Critical Needs and Gaps in Understanding Prevention, Amelioration, and Resolution of Lyme and Other Tick-Borne Diseases

On October 11–12, 2010, the Institute of Medicine (IOM)’s Committee on Lyme Disease and Other Tick-Borne Diseases: The State of the Science convened a workshop in Washington, DC. The committee was charged with bringing together a diverse group of scientists, physicians, and the public to discuss a breadth of scientific topics and approaches to understand and decrease the burden of tick-borne diseases. The workshop also provided an opportunity for the patients and their advocates to discuss their concerns and to provide input to the discussion. During the opening sessions and throughout the two days, many patients shared their personal stories to illustrate the burden that these diseases place on individuals, families, and society and provided context for the ensuing scientific discussions.

The plenary session of the workshop covered an integrated view of tick-borne diseases from the pathogen through human disease and including the environmental factors that modulate transmission. Richard S. Ostfeld of the Cary Institute of Ecosystem Studies noted that throughout the 20th and 21st centuries, the number of infectious diseases in humans has been increasing as approximately 335 human infectious diseases have emerged since 1940. Approximately 30 percent of those diseases are vector-borne, which includes tick-borne diseases.

The Burden of Tick-Borne Disease and Opportunities for Prevention

Gary Wormser of the New York Medical College noted that Lyme disease is the most commonly reported vector-borne infection in the United States.
*Borrelia burgdorferi* is the only recognized pathogen to cause Lyme disease in the United States, and it can be differentiated into 16 to 45 subtypes that may vary in infectivity and/or pathogenicity. The reported incidence rate of Lyme disease has increased steadily from 10,000 cases in 1992 to approximately 30,000 cases in 2009. Similar increases in the incidence rates for other tick-borne diseases have been reported. Peter Krause of Yale University’s School of Public Health, for example, noted an increase rate of babesiosis from 1991 to 2009 in the Northeastern United States, although the actual numbers of infections are likely to be underestimated. David Weber of the University of North Carolina discussed the factors that can influence risk to tick-borne diseases, such as geographic proximity to the tick environment, occupation, and recreational preferences. For some individuals and diseases, genetic factors and the state of their current health (for example, immunocompromised individuals) can influence the severity of disease. Paul Mead of the Centers for Disease Control and Prevention noted that for tick-borne diseases, prevention is clearly preferable to treatment, and it should be a foremost concern. Unfortunately, current methods and opportunities for prevention are limited, and there is an urgent need for new methods and new approaches.

**Ticks and Transmission of Pathogens to Humans**

Ulrike Munderloh of the University of Minnesota noted that ticks are efficient vectors of multiple pathogens due to their potential interactions with several different vertebrate hosts during their life cycle. As a result, they have the opportunity to acquire a large array of different types of organisms that are present in the blood of these hosts. The microbial community can influence the acquisition, transmission, and virulence of human pathogens. Furthermore, as the tick feeds for extended periods, it interacts with its vertebrate host and has the ability to suppress the host’s immune system by dampening down the immune response and binding up antibodies that the host might have made in an attempt to rid itself of the blood-sucking parasite. Howard Ginsberg of the United States Geological Survey also noted that ticks and their hosts can be influenced by environmental factors, and complex interactions influence the transmission of tick-borne diseases, such as tick density, diversity of the potential hosts, geographic distribution of ticks, and the length of the season during which ticks and their hosts are active.

Understanding pathogenesis of an infectious disease at the cellular and molecular levels is critical for discovering, developing, and implementing methods to prevent infection, and to improve patient outcomes after treatment. Janis Weis of the University of Utah noted that differences in the severity and spectrum of disease among patients infected with *Borrelia burgdorferi* is one of the hallmarks of Lyme disease. The reasons for this variation include both genetic differences among strains of the bacterium and differences in the host responses. Understanding how *B. burgdorferi* traffic to and colonize various tissues is important in shedding light on the reasons for differences in the organ-specific manifestations and severity of disease. Advances in visualization techniques, such as those used by Linda Bockenstedt of Yale University, have allowed for imaging to track the progression of infection and cellular trafficking in real time.

**Diagnostics and Diagnosis of Tick-Borne Diseases**

Throughout the workshop various presenters and workshop participants discussed the current diagnostic tests for tick-borne diseases. Juan P. Olano of the University of Texas Medical Branch noted that antibody detection (serological techniques) is the most common diagnostic method used in
infectious diseases, but as reiterated throughout the workshop, a serologic diagnosis is frequently rendered too late to be of clinical value for therapeutic decisions because the immune response requires time to develop so that pathogen-specific circulating antibodies can be reliably detected. Maria Aguero-Rosenfeld of New York University and Bellevue Hospital Center noted that microbiologists share some of the concerns that patients have about the current diagnostic tests for Lyme borreliosis and other tick-borne diseases. She noted that education is critical and that physicians need to be educated on the availability of the tests and their limitations.

The Way Forward—Themes from the Workshop

The following themes that emerged during the workshop are not intended to be and should not be perceived as a consensus of the participants, nor the views of the committee, the IOM, or its sponsors. The purpose is to concisely reflect the breadth of topics discussed and individual ideas for addressing the research gaps for tick-borne diseases. Themes include:

- the risk of tick-borne diseases as they relate to ecological fragmentation and reduced wildlife diversity;
- the tick microbiome and its role in transmission of pathogens to humans;
- the relative contributions of changes in surveillance, clinical recognition, and testing patterns to the rising incidence of all of the major tick-borne diseases;
- the impact of coinfection in severity of human tick-borne diseases;
- biological understanding of persistent symptoms;
- research based on animal models for the testing of hypotheses related to the clinical manifestations and severity of symptoms or disease;
- the role of the immune response to tick-borne infection and its effect on bacterial load and disease manifestations;
- the current status of diagnostic tests and biomarkers for tick-borne diseases;
- the role of central system sensitivity and fatigue and other sequelae, as possible biomarkers of tick-borne diseases;
- measurement of qualitative symptoms reported by patients;
- biorepositories for tick-borne diseases;
- syndromic-based diagnostics for tick-borne diseases;
- research and development of safe, effective, multipathogen human and animal vaccines for tick-transmitted diseases;
• land-use practices and public education as current tools to improve mitigation and prevention of tick-borne diseases;
• social and behavioral considerations for tick-borne disease prevention interventions;
• educational programs for the public;
• research funding gaps for other tick-borne diseases;
• contribution of a national integrated research plan for advancing the science on tick-borne diseases; and
• the merits of a long-term study of Lyme disease and other tick-borne disease patients.