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Introduction  

Chairman Blunt, Ranking Member Murray, and distinguished Subcommittee Members, thank you for inviting me to share my perspective on “Saving Lives through Medical Research.” My name is Dr. Stacey Schultz-Cherry, and I am a member of the faculty in the Department of Infectious Diseases at St. Jude Children’s Research Hospital in Memphis, Tennessee. As you may know, St. Jude’s mission is to advance cures and means of prevention for pediatric catastrophic diseases through research and treatment. Since St. Jude opened its doors in 1962, no child is denied treatment based on race, religion or a family's ability to pay.  

St. Jude also is at the forefront of the ongoing battle against pandemic influenza as well as other emerging viruses. In addition to my faculty position, I serve as the Deputy Director of the World Health Organization (WHO) Collaborating Center for Influenza at St. Jude, which is focused exclusively on the threat to humans from influenza viruses that emerge from animals. We work closely with other WHO centers around the world to guide global influenza research and response. St. Jude produces and distributes materials for vaccines for use against emerging viruses, including pandemic threats.  

As an institution, St. Jude is grateful for the wonderful relationships we have with so many Members of this Subcommittee and your staffs, and we welcome all of you to visit us in Memphis to see what a difference our work makes in the lives of the children around the globe.  

Today I would like to talk about how critical it is to have adequate funding for medical research and the consequences of insufficient support for basic research on infectious diseases. Federal support for medical research is critical to be prepared for the threat of emerging and reemerging diseases, to secure the United States’ position as a global leader in medical research, to ensure that as a country we are able to attract and retain the brightest minds to medical research, and to continue to create the conditions under which ground-breaking medical discoveries are made. I will address each of these in turn.
1) **Threat: Ongoing Threats Posed by Emerging and Reemerging Diseases**

Zika, Ebola, antibiotic-resistant bacteria, Chagas, SARS and MERS, influenza viruses, even measles and mumps: these are just a few examples of the recent threats we have faced from emerging and re-emerging infectious diseases. Since 1980, approximately one to three new human infectious diseases have been identified each year; others have “re-emerged,” causing greater numbers of cases than before and/or affecting different populations and regions than in the past\(^1\). According to the Centers for Disease Control and Prevention (CDC), greater than 60 percent of all known infectious diseases in people are spread from animals and 75 percent of the new or emerging infectious diseases in people have an animal source.

While many of these infections historically have been problems of the developing world, the recent Ebola and ongoing Zika outbreaks in the United States highlight that infectious diseases know no boundaries. During the Munich Security Conference in February 2017, Bill Gates was quoted as saying “Whether it occurs by a quirk of nature or at the hand of a terrorist, epidemiologists say a fast-moving airborne pathogen could kill more than 30 million people in less than a year. And they say there is a reasonable probability the world will experience such an outbreak in the next 10 to 15 years.”

The cost of these outbreaks is staggering. Estimates of the economic cost of an influenza pandemic range from $374 billion (in 2014 US dollars) for a mild pandemic to $7.3 trillion for a severe pandemic with 12.6 percent loss of gross domestic product (GDP)\(^2\). The cost to human life could be even greater. Take for example Zika virus, which has been called an “epidemic on delay.” The impact on babies born to infected mothers or people developing Guillain-Barre syndrome after infection are well-appreciated, but the long-term effects of the epidemic are unknown. Whether infection results in future health effects or long term neurological deficits in infected people of all ages remains to be seen.

Further, there is a burden of disease caused by a group of infections typically only seen in the developing world that is largely hidden and that is known as the neglected infections of poverty. These diseases occur primarily in the Mississippi Delta and elsewhere in the Southern United States, as well as in disadvantaged urban areas and peoples living in Appalachia\(^3\). In several of these areas, many of the diseases we are most concerned about such as Zika, dengue, and diseases of animals that can transmit to humans (for example rabies), not only occur but thrive and could be a source for a widespread disease threat.

How do we prepare for these continued threats? Stable funding for the National Institutes of Health (NIH) to build relationships and capacity with partners across the United States, especially in these areas considered “high risk”, and around the world is key not just to preparing for but possibly predicting the next emerging/reemerging infectious disease threats. These monies must go beyond the basic research, and must include research and surveillance at the animal-human interface, which is the source of most emerging infectious diseases.

We know from our own work at St. Jude Children’s Research Hospital that this approach works. The 1997 outbreak of highly pathogenic H5N1 avian influenza in humans in Hong Kong highlighted the need for global influenza surveillance to protect human health. In response, in
1999, the National Institute for Allergy and Infectious Diseases (NIAID) awarded a contract to St. Jude to set up continuous surveillance of aquatic birds and live bird markets in Hong Kong in collaboration with partners in Hong Kong, Southeast Asia, and the United States. In addition to this early warning system, this contract provided training and capacity building in this region of the world and fed invaluable information and reagents into the WHO and CDC influenza response systems. Ultimately, this program developed a candidate seed vaccine strain. An unexpected second benefit of this program was the detection and characterization of the causative virus of SARS in 2003 by one of our Hong Kong collaborators, Dr. Malik Peiris.

Given the success of the initial contract awarded to St. Jude, NIAID established the Centers for Excellence in Influenza Research and Surveillance (CEIRS) network. The first seven year contract, which funded five centers, resulted in the expansion of animal influenza surveillance programs internationally and domestically and focused on several high priority areas in influenza research. These projects provided key information on influenza virus-induced disease and immunity, assisted in the development of the Influenza Research Database, (an NIAID-funded program that provides datasets and bioinformatics tools to the global research community), and made important contributions to influenza reagent developments and data sharing. Equally important were the training and lab capacity-building activities the Centers supported within the U.S. and around the world. These activities enhance influenza research and response, and build infrastructure that can be applied to other infectious diseases. Arguably, some of the most important activities under the 2007-2014 contracts were a response to the 2009 H1N1 pandemic, in which the CEIRS network was instrumental in conducting early virus characterization studies and pre-clinical evaluation of vaccine material.

We are now in our second generation of the CEIRS network contracts. While the focus remains on influenza viruses, we have seen the emergence of MERS and Zika viruses. The response capabilities and collaborations established with partners within the U.S. and around the world have made it possible for the CEIRS network to rapidly respond to any emerging threat. CEIRS scientists again were among the first to identify and characterize the virus that causes MERS, determine that camels were a key source for human infections, and continue to “look for” MERS in animal and humans around the world. The new capabilities conferred through CEIRS also allowed us to respond to Zika rapidly. Given our long-term CEIRS-funded studies in Colombia, South America, NIH was able to establish Zika studies quickly in an area with an emerging Zika epidemic. However, our studies go beyond Zika infection. We want to understand what happens to a pregnant woman and her child when she gets co-infected with influenza virus and Zika, dengue or even chikungunya virus, a real threat to pregnant women throughout the Americas, especially in an influenza epidemic year like we are facing currently. These critical studies for human health would be impossible without sustained NIH funding.

If there were any doubt that these threats are real and can strike at any time, the USDA APHIS confirmed on Monday that highly pathogenic avian H7 influenza virus was identified in a commercial breeder flock in Lincoln County, Tennessee. The source of the virus appears to be wild birds. The threat to humans is currently unknown.
2) **Competition: The U.S. as a Global Leader in Medical Research**

The U.S. long had been the leader in biomedical research. Unfortunately, this trend is changing. A recent publication by Moses, *et al.* in the Journal of the American Medical Association (JAMA) used publicly available data from 1994 to 2012 to show that the decrease in US funding for biomedical research correlated with a decrease in the U.S. share of life sciences patents, with those considered most valuable decreasing from 73 percent in 1981 to 59 percent in 2011\(^4\).

This is also evident when reviewing publications from U.S. and foreign investigators. In 2009, the U.S. led the world in research productivity, with 33 percent of published biomedical research articles and numbers of articles from U.S. investigators increasing at 0.6 percent per year from 2000 to 2009. We also led the world in the numbers of most highly cited biomedical research articles with 63 percent of the top cited articles in 2000 and 56 percent in 2010. Yet, during the same period, the number of articles published in China increased by 18.7 percent annually and the number of highly cited literature from China continued to increase. After controlling for the share of the world’s biomedical research articles using a citation index, publications from the U.S. declined −0.2 percent from 2000 to 2010 per year as the rest of the world increased by approximately 1 percent per year\(^4\). The trend is even more concerning when considering the number of biomedical research articles submitted to major infectious disease journals.

Figure 1 illustrates the trends from four major infectious disease journals from 2010 through 2016. Overall, the number of submissions from foreign investigators has continued to increase as compared to those from U.S.-based scientists, but there are a few trends. In one journal, U.S.-based submissions were consistently lower than those received from foreign investigators (Figure 1B). However, most journals showed progressive decreases in submissions from US-based investigators. Figure 1C highlights a dramatic shift in one journal; where in 2010 60 percent of submissions were from U.S.-based scientists dropping to 37 percent in 2015. In all cases, the majority of foreign-based submissions come from China.

There are different explanations for these changes, and understanding journal trends and US competitiveness in scientific research will require careful analysis.
3) **Preparation: Encouraging the Next Generation of Medical Researchers**

A key to fighting infectious disease threats is training the next generation of scientists, including the physician-scientists and Doctor of Veterinary Medicine-scientists that likely will be at the frontline of the fight. One of the highlights of my career has been mentoring the next generation of scientists. It is something that I take seriously and will be a major focus during my term as the President of the American Society for Virology. Yet over the past five years, we have seen a disturbing trend: increased numbers of trainees do not want to pursue faculty positions in an academic setting. A recent study by the University of California at San Francisco (UCSF), a world renowned biomedical research institution, tracking their trainees’ careers showed that only 37 percent of U.S.-employed postdoctoral alumni were in faculty positions, which included non-tenure track faculty-like full time research or teaching positions with the majority of these employed at research institutions. The outcome is very different for UCSF postdoctoral alumni that left the U.S. In that case, 54 percent were in faculty positions.

When I ask a trainee why he or she does not want to pursue a career in academic research, not receiving NIH funding is a primary concern. Trainees know that the lack of funding will make it difficult to be productive and ultimately obtain tenure. The low NIH payline (determined by the score you receive during the peer review process) also requires that young investigators spend more time writing grants rather than performing research. Stability of funding may be even more important for the careers of young scientists than the overall size of the Department of Health and Human Services or NIH. Boom-and-bust cycles wipe out generations of young scientists and discourage people from taking a chance in research careers. This means that only older scientists stay in the game. In 2011, the average age of first-time R01 grantees was 42 for Ph.D.s and mid-to-late 40s for M.D. and M.D.-Ph.D. scientists. It is likely even higher now. We also are seeing a skewing in the age of NIH-funded Principal Investigators (PIs). In the 1980s the majority were 35 and younger with less than 1 percent over age 66. Since the 2000’s this has reversed, with the majority of NIH PIs now older than 66.

In many cases, young investigators are required to have funding before they even can apply for faculty positions, making it difficult if not impossible for many to find their first “real job.” “Erik” is an example of this. He came to my laboratory as a postdoctoral fellow to study the impact of obesity on influenza infection and vaccination response, after receiving his Ph.D. in nutrition from the University of North Carolina at Chapel Hill. This is a very creative, ambitious and productive young scientist at the interface of nutrition and infectious diseases. In spite of an outstanding CV, he was having difficulties finding a faculty position because he did not already have independent NIH funding. Many departments were concerned that it could be difficult for him to obtain funding for his work, despite the cutting edge research he was doing. Instead of staying in the U.S., Erik has decided to accept a position as the Head of Virology at one of the Institute-Pasteur laboratories. While I am excited to see him begin his independent career and know that he will be successful, it is discouraging that he has to leave the U.S. to pursue his dreams to be a PI.

It is not only the careers of young investigators that are of concern, but those of the mid-level PIs like me. In many cases, we are the “workhorses” of our fields, serving as journal editors, NIH study section members, teachers for undergraduate, graduate, medical, and professional students, heads of admissions committees, even becoming Presidents of our respective societies. Yet
unlike our more junior colleagues, we are “too old” to apply for many of the funding opportunities specific for young investigators, and may not have the “name recognition” of our more senior colleagues. While on the faculty at the University of Wisconsin-Madison, several of my colleagues at the Associate Professor-level and even Professor-level had to close their research laboratories due to a lack of funding. While they were able to provide other invaluable contributions to the department and university it was a significant loss to basic research. In summary, not only are we failing to bring young people into infectious disease research, but we also are losing many of our “soldiers” in the fight. This will leave us ill-prepared to face future threats, which we know will continue.

4) **Discovery: Basic Research is the Foundation for Important Medical Discoveries**

Federal funding for basic research is an important foundation of societal progress, sustainability, economy and obviously the health and well-being of the population. Without funding for basic research and especially funding for high-risk, innovative research, we will never develop a universal influenza vaccine, new antibiotics to combat antibiotic resistant microbes, or crucial new cancer therapies. In terms of infectious disease research, in order to be at the forefront of the next threat, we need to understand what is happening in our animal populations (domestic and wildlife), and appreciate that our population is aging and expanding, which can impact infectious disease emergence, transmission, disease severity and even efficacy of our therapeutic strategies.

Over the weekend, a global electronic reporting system for outbreaks of emerging infectious diseases and toxins called “ProMED-mail” posted notifications on new meningococcal meningitis, measles and mumps outbreaks on college campuses across the US; the continued westward spread of highly pathogenic avian H5 influenza virus; four new human cases of avian H7N9 influenza infection in humans; and an outbreak of an undiagnosed respiratory disease in Hong Kong, all highlighting the ongoing threat posed by infectious diseases. The next Jonas Salk, George Washington Carver, Marie Curie, or Jane Goodall may be working in our laboratories. Let’s not lose any of them.

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I extend my sincere appreciation to the Subcommittee for asking me to share my views with you today, and I look forward to answering any questions you have.