Institute on Science for Global Policy

Program
on
Emerging and Persistent Infectious Diseases
(EPID)

Strategic Roadmap

Revised August 2010*

*In the process of being revised in 2011

Institute on Science for Global Policy (ISGP) Program

on

Emerging and Persistent Infectious Disease (EPID)

Strategic Roadmap

ISGP programs use a unique format of multiple, invitation-only conferences and caucuses emphasizing debate between scientists and policy makers. Currently, the ISGP is addressing Emerging and Persistent Infectious Diseases (EPID). For each two-year series of ISGP conferences, held at venues in the United States and internationally, the ISGP prepares a Strategic Roadmap that describes the content for each of the seven to eight (7-8) conferences devoted to that scientific and technological (S&T) topic. The EPID version of the Strategic Roadmap is presented here for your review and comment.

The ISGP began the preparation of the EPID Strategic Roadmap by soliciting viewpoints and recommendations from scientific and policy experts in the seven countries participating in and supporting ISGP programs (the United States, the United Kingdom, Italy, France, Germany, Japan, and Singapore). Emphasis was placed on identifying those S&T topics that could be reasonably anticipated to have major impact on domestic and global policies. Of the S&T topics suggested (see the ISGP brochure), EPID was uniformly considered to be of major importance and certainly expected to have significant impact on public policies worldwide.

The EPID Strategic Roadmap provides a view of how both individual countries, as well as the international community, could effectively evaluate the credible S&T options capable of addressing a complex, dynamic topic such as EPID. The topics for each ISGP conference and their agenda were derived from the interviews and correspondence with more than 100 international subject matter experts in S&T and in policy. When combined with a comprehensive review of the credible S&T and policy literature on EPID, the resultant EPID Strategic Roadmap shows how these ISGP conferences can assist governments to efficiently obtain an accurate understanding of the S&T options that underlie effective domestic and international policies concerning EPID.

This document articulates why many scientists and policy makers view EPID as a critical policy issue. The content and format for each of these proposed EPID conferences are presented separately below.

All of these issues are presented here to solicit comments.

Dr. George H. Atkinson
Director
Institute on Science for Global Policy

Institute on Science for Global Policy Overview

Mission and Rationale

- Many of the most significant global challenges for 21st century societies are directly related to the remarkably rapid and profound scientific and technological achievements of our time. Success in fostering safe, secure, and prosperous "knowledge-based" societies often reflects how well governments recognize the opportunities and risks associated with existing, emerging, and "at-the-horizon" science and technology (S&T) and how effectively governmental policies balance short- versus long-term issues. Unfortunately, the gap between science-based understanding and many political and governmental agenda remains large.
- To formulate and implement realistic policies and to guide societal investments of financial and human resources, governments increasingly require anticipatory S&T roadmaps based on "actionable decisions" derived from an accurate understanding of both the S&T advances and the global perspectives of their potential societal impact.
- The **Institute on Science for Global Policy (ISGP)** was established to operate directly with selected governments and at the center of an international network of outstanding academic institutions. The ISGP seeks to significantly improve the capability of governments to effectively bridge the increasingly critical nexus between S&T understanding and major societal issues that shape domestic and international policies in the 21st century.

Structure and Process

- The establishment of the ISGP in association with US and international universities, recognized for their openness to new ideas, distinguished teaching, research, and scholarship, and commitment to public service, is invaluable for creating the public credibility needed to distinguish ISGP programs from more parochial science policy activities. ISGP programs attempt to not only shape current policy decisions, but also to foster public respect for the role of S&T in policy, and to create ongoing institutional commitments to incorporate globally-credible S&T understanding into strategic public policies.
- Operationally, the ISGP focuses on attracting globally recognized S&T scholars, from a range of generations, to accurately describe S&T advances and to participate in critical debates with influential governmental and societal decision makers concerning how they can shape actionable policy decisions. ISGP conferences occur within "not for attribution (Chatham House rule)" environments designed to promote the discussions needed to clarify areas of agreement and differences. These debates focus on creating the in-depth understanding of both the S&T issues as well as the challenges attendant to formulating and implementing policies in increasingly global societies.
- ISGP programs use a unique format based on multiple conferences and caucuses to address a specific S&T topic previously vetted as a priority with participating governments and academic institutions (several separate S&T topics are simultaneously investigated in different series of conferences led by different teams of ISGP staff).
- The ISGP fully controls the selection of invited S&T presenters and the specific topic addressed in each conference. Each S&T expert invited by the ISGP to participate in a conference must first write a three-page position paper identifying the central S&T issues, reasons why governments/societies need to be attentive (both in the short- and

long-term), and potential "actionable decisions" together with their foreseeable consequences. These position papers are organized around three categories: current realities, scientific opportunities and challenges, and policy issues. All these position papers are made available to all participants and presenters prior to convening each ISGP conference, and are the focal points for all debates, discussions, and caucuses.

- The format of each ISGP conference almost exclusively involves questions to the S&T presenters as formulated by the international policy audience selected solely by the participating governments (typically 10 per country). A 90-minute period begins with a short (5 minute) statement by each presenter summarizing the views expressed in his/her position paper. The policy audience is then given remainder of the 90-minue period to discuss, question, and debate the S&T expert. The emphasis remains on presenting credible scientific options that are debated from the policy makers' perspective in order to clarify understanding in the non-S&T audience.
- In each conference, ISGP organizes two types of caucuses: one for each country's delegation by itself and one plenary session for all participating countries. Both are designed to discuss the "next steps" to be considered in formulating and implementing policy.
- The in-depth understanding of existing, emerging, and "at-the-horizon" S&T derived from ISGP programs is anticipated to help shape public policy, and to influence the allocation of the human and financial resources needed to address their impact on societies, both domestically and internationally.
- The long-term, enduring success of ISGP programs depends on the quality of participation from the global S&T and policy communities in government, academe, the private sector and foundations.
- It is anticipated the policy perspectives gained from ISGP conferences are annually shared through a report on the "**State of Global Science Policy"** derived from the ISGP conferences themselves. It can also be anticipated that an open, public, senior-level ISGP conference will be convened to heighten public recognition of the importance of S&T in global policy, to stimulate societal debate, and to shape policy worldwide.

Academic Programs

- The global character of the ISGP is reflected in its "international network of affiliated universities." Students and professors from these affiliated institutions are encouraged to participate in ISGP programs. By cooperating with the pre- and postdoctoral educational programs at these universities, the ISGP seeks to establish itself as "practical policy laboratory" where one can experience how S&T understanding can, and cannot, effectively influence policy decisions. By engaging an international group of students in the real decision-making process, the next generation is exposed to the challenges permeating S&T-policy discussions.

"It's about listening to what our scientists have to say, even when it is inconvenient – especially when it is inconvenient."

– U.S. President Barack Obama, 2009

Institute on Science for Global Policy

Emerging and Persistent Infectious Diseases (EPID)

Introduction

Infectious diseases are a leading cause of human suffering and death, a major threat to international commerce, and an increasingly critical source of political instability across the globe. While infectious disease outbreaks sporadically grab the public imagination and headlines (e.g., SARS, mad cow disease, flesh-eating bacteria, and the swine flu), the news media rarely identifies the complexity of scientific and technological (S&T) factors that must be considered to establish the domestic and international policies needed to effectively combat infectious diseases.

The HIV/AIDS epidemic produced many headlines twenty years ago, and despite a massive research effort a preventative vaccine remains unavailable. Many examples of S&T challenges related to infectious diseases are less well publicized:

- While more is understood about the genetic sequences of microbes and the linkages between hosts and parasites, much uncertainty remains about the potential of new therapies derived from this understanding.
- Each line of inquiry re-confirms the enormous scale of the EPID challenges as viewed through the vast number of pathogens, as well as their adaptability to new environments.
- Dramatic decreases in infectious diseases resulting from a combination of the use of vaccines, the development of antibiotics, improved nutrition, and the provision of clean water were interpreted as bringing the end to the era of infection. This optimism was unfounded.
- New health issues such as cancer were identified as priorities for research. This shift in emphasis led to the defunding of vector control programs and an erosion of basic public health infrastructure. These policies have contributed to ensuring that infectious diseases continue to have major impact worldwide.

In a world experiencing a rapidly increasing population (nearly 9 billion people are expected to inhabit the planet before 2050), the combination of emerging and persistent infections and chronic conditions is dramatically altering societal capabilities to deal with human health. As a consequence, EPID has the potential for dominating policy decisions, including those directly determining national security and prosperity.

If in retrospect the optimism concerning the elimination of infectious diseases seems misplaced at the outset of the 21st century, what are the rational prospects for bridging the foreseeable limits offered by modern scientific and medical research? Can we find a better balance between realism and ambition in a world of multidrug resistance, global climate change and limited vaccine capacity? Which new lines of inquiry, cooperative research agenda, coordinated applications, methodologies for shared information, efficiencies in transforming existing health systems, and perhaps of utmost importance, anticipatory domestic and international policies are capable of achieving more effective results?

The Scope of Emerging and Persistent Infectious Diseases

Elimination and control of infectious pathogens remains complex and elusive. Unidentified pathogens continue to emerge in increasing number and greater severity:

- Human immunodeficiency virus (HIV), responsible for acquired immunodeficiency syndrome (AIDS), killed more than 25 million people between 1981 and 2006.
- The sudden appearance of the SARS coronavirus and its more surprising disappearance highlighted the unpredictability of viral pathogens.
- Prions, infectious agents comprised entirely of proteins, were identified as the causative agent in a number of diseases in mammals, including bovine spongiform encephalopathy (mad cow disease) in cattle and Creutzfeldt-Jakob disease in humans.

Pathogens, believed to be susceptible to control efforts, have proven to be more difficult to eradicate than anticipated:

- *Mycobacterium tuberculosis*, the bacteria responsible for tuberculosis (TB), is estimated to have caused 1.6 million deaths in 2005.
- *Plasmodium falciparum* and related protozoans, responsible for malaria, cause 247 million malaria cases, killing more than 881,000 people annually, mostly African children.

Evolution by pathogens has reduced the efficacy of therapeutic agents:

- Hospital-acquired infections kill more than 200,000 people annually worldwide; many of these infections are resistant to antibiotics.
- In 2007, five percent (~511,000 cases) of the estimated 10.4 million episodes of TB were multidrug resistant; and strains of TB, resistant to at least one of the common therapeutics, was documented in every country surveyed.
- Chloroquine-resistant *Plasmodium falciparum* has spread over most of the globe rendering effective and inexpensive therapies useless.

The economic impact of human and animal pathogens continues to grow:

- The SARS epidemic is estimated to have lowered the gross national product of Hong Kong by 2.6 percent, of China by 1.1 percent, and of Taiwan and Singapore by 0.5 percent each.
- In 2001, an outbreak of foot-and-mouth disease in the United Kingdom is estimated to have cost the economy over £8bn.
- In 2004, it is estimated that 45 million poultry were culled or died during the first large outbreak of avian influenza in Vietnam.

Infectious diseases remain a critical concern, as chronic conditions are increasing:

- Chronic diseases of aging populations and conditions associated with diet and lifestyle (e.g. diabetes) are making increasing demands worldwide on resources devoted to healthcare.
- The burden of chronic diseases in developing nations is also increasing rapidly, because the scourge of infectious diseases has not been eliminated, or significantly controlled.
- The current circulating H1N1 influenza strain has a higher morbidity and mortality among those people with underlying chronic conditions.

EPID Strategic Roadmap

Over the past 18 months, the ISGP staff has interviewed or corresponded with more than one hundred internationally recognized scientific and medical experts to solicit their views and recommendations concerning EPID. Representing the fields of virology, immunology, infectious disease, veterinary sciences, genetics, vaccine development, public health surveillance, medicine, as well as public policy, each interviewee was asked to delineate the most important scientific and technological challenges and opportunities associated with EPID, and to suggest governmental and societal policies they would recommend be considered for confronting these challenges.

Overarching Views

This interview process identified a wide variety of topics, issues, recommendations and challenges associated with EPID. Despite the diverse backgrounds of these experts, they consistently identified a similar set of thematic areas that needed to be examined. Collectively, these areas were identified as critical, both now and in the foreseeable future, in determining how scientific understanding, technological advances, and governmental and societal policies can mitigate the spread and severity of infectious diseases. Their observations and recommendations were used by the ISGP to construct the EPID Strategic Roadmap. The Roadmap is presented here for comment and will be a central agenda item at the Global Perspectives conference to be convened in Tucson, Arizona in December 2009.

A variety of overarching views and observations appeared throughout essentially all interviews and correspondence and characterize the entire series of 7-8 conferences to be convened over two years:

- The time required to produce and to distribute vaccines and other therapeutics is significantly longer that the time EPID travels between widely separated communities worldwide, thus the capacity of vaccines to dramatically alter pandemic outcomes is not optimal.
- The threat of pandemics is real. In the case of influenza virus, the best predictor of the number of deaths expected from a specific strain comes from our understanding of that strain's transmission and virulence characteristics.
- Global climate changes are expected to cause an increase in the spread of pathogens and disease vectors such as mosquitoes, ticks and rodents.
- The increasing number of sprawling mega-cities is producing population densities at levels rarely seen in human history while the rapid, ubiquitous migration of human populations (both legal travel and illegal border crossing activities) is expanding the rate and efficiency at which infections are spread.
- The high population density, poor sanitary conditions, and inadequate public health infrastructure found in both developed and developing countries have produced environments ripe for the spread of pathogens and for increasing the distribution of persistent infectious diseases. These conditions can be anticipated to cause the distribution and abundance of pathogens to reach dangerously high levels.
- Environmental degradation, intentional deforestation, and increasing encroachment of human activity into wilderness areas are anticipated to result in greater

exposure of humans to reservoirs of potentially harmful diseases from animals and parasites. This exposure, coupled with rapid international travel and trade, increases the likelihood that diseases will spread to regions not previously affected. Simultaneously, the chronic lack of access to clean water for many people ensures that the conditions for microbe transmission and adaptation will continue to expand.

- The decreasing sensitivity of pathogens to antimicrobial compounds and the increasing resistance of vectors to insecticides are inevitable. Expanded efforts to develop new antimicrobial compounds and novel strategies for controlling vectors and pathogens are required if the anticipated resistance materializes.

- Much of the difficulty in predicting and tracking infectious disease outbreaks is caused by the lack of health infrastructure for patient monitoring and disease surveillance. Strengthening healthcare systems worldwide is vital, but under-appreciated. Steps to translate research insights into clinical practice and to ensure appropriate drug and care management are vital to bolstering healthcare systems and thereby, to preventing the spread of disease.

- Improving global living standards are driving a greater demand for animal protein. This demand has increased reliance upon industrialized, high-density production of farm animals that routinely requires antimicrobial supplements. Industrialized agriculture approach increases susceptibility of animal populations to disease outbreaks and also increases the susceptibility of human populations to zoonotic diseases.

- Changes in diet and lifestyle are producing expensive healthcare burdens in different areas of the world. This chronic disease burden is growing annually. An estimated 35 million people die from heart disease, stroke, cancer, and other chronic diseases. Eighty percent of these deaths will occur in low-income and middle-income countries and the death rates are often higher for the most productive portion of the population in these countries. The impact on national prosperity is yet to be known.

Scaling policies to the challenges:

In addition to these areas of general agreement, contributors to the EPID Strategic Roadmap also identified a need to scale interventions and policies to the size of the challenge. No single scientific advance, technological opportunity, or policy commitment was viewed as individually capable of solving the complex issues underlying the global threats of EPID. The informants almost all agreed that fundamentally altering the impact of EPID requires the commitments of governmental and societal institutions to efforts at a scale defined by the size of the current realities, and that smaller scale interventions might exacerbate the problem by creating conditions for pathogen adaptation.

Examples taken from HIV/AIDS, influenza, malaria, dengue fever, tuberculosis illustrate what could be reasonably anticipated from insufficiently scoped responses. While the magnitude of the global challenges posed by EPID are dramatic and require significant advances in many technical fields simultaneously, there was broad consensus that the most critical issues pertain to linking credible scientific and technological understanding to effective domestic and international policies.

This latter goal is, of course, fundamental to the mission of the ISGP.

ISGP Conference Topics for EPID

These observations and recommendations were integrated by the ISGP into a series of

EPID conferences to be convened over a two-year period at venues worldwide. The initial six EPID conferences focus on six separate thematic topics:

Pandemics and Viral Mutations

- Pandemic strains of influenza have been extraordinary burdens on human health and welfare. What order of magnitude change is required to ensure that the ubiquitous threats from new influenza strains are minimized? What combination of genomic mapping, zoonotic DNA sequencing, vaccine production innovation, environmental modeling, distribution of diagnostic capacity, sample sharing, cytokine manipulation, demographic understanding and comprehension of antimicrobial resistance is required to effectively combat pandemics in 21st century societies (e.g., H1N1)?

Vaccine Technologies

- Incorporating S&T advances, including the development of more effective and efficient vaccination technologies, remains central to all EPID strategies. The need to address policy issues that have stymied public and private sector investment in vaccine development is perhaps the most important issue blocking immediate improvements in infectious disease management programs.

Surveillance

- Current surveillance capabilities have been insufficient to detect or predict the development and spread of emerging human pathogens. Massive convergence in information technologies, new concepts and tools for data modeling and analysis, and increasing global telecommunication capacity can dramatically improve the global surveillance of infectious diseases and fundamentally transform the processes by which nations address the threats posed by EPID. The prospect of a rapid response infrastructure based upon real-time genetic monitoring of viral isolates is within reach for the first time.

Drug Resistance

- The evolutionary pressures that lead to drug resistance demand multiple fronts be developed to attack pathogens. Novel approaches to the development of antimicrobials that can be applied against multiple pathogens could break the cycle of single drugs for single diseases. Changes to domestic and international policies that have stymied private sector investment in the development of new antimicrobials can increase the availability of new therapeutic options.

Animal and Human Health: Zoonotic Diseases

- More effective infectious disease prevention and mitigation strategies will require increased understanding of zoonotic pathogens. Since animal populations remain the largest reservoir of emerging infections in humans, predicting the changes and conditions for change in this reservoir is essential for protecting human health.

Environmental Change

- Scientific understanding of how changes in natural and man-made environments affect the emergence and spread of infectious diseases is at best limited, and often contradictory. While it has long been recognized that infectious diseases dynamics are intimately related to climate, the scale and diversity of the climate disruptions now occurring, and anticipated, has redefined the climate change/disease debate. By obtaining an in-depth understanding of the relationship between environmental conditions, infectious disease outbreaks and human health, policy makers are better positioned to make informed choices.

While these six topics form the basis of separate EPID conferences, it is recognized that there are overlapping aspects throughout and that conference topics over time could change as the need arises. Each of the initially proposed EPID conference is described in more detail below using current realities, scientific challenges and opportunities, and policy issues to illustrate the areas that can be anticipated to comprise the debates and discussions. New ideas are also likely to be raised as the conferences are organized and participants selected. In all cases, the ISGP seeks to develop an agenda that addresses the questions relevant to policy issues faced in each participating country as well as internationally.

ISGP Strategic EPID Roadmap
Conference Schedule

Date	Title	Location
December 2009	ONE Global Perspectives	Ventana Canyon Resort, Tucson, AZ
October 2010	TWO Emerging and Persistent Infectious Diseases: Focus on Surveillance	Airlie Conference Center Warrenton Va.
May/June 2011	THREE Emerging and Persistent Infectious Diseases: Focus on Prevention	San Diego, Calif.
October/November 2011	FOUR Emerging and Persistent Infectious Diseases: Focus on Mitigation	Europe (UK, France, Italy, or Germany)
February/March 2012	FIVE Emerging and Persistent Infectious Diseases: Focus on Zoonosis	North America (USA or Canada)
September/October 2012	SIX Emerging and Persistent Infectious Diseases: Focus on Environmental Change	Europe or Asia (UK, France, Italy, Germany, or Japan)
January/ February 2013	SEVEN Emerging and Persistent Infectious Diseases: Policy Review Forum	USA

(This page intentionally left blank)

Pandemics & Viral Mutations

Galvanized by the emergence in 1997 of a lethal strain of avian influenza (more than 50% of individuals with confirmed cases have died) many nations have developed pandemic preparedness plans. Additionally, countries have stockpiled antiviral medications, invested in vaccine research and production, and strengthened international surveillance efforts. In spite of these efforts, a novel 2009 influenza A virus (subtype H1N1; swine flu) outbreak that began in Mexico spread within months around the globe, thereby becoming the first pandemic of the 21st century. Few existing preparatory measures appear to have significantly changed the early course of the H1N1 outbreak.

As of September 2009 the severity of this 2009 novel H1N1 influenza virus is comparable to the seasonal influenza. By contrast, the 1918-19 influenza pandemic, also a swine flu, caused the largest number of deaths of any event in the last century, killing 50 million people worldwide. Humankind remains uniquely vulnerable to variations in the genetics of influenza viruses.

Many questions critical to effective influenza policy remain unanswered. What order of magnitude change is required to ensure that new influenza strains no longer threaten all aspects of global societal structure? Can the application of new scientific knowledge and technology significantly reduce the threat of influenza pandemics? Can improvements in sharing clinical samples (animal and human), the wider distribution of diagnostic tools, and an expanded analytical capacity improve front-line identification and timeliness of response? Can occurrence mapping, environmental modeling, demographics, and tracking of vectors and zoonotic pathogens improve prediction to acceptable levels of dependability?

Current Realities

- The inability to assess how mutations of the influenza genome will change the lethality and/or the transmissibility of different strains significantly limits effective mitigation strategies.
- Neither scientific knowledge, nor technological innovation, nor societal responses appear to have significantly protected us from the H1N1 influenza pandemic. The single best predictor of the severity of an outbreak remains the genetic composition of the virus, information generally available only after the onset of the disease.
- High-density production of farm animals increases the susceptibility of animal disease and increases its potential zoonotic transfer to human populations (e.g., influenza). The transmission of the 2009 H1N1 between swine and humans, and the continuing circulation of H5N1 influenza virus in bird populations, illustrates the importance of monitoring and tracking the spread of influenza virus in animals, both domestic and wild.
- Due to their lengthy production times, current egg- and cell-based vaccine technologies remain inadequate for early prevention of viral transmission. Vaccine production cycles are longer than the time it takes for a pandemic influenza strain to spread worldwide.
- A global vaccination effort would be extremely difficult to implement due to limited vaccine production and distribution, the complexity of determining the needs of different countries, and the practicalities of monitoring large populations for negative effects.
- The absence of inexpensive diagnostic kits capable of rapid, point-of-care detection and identification of influenza prevents effective management of influenza outbreaks and

hinders effective disease surveillance.

- The rapidity with which the influenza virus is able to develop resistance to antiviral compounds threatens to reduce the utility of the few antiviral drugs available.

Scientific Challenges and Opportunities

- Better understanding of the genetic basis for influenza transmission (e.g., human to human and animal to human), virulence, and antiviral resistance can lead to tailored and more effective control measures. Expansion of research in these areas can provide more practical options for combating early stages of the pandemic.
- Improving the surveillance of agricultural and wild animal reservoirs of the influenza virus improves the potential for their detection prior to human infection.
- Greater emphasis on research and development of inexpensive and effective vaccines targeted at meat and poultry populations can help mitigate the spread of influenza from zoonotic reservoirs.
- Combining results from operations research and a practical understanding of distributed analytics with real-time genetic coding of clinical isolates promises for developing a more effective rapid-response infrastructure for pandemics.
- Pre-pandemic vaccination programs, individual inherited susceptibilities and health status (e.g., co-infections, age, nutrition, and other chronic diseases) play important roles in the transmission and severity of influenza infection. Integrated analysis of these factors can enable improved outcomes from existing health care delivery options.
- Industry and academic research and development efforts aimed at producing novel influenza antiviral compounds are needed ensure that efficacious medicines are available to help mitigate the impact of novel influenzas prior to vaccine availability.
- Improved understanding of the potential role of pre-pandemic vaccinations could improve targeting of new and/or limited supplies of vaccines.

Policy Issues

- What integrated international regulatory capacity will be required to succeed with a universal global vaccine and vaccination program?
- How can personal genetic data be protected while creating a global influenza surveillance system focused on determining pre-existing exposure to novel strains?
- What agricultural practices can be modified to develop a sufficiently robust protective system for human health? Must turkey, duck and pig production be separated? Can new bio-security measures contribute to better management models for animal facilities?
- How should infectious disease research priorities be adjusted to address the bio-security threats believed to exist to human health? Two specific bio-security threats, anthrax and smallpox, have received the largest US dollar support in the last ten years while other equally, or more, dangerous infectious diseases have received less funding.
- What are the complementary drug and vaccine development efforts (pneumonia, childhood respiratory diseases) needed to break the cycle of mortality associated with influenza?

Institute on Science for Global Policy

Vaccine Technologies

Vaccination has proven to be a safe, cost-effective option for dramatically reducing death and disability associated with infectious disease. Vaccination saves millions of lives each year by preparing the immune system to respond to pathogens before an infection becomes debilitating or life threatening. To date, the majority of vaccines have been formulated using attenuated (reduced virulence) versions of the live organism. These are administered to at-risk populations through one or more rounds of immunization, with special attention to people who are immunocompromised. There are more than 50 licensed vaccines for 24 infectious diseases worldwide.

Traditional vaccine development and production processes have limitations and the current development picture for new vaccines is not encouraging. There is currently no vaccine for HIV despite considerable investments in its development; only three vaccines are undergoing clinical trials for neglected tropical diseases (hookworm, leishmaniasis and schistosomiasis); and a single candidate vaccine to prevent malaria has just entered Phase III clinical trials.

Advances in basic and applied biomedical sciences can significantly improve the development of new vaccines and transform the processes by which nations use vaccination programs as a counter to pathogens.

Current Realities

- The lengthy development process for vaccines often prevents vaccination from being a component of mitigation or prevention strategies for newly emerging infectious diseases.
- For the foreseeable future, research and development of vaccines will continue to be a for-profit endeavor. Private sector investment in vaccine development for developing nations is hindered by the lack of country-level data on disease burden and the absence of reliable information regarding country willingness and ability to adopt new vaccines.
- Effective vaccine development programs have been undermined by gaps in our understanding of the immune response system. Though widely recognized as factors impacting the immune system, the influence of co-infections (age, immune status, and nutrition) on the human immune system is not well enough understood to effectively shape infectious disease control efforts.
- Even if safe, effective and affordable vaccines were available, barriers exist in many developing nations that prevent the implementation of large-scale vaccination programs (e.g., political instability; an absence of vaccine refrigeration facilities; and few who can properly administer the vaccine). Currently the adoption of newly developed vaccines by developing nations lags far behind industrialized nations by approximately 15 years.
- Given the rapidity with which diseases spread, the inability of some nations to effectively vaccinate their populations endangers all nations.

Scientific Challenges and Opportunities

- Incorporating a greater understanding of the role that genetic differences and health status (e.g., co-infections, age, nutrition, and other chronic diseases) play in the immune system response can lead to more effective vaccination programs, and potentially tailored to the needs of individuals.

- Improving disease surveillance and more accurately modeling country-level disease burden can improve the ability of the private sector to forecast demand. Such information can lead to greater investment in research and development of programs designed to address specific populations.
- Identifying the gene-based susceptibility to infection shifts the research and treatment focus to the individual and away from the vaccine/pathogen. Vaccines are useful and historically the correct approach, but attention to individual vulnerability is an important complementary approach yet to be fully used.
- Genomics and proteomics are research domains and techniques that unravel the nature of, and relationships between, genes and their protein products. These fundamental biological insights will influence vaccine technology research by decreasing both the costs associated with new, even individually tailored, vaccines and their production times. Speeding the incorporation of advances from research on genes and the basic proteins that control human characteristics into the development of vaccines could decrease the cost associated with the development of new and/or improved vaccines by getting to market more quickly.
- Advances in basic, preclinical and clinical studies of potentially revolutionary new vaccine technologies (e.g., DNA vaccines, universal influenza vaccines, etc.) are needed to understand the impact that these technologies may have on future vaccine development activities.
- Improving vaccine delivery and administration technologies can decrease the cost and logistical burden of vaccine programs and result in more rapid utilization of newly developed vaccines in developing nations. Immune response boosting adjuvants, stabilizing agents that mitigate the need for refrigeration, and alternative routes of administration are examples of potential technologies that could dramatically reduce the cost of large-scale vaccination programs.

Policy Issues

- Public skepticism about vaccine safety has grown substantially in the past two decades. How can scientists and policymakers demonstrate to the public an accurate understanding of the safety and efficacy of vaccines, and thus avoid the re-emergence of preventable diseases (e.g., measles, mumps) through the underuse of vaccines?
- Manufacturers are reluctant to invest in new vaccine strains due to small potential markets. How can the uncertainty of adoption of new vaccines in developing nations be overcome? Can the availability of country-level data be improved to a level to ensure the development of new vaccines by the private sector?
- Can the lack of public health immunization infrastructure in many parts of the world be overcome to ensure a broad based capability to provide vaccines safely all across the globe?
- Which organizations can lead to the development of secure systems for sharing of personal genetic data that will enable the development of next generation vaccines geographically tailored to genomic variations

Surveillance

Epidemiological reviews of recent infectious disease outbreaks consistently highlight gaps in surveillance of emerging infectious diseases. The SARS outbreak clearly illustrates the need for better early-warning systems, and descriptions of the ongoing H1N1 influenza outbreak have stressed the weakness in surveillance systems' abilities to detect the magnitude of an epidemic at the outset. Without this type of surveillance-based information regarding disease progression, interventions and policies essentially develop from guesswork and thus, have the potential to do more harm than good.

Surveillance enables visualization of current patterns in disease progression. When studied further, these patterns offer insight into the pathogenic movement of the disease in question. Additionally, establishing interdisciplinary insight into future disease threats through varied sources of data, such as diagnostic laboratories, veterinarians, food distributors, or school absenteeism records, etc., can enhance these surveillance systems. These data help validate overarching societal decisions and thereby, create confidence in the comprehensive policies needed to contain pandemics.

Current Realities

- Currently, the global surveillance system is inadequate to justify large-scale decisions in response to disease outbreaks. There are too many areas of the world without coverage, too few links between animal and human health observations, and too few diagnostic tools available in all settings. Even though technologies exist, too few have been deployed.
- Successive new outbreaks (HIV, SARS, influenzas) have been missed, or characterized so poorly, to have undermined and misdirected response efforts.
- Current epidemiological and disease surveillance efforts are not aligned to adequately address the impact of global climate change on the spread of pathogens and vectors.
- Integration of information technologies, new tools for data analysis, and increasing global telecommunication capacity have been used to improve and expedite a number of commercial and scientific activities including the marketing of drugs, economic surveillance, fraud detection and scientific discovery. However, the application of geospatial information acquisition and its transfer to disease surveillance and mitigation has not been optimized. Many such technological advantages have yet to be utilized within the surveillance community.

Scientific Challenges and Opportunities

- Improving disease surveillance, and especially obtaining more accurately modeling for country-level disease burdens, can improve the ability of government agencies and the private sector to forecast demand for many aspects of disease control (e.g., vaccine production and distribution).
- The ability to identify and characterize potential sentinel events, such as the honey bee colony collapse and the unusual respiratory illnesses in restaurant staff handling live

animals prior to spread of SARS, would help to integrate disease information from animal and human health surveillance.

- Fully exploiting new mathematical modeling and analytical capabilities being developed in conjunction with massive computing complexes could advance our understanding of pathogens spread.
- The incorporation of available geospatial data with disease surveillance data would significantly improve the effectiveness of the global surveillance system. There are good S&T options to support such integration into public health planning.
- Developing rapid and inexpensive diagnostic tests for antimicrobial susceptibility is a critical need. These tests could promote the appropriate utilization of available antimicrobial compounds as well as significantly improve the ability to conduct effective surveillance of antimicrobial resistance.

Policy Issues

- Has the experience with SARS been widely appreciated enough to ensure a new era of international and scientific collaboration? Have these events made it clear that rapidly obtaining accurate information on sentinel biological, epidemiological, and changing environmental conditions is vital to national and international security? Will the new International Health Regulations encourage further lowering of legal, trade and other regulatory barriers to sharing such vital information across borders?
- How can the burden of the cost for surveillance be better distributed to ensure greater integration of human and animal health data? Will adding the cost burden to the food production system undermine safety efforts? As the increasing price of food production alters the nutritional status of poorer countries and increases the spread of disease, how are controls over food safety affected?
- Are diplomatic communications attuned sufficiently to the global spread of disease to ensure the early warning of outbreaks can be shared without inducing panic or economic sanctions? How can these communications through diplomatic channels lead to earlier actions to halt spread at the source?
- Surveillance without the ability to respond can become an issue of equity of access to resources. What pre-pandemic polices are useful in promoting broad access to the resources across borders needed to protect all nations?
- How can improved surveillance systems be connected to the development of infrastructures that use the information effectively to mitigate the emerging or persistent infection?

Drug Resistance

Bacteria, viruses, fungi, and parasites all have the ability to develop resistance to pharmaceutical agents. The evolution of drug resistance is a natural phenomenon exacerbated by abusive of antimicrobial drugs, poor patient observance, and poor quality of available drugs. In many industrialized nations, the declining efficacy of antibiotics and other antimicrobial drugs causes significant loss of life and heavily taxes the health-care infrastructure. The estimated annual cost in the United States associated with antimicrobial resistance is at least $5 billion, and in the European Union (EU) the costs of methicillin-resistant *Staphylococcus aureus* (MRSA) alone exceed the entire EU budget for antibacterial research programs.

The impact of drug resistance in developing nations is even more profound. Globally, HIV/AIDS, malaria and tuberculosis combine to account for the largest number of deaths from infections. Each of the pathogens responsible for these illnesses has developed resistance to what were once considered first-line antimicrobial therapies.

Pathogens and disease vectors are not restricted by political and regional boundaries. The evolution of drug resistance in one area can threaten the global effectiveness of therapeutic compounds elsewhere. In the late 1950s and 1960s, chloroquine-resistant *Plasmodium falciparum* emerged on the Thai–Cambodian border and subsequently spread over most of the globe, rendering an effective and inexpensive therapy essentially useless. Research and development on new antimicrobial agents has not kept pace with the decreasing efficacy of currently available pharmaceutical products. The declining efficacy of antimicrobial compounds and the dearth of new drugs are fundamentally degrading the ability of nations to address the threats posed by EPID.

Current Realities

- Decreasing pathogen sensitivity to antimicrobial compounds and increasing vector resistance to insecticides results in both the spread of and increased morbidity.
- The increasing demand in developed countries for meat products has increased the reliance upon the industrialized, high-density production of farm animals whose health is routinely reliant on antimicrobial supplements. The extensive use of antibiotics in animal production increases the likelihood of the development of drug resistance.
- Predicting the paths of pathogen resistance is neither simple nor directly related to previous use of particular antimicrobial therapies. In the 2008-09 seasonal influenza strain there was greater than 95% resistance to Tamiflu in countries without extensive prior usage of the drug.
- The importance antimicrobial resistance in many communities is exacerbated by (i) the spread of vectors (e.g., mosquitoes, ticks and rodents), (ii) changes in the distribution and abundance of pathogens, and (iii) human migration.
- Current capacity to track the global spread and distribution of antimicrobial resistance is inadequate due the large variety of pathways and number of pathogens to be monitored.

Scientific Challenges and Opportunities

- Improving our understanding of how developed resistance occurs *via* the transfer and dissemination of resistant genes spreads from one organism to another is a key component of combating drug resistance.
- Surveillance of antibiotic resistance is critical to provide early warning of emerging disease problems. This includes monitoring changing patterns of resistance, and the ability to routinely evaluate prevention and control measures.
- Incorporating a greater understanding of the role that genetic differences and health status (e.g., co-infections, age, nutrition, and other chronic diseases) play in immune system response can lead to tailored and more effective use of antimicrobial therapies.
- Increased efforts to identify and develop novel technologies, (e.g. blood spectrum antimicrobials) need to be encouraged and supported. Such novel discovery methods can minimize disease infection, speed the onset of adaptive immunity, or otherwise boost human immune function.

Policy Issues

- For the foreseeable future, research and development of new antimicrobial drugs will continue to be a for-profit endeavor. Private sector investment in antimicrobial development is hindered by regulatory, financial and liability concerns.
- What is the best process for ensuring international synchronization of governmental recommendations regarding antimicrobial use? Are the differences between nations in recommendations about appropriate medical use of antimicrobial drugs fostering conditions for adaptation and the development of resistance? For example, are the varieties of government policy statements about the use of antiviral drugs in the current H1N1 outbreak confusing the public, and could they increase the likelihood for resistant strains to circulate unnoticed?
- How can there be increased coordination at the national and international level regarding the harmonization of antimicrobial biomarker discovery? Will the development of novel animal models and in vitro technologies lead to decreases in the cost and risk associated with product development? Can the use and validity of surrogate markers in clinical trials improve the development and approval of novel pharmaceutical products?
- What are the best options for promoting investment by the pharmaceutical industry in the development of new antimicrobial compounds (tax incentives; guaranteed markets; supplemental intellectual property protections etc)?
- How can the global burden of cleaning microbial compounds from the waste stream and water systems be shared?

Environmental Change

Scientific understanding of how changes in natural and man-made environments affect the emergence and spread of infectious diseases is at best limited, and often contradictory. As the effect of human induced environmental changes (urbanization, the availability of water and food resources, deforestation, changes in ocean chemistry and the frequency and severity of natural disasters) becomes clearer, it is expected that we will increasingly encounter an array of infectious diseases that have greater impact on human health. By obtaining an in-depth understanding of the relationship between environmental conditions and human health, policy makers are better positioned to make fully informed choices.

While it has long been recognized that infectious diseases dynamics are intimately related to climate, the scale and diversity of the climate disruptions now occurring, and anticipated, has redefined the climate change/disease debate. For example, water, both in excess and scarcity, is closely tied to many infectious diseases. It is evident that the global water supply, already taxed by rising populations, faces extreme threats from changes in precipitation patterns thought to be part of climate change. Attention to effectively managing the quantity and quality of current water supplies could mitigate the magnitude of future infectious diseases, at least as it relates to water.

As the environment alters the infectious disease patterns we have historically experienced, existing health infrastructures will be challenged in new ways. Health systems unable to manage the burden of existing infectious disease will be the least able to protect their citizens from those disease outbreaks connected to global climate change. We do not yet understand in detail how the range of anticipated environmental disruptions will affect infectious diseases, but it appears clear that environmental changes will play a major role in influencing the severity and spread of disease worldwide.

Current Realities

- The speed and magnitude of the global environmental changes occurring today will have consequences for infectious diseases. Currently, the limited understanding of how environmental changes will impact diseases inhibits policy makers' ability to determine the most effective public health solutions to infectious disease challenges.
- The focus of environmental studies has been on diseases occurring primarily in local areas. The results have provided insights into developing effective disease prevention strategies within these confined communities. For example, satellite images of a neighborhood in a Kenyan city allowed health workers to find clusters of malaria incidences and target those areas for treatment, reducing the overall rate of infections throughout the community. This also allowed the environmental conditions contributing to these "hot spots" to be better understood, thereby also revealing some of the root environmental causes for infections.
- Although poor sanitation, due largely to a lack of clean water, presents one of the most critical present day environmental challenges in the fight against infectious disease, the technology needed to produce larger quantities of clean water is readily available. The

political will to incorporate these capabilities into communities remains a significant barrier to improving human health.

Scientific Challenges and Opportunities

- With the widespread availability of geographic information software, scientists are helping local communities map how environmental factors are changing the spread of infectious diseases and developing targeted public health solutions. However, the public health data and epidemiology skills essential to the analysis are frequently difficult to locate and apply.
- The general infectious disease risk can be understood in part by studying specific environmental factors. For example, in the United States the prevalence of lyme disease was assessed through field research, and combined with NASA Earth-observing data on climate variables. Models were developed to map where lyme disease would likely become prevalent in the future under various climate change scenarios while recognizing that the severity of the disease is often largely determined by climate. Unfortunately, there are few evidence-based studies of this kind.
- Changes to the global climate will result in new patterns of storm severity, droughts and flooding. Infectious disease epidemics frequently follow natural disasters, which increase exposure to disease, while at the same time reducing access to medical treatment. Research into understanding extreme weather patterns and modeling them can improve the predictive capabilities of existing models, thereby providing better warnings and more quickly repair the damaged infrastructure affecting disease control.
- While it is known that various environmental factors have complex and interacting (non-linear) relationships with appearance and severity of infectious diseases, there is little quantitative understanding of these relationships. Mathematical methods from other disciplines (e.g., optics, bio-informatics) are available to quantatively model these phenomena and to provide new insight into anticipating how climate change affects disease detection and control.

Policy Issues

- Currently, the satellite images and geospatial data required for environmental research are often costly and difficult for researchers to obtain. Can improving access to these data and reducing cost barriers to the distribution of data for research accelerate the pace of discovery in this field? Can new international data-sharing standards be developed with the speed required to enable effective research?
- Understanding the environment-disease relationship at the local level requires a commitment to obtaining credible information on the epidemiology of disease occurrence. Can local information be provided to policy makers on the infectious disease consequences of actions that alter the environment, such as infrastructure projects, natural resource extraction, and energy production?
- Climate change also affects diseases of animals and, therefore, the human food supply. What is the correct balance of policies to ensure the safety of the food supply while enhancing disease monitoring?

Animal Health and Human Health: Zoonotic Diseases

The majority of emerging diseases infecting humans today are zoonotic in origin, i.e., infections spread to humans by animals. More than 60% of all human pathogens are zoonotic and have represented 75% of all emerging pathogens during the past decade. HIV/AIDS, SARS chikungunya, and nipah virus are zoonotic diseases that were generally unheard of prior to 1980, but are now commonly recognized as significant threats to human health. Animals represent the largest reservoir for infectious diseases, and predicting the changes and conditions for change in this reservoir is a complex scientific challenge. Meeting this challenge requires controlling patterns of human-animal contact, monitoring changes in wildlife population and trends in animal production, researching host-pathogen transfer, and supervising the mobility of food, humans, and animals.

Animal farming increases the risk of contracting a zoonotic disease, primarily by bringing humans in close contact with animals and their waste. The risks posed by proximity are exacerbated when unsanitary meat processing conditions are used, as is often the case in resource-poor parts of the world. Further, the extensive use of antimicrobials in animal farming is spawning resistances that can cross the species barrier making zoonoses more challenging to treat in both animals and humans.

Prevention is the primary tool and can be applied by improving sanitation and meat treatment protocols. However, in the inevitable instance of an animal disease being transferred to humans, surveillance is essential for early detection. During the recent rapid and uncontrolled spread of H1N1 (swine flu), our current global surveillance and containment systems were tested and often found wanting. It is clear that efforts to curb disease spread are ineffective in the absence of international cooperation and communication concerning both human and animal populations.

Current Realities

- Projections of human population growth indicate that there will be almost nine billion people on earth by 2050.
- By 2020, demand for animal protein is expected to grow by 50%. Given that there have been increasing incidents where meat production has occurred under conditions that lack adequate sanitation and/or access to modern veterinary technology, it is expected that animal to human disease transmission will increase.
- Although many animal pathogens have emerged as possible zoonotic diseases, surveillance of the animal reservoir designed to search for the next zoonotic challenge to human health remains inadequate.
- The procedure for addressing some zoonotic diseases requires extermination of the animal host, which by itself can pose serious threats to the availability of food supplies.

Scientific Challenges and Opportunities

- Predicting future zoonotic infections will require a more detailed understanding of the genetics and biology of pathogens in animal species. The monitoring of high-risk pathogens (e.g., the family of RNA viruses, such as influenza) involves studies in high-risk environments (e.g., mega-cities) and with high-risk animals (e.g., pigs). While effective scientific techniques are available, the commitment to use these resources widely enough has yet to be made.
- While emerging zoonotic diseases have recently captured public attention, long-standing scientific challenges remain to be solved in examining those neglected zoonoses still contributing significantly to global mortality. These include anthrax, bovine tuberculosis, rabies, sleeping sickness, *Salmonella*, and *E. coli*.
- The efforts of veterinary medicine devoted to addressing zoonotic diseases in the animals are often insufficient to meet the recognized challenge, especially in the developing world. There is a vast gap in understanding current diseases of animals, without including the pathogens that may be emerging from these hosts. Developing a taxonomy of diseases most likely to jump the species barrier is a critical need.
- Developing more effective methodologies for studying zoonoses requires enhanced scientific collaboration between the veterinary and human medical research communities, especially concerning how animal diseases transfer to humans.

Policy Issues

- The spread of H1N1 illustrated the continued need to enhance our integrated global alert and response system for both humans and animals. Currently, significant gaps in the global system exist, in part because of the lack of strong national public health systems and capacity. How can an international system for coordinated response be developed for the next zoonotic disease, especially for monitoring animal populations?
- How can predictive data mining be deployed to search for the most likely high-risk pathogens in animal populations? How will this information be effectively incorporated into the analysis of changes in vector competence and the evolutionary adaptation of pathogens?
- The deterioration of animal health places food security at risk at all levels. Clearly, the economic and health consequences of disruptions in food supply can be dramatic. How can we develop effective food security strategy based on an integrated monitoring of animal pathogens?
- A quantitative understanding of the human and animal movement across borders and its relationship to zoonosis is essential for developing policies to control disease spread. What new regime of policy is needed to incorporate these needs into the overall issues concerning international travel and trade?