

**An H5N1 Pandemic:
The Virginia Tech Campus
as a Model of State, National, and Global
Emergency Preparedness**

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April 2013

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Abstract Experts suggest the likelihood of another human influenza pandemic to be high, or maybe even inevitable.^{1,2} There's a good chance that it could be H5N1, and the possible effects are worrisome.³ No one can know for sure when the next pandemic will occur.¹ A pandemic has no regard for borders; once it begins, it has serious economic implications all levels. Organizations at all levels have put programs in place to prepare for such an event, and models allow them to better prepare by estimating illnesses, hospitalizations, deaths, and other factors pertinent to public health. Virginia Tech, a community in itself, will not be except from the fallout, and must ensure preparedness with regard to resources, expertise, and services in order to mitigate the effects of a full-blown pandemic.⁴

INTRODUCTION

Influenza, a virus of the respiratory system, infects approximately five to 20% of people in the United States each year. Some 200,000 will require hospitalization for flu-related complications, and thousands will die. These figures alone are enough to cause concern.^{5,6}

There is, however, another virus that's causing considerable uneasiness to human and animal health experts alike. The virus is the highly pathogenic avian influenza – specifically H5N1.⁵ In the poultry population, it is “unprecedented in its virulence, extent, and longevity.”⁷

Though it originated in birds, it has made the species jump and is also able to infect humans. H5N1 is not currently able to spread easily between people, but viruses are constantly mutating and it's a very real possibility that it could happen – especially with human intervention. The result could be a pandemic, with serious implications across the globe.⁵

There's speculation that an H5N1 pandemic would cause 1.7 million deaths in the United States alone. Add to that the estimated 700,000 hospitalizations and 40 million outpatient visits, and it doesn't take long for the numbers to add up at an alarming rate. Global mortality could be between 180 million to 360 million people.⁸

Therefore, rapid detection is essential for minimizing the likelihood of a pandemic.⁷ This is best accomplished by constant surveillance and preparedness at all levels to ultimately decrease the morbidity, mortality, and social disruption a pandemic would cause.^{4,9}

Are we really prepared for such an event? “We” being the international community. “We” being the United States. “We” being Virginia. “We” being the New River Valley. “We” being the Virginia Tech community. This paper will discuss organizations and programs critical to preparedness for an influenza pandemic, as well as considerations that must be addressed specific to Virginia Tech.

BACKGROUND

ORIGINATION

The H5N1 virus subtype was first seen in birds in China in 1996. The first human infection was confirmed a year later in Hong Kong.¹⁰ There were 18 cases reported, with six deaths. This occurred concurrently with an epizootic, or an epidemic in nonhumans. The entire domestic poultry population within the territory was killed in an effort to stop the panzootic (a disease affecting animals of many species, especially over a wide area).¹¹ H5N1 re-emerged in 2003-2004 and spread from Asia to Europe and Africa. The result has been millions of infected poultry, several hundred infected humans, and many human deaths.¹⁰

PREVIOUS PANDEMICS

In the 20th century, three influenza pandemics occurred worldwide: 1918-19, 1957, and 1968. All three pandemics appeared without warning, spread globally at a rapid rate, and caused illness in more than 25% of the total population. There's one other thing they had in common: all three originated in the avian population – much like the H5N1 influenza virus.

In the latter two pandemics, one to four million people each died. However, estimates from the 1918-19 “Spanish” influenza vary. Some estimate the number to be 20 million people,¹ while others gauge the loss at 40-50 million people.⁴ Mortality statistics for that time period are somewhat limited, but indicate that 25- to 29-year-olds experienced the highest mortality. More than twice as many 20- to 34-year-olds died as compared to individuals over 50.³

In 2009 another pandemic occurred, this time porcine instead of avian in origin. The response to this pandemic was a bit different than the ones of the previous century. Many local, state, national, and international organizations had beefed up preparedness for such an event and were better able to inform and advise the public. There were 100,000 people who became ill, and 400 of them died – a considerably different statistic than prior pandemics.¹² See **Figure 1**.

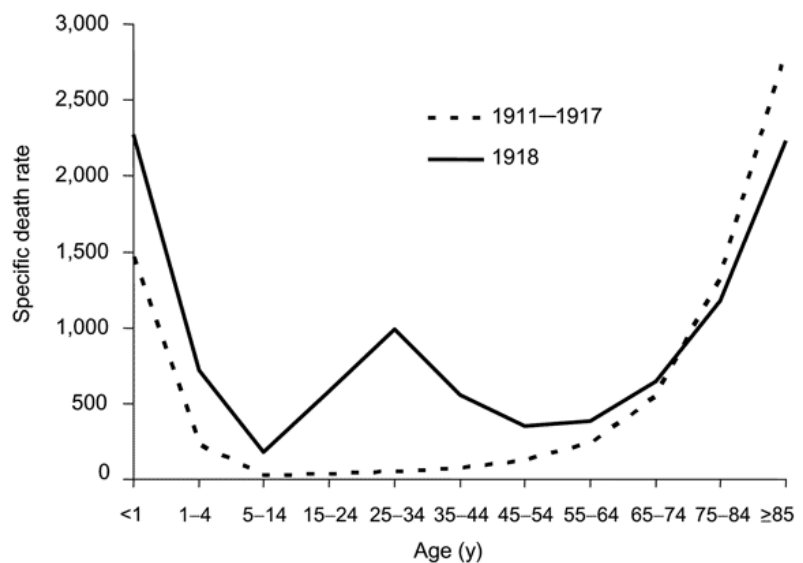


Figure 1: Death rate by age for the 1918 influenza pandemic compared to the previous seven years.

<http://wwwnc.cdc.gov/eid/article/12/1/05-0979-f2.htm>

PATHOGENESIS

Influenza viruses

Three types of influenza viruses exist: A, B, and C. Only types A and B cause seasonal epidemics in the United States – typically between October and May. All known influenza type A viruses originate from wild aquatic birds. Wild ducks, geese, swans, gulls, shorebirds and terns are the most common. However, influenza type A virus can also infect other species such as humans, birds, pigs, horses, dogs, marine mammals, and other animals.¹³

Agent

H5N1 is an RNA virus and is a subtype of the:

- species Influenza A virus
- genus Influenzavirus A
- family Orthomyxoviridae¹⁴

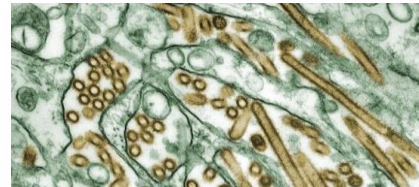


Figure 2: Transmission electron micrograph of avian influenza A H5N1 viruses (gold)

<http://phil.cdc.gov/Phil/home.asp>

Membrane proteins

Influenza type A viruses are divided into subtypes based on two proteins on the virus' surface – hemagglutinin (HA) and neuraminidase (NA). The HA is responsible for binding the virus to the cell that is being infected. The NA facilitates the release of progeny virus from the infected cells.¹³

For example, the H5N1 influenza A virus subtype that will be discussed here has an HA type 5 protein and an NA type 1 protein. With the 17 known HA subtypes and 10 known NA subtypes, many combinations of proteins are possible. There are currently only two influenza A viruses subtypes in general circulation among humans, H1N1 and H3N2.¹³

Clades

H5N1 viruses that are moving through the avian population continue to change and mutate. The result is the development of different subgroups, or 'clades,' within the H5N1 virus. Most of the clades are specific to a particular area or geographic location. Because H5N1 continues to evolve, it's extremely important to monitor its spread in the avian population in an effort to mitigate the risk of spread to humans.¹⁵

Pathogenicity designation

Avian influenza A viruses are organized into two categories: low pathogenic avian influenza (LPAI) and highly pathogenic avian influenza (HPAI). Most of the H5 viruses are LPAI. The classification is based on the molecular characteristics of the virus and their ability to cause disease.¹³

While they both can spread rapidly in poultry flocks, their outcomes may be considerably different. Poultry infected with LPAI may show mild illness such as a drop in egg production or may not show any disease at all. HPAI may result in severe disease that affects multiple organs and tends to have high mortality rates, sometimes as high as 100% with 48 hours.^{10,13} The H5N1 discussed here is considered to be HPAI.

Nomenclature

HPAI H5N1 is a general term that's used, but each isolate that is identified has a "complete" name consisting of the following:

- genus of influenza
- host species of origin (if other than human)
- geographic origin
- strain number
- last two numbers of the isolation year
- hemagglutinin protein type
- neuraminidase protein type

An example of a human strain would be A/Hong Kong/03/68(H3N2); an example of an animal strain would be A/chicken/HK/5/98(H5N1).¹⁴

TRANSMISSION AND INFECTION

Human influenza is primarily transmitted three ways: by direct contact with infected individuals; by contact with contaminated objects called fomites (such as doorknobs); and by inhalation of virus-laden aerosols. H5N1 transmission may be through similar means.¹⁶ See **Figure 3**.

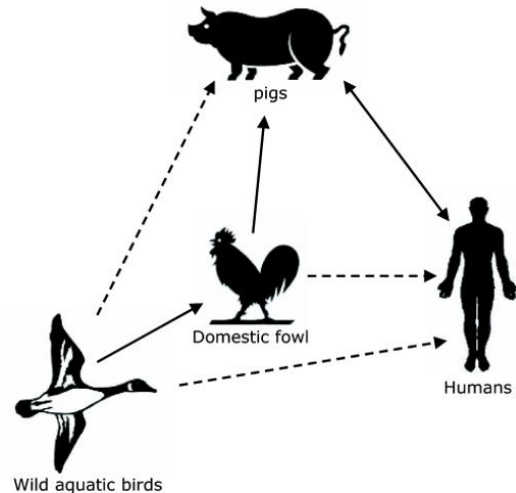


Figure 3: Transmission of H5N1

Solid lines represent frequent and/or confirmed transmission events. Dotted lines represent possible and/or occasional transmission events.
http://openi.nlm.nih.gov/detailedresult.php?img=2702078_imgm-03-158-g001&req=4

Animal to Animal

Most common transmission between animals is through saliva, nasal secretions, and feces.¹¹ Respiratory droplets larger than five microns are required for spread via aerosol.¹⁷ Other birds can pick up the virus via direct contact with these bodily excretions, or by contact with surfaces contaminated by the excretions.¹¹ Infection of other species, including mammals such as tigers, cats, dogs, or parrot, may increase the likelihood of the H5N1 more easily adapting and spreading to the human population.¹⁸

Migratory birds are one of the most common carriers of H5N1. As such, the main flight pathways of migratory birds are a potential risk factor for global spread of the avian influenza and the H5N1 virus in particular. Three of these are associated with the spread and include Northern to Southern Hemispheres, Asia to Europe, and Asia to Africa. The "hot zones" for HPAI spread correspond to these flight paths and to deltas in Bengal, Nigeria, Egypt, and Vietnam.¹⁸ However, since it was first discovered, the H5N1 virus has been slowly expanding its host range. It has also been spreading geographically within affected countries and to those previously unaffected as well. This pattern continues to repeat itself.⁴

Animal to Human

Exposure to live poultry is the primary risk factor associated with human disease; onset of symptoms usually occurs a week or so after contact. Those involved in poultry butchering, culling, or other aspects of the poultry market are typically at a higher risk of infection.¹⁶

Many people or families in areas where H5N1 is more frequent, such as Asia, live in close contact with animals. They keep small backyard free-ranging flocks where chickens and ducks congregate. They may use these animals for food, which means they're handling raw poultry. Or they may trade them informally with others, making it difficult to control the spread of the infection in the animal population.⁴

Human to Human

Though sustained human- to-human transmission of H5N1 has not yet been observed, it has occurred sporadically. Most observations have been within household clusters, with one being transmitted from child to mother. According to a 2005 World Health Organization (WHO) report, healthcare workers who did not utilize appropriate personal protective equipment when dealing with affected individuals experienced only a small risk of nosocomial infections.¹⁶

High population density can be a factor contributing to virus spread and also to its mutagenesis into more easily transmissible forms. These individuals typically live in poverty, sometimes extreme, and are not even aware of the risk factors that increase their susceptibility to H5N1 infection.⁴

Environment to Human

Virus particles are not viable for very long in dry environments: 24 to 48 hours on nonporous surfaces and less than 12 hours on porous surfaces. However, in water or in other moist environments that are protected from the sunlight, they can survive for weeks.¹⁹ This opens up other modes of H5N1 transmission, which would increase risk of infection. One possibility is water exposure leading to either oral ingestion or direct intranasal or conjunctival contact. In many places, poultry feces is commonly used as fertilizer. If it includes feces from infected poultry and is not treated prior to spreading, there is a possible risk of virus transmission.¹⁶ Fomites have been suggested as another factor in transmission of H5N1, though the role or importance have not been determined.^{14,16}

PREVENTION

Once detected in an animal population, the infected animals are destroyed, as are any animals suspected of being infected. This is the most effective means of preventing further H5N1 spread and has resulted in the slaughter of millions of birds, most of them from Asia.¹¹

Travelers to areas where H5N1 outbreaks have occurred are advised by the Centers for Disease Control and Prevention (CDC) to avoid poultry farms and animals in live food markets. In addition, they should avoid contact with surfaces contaminated by animal feces.¹¹

The U.S. bans poultry and poultry products imported from countries where H5N1 is endemic. Proper handling and preparation of poultry products and eggs will prevent infection with HPAI H5N1.¹¹

The goal is to decrease human risk to H5N1 from the avian population through infection control in poultry, communication with the animal health sector, and raise awareness among communities most prone to the infections.⁴

PANDEMIC POTENTIAL

Requirements

In order for a pandemic to occur, three things must happen. First, a new virus strain must develop that has no circulating immunity within the human population. Second, the strain must be able to replicate and cause disease in humans. And finally, the virus must be easily transmitted from person to person.¹⁸

Up to this point, the first two of the three prerequisites have occurred. The only thing lacking for an H5N1 pandemic is the ease of transmission among humans. Though it has spread between humans, there has been no indication that it is becoming naturally more transmissible to humans or from human to human.²⁰

For each human case of H5N1 infection that emerges, the odds of a deadlier strain increase as well. It could very well be a strain with a genetic makeup that is better suited to human hosts, thus increasing the potential for efficient and sustained transmission among humans and completing the third and final pandemic requirement.^{4,18}

Capacity for genetic change

Type A viruses can undergo two types of changes that could lead to emergence of a pandemic influenza strain from the avian lineage. The first is referred to as “antigenic drift” and are small changes in the virus that happen slowly and continually over time. Eventually, the body’s immune system no longer recognizes the virus and sees it as foreign.^{14,21} The H5N1 virus has changed since its emergence in 1997, and it continues to evolve through (antigenic) drifts.¹⁸

The second is referred to as “antigenic shift” and results in abrupt changes to the virus. The HA and/or NA proteins are involved in the genetic reassortment, and a new subtype results. This is what happened to cause the 2009 H1N1 pandemic.^{14,21}

Biosafety and Biosecurity

In a continuing effort to “get ahead” of an H5N1 pandemic, considerable research is being conducted. The HPAI strains such as H5N1 are considered agricultural Select Agents. Thus they require personnel and facilities to be registered with CDC or United States Department of Agriculture – Animal and Plant Health Inspection Service (USDA-APHIS) for possession, use, storage, and/or transfer in accordance with the Agricultural Bioterrorism Protection Act of 2002.¹⁴

Registered laboratories must secure the H5N1 against theft, loss, or release. Any laboratory that is unregistered and diagnoses H5N1 in a specimen must transfer or destroy that specimen within seven day of identification.¹⁴

Engineered Mutagenesis

Within the last few years, several in the scientific community have undertaken studies to understand why the H5N1 influenza virus is not easily transmissible between humans. In an effort to stay ahead of the virus, they have also been conducting research to determine whether genetic changes in the virus would increase that transmissibility. This research, however, is not without risks, and it comes with a myriad of opinions.^{22,23}

Influenza viruses that are adapted to humans have HA proteins that bind specifically to the long α 2-6 glycan receptors of epithelial cells in the human upper respiratory tract. H5N1 strains that are currently circulating do not have binding affinity for these receptors.¹⁴

However, scientists at two different institutions have made considerable progress in increasing that binding affinity. Using the ferret as the animal model for their study, both groups have engineered a form of H5N1 that does more easily pass from human to human than the H5N1 that occurs naturally. This new form was achieved with only a few genetic modifications.²⁴

Anthony Fauci, MD, is the director of the National Institute of Allergy and Infectious Diseases, and was a proponent of the moratorium. He, like the World Health Organization (WHO) and most in the scientific community, agree that conducting research to understand lab-modified H5N1 is critical and should continue – that the benefits outweigh the risk. He also believes that the concerns raised are “genuine and legitimate.”²⁴ There has, however, been considerable controversy over what to actually do with the knowledge gained from the research that’s already been conducted.²²

Because of this controversy, a group of global health and influenza experts originally placed a 60-day moratorium on research with new laboratory-modified H5N1 viruses. However, that moratorium hit the eight-month mark last October, without a proverbial light at the end of the tunnel.²⁴

There were also differing thoughts on whether the studies and their results be made available to the public. Research in the biological sciences generally has a “culture of openness.” Typically, a primary goal for those in research is to be published. Reporting the methods and results of a study allows others in the scientific community the opportunity to replicate a procedure, learn from it, and pass the knowledge along.²³

It was suggested that the H5N1 studies be published in redacted form, leaving out methods and possibly other key pieces of information. A WHO panel determined this would be impractical, that “knowledgeable scientists” would be able to determine the procedure with little difficulty.²³ The authors of the two papers did revise them to clarify some points. After that, the National Institutes of Health (NIH) endorsed the recommendation to publish the full H5N1 studies. NIH director Francis Collins, MD, PhD, along with the Department of Health and Human Services (HHS) Secretary Kathleen Sebelius, both agreed that information from this research is important to public health preparedness efforts on both the national and global levels and should be available for others to utilize.²⁵

In the May 2012 issue of *Nature*, Yoshihiro Kawaoka, DVM, PhD, of the University of Wisconsin and the University of Tokyo, reported that in as few as four mutations the surface of the H5N1 virus could be changed to promote spread among mammals. The following month, the study by Ron Fouchier, PhD, of Erasmus University in the Netherlands was published in *Science*. This research indicated that in as few as five mutations, H5N1 could become more easily transmissible.²⁴

The goal of the moratorium wasn’t to punish researchers. It was to utilize the period as a time of “cautious study” to look into some of the looming issues about H5N1 research – its safety, its benefits, its potential risks, and any other pertinent factors.²⁴

Biosafety, biocontainment, and bioterrorism are three of the concerns that have been raised during this process. What BSL conditions are adequate or appropriate for

working with H5N1? Who should be able to do research on engineered H5N1? These are only two of many questions that are of importance to both the researchers and the stakeholders. With H5N1 research being conducted in numerous locations, any course or direction taken must have global consideration. This research “pause” could be compared to the one that occurred during the time of recombinant DNA research.²⁴

In January 2013, the same group who called for the moratorium a year earlier announced that research on H5N1 transmission could move forward. This would, however, be allowed only in countries that had released guidelines pertaining to biosafety standards of such research. At that time, the United States did not have those required standards in place and therefore H5N1 studies could not resume – nor could it resume in any country that receives grant money from the United States for the project.²⁶

With the very real threat of a pandemic, continuing to study H5N1 is vital for gaining a better understanding of how the virus becomes airborne. This information could improve influenza surveillance and allow public health officials to get a jump on H5N1 mutations that are potentially dangerous and show pandemic potential. The result would be a decreased public health threat associated with H5N1.^{23,26}

Though the research has been intended for good, “we can’t ignore the small possibility it may be used for harm” says David R. Franz, a former commander in the U.S. Army Medical Research Institute of Infectious Diseases.²⁷ Franz was referring to the possibility of the misuse of information gained from H5N1 research as an intentional act of bioterrorism.^{23,27} Dr. Thomas Inglesby, a bioterrorism expert and director of the Center for Biosecurity of the University of Pittsburgh Medical Center, was one of the naysayers. “It’s just a bad idea for scientists to turn a lethal virus into a lethal and highly contagious virus. And it’s a second bad idea for them to publish how they did it so others can copy it,” says Inglesby.²⁸

Another concern is the potential for accidental release of modified H5N1. Professor Robert May from the University of Oxford expressed concerns about laboratories and said “These are not bad people, they are good people with good intentions, but they look through rose-coloured glasses at the security of the laboratories” and indicates that “it will get out” as evidenced by past history; over 1000 cases have been reported of humans being infected in labs with extremely high standards.²⁶

Yet another concern is that of “blanket secrecy.” This would result in researchers working exclusively for their own benefit. Collaboration among scientists would be hindered, information-sharing would not happen, and vital information would not be passed along to colleagues. However, in our very electronic world, it’s difficult to stop the flow of information.²⁷

CLINICAL MANIFESTATION

Incubation

The incubation period for normal seasonal influenza is approximately two to three days; for H5N1, however, it may be longer. Available information has shown an incubation period ranging from two to eight days, though up to 17 days may be possible.

WHO guidelines currently recommend using seven days as a guideline for “field investigations and monitoring patient contact.”¹⁰

Initial Symptoms

The primary initial symptom of an H5N1 infection is a fever, which is usually above 38°C. Lower respiratory symptoms are also common and manifest early in the course of the illness. Other symptoms typical of the seasonal flu may or may not be present, such as upper respiratory issues of cough and sore throat.^{11,16}

Vomiting, diarrhea, abdominal and chest pain, and bleeding from the nose and gums have also been reported. Watery diarrhea may be more common with H5N1 infection than influenza caused by human viruses, and the symptoms may appear several days prior to respiratory symptoms in an infected individual.¹⁶

Clinical course and Management

Within a few days after onset of symptoms, breathing tends to become difficult and the individual may require ventilator support.^{10,16} Pneumonia may develop, which is usually viral in origin as opposed to bacterial. Sputum production is variable, and it may or may not be bloody. In one study, it took between 3 and 17 days (average of 7) after the onset of fever for radiographs to show irregularities. The pneumonia may also progress into acute respiratory distress syndrome.¹⁶

Cytokines are hormones that aid in immune system regulation. When functioning appropriately, they help fight infections and regulate bodily processes. The H5N1 virus causes overproduction of certain cytokines, or what’s referred to as a cytokine storm. When levels of certain cytokines become too high, this leads to an inflammatory cascade response and possible damage to the body. The H5N1 virus is somewhat resistant to the “good” cytokines, but concurrently decreases production of cytokines with anti-inflammatory properties. This may lead to a toxic-shock-like syndrome, and ultimately to death.¹¹

Multiorgan involvement may result in hepatitis, renal dysfunction, neurologic signs, sepsis-like syndromes, and cardiac compromise. Laboratory findings may include leukopenia, thrombocytopenia, as well as increased aminotransferase, glucose, and creatinine levels.^{16,29}

Specimen Collection and Handling

The quality of the sample is a large determinant of the accuracy of a diagnostic test. Thus, specimen collection is critical.³⁰ The WHO has developed an eighty-page ‘guide for field operators’ that addresses all the pertinent aspects of specimen collection. It includes detailed directives for what specimens to collect and how to collect them for both suspected and contact cases. In addition, it provides instructions for how to store, aliquot, package, and ship specimens.¹⁹

Following proper procedures will allow a medical professional to safely obtain high-quality specimens, which in turn will significantly improve the prospect of a correct laboratory test result (i.e. a positive result in a patient that is truly infected with H5N1). A high-quality specimen will also increase the likelihood of detection and identification of a respiratory pathogen other than H5N1.¹⁹

Virologic diagnosis

Traditional diagnosis of influenza type A infections has been conducted in a clinical microbiology lab using cell culture or direct fluorescent antibody assays.³¹ These, however, can be time consuming, expensive, and require specialized training. They're also potentially more dangerous because of the use of viable virus. When utilizing this method, all testing should be performed in biosafety level (BSL)-3 containment to reduce the risk of exposure to laboratory personnel.^{31,32}

Not only has the H5N1 virus evolved, so have the testing methods. That progress has grown out of necessity. Over the last several years, various polymerase chain reaction (PCR) methods have gradually been replacing cell culture. PCR offers several benefits over traditional methods. It's more sensitive and doesn't require the use of live virus. It is also safer and may be handled in BSL-2 containment. Turnaround time is significantly reduced compared to traditional culture, with results being available in hours instead of days.³¹

Because of pandemic concerns, development of a rapid and reliable test that can be used on-site has been the goal. Several different test types have been produced, but the challenge and limitation has been to produce one that can detect both virus type and subtype.³¹

In 2012, a rapid antigen test was developed that met that challenge. The test has shown impressive specificity and sensitivity. It has the ability to detect all existing H5N1 strains and can do it within a few hours. And it's all in one test, which saves time and money.³²

There are a number of diagnostic tests available, and the scope is too large to investigate further for this paper. The laboratory is a vital component of diagnosis during an influenza outbreak of any kind. It can confirm a clinical diagnosis for a patient, as well as aid in research by determining genetic characterization and changes.^{19,30}

Treatment

When a case is confirmed in the laboratory, typical treatment is administration of antiviral drugs.¹⁴ Neuraminidase inhibitors, particularly when administered soon after onset of illness, have been shown to decrease the risk of pneumonia, decrease mortality, and decrease hospitalization considerably.²¹ Oseltamivir, marketed as Tamiflu[®], is the primary recommended antiviral treatment; zanamivir, marketed as Relenza[®], is another. Dosage and administration is on a case-by-case basis and considers other comorbidities experienced by the patient.¹⁴

CURRENT H5N1 SITUATION

The WHO provides a monthly update for H5N1 infections. Between 2003 and February 15th of this year, there have been 620 cases of human H5N1 infections. This was an increase of 10 cases from the previous month. A case is defined as one that has been confirmed positive in the laboratory. The 620 cases have occurred in 15 countries, and 367 (or 59%) have died.^{33,34}

IMPACTS

Public Health

Unlike seasonal flu infections, the case fatality ratio (CFR) for those infected with H5N1 is considerably high.^{10,16} In the first outbreak in Hong Kong, the mortality rate was 33%, or six deaths out of the 18 cases reported. The ages ranged from one to 60 years old, with illness being more severe in those greater than age twelve. Fifty-one household contacts were discovered, most with a history of exposure to poultry. 9 In the 2004-2005 outbreaks, however, the rate was as high as 100% in certain areas; the average was about 60%.²⁹ See Table 1.

Another difference between seasonal flu and H5N1 infections is the age of those affected. Children and young adults tend to be more susceptible to the virus. It's hypothesized that older people have most likely been infected with a human influenza A virus at some point in their lives, may provide them with some immunity. Though the previous influenza A exposure would not prevent the individual from becoming infected with H5N1, it could decrease the severity of infection.³⁵

	2003-2009	2010	2011	2012	2013*	Total
Cases	468	48	62	32	10	620
Deaths	282	24	34	20	7	367
CFR	60%	50%	55%	63%	70%	59%

CFR = Case Fatality Ratio

Source: WHO/GIP
*Data as of February 15, 2013

The median age for all confirmed H5N1 cases between 2003 and 2009 was 19. In 2010 there were 48 human cases of H5N1 diagnosed in individuals ranging in age from one to 59 years. Forty of those, or 83%, were less than 40 years old, with a median age of 25 years. Though the CFR differed by country in 2010, overall half of those diagnosed with the infection died. In fact, when all cases between 2003 and 2010 are considered, those <20 years old had a considerably lower risk of death than those >20 years old (52% versus 66%).³⁶ In a 2008 epidemiological report of 340 confirmed H5N1 cases, the WHO indicated that 90% of the infections occurred in individuals less than 40 years old.¹⁶

Some believe that the CFR numbers that have been published are too high and there are several missed cases. The belief is that more individuals have actually been infected, but the symptoms were not severe enough to seek treatment and the infection did not progress into a full-blown case. This conclusion is based on a analysis of seroprevalence studies performed on populations that have been exposed to H5N1. Wang and colleagues believe the infection rate could be 1% to 2%, which they believe translates into millions of infections globally. Others flu experts disagree, and the debate continues.³⁷

Trade/economic

"A pandemic would have significant implications for the economy, national security, the national healthcare system, and the basic functioning of society," according to the Department of Homeland Security's (DHS) *Pandemic Influenza: Best Practices and Model Protocols*.³⁸ While morbidity and mortality will be high during a pandemic, an

H5N1 influenza pandemic could prove to be economically disastrous as well. Losses would result through direct, indirect, or other means.⁴

In the United States alone, the estimated economic impact is between \$71.3 and \$166.5 billion.³⁹ For the countries where H5N1 is endemic, such as some in Asia, direct costs are probably the most significant source of loss.⁸ Animals either die because they are infected, or are culled in order to stem the spread. This has the potential to significantly compromise the livelihood of those involved.³⁸ The impacts are bi-directional and seen both in the input and distribution channels, including breeding farms, feed mills, and with poultry traders.⁸ The loss of income from poultry trade could severely impact the government's financial situation. It's seen not just at the local or national levels, but in international trade as well.¹⁰ Consumers may become wary of poultry for fear of potential infection, causing a downward trend in poultry consumption altogether.²

National and international trade of livestock and poultry has been a considerable source of economic growth for the countries where H5N1 is now endemic. In 2006, the Southeast Asia economies accounted for one-fourth of the global poultry trade. Because of the H5N1 outbreaks there, importers of poultry have decreased the quantity received from the affected countries and instead have chosen other suppliers such as the United States or Brazil. Global prices have risen, due in part to the fact that Southeast Asia's comparative advantage is not nearly as great as it once was. A country with a reputation for "diseased products" may see a backlash with regard to the exportation of other important products as well.²

Whether it's by choice or by government-sanctioned trade barriers due to health and safety concerns, the result can be in an uncertain future for trade and ultimately for a nation's Gross Domestic Product (GDP). When a country can't export a major product such as poultry, the non-diseased poultry stays in the country and is sold domestically at a lower price.²

During the 2003 H5N1 outbreak over 150 million birds died or were destroyed, with an economic impact estimated at \$8 – \$12 billion.⁴ It's estimated that a one-year-long pandemic could cause a loss as high as \$800 billion of global GDP. The "Spanish" influenza of 1918 came in three waves and occurred over two years.⁸

As the H5N1 animal outbreaks have gradually advanced away from the point of origin in developing countries, other developed countries are keeping a keen eye out. There exists for them the utmost concern of an epidemic within their own borders, which might lead to economic stresses for them as well. Even though developed countries may have more resources and technology to deal with an outbreak, they will still incur social and economic costs because of a pandemic. And in the back of the minds of most is the concern previously discussed – of the strain undergoing mutagenesis and becoming more easily transmissible among humans.²

Indirect costs may also be factors in economic losses. If travel restrictions are put in place in a country because of a pandemic, H5N1 or otherwise, the result would be a decline in international tourism – and a concurrent decrease in revenue because of it.⁸

Other costs involved include those for prevention, control, and laboratory testing of products. The government will incur additional costs for vaccines, medications, personnel for culling and cleanup, surveillance and diagnostics, and a host of other factors. Compensation to farmers with infected poultry must also be a consideration.

This gives the farmers an incentive to report an outbreak and not attempt to conceal infected birds. It can, however, pose a financial strain on a government.^{2,8} Though the short-run cost of containing an H5N1 outbreak may be enormous, affected countries still agree that this is a better scenario than dealing with the financial implications for a lengthier period of time.²

Infrastructure

The functioning of critical infrastructure may be in danger as well. In the event of a pandemic, workers will be absent across many sectors due to personal illness or illness in family members. If an individual is not sick, there is the fear or concern of infection, which may lead to changes in routine. Depending on the severity, public health directives, quarantines, or restrictions may be given in an effort to minimize contact with others.²

The service sector may suffer considerably during a pandemic when individuals are trying to avoid becoming infected. The movement of goods and services may be delayed or stalled completely if there's a shortage of healthy workers. The operation of schools and universities will also be impacted at all levels.⁸

An additional area of concern will be that of public service responders. With an anticipated 30-40% of the workforce out due to illness, the challenge will be to adequately care for those in need. Under normal circumstances, when responders in one area or community are overwhelmed, they may ask for assistance from another area or community. This, however, will not be applicable during a pandemic since the relief area will also be dealing with similar losses and issues. Therefore it's particularly important that public service sectors coordinate with each other and conduct proper training.³⁸

The healthcare sector will be inundated as well. Hospitals will be up to or even above capacity trying to serve the worst of the infected, which will include the immunocompromised or those with other co-morbidities. Those who are ill but not sick enough to need hospital care will most likely visit their general practitioner, possibly more than once. Staffing issues will play a role here, just as in any other sector of the infrastructure, raising the question of whether the medical facilities will be able to adequately meet the demand.⁴⁰

While the service sector aspect is vital, the business, individual, family, and community impacts must be addressed as well. Prioritization of services and of prophylaxis allocation during a pandemic may create feelings of inequality as some may question why others are being taken care of first.³⁸

Telecommunications may be affected as those unable to move from their location try to make contact with other friends and loved ones. Many will utilize electronic resources in search of information and updates.³⁸

INTERNATIONAL LEVEL PREPAREDNESS MEASURES

WORLD HEALTH ORGANIZATION

The WHO plays a central role among the many international organizations that contribute to global preparations against pandemic influenza. This includes disease

surveillance, which requires constant information-gathering over its entire six regions. It coordinates with other agencies to share information and organize activities. It also plays a role as an advocate with national authorities for the establishment of cost-effective public health measures. These may include communication and information-sharing, education, human resources, capacity building, or coordinating technical support. This enhances collaboration among countries and across the six regions that comprise the WHO.⁴

In 1999, the WHO published the Influenza Pandemic Plan, the goal of which was to help its Member States become better prepared to respond to future threats of pandemic influenza. The guidelines have been updated twice since then and are now called the Regional Pandemic Preparedness Plan. The WHO plan addresses detection, verification, diagnosis, surveillance, response, antiviral stockpiles, facility surge capacity, and information management.⁹ WHO also prepared and made available a checklist and other guidelines to serve as a framework for pandemic preparedness planning.⁴¹

The WHO has defined pandemic stages in an effort to provide a common framework for preparedness and planning efforts on local, regional, state, national, and international levels.¹⁸ See **Table 2**.

Table 2: Summary of WHO Global Pandemic Phases		
Phase		Definition
Inter-pandemic period	1	No new influenza virus subtypes have been detected in humans. An influenza virus subtype that has caused human infection may be present in animals. If present in animals, the risk of human infection is considered to be low.
	2	No new influenza virus subtypes have been detected in humans. However, a circulating animal influenza virus subtype poses a substantial risk of human disease
Pandemic alert period	3	Human infection(s) with a new subtype, but no human-to-human spread, or at most rare instances of spread to a close contact.
	4	Small cluster(s) with limited human-to-human transmission but spread is highly localized, suggesting that the virus is not well adapted to humans.
	5	Larger cluster(s) but human-to-human spread still localized, suggesting that the virus is becoming increasingly better adapted to humans, but may not yet be fully transmissible (substantial pandemic risk).
Pandemic period	6	Pandemic: increased and sustained transmission in general population.
Post-pandemic period		Return to the Interpandemic period (Phase 1)

<http://www.dhhs.gov/pandemicflu/plan/pdf/AppC.pdf>

The pre-pandemic phase would focus on strengthening the early warning system and looking for ways to decrease the chance of human infection. The next phase would include early use of antivirals to help contain or delay the spread of the virus at the source. When an episode is declared a pandemic and has spread internationally, efforts would focus on decreasing morbidity, mortality, and “social disruption.”⁴ When Phase 4 is reached and sustained transmissions are noted, additional measures must be taken. One action is deployment of stockpiled antiviral drugs. Non

pharmaceutical measures may include the following: movement restrictions, social distancing, isolation, or quarantine.¹⁸

An example of the use of the alert phase system is the 2009 pandemic. On April 27th 2009, the WHO increased the pandemic phase alert from Phase 3 to 4. Just two days later it was increased another level to Phase 5. Less than six weeks later, it was raised yet again to Phase 6, at which time the first pandemic of the 21st century was declared. Though the culprit at that time was the H1N1 swine influenza, the reality is that the same thing could happen with the H5N1 avian influenza.⁴²

The WHO has also developed a Pandemic Severity Index (PSI) to categorize the severity of a pandemic. It's based on case fatality ratio and provides a framework for integration of non-pharmaceutical intervention and implementation. The PSI lists interventions by setting – home, school, and workplace/community. It provides individuals in those settings with a guide for recommended actions based on the index level. These include isolation and treatment, voluntary home quarantine, dismissal of students from public and/or private institutions, and use of social distancing.⁴³

In 2011, the WHO published a comparative analysis of national pandemic influenza preparedness plans. They evaluated publicly available plans that were in place for 119 countries at the emergence of the 2009 influenza pandemic. A checklist based on the guidelines mentioned above was constructed to assess 88 key indicators. Positive key findings included the following:

- Most WHO member states have a plan
- Most had formed a planning committee and designated agency response coordination
- Most addressed all pandemic phases and data collection/exchange
- Most addressed the use of antiviral drugs and vaccines, with the majority designating priority groups to receive them.
- Most addressed communication methods to keep non-health authorities and the public informed.
- Most identified laboratories for virus identification and further characterization.

Other factors that may be cause for concern included the following:

- Over half of the plans were developed based exclusively on an H5N1 pandemic. Most should be generic and applicable to any pandemic.
- Planning detail was lacking in some areas. Crucial elements should be identified.
- Disparities were found among countries by region, gross national income, and level of health. Ideally plans would cover all of those equally.
- Lack of integration (or sub-national level planning) was apparent. Plans should be integrated into the national disaster plan.⁴¹

There are hurdles to implementing a regional preparedness plan. Two of the primary ones are financial and technical limitations. Once a plan is implemented, experience, response in other countries, or scientific advancement may prompt adjustments and adaptations to strategies.⁴ Several WHO programs aid in surveillance and preparedness for pandemic influenza.

The Global Influenza Surveillance and Response System (GISRS)

GISRS, which prior to 2011 was known as the Global Influenza Surveillance Network, has been in use by WHO for over 50 years. It is the international network of influenza laboratories which provides continual influenza surveillance. They aid in assessment of risk as well as preparedness for pandemic influenza. The GISRS has four primary components, listed below, along with their basic function.

- National Influenza Centres (NIC) – The backbone of the GISRS. There are four in the United States, and 140 throughout the world. The NICs perform preliminary testing on specimens from their own country, then send them to the WHO for further classification. This information helps determine the composition for the influenza vaccine each year.⁴⁴
- H5 Reference Laboratories (H5RL) – Laboratories created specifically for GISRS to address the public health concern resulting from H5N1 infection in humans. The goal is to improve diagnosis reliability at the national and regional levels until more laboratories have testing capability.⁴⁵
- Collaborating Centres on Influenza (CC) – Key institutions with “relevant expertise.” They have a formal partnership with WHO, and have more global responsibility and technical capacities than NIC or H5RL.⁴⁵ There are over 800 CC in over 80 WHO Member States.⁴⁴
- Essential Regulatory Laboratories – Associated with national regulatory agencies. They play a significant role in development, regulation, and standardization of human influenza vaccines.⁴⁵

Pandemic Influenza Preparedness (PIP) Framework

The process for this framework was initiated in 2007 and became effective May 2011. It brought together WHO Member States, institutions, organizations, and industry to address pandemic influenza preparedness on a global level.⁴⁵

It does that two ways: first by facilitating among stakeholders the sharing of influenza viruses with pandemic potential, and second by increasing the stakeholders’ access to pandemic influenza vaccines. This benefit-sharing system aids in the overarching goal of strengthening the WHO GISRS previously discussed.⁴⁵ Though the WHO is the organization with “international legal mandate,” it does not facilitate the development of response capacity on an international level. This responsibility is left up to the Member States. Therefore, the United States has put programs in place at the national level for dealing with pandemic influenza.⁴

FluNet

Influenza virological surveillance is conducted through a program called FluNet. The information entered, such as virus subtype, provides epidemiological data and helps to track the virus globally. The information is available to the public online and in real-time and may be accessed in a variety of formats. A newer program, FluID, combines regional epidemiological data into a single global database and complements the FluNet program.⁴⁴

Vaccines and Antivirals

In May 2006, the WHO organized a group to prepare a Global Action Plan (GAP), with the goal of decreasing the gap between the potential vaccine supply and demand. It included three primary approaches:

- Increase in seasonal vaccine use
- Increase in vaccine production capacity
- Research and development⁴⁶

Only 46% of the WHO Member States were incorporating seasonal influenza vaccination into their national immunization programs in 2010.⁴⁷

GAP has spurred a significant increase in influenza vaccine manufacturing. Global production capacity nearly tripled to over 900 million doses within three years of the program's inception. The goal is 1.7 billion doses by the year 2015. With improvements in technology, such as live attenuated vaccines and adjuvants, even more doses are possible.⁴⁷

However, the 2009 H1N1 pandemic proved that production increase alone was not enough. Developed countries received vaccine much sooner than developing countries – if they received any at all. This disparity indicated that gaps still existed in availability and distribution.⁴⁷

Eleven manufacturers in low- and middle-income countries have received seed funding from the WHO for influenza vaccine production. These grants do have a requirement; the manufacturer must sell 10% of their vaccine production at an “affordable price” to United Nations agencies for distribution in countries that are not able to produce vaccine.⁴⁷

In the event of a pandemic, antivirals may be used in the initial response for treatment and prophylaxis of exposed individuals. As such, the WHO has included this consideration in its protocol for “rapid response and containment.” It maintains a stockpile of five million treatment courses of Tamiflu[®], which was donated by Roche. These doses will be used for targeted antiviral prophylaxis for known case contacts. They may also be directed toward mass antiviral prophylaxis for nearby or at-risk populations.⁴² The goal of the US federal pandemic influenza plan is to stockpile enough antivirals to treat about 25% of the US population.²¹

WORLD ORGANISATION FOR ANIMAL HEALTH (OIE)

Though this paper's primary focus is the impact of H5N1 on humans and the preparedness at different levels, there is a priority placed on curbing avian influenza at the source. Surveillance, control, and mitigation strategies facilitate this goal. A speedy detection in poultry, with rapid culling of the exposed and infected animals, can considerably decrease the chance of an outbreak. If surveillance on the human side also detects cases quickly and treatment/containment measures are put in place, it's quite possible that the pandemic could be averted altogether.^{4,8}

The OIE works to improve the health of animals at the global level, in part by preparing and publishing international animal health standards. Part of this task also includes fighting animal diseases. When any of the 178 Member Countries of OIE detects an animal disease in its area, it agrees to report this information. The information is shared with other members in an effort to promote transparency and

prevent an outbreak elsewhere. Members access information through the OIE's web interface – World Animal Health Information Systems.⁴⁸

The OIE also gathers and distributes scientific information pertinent to disease control and eradication in animals. In addition, they offer technical assistance to Member Countries and provide expertise to poorer nations to decrease loss of livestock and promote public health. They also provide training for the Veterinary Services section.⁴⁸

OIE and the Food and Agricultural Organization of the United Nations (FAO) have joined forces to specifically reduce risks to animal and public health from animal influenza viruses. The program is called OFFLU and is somewhat similar to the PIP that is administered by WHO. It promotes sharing of scientific data within the network, and also of biological materials such as virus strains.⁴⁸

The Crisis Management Centre – Animal Health was developed by the OIE in response to the rapid spread of HPAI H5N1. It provides speedy technical advice and support to countries experiencing an immediate animal health crisis. Upon request, an expert team is sent to the area to provide guidance. This group collaborates extensively with the WHO.⁴⁸

The laboratory structure of the OIE is similar in nature to that of the WHO. There are 236 Reference Laboratories in 37 countries, each functioning as a world reference center of expertise on specific diseases or pathogens. There are 41 Collaborating Centres in 22 countries that primarily provide research, expertise, technique standardization, and dissemination of information on specific diseases or pathogens. Eight of the reference laboratories have expertise in HPAI, one of which is in Ames, IA.⁴⁸

OIE, along with WHO and the FAO, promote in a concept called One Health. Sixty percent of pathogens that cause disease in humans originate in animals. The goal of One Health is to prevent and control zoonotic pathogens and other diseases at the level of the animal, thus protecting human health.⁴⁹ To facilitate this, the OIE *Terrestrial Animal Health Code* dictates that two subtypes of avian influenza must be reported to the OIE: H5 and H7.⁵⁰

GLOBAL EARLY WARNING SYSTEM FOR MAJOR ANIMAL DISEASES (GLEWS)

This program combines the disease surveillance and intelligence methods of three major international organizations - the OIE, FAO, and WHO. Combining the alert mechanisms of these organizations prevents duplication of efforts and benefits the entire international community because animal diseases can be better predicted, prevented, and controlled. The belief with the GLEWS system is that dealing with an animal health issue early in its development is better than doing so after it has spread and caused considerable economic problems. Collaboration leads to a comprehensive analysis of a situation and allows joint dissemination of information.⁵¹

NATIONAL LEVEL PREPAREDNESS MEASURES

U.S. DEPARTMENT OF HOMELAND SECURITY (DHS)

The Federal Emergency Management Agency (FEMA) is part of the DHS. FEMA is responsible for coordination of the federal government in “preparing for, preventing,

mitigating the effects of, responding to, and recovering from all domestic disasters, whether natural or man-made, including acts of terror.” Pandemic influenza would fall into these categories.⁵²

Part of this includes the National Response Framework (NRF), which is a guide to how the U.S. conducts all-hazards response at all levels – from the smallest incident to the largest disaster. There are five key principles upon which the NRF is based:

- Engaged partnership – Communication and support between leaders at all levels is required so no one becomes overwhelmed.
- Tiered response – Incidents are managed at the lowest level, with additional support given when needed.
- Scalable, flexible, and adaptable – Operations capabilities must be able to change in size, scope, and complexity as an incident changes.
- Unity of effort – A clear understanding of roles and responsibilities is possible through the Incident Command System.
- Readiness to act – Balancing the risk with the instinct and ability to act is part of an effective response.⁵³

The National Incident Management System is a companion document to the NRF that enables Federal, State, tribal, and local governments, as well as the private sector and non-governmental organizations to work together to complete the mission of FEMA and the DHS.⁵³

The DHS also has a plan specific to pandemic influenza on the national level. It delineates the basic roles for emergency and public service organizations, with specific sections addressing mitigation, preparedness, response, and recovery for each.³⁸

CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)

The CDC is a federal agency that works under HHS. It is recognized as the lead federal agency for protecting the health and safety of people in the United States. It works with state health departments and other organizations to identify potential health or disease issues and control the spread of infectious diseases and to promote healthy decision-making. The CDC also conducts epidemiological and laboratory surveillance such as that for H5N1 avian influenza.⁵⁴ Several programs within the CDC aid in accomplishing these goals with respect to H5N1 avian influenza.

Genetic Changes inventory

Since the discovery of H5N1 in humans in 1997, the virus has continued to evolve and undergo genetic change. Some of those genetic changes may increase the likelihood that it will develop into a form that’s more easily transmissible in humans. Early detection of these changes leads to improved surveillance and ultimately better pandemic preparedness.⁵⁵

CDC researchers and other international influenza experts collaborated to compile the H5N1 Genetic Changes Inventory to catalogue known HPAI H5N1 genetic changes.²⁰ It is a molecular-based surveillance tool that uses changes in amino acid sequence of the viral protein. It helps those conducting influenza surveillance and research to identify specific mutations that may threaten or have an impact on human health. It may also be beneficial in determining if the susceptibility to existing antiviral drugs has changed, possibly indicating adaptation to mammalian species. If research

or surveillance identifies a H5N1 virus with “mutations of concern,” it is submitted to a WHO CC or WHO H5RL for characterization and assessment of risk.⁵⁵

Laboratory Response Network

In the late 1990s, there was considerable concern about the ability of the nation’s laboratories to adequately deal with threats from biological or chemical agents in a timely manner. Turn-around-time was catalogued in days, not hours, because traditional culture methods were still in use. Most state and local labs did not have the capability for rapid molecular testing.⁵⁶

This led CDC’s HHS to start the Laboratory Response Network (LRN) in an effort to improve the nation’s laboratory capacity. Since its inception in 1999, many labs have been able to renovate facilities to comply with safety and containment regulations, purchase state-of-the-art analytical equipment, and hire and train additional staff. As of April 2012, there were 157 labs in the LRN from all 50 states, as well as Canada, the United Kingdom, Australia, Mexico, and South Korea.⁵⁶

The goal of the LRN is to provide quick detection of a disease outbreak to enable a rapid local response. Locating facilities near densely populated areas helps LRN accomplish this; 87% of the U.S. population is located within 100 miles of an LRN laboratory. If the LRN does not perform a test or reaches test capacity, it will transfer the specimen to a partner lab with the appropriate capabilities.⁵⁶

The LRN consists of laboratories from several different sectors: federal, state and local public health, environmental, military, veterinary, food testing, and international. LRN played an integral role in validation of an H5N1 assay and reagent kit. The FDA facilitated a speedy approval of the *in vitro* diagnostic test and made it publicly available in 2006. This provided a low-cost, high-confidence H5N1 surveillance and detection tool.⁵⁶

The LRN and the DHS have joined forces with the Environmental Protection Agency on an environmental surveillance program called BioWatch. In this program, air samplers monitor large, densely-populated areas across the U.S. on a 24-hour basis. Samples obtained through the BioWatch program are sent to LRN laboratories and analyzed for multiple agents that are considered threats.⁵⁶

The Division of Notifiable Diseases and Healthcare Information (DNDHI)

DNDHI is in CDC’s Public Health Surveillance and Informatics Program Office; Office of Surveillance, Epidemiology, and Laboratory Services. It plays a key role in public health surveillance through science and cooperation among organizations. It collaborates with other CDC programs, state and local health departments, and other partners to provide a picture of what’s happening on the regional and national levels for public health issues. It has also been instrumental in developing standards for syndromic data surveillance and helping states to implement electronic health records (EHR). In addition, the DNDHI maintains a list of nationally notifiable conditions and case definitions.⁹ A notifiable disease is any disease that is required by law to be reported to state and/or local health departments.⁵⁷

BioSense is a syndromic surveillance tool, which is a system for collecting and analyzing medical data to detect and monitor disease outbreaks and harmful effects of

exposures to hazardous conditions.^{9,58} The latest version, BioSense 2.0, launched in November of 2011. This program allows health officials to track any health issue anywhere in the United States. It combines health data from the local and state levels to provide a “near real time” view of what’s going on nationally with all health hazards or concerns.⁹

BioSense 2.0 uses multiple sources to gather information on emergency department visits and hospitalizations. These sources include the Department of Veterans Affairs, the Department of Defense, over 100 hospitals that report to the CDC, and emergency department monitoring data provided by some state or local health departments. All of this information better enables our health care officials to make decisions and prepare and organize responses. It simplifies data collection, storage, and sharing, thus saving health departments time and money. The technology also allows health departments to keep up with the latest advances in electronic health records.⁹

The *National Notifiable Diseases Surveillance System* (NNDSS) is another tool used by CDC and is administered by the DNDHI. Through this comprehensive program, health departments at the tribal, territorial, local, and state levels collect, manage, and monitor information about specific diseases or conditions in their areas and voluntarily share a portion of it with the CDC. Epidemiologists then compile, analyze, interpret, and disseminate valuable health-related information.^{57,58}

The NNDSS helps to determine which diseases or conditions should be notifiable, and provides statistics on these diseases and conditions. It enables epidemiologists and others to define what a case is for these notifiable diseases and conditions, and enables more consistent reporting across states. The NNDSS: collects data from 57 state, territorial, and local reporting jurisdictions each week and uses the data to identify disease trends; monitors infectious disease morbidity for reportable diseases; and publishes national health trends and data in the *Morbidity and Mortality Weekly Report*.⁵⁷

This information is used to identify high-risk populations or geographic areas to determine what programs may need to be implemented, and to assess prevention and control programs that are already in place. This ultimately aids in prevention and containment strategies on the national and global levels, and contributes to public health policy development.⁵⁷

The National Electronic Disease Surveillance System (NEDDS) is an integral part of the NNDSS. It provides the information technology standards and support so the tribal, territorial, local, and state agencies have a means to efficiently and securely manage and share data with CDC and other health agencies. NEDDS uses healthcare industry standards to ensure that health information data are integrated into a single location and consistently transmitted between healthcare providers and the health departments using. It also defines the content of the data messages sent (such as disease diagnosis, patient demographics, or laboratory results). Every state is adopting or is already using a NEDSS-compatible system to transmit case notifications to NNDSS.⁵⁷

Strategic National Stockpile (SNS)

In 1999, at the direction of Congress, HHS and CDC established the SNS. In the event of a large-scale natural disaster or an act of terrorism, local and state supplies will be used quickly. The SNS ensures that sufficient quantities of medical supplies and pharmaceuticals will be readily and rapidly available. When an emergency occurs, a state's governor (or office) must request assistance. When federal authorities deem use of the NPS necessary, the "Push Package" of supplies is provided to the state within 12 hours of the declaration. States and localities have their own procedures for how the supplies and pharmaceuticals are dispensed.⁵⁹

Supplies in the SNS program undergo quality assurance and quality control checks on a regular basis to ensure efficacy. HHS and CDC take many things into consideration when deciding what supplies and pharmaceuticals should be included in the NPS.⁵⁹

Vaccines and Antivirals

Depending on the period (Interpandemic, Pandemic Alert, and Pandemic), HHS agencies and state and local health departments have different roles and responsibilities.

During the Interpandemic and Pandemic Alert Periods, state and local health departments should work to increase seasonal influenza vaccination to potentially enhance protection against a pandemic strain. This may foster public confidence and allows the public to become more familiar with the vaccination process should it be necessary during a pandemic. Pneumococcal vaccination is also recommended – usually for those who are eligible for an influenza vaccine. This may decrease the likelihood of secondary bacterial infection during a pandemic.²¹

When the Pandemic Period is reached, several things happen. If stockpiled vaccine of the pandemic subtype is available, these doses would be administered to designated groups. It would take approximately four to six months for a monovalent vaccine directed against the circulating strain to be developed and put into production. HHS would direct manufacturers to shift from seasonal to pandemic influenza vaccine production and maintain highest production capacity.²¹

When a strain-specific vaccine is available, manufacturers will distribute directly to the states. Organizations will be identified to administer the vaccine to priority groups. Priority groups are those whose functions are essential to maintain continuity of operations. Per HHS guidelines, state, local, and tribal plans should be developed to determine priority groups and how they will be identified, as well as plans for delivering vaccines (and antivirals) to these groups. HHS has provided vaccine priority group recommendations, which is divided into tier and sub-tier categories.²¹

Topping the HHS list are the vaccine and antiviral manufacturers and others essential to manufacturing – about 40,000 according to HHS estimates. The rationale behind this is that vaccines containing the circulating H5N1 virus strain will not be readily available at the onset of a pandemic. Thus the manufacturing sector will need to be ready to operate at full production when that time arrives.²¹

Also included in the top tier/sub-tier are medical/public health workers and others who are involved in direct patient care/contact – about 8.9 million people. These individuals are needed to provide care to others who will be affected. As many as

possible will be needed because facilities will be at or above capacity. The remainder of the list is divided according to morbidity and mortality risk, workforce need, and critical infrastructure need. Depending on the situation and disease epidemiology, however, these may require adjustment.²¹

It's likely that a vaccine against pandemic influenza will require two doses since most individuals have never been exposed to the specific strain. The first dose would prime the system while the second dose provides the actual protection. They're usually administered about a month apart. It's also important for state and local health departments to develop a system to report and investigate adverse reactions attributed to immunization.²¹

As with the vaccines, HHS has also prepared recommendation for antiviral drug priority groups. The rationale, however, is a bit different. With the vaccines, tiers and sub-tiers lower down the recommendation list would receive vaccine as more is produced. For antiviral drugs, the amount of drug that is stockpiled would be known, so health planners would know at the onset of the pandemic how many priority groups would be covered.²¹

ANIMAL AND PLANT HEALTH INSPECTION SERVICE (APHIS)

The organization within the United States responsible for coordination of efforts on the animal side is APHIS. Established in 1972, APHIS is a part of the United States Department of Agriculture. Its efforts are concentrated on preventing the introduction of foreign pests and diseases and promoting U.S. agriculture. Several things work together to help make that happen.⁶⁰

HPAI Response Plan - In September 2012, USDA-APHIS published an updated version of the Foreign Animal Disease Preparedness and Response Plan (FAD PReP) – *Highly Pathogenic Avian Influenza (HPAI) Response Plan: The Red Book*. It provides strategic guidance for responding to an animal health emergency caused by HPAI in the U.S.⁶¹

Though HPAI has previously been detected in poultry in the U.S., there is currently no evidence that it is here now. As mentioned previously, however, it is endemic in other parts of the world. In the event of an HPAI outbreak in the U.S. (such as from H5N1), the goals of the HPAI Response Plan are three-fold. First, to detect, control and contain infection in the poultry population. Second, to eradicate HPAI while maintaining public health as well as the welfare of the economy, animal health, and the food supply. And third, to promote continuity of operations for animals and their products that are not infected.⁶¹

National Poultry Improvement Plan (NPIP)

NPIP is a national program in collaboration with state and federal departments of agriculture and industry representatives. It was initially originated to eliminate Pullorum Disease caused by *Salmonella pullorum*. It has since been expanded to cover other poultry diseases of concern, including Avian Influenza. The main objective of this program is to use new diagnostic technology to effectively improve poultry and poultry products throughout the United States. NPIP provides certification that poultry and poultry products destined for interstate and international shipments are disease free.⁶²

National Animal Health Laboratory Network (NAHLN)

NAHLN is comprised of laboratories that use common testing methods and software to complete diagnostic testing and share information. It's a collaborative effort between APHIS, the National Institute of Food and Agriculture, and the American Association of Veterinary Laboratory Diagnosticians. The state and university laboratories in the NAHLN perform routine diagnostic testing, conduct targeted surveillance, and develop new assays. As of March 2013, there were 60 NAHLN laboratories across the U.S. Only one is located in Virginia – the Harrisonburg Regional Laboratory – but it does not perform avian influenza testing.^{60,63}

National Veterinary Services Laboratory (NVSL)

NVSL is operated by the USDA and has two locations in the U.S. Its Ames, IA location is an OIE reference laboratory for identifying and confirming HPAI. It is the national veterinary diagnostic reference and confirmatory laboratory on the federal level. The NVSL plays a significant role in training, proficiency testing, and method validation for diagnostic testing.⁶¹

These laboratories are the early-indicators for a disease outbreak. They have the capacity to rapidly analyze a large number of specimens. Their infrastructure resources in terms of facilities, equipment, and personnel enable them to provide necessary surveillance before, during, and after an outbreak.⁶¹

STATE AND LOCAL PREPAREDNESS MEASURES

STATE

The Commonwealth of Virginia Emergency Operations Plan (COVEOP) provides the framework and structure for overall emergency management in Virginia. It's the coordination plan needed to provide state assistance to local governments, businesses, and individuals impacted by an emergency situation. COVEOP is comprised of the following:

- a basic plan and appendices
- a section of 17 emergency support functions, which includes definition of roles and responsibilities for lead and support agencies
- support annexes
- hazard-specific annexes (two of which are secure).⁶⁴

COVEOP works in coordination with the FEMA's NRF to enable Virginia to receive disaster assistance from the federal government. It ultimately improves Virginia's ability to respond to and recover from disasters – whether from human-caused or natural sources.⁶⁴

Virginia has a Continuity of Operations Plan (COOP) that identifies “mission essential” functions for the state in the event of an emergency or disaster. Local governments have their own COOP as well in order to maintain their readiness. Virginia's Department of Emergency Management website also provides guides, plans,

and templates that can be used for hazard preparedness, response, and mitigation (<http://www.vaemergency.gov/em/plans>).^{65,66} This includes a Pandemic Influenza Annex manual, worksheet, and templates that will enable the organization to be better prepared to manage limited human resources during such an event.⁶⁶

LOCAL

After 9/11, grants were given to ramp up emergency preparedness. The Office of Emergency Preparedness was developed for each of the 35 health districts within Virginia. See **Figure 4**. It put in place the following for each district:

- an epidemiologist – to concentrate on disease aspects
- an emergency planner – for logistics and implementation.⁶⁷

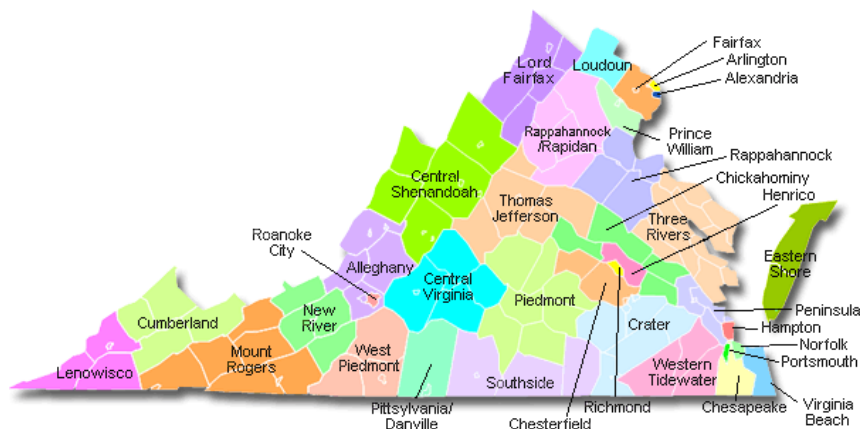


Figure 4: Health Districts in Virginia

<http://www.vahealth.org/dcn/General%20Info/map.htm>

There are five jurisdictions within the New River Health District

(NRHD): the counties of Pulaski, Montgomery, Floyd and Giles, as well as Radford City. Each jurisdiction has its own health department. The NRHD, along with three other planning districts, comprise the Near Southwest Region in Virginia.⁶⁷

Paige Bordwine, MT(ASCP), MPH, is the NRHD Epidemiologist. H. David Linkous is the NRHD Emergency Planner. Both Bordwine and Linkous work out of the district office at the Montgomery County Health Department (MCHD) in Christiansburg, VA. I spoke with each of them about pandemic influenza preparedness.^{40,67}

The Office of Emergency Preparedness (OEM) for the state gives the directive to MCHD regarding what “pieces” must be in a plan or program. It is then MCHD’s responsibility to put a program and guidelines together to meet the needs of the requirement and work with the locals for implementation.⁴⁰

Surveillance

There are three facilities in the NRHD that provide sentinel surveillance for currently-circulating influenza. Sentinel surveillance is not intended to count every person who has the disease, which would be a difficult task since many who are infected are never seen by a physician.⁶⁸ It is useful in detecting trends over time, and is less costly and more flexible for participating providers than population-based surveillance. It also allows for collection of individual patient-related data.⁶⁹

The sentinel providers in the NRHD collect specimens on patients with flu-like illnesses. Each provider is asked to collect two specimens per month throughout the

influenza season (October – May).⁷⁰ These specimens are sent to the state lab for testing. During a pandemic alert period, the CDC and Virginia Department of Health (VDH) may authorize collection of additional specimens if the patient meets epidemiological criteria.⁷¹

All confirmatory influenza testing in Virginia is performed at the Division of Consolidated Laboratory Services (DCLS), a division of Virginia Department of General Services. To improve efficiency, laboratories from several Virginia agencies were combined to form DCLS in 1972. DCLS is Virginia’s confirmatory lab for the LRN, and is the PulseNet Regional laboratory for the Central Atlantic states.⁷² Positive results for novel influenza subtypes are immediately reported to CDC.⁷¹

Emergency departments and acute care centers also provide year-round surveillance for flu-like illnesses. They submit “chief complaint” data on a daily basis to the VDH to be used for syndromic surveillance. Health officials at the VDH evaluate the data for patterns and are prepared to intervene if necessary.⁷¹

State health officials can compare weekly results for each of Virginia’s five health planning regions to a base value.⁶⁸ All of this information is used to form a “dynamic picture” of influenza’s impact and keep medical, emergency, and even school personnel apprised of the current or a developing situation.⁷⁰

On a weekly basis the VDH assesses the level of influenza-like activity within the state and electronically transmits that data to the CDC.⁷¹ In order for the weekly flu activity from Virginia to accurately be compared to that of other states, the CDC established national definitions of flu activity levels. See **Table 3**.

Table 3: CDC’s National Definitions of Influenza Activity Level	
Activity Level	Definition
No Activity	No laboratory-confirmed cases of influenza and no reported increase in the number of influenza-like illness
Sporadic	Small numbers of laboratory-confirmed influenza cases or a single laboratory-confirmed influenza outbreak has been reported, but there is no increase in cases of ILI
Local	Outbreak of influenza or increases in ILI cases and recent laboratory-confirmed influenza in a single region of the state
Regional	Outbreaks of influenza or increases in ILI and recent laboratory-confirmed influenza in at least 2 but less than half the regions of the state
Widespread	Outbreaks of influenza or increases in ILI cases and recent laboratory-confirmed influenza in at least half the regions of the state.

<http://www.vdh.virginia.gov/Epidemiology/Surveillance/Influenza/index.htm?mode=printable>

The surveillance may sound time-consuming and unnecessary, but this data provides important information. This was especially true in the 2009 pandemic. Through this type of surveillance and testing it was determined that the H1N1 novel influenza strain was resistant to Tamiflu[®]. Knowing this allowed health care professionals to better treat affected individuals earlier in the course of the illness.⁴⁰

On a regular basis, Bordwine receives a list of clients with reportable diseases, as well as information pertinent to the case. MCHD utilizes VEDS, an electronic laboratory records program, to securely transmit data on reportable diseases to the VDH and to the CDC. Any cases from Virginia Tech that tested positive would be included in that information.⁴⁰

One issue that health providers run into pertains to the rapid influenza tests used for diagnosis. These tests are not always going to be accurate; it depends on the antigens present. According to Bordwine, about 40% of tests performed on a novel strain are not picked up by a rapid test. In this situation, state and local health officials must send guidance and recommendations to physicians about how to proceed.⁴⁰

VIRGINIA TECH PREPAREDNESS MEASURES

VIRGINIA TECH BACKGROUND AND STATISTICS

Virginia Tech's main campus is located in Blacksburg, in the New River Valley of Virginia, and encompasses 2,600 acres. In the fall of 2011, VT had nearly 31,000 undergraduates, graduates, and professionals enrolled at the main campus. These students represented 44 states and territories within the United States and 29 countries around the world. Through the residential facilities, the campus is capable of housing over 9,000 students. In addition, there are nearly 6,900 full-time faculty and full- and part-time support staff for all of the college programs within the university.^{73,74}

Virginia Tech offers more degree programs and awards more diplomas than any other university in the Commonwealth of Virginia, and was ranked 28th among national public universities in 2011. The university operating budget for 2011-2012 was \$1,145,971.⁷³

On any given day, thousands of students, faculty, and staff interact with each other at the Blacksburg campus, providing a prime opportunity for a pandemic. What would happen if someone were exposed to the H5N1 virus unknowingly and then ended up on the VT campus? How would it be detected? What would happen if others became infected with the virus? How many people would be impacted? How would Virginia Tech maintain function – or would it be able to? There are dozens of questions to ask.

Should that happen, the most direct response will come from state and local authorities, public health officials, medical providers, and other public services. Because of issues previously discussed, Virginia Tech, a community in itself, will most likely be faced with the task of responding to an influenza pandemic with minimal external resources.

To attempt to understand how a pandemic influenza event would be handled at Virginia Tech, one must have a basic understanding of how VT addresses any type of emergency. These, along with more specific plans, are modeled after those of the state, national, and international organizations previously discussed.

PROGRAMS

VT OEM

Dealing with a pandemic or any other crisis starts with Virginia Tech’s Office of Emergency Management (VTOEM). While the focus is on emergency preparedness, VTOEM also strives to “improve the disaster resiliency of the university.” Should an H5N1 pandemic occur, VTOEM would be the central organization at Virginia Tech responsible for coordinating response to, operations during, and recovery from such an event. Planning is based on the four phases of emergency management: preparedness, response, recovery, and mitigation.⁷⁴ See **Figure 5**.



Figure 5: Phases of Emergency Management
Virginia Tech Crisis and Emergency Management Plan

VT’s emergency management website has a page specifically devoted to the flu. It addresses seasonal influenza and pandemic influenza and discusses the distinction between the two. Similar to the SHC website, it also includes information about staying healthy, how the flu spreads, and symptoms.⁷⁵

University Plans

The *Crisis and Emergency Management Plan* (CEMP) is main component of Virginia Tech’s emergency management program. It provides basic instructions to campus personnel when responding to an incident. The CEMP provides guidance for the following: incident response structure, chain of command, Emergency Notification System protocols, Emergency Operations Center management, continuity of operations, plan administration and maintenance, training and exercises, and departmental support mechanisms and functions.^{74,76}

The OEM at VT is responsible for the CEMP. The Code of Virginia requires that Virginia Tech must completely review and revise the CEMP every four years. This requirement applies to all higher education institutions to ensure that the plan remains current. The institution’s Board of Visitors must formally adopt the plan and its revisions.^{74,76}

The latest version of the CEMP was made available in January, 2012. The base plan, six annexes, and three appendices combine to make the public version of the document 377 pages long. Though lengthy, it does not include the CEMP in its entirety; certain parts are secure and available only to approved groups or individuals.⁷⁴

The public version omits certain information of the base plan, such as who receives the CEMP, hazard indices vulnerability assessments developed specifically for VT, and succession of decision-making

Table 4: Virginia Tech CEMP Annex List	
Annex	Content
A	Emergency Notification System Protocols
B	Emergency Operations Center Plan
C	Emergency Support Functions
D	Infectious Disease Outbreak Control Plan
E	Disaster Mental Health Plan
F	Lane Stadium Evacuation Plan

Virginia Tech Crisis and Emergency Management Plan

authority for critical incident management. In addition, only four out of the six annexes are available in the public version. Contents of Annex C Emergency Support Functions and Annex F Lane Stadium Evacuation Plan are considered confidential and therefore not available for public viewing.⁷⁴ See **Table 4**.

The *Virginia Tech Hazard Mitigation Plan* (HMP) was developed in 2006 as a complementary document to the CEMP. This is a risk management tool used to identify natural, human-caused, and technological hazards that could impact the Virginia Tech campus specifically. The identified hazards were evaluated to assess building vulnerabilities, potential impact, and mitigation strategies for each hazard.^{74,77}

The HMP guides decision-making at the campus. It is a factor when considering land use, construction of new facilities, or renovation and use of existing facilities.

The Emergency Notification System (ENS) is used to provide “rapid incident communication” to faculty, staff, students, and parents of the Virginia Tech community. The ENS is more commonly known as VT Alerts.⁷⁸

Message delivery methods for the ENS include the VT homepage, broadcast emails to all vt.edu accounts, the weather/emergency hotline, outdoor sirens, classroom message boards, text messages, phone alerts, and computer alerts. This broad expanse of delivery also allows visitors, vendors, and contractors to be notified of critical information. Depending on the situation and location, specific regions in the Commonwealth may be targeted via one of these methods by the ENS.^{74,78}

Departmental Plans

The *Emergency Action Plan* (EAP) addresses immediate life-saving action at the department level during an emergency. It provides information on hazards located within that particular facility, as well as emergency contact information for that location. Its components include evacuation, shelter-in-place, emergency responder contact, and emergency procedures. Each area should ensure the EAP is easily accessible by all employees.⁷⁴

A *COOP*, just as it is required for the state, is required for each unit at Virginia Tech and for Virginia Tech as a whole. It is basically a plan that indicates how to proceed if a unit within Virginia Tech or Virginia Tech as a whole should suffer a natural or manmade loss. It addresses which functions are essential to sustain the unit or whole entity until normal operations are able to resume. The Virginia Tech COOP specifically addresses three types of disruptions: loss of facility, loss of services (such as computer service, basic utilities, and intellectual property), and loss of human capital.⁷⁴

The last area could be of critical importance during a pandemic influenza outbreak such as H5N1. If an H5N1 pandemic does occur on the Virginia Tech campus, all faculty, staff, and students will be affected at the same rate as the general population. Therefore supervisors and/or managers who normally direct day-to-day operations will be among the ones with the illness.⁴⁵

It's estimated that as many as 40% of the workforce may be affected by pandemic influenza during its peak and unable to work for two weeks or more. Once

established, the spread of pandemic influenza will be rapid and occur in waves – and very tough to stop after it begins. Therefore, planning prior to the event will ensure the pandemic influenza response will be more effective.⁴⁵

Because of this concern, a separate Pandemic Influenza annex to the VT COOP has been prepared. 20 The VT COOP Pandemic Influenza Annex is also secure and confidential to certain and not accessible by the public. It would address a number of logistical considerations should a pandemic occur.⁷⁶

Schiffert Health Center (SHC)

SHC operates on the main VT campus. It's a medical facility that offers services to full-time VT students who have paid the health fee. Part-time students may be treated on a "fee for service" basis or may choose to "purchase the health fee."⁷⁹

Dr. Noelle Bissell is the Medical Director for SHC. The center places a high priority on influenza prevention. There is a heavy push each year, particularly during student orientation, for flu vaccination for faculty, staff, and students. This is the "front lines" for students on campus.⁸⁰ The SHC website (<http://www.healthcenter.vt.edu>) provides valuable health information for students, including influenza information.⁷⁹

Dr. Bissell walked me through what typically happens at SHC when a student presents with an illness suspected to be the flu. When a student arrives, he checks himself in at a computer kiosk at SHC.⁸⁰ These keyboards are cleaned regularly with Super Sani-Cloth[®] disposable wipes, which contains a germicide that kills 26 microorganisms in two minutes on hard, non-porous surfaces.⁸¹ Signs are posted to signify separate "well" and "sick" waiting areas. There are also signs posted to indicate that those with influenza symptoms are required to wear a mask. Hand sanitizers are readily available for use. Over 90% of the SHC staff have received the influenza vaccine, and they all take appropriate precautions according to CDC guidelines.⁸⁰

If the student exhibits flu-like symptoms during a known influenza outbreak, the clinical staff will typically not administer an influenza test. Per Dr. Bissell, "most young healthy adults recover uneventfully," therefore antivirals are not prescribed. The diagnosis of flu-like illness is used, and the student is given information on self isolation and on how to manage symptoms.⁸⁰

Antivirals are usually reserved for "sicker" individuals or those who have co-morbidities such as diabetes, asthma, or rheumatoid arthritis. The SHC pharmacy does not maintain antivirals for influenza in stock; the student must obtain these from an outside pharmacy. By following this protocol, the clinical staff hopes to avoid unnecessary treatment, avoid contributing to the drug resistance, and avoid antiviral shortages in an epidemic.⁸⁰

A student is advised to contact the SHC if one or more of the following occurs: he isn't recovering, he develops additional respiratory symptoms, or if his fever continues. Ideally, the student would be seen the same day should any of these occur. If that's not possible, triage protocol would be followed (under revision at this time). Alternately they may be referred to a local emergency department.⁸⁰

However, if a student presents with flu-like symptoms in the absence of a known outbreak or during months typically not associated with influenza (such as summer), the clinical staff would most likely test. At SHC, testing is for influenza A or B only. If the SHC clinical staff feels additional testing is necessary, the MCHD is notified. A MCHD

employee will either come to the VT campus to collect the specimen, provide specimen collection materials to SHC staff, or the student will go to the MCHD in person for testing.⁸⁰

Virginia Tech’s SHC is not directly part of a regional or state electronic lab reporting system. It does, however, track internally the number of “influenza” and “flu-like illness” diagnoses made at the center. According to Dr. Bissell, SHC clinical staff follows CDC’s Flu Map to monitor the location and status of seasonal influenza. There is no “threshold number” of cases to dictate it, but SHC will send out information through VT email to faculty, staff, and students to apprise them of the situation and give reminders of protection methods.⁸⁰

Per Dr. Bissell, there is a trend of increased influenza cases when students return to the VT campus and the surrounding area after being out of town on break (such as summer, Thanksgiving, or Christmas breaks). There appears to be no increased incidence of influenza in international students.⁸⁰

If there’s a question about what’s circulating at VT, SHC might be provided with 40 kits by the MCHD. SHC medical staff would use those kits to collect specimens from 40 individuals with flu-like illness, which are sent to the state lab for testing. When 15 or more of them are positively identified as the novel strain, SHC would treat all students who presented with flu-like illnesses the same.⁴⁰

If the SHC clinical staff specifically suspects an avian or animal strain of influenza based on clinical presentation, travel history, or physical contact with birds, SCH would immediately contact MCHD to for guidance on how to proceed.⁸⁰ Other providers in the area would follow the same protocol as well, utilizing the 24/7 emergency number for the MCHD if necessary.⁷¹

Estimations

Part of HHS’ national influenza pandemic plan is the requirement for each state to develop its own plan specific to their needs. Therefore health planners in Virginia must be able to estimate the number of deaths, hospitalizations, and outpatient visits with regard to particular localities. This is necessary since the national plan may not provide an accurate estimate of impact for individual areas in a state.¹ There is no way to know exactly how many in Virginia will be affected by the next pandemic. Modeling studies suggest that without vaccination or drugs, it could be significant. **Table 5** shows the effect a “medium-level” pandemic, such as that from 1968, is estimated to have on Virginia and the United States.

Table 5: Estimates of “Medium-Level” Pandemic		
	Virginia	United States
Deaths	2,700 to 6,300	89,000 to 207,000
Hospitalizations	12,000 to 28,500	314,000 to 734,000
Outpatient visits	575,000 to 1.35 million	18 to 42 million
People becoming sick	1.08 million to 2.52 million	20 to 47 million

<http://www.vdh.virginia.gov/lhd/CentralShenandoah/EPR/panflu.htm>

While no one can definitively answer how many people from the Virginia Tech and Blacksburg area would be affected by an H5N1 pandemic, two software programs can provide estimates. CDC developed them to assist local and state public health officials comply with the aforementioned requirements of the plan and to prepare for the next influenza pandemic.⁸²

FluSurge models the impact of an influenza pandemic on the demand for hospital-based services. FluAid provides estimates of potential impact specific to a locality in terms of the total numbers of deaths, hospitalizations, and outpatient visits. It is not, however, an epidemiologic model and therefore cannot predict when or how someone will become ill.¹

In 2007, the Office of the Chief Medical Examiner in Virginia used FluAid 2.0 to estimate deaths by city and county throughout the state. The calculation estimations were based on population counts and total deaths during the year 2004. An excerpt of that data, containing only data for the NRHD, is shown in **Table 6**.⁸³

Table 6: Estimated Deaths of Virginia's New River Health District for 2004					
New River Health District	Total Population in 2004	Total Deaths in 2004	Total projected flu deaths for 6 months		
			0.6/1000 ^a	1.52/1000 ^b	7.35/1000 ^c
Floyd County	14465	89	9	22	106
Giles County	16985	182	10	26	125
Montgomery County	83983	610	50	128	617
Pulaski County	35145	316	21	53	258
Radford City	14762	69	9	22	109
^a Estimated, average mortality rate (0.6deaths/1000 people) by VDH for a "medium level" pandemic					
^b Estimated mortality rate (1.52 deaths/1000 people) based on a worst-case scenario using a 35% attack rate modeled after the 1958 & 1968 pandemics.					
^c Estimated mortality rate based on a 35% attack rate modeled after the 1918 pandemic,					

http://www.vdh.state.va.us/medExam/documents/PanFluDeathEstimates_Planning%20District.pdf

Fast-forward to 2011 for the NRHD. Between 2004 and 2011, population increased for all but one of the jurisdictions. For two, Radford City and Montgomery County, it was a considerable increase. See **Table 7**. FluAid estimates based on 2011 population data would be considerably more for both Montgomery County and Radford City.⁸⁴

Where would Virginia Tech, a community in itself, fit into this? Using information from the State Council of Higher Education for Virginia (SCHEV) and FluAid 2.0, I attempted to answer this question. According to SCHEV data, there were 9,208 students 17 – 44 years of age living on the Virginia Tech campus in fall of 2012.⁸⁵

NRHD jurisdiction	Population change
Floyd County	6.3%
Giles County	0.8%
Montgomery County	12.4%
Pulaski County	- 1.5%
Radford City	11.2%

<http://www.vdh.state.va.us/HealthStats/stats.htm>

In FluAid 2.0, populations are broken down into three categories: 0-18, 19-64, and 65 and older. Per the modeling instructions, these age ranges could be modified slightly. To make the Virginia Tech estimations, I altered the middle category to reflect ages 17 – 64 and placed the entire on-campus resident population into that category.

(The program would not accept zeros for the other two categories; the minimum value of one was entered into each one to enable the program to function. Their values for parameters in question, however, essentially remained at zero.)⁸²

The program allows the user to alter the percentages of high risk individuals in each age group. Per Dr. Bissell’s previous comment, most in the age group of those on-campus are healthy with no co-morbidities. Therefore I used the recommended rate of 14.4% for this age group.⁸²

FluAid 2.0 provides default factors for the age groups and risk group to calculate minimum, most likely, and maximum death rates per 1,000 of the population. The user may enter different factors into the calculation table if desired.⁸²

In addition, three gross attack rates are calculated. The gross attack rate is considered to be the percentage of the population that will have a clinical case of influenza. For this model, a clinical case of influenza is one that causes an economic impact, such as a person missing part of a day of work (or school) or going to a physician’s office. These percentages may be altered by the user as well. I used the recommended rates of 15%, 25%, and 35%.⁸²

The model and calculations represent the impact that a 1968-type influenza pandemic would have on a population. However, the model may be altered to simulate a 1918-type influenza pandemic. To do this, a scale-up factor of 8.22 is multiplied by the default factors previously mentioned and entered into the calculation tables.⁸²

Death rates for the on-campus Virginia Tech population is presented in **Table 8**.

Note: FluAid 2.0 can also be used to estimate hospitalizations, outpatient visits, vaccination coverage, and impact on the healthcare system. Those parameters, however, were not included in the scope of this estimate and discussion.⁸²

Pandemic Type	Gross Attack Rates		
	15%	25%	35%
1968 type	3	5	7
1918 type	24	39	55

Calculated using FluAid 2.0 (<http://www.cdc.gov/flu/pandemic-resources/tools/fluaid.htm>) and Virginia Tech fall on-campus enrollment (<http://research.schev.edu/>)

Planning Considerations

If a pandemic similar to 1918 hits, major decisions will have to be made. At what point are classes cancelled? At what point does Virginia Tech send on-campus

residents home? There is no magic number says Grady DeVilbiss, Virginia Tech's Emergency Planner. Decisions are made by the VTOEM based on the individual situation.⁷⁶

If a resident lives within a couple of hours and has a full tank of gas, that's probably feasible. If the student is from several hours away and there are no gas stations open (or must fly), how should that be handled? What about international students? They typically don't have many options and would have to remain on campus.⁴⁰

It's possible that local, state, or national travel restrictions may be put in place by health officials. Faculty, staff, and students who live off-campus would not be coming to campus at all. This would also mean that none of the students living on campus would be able to leave, resulting in a shelter-in-place situation.⁴⁰

When a shelter-in-place directive is given to the students on campus, additional questions must be asked and decisions made.

- Is the amount of food storage adequate if the infrastructure shuts down? How will food be distributed to the students? Will there be adequate personnel to do so?
- How will physical plant services operate on-campus? How will HVAC, water, and sewer issues be handled?
- How will research animals be managed? Virginia Tech's research expenditures topped \$450 million for the 2011 fiscal year, ranking 41st out of over 900 institutions and topping the list for Virginia. That correlates to a significant number of research animals on campus that will require care.
- How will the vaccines that have been allotted be designated and administered? The decision on dosage allocation would be made by the SHC director, the emergency planner, and others in the VTOEM.
- How would student health and welfare be handled? There would be a significant number of students experiencing illness. The local clinics and hospitals would be to capacity and unable to handle the infected individuals from Virginia Tech. SHC and the VTOEM would have to provide healthcare and further direction.
- How will body storage be handled? If the pandemic mimics the 1918 episode and causes 35% gross mortality rates, close to five dozen on-campus residents may die. The surrounding community would be dealing with their own deaths. Morgue space at hospitals and funeral homes would be at capacity and unable to take additional bodies; Virginia Tech would have to take care of their own. This might entail bringing in refrigerated trailers manufactured for this purpose, or having the capability to convert current coolers on campus into morgue space.⁴⁰

The questions posed are just a handful of the decisions that the Virginia Tech administration and emergency officials would have to be prepared to make in the event of an H5N1 pandemic influenza outbreak. These issues, as well as many others, should be addressed in Virginia Tech's Pandemic Influenza Annex to their COOP. It is a secure document, however, and inaccessible by the general public.

SUMMARY

It's been over 40 years since the last pandemic, but the underlying threat remains for another one. Though no one knows for sure, it could very well be H5N1. When it does occur, the result will be a global health emergency.

Pre-event planning is critical to ensure a prompt and effective response, as its spread will be rapid and difficult to stop once it begins. Proper planning along with adequate resources may sustain essential operations and services. By using various tools from the global level all the way down to the local level, there is potential to reduce the effects of the pandemic. 9

Sixty percent of pathogens that cause disease in humans actually originate from animals. 82 Therefore it is critical to protect human health by curbing avian influenza at the source through surveillance, control, and mitigation. 10, 23

Thanks to evolving technology, detection, control, and prevention of influenza viruses with pandemic potential have improved considerably since the 1918 pandemic. 50 Lessons have also been learned and public health has benefitted on all levels. All involved in emergency preparedness are coming to understand that a pandemic can be better fought jointly and cooperation with others. Actions taken in one country may have an impact on the rest of the world as well. 11, 22 The organizations discussed here play vital roles in this unity. However there are many others with plans in place, particularly at the local levels, that contribute to overall preparedness.

Local, state, national, and global organizations are all vital to H5N1 pandemic preparedness, and Virginia Tech is following their directives. Required documents are in place and emergency plans have been made. However, since some documentation is secure, the stakeholders at the University have to trust that all the pertinent issues are addressed in those secure plans. Until an actual pandemic influenza occurs at Virginia Tech, though, no one can be sure that the preparedness efforts are enough.

ACRONYMS

APHIS	Animal and Plant Health Inspection Service
BSL	Biosafety Level
CC	Collaborating Centres on Influenza
CDC	Centers for Disease Control and Prevention
CEMP	Crisis and Emergency Management Plan
CFR	Case Fatality Ratio
COOP	Continuity of Operations
COVEOP	Commonwealth of Virginia Emergency Operations Plan
DCLS	Division of Consolidated Laboratory Services
DHS	Department of Homeland Security
DNDHI	Division of Notifiable Diseases and Healthcare Information
EAP	Emergency Action Plan
ENS	Emergency Notification System; VT Alerts

ACRONYMS

FAO	Food and Agricultural Organization of the United Nations
FEMA	Federal Emergency Management Agency
GAP	Global Action Plan
GDP	Gross Domestic Product
GISRS	Global Influenza Surveillance and Response System
GLEWS	Global Early Warning System for Major Animal Diseases
H5RL	H5 Reference Laboratories
HA	Hemagglutinin
HER	Electronic Health Records
HHS	Department of Health and Human Services
HMP	Hazard Mitigation Plan
HPAI	Highly pathogenic avian influenza
LPAI	Low pathogenic avian influenza
LRN	Laboratory Response Network
MCHD	Montgomery County Health Department
NA	Neuraminidase
NAHLN	National Animal Health Laboratory Network
NEDDS	National Electronic Disease Surveillance System
NIC	Nation Influenza Centres
NIH	National Institutes of Health
NNDSS	National Notifiable Diseases Surveillance System
NPIP	National Poultry Improvement Plan
NRF	National Response Framework
NRHD	New River Health District
NVSL	National Veterinary Services Laboratory
OEM	Office of Emergency Management
OIE	World Organisation for Animal Health
PIP	Pandemic Influenza Preparedness Framework
PSI	Pandemic Severity Index
SCHEV	State Council of Higher Education for Virginia
SHC	Schiffert Health Center
SNS	Strategic National Stockpile
USDA	United States Department of Agriculture
VDH	Virginia Department of Health
VTOEM	Virginia Tech Office of Emergency Management
WHO	World Health Organization

REFERENCES

1. FluAid 2.0. August 29, 2001; Centers for Disease Control and Prevention website. Available at: <http://www.cdc.gov/flu/pandemic-resources/tools/fluaid.htm>. Accessed March 21, 2013.
2. Elci C. The impact of HPAI of the H5N1 strain on economies of affected countries. *International Conference on Human and Economic Resources*. Izmir, Turkey 2006.
3. The threat of pandemic influenza: are we ready? Workshop summary. 2005; The National Academies Press website. Available at: <http://www.nap.edu/openbook.php?isbn=0309095042>. Accessed February 18, 2013.
4. Regional influenza pandemic preparedness plan (2006-2008). January 2006; Mekong Basin Disease Surveillance website. Available at: [http://www.mbdsoffice.com/data020408/Searo%20Influenza%20Pandemic%20Preparedness%20Plan\(2006-2008\).pdf](http://www.mbdsoffice.com/data020408/Searo%20Influenza%20Pandemic%20Preparedness%20Plan(2006-2008).pdf). Accessed March 3, 2013.
5. Learning what H5N1 needs to spread. National Institutes of Health website. Available at: www.nih.gov/researchmatters/july2012/07092012H5N1.htm. Accessed January 5, 2013.
6. Seasonal influenza. Centers for Disease Control and Prevention website. Available at: <http://www.cdc.gov/flu/about/qa/disease.htm>. Accessed March 15, 2013.
7. Chung P, et al. Expert consultation on diagnosis of H5N1 avian influenza infections in humans. *Influenza Other Respi Viruses*. 2007;1(4):131-138.
8. *Spread of avian flu could affect next year's economic outlook*: The World Bank East Asia and Pacific Region; 2006.
9. Advancing public health surveillance through science and collaboration. June 25, 2012; Centers for Disease Control and Prevention website. Available at: www.cdc.gov/osels/phsipo/dndhi/dndhi_overview.html. Accessed November 18, 2012.
10. Avian influenza key facts. April 2011; World Health Organization website. Available at: http://www.who.int/mediacentre/factsheets/avian_influenza/en/. Accessed September 15, 2012.
11. Avian influenza mutation, H5N1. Avian Influenza website. Available at: www.avianinfluenza.org/mutated-avian-influenza-virus-h5n1.php. Accessed September 23, 2012.
12. Lister S. The 2009 influenza pandemic: an overview. August 6, 2009; U.S. Department of State website. Available at: <http://fpc.state.gov/documents/organization/128854.pdf>. Accessed January 23, 2013.
13. Influenza type A viruses and subtypes. March 22, 2012; Centers for Disease Control and Prevention website. Available at: www.cdc.gov/flu/avianflu/influenza-a-virus-subtypes.htm. Accessed January 13, 2013.
14. Avian influenza (bird flu): implications for human disease. April 12, 2012; CIDRAP website. Available at: http://www.cidrap.umn.edu/cidrap/content/influenza/avianflu/biofacts/avflu_human.html. Accessed November 12, 2012.
15. Avian Influenza A virus infections in humans. June 21, 2012; Centers for Disease Control and Prevention website. Available at: www.cdc.gov/flu/avianflu/avian-in-humans.htm. Accessed February 25, 2013.
16. Avian influenza A (H5N1) infection in humans. *New Engl J Med*. 2005;353(13):1374-1385.
17. Updated unified nomenclature system for the highly pathogenic H5N1 avian influenza viruses. October 2001; World Health Organization website. Available at: www.who.int/influenza/gisrs_laboratory/h5n1_nomenclature/en/index.html. Accessed February 25, 2013.

18. *An assessment of H5N1 situation, trends and epidemiological insights* May 2008.
19. *Collecting, preserving and shipping specimens for the diagnosis of avian influenza A(H5N1) virus infection - guide for field operations*: World Health Organization; October 2006.
20. Public health threat of highly pathogenic avian influenza A (H5N1) virus. June 22, 2012; Centers for Disease Control and Prevention website Available at: www.cdc.gov/flu/avianflu/h5n1-threat.htm. Accessed December 28, 2012.
21. HHS pandemic influenza plan. November 2005; Flu.gov, website managed by the U.S. Department of Health and Human Services Available at: <http://www.flu.gov/planning-preparedness/federal/hhspandemicinfluenzaplan.pdf>. Accessed January 13, 2013.
22. WHO concerned that new H5N1 influenza research could undermine the 2011 Pandemic Influenza Preparedness Framework. December 30, 2011; World Health Organization website. Available at: http://www.who.int/mediacentre/news/statements/2011/pip_framework_20111229/en/. Accessed December 28, 2012.
23. Influenza FAQs: H5N1 research issues. March 2012; World Health Organization website. Available at: http://www.who.int/influenza/human_animal_interface/avian_influenza/h5n1_research/faqs/en/index.html. Accessed December 28, 2012.
24. Schnirring L. Experts ponder H5N1 research moratorium issues. October 9, 2012; CIDRAP website. Available at: <http://www.cidrap.umn.edu/cidrap/content/influenza/avianflu/news/jun2212cfr.html>. Accessed December 28, 2012.
25. NIH endorses recommendation to publish H5N1 studies. April 20, 2012; CIDRAP website. Available at: <http://www.cidrap.umn.edu/cidrap/content/influenza/avianflu/news/apr2012nih.html>. Accessed December 28, 2012.
26. One year later, moratorium lifted on bird flu research. *ASCP Daily Diagnosis* January 24, 2013.
27. Schorow S. Fears of bioterrorism or an accidental release. *Harvard Gazette*. February 16, 2012.
28. Greenfieldbroyce N. Bird flu research rattles bioterrorism field. November 11, 2011; National Public Radio website. Available at: <http://www.npr.org/blogs/health/2011/11/17/142453447/bird-flu-research-rattles-bioterrorism-field>. Accessed March, 2013.
29. de Jong MD. H5N1 transmission and disease observations from the frontlines. *Pediatr Infect Dis J*. October 2008;27(10):S54-S56.
30. Vivi Setiawaty KP, Ondri Sampurno. Establishing a laboratory network of influenza diagnosis in Indonesia: an experience from the avian flu (H5N1) outbreak. *J Clin Epidemiol*. 2012;4:209-212.
31. Pourmand N, Diamond L, Garten R, et al. Rapid and highly informative diagnostic assay for H5N1 influenza viruses. *PLoS ONE*. December 2006;1(1):1-9.
32. Made-in-Singapore H5N1 diagnostic kit - detects all known strains of H5N1 virus with a single test. May 29, 2012; Eureka Alert! website. Available at: www.eurekaalert.org/pub_releases/2012-05/afst-mhd052912.php. Accessed February 25, 2013.
33. Influenza at the human-animal interface - summary and assessment as of 15 February 2013. World Health Organization website. Available at: http://www.who.int/influenza/human_animal_interface/Influenza_Summary_IRA_HA_interface_15Feb13.pdf. Accessed March 9, 2013.

34. Cumulative number of confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2013. World Health Organization website. Available at: http://www.who.int/influenza/human_animal_interface/EN_GIP_20130215CumulativeNumberH5N1cases.pdf. Accessed March 9, 2013.
35. Chen J-M, Chen, Ji-Wang, Dai, Jian-Jun, Sun, Xing-Xue. A survey of human cases of H5N1 avian influenza reported by the WHO before June 2006 for infection control. *Am J Infect Control*. 2007;35(5):351-353.
36. Weekly epidemiological record - update on human cases of highly pathogenic avian influenza A(H5N1) virus infection 2010. April 22, 2011; World Health Organization website. Available at: <http://www.who.int/wer/2011/wer8617.pdf>. Accessed February 24, 2013.
37. Debate over H5N1 fatality rate flares again. June 22, 2012; CIDRAP website. Available at: <http://www.cidrap.umn.edu/cidrap/content/influenza/avianflu/news/jun2212cfr.html>. Accessed June 25, 2012.
38. *Pandemic Influenza Best Practices and Model Protocols*: U.S. Department of Homeland Security;2007.
39. Impact of pandemic influenza. August 17, 2012; Virginia Department of Health website. Available at: <http://www.vdh.virginia.gov/lhd/CentralShenandoah/EPR/panflu.htm>. Accessed March 14, 2013.
40. Bordwine P. Personal interview. February 4, 2013.
41. Comparative analysis of national pandemic influenza preparedness plans. January 2011; World Health Organization website. Available at: http://www.who.int/influenza/resources/documents/comparative_analysis_php_2011_en/. Accessed March 1, 2013.
42. Preparing for and responding to influenza pandemics: roles and responsibilities of Roche. June 2012; Roche website. Available at: http://www.roche.com/roles_responsibilities_influenza Accessed March 10, 2013.
43. *Commonwealth of Virginia emergency operations plan, pandemic influenza plan, volume VI*: Virginia Department of Emergency Management;September 2009.
44. Global influenza surveillance and response system (GISRS). World Health Organization website. Available at: http://www.who.int/influenza/gisrs_laboratory/en/. Accessed March 18, 2013.
45. Pandemic influenza preparedness framework for the sharing of influenza viruses and access to vaccines and other benefits. 2011; World Health Organization website. Available at: http://whqlibdoc.who.int/publications/2011/9789241503082_eng.pdf. Accessed March 1, 2013.
46. Global action plan for influenza vaccines. World Health Organization website. Available at: http://who.int/influenza_vaccines_plan/objectives/en/index.html. Accessed March 25, 2013.
47. Report of the second WHO consultation on the global action plan for influenza vaccines (GAP). July 12-14, 2001; Geneva, Switzerland.
48. The World Organisation for Animal Health (OIE) - about us. The World Organisation for Animal Health (OIE) website
Available at: <http://www.oie.int/about-us/>. Accessed March 1, 2013.
49. Animal health: a multifaceted challenge. World Organisation for Animal Health website. Available at: http://www.oie.int/fileadmin/Home/eng/Media_Center/docs/pdf/Key_Documents/ANIMAL_HEALTH-EN-FINAL.pdf. Accessed March 1, 2013.
50. One health. World Organisation for Animal Health website. Available at: <http://www.oie.int/en/for-the-media/editorials/detail/article/one-health/>. Accessed March 15, 2013.

51. The global early warning system for major animal diseases including zoonoses. The Global Early Warning System website. Available at: <http://www.glews.net/>. Accessed March 1, 2013.
52. About the agency. Federal Emergency Management Agency website. Available at: <http://www.fema.gov/about>. Accessed March 5, 2013.
53. *National Response Framework*: U.S. Department of Homeland Security;2008.
54. Centers for Disease Control and Prevention, mission statement. <http://www.cdc.gov/maso/pdf/cdcmiss.pdf>. Accessed March 24, 2013.
55. H5N1 genetic changes inventory. June 21, 2012; Centers for Disease Control and Prevention website. Available at: <http://www.cdc.gov/flu/avianflu/h5n1-genetic-changes.htm>. Accessed November 12, 2012.
56. The laboratory response network partners in preparedness. July 2, 2012; Centers for Disease Control and Prevention website. Available at: <http://www.bt.cdc.gov/lrn/>. Accessed February 18, 2013.
57. National notifiable diseases surveillance system. Centers for Disease Control and Prevention website. Available at: http://www.cdc.gov/osels/phsipo/docs/pdf/factsheets/DNDHI_NNDSS_12_232372_L_remediated_10_26_2012.pdf. Accessed December 3, 2012.
58. Division of notifiable diseases and healthcare information. Centers for Disease Control and Prevention website. Available at: http://www.cdc.gov/osels/phsipo/docs/pdf/DNDHI_Overview_12_232372_J_REM_5_25_2012.pdf. Accessed December 8, 2012.
59. Strategic national stockpile (SNS). Centers for Disease Control and Prevention website. Available at: <http://www.cdc.gov/phpr/stockpile/stockpile.htm>. Accessed March 1, 2013.
60. About APHIS. http://www.aphis.usda.gov/about_aphis/. Accessed March 1, 2013.
61. Foreign animal disease preparedness and response plan (FAD PReP) - highly pathogenic avian influenza (HPAI) response plan: the red book. September 2012; Foreign. Available at: http://www.aphis.usda.gov/newsroom/hot_issues/avian_influenza/contents/printable_version/summary_hpai_response_plan.pdf. Accessed March 3, 2013.
62. Poultry disease information. U.S. Department of Agriculture Animal and Plant Health Inspection Service website. Available at: http://www.aphis.usda.gov/animal_health/animal_dis_spec/poultry/. Accessed March 1, 2013.
63. Animal health: about NAHLN. U.S. Department of Agriculture Animal and Plant Health Inspection Service website. Available at: http://www.aphis.usda.gov/animal_health/nahln/about_nahln.shtml. Accessed March 25, 2013.
64. *Commonwealth of Virginia emergency operations plan (COVEOP)*: Virginia Department of Emergency Management;2012.
65. *Pandemic Influenza Annex Manual for Continuity of Operations (COOP) Planning*: Virginia Department of Emergency Management;November 2007.
66. Plans. Virginia Department of Emergency Management website. Available at: <http://www.vaemergency.gov/em/plans>. Accessed March 15, 2013.
67. Linkous D. Personal interview. February 4, 2013.
68. Virginia 2012/2013 influenza surveillance activity level. Commonwealth of Virginia website. Available at: <http://www.vdh.virginia.gov/Epidemiology/Surveillance/Influenza/index.htm?mode=printable>. Accessed March 21, 2013.

69. Sentinel surveillance method. January 4, 2010; Centers for Disease Control and Prevention website. Available at: <http://www.cdc.gov/abcs/reports-findings/downloads/sentinel-method.pdf>. Accessed March 14, 2013.
70. 2012-13 sentinel influenza surveillance in Virginia: some frequently asked questions. November 2012; Virginia Department of Health website. Available at: http://www.vdh.virginia.gov/Epidemiology/Surveillance/Influenza/Sentinel_Surveillance/FluSurveill_FAQs_final.pdf. Accessed March 14, 2013.
71. *Virginia Department of Health Emergency Response Plan, hazard specific appendix 8: pandemic influenza, supplement 1: disease surveillance* August 2010.
72. Division of consolidated laboratory services. Commonwealth of Virginia website. Available at: <http://www.dgs.state.va.us/divisionofconsolidatedlaboratoryservices/tabid/453/default.aspx>. Accessed February 4, 2013.
73. *University Facts & Figures 2011-2012*: Virginia Tech;2012.
74. Virginia Tech crisis and emergency management plan (CEMP) public version. January 2012; Virginia Tech website. Available at: <http://www.emergency.vt.edu/programs/plans/CEMP-public-07312012.pdf>. Accessed January 18, 2013.
75. Flu overview. Virginia Tech website. Available at: <http://www.emergency.vt.edu/guides/health/flu.html>. Accessed March 11, 2013.
76. DeVilbiss G. Personal Interview January 14, 2013.
77. Hazard mitigation plan. Virginia Tech website. Available at: <http://www.emergency.vt.edu/programs/plans/hazard-mitigation.html>. Accessed March 11, 2013.
78. About VT Alerts. Virginia Tech website. Available at: <http://www.alerts.vt.edu/>. Accessed March 11, 2013.
79. Schiffert Health Center. Virginia Tech website. Available at: <http://www.healthcenter.vt.edu/>. Accessed January 25, 2013.
80. Bissell N. Personal Interview. January 10, 2013.
81. Sani-Cloth® AF3 germicidal disposable wipe. PDI Incorporated website. Available at: http://www.pdipdi.com/healthcare/surface_disinfect.aspx. Accessed February 5, 2013.
82. Meltzer M. Using FluAid and FluSurge to estimate the potential impact of the next influenza pandemic upon Locale Y. March 22, 2006; Centers for Disease Control and Prevention Website. Available at: <http://www.cdc.gov/flu/pandemic-resources/tools/downloads/pandemic-impact-estimate-instructions.pdf>. Accessed January 13, 2013.
83. Estimations of deaths in Virginia caused by pandemic flu by planning district. 2007; Virginia Department of Health website. Available at: http://www.vdh.state.va.us/medExam/documents/PanFluDeathEstimates_Planning%20District.pdf. Accessed February 4, 2013.
84. Virginia Department of Health statistical reports and tables - total Virginia population 2011. Virginia Department of Health website. Available at: <http://www.vdh.state.va.us/HealthStats/stats.htm>. Accessed March 15, 2013.
85. Virginia college navigator report. State Council of Higher Education for Virginia website. Available at: <http://research.schev.edu/>. Accessed March 19, 2013.