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The Forum of Microbial Threats was established to provide a structured opportunity for stakeholder discussion and scrutiny of critical and possibly contentious scientific and policy issues of shared concern related to research on and the prevention, detection, and management of infectious diseases and dangerous pathogens. Because of the unofficial nature of its deliberations coupled with the neutrality of the Institute of Medicine, the Forum remains uniquely positioned to stimulate original thinking about new as well as long-standing problems in these areas.
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FORUM ON MICROBIAL THREATS

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Introduction

The Forum was established to provide a structured opportunity for stakeholder discussion and scrutiny of critical—and possibly contentious—scientific and policy issues of shared concern related to research on and the prevention, detection, and management of infectious diseases and dangerous pathogens. Because of the unofficial nature of its deliberations coupled with the neutrality of the Institute of Medicine, the Forum remains uniquely positioned to stimulate original thinking about new as well as long-standing problems in these areas. Indeed, it is expected that the Forum will continue to:

- promote a regular and ongoing exchange of information and ideas about critical issues among policymakers, public and private sector leaders, individuals, and groups who shape and influence public policy and opinion;
- clarify policy and research issues and identify options that require additional emphasis and research, and encourage leading scientists, public health professionals, medical care providers, private industry, and others to further explore these areas;
- inform public and private sector decision- and policymakers about the scientific basis and public health needs and understanding related to infectious diseases in the United States and worldwide; and
- formulate priority and collaborative initiatives that require in-depth exploration, review, and/or analysis of existing data and research, particularly in instances where new strategies are necessary to advance progress on the emergence, detection, and response to infectious diseases.

Framework of the Forum

The Forum’s work continually evolves to address the ever-changing challenges at the intersection of infectious diseases and human health, development, and security. Through public debate and private deliberation, the activities of the Forum seek to facilitate open discussion and inquiry into the most pressing and cross-cutting set of issues in light of recent or groundbreaking advances that may lead to further innovation or resolution. In recent years, the result of such cross-sector dialogue has fostered action toward addressing priority issues in infectious disease research and public health policy; the use of new scientific and policy tools, and; opportunities for more effective collaboration between the private and public sectors represented on the Forum. The activities of the Forum have highlighted and brought to the fore some of the most important infectious disease issues of the last decade that have included cutting-edge research findings and deliberations that provide not only the most up-to-date information, but also models that are useful in predicting what is not yet fully understood.

Building on the findings and recommendations of the 2003 IOM report, Microbial Threats to Health: Emergence, Detection, and Response, the Forum will continue to be a regularly convening mechanism of representatives from the upper policy levels of all the major stakeholders who represent a wide range of organizational interests and a breadth of scientific and policy expertise. Forum members serve anywhere from an 18-
month to a three-year term. The strength of the Forum activity rests in the diversity of its expert membership and the commitment of its individual members to attend these activities on a regular and continuing basis. Individuals and representatives from organizations with relevant expertise are invited to Forum meetings on an ad hoc basis to provide additional testimony and perspectives in particular areas of interest or concern, and in some cases, in the form of written documentation and review papers. In all of its activities, the Forum seeks to strengthen and forge global links among the public health, medical care, agricultural, veterinary, academic research, policymaking, and pharmaceutical and biotechnology industry, and national security communities that are involved in the research, surveillance, detection and response to domestic and global infectious disease challenges.

The Forum members continue to organize around activities designed to solve problems and identify critical issues in the field. Topical, issue-oriented, public workshops are followed by published summary reports. The Forum also will continue to meet in closed-session planning meetings to discuss topics of particular sensitivity, urgency, and interest to U.S. government agencies, public health specialists, public and private sector interest groups, and U.S.-based funders and implementers of research and control activities related to infectious diseases and dangerous pathogens. These planning meetings will seek to foster active and innovative collaboration among multiple sectors focused on the timely resolution of critical problems.

The Forum will convene three (3) public workshops and two (2) closed-session planning meetings each year. The subject area and scope of the working group session and workshops will continue to be determined by the Forum members. It is important to note here that the active engagement and participation of the members of the Forum has been and must continue to be both substantial and consistent in shaping the direction and format of Forum activities.

Based on the outcomes of workshop and working group discussions, Forum members are able to recommend the formation of IOM study committees on issues where remaining questions and priorities clearly warrant further study. Such a committee would function independently of the Forum (though it may include some Forum members) and would offer conclusions and recommendations on the identified topic. The recommendations for IOM ad hoc committee studies would be presented to the parent Board on Global Health (BGH) and developed through consultation with its members and other relevant Boards of the National Academies.

**Issues and Activities**

Against the backdrop of changing infrastructures, technology, and the continuing challenges posed by infectious diseases and dangerous pathogens in the United States and globally, the Forum focuses on five broad areas of inquiry: surveillance and detection; emerging tools and technology for diagnosis and treatment; research directions and priorities; education, training, and public communication; and, opportunities to strengthen public-private sector partnerships. It is anticipated that these overarching themes will continue to guide the activities of the Forum.

With this multi-faceted framework for examining a range of microbial threats, the Forum will examine both naturally occurring and intentionally-introduced pathogens and diseases. In 2004, the Forum has established parallel tracks of activities that will continue to address the threats to human health, the economy, and development posed by the worst that Mother Nature can muster. Additionally, through its public and closed-session activities, the Forum will consider topics defined as biosecurity threats. This track of activities seek to engage a broader set of international and national security researchers and policymakers and will stimulate opportunities to develop complementary and synergistic activities within the overall portfolio of the Forum’s efforts. In this context, important areas for exploration might include: what investments are currently being made to identify and respond to a naturally-occurring disease outbreak or intentionally engineered pathogen; how to best utilize these resource investments in an integrated fashion within and across government agencies; and how
to educate and advise the public, public health, and first responder communities on how to make wise use of these tools and technologies for local and regional emergencies.

**Recently Completed Workshop Activities:**

- **March 14 – 15, 2011: Synthetic and Systems Biology**

  Humans have been modifying the genetic characteristics of plants and animals for millennia by breeding species together to promote certain traits and reduce others. The discovery of the structure of DNA in 1953, followed by the invention of DNA recombinant technology two decades later, paved the way for the very powerful potential to efficiently and effectively manipulate nuclear and cytoplasmic genes to express specific traits in an organism within a single generation. In the last several decades, researchers have been able to work directly with DNA to genetically engineer changes in cells, leading to advances such as the ability to mass-produce safe and affordable insulin for diabetics. These advances in our understanding of the basic building blocks of life, combined with a concurrent explosion in technology, have allowed researchers to come tantalizingly close to being able to “design” new organisms—in effect creating life.

  This new scientific discipline, which applies engineering principles to design biological systems that behave in a specific way, is known as synthetic biology. Synthetic biology holds promise for a wide range of applications for health, energy and the environment. The field could create an explosion of new industries and revolutionize the way we prevent, diagnose, and treat disease; address energy and environmental challenges; build buildings, aircraft, and cars; and even design and understand computers. Indeed, microbes are already being engineered to produce useful medicines such as artemisinin and the same approaches may be applied to more easily produce other drugs. Other possible applications include biological sensors to detect infections, fine tuning existing drugs, and techniques to improve tissue reconstruction.

  On May 14-15, 2011, the Institute of Medicine’s Forum on Microbial Threats held a public workshop to explore the scientific and policy dimensions of recent developments in genetic engineering and their applications to emerging infectious diseases. Through invited presentations and discussions, this workshop considered the use of genetic engineering, synthetic genomics, synthetic biology, other molecular biology approaches for understanding microbial emergence and evolutionary diversity. Workshop participants also discussed the applications of these advanced technologies in the life sciences and engineering disciplines to contribute to improvements in human and animal health, agriculture, and biodiversity. An individually-authored summary of the workshop is being prepared in accordance with institutional policy and procedures.


  In the past several decades, emerging fungal diseases of plants, animals, and humans have devastated natural ecosystems and agricultural crops, triggered global population declines and extinctions in wildlife, altered the tree population diversity and ecosystem dynamics in temperate and tropical forests, and have contributed to death and disability in humans. While the frequency of many known fungal diseases may be on the rise due to “host factors” others such as *Cryptococcus gattii*, are emerging in new geographic ranges with altered virulence characteristics.

  *Cryptococcus gattii*, a pathogenic environmental fungus believed to have been introduced onto Vancouver Island, British Columbia, Canada in 1999, is causing a growing epidemic of human and animal disease and death in the Pacific Northwest. Several novel diseases of animals have also been associated with fungal pathogens. —Bat white nose” syndrome and amphibian chytridomycosis currently threaten massive population declines and in some cases, species extinction in New World bats and amphibians, respectively. In 2009, a new virulent strain(s)
of wheat yellow ‘stripe’ rust was identified and quickly spread to five continents threatening the world’s wheat supply. These pathogenic strains of yellow stripe rust have been described by some as a severe threat to the world’s wheat supply."

The emerging fungal diseases not only share features that allow them to become established in new ecological niches and new host ranges, but also present common opportunities for coordinated global disease surveillance and response. On December 14 - 15, 2010, the Institute of Medicine’s Forum on Microbial Threats hosted a two-day public workshop to explore the scientific and policy dimensions of the emerging fungal diseases. Through presentations and discussions, workshop participants discussed the evolutionary, genetic, and ecological origins of fungal pathogens and the role of fungi in the carbon cycle, reviewed their influence on human, plant, and animal health and on economic productivity, and considered opportunities for coordinated global engagement for surveillance and response to these enigmatic pathogens. The summary report of this workshop is in press.

♦ September 21 – 22, 2010: The Causes and Impacts of Neglected Tropical and Zoonotic Diseases - Implications for Global Health and Opportunities for Novel Intervention Strategies

Although medically diverse, neglected tropical diseases share features that allow them to persist in conditions of poverty, where they cluster and frequently overlap. Approximately 1.4 billion people—one-sixth of the world’s population—suffer from one or more neglected tropical diseases. Conflict situations or natural disasters aggravate conditions that are conducive to the spread of these diseases. Around half of the world’s population is at risk of NTD infections. The human NTDs are diseases of poverty, afflicting the world’s poorest, and trapping them in a cycle of poverty. The global burden of the neglected tropical diseases is equivalent to at least half of the combined global burden of HIV/AIDS, tuberculosis (TB), and malaria.

Several NTDs are zoonoses -- infections that can be transmitted between animal and human hosts, sometimes by means of a vector, or carrying species (for example, the parasite that causes African trypanosomiasis, or sleeping sickness, infects livestock and wild animals as well as humans, and is transmitted by the bite of a mosquito). Additional neglected zoonotic diseases (NZDs) such as brucellosis, bovine tuberculosis, and rabies, which are not typically included among the NTDs, profoundly affect impoverished people not only through their direct effects on human health, but also by sickening and killing the livestock upon which their livelihoods depend.

NTDs and NZDs not only share features that allow them to persist in conditions of poverty, where they cluster and frequently overlap, but also present common opportunities for effective, integrated, intervention and control strategies. On September 21st and 22nd, 2010, the Institute of Medicine’s Forum on Microbial Threats hosted a two-day public workshop to explore the scientific and policy dimensions of NTDs and NZDs. Through presentations and discussions, workshop participants discussed the evolutionary, genetic, and ecological origins of NTDs and NZDs, reviewed their influence on human and animal health and on economic productivity, and considered opportunities for medical diplomacy and global engagement to reduce the profound, yet long-hidden, consequences of these diseases. The summary report of this workshop was released in May 2011.


Infectious diseases remain among the leading causes of morbidity and mortality on our planet. Resistance in microbes-bacterial, viral, or parasitic worms-to therapeutics is not surprising or new. It is, however, an increasing challenge as drug resistance accumulates and accelerates, even as the drugs for combating infections are reduced in power and number. Today some strains of bacteria and viruses are treatable with only a single drug, and some
no longer have effective treatments. The disease burden from multi-drug resistant strains of organisms causing AIDS, tuberculosis, malaria, influenza, pneumonia, and diarrhea is growing in both developed and developing countries.

The Institute of Medicine’s Forum on Microbial Threats hosted a public workshop on April 6th and 7th, 2010, in Washington DC, to explore the scientific and policy dimensions of the global spread of antimicrobial resistance. Through invited presentations and discussions, this workshop explored the evolutionary, genetic, and ecological origins of antimicrobial resistance and its increasing impact on human and animal health worldwide. Participants discussed host and environmental factors associated with the expansion and impact of antimicrobial resistance; strategies for extending the useful life of antimicrobials; alternative approaches for treating infections; incentives and disincentives for prudent antimicrobial use; and prospects for the discovery and development of novel antimicrobial therapeutics. The summary report of this workshop was released in late 2010.

- **September 15-16, 2009: The Domestic and International Impacts of the 2009 Influenza A H1N1 Pandemic: Global Challenges, Global Solutions**

  In March and early April 2009, a new influenza A (H1N1) virus (S-OIV) emerged in Mexico and the United States. During the first few weeks of surveillance, the virus spread worldwide to 30 countries (as of May 11) by human-to-human transmission, causing the World Heath Organization to raise its pandemic alert to level 5 of 6. On June 11, 2009, the World Health Organization (WHO) raised the worldwide pandemic alert level to Phase 6 in response to the ongoing global spread of the novel influenza A (H1N1) virus. More than 100 countries have now reported cases of human infection with the novel swine origin H1N1 Influenza A virus—a number that has been increasing as the virus moves from the Northern to the Southern Hemisphere. The story of how this new influenza virus spread out of Mexico to other parts of North America and then on to Europe, the Far East, and now Australia and the Pacific Rim countries has its origins in the global interconnectedness of travel, trade, and tourism.

  This novel origin influenza A virus has now become the first influenza pandemic of the twenty-first century. In order to better understand the domestic and global scientific, public health, and policy dimensions of this new pandemic, the IOM’s Forum on Microbial Threats convened a public workshop on **September 15-16, 2009**, to explore issues concerning: (1) viral evolution, epidemiology, and surveillance for the new H1N1 Influenza A virus; (2) the economic and public health impacts of the global response to the H1N1 Influenza A virus; (3) the application of lessons learned from the infection patterns and experiences with the H1N1 influenza A virus in the Southern Hemisphere to countries north of the equator; and (4) vaccine and drug development, availability, accessibility, and equity. The pre-publication version of the summary report of this workshop was released electronically on December 29, 2009. The final version of this report was released in September 2010.

**Future Workshops:**

Planning for the next 18 months has begun and the following topics have been proposed for exploration through workshop/symposia activities:

- "One Health” and Food Safety
- The future of new diagnostic modalities for rapid disease detection in primary and emergency care settings;
- Domestic and international “real time” surveillance for “unusual disease outbreaks” in human, plant and animal populations;
- The potential to exploit environmental monitoring as a tool for the detection and identification of “novel” agents;
- Surveillance, Prediction, and Public Health Response to Emerging Infectious Diseases
The Possible Role of the Microbiome and Microbial Community Composition in Health and Disease

Microbial Forensics

Recently Completed Working Group Planning Meetings

With representation from the three major sectors involved with issues surrounding emerging, resurgent, and endemic infectious diseases and the threat of dangerous pathogens, a primary objective of the Forum is to facilitate debate and discussion among the members. Closed-session working group discussions of Forum members provide an opportunity to explore complex, cross-cutting, and highly charged issues in a neutral setting—allowing provocative, off-the-record exchange about contentious and problematic issues as well as opportunities for innovation.

June 28–29, 2011: Discussion on Microbial Forensics and Detection Technology and Discussion of the Microbiome and Microbial Ecology.

On June 28, 2011, the Forum hosted a one day discussion meeting to explore the topics of microbial forensics and detection technology and also to discuss the microbiome and microbial ecology. Invited speakers and discussants included Bernie Goldstein (University of Pittsburgh), Tim Stearns (Stanford University), Paul Keim (Northern Arizona University), David Relman (Stanford University), Sarkis Mazmanian (California Institute of Technology), Jeremy Nicholson (Imperial College London), and Forest Rohwer (San Diego State University), Cameron Currie (University of Wisconsin at Madison), and Jonathan Eisen (University of California, Davis).

- June 28, 2011: Morning Session — Microbial Forensics and Detection Technology. The discussion leaders included Bernie Goldstein from the University of Pittsburgh; Tim Stearns from Stanford University; and Paul Keim, from Northern Arizona University.

Forum members were briefed on the findings and conclusions of the IOM/NRC report: BioWatch and Public Health Surveillance: Evaluating Systems for the Early Detection of Biological Threats by the Chair of this consensus committee Dr. Bernard Goldstein. The BioWatch program began in 2003 to detect certain biological agents released in aerosolized form. While BioWatch has the potential to provide a more timely alert than the public health and health care systems — under a narrow set of circumstances — the promise remains theoretical. The program’s current emphasis on detection technology over the information needs of users and the program’s lack of integration with the public health system limit this system’s contribution to national biosurveillance. Dr. Tim Stearns discussed the findings of a 2008 JASONs study on Microbial Forensics. Microbial forensics is an increasingly useful tool for natural and intentional outbreaks of infectious disease, but findings need to be supported by other evidence (e.g., derived from field work or intelligence work). In the short term, efforts to standardize methods and tools are needed (e.g., sample collection, reference library, bioinformatics tools) and longer-term goals should include development of novel methods to investigate microbial characteristics (e.g., transcriptome analysis, epigenetic modifications). Dr. Paul Keim of Northern Arizona University discussed whole genome sequencing, how this technology is revolutionizing the field and presented several examples of how detailed genomic information can be used to understand the ecological and evolutionary forces that shaped the phylogeography of recently emerged diseases, such as the geographic origins of several historical plague (Y. pestis) epidemics and the recent cholera epidemic in Haiti.

- June 28th – Afternoon Session — The Microbiome and Microbial Ecology

The Forum hosted a half-day discussion on June 28, 2011 to explore research on the Microbiome and Microbial Ecology. Participants included: David Relman, Stanford University; Sarkis Mazmanian, California
Institute of Technology; Jeremy Nicholson, Imperial College London; Forest Rohwer, San Diego State University; Jonathan Eisen, University of California, Davis; and Cameron Currie, University of Wisconsin at Madison.

Microbial ecology characterizes microbial diversity, and the complex relationships between microbes and their environment. Recent studies on the human microbiome have begun to reveal the complexity of these interactions within the human body and the effects of the environment on community composition – over space and time. Potential benefits from these interactions include: food digestion, nutrition (vitamins, energy), xenobiotic processing, metabolic regulation, development, the “education” or regulation of the human immune system, epithelial —homeostasis”, barrier integrity, and colonization resistance to pathogens. Research on these interactions will help to characterize microbial contributions to —health” and —disease”. Studies on leafcutter ants have revealed a complex web of symbiotic interactions, among ants, bacteria, and fungi that are associated with fungal —gardens” cultivated by ants for food and transmitted from colony to colony. These associations are ancient and underscore the role microbes have played in driving adaptation and evolution of organisms. To date, most microbiome or microbial ecology studies have focused on bacteria, but viruses also play an important role in the dynamics of complex biological systems. The phylogenetic diversity of microbes is poorly sampled and a more systematic approach to sampling and analysis would greatly benefit the field. Improving the quantity, quality, and diversity of microbial sequence data is essential for understanding microbial biogeography, phylogeny, function, and community composition.

- June 29, 2011:

The Forum held a private half-day planning meeting on June 29, 2011 to discuss future workshop topics and to identify potential speakers to invite to future meetings. After closed deliberations, the Forum decided to host a public symposium on Biosurveillance on September 20-21, 2011.


- June 15, 2010:

The Forum hosted a half-day discussion on June 15, 2010, to learn more about Communicating Science in a Multi-Medium Environment”. The participants in the wide-ranging panel discussion -- moderated by Dr. Jim Hughes, co-chair of the Forum -- included Dr. Scott Keeter, Director of Survey Research at the PEW Research Center; Dr. Richard Besser, former acting-Director of the Centers for Disease Control and Prevention and currently Senior Medical Editor for ABC News; Dr. Joe Palca, Science Reporter for National Public Radio; and, Ms. Maggie Fox, Health and Science Editor for Reuters.

June 15 – 16, 2010: Discussion of the Emerging Fungal Diseases of Plants, Animals, and Humans – is there a role for the Forum to host a public workshop on this topic?

The Forum on Microbial Threats organized a one-day meeting on June 15, 2010 and part of June 16, 2010 to learn more about the nature and potential impact of the emerging fungal diseases of humans, plants and animals. In the past several decades, emerging fungal diseases of plants, animals, and humans have devastated natural ecosystems and agricultural crops, triggered caused global population declines and extinctions in wildlife, altered the tree population diversity and ecosystem dynamics in temperate and tropical forests, and contributed to death and disability in humans. While the frequency of many known fungal diseases may be on the rise due to —host factors” others such as Cryptococcus gattii, are emerging with altered virulence and geographic ranges.
Cryptococcus gattii, a pathogenic environmental fungus believed to have been introduced onto Vancouver Island, British Columbia, Canada in 1999, is causing a growing epidemic of human and animal disease and death in the Pacific Northwest. Several novel diseases of animals have also been associated with fungal pathogens. —Bat white nose— syndrome and amphibian chytridmycosis currently threaten massive population declines and in some cases, extinction of species of New World bats and amphibians, respectively. In 2009, a new virulent strain(s) of yellow `stripe' rust of wheat, was identified and quickly spread to five continents threatening the world's wheat supply. These pathogenic strains of yellow stripe rust have been described by some as —a severe threat to the world's wheat supply."

**June 16, 2010:**

Based upon this briefing and discussion the Forum decided to host a 2-day formal public workshop on —coming fungal diseases”— on December 14 – 15, 2010 in Washington, DC. The Forum on Microbial Threats also held a half-day private planning meeting to discuss future workshop topics and identify potential speakers to invite to future meetings.

**PUBLICATIONS AND DISSEMINATION**

**Workshop Summaries**

Reports of Forum workshops have highlighted and brought to the fore some of the most important infectious disease threats of the last decade. Through dissemination to public leaders, private industry, and policymakers, the summary reports have served as a useful decision-making tool and record of these innovative proposals and ideas.

After each workshop, a report summarizing the proceedings of the workshop is prepared, reviewed according to National Research Council report review procedures, and published by the National Academy Press. The workshop summary presents lessons learned from described experiences, delineates a range of pivotal issues and their respective problems, and puts forth response and research agendas as described by the workshop discussants.

Reports of the Forum's workshops and meetings will continue to be distributed to Forum members, sponsors, meeting attendees, and other interested constituencies. These reports summarize the proceedings of the workshop or meeting, but do not contain consensus advice or recommendations regarding government policy. Workshop or meeting summaries include a disclaimer indicating that the individual views described therein are those of the speakers/presenters and not necessarily those of the National Academies or Forum members. The National Academy Press publishes the reports.

The following is a list of published or in press workshop summary reports of the Forum on Microbial Threats.


The Domestic and International Impacts of the 2009-H1N1 Influenza A Pandemic: Global Challenges, Global Solutions National Academies Press (2010)


Global Climate Change and Extreme Weather Events: Understanding the Contributions to Infectious Disease Emergence National Academies Press (2008)


Ethical and Legal Considerations in Mitigating a Pandemic Disease Event National Academies Press (2007)


