



Testimony by the Alliance for the Prudent Use of Antibiotics (APUA)
Subcommittee: Federal Workforce, Postal Service and District of Columbia
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The 2009 H1N1 Pandemic: Lessons for the Public and Federal Workforce Protection

Thank you Congressman Lynch and Committee members, for this opportunity to testify on behalf of the Alliance for the Prudent Use of Antibiotics concerning how best to protect front-line workers and the public during a crisis such as the current influenza pandemic. Established in 1981 as an independent public health organization, APUA's mission is to strengthen society's defenses against infectious disease by promoting appropriate antimicrobial access and use and controlling antimicrobial resistance on a worldwide basis. Based in Boston, with affiliated chapters in over 60 countries, APUA represents the world's largest international network totally dedicated to research and education, concerning antibiotics and resistance, with the goal of preserving the power of these life saving drugs.

Background

Infectious disease epidemics and pandemics have occurred throughout human history. They remain the major cause of death worldwide and they will not be conquered during our lifetimes. Today our focus is on the threat of influenza pandemics, however many other infectious diseases also pose major threats to our national security (Taubenberger, & Morens, 2008). Infectious agents are subject to genetic change and evolution, spurred on by modern transport and population growth and crowding. Many of these diseases may be prevented, and new diseases will also emerge, but it is impossible to predict their individual emergence in time and place.

As of Friday May 8th, 2009 there have been 896 reported cases of H1N1 in the U.S. in 41 states and Dr. Richard Besser of the CDC, states that "We are still on the upswing of the epidemic curve." Only about 10 percent of those infected had a travel history to Mexico said Besser. Of the confirmed cases only about 5% have been hospitalized. Even if swine-flu symptoms are mild, the ease with which the new virus can spread among a world population with no natural immunity makes it a threat (Randall, 2009). The public health investments of Congress over the past ten years have paid off in the latest round on H1N1 Flu, and these need to be expanded. Dr. Richard Besser of the CDC and Dr. Alfred DeMaria, in the Massachusetts Department of Public Health are examples of public health servants who have performed brilliantly as scientists and communicators to identify and mitigate disease episodes.

The 1918 Influenza Pandemics

The 1918 influenza A pandemic claimed more than 50 million lives worldwide in less than a year and is considered one of the worst disasters in history. Approximately one in four people in the U.S. became ill and 500,000 died. The unusually high fatality rate among previously healthy young adults meant the loss of a disproportionate number of society's most productive members. The elderly, the very young, and those with chronic disease are most at risk of death from the viral infection itself or from complications resulting from secondary bacterial pneumonia. Two to three percent of those who fell ill during the 1918 flu died, compared to .10 percent for other influenza pandemics. (Taubenberger & Morens, 2006)

This first wave of the 1918 influenza spread rapidly, circling the globe in less than five months. The disease resurfaced in a more virulent form in the United States in August of 1918, causing large numbers of deaths in many U.S. cities as it spread from the East Coast to California. Health authorities reacted by requiring citizens to wear masks in public places and by taking other steps that were presumed to prevent the spread of disease. Many of these efforts were not put in place, however, until the worst of the epidemic had passed.

Some characteristics of the 1918 pandemic appear unique: most notably, death rates were 5–20 times higher than expected. Clinically and pathologically, these high death rates appear to be the result of several factors, including a higher proportion of severe secondary bacterial infections of the respiratory tract, rather than involvement of organ systems outside the normal range of the influenza virus. Finally, in 1918, three separate recurrences of influenza followed each other with unusual rapidity, resulting in 3 explosive pandemic waves within a year's time.

The History of Selected H1N1 Viruses:

Sequence and phylogenetic analysis of the completed 1918 influenza virus genes shows them to be the most avian-like among the mammalian-adapted viruses. This finding supports the hypotheses that pandemic virus contains genes derived from the avian-like influenza virus strains and that the 1918 virus is the common ancestor of human and classical swine H1N1 flu viruses. This information will help to elucidate how pandemic influenza virus strains emerge and what genetic features contribute to virulence in humans. (Taubenberger, JK 2006)

All influenza A pandemics since then have been caused by the descendants of the 1918 virus, including H1N1 virus. (Taubenberger, & Morrens, 2006). Since 1977, H1N1 viruses have circulated globally to produce seasonal epidemics, causing approximately 36,000 US deaths annually. It is unclear, however, whether continuing co-circulation, coupled with an increase in influenza vaccines will increase or decrease pandemic risk or influence the subtype of the next pandemic virus (Taubenberger, et al 2007).

The core work of APUA to control emergence of antibiotic resistance is given a special relevance to this danger by recent evidence that secondary bacterial infection was a major contributor to the 1918 influenza death rate and also by recent changes in methicillin-resistant *Staphylococcus aureus* (MRSA). MRSA has spread widely in the community in recent years and on multiple occasions has acquired resistance to vancomycin, the drug that has been relied on for treating it. MRSA will thus be a very likely major contributor to the mortality of future influenza infections, and preventing its further acquisition of antibiotic resistances is necessary to keep those infections from becoming untreatable.

The Ecology of Infectious Diseases: Bacterial Transfer between Humans and Animals

Ecology, the study of how living organisms interact with other species and their environment, is a relatively new scientific enterprise which holds keys to understanding infectious diseases. (Summers, 2002) The continuous exchange of bacteria between humans and their environment and exchange among the genetic elements of these bacteria means that imposition of selection on any microbial ecosystem will result in proliferation of highly resistant bacteria (Summers, 2002).

Discovering new antibiotics will buy us time, but the same ancient molecular mechanisms will ensure their eventual loss of efficacy as well. All sectors that use antibiotics—human medical, veterinary, and horticultural—need to cooperate in devising novel methods to stop unnecessary use of these agents and to minimize proliferation of resistant bacteria while meeting their respective therapeutic needs. The simple ecological principle is that everything is connected to everything else (McEwen, & Fedorka-Cray 2002). After all the 2009 H1N1 flu virus is a mix of swine, human, and avian flu, which

originated in swine. Since it has mutated to be transmissible from human to human, contact with swine is no longer the primary concern.

Food animals in the United States are often exposed to antimicrobials to treat and prevent infectious disease or to promote growth. Many of these antimicrobials are identical to, or closely resemble, drugs used in humans. Precise figures for the quantity of antimicrobials used in animals are not publicly available in the United States, and estimates vary widely. Transfer of resistance genes and bacteria among animals and animal products and the environment is prolific. Factory farms are an ideal environment for bacterial gene exchange. To slow the development of resistance, some countries have restricted antimicrobial use in feed, and some groups advocate similar measures in the United States. Alternatives to growth promoting and prophylactic uses of antimicrobials in agriculture include improved management practices, wider use of vaccines, and introduction of probiotics. The EU is far more proactive in instituting protections such as monitoring programs, prudent use guidelines, educational campaigns, and a ban on use of critically important human antibiotics for animal growth promotion (McEwen, & Fedorka-Cray 2002).

Public Health Protections Worth the Investments

While the bad news is the omnipresence of infectious disease, the good news is the well-known prevention and control measures which Congress can support in order to protect federal workers and the public from infectious disease epidemics. Due to the complexity of infectious diseases and the problems of drug resistance, infection prevention is by far the preferable intervention (Salyers, & Whitt, 2005).

- a. **Surveillance:** Surveillance is the foundation of the public health system and disease prevention and control efforts. A good public health surveillance system requires local laboratory infrastructure to recognize new or emerging infectious diseases, and to track the prevalence of more established ones. Any disease that is not on CDC's current list of notifiable illnesses may go undetected or may be detected only after a severe outbreak. We live in a global village where bacteria and viruses know no boundaries. Thus it is necessary to link U.S. domestic and international public surveillance efforts and other surveillance programs such as APUA's commensal resistance tracking program for U.S. AMRIID and the WHONET program of resistance surveillance at hospitals. Surveillance and genomic sequencing of large numbers of animal influenza viruses will help us understand the genetic basis of host adaptation and the extent of the natural reservoirs of influenza viruses. (Taubenberger, & Morens, 2006)
- b. **Basic Research:** Understanding infectious diseases requires multidisciplinary research over dedicated periods of time. Genetic analysis and bioinformatics, while expensive, allow acceleration of research findings critical to public health. Many basic questions remain about how to live with and battle microbes. The dramatic increase in funding for HIV research over the last two decades has proven to produce good results, while other disease states, like resistant bacterial diseases are still under-funded and less understood. The expansion of National Institutes of Health-supported research is fundamental to our understanding of the microbial world. The Department of Defense infectious disease programs and laboratories, such as the AMRIID project and NBACC, should also continue to receive priority support.
- c. **Vaccines:** Vaccines are helpful, but they should not be viewed as the entire solution for defeating emerging microbial threats to health. Because viruses continue to mutate, they tend to stay one step ahead of the vaccine. The potential value of vaccination and the speed with which vaccines can be developed depend on many factors, such as the existing scientific knowledge of the agent (or a similar organism), its molecular biology, rate of

transmission, pathogenesis, how the human immune system responds to natural infection, and the nature of protective immunity. Economic factors may also impede vaccine development, which requires an extensive, up-front investment in research.

- d. Sanitation: Clean water supplies, personal hygiene, and safe food handling are now fundamental public health practices in the U.S. that protect us from infectious diseases.
- e. Antimicrobial Treatments: Antimicrobial is the name for a chemical that either kills or prevents the growth of microbes such as bacteria, viruses, fungi or protozoa. Different microbes require different types of antimicrobials for treatment—for example, antibiotics for bacteria, antivirals for viruses.

Antivirals: Some viral infections can be successfully controlled with currently available antiviral drugs. Unfortunately, as has been the case for antibiotics, resistance to antiviral drugs has been reported. Ultimately, control of the viral infection relies on the individual's immune response. Individuals who are immunocompromised, with chronic or recurrent viral infections, often develop drug-resistant viruses. Because resistance to antiviral drugs appear to occur quite rapidly in such individuals, appropriate use and availability of drugs with alternative mechanisms of action are important. Sufficient data are not yet available, however, to recommend limitations on the use of antiviral drugs (Salyers, & Whitt, 2005). In terms of resistance however, clearly prudent use of these therapeutics means using them only for viral infections and making sure the dose and length of treatment is as recommended. Inadequate dosing helps develop antiviral resistance. As with antibiotics, these agents should not be misused, stockpiled or demanded from physicians. A single individual's error leading to the emergence of resistance can be devastating to a whole community. The influenza threat is a moving target. Scientists who develop antiviral compounds face a daunting challenge. There are only a few known targets that can be hit by antiviral compounds. In HIV treatment, resistance to AZT and to protease inhibitors has already appeared (Salyers, & Whitt, 2005).

Antibiotics for Bacterial Diseases: Antibiotics are antibacterial compounds that have no efficacy against viruses. Thus we should not take antibiotics for the common cold or to treat an influenza virus. Antibiotics are effective however against bacterial infections such as pneumonia. In the 1918 Great Flu Epidemic more people died from secondary bacterial infections (pneumonia) than from the flu virus. The usefulness of antimicrobial drugs can be ensured only if they are used carefully and responsibly. To assure the availability and usefulness of antimicrobials and to prevent the emergence of resistance, resistant infections cost 10 to 100 times more to treat compared to non-resistant infections. Thus any investments, which will improve antibiotic use and preserve the power of existing drugs is a good one. APUA recommends that clinicians, the research and development community and the U.S. government introduce measures which include the education of health care personnel, veterinarians, and users in the agricultural sector and the general public regarding the importance of rational use of antimicrobials.

Hygiene and Antiseptics: Washing hands and surfaces with ordinary soap and water is a surprisingly effective way to remove germs and clean surfaces. Alcohol and common household bleach are also good old-fashioned stand-bys and have not been shown to prompt resistance. One of the greatest advances in human health during the past century was the discovery that our natural defenses could be augmented with externally

provided chemical defenses: antiseptics and disinfectants. In almost all cases, antiseptics and disinfectants are benevolent agents that, when properly used, make an enormous contribution to protecting people, especially those facing surgery (Salyers, & Whitt, 2005). Resistance to antiseptics and disinfectants is still poorly understood, but does occur. Already, antiseptics are being used as an important part of the strategy for combating methicillin-resistant *Staphylococcus aureus* strains. Overuse and abuse of antiseptics and disinfectants could reduce effectiveness of key antiseptics and disinfectants and potentially of antibiotics. (Salyers, & Whitt, 2005)

Conclusions: The H1N1 virus outbreak of April and May 2009 clearly illustrates the value of an effective public health infrastructure and the need for coordination with other disease surveillance programs around the world. This pandemic also underscores the dangers of drug resistance, which could leave US citizens defenseless against death-causing microbes. Influenza drugs develop resistance quickly and overuse of Tamiflu or any antimicrobial will hasten drug resistance. We are concerned that if the virus mutates and becomes resistant to all antivirals the US will be left extremely vulnerable during a subsequent wave. While there is a lot of bad news out there right now, there is also the good news. First, Congress has had good payoff from its ten year build up of our public health infrastructure. The U.S. leaders in place have proven highly effective in this test run of our pandemic response. Sanitation is a cost effective intervention and there are simple messages and methods to make this intervention work at home, on the job and in all public areas. Public awareness of the need for prudent use of antimicrobials, antiseptics, and vaccines will help to minimize antimicrobial resistance. Basic research regarding antibiotic treatment, diagnostics, and vaccines is informing our interventions but needs to be expanded. Finally, the STAAR Act introduced by Representative Jim Matheson (D-VT) provides an opportunity for Congress to take leadership in advancing APUA's mission to "preserve the power of antibiotics." Thank you and the federal agencies here today for their dedication and attention.

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