opportunity to speak make no more than one or two of these key points at any one encounter with the doctor.

## **Provide them with information but not too much**



Most doctors have stopped educating themselves because today's work stress and frustration leave them too tired to do much at the end of the day. Patients often give us things they cut out from the newspaper or downloaded from the Internet touting this or that idea or alternative treatment. The common response is to accept the proffered material and as soon as we can after leaving the exam room deposit it into the nearest waste can. Doctor's think, "Hell, I don't have time to read this 3 foot high pile of medical journals that have really important new information that could help me practice medicine better. Where would I ever find the time to read some off the wall BS about pandemic flu given to me by a patient?" Please don't take offense; my purpose is not to insult you but to give you an inside look at the typical doctor's frame of mind these days.

The point I am trying to make is to give the doctor no more than one thing to read at a time. The chances or them of reading them are low but some might. My essays have hooks designed to get their attention. Most won't even take a look at it. So, don't be surprised if your doctor doesn't.

## **The bird flu is not going away so be persistent**

Unfortunately, this story is not going away. If it does, that would be great but it is probably not going to. As the virus adapts to humankind the number of cases, deaths, and the geographic reach will all increase. During the ante-pandemic phases (4 and 5) this increase will be linear but still pretty impressive. At some point it will be obvious to doctors that the virus is not going away and its activity is increasing. There will be more articles in the medical and lay press that support the case that a pandemic is coming. There will be counter arguments too. What will be undeniable though is the growing number of cases and increased pace of

the human infections compared with the past. Seeing this is the time when many doctors are going to begin to see the risk more clearly. It will be an opportune time to ask for their help with your stockpile.

## **Doctor's have their patient's best interests at heart**

It is OK to bend the rule when it comes to a life and death issues.

Chances are there will be some doctors who will never come around. Unusual measures might be needed. If you have a chance to travel overseas to a country that allows people to buy the drugs you need without a prescription, go for it. You might have a friend that lives in one of these countries or who is planning to visit one. Ask them to help you out by buying the drugs there and mailing them to you. Some people have had success buying these drugs over the Internet from an offshore pharmacy without a prescription. This is a risky proposition and not one I prefer.

## **Canadian Internet Pharmacies**

I have purchased drugs from Canadian Internet Pharmacies and they have always required a prescription and even called the doctor's office to verify that they really wrote it. The drugs provided were manufactured in a variety of countries outside the US. They were just as good as the drugs purchased in my local US drug store. Obtaining drugs from pharmacies that don't require a physician prescription is risky. These Internet providers are those that sell counterfeit drugs.

The very best option is to enlist your doctor's assistance. This means being patient and persistent. Keep your cool. The advice provided here is crafted to help you understand your doctor better. Doing so improves but does not guarantee your quest will succeed. Don't give up on your doctor. He or she remains your best bet for obtaining a prescription for the drugs you and your family needs to survive the pandemic.

# Chapter 2: Consumer Drug Stockpiling

## Pros and Cons

Some in the medical, public health, and ethics communities have vigorously opposed the desire by consumers to stockpile prescription pharmaceuticals for future use during the next pandemic. Editorials and position statements in opposition to stockpiling have appeared in leading peer reviewed medical journals.<sup>9, 10, 11, 12</sup> These objections have been widely publicized in the lay press. It is important for individuals desiring to stockpile and their doctors who must decide whether to help them, understand the reasons behind this opposition.

The arguments put forth all have merit and usually have to do with one of several concerns.

- The concern that consumers would use the stockpiled drugs improperly or inappropriately in a fashion that might be wasteful, dangerous, or in the case of antimicrobials increase resistance to the drug
- The concern that widespread stockpiling could result in shortages of drugs for treatment of patients needing them today
- The concern that it is unfair for the affluent to gain access to these drugs ahead of those unable to buy them
- The concern that stockpiling would cost too much
- The concern voiced by the public health community that consumer stockpiling could interfere with their ability to influence who is given priority for antiviral therapy

These concerns have solid foundations and at first blush make sense. A lot of people support them including physicians in private practice who control the prescription pad. While these doctors are the ones who actually have to carry out the policy, most of those making them are not physicians and only a few who are have any direct patient contact.

As a physician in private practice, I can see both sides of this issue but am alarmed by an overlooked but critical flaw in the assumptions underlying these concerns. The arguments err not from a substantive or ethical standpoint. On the contrary, they are all well founded medically and ethically. The problem relates to the fact that their views are valid only if the medical, economic, and government infrastructure remain functional during the pandemic. This is likely to be the case if the pandemic is mild or moderate in severity. Under the conditions of a severe influenza pandemic, there is great risk that this infrastructure may buckle temporarily. If that happens, access to drugs of all types and advanced medical care could become extremely limited.

In the sections below, I provide a detailed analysis of the current concerns over consumer stockpiling and explain how the well intended policies designed to undermine this practice might well result in catastrophic unintended health consequences for patients.

**D) Consumers would use the stockpiled drugs improperly or inappropriately in a fashion that might be wasteful, dangerous, or in the case of antimicrobials increase resistance to the drug.**

The consumers I have encountered desiring to obtain a stockpile of drugs for use during the pandemic are on the whole, serious and responsible people who have looked carefully at the issue. Many have learned how to use these drugs properly and appropriately and if not are willing to learn. It is anachronistic to maintain that people wishing to stockpile prescription drugs for the pandemic would behave irresponsibly. Our patients are better educated and informed today than ever before. Viewing them in this paternalistic manner is no longer appropriate nor is it accepted in the modern clinical interchange. Physicians acting thus are perceived as condescending by patients, a view that is pure poison to the development and maintenance of a healthy therapeutic relationship.

While some consumers may not use these drugs properly, applying this stereotype to all of them is unwarranted. The person best able to decide whether the patient is likely to use the drugs responsibly or not is their personal physician. This decision should be made on a case-by-case basis by the patient's physician rather than across the board by fiat.

## **II) Widespread stockpiling could result in shortages of drugs for treatment of patients needing them today**

The numbers of people wanting to establish drug stockpiles for use during the pandemic is not large today. True, as the risk of a pandemic rises, more people will come to see the need to obtain a supply of drugs they use everyday for their chronic medical problems as well as those special items held in reserve for use during the pandemic.

All understand the need for patients with chronic medical disorders to continue drug treatment during the 12- to 18-months the pandemic is expected to last. If treatment were interrupted, the incidence of complications of these conditions would surely increase placing an even greater burden on the pandemic ridden healthcare system.

The pharmaceutical industry will have little difficulty satisfying this small additional demand today. Once a person has obtained an adequate drug stockpile, they are no longer in the marketplace for a greater supply. As the need for stockpiling becomes more widely appreciated, more people will wish to do so. These new entrants will take the place of those who have gone before soaking up the marginal drug supply.

Stockpiling occurring in this fashion would be orderly and not lead to shortages of drugs for current use. On the other hand if everyone tried to purchase their stockpile at the same time, shortages would abound. This of course is what will happen at some point in the run up to the pandemic but probably not until the emergency is upon us.

Orderly stockpiling by consumers of drugs taken daily for chronic medical conditions as well as a select few prescription and OTC drugs for influenza treatment is an important way to mitigate the risk inherent in a breakdown in drug availability during the emergency. Instead of opposing this approach categorically, we should be advocating the orderly stockpiling of drugs so that people who need them will not be denied access if the pandemic is more severe than some envision.

**III) It is unfair for the affluent to gain access to these drugs ahead of those unable to buy them.**

It is doubtful that the majority of consumers will purchase a drug stockpile even if this practice was widely advocated. Most people who wish to obtain a drug stockpile say their primary motivation is to provide as much protection they can for their family from illness during an influenza pandemic. This motivation cuts across all socio-economic groups. While it is true that the affluent can more easily afford the cost of preparing for this emergency, they do not seem to be doing so in any greater numbers than the middle class. All are constrained in their preparations by having to obtain a prescription from their physician. If a person of modest means wishes to use their disposable income for this purpose, this should be their choice.

That the poor have little access to medical care in the first place and no funds to prepare for the pandemic in the second is a great shame. While this condition is deplorable for a nation as wealthy as the US, it is not something that can be rectified quickly. In my view, using this social ill as an excuse to prohibit those desiring to stockpile because it is unfair is misguided. In a perfect world all groups should have access to the drugs they need. In this regard, it is wrong to frustrate the efforts of those who can afford to stockpile drugs in the same way it is that those who cannot afford them are denied access to needed medications. I was taught by a wise man that two wrongs do not make a right, an aphorism that seems applicable here. It is illogical then to take the position that since adverse societal conditions prevents one group of deserving people from

obtaining a needed resource, that the same resource should be denied to all groups.

#### **IV) Stockpiling would cost too much**

In the event that 10% of the US population stockpiled a 6-month supply of drugs taken daily and those for emergency use during the pandemic, the one-time cost would be about \$14 billion. Since the drugs purchased is intended for future use, when this occurred, the expenditure would be recovered. If the next pandemic was mild or moderate and drug availability remained intact, it would no longer be prudent to maintain a stockpile and patients would consume their stored drugs. This would lower their drug expenditures in the future. The true cost of obtaining a stockpile then is the carrying cost of the inventory between the time it was purchased and consumed. This is a small premium to pay for the value of having uninterrupted drug therapy available to the consumer. Of course, if a severe pandemic results in loss of access to these drugs, the premium paid for carrying the stockpile will pale compared to health benefits derived from patients being able to continue therapy.

#### **V) The public health community's ability to influence who is given priority for antiviral therapy would be undermined if consumers were allowed to stockpile drugs**

The well-intentioned plans of the public health community would be impossible to implement without an intact medical delivery system. It is conceivable that the millions of courses of drugs stored in the country's Strategic National Stockpile for use during the emergency could well remain locked up in guarded federal warehouses or stolen and available only on the black market in the event of a severe pandemic.

The current plan proposed by the US Department of Health and Human Services to distribute these drugs from federal National Strategic Stockpile warehouses to the state health departments and thence to those on a priority list strikes me as too complex to work effectively.<sup>13</sup> While

it is not possible to see the future, it is not difficult to predict a serious influenza pandemic will adversely affect transportation and communications. In a move that could exacerbate distribution of drugs from the National Strategic Stockpile, in an executive order, President Bush has designated the US Department of Homeland Security as the lead agency during an influenza pandemic. There is already conflict between these two agencies over this turf. The US DHS has released their own pandemic plan, which is at odds with the one the US DHHS released in November 2005.<sup>14</sup> If past performance is any guide to the future, one only needs to consider the way in which the US DHS managed the Hurricane Katrina emergency in August 2005. Of course, that emergency lasted only a short time and was regional in nature. By comparison, a serious influenza pandemic will last 12- to 18-months and affect the entire country at roughly the same time and to the same extent.

Under these circumstances, it is unlikely that those meeting the criteria used by the CDC as eligible to receive priority access to antiviral therapy would receive this drug in a timely manner. To be an effective treatment of influenza, Tamiflu must be started within 48 hours of developing influenza symptoms. It is doubtful that any country in the grasp of a nationwide medical emergency on the scale of pandemic influenza could effectively coordinate this effort.

Consider the following:

- The US DHHS proposes to transport the drugs stored in the National Strategic Stockpile to the states where they will be turned over to the state health departments
- The state health departments are responsible to distribute the drugs to the county health departments.

This is a fine plan but exactly how do the drugs reach those that need them?

- Will the local health department keep control of the drugs or will they distribute them to area pharmacies or directly to the doctor's offices?

- Are there plans for increased security to guard the drug supply and protect those who control it?
- Will a prescription be required by the agency destined to dispense the drug?
- Who will determine if an individual person meets the CDC definition of someone on the priority access list?
- Will making this determination delay antiviral therapy beyond the therapeutic window making the entire exercise futile?

Implementing a plan this complex might not work even if the pandemic were mild or moderate and would certainly be at risk should there be a severe pandemic. In my view, the only way to ensure that those meeting the criteria for priority use of antiviral drugs established by the public health community would be to provide these people with a personal stockpile of the medications to keep at home for use in the event they developed influenza. This in fact is the approach take by many doctors for their families and friends and a number of S&P 500 corporations who have purchased Tamiflu stockpiles for use by their employees.

## **The unintended consequences of the present policy**

The longer the medical, public health, and ethics community remains in lock-step opposition to patient stockpiling, the more severe the shortages will be when doctors wake one morning to see the approaching pandemic and break ranks. This is sure to occur, as physicians owe their primary loyalty to their patients. Their patients will clamor for what protection pharmaceuticals will provide from the terror of pandemic influenza. Once physicians begin to think the pandemic is coming soon, it will be very difficult for them to refuse. Depending on the level of panic and chaos in the doctor's office, there may not be much time to instruct the patients in the proper use of the drugs prescribed. Without proper guidance, it is unlikely consumers will use the drugs prescribed appropriately. I have no doubt that this will happen and depending on the timing of the doctor's change of heart, could indeed result in all the

worst predictions voiced by those who currently oppose consumer stockpiles. Ironically then, one way to guarantee the concerns of those in opposition to consumer stockpiling becoming manifest is by adhering to their current recommendations.

## Chapter 3: Stocking Up on Regular Medications

We may experience shortages or the temporary unavailability of many key drugs during the next influenza pandemic. This scenario is likely to coincide with the height of the pandemic when drug production and distribution could come to a temporary halt. Pharmaceutical manufacturing during the 12- to 18-month pandemic period could experience production interruptions due to shortages of basic materials and absentee staff. Getting these complex facilities up and running again will take much longer than the time they were closed because of safety, regulatory, and legal concerns.



Some chronic medical conditions are of sufficient severity that great harm could occur to someone unable to continue their drug treatment. Other drug treatments, while important to long-term health or present comfort may be ignored in the short term without risk of

significant harm. For critical medications, a prudent course for consumers is to stockpile a six-month supply to insure that they will be able to maintain continuous therapy should we experience a severe influenza pandemic.

### **Stockpile rotation, expiration dates, and storage**

Those who are able to establish a stockpile would still purchase their regular 30- or 90-day supply of medications for day-to-day use. To keep the drug stockpile fresh, rotate supplies so that each time a new prescription is obtained, put it in the stockpile and pull out a month's worth of the same drug with the least amount of time left before expiration. Drug expiration dates are printed on the container's label.

These dates are very conservative, meaning that almost every drug is still good long after its expiration date especially if the drug has been stored properly.

To keep drugs in good condition, the most important consideration is that they be stored properly. Humidity, temperature, air, and sunlight are the factors that most affect drug longevity. It is usually best to keep drugs unopened in their original packaging especially those provided by the manufacturer or the pharmacist. Store the drug stockpile in an airtight plastic container at room temperature. Keep them away from moisture and in the dark. Both heat and freezing temperatures can cause drugs to deteriorate and must be avoided.

## **Critical medications**

Medications in the critical “must take” category include those for chronic medical conditions like diabetes, hypertension, emphysema, chronic bronchitis, asthma, coronary artery disease, and hypothyroidism. This simple list is for illustration purposes only. There are many other conditions for which treatment must be continued during the pandemic period. My advice is to discuss this with your doctor. He or she is responsible for advising you on the need for stockpiling a particular drug or not. For the ones he or she recommends you stockpile, you will need a prescription for a 6-months quantity of drug not just a one-month supply with five refills. For instance, if you take one tablet daily, a 6-month supply means obtaining a prescription for 180 tablets.

## **Contraception critical for women of childbearing age**

Women who are of childbearing age and sexually active should consider what to do about contraception during the pandemic. During past influenza pandemics, pregnant women had some of the highest mortality rates of any group. If you are currently using birth control pills, the supply of these drugs could be



affected in the same way that others are. Stocking up on an alternative contraceptive method like condoms or a diaphragm is probably the most prudent and cost-effective course to take.

### **Patients with special medical problems**

Patients with organ transplants, insulin dependent diabetes, active rheumatoid arthritis, AIDS, active systemic lupus erythematosus, other connective tissue diseases, and those taking anti-coagulants will present special management difficulties during a pandemic emergency, especially if the drug supply chain is disrupted. This issue should be discussed with your doctor who may be able to help find available options even during the emergency.

A person on major tranquilizers for psychiatric problems like bipolar disorder and schizophrenia also need to establish a 6-month supply of medication. Similarly, patients on antidepressants for either depression or anxiety disorders should try and continue these medications during the crisis. Discuss this with your doctor and get his or her opinion.

### **Non-critical medications**

Chronic medical conditions for which medical therapy is optional--meaning that it may be possible to go without treatment in the short-term without much harm--include cholesterol lowering drugs, osteo-arthritis treatment, and medication for GERD (indigestion and heartburn), migraine headaches, sleeping pills, osteoporosis treatments, and hormones. Some patients on anti-seizure medications may find that they can cope without their medication. They may have an occasional seizure but as long as they are not driving, they can survive. If a patient's seizures are frequent without treatment, the patient should consider obtain enough medication for six months.

### **Rely on your doctor's advice and guidance**

Advice about what medications you need to stockpile ultimately needs to come from your doctor. She or he is the only person who can competently guide you in these matters. My purpose in writing about

pharmaceutical use is not so much to tell you what to do as to give you a heads-up that this is an important issue for which you and your doctor need to consider.

# **Chapter 4: Supporting Consumer Drug Stockpiling**

There are a number of unintended adverse consequences that accrue if physicians deny their patient's request for help in obtaining a stockpile of drugs for use during the coming influenza pandemic. While no one can say when the next pandemic will occur, we are presently overdue and H5N1 bird flu seems to be shaping up as the likely candidate. Its resemblance in many regards to the devastating 1918 Spanish Flu and the fact this virus looks to be on the verge of becoming pandemic are adequate reason to take this threat seriously.

## **What patients need and why**

There are two types of drugs patients need to stockpile now in order to be adequately prepared to cope with the possibility of a severe pandemic. Stockpiling is reasonable because the risk a severe pandemic could temporarily block ready access to both physicians and to pharmaceuticals. It makes sense for patients to secure an adequate supply of the drugs taken daily for chronic disease as well as a select few held in reserve for treatment of influenza during the pandemic. It is ironic that the concerns expressed by those opposing consumer stockpiles along with a variety of excess adverse health outcomes are much more likely to develop if physicians refuse to help their patients obtain the drugs needed to sustain them during the pandemic. Support for this view is provided in the following analysis.

## **Stockpiling a 6-month supply of regular medications**

Preventing consumers from establishing an adequate stockpile of drugs they rely on day in and day out places patients at greater risk of harm should the pandemic be so severe that it affected the conventional supply chain. If patients were suddenly without their regular medications and had no effective treatments for the symptoms or complications of

influenza, it is not hard to envision the consequences. The incidence of catastrophic health events like myocardial infarction, cerebrovascular accident, bacterial pneumonia and sepsis would all rise in this group.

At this point, only a few patients desire to obtain a drug stockpile and even fewer physicians' support these efforts, a circumstance that is likely to change as the pandemic becomes increasingly likely.

Patients making preparations for pandemic influenza are quite serious about doing it right. They have studied the issue and planned their strategy. Stockpiling a 6-month supply of the drugs they take daily for management of their chronic medical problems is a rational way to insure that therapy for these serious disorders can be continued in the event that a chain of pandemic related events interrupts routine pharmaceutical manufacture or delivery.

### **Stockpiling drugs for treatment of pandemic influenza**

Helping patients have an adequate supply of medication on hand useful in the treatment of influenza together with clear instructions for when and how to use them is also a responsible act for the primary care physician. Ideally, this stockpile would include the antiviral agent Tamiflu, and medications for nausea, pain, cough suppression, anxiety, and an antibiotic with good coverage for the bacterial causes community acquired pneumonia. For instance, the Flu Treatment Kit I recommend in *The Bird Flu Manual* contains oseltamivir, promethazine, hydrocodone, diazepam, and the antibiotic azithromycin. I also include probenecid for use as a Tamiflu dose multiplier. Probenecid inhibits renal excretion of oseltamivir by 60% in the same way it does with penicillin having the effect of doubling its peak serum level and increasing its half-life by 2.5 times above that seen without concomitant use.

## **Pandemic threats to the pharmaceutical supply**

Today all pharmaceutical companies, wholesalers, and retail pharmacies have implemented the just-in-time method to control inventory. This management technique keeps inventories lean freeing up operating capital for other purposes. A demand spike, especially if prolonged for any drug will result in a short-term shortage until the manufacturer can scale up production sufficiently. Most drug makers can increase production quantities without the need to add equipment or staff. There is an upper limit that can't be exceeded without sacrificing quality. To meet demand beyond this level requires the addition of manufacturing facilities and staff as was done in 2005 by Roche to meet the huge increase in demand by countries seeking to add Tamiflu to their national strategic stockpiles.

During an influenza pandemic, the vast increase in demand for both OTC and prescription drugs useful in the management of flu will lead to prolonged shortages in a large number of these products. This includes OTC drugs for treatment of pain and fever like aspirin, acetaminophen, ibuprofen, and naproxen, cough syrup employing dextromethorphan, antihistamines like diphenhydramine, and decongestants like pseudoephedrine. These products will fly off the drugstore shelves faster than they can be replaced. Manufacturers will be operating at full capacity to meet this demand but at some point, flu related absenteeism or a lack of raw materials could affect their ability to produce or deliver their products.

These same dynamics apply to prescription drugs, especially those useful in the treatment of influenza, its symptoms and complications. Obviously the antivirals Tamiflu and Relenza will be remain in continual short supply beginning even before the actual start of the pandemic and extending during the entire 12- to 18-month pandemic period. Narcotic containing cough suppressants and pain relievers, antiemetics in the phenothiazine class, prescription antihistamines, and

oral and IV antibiotics will all be in continuous short supply or temporarily unavailable.

Disturbingly, few know that more than 80% of the raw materials for drug manufacture and in some cases the finished pharmaceutical used in the US are imported, mainly from the EU and Asia.<sup>15</sup> Disruptions in collection and processing these raw materials in the country of origin, their diversion to regional manufactures or distributors to meet increased local demand, or interruption in the transportation or distribution of these materials to or within the US are all easily predicable consequences of a severe pandemic. This can only aggravate shortages of the drugs that will predictably already exist in the US due to significantly increased demand.

## **Risky business: Our dependence on disposable medical supplies**

Shortages of a wide variety of disposable medical supplies will also plague the delivery of quality healthcare and affect safety. The N-95



respirator mask has gotten most attention in this regard but this is just the tip of the iceberg.<sup>16</sup> The supply of everything from latex gloves, shoe covers, syringes, hypodermic needles, sterile saline for IV drug preparation, to the polyethylene IV tubing and intravenous catheters used to administer drugs and fluids will become terribly scarce and very quickly after the onset of the pandemic. After initial shortages develop, intermittent re-supply can be expected to occur in the beginning months of the pandemic but the

deliveries will never meet the increased demand. There will not be enough time to add manufacturing capacity even if this was warranted from a long-term business prospective, which it is not because manufacturers see that the increased demand will last only as long as the pandemic.

Manufacturers of disposable medical equipment and supplies will be able to ramp up production in the same way as pharmaceutical companies, but only so long as their employees remain healthy and their raw material suppliers can continue to deliver. In the event of a severe pandemic, worldwide influenza related conditions are likely to reduce or even halt production. These conditions include absenteeism of the plant workforce, inadequate supplies of raw materials, and loss of critical inputs required to operate the plant such as reliable electric, natural gas, or water utility service. Civil disorder or the threat thereof could also result in plant closure.

If these conditions develop it is easy to predict they will be extremely disruptive to the operation of the healthcare economy including provision of direct patient care and those responsible for the manufacture of drugs and medical supplies.

## **Medical first responder and healthcare worker absenteeism**

A further complication is the growing uncertainty that medical first responders and healthcare workers will remain at their posts during the pandemic.

### **First responders**

The lessons learned by first responders to the 911 tragedies in New York City remain fresh in the minds of their colleagues everywhere. The collapse of the buildings killed hundreds of first responders but many more who survived have become disabled due to inhaling the toxic air at the disaster site during the rescue attempt and ensuring weeks spent

recovering the deceased's remains. The US EPA made public statements declaring the air within the vicinity of the disaster was safe. Subsequently we have learned that these declarations were false. The medical first responders and rescue crews believed them and remained at work for weeks.

Some are now disabled with pulmonary fibrosis and other respiratory disorders and are no longer able to work. Others have been fired with some being abandoned by the authorities. The front of our healthcare system in



every city across the US is composed of these same first responders. Given this experience, one wonders what their reaction will be when asked to risk their health during a severe influenza pandemic?

## **Healthcare workers**

The healthcare system needs all its workers to operate properly, not just the allied technicians and medical professionals. In hospitals, this includes the clerical, janitorial, IT, facilities maintenance, nursing aids, kitchen, and security staff who do all the heavy lifting needed to keep the facility open. These are the people that pay the hospital's bills and collect its money, keep the hospital clean and sanitary, keep the computers running, maintain and repair the physical plant, bath the patients, change their bed linen, and help patients use the bedpan. They are those who prepare and deliver food to the patient's rooms and feed the staff. They are responsible for patient and hospital staff security and safety. Despite the fact that these healthcare workers are some of the lowest paid in the economy as a whole, no hospital could remain functional without them.

## **The sacrifice of those who serve**

Hospital workers, medical first responders, and the ancillary and professional medical staff will by virtue of their work be repeatedly exposed to the influenza virus irrespective of the precautions taken. They will carry the virus home with them exposing their families and friends. As was seen during the 1918 and 1957 pandemics, people in these professions are predicted to have the highest clinical attack rates and case fatality rates of any group during the coming pandemic.

Most health care workers are presently unaware of their increased health risk despite being well known within the public health community. This fact and because it is in the public interest that healthcare workers and first responders live to provide care for others is why these groups head the CDC's priority list for access to scarce drugs and vaccines during the pandemic. Unfortunately, the same protection does not extend to the families of healthcare workers or first responders. No doubt, as the pandemic approaches and certainly once it arrives, this fact will become better known.



Healthcare workers and medical first responders are among some of the most dedicated people in our society and many will remain at their posts irrespective of the risk, but not all. It is easy to see that healthcare workers in every category will be significantly reduced due to the combined effects of illness and death due to influenza and to those who resign their position or simply fail to return to work due to concern about becoming ill

themselves and/or infecting their family members. While volunteers can help keep the hospital clean, prepare food, and bath patients, when it comes to highly technical roles in the laboratory, respiratory, radiology, or ICU there will be no relief.

As soon as physicians, nurses, and healthcare administrators come to a more realistic appraisal of the conditions that could emerge during a severe pandemic, the sooner they can begin planning appropriately for it.

Preparing for this pandemic makes a lot of sense despite the fact that most hospitals and few doctors have done very little so far. Those that plan now will be in a much better position to weather the storm when it comes and recover more quickly once it is over.

This essay was written to foster insight into the risk our highly structured and technology dependent healthcare and health economic system faces from a pandemic event. The widespread use of just-in-time inventory methods up and down the supply chain means that no one has more than a few days or weeks supply of anything on hand at any one time. Globalization of the supply and manufacturing chain is another factor increasing our vulnerability. As appreciation of these risks increase, it becomes apparent that taking steps to prepare for the possibility of a disruption in the supply of drugs as well as a whole host of other healthcare materials and supplies becomes a rational act.

Those who accept this analysis will also see that there are actions that can be taken to help reduce the consequences. One of these actions is for people to obtain a stockpile of their regular and influenza treatment medications for emergency use. Patients are not able to do this easily without the help of their physicians. It is my hope that physicians will see the value of helping their patients prepare for the coming pandemic in every way possible including supporting their effort to obtain a stockpile of necessary drugs.

## Chapter 5: Obstetric care during the pandemic

The care and treatment of women who are pregnant at the start of the pandemic or become pregnant during the emergency is an area where planning and preparation can make a huge difference in patient outcomes. Pregnant women are at exceeding high risk for death during pandemic influenza, as will be their newborn infants. Pregnant women had one of the highest case fatality rate of any group during the Spanish Flu in 1918. Without planning, those giving birth in a hospital overflowing with influenza patients will be at increased risk as will their newborn of contracting fatal influenza. They could also be exposed to people with influenza when visiting the doctor for pre-natal visits or going to the hospital for routine tests.

It is likely that during the pandemic, pregnant women will be advised to shelter in place at home avoiding exposure to crowded shopping centers, grocery stores, or their other children's schools. This precaution will need to be continued until well after the birth of the infant because while the mother's risk from flu will wane, the infants will remain high during the first few years of life.



A logical response to this dilemma is for community health planners to designate one area hospital for prenatal, obstetrics and postnatal use only. No patient, pregnant or otherwise with influenza would be seen in this facility. Isolating the care of this group in a designated facility is the type of planning that can be expected to reduce the number of avoidable deaths during the pandemic without increasing costs to the community.

Providing pregnant women with a stockpile of drugs for use during the pandemic also makes sense. Their obstetrician in concert with their primary care physician would be responsible for making this decision and for instructing the patient on the timing and appropriate home use of this and other drugs that might be prescribed. The risk of using these drugs during pregnancy, especially Tamiflu (US FDA Category C) would need to be carefully weighed against the risk of maternal and fetal morbidity and mortality from pandemic influenza. Treatment of severe influenza in this special group of patients will be complex. An issue like this is one that deserves the attention of a multidisciplinary expert panel whose report would include guidelines for obstetricians and primary care physicians to follow during the pandemic. Their views and suggestions on how these patients can be safely managed will be of inestimable value to doctors during the pandemic.

### **So shall ye sow, so shall ye reap**

The concerns developed in this essay are presented in order to help foster a clearer understanding of the potential risk we face from a severe influenza pandemic resembling the 1918 Spanish Flu. The above vignettes represent only the most easily foreseen events that are likely to occur given the nature of pandemic influenza. My purpose in presenting them is to provide primary care physicians and those specializing in obstetrics with a rational underpinning for why it is prudent and good medical practice to help their patients obtain a personal drug stockpile for use during the pandemic. This includes the drugs they take daily for management of chronic disease as well as a few select prescription and OTC drugs that will be very useful to have on hand for management of influenza or its complications.

# Chapter 6: Tamiflu Treatment and Resistance

An excerpt from *The Bird Flu Manual*

If you have access to Tamiflu, the dose for seasonal flu is one tablet twice daily for 5 days. The studies found that in seasonal flu it is best to begin Tamiflu within two days of the beginning of symptoms. There is almost no information on how to use Tamiflu for treatment of Bird Flu patients but I hope that the Chinese, Indonesians, and Vietnamese will be publishing their experience soon. This will provide us with important guidance on the optimal dose and length of treatment needed to obtain the best patient outcome. I will be providing updates on our [www.birdflumanual.com](http://www.birdflumanual.com) website on this as they become available. The effective use of Tamiflu may be very different during pandemic conditions compared with seasonal flu. Until more is known, I plan to start Tamiflu in every patient in whom I think it will help, irrespective of how long they have been sick, as long as I think the patient has a good chance of survival, and active viral reproduction is occurring in the patient.

Remember, during seasonal flu viral reproduction and shedding in children and adolescents can last for up to two weeks after they become ill. This is twice as long as in adults.

Some strains of H5N1 are resistant to Tamiflu as well as amantidine. The HHS Pandemic Influenza Plan does not recommend stockpiling of drugs from the amantidine class, as most H5N1 has been resistant to them. There has been fairly heavy agricultural use of these generic antivirals in Asia in an attempt to prevent the virus from infecting domestic poultry and swine. Unfortunately this technique failed to protect the farm livestock but did select out a potent strain of H5N1 that was completely resistant to this entire family of drugs. Recent reports

indicate that seasonal flu is becoming increasingly resistant to the amantidine class too.

Since the Tamiflu resistant strains are less lethal than the Tamiflu sensitive ones, it makes good sense to use this drug irrespective of whether or not Tamiflu resistant strains are circulating or not. There is recent data on Tamiflu resistance from viral specimens isolated from a girl in Vietnam. This developed while she was taking prophylactic doses of the drug, 75 mg daily. When she fell ill, her doctors increased her dose to 1 tablet twice daily and she recovered. It was only later that they discovered that the strain she came down with was resistant.

It seems that the mechanism by which the influenza develops resistance to the antiviral drug also leads to a much less lethal virus. This means we gain by using Tamiflu, whether the viral strains circulating in the community are resistant or not. The strains which are sensitive to it, and which the drug eliminates, are much more lethal than the resistant ones. So, my advice is to use the Tamiflu if you have it and don't worry about resistance. If the strain you are treating is Tamiflu sensitive, great, the Tamiflu will help. If not, great, the patient is infected with a lower risk strain of Bird Flu and employing the Tamiflu in them prevents the emergence of the more lethal coexisting Tamiflu-sensitive strains.

Don't worry too much about not being able to get the very latest sensitivity and specificity data from CDC. It will be important to keep up with this as long as you can, but I expect that as the pandemic spreads the quality and timeliness of medical information coming out of health agencies like the CDC and local health departments will deteriorate.

## **Questions about the current Tamiflu regimen**

In a NIH sponsored mouse study, there was the concern that Bird Flu may require much higher doses of Tamiflu to achieve a meaningful response to treatment. Human infectious disease specialists have expressed the same sentiments. In my opinion, it is not likely the strain

of pandemic flu that ultimately emerges will be nearly as lethal as the strain infecting birds or people is at the earlier stages of the strain's adaptation. Second, we now understand that we can achieve much higher plasma levels of Tamiflu by the co-administration of probenecid. Using this combination boosts the effective stockpile of Tamiflu by a factor of at least 2.5 by decreasing the excretion of the drug in the urine. I plan to make use of this method to stretch my Tamiflu supply or if need be dramatically raise the plasma concentration of the drug. It is very important that the drug be used for a long enough time and at a high enough dose to be effective against the flu.

At the present time, there is discussion among the public health and infectious disease community about raising the dose and length of treatment. My current plan is to use Tamiflu 75 mg capsules twice daily with probenecid 500 mg 2 times daily both for 10 days. This will give my patient drug levels that are twice the level recommended for seasonal flu for twice as long. It is my guess that experts will suggest that the dose and course of Tamiflu treatment for pandemic flu will be increased. Fortunately, studies of Tamiflu in adults show that it is safe to take a dose this high, although the incidence of side effects is greater. I am unaware of any studies on the safety of using the drug for more than 5 days in adults, but do not anticipate that there will be new problems or unexpected concerns. This will be something that I will be studying closely and I suggest that you keep up with it too.

It is possible that the severe shortage of Tamiflu will be used to prevent any new recommendations that call for higher doses of the drug to be used from being released. This is already controversial and as the pandemic approaches it will surely become an even hotter issue. I will be keeping a close eye on this discussion and update my recommendations on the BFM web site as mentioned. In contemplation of the pandemic influenza dose being increased, I have advised adults to obtain a double supply of Tamiflu (twenty 75 mg capsules) and enough probenecid to take with it for a 10-day course.

## **Probenecid, a Tamiflu dose multiplier**

To obtain the benefits of this combination, probenecid should be given in a dose of 500 mg by mouth 2 times daily. Doing so safely reduces renal excretion of oseltamivir carboxylate by 60%, doubles the plasma concentration, and increases the half-life by 2.5 times. Over all, the area under the receiver operator curve is increased by 2.5 times that of giving the same dose without probenecid. In clinical trials of Tamiflu given at higher doses, there were no significant increases in side effects or any new or dangerous side effects. Recent anecdotal reports from Japan that a dozen children have died after receiving Tamiflu treatment during flu season was evaluated by a specially convened outside panel for the US FDA in November 2005. The outside FDA panel reviewed these deaths in 2006 and concluded they were due to influenza and not Tamiflu.

In November 2006 Tamiflu use in 103 Japanese children was linked to hallucinations and the US FDA has ordered this adverse reaction be added to the drug's Product Circular. It is of note that Japanese physicians routinely prescribe Tamiflu at much higher doses to adults and children than that used in the US and this fact is probably responsible for the increased incidence of hallucinations attributed to the drug.

Probenecid side effects are infrequent and mild. These include headache, precipitation of acute gout, nausea, anorexia, and rash. Very rarely is it related to serious kidney, liver, or blood disorders but these are not likely to occur when taken for no more than ten days. Probenecid increases the plasma levels of a number of drugs. Common drugs affected include allopurinol, aspirin and aspirin-like NSAIDs (like ibuprofen and naproxen), antibiotics in the  $\beta$ -lactam family (penicillin class), thiazide diuretics, and benzodiazepines (like Valium and Ativan). Lowering the doses of these other drugs by half while using probenecid should avoid any problems. If gout occurs during treatment, give the patient ibuprofen or naproxen at half the usual therapeutic dose. Gout occurs due to the acute lowering of the serum uric acid by probenecid.

You are already keeping the patient well hydrated as treatment for their underlying infection, which is the best way to prevent the renal complications of hyperuricosuria, caused by probenecid. The short treatment course of probenecid lowers the risk of any complication except for gout and this is easily managed.

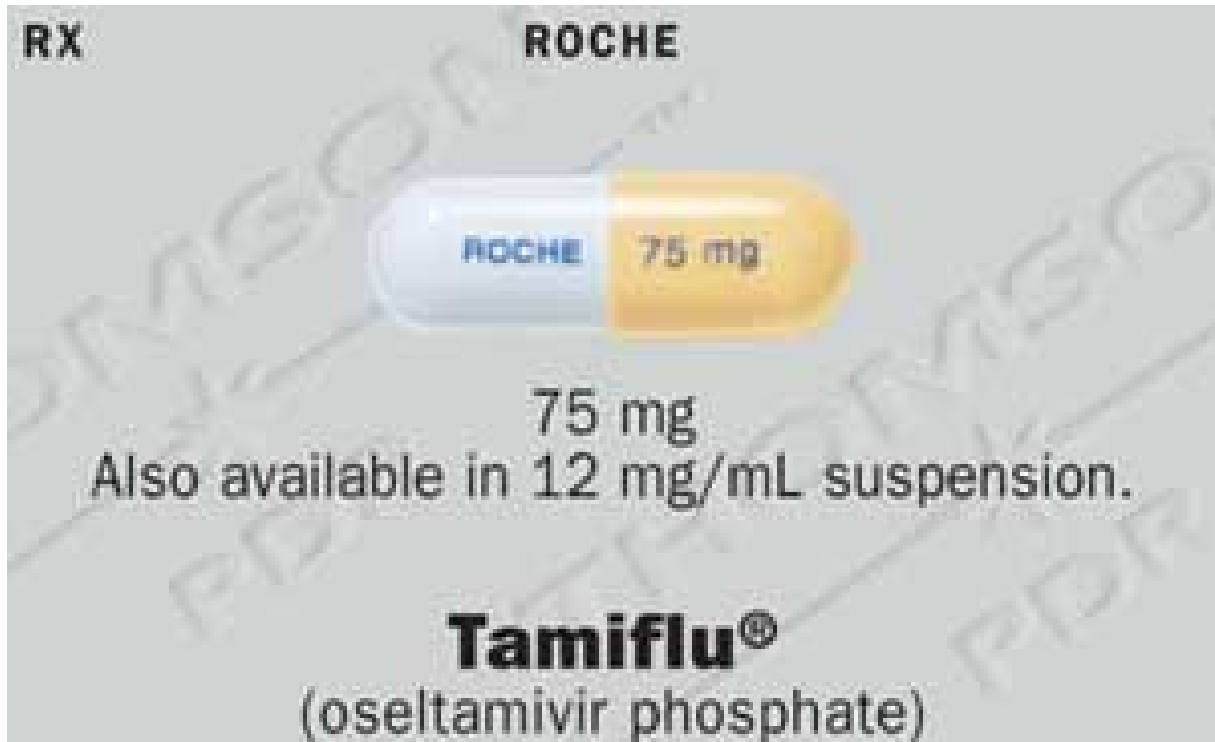
# Chapter 7: Support for a Personal Tamiflu Stockpile

It is responsible and ethical for physicians to prescribe Tamiflu for their patients to stockpile and use later during pandemic bird flu. Presently the risk of an influenza pandemic is high. Roche and its licensees have significantly ramped up production of Tamiflu beginning in the spring of 2006. This has alleviated the severe supply shortage seen in 2005. There will not be an effective H5N1 pandemic influenza vaccine until about 6 months after the pandemic strain first emerges. Even then supplies of the vaccine will be limited with only enough for about 10% of the population. There is doubt regarding the ability of the US Government and organized medicine to respond effectively to an emergency on the scale of a severe influenza pandemic. These factors are those that have led me to support the practice of helping my patients establish a Tamiflu stockpile for use during the pandemic. Nationally there is a woeful lack of preparation to respond to this serious public health issue. My position differs from most government and medical bodies who have expressed an opinion. In this brief essay, I provide the rationale for why I think it is both a good medical practice and ethical for doctors to prescribe and patients to obtain Tamiflu prior to the pandemic.

## **The Tamiflu shortage**

The World Health Organization (WHO) has recommended that every country establish a stockpile of enough drugs to treat 20% of its citizens in preparation for a possible avian influenza pandemic.<sup>17</sup> Most of the developed nations followed the WHO recommendations except for the US who hesitated placing their order in the fall of 2005. The CBO stated in a recent study of the macroeconomic effect of influenza pandemic on the US, that by the end of 2005, the US Strategic National Stockpile would contain enough Tamiflu for 4 million five-day treatment courses and 84,000 Relenza treatment courses.<sup>18</sup> This is enough for about 1.4%

of the US population assuming that the standard treatment regimen will be effective for bird flu. This dose and the length of treatment with Tamiflu for bird flu is currently under review by infectious disease and public health experts. There is a good chance that they will recommend that the dose and course of therapy both be doubled.<sup>19</sup> If so, this would reduce the coverage by 75%.

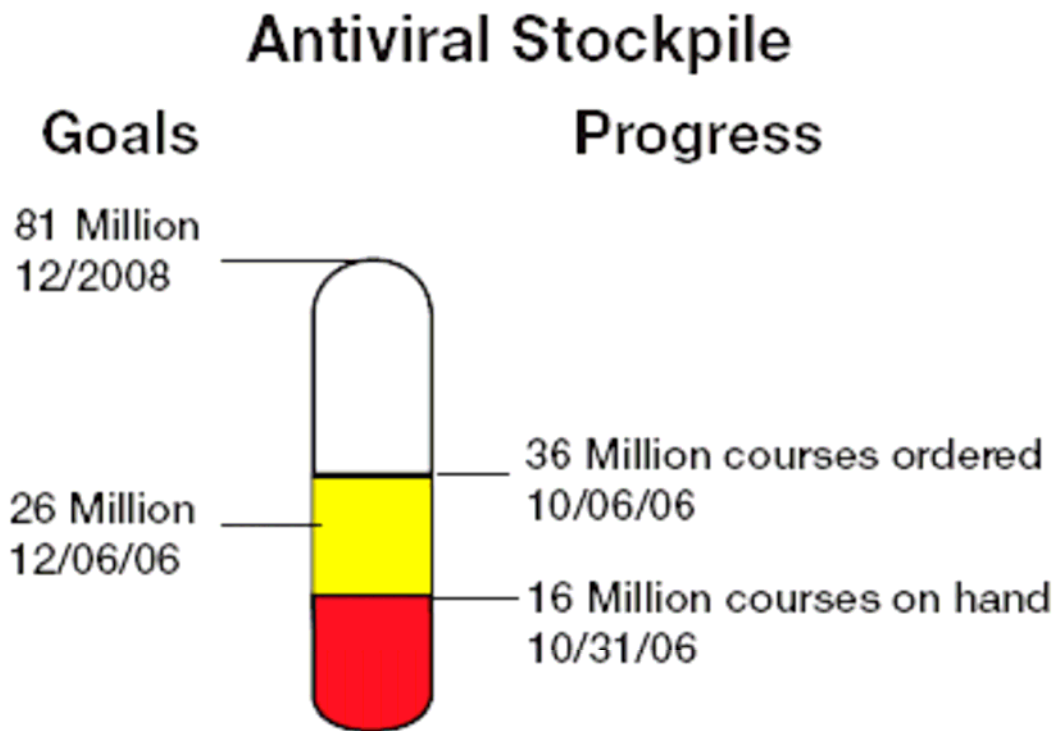


When the US finally placed an order for 12 million additional treatment courses from Roche, the company informed the US that Roche was already at full manufacturing capacity worldwide and the orders were to be filled on a first come first serve basis. Since the US was one of the last countries to order the drug, Roche informed the US Department of Health and Human Services (US DHHS) in October 2005 that it would not even begin to fill the US order until late 2007.<sup>18</sup>

This resulted in pressure being applied by various stakeholders, both political and commercial. In response, Roche addressed this problem in November 2005 by issuing licenses to manufacture Tamiflu to pharmaceutical companies worldwide. Roche also found a synthetic

substitute for the main and most expensive ingredient of the drug, star anise, which is a botanical grown only in China. It took the Roche licensees 6 months to retool and begin Tamiflu production. Since the spring of 2006 these new supplies began to be shipped. The US DHHS announced in November 2006 that the US National Strategic Stockpile of Tamiflu stood at 16 million effective 5-day courses with 20 million more expected by March 2007, enough for 11% of the US population.<sup>20</sup>

The US States have ordered 31 million courses of Tamiflu as well. By December 2008, 81 million courses of the drug are projected to be on hand, enough to cover 25% of the US population.



Today supplies of the drug for present use and that destined for the national stockpiles are being met around the world. While more drug is needed, the supply of Tamiflu is now sufficient to allow for limited individual stockpiling to occur without there being any concern about causing shortages for present use or interfering with the national authorities desire to fill their stockpiles.

## **The lack of a pandemic flu vaccine**

The pandemic strain of H5N1 has yet to emerge. Until it does so, only prototype vaccines, of unforeseeable efficacy, can be made using viral isolated samples obtain earlier human cases of bird flu isolated in Viet Nam and Indonesia. When the actual pandemic virus begins to spread, there will not be any vaccine doses available for anyone for at least six months. Using current technology with some luck thrown in, it is



estimated that supplies will be limited to only 30 million effective doses being available at 6-month intervals. This quantity is enough to vaccinate no more than 10% of the US population. If the pandemic lasts for 18 months, vaccination will be an option for about 30% of Americans. During this period, Tamiflu (and Relenza) will be the only option

for effective medical treatment of pandemic flu available to most people.

## **Would personal stockpiles Tamiflu be properly used?**

In the December 22, 2005 issue of the New England Journal of Medicine, Anne Moscona, M.D. argued “personal stockpiling of oseltamivir is likely to lead to the use of insufficient doses or inadequate courses of therapy. Shortages during a pandemic would inspire sharing of personal supplies, resulting in inadequate treatment. Such under-treatment is of particular concern in children — the main source for the dissemination of influenza within the community, since they usually have higher viral loads than adults and excrete infectious virus for longer periods. The habit of stopping treatment prematurely when symptoms resolve (a well established tendency with antibiotic therapy) could also lead to sub-optimal treatment of influenza and promote the development of drug resistance.” Her conclusion is “Improper use of personal stockpiles of oseltamivir may promote resistance, thereby lessening the usefulness of our frontline defense against influenza, and should be strongly discouraged.” These sentiments are being widely supported in the public health and infectious disease community.<sup>21 22 23</sup> , ,

I disagree with these assumptions for several reasons. First, the idea that people who use Tamiflu out of their private stockpile will misuse it is an unwarranted generalization. While there are segments of the population that may be unable to self-administer drugs properly, these are probably not the same people who are interested in obtaining a personal Tamiflu stockpile. In my experience, the people who have requested a Tamiflu prescription from me for the purpose of establishing a personal stockpile have researched the issue thoroughly and are very clear on the



indications for use, timing of the dose, and treatment course. They probably know these things better than most doctors who rarely prescribe Tamiflu. Interestingly, this lack of experience prescribing Tamiflu is often due to the fact that by the time most patients seek treatment for the flu, it is too late in the

course of the illness to start it. To be effective, Tamiflu must be initiated within a 48-hour therapeutic window after the onset of symptoms.

For the administration of the Tamiflu in a timely manner, I can hardly think of a better place for the drug to be stored than in the house of the person coming down with the flu. With respect to being able to take the drug within 2 days of the beginning of symptoms, what could be better? It is important that the person deciding when to start the Tamiflu have a good grasp of what flu symptoms are so they don't waste their precious drug. I provide this information to my patients and find that similar information is available in many places on the Internet today.

I advocate physicians prescribe drugs for their patients that will be useful for the management of influenza before they become scarce, an event likely to accompany the pandemic as it emerges. Specifically, I think it is prudent for patients to have Tamiflu, over-the-counter and other prescription drugs stored at home for personal use during a pandemic. As is the case any time we prescribe drugs, a key responsibility of the prescribing physician is to ensure that the patient is provided with specific advice on how to use these medications properly

and when to do so. An influenza pandemic could begin at any time now. Under these circumstances and considering the inadequate national pandemic preparedness, I think it is both prudent and

responsible for practicing physicians to give patients access to Tamiflu if they want it. This is especially so since it is well understood that once the pandemic starts, most people will have no chance at all of getting any or for that matter even getting in to see their doctor whose office is likely to be



overwhelmed by patients sick with flu. For these reasons, the only way I see that a patient with pandemic flu has any chance of benefiting from Tamiflu within the therapeutic window is if they already have it on hand.

## **Bird flu resistance to Tamiflu**

One of the arguments used by opponents of patient stockpiles of Tamiflu is that their misuse or even their use of the drug could result in higher rates of oseltamivir resistant H5N1 bird flu. Based on our experience with all other anti-infective agents, this is a true statement and will happen irrespective of whether it is used properly or not. *A unique and truly interesting fact concerning Tamiflu resistant strains of influenza is that they are less infective and have lower virulence and lethality compared with non-resistant strains.* This means that inducing Tamiflu resistance in the pandemic bird flu strain could have beneficial effect. In fact, I think it might give us something we can exploit to lower the severity of bird flu infections. This finding has to do with the way the virus has to alter the neuraminidase receptor to avoid Tamiflu. While making this change allows the flu to escape the effect of Tamiflu it also partially cripples itself by making it much harder for it to enter and leave the cell. In other words, bird flu without the Tamiflu resistance mutation

is much more deadly than those with it. So, this may mean that Tamiflu could be useful for treatment of bird flu even if there is a high prevalence of Tamiflu resistant avian influenza strains in the community. The drug would be useful by selecting out the weaker members of the viral family as the ones that got through the Tamiflu defense while screening out the stronger members.

In summary, the facts that support the establishment of personal Tamiflu stockpiles by individuals who desire to do so include:

- A) The increase in Tamiflu supplies now allow for limited personal stockpiles of the drug to be obtained without the risk that this will cause shortages of the drug for current use or interfere with the US Government's efforts to obtain a supply of the drug for the National Strategic Stockpile.
- B) The unavailability of an efficacious pandemic vaccine for a least 6 months after the beginning of the pandemic that will be adequate for no more than 30% of the population during the course of the pandemic.
- C) The probability that during the pandemic, patients with influenza will have great difficulty gaining timely access to their physician sufficient to receive a prescription for Tamiflu to begin it within the 48-hour therapeutic window required.
- D) That Tamiflu resistance may not be as bad a problem as it is being made out to be and in fact may improve the chances of survival for some patients.
- E) Lack of confidence in the US, state, and local government's ability to distribute Tamiflu and vaccine in an efficient and timely manner during the chaos expected during a severe pandemic.
- F) Lastly, I think patients have a right to make this decision for themselves and that those who chose to obtain a personal supply of Tamiflu will use it responsibly.

I support the practice of prescribing drugs for the treatment of influenza for patients to stockpile in anticipation of a pandemic as long as

practitioners writing these prescriptions fulfill their obligation to ensure that the patient has thorough instructions on how and when to employ these agents including Tamiflu.

## Chapter 8: Flu Treatment Kit Substitutes and Alternatives

In *The Bird Flu Manual*<sup>24</sup> I have recommended a list of prescription and over-the-counter (OTC) drugs in the Flu Treatment Kit section that will be useful for the treatment of pandemic influenza and its complications. This text also provides the reader with guidance for when and how to use these drugs for treatment of flu. The drugs listed in the pamphlet, *Good Home Influenza Treatment*, include only non-prescription OTC drugs as it is written for use by those without access to a doctor willing to assist them obtain a stockpile of prescription drugs for use during the pandemic.<sup>25</sup> The pamphlet includes specific guidelines for use of these OTC drugs in treatment of pandemic influenza. The drugs specified in these publications are commonly available in pharmacies, grocery stores, and over the Internet. They are inexpensive generic drugs except for one, the antiviral Tamiflu. Generic drugs are a good value and many of these older drugs remain as effective as some costly branded products with the same US FDA approved indications.

The US FDA has greatly expanded the number of drugs available OTC that are effective but do not require a doctor's prescription. Some of these products will be very important to have on hand for flu treatment. Those interested in preparing for the coming pandemic should purchase an appropriate quantity of these OTC drugs for their stockpile. Recommended quantities are provided in the Flu Treatment Kit sections of the above publications.

If your physician is willing to help you, now is the time to purchase a stockpile of prescription drugs you will need to have on hand during the pandemic. This includes the drugs that will be useful for management of flu and also those that you take everyday for treatment of the chronic medical disorders you may have.

## **The value of using drugs properly**

It is important that people use these drugs properly in order to get the intended benefit and to avoid unnecessary side effects. Advice on when and how to use the drugs listed in the Flu Treatment Kit are included in the above referenced publications.

This article discusses possible substitutes for the drugs specified in the above two publications. There are several simple reasons why I recommended these particular drugs. The first is they are the ones that I have prescribed for treatment of flu for many years and over this time have found them to be very effective and safe for the uses recommended. These drugs are versatile in that they provide a broad range of benefits and uses beyond their US FDA approvals. Having fewer drugs to deal with simplifies the task of learning how and when to use them safely. All the specified drugs except Tamiflu are generic which helps to keep the cost of stockpiling down. Lastly, the drugs are widely available throughout the world.

In the table below, you will find the drug specified in the Flu Treatment Kit listed in the first column, the recommended indication in the second, and the trade or brand name of the product in the third. Possible substitutes, if any, are listed to the right in the adjacent column. In some cases the suggested substitute is actually an alternative treatment rather than a true substitute. Some alternatives have similar mechanisms of action and effects. If you need to use a substitute for any of the drugs specified in *The Bird Flu Manual* and you intend to compound them for use as an oral solution, you will need to review the drug's Product Circular to find what doses are recommended for use in children and adults and adjust the formula according. If your doctor is prescribing these drugs, he or she will provide you with this guidance.

<b>Possible OTC Drug Substitutes for OTC drugs listed in the Flu Treatment Kit</b>				
<b>Index FTK OTC Drug</b>	<b>FTK Indication</b>	<b>Drug Trade Name</b>	<b>OTC Substitute</b>	<b>OTC alternative</b>
Acetaminophen	Pain and fever	Tylenol®		Ibuprofen, naproxen, aspirin
Ibuprofen	Pain and fever	Motrin®	Naproxen, aspirin	Acetaminophen
Diphenhydramine	Nose and ear congestion	Benadryl®	Loratadine, clemastine fumarate, Doxylamine Succinate, dexbrompheniramine, chlorpheniramine maleate	Saline nasal sprays, Cromolyn Sodium (NasalChrom®), Phenylephrine Hydrochloride (Neo Synephrine®), Pseudoephedrine, Oxymetazoline Hydrochloride (Afrin®), Propylhexedrine (Benzedrex inhaler®)
DM contain cough syrup <sup>1</sup>	Cough suppressant	Robitussin DM®	Many other private-label store brands	Guaifenesin 600 mg (Expectorant)
Loperamide 2mg	Diarrhea	Imodium AD®		Bismuth subsalicylate (Pepto-Bismol®, Kaopectate®)
Meclizine	Nausea	Antivert®	Dimenhydrinate (Dramamine®), Diphenhydramine, Cyclizine Hydrochloride (Marezine®)	Dextrose + fructose + phosphoric acid combinations (Emertrol®)

<sup>1</sup> DM is the abbreviation for dextromethorphan, an effective non-narcotic cough suppressant.

<b>Possible OTC or Prescription Drug Substitutes for Prescription drugs listed in the Flu Treatment Kit</b>				
<b>Index FTK Rx Drug</b>	<b>FTK Indication</b>	<b>Drug Trade Name</b>	<b>Rx Substitute</b>	<b>OTC Substitute</b>
Oseltamivir	Influenza Antiviral	Tamiflu®	Relenza®	None
Promethazine	Nausea, vomiting, nasal congestion, abdominal cramps	Phenergan®	Chlorpromazine	For all: Dimenhydrinate (Dramamine®), Diphenhydramine, Cyclizine Hydrochloride (Marezine®) and meclizine (but much less effective than promethazine)
Hydrocodone	Pain, cough suppressant, diarrhea and as bowel antispasmodic	Lortab®, Vicodan®	For all: Codeine For diarrhea and bowel spasm: Lomotil®, paregoric	For pain: Acetaminophen, ibuprofen, aspirin, and naproxen For cough: DM containing cough syrup; For diarrhea and bowel spasm: loperamide, For diarrhea, Bismuth subsalicylate
Diazepam	Muscle spasm, anxiety, insomnia	Valium®	Xanax®, Ativan®, Librium® for all	For anxiety: valerian For insomnia: Acetaminophen plus diphenhydramine, valerian
Azithromycin	Bacterial infections complicating influenza	Zithromax®	Erythromycin, Ketek®, ciprofloxin for all	None
Probenecid	Oseltamivir dose multiplier	Benamid®	None	None

# References

---

- <sup>1</sup> Osterholm M, Preparing for the next pandemic., N Engl J Med 2005;352:1839-1842
- <sup>2</sup> Elodie Ghedin<sup>1</sup>, Naomi A. Sengamalay<sup>1</sup>, K. Taubenberger, et al., Large-scale sequencing of human influenza reveals the dynamic nature of viral genome evolution Nature 2005;437; 1162-6
- <sup>3</sup> The US Department of Health and Human Services Pandemic Influenza Plan. November 2, 2005
- <sup>4</sup> Defined for this purpose as the 325,000 active US Internists, Family Practitioners, and Pediatricians.
- <sup>5</sup> Tamiflu Product Circular, Roche Pharmaceuticals (Published in the PDR).
- <sup>6</sup> You can find the drugs I recommend for flu treatment on the [www.BirdFluManual.com](http://www.BirdFluManual.com) website on the Resources section in the Influenza Drugs folder. Specific flu indications, doses and patient instructions are found in *The Bird Flu Manual*, Booksurge Publishing, Charleston, SC September 2006,
- <sup>7</sup> Moscona A., Oseltamivir Resistance — Disabling Our Influenza Defenses. N Engl J Med 2005 353;25
- <sup>8</sup> Joint Position Statement of the Infectious Diseases Society of America and Society for Healthcare Epidemiology of America on Antiviral Stockpiling for Influenza Preparedness October 31, 2005; <http://www.idsociety.org>
- <sup>9</sup> Moscona A., Oseltamivir Resistance — Disabling Our Influenza Defenses. N Engl J Med 2005 353;25
- <sup>10</sup> Joint Position Statement of the Infectious Diseases Society of America and Society for Healthcare Epidemiology of America on Antiviral Stockpiling for Influenza Preparedness October 31, 2005; <http://www.idsociety.org>
- <sup>11</sup> Brett AS, et al., Run on Tamiflu NEJM 2005 353,25
- <sup>12</sup> Harvard Vanguard Medical Associates. Avian influenza (bird flu): frequently asked questions. (Accessed November 17, 2005, at <http://www.harvardvanguard.org/flu/avian.asp>)
- <sup>13</sup> The US Department of Health and Human Services Pandemic Influenza Plan. November 2, 2005
- <sup>14</sup> US National Strategy for Pandemic Influenza US DHS 2May2006
- <sup>15</sup> Michael Osterholm, PhD, Director of CIDRAP in testimony before the US Congress in December 2005.
- <sup>16</sup> Reusability of Facemasks IOM Apr2006
- <sup>17</sup> WHO Global Influenza Pandemic Preparedness Plan, July 2005
- <sup>18</sup> A Potential Influenza Pandemic: Possible Macroeconomic Effects and Policy Issues. The Congress of the US, The Congressional Budget Office, December 8, 2005, US Government Printing Office.

- 
- <sup>19</sup> Moscona, A., Tamiflu Resistance — Disabling Our Influenza Defenses N Engl J Med 2005: 353; 25
- <sup>20</sup> Pandemic Planning Update US DHHS 13Nov2006
- <sup>21</sup> Joint Position Statement of the Infectious Diseases Society of America and Society for Healthcare Epidemiology of America on Antiviral Stockpiling for Influenza Preparedness October 31, 2005; <http://www.idsociety.org>
- <sup>22</sup> Brett AS, et al., Run on Tamiflu NEJM 2005 353,25
- <sup>23</sup> Harvard Vanguard Medical Associates. Avian influenza (bird flu): frequently asked questions. (Accessed November 17, 2005, at <http://www.harvardvanguard.org/flu/avian.asp>)
- <sup>24</sup> Woodson, Grattan. The Bird Flu Manual, Booksurge Publishing, Charleston, SC, September 2006.
- <sup>25</sup> Woodson, Grattan. Good Home Influenza Treatment, available as a free download from [www.BirdFluManual.com](http://www.BirdFluManual.com) in the Home Influenza Treatment folder of the Resource section.