

Emerging infectious diseases as a global health threat

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In 1998, Nobel Laureate Dr Joshua Lederberg, internationally recognized as bringing forth the attention and importance to emerging infectious diseases, wrote

*Our relationship to infectious pathogens is part of an evolutionary drama. Here we are; here are the bugs. They are looking for food; we are their meat. How do we compete? They reproduce so quickly, and there are so many of them. They tolerate vast fluctuations of population size as part of their natural history; a fluctuation of 1% in our population size is a major catastrophe. Microbes have enormous potential mechanisms of genetic diversity. We are different from them in every respect. Their numbers, rapid fluctuations, and amenability to genetic change give them tools for adaptation that far outpace what we can generate on any short-term basis.*¹

Dr Lederberg, a genetic microbiologist, captured in this paragraph the power and flux of a dynamic world of shifting microorganisms in our environment and their need to adapt to a changing world and its effects on human health. Certainly, infectious diseases have emerged and re-emerged since the dawn of time. Our concepts of emerging infectious disease are currently defined as infections that have newly appeared in a population, or have existed previously but are rapidly increasing in incidence and/or geographic range.²

Infectious diseases are responsible for greater than 25% of the world's annual death rate and represent a large burden of disease and economic impact.² This impact on the world's population is disproportionate and largely impacts developing countries and, in particular, infants and children. As such, most of the emerging disease threats come from developing countries. In a workshop on the emergence of infectious diseases chaired by Dr Lederberg, important factors in infectious disease emergence and re-emergence were put forth and include: (1) increased human intrusion into tropical forests; (2) lack of access to health care; (3) population growth and changes in demographics; (4) changes in human behaviors; (5) inadequate and deteriorating public health infrastructure;

(6) misuse of antibiotics and other antimicrobial drugs; (7) microbial adaptation; (8) urbanization and crowding; (9) modern travel; and (10) increased trade and expanded markets for imported foods.³ Of all the factors contributing to the genesis of emerging infectious diseases, certainly human population growth and associated human activities are key factors which shape the landscape of emerging infections. The economic growth of many developing countries has resulted in an increase in urbanization and the detritus of society that results in increased breeding sites for vector-borne diseases. Deforestation for agriculture, decreased biodiversity, increased demand for dietary proteins, drugs and health products and the concomitant increase in farm or market animals by intensive farming and food manufacturing has resulted in the introduction of zoonotic infections into the human population.^{4–7} As such, we have witnessed major outbreaks caused by avian influenza A H5N1 virus, severe acute respiratory syndrome (SARS) coronavirus, Nipah virus and, recently, pandemic swine origin influenza A virus H1N1.⁸ International air travel and animal trading have allowed the rapid dissemination of a new emerging infection across the globe within days.

To achieve our goals to meet the challenges of emerging infectious disease threats requires new tools and a comprehensive set of surveillance data on human and animals from syndromics to genomics, rapidly tailored diagnostic tests, ready-to-use antimicrobials with matched activity, and novel treatment that can modulate our immune system to decrease damage triggered by infection. New drugs that can restore or regenerate organ functions other than just inhibiting microbes, relevant models of pathogenesis and immune response to microbes, and safe and effective vaccines being available within a short time during the incubation period of the pathogen are also important tools. This special thematic issue of the journal *Experimental Biology and Medicine* (EBM) is focused on the emergence of infectious disease threats and takes a translational approach to put forth new concepts and potential tools to meet these threats and is concentrated on five important conceptual

areas to derive these tools. These areas are: (1) pathogen adaptation and how pathogens rapidly evolve to emerge; (2) host adaptation and how human factors can mediate diseases severity; (3) tools to measure the impact of climate change on the emergence of infectious pathogens; (4) mathematical and engineering tools that can be applied towards understanding pathogen transmission in a population; and (5) new technologies that can be utilized to create new diagnostics and biomarkers for protection or susceptibility to new pathogens.

In this issue we have brought together experts in the field to present their novel research in these focus areas and describe new technical capabilities to address emerging infectious disease threats. These tools include mathematical modeling for predicting epidemics; structural biology and molecular docking to understand microbe-receptor binding changes which may allow jumping of interspecies barriers or new tissue tropism; the use of microfluidics to allow minimal volumes of clinical samples for testing hundreds of microbes within a short time using nucleic acid amplification or immunoassays; new generations of ultra-high-throughput gene sequencing and bioinformatics that will allow a comprehensive collection of viral, bacterial and fungal genomes found in human and animals during states of health and disease; metabolomic profiles of microbes and hosts identified by liquid chromatography-nuclear magnetic resonance-mass spectroscopy which can be useful for rapid diagnosis using novel biomarkers of infection; the use of systems biology to study various aspects of host-microbe interaction; and computational infrastructure to link up the first-generation investigations with genomics, metagenomics and proteomics on virus-host interactions with the more recent data from complementary high-throughput technologies, such as chemical genetics, siRNA and microRNA screens, and next-generation sequencing. Also presented are new animal models using humanized mice and other mammalian models to study the microbe-induced host response and the effects of antivirals, immunomodulators and vaccines so that safe and rapidly effective vaccines can be produced within the shortest possible time.

A comprehensive understanding of the spectrum of microbes (including yet undiscovered ones) and their genomes, phenomes, and antimicrobial resistance existing in human and animals would enhance preparedness of our community against emerging infectious diseases and outbreaks. With this information it is possible for us to estimate their potential of jumping from animal to human or causing a major epidemic, design appropriate diagnostic tests or prototype vaccines, and predict their antimicrobial susceptibility and perhaps transmissibility. We may even link up novel microbes causing a human disease syndrome without a previously known etiology. This new knowledge will also shed light on how emerging microbes cross species barriers between animals and humans. Together with

realtime surveillance and mathematical modeling in epidemiology, such knowledge will provide the necessary information in the control of infectious disease outbreaks and many public health decisions. Using technology of microfluidics, any patient or animal with an unusual disease can be screened for hundreds of different microbes or drug resistance, and many known and novel biomarkers of disease and severity, by nucleic acid amplification or antibody reaction within hours. This will immediately differentiate the sick from the healthy, and the known human infections from novel infections from animal microbes. This will allow the more optimal use of antimicrobials, isolation procedures, and rapid contact tracing with improved efficiency and decreased wastage. Our understanding of the host-microbe interactions using systems biology or chemical genetics will provide us with new targets for more effective inhibition of microbes, and new ways to modulate our immune system to improve microbial killings while decreasing the peripheral damage due to the concomitant inflammatory response of the host. Those patients who were previously considered hopeless due to severe end organ damage may benefit from our stem cell technology and regenerate their failed organs.

Emerging infectious diseases are a global health threat and new tools are needed to address these threats. It is our hope that issues such as this issue of *EBM* will better inform the readers on potential technologies that can be used and, more importantly, to stimulate the imagination and scientific creative forces needed to address this global health threat.

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