Tick-Borne Disease Working Group

Welcome

Leigh Ann Soltysiak, M.S. (Co-Chair)
Owner, Principal, Silverleaf Consulting, LLC; Adjunct Professor, Stevens Institute of Technology, Entrepreneurial Thinking

David Hughes Walker, M.D. (Co-Chair)
Professor, Department of Pathology, The Carmage and Martha Walls Distinguished University Chair in Tropical Diseases; and Executive Director, UTMB Center for Biodefense and Emerging Infectious Diseases
Review of Meeting #10 Agenda

1. Welcome
2. New Member Introductions
3. Overview of the Working Group’s Mission, Vision, Values
4. Update from June 4, 2019 (Meeting #9) to Today
5. What We Hope to Accomplish Today
6. Introduction of Subcommittees Updates
7. Alpha-Gal Subcommittee Update
8. Babesiosis and Tick-Borne Viruses Subcommittee Update
9. Clinical Aspects of Lyme Disease Subcommittee
10. Ehrlichiosis and Anaplasmosis Subcommittee
11. Pathogenesis and Physiology of Lyme Disease Subcommittee
12. Rickettsiosis Subcommittee
13. Tick Biology, Ecology, and Control Subcommittee
14. Training and Education Subcommittee
15. Discussion of Public Comment Subcommittee
16. Topic Development Brief Update – Causes of increased Tick-Borne Diseases
17. Topic Development Brief Update – Lyme Diagnosis/Persistent Infection
18. Topic Development Brief Update – Persistent Symptoms
19. Public Comments
20. Quick Recap of the Morning
21. Federal Inventory
22. Discussion of Next 2 In-person Meetings
23. Recap of Decisions Made / Next Steps
24. Adjournments
New Member Introduction

Kevin R. Macaluso, PhD, MS
Locke Distinguished Chair
Chair of Microbiology and Immunology
College of Medicine
University of South Alabama
Mission Statement

The Tick-Borne Disease Working Group’s mission, as mandated through the 21st Century Cures Act, is to provide expertise and to review all efforts within the Department of Health and Human Services related to all tick-borne diseases, to help ensure inter-agency coordination and minimize overlap, and to examine research priorities. As part of this mandate, and in order to provide expertise, we will ensure that the membership of the working group represents a diversity of scientific disciplines and views and is comprised of both federal and non-federal representatives, including patients, and family members or caregivers, advocates of non-profit in the interest of the patient with tick-borne illness, scientists and researchers. A major responsibility of our mission will be develop and regularly update the action of HHS from the past, present and the future.

https://www.hhs.gov/ash/advisory-committees/tickbornedisease/index.html
One Common Purpose

**SHARED VISION:** A nation free of tick-borne diseases where new infections are prevented and patients have access to affordable care that restores health.
RESPECT: Everyone is valued
We respect all people, treating them and their diverse experiences and perspectives with dignity, courtesy, and openness, and ask only that those we encounter in this mission return the same favor to us. Differing viewpoints are encouraged, always, with the underlying assumption that inclusivity and diversity of minority views will only strengthen and improve the quality of our collective efforts in the long term.

INNOVATION: Shifting the paradigm, finding a better way
We strive to have an open mind and think out of the box. We keep what works and change what doesn’t. We will transform outdated paradigms when necessary, in order to improve the health and quality of life of every American.

HONESTY & INTEGRITY: Find the truth, tell the truth
We are honest, civil, and ethical in our conduct, speech, and interactions with our colleagues and collaborators. We expect our people to be humble, but not reticent, and to question the status quo whenever the data and the evidence support such questions, to not manipulate facts and data to a particular end or agenda, and to acknowledge and speak the truth where we find it.

EXCELLENCE: Quality, real-world evidence underlies decision-making
We seek out rigorous, evidence-based, data-driven, and human-centered insights and innovations—including physician and patient experiences—that we believe are essential for scientific and medical breakthroughs. We foster an environment of excellence that strives to achieve the highest ethical and professional standards, and which values the development of everyone’s skills, knowledge, and experience.
Core Values (2 of 2)

COMPASSION: Finding solutions to relieve suffering
We listen carefully with compassion and an open heart in order to find solutions which relieve the suffering of others. We promise to work tirelessly to serve the greater good until that goal is achieved.

COLLABORATION: Work with citizens and patients as partners
The best results and outcomes won’t be created behind closed doors, but will be co-created in the open with input of the American public working together with these core values as our guide. We actively listen to the patient experiences shared with us, respect the lived experiences of patients and their advocates, and learn from their experiences in our pursuit of objective truth. Across diverse audiences, we communicate effectively and collaborate extensively to identify shared goals and leverage resources for maximum public health impact.

ACCOUNTABILITY: The buck stops here
We, as diligent stewards of the public trust and the funds provided by our fellow citizens, pledge to be transparent in all of our proceedings and to honor our commitments to ourselves and others, while taking full responsibility for our actions in service to American people.
Objectives and Progress from last meeting

• Provide expertise/review all efforts within HHS related to all tick-borne diseases, to help ensure inter-agency coordination and minimize overlap, and to examine research priorities, duties include:
  (A) Not later than 2 years after the date of enactment of the authorizing legislation, update a summary of:
    (1) ongoing tick-borne disease research, including research related to causes, prevention, treatment, surveillance, diagnosis, diagnostics, duration of illness, and intervention
    (2) advances made pursuant to such research;
    (3) federal activities related to tick-borne diseases, including: (a) epidemiological activities related to tick-borne diseases; (b) basic, clinical, and translational tick-borne disease research related to the pathogenesis; prevention, diagnosis, and treatment of tick-borne diseases
    (4) gaps in tick-borne disease research described in clause 3b;
    (5) the Working Group's meetings; and the comments received by the Working Group
  (B) Make recommendations to the Secretary regarding any appropriate changes or improvements to such activities and research; and
  (C) Solicit input from States, localities, and non-governmental entities, including organizations representing patients, health care providers, researchers, and industry regarding scientific advances, research questions, surveillance activities, and emerging strains in species of pathogenic organisms
Tick-Borne Disease Working Group

What We Hope to Accomplish Today

• Meeting Purpose
  o Sub-Committee Updates
  o Topic Development Updates
  o Public Comments -Federal Inventory Activity
  o Next Meeting Planning
  o Summary of Decisions
June 4, 2019
- New Public Members sworn in
- 1st Meeting of the 2020 TBDWG

June/July
- Formation of Subcommittees
- Subcommittee work

January 10, 2020
- Subcommittee Reports to Working Group Due

March 3-4, 2020
- Meeting #12 in-person

November 2020
- Report to be submitted to Assistant Secretary of Health and Congress
- Final Report to Congress accessible on the TBDWG website

January 28-29, 2020
- Meeting #11 in-person

Timeline for 2020 Report to Congress
Tick-Borne Disease Working Group

Introduction of Subcommittees Updates

- Alpha-Gal
- Babesiosis and Tick-Borne Viruses
- Clinical Aspects of Lyme Disease
- Ehrlichiosis and Anaplasmosis
- Pathogenesis and Physiology of Lyme Disease
- Rickettsiosis Subcommittee
- Tick Biology, Ecology, and Control
- Training and Education
- Discussion of Public Comment
Tick-Borne Disease Working Group

Alpha-Gal Subcommittee Update
Tick-Borne Disease Working Group

Alpha-Gal Subcommittee Co-Chairs

Scott Palmer Commins, MD, PhD
Associate Professor of Medicine & Pediatrics;
University of North Carolina; Member,
UNC Food Allergy Initiative, Thurston Research Center

Angel M. Davey, PhD
Program Manager, Tick-Borne Disease Research Program,
Congressionally Directed Medical Research Programs,
U.S. Department of Defense (DoD)

Leigh Ann Soltysiak, MS
Founder, Principal Silverleaf Consulting, LLC;
Adjunct Professor, Entrepreneurship Thinking,
Stevens Institute of Technology
Tick-Borne Disease Working Group

Alpha-Gal Subcommittee Members

**Charles Apperson, PhD**
Professor Emeritus, Arthropod Vector Biology & Management, Dept. of Entomology, NC State

**Beth Carrison**
AGS Patient/Advocate and Co-founder of Tick-Borne Conditions United

**Shahid Karim, PhD**
Professor, Arthropod Vector Biology, Tick-Borne Diseases, Functional Genomics, Biological Sciences, Univ. of Southern Mississippi

**Stephen M. Rich, PhD**
Professor of Microbiology Director of the Laboratory of Medical Zoology UMASS

**Sarah Stuart**
Alpha-Gal Advocate/Patient

*Public comments are included throughout*
Report Goals:

• Solicit scientific/clinical research and real-world experience in support of alpha-gal syndrome (AGS):
  - Causes
  - Prevention
  - Diagnosis / Diagnostics
  - Tick-species Correlation
  - Treatment
  - Surveillance
  - Intervention
  - Duration of Illness

• Seek expert opinion and cross-functional stakeholder guidance to enhance understanding of AGS

• Identify areas of additional research need

• Provide recommendations to the TBDWG with the goal of advancing human protection and disease recovery from AGS
Distinct Factors

• Alpha-Gal Syndrome (AGS) is an allergic reaction to mammalian meat (may include dairy, cheese, gelatin)

• It is associated primarily with bites from the lone star tick; and is not currently recognized/reportable as a tick-borne disease per NIH/CDC

• Individual child or adult patient symptoms may vary (hives, itching, redness, anaphylaxis, gastrointestinal distress, cramping, diarrhea, nausea, vomiting, etc.)
Tick-Borne Disease Working Group

Alpha-Gal Subcommittee Update (3 of 9)

Distinct Factors

• **Lifestyles may be significantly altered.** Co-factors (*e.g.*, physical activity, alcohol, stress, *etc.*) may affect individual allergic reactions and exposure as mammalian products are ubiquitous (*located within foods, medicines, bioprosthetics*)

• **AGS does not appear to be due to a pathogen.** Studies related to the etiology of AGS implicate tick bites but have not demonstrated the factor within ticks (or humans) that triggers the allergic immune response
Factors Similar to Other Tick-Borne Diseases

- AGS drastically affects the lives of not just the patients, but also their family/caregivers (physical, emotional, psychosocial, financial)
- No on-label product options exist for alpha-gal allergy (FDA approved); treatment plans are “off-label” (may impact payer coverage) and/or a clinical protocol
Background and Identified Needs

- AGS is an allergy that develops in response to tick bite(s) but there is no current evidence of an infectious or pathogenic etiology.
- Accumulating data suggest increasing AGS incidence and expanding geographic risk.
- Establishment of an AGS diagnosis code and development of diagnostic marker(s) would further aid in understanding AGS prevalence.
- AGS is managed differently from other tick-borne conditions and requires effective labeling, education, and training; no FDA-approved treatment for food allergy.
- Including human tick-bite data in epidemiological investigations and linking with clinical data would overcome limitations in alpha-gal surveillance and assess risk.
Tick-Borne Disease Working Group

Alpha-Gal Subcommittee Update (6 of 9)

Major Challenges & Issues

Information/insights needed to train, educate, and influence patient outcomes:

• Accurate data on the **scope/incidence** of AGS (*diagnostic data*)
• Knowledge of how to **identify individuals pre-disposed** to AGS (*why do some people bitten by the lone-star tick not develop the allergy and others do?*)
• **Treatment guidelines/plan** (*includes increased awareness for providers (EMS, clinicians) and payers, and patient support with coordinated nutritional care*)
• **Validated resources** related to foods and other products containing alpha-gal
Alpha-Gal Subcommittee Update (7 of 9)

Methods

- Invited subcommittee members to include academic researchers, scientist clinicians, and patients/patient advocates
- Weekly conference calls, beginning 16 July 2019
- Subcommittee identified experts in areas known to be priorities in fields of alpha-gal research and patient care; had expert speaker presentations during calls to clarify key issues/concerns
- Members submitted content for framing preliminary report, exchanged agendas, meeting summary notes, and meeting presentation drafts
Tick-Borne Disease Working Group

Alpha-Gal Subcommittee Update (8 of 9)

Presentations to Date:

• **Dr. William Nicholson** (Division of Vector Borne Diseases, CDC) – *Alpha-gal Allergy Following Tick Bite-What do we really know?*

• **Dr. Stephen Rich** (Laboratory of Medical Zoology, UMASS) – *Tick-Borne Disease Surveillance and Exposure*

• **Dr. Thomas Mather** (Tick Encounter Center, Univ. of Rhode Island) – *Presentation focused on interventions/prevention*

• **Dr. Scott Commins** (Univ. of North Carolina) – *Alpha-gal Diagnosis and Management*

• **Ms. Beth Carrison** (Co-founder, Tick-Borne Conditions United) – *Alpha-gal Syndrome Patient Perspectives and Experiences*
Next Steps

- **Continue weekly conference calls** (expert speaker presentations to clarify key issues/concerns, reconcile research, public opinion, and federal information)

- **Advance subcommittee report draft** prior to January 2020 (complete Background and Methods section, and move forward with Results and Potential Actions)
Acknowledgements.

Thank You!

to the Subcommittee Members and invited speakers for your hard work and efforts in making this report successful, and especially to the public and patients for your interest and support.
Tick-Borne Disease Working Group

Babesiosis and Tick-Borne Viruses Subcommittee Co-Chairs

C. Ben Beard, MS, Ph.D.
Deputy Director, Division of Vector-Borne Diseases
Centers for Disease Control and Prevention

Eugene Shapiro, MD
Professor of Pediatrics, Epidemiology, and Investigative Medicine
Yale University School of Medicine
Tick-Borne Disease Working Group

Babesiosis and Tick-Borne Viruses Subcommittee Members

**Bryon Backenson, M.S.**
New York State Department of Health Bureau of Communicable Disease Control

**Alan Barbour, MD**
University of California Irvine School of Medicine and School of Biological Sciences

**Greg Ebel, PhD**
Department of Microbiology Immunology and Pathology Colorado State University

**Richard I. Horowitz, MD**
Hudson Valley Healing Arts Center

**Anne Kjemtrup, DVM, MPVM, PhD**
California Department of Public Health Division of Communicable Disease Control

**Anna Schotthoefer, PhD**
Marshfield Clinic Research Institute Integrated Research and Development Laboratory

**Sam R. Telford III, M.S., S.D.**
Cummings School of Veterinary Medicine at Tufts University Department of Infectious Disease and Global Health

**Monica White**
President/Co-founder Colorado Tick-Borne Disease Awareness Association
Goals of this report

• To review the state of the science regarding the epidemiology, ecology, diagnostics, treatment, and prevention of infections due to *Babesia* spp., tick-borne relapsing fever spirochetal agents, and tick-borne viruses

• To define key research questions and clinical and public health priority needs regarding these pathogens

• To provide input to the HHS Tick-Borne Disease Working Group on potential recommendations to include in their report
Subcommittee proposal

• To officially rename the subcommittee the “Babesiosis and Tick-Borne Pathogens Subcommittee”

• Rationale:
  • There are other important tick-borne agents that are not captured under any of the other subcommittees, such as tularemia and both hard and soft tick-transmitted relapsing fever agents
  • There are important needs relating to these pathogens, and this subcommittee report would be an appropriate place to address them
### Babesiosis and Tick-Borne Viruses Subcommittee Update (3 of 8)

Table 1. Pathogens addressed by the Babesiosis and other tick-borne pathogens subcommittee

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Babesia microti, Babesia duncani</em></td>
<td>Babesiosis</td>
</tr>
<tr>
<td><em>Borrelia hermsii, B. turicatae, B. parkeri</em></td>
<td>Tick-borne relapsing fever</td>
</tr>
<tr>
<td><em>Borrelia miyamotoi</em></td>
<td>Borrelia miyamotoi disease</td>
</tr>
<tr>
<td>Bourbon virus</td>
<td>Bourbon virus disease</td>
</tr>
<tr>
<td>Colorado tick fever virus</td>
<td>Colorado tick fever</td>
</tr>
<tr>
<td>Heartland virus</td>
<td>Heartland virus disease</td>
</tr>
<tr>
<td>Powassan virus</td>
<td>Powassan virus disease</td>
</tr>
<tr>
<td><em>Francisella tularensis</em></td>
<td>Tularemia</td>
</tr>
</tbody>
</table>
Background

- In 2017, 59,349 cases of tick-borne diseases were reported to CDC, the highest number of tick-borne disease cases ever reported in a single year in the U.S.
- Of these, there were 2,368 babesiosis cases, 230 tularemia cases and 33 Powassan virus infection cases reported.
- There are significant gaps in our understanding of the ecology and emergence of some of these pathogens.
- Some of these diseases can pose unique challenges for diagnosis and treatment.
Major challenges and issues that are being addressed in this subcommittee report – work in progress

• Better understanding of the ecology and natural history
• Improved surveillance for Babesia to capture species and travel history of patients
• Improved diagnostic assays, particularly for *Borrelia miyamotoi*
• Multiple pathogen interaction within vectors and hosts and subsequent impact on transmission
• Co-infections in patients and the impact on clinical symptoms, disease severity, and treatment response, particularly in the case of *B. miyamotoi* and *B. burgdorferi*
Methods

• Subcommittee members were invited to participate with an effort to include representation from university researchers, government scientists, public health professionals, physicians, and patients/patient advocates, following the guidance from the 21st Century Cures Act

• Meetings have been held bi-weekly by conference call, beginning July 18, 2019 to date, expected to continue through January 10, 2020

• During the meetings, there were presentations both by outside subject matter experts and by subcommittee members to provide background and context for identifying key issues and concerns
Presentations to the subcommittee

• Dr. Susan Montgomery (CDC) – Babesiosis
• Dr. Chourki Ben Mamoun (Yale School of Medicine) – Babesiosis
• Dr. Alan Barbour (UC Irvine) – Relapsing fever spirochetes
• Dr. Greg Ebel (Colorado State University) – Tick-borne viruses
• Mr. Bryon Backenson (New York State Department of Health) – Powassan virus cases in New York
Next Steps

- Continue efforts aimed at identifying issues, questions and concerns to be highlighted in the report
- Complete Background and Methods section of the report
- Begin work on the Results and Potential Actions section of the report
Acknowledgements. . .

Thank you!

to all of the Subcommittee Members for all of your hard work and efforts in making this report successful
Tick-Borne Disease Working Group

Clinical Aspects of Lyme Disease Subcommittee Update
Tick-Borne Disease Working Group

Clinical Aspects of Lyme Disease Subcommittee

Co-Chairs

• CDR Rebecca Bunnell, MPAS, PA-C, Senior Advisor, Learning and Diffusion Group, Innovation Center, Centers for Medicare and Medicaid Services

• Sam T. Donta, MD, Professor of Medicine (retired);
  Infectious Disease Consultant, Falmouth Hospital
Tick-Borne Disease Working Group

Clinical Aspects of Lyme Disease Subcommittee Members

John Aucott, MD
Director, Johns Hopkins Lyme Disease Clinical Research Center

Rex G. Carr, MD, FAAPMR
Specialist in Physical Medicine and Rehabilitation Medicine Physician

Elizabeth Maloney, MD
Family Physician, President, Partnership for Tick-Borne Diseases Education

Katherine Murray Leisure, MD
Infectious Disease Specialist

James K. Mingle
President & CEO, MyCareTeam

Brian A. Fallon, MD, MPH
Professor, Clinical Psychiatry Director, Lyme & Tick-Borne Diseases Research Center, Columbia University Irving Medical Center
Goals of the Subcommittee Report

• Identify gaps in current clinical research related to the persistence of Lyme disease
Background

- The subcommittee is focused on identifying the gaps in our understanding of the diagnosis and treatment of persistent Lyme disease.
Major challenges and issues that are being addressed in this subcommittee report:

- Differential diagnosis of persistent Lyme disease
- Laboratory issues in the diagnosis of persistent Lyme disease
- Other diagnostic modalities (eg, SPECT, PET scans)
- Treatment issues
- Nontick transmission, including congenital and intrapartum Lyme disease and sexual transmission
Methods: Presentations from Invited Experts

- Meeting 2 (July 31): Marianne J. Middelveen, MS, a researcher with Atkins Veterinary Services of Calgary, described her controversial findings regarding the possibility of human sexual transmission of *Borrelia burgdorferi*.

- Meeting 3 (August 14): Subcommittee Co-Chair Sam Donta spoke about the challenges surrounding the clinical diagnosis of persistent Lyme disease.

- Meeting 4 (August 28): Steven Schutzer, MD, of the Rutgers New Jersey Medical School described his work investigating the proteomics of cerebral spinal fluid in healthy individuals compared with patients with persistent Lyme disease, chronic fatigue syndrome, or multiple sclerosis to identify potential disease biomarkers.

- Meeting 5 (September 11): Subcommittee member John Aucott, MD, of Johns Hopkins Lyme Disease Clinical Research Center gave an overview of biomarkers in previously treated patients with persistent symptoms of Lyme disease.
Next Steps

Proposed presentations:

- Dr. Brian Fallon and Dr. Sam Donta on SPECT and PET scans in patients with persistent symptoms
- Dr. Sam Donta and Dr. Rex Carr on antibiotic treatment options for patients with persistent Lyme disease
- Dr. Ying Zhang of Johns Hopkins and Dr. Kim Lewis of Northeastern University on in vitro and in vivo persistence models and their connection to antibiotic treatment
Acknowledgements.

Thank You!

to all of the Subcommittee Members for all of your hard work and efforts in making this report successful
Tick-Borne Disease Working Group

Ehrlichiosis and Anaplasmosis Subcommittee Update
Tick-Borne Disease Working Group

Ehrlichiosis and Anaplasmosis Subcommittee

Co-Chairs

• Dennis M. Dixon
• David Walker
Tick-Borne Disease Working Group

Ehrlichiosis and Anaplasmosis Subcommittee

Members

**John Branda, MD**
Harvard University
Massachusetts General Hospital
Clinical Microbiology/Pathology

**Stephen Clark, PhD**
Retired, Associate Professor Emeritus at the University of Connecticut School of Medicine

**J. Stephen Dumler, MD**
Professor and Chair, Joint Department of Pathology
Uniformed Services University of the Health Sciences
Walter Reed National Military Medical Center Joint
Pathology Center Research Center

**Harold Horowitz, MD**
Professor, Department of Medicine (Infectious Diseases)
Cornell University – Weill Medical College

**Bobbi Pritt, MD**
Professor, Department of Laboratory Medicine and Pathology
Vice Chair of Education
Director, Clinical Parasitology
Co-Director, Vector-borne Diseases Laboratory Services

**Daniel Sexton, MD**
Professor of Medicine (Infectious Diseases)
Duke University School of Medicine

**Gregory A. Storch, MD**
Professor of Pediatrics (Infectious Diseases), Medicine, and Molecular Microbiology
Chief, Division of Pediatric Laboratory Medicine
Washington University
Goals of the Subcommittee Report

- To describe the health impact of human anaplasmosis and ehrlichioses in the US
- To determine the obstacles to reduction in the morbidity and mortality of anaplasmosis and ehrlichioses in the US
- To identify gaps in knowledge and implementation that research may resolve
Important Issues to be Addressed by the Subcommittee

- Surveillance
- Clinical diagnosis
- Laboratory diagnostics
- Treatment
- Prevention
Ehrlichiosis and Anaplasmosis Subcommittee Update (3 of 6)

Major Challenges and Issues Being Addressed in the Subcommittee Report

Anaplasmosis:

- Cases more than doubled: 2782 cases in 2013, 5762 cases in 2017
- Passive surveillance results in underreporting by an estimated 11-fold
- Clinical diagnosis is difficult
- Seroprevalence of 10-15% in endemic areas determined 20 years ago and prevalence of anaplasmosis in deer ticks (9% adult and 5% of nymphal ticks) suggests very high incidence of infection
- Prevalence in ticks is confounded by a deer-specific A. phagocytophilum strain that does not infect humans
Major Challenges and Issues Being Addressed in the Subcommittee Report (continued)

_Ehrlichia chaffeensis, E. ewingii, E. muris eauclairensis:_

- Human monocytic ehrlichiosis (E. chaffeensis) is a life-threatening disease
- Clinical diagnosis is difficult
- Utilization of laboratory diagnostics, accurate clinical diagnosis, and reporting of cases are inadequate
- Passive surveillance and misdiagnosis result in estimated 50-fold underreporting
- Seroprevalence of 8-20% in the Lone Star tick region suggests underdiagnosis
- Cross reactive serology among _Ehrlichia_ confounds diagnosis
- No generally available laboratory diagnostic test during the acute stage of disease
- Lack of a vaccine
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Ehrlichiosis and Anaplasmosis Subcommittee Update (5 of 6)

Methods

Presentations and discussion among subcommittee members:

- Treatment
- Surveillance/Epidemiology
- Clinical diagnosis
- Laboratory diagnostics
- Pathogenesis
Next Steps

• Complete presentations

• Develop specific suggested recommendations that Congress and HHS could authorize and implement to address the obstacles and gaps in knowledge
Acknowledgements... Thank You!

to all of the Subcommittee Members for all of your hard work and efforts in making this report successful
Tick-Borne Disease Working Group

Pathogenesis and Physiology of Lyme Disease Subcommittee Update
Tick-Borne Disease Working Group

Pathogenesis and Physiology of Lyme Disease Subcommittee Co-Chairs

• Sam T. Dona, MD, Professor of Medicine (retired); Consultant, Infectious Diseases

• Leith Jason States, MD, MPH, Acting Chief Medical Officer, Office of the Assistant Secretary for Health, U.S. Department of Health and Human Services
Tick-Borne Disease Working Group

Pathogenesis and Physiology of Lyme Disease
Subcommittee Members

Wendy Adams
Research Grant Director, Bay Area Lyme Foundation

Troy Bankhead, PhD
Associate Professor, School of Veterinary Microbiology and Pathology, Washington State University

J. Nicole Baumgarth, DVM, PhD
Professor, Center for Comparative Medicine and Dept. of Pathology, Microbiology & Immunology, University of California, Davis

Monica E. Embers, PhD
Director of Vector-borne Disease Research, Division of Immunology, Tulane National Primate Research Center

Robert Lochhead, PhD
Assistant Professor of Microbiology and Immunology at the Medical College of Wisconsin

Brian Stevenson, PhD
Professor, Department of Microbiology, Immunology & Molecular Genetics, University of Kentucky College of Medicine
Goals of the Subcommittee Report

The Subcommittee is addressing the following topics in its discussions:

- What are the initial events and mechanisms involved in the entry of *Borrelia burgdorferi* into host tissues?
- What are the events and pathophysiology involved following entry of *B. burgdorferi* into host tissues?
- What are the pathogenic and pathophysiologic mechanisms involved in the development of symptoms and signs?
- What underlies the persistence of *Borrelia* in host tissues?
- Is there a role for autoimmunity in the process of persistent symptoms?
- Is there a role for antibiotic tolerance in “resistance” to successful antibiotic treatment (and how are biofilms involved in antibiotic resistance)?
Background

• The Pathogenesis and Physiology of Lyme Disease Subcommittee is focused on establishing what is known about the mechanisms underlying pathophysiology of Lyme disease and, importantly, addressing persistent Lyme disease in a meaningful way that leads to tangible next steps that can inform better patient care.
Major challenges and issues that are being addressed in this subcommittee report:

• Understanding the mechanisms that lead to transmission of the bacteria from ticks to hosts and of their persistence
• Detection of persistent *B. burgdorferi* in vivo
• The role of *B. burgdorferi* peptidoglycan persistence in the pathogenesis of Lyme arthritis
• Is inflammation in patients with persistent symptoms of Lyme disease driven by low-level persistent infection or a dysregulated immune response?
Methods: Presentations from Invited Experts

- Meeting 2 (July 30): Brandon L. Jutras, PhD, of Virginia PolyTechnic Institute and State University spoke about peptidoglycan as a tool to understand spirochete biology and pathogenesis, its relationship with arthritis, and its recycling pathway.

- Meeting 3 (August 13): Subcommittee member Brian Stevenson, PhD, described the establishment of *B. burgdorferi* in tissues and identified a number of questions for future research.

- Meeting 4 (August 27): Jenny A. Hyde, PhD, of the Texas A&M University College of Medicine outlined how *B. burgdorferi* impacts gene regulation during colonization, dissemination, and tissue-specific infection in mice; the use of bioluminescence in mice to visualize the kinetics of infection with different strains of the pathogen; and real-time evaluation of gene expression in the skin, heart, and joints of a mammal infected with *B. burgdorferi*.

- Meeting 5 (September 10): Subcommittee members Monica E. Embers, PhD, and Nicole Baumgarth, DVM, PhD, addressed how *B. burgdorferi* interacts with the immune system/immune suppression.
Next Steps

• Proposed and planned presentations:
  • Mark Wooten, PhD, of the University of Toledo will discuss intravital microscopy imaging that allows direct visualization of the interactions between *B. burgdorferi* and different immune cell populations within the intact skin of infected mice (September 24).
  • Michal (Mikki) Tal, PhD, of Stanford University, on CD47 mimics for *B. burgdorferi* (TBD)
  • Subcommittee member Troy Bankhead, PhD, will present on surface lipoprotein E (VlsE) and its ability to shield antigenic proteins (date TBD).
  • Why *B. burgdorferi* persists in host tissue (TBD)
  • Antibiotic tolerance as a possible means for resistance to antibiotic treatment (TBD)
Acknowledgements... to all of the Subcommittee Members for all of your hard work and efforts in making this report successful

Thank You!
Tick-Borne Disease Working Group

Rickettsiosis Subcommittee Co-Chairs

• Estella Jones and Todd Myers
• David Walker
Tick-Borne Disease Working Group

Rickettsiosis Subcommittee Members

Lucas Blanton, MD
Associate Professor of Internal Medicine (Infectious Diseases)
University of Texas Medical Branch at Galveston

Karen Bloch, MD, MPH, FIDSA, FACP
Associate Professor of Medicine (Infectious Disease) and Health Policy
Vanderbilt University Medical Center

Christina M. Farris, PhD
Viral and Rickettsial Diseases Department
Naval Medical Research Center

Vance Fowler, MD
Professor of Medicine
Duke University

Tony Galbo
Father of a child who died of Rocky Mountain spotted fever

David N. Gaines, PhD
State Public Health Entomologist
Virginia Department of Health

Christopher D. Paddock, MD, MPHTM
Rickettsial Zoonoses Branch
CDC

Hayley Yaglom, MS, MPH
One Health Genomics Epidemiologist
Translational Genomics Research Institute
Background

- Established in December of 2016, Section 2062 of the 21st Century Cures Acts Legislation pertains to advancing research on tick-borne diseases
- As tick populations continue to grow and infected ticks expand geographically, the threat to human health intensifies
- In response, the HHS Secretary formed the Tick-Borne Disease Working Group (TBDWG) to identify gaps in research, education, prevention, and access to care
Tick-Borne Disease Working Group

Rickettsiosis Subcommittee Update (2 of 6)

Goals of the Subcommittee Report

• To describe the health impact of tickborne rickettsial diseases in the US
• To determine the obstacles to reduction of the morbidity and mortality caused by tickborne rickettsial diseases in the US
• To identify gaps in knowledge and implementation that research may resolve
Rickettsiosis Subcommittee Update (3 of 6)

Important Issues to be Addressed by the Subcommittee

• Species of *Rickettsia* pathogens in the United States
• Epidemiology
• Surveillance – clinical and environmental
• True incidence of the diseases
• Prevalence of Lone Star ticks in different geographic areas
• Point-of-care diagnostic tests
• Treatment of children under 12 with doxycycline
• Undertreating versus overtreating
• Public and clinician education
Major Challenges and Issues Being Addressed in the Subcommittee Report

• More than 6000 cases of tickborne spotted fever rickettsioses reported annually based on passive surveillance
• 99% of reported cases are not confirmed
• Serologic diagnosis does not distinguish among five SFG rickettsiae that may stimulate antibodies and range from 23% fatal without appropriate treatment to subclinical infection
• Case diagnostic reporting criteria likely includes many patients who did not have active tickborne rickettsial infection
• 10-20% of healthy persons in the Lone Star tick region have anti-spotted fever group rickettsial antibodies
• Passive surveillance results in many unreported cases
• There is no generally available test for diagnosis of acute infection
• Knowledge and awareness of illness and treatment by many physicians is lacking
• Diagnosis based on clinical manifestations early in the course of illness is very difficult
• Only specific antibiotics are effective
Methods

The Rickettsiosis Subcommittee was established to leverage member expertise, balance a range of perspectives, and thoroughly examine several aspects of diagnostics, treatment and prevention of a range of tick-borne rickettsial diseases.

Presentations and discussions among subcommittee members:

• Physician education (medical students, residents, continuing medical education) and other health care providers
• Surveillance/epidemiology
• Approach to the clinical diagnosis
• Laboratory diagnostics
Next Steps

- Complete presentations
- Develop specific suggested recommendations that Congress and HHS could authorize and implement to address the obstacles and gaps in knowledge
Acknowledgements. . .

Thank You!

to all of the Subcommittee Members for all of your hard work and efforts in making this report successful
Tick-Borne Disease Working Group

Tick Biology, Ecology, and Control Subcommittee Update
Tick-Borne Disease Working Group

Tick Biology, Ecology, and Control Subcommittee

Co-Chairs

Adalberto (Beto) Pérez de León, DVM, MS, PhD
Director
Knipling-Bushland U.S. Livestock Insects Research Laboratory
U.S. Department of Agriculture—Agricultural Research Service

Kevin Macaluso, PhD
Locke Distinguished Chair
Professor and Chair, Department of Microbiology and Immunology
University of South Alabama College of Medicine
Tick-Borne Disease Working Group

Tick Biology, Ecology, and Control Subcommittee

Members ~250 years of relevant experience

Trey Cahill, MS
Public Health Analyst | Location Intelligence (GIS) Health Regulation & Licensing Administration

Neeta Pardanani Connally, PhD, MSPH
Associate Professor and Director, Tickborne Disease Prevention Laboratory Department of Biological & Environmental Sciences Western Connecticut State University

Maria Diuk-Wasser, PhD
Associate Professor Dept. of Ecology, Evolution and Environmental Biology Columbia University

Lars Eisen, PhD
Research Entomologist; Division of Vector-Borne Diseases, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention

Lonnie Marcum, PT, BSHCA
Physical Therapist, Health and Science Writer for LymeDisease.org

Howard Ginsberg, PhD
Research Ecologist & Field Station Leader of the USGS Rhode Island Field Station, Professor in Residence at the University of Rhode Island
Tick-Borne Disease Working Group

Tick Biology, Ecology, and Control Subcommittee Members (cont.)

R. Michael Roe, PhD
William Neal Reynolds Distinguished Professor
Department of Entomology and Plant Pathology
North Carolina State University

Bob Sabatino
Founder & Executive Director
Lyme Society INC

Daniel Sonenshine, PhD
Guest Researcher, LMVR, NIAID, NIH Eminent Professor of Biological Science, Old Dominion University

Kirby C. Stafford III, PhD
Chief Entomologist, State Entomologist Department of Entomology Center for Vector Biology and Zoonotic Diseases NE Regional Center for Excellence in Vector Borne Diseases

Pete D. Teel, PhD
Regents Professor and Interim Department Head
Department of Entomology Texas A&M University

Stephen Wikel, PhD
Professor and Chair Emeritus of Medical Sciences
St. Vincent's Medical Center Quinnipiac University
Goals of the Subcommittee Report

• This report will analyze information on tick biology, ecology, and control related to the problem with tick-borne diseases.
• We will review how biological and ecological drivers of tick populations may be impacting existing control technologies to manage tick-borne disease transmission.
• A gap analysis of national tick biology and ecology research strategies and implementation capacity for effective tick control that can mitigate the health burden of tick-borne diseases will be included.
• A priority issue for consideration is advancing integrated tick management taking an area-wide approach to disrupt tick-host-pathogen interactions, which presents a great opportunity to prevent tick-borne disease morbidity and mortality.
Background

Tick-borne diseases threaten the health of humans, domestic animals, and wildlife.

Infected ticks transmit the microbes causing these diseases when they bite humans and other animals.

These infectious diseases are generally zoonotic because, before biting a human, a tick acquires microbes by blood feeding on an infected animal.

There has been a steady increase in tick-borne disease incidence.

The geographic distribution of this trend is expanding.
Tick-Borne Disease Working Group

Tick Biology, Ecology, and Control Subcommittee Update (3)

Challenges and issues addressed in this subcommittee report

• Drivers for the increase in tick vector populations
• Drivers for the geographic range expansion of tick vector
• Risk for the introduction of foreign tick vectors and disease-causing agents into the United States
• Potential benefits of emerging tick control technologies
• Barriers for innovation in area-wide integrated tick management
Methods

• The subcommittee identified experts in tick biology, ecology, and control who are actively examining the factors that contribute to the recognized increase in tick-borne diseases.

• Experts presented on the state of scientific knowledge and limitations of practices influencing the effectiveness of current tick control strategies.
# Tick-Borne Disease Working Group

**Tick Biology, Ecology, and Control Subcommittee Update (5a)**

<table>
<thead>
<tr>
<th>Speaker</th>
<th>Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stephen Wikel, PhD</strong></td>
<td>Overview of Work Completed by the 2018 Disease Vectors, Surveillance, and Prevention Subcommittee</td>
</tr>
<tr>
<td>St. Vincent’s Medical Center, Quinnipiac University</td>
<td></td>
</tr>
<tr>
<td><strong>Kirby Stafford, III, PhD</strong></td>
<td>Concepts Vector Control: Integrated Tick Management</td>
</tr>
<tr>
<td>The Connecticut Agricultural Experiment Station</td>
<td></td>
</tr>
<tr>
<td><strong>Rebecca Eisen, PhD</strong></td>
<td>Tick Surveillance as a Public Health Tool</td>
</tr>
<tr>
<td>Division of Vector-Borne Diseases, CDC</td>
<td></td>
</tr>
<tr>
<td><strong>Richard S. Ostfeld, PhD</strong></td>
<td>The Tick Project: Testing Environmental Interventions to Prevent Lyme and Other Tick-Borne Diseases in Our Communities</td>
</tr>
<tr>
<td>Cary Institute of Ecosystem Studies</td>
<td></td>
</tr>
</tbody>
</table>
**Tick-Borne Disease Working Group**

**Tick Biology, Ecology, and Control Subcommittee Update (5b)**

<table>
<thead>
<tr>
<th>Speaker</th>
<th>Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chris Przybyszewski, US Biologic</td>
<td>Integrated Tick Management Solutions: Reservoir-Targeted Vaccines and Predictive Analytics</td>
</tr>
<tr>
<td>Ed Clark</td>
<td>Interface Between Invasive Species and Tick-Borne Diseases (White Paper)</td>
</tr>
<tr>
<td>Ernesto Dominguez, DVM</td>
<td></td>
</tr>
<tr>
<td>Jeff Morisette, PhD</td>
<td></td>
</tr>
<tr>
<td>National Invasive Species Council</td>
<td></td>
</tr>
<tr>
<td>Jean Tsao, PhD</td>
<td>Factors Contributing to the Spread of <em>Ixodes scapularis</em></td>
</tr>
<tr>
<td>Midwest Center of Excellence, Vector-Borne Disease</td>
<td></td>
</tr>
</tbody>
</table>
Next Steps

- Assimilate shared knowledge, review the scientific literature
- Contribute expertise of the membership to identify causes for the increase in tick-borne diseases related to tick biology and ecology
- Recommendations will emphasize research and development work to reverse the alarming trends with tick-borne diseases
- Fundamental: area-wide integrated management interventions targeting vector-host-pathogen interactions to disrupt vulnerabilities in the biology and ecology of ticks
Acknowledgements

Thank you!

• To the public for your interest in this effort
• To the Subcommittee Members for your dedication in making this effort successful
• To the invited speakers for sharing their expert knowledge
Tick-Borne Disease Working Group

Training and Education Subcommittee Update
Tick-Borne Disease Working Group

Training and Education Subcommittee Co-Chairs

Pat Smith

- President, Lyme Disease Association, Inc.
- CDMRP Programmatic Panel Member

Rebecca Bunnell, MPAS, PA-C

- CDR, United States Public Health Service
- Senior Advisor, Learning & Diffusion Group, CMS Innovation Center
Tick-Borne Disease Working Group

Training and Education Subcommittee Members

Doug Fearn
President, Lyme Disease Association of Southeastern Pennsylvania, Inc.

Megan Dulaney, MS
Patient Representative
Senior Interagency Liaison & Policy Advisor
Henry M. Jackson Foundation for the Advancement of Military Medicine in support of DoD Health Affairs & Center for Global Health Engagement, Uniformed Services University

Lorraine Johnson, JD, MBA
Health Care Policy Expert CEO, LymeDisease.org

Elizabeth Maloney, MD
Family Physician
President, Partnership for Tick-Borne Diseases Education

Sheila M. Statlender, PhD
Clinical Psychologist, Private Practice
Chair, Massachusetts Lyme Legislative Task Force
Goals of the Subcommittee Report

- Delineate obstacles preventing health care providers from providing prompt diagnosis and optimal treatment and suggest viable solutions for congressional consideration and action.
- Delineate obstacles that prevent patients from receiving prompt diagnosis and optimal treatment given their stage of disease and suggest viable solutions for congressional consideration and action.
- Delineate reimbursement obstacles and suggest viable solutions for congressional consideration and action.
Tick-Borne Disease Working Group

Training and Education Subcommittee Update (2 of 10)

Goals of the Subcommittee Report

• Identify deficiencies in health care provider training and suggest revisions for Federally sponsored educational resources

• Identify deficiencies in patient/public health education and suggest revisions for Federally sponsored educational resources
Important issues Subcommittee will focus on

- Access to Care for patients with Lyme and TBD
- Reimbursement for patients with Lyme and TBD
- Clinician Training for Lyme and TBD
- Patient/Public Health Education on Lyme and TBD
- Diagnostic errors: factors related to delayed diagnosis and misdiagnosis including inappropriate psychiatric diagnosis
- Shared medical decision-making
Tick-Borne Disease Working Group

Training and Education Subcommittee Update (4 of 10)

Major challenges & issues to be addressed in this subcommittee report

- How to identify factors that delay early diagnosis and treatment
- How variance in treatment guidelines impact accurate diagnosis and treatment
- How delayed diagnosis impacts treatment outcomes and costs
- The role of shared medical decision-making in diagnostic and treatment approaches
- Misdiagnosis by geography
Major challenges & issues to be addressed in this subcommittee report

- How educational resource content development and approval process, as well as information distribution, impact treatment
- How variance in guidelines and lack of peer review and stakeholder input to updates for educational curriculum in training programs as well as continuing education for clinicians, affect diagnosis, treatment, prevention
- How geographic restrictions, such as definition of high incidence states in case definitions/guidelines, and misuse of surveillance criteria impact treatment, e.g., for establishing clinical diagnosis or providing standards for reimbursement
- How government laws, policies, procedures impact treatment
Methods

• Subcommittee will have held five meetings as of tomorrow
• The meetings include presentations by subject matter experts that incorporate:
  • A diversity of topics
  • Diverse viewpoints
  • Geographic diversity
Methods

Expert speakers have presented to Subcommittee on various topics

• *Historical perspectives of Lyme disease issues*, Lorraine Johnson, JD (LymeDisease.org)

• *Communications issues*, Sue Partridge, CDC

• *ILADS, NICE* *Guidelines* Elizabeth Maloney, MD (Partnership for TBD Ed.)

*National Institute for Health and Care Excellence (tomorrow’s mtg.)*
Upcoming speakers scheduled (7 more meetings scheduled; 12 meetings in 2019)

- *Cost of Illness Study*, John Aucott, MD (JHU)
- *Legal Issue for Physicians*, Elliott Pollack, LL.B., (Pullman & Comley LLC)
- *Report Stats on geographic diversity, urban, suburban*, Robin Gelburd, JD, (Fair Health)
- *Patient Perspectives: Civilian & Military Health Considerations*, Megan Dulaney perspective
- *Patient Perspectives: Civilian & Military Health Considerations*, Nicole Malachowski perspective
- *IDSA Guidelines*, Paul Auwaerter, MD, (JHU)
- *Quality of life and access to care*, Lorraine Johnson, JD, (LymeDisease.org)
Next Steps

- Investigating two more potential speakers
- Divide up topics and assign Subcommittee members to focus on each of them
- Write report to address goals, important issues, and major challenges
- Suggest recommendations for Federal action
- Decide on peer review to be cited in written report to Congress
- Ensure that the Subcommittee report also reflects minority opinions
Proposing Subcommittee title change

Change the title of the subcommittee from “Training and Education” to “Training and Education, Access to Care and Reimbursement”

Rationale

• Discussion at Working Group meeting equally focused on all of these topics for this committee
• Nomenclature at the meeting included language on Access to Care & Reimbursement
• Legislation that established the Working Group was initiated and written by Lyme patients and advocates with legislators to achieve life saving support for their medical condition(s)
• Ensure goals and recommendations outlined in the written report capture the interest of the report audience (Congress) and are actionable
Acknowledgements... 

Thank You!

Subcommittee Members
Expert Speakers
Staff

- For your contributions to this report
- For your future commitment to ensure that this report will be a significant step forward for Lyme & tick-borne disease patients/their families and for future tick-borne disease sufferers
- Working Group for your time
Public Comment Subcommittee

- Formed at public meeting #7 on July 24, 2018
- Meets monthly
- Since Subcommittee formation, we’ve reviewed nearly 1,000 written comments tickbornedisease@hhs.gov
- New Volunteers
  - Working Group members who have volunteered to date
    - Scott Commins
    - Angel Davey
    - Leigh Ann Soltysiak
  - Chair or Co-Chairs from new volunteers
Purpose of this activity

• Assess available literature related to the Key Question
• Determine whether a systematic literature review will have an impact, is feasible, and the potential value of the review
Tick-Borne Disease Working Group

Process

1. Develop a key question, guiding questions, and PICOTS

2. Conduct a literature search using EBSCOhost and Government websites
## Tick-Borne Disease Working Group

### Process – Key Question and PICOTS

<table>
<thead>
<tr>
<th>Key Question and PICOTS</th>
<th>Topic Information</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Key Question</strong></td>
<td>Considering tick biology, ecology, and control, what are the causes for the increased number of tick-borne disease cases in the United States?</td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>People diagnosed with tick-borne diseases in the United States and globally</td>
</tr>
<tr>
<td><strong>Interventions/Indicators</strong></td>
<td>Understanding how climate variability, environmental change, host and vector population increases, and range expansion increase the risk of tick-borne disease transmission so we can adapt interventions</td>
</tr>
<tr>
<td><strong>Comparators</strong></td>
<td>Compare findings from interventions/indicators to each other</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Identifiable causes for an increase in tick-borne diseases to adapt integrated tick-management interventions targeting the vector-host-pathogen interface by disrupting vulnerabilities in the biology and ecology of ticks</td>
</tr>
<tr>
<td><strong>Timing</strong></td>
<td>Past 50 years (1968–2018)</td>
</tr>
<tr>
<td><strong>Setting</strong></td>
<td>Geographic areas with increased risk of tick-borne disease transmission in the United States</td>
</tr>
</tbody>
</table>
Key Question: Considering tick biology, ecology, and control, what are the causes for the increased number of tick-borne disease cases in the United States?

Guiding Questions

• Is the problem with ticks and tick-borne diseases particular to the United States or is it a global issue?

• If it is a global problem, what are the particular drivers (e.g., climate variability, environmental change, host and vector population increases, range expansion) for the problem with ticks and tick-borne diseases in the United States during the past 50 years?

• What are the challenges for implementation research on integrated tick management focused on controlling host and vector populations to decrease the risk of tick-borne disease transmission?
Process – Search Criteria

• A literature search was conducted using EBSCOhost and Government websites

• Key words and exclusion criteria were derived from the criteria set forth in the PICOTS. Articles were excluded when:
  • Full article missing or there was not enough information in the abstract
  • Article not from a peer-reviewed scholarly journal
  • Article not relevant to topic area
## Findings

A preliminary assessment of the literature identified the following key themes:

- Effect of the climate on tick biology and ecology
- Interaction of climatic and environmental factors
- Variation in host availability
- Increase in tick abundance
- Changes in the geographic distribution of ticks
- Changes in the prevalence of pathogens in tick populations
Tick-Borne Disease Working Group

Summary of Findings

• Appropriateness and Importance
  This topic is both appropriate and important.
• Desirability of a New Review/Duplication
  A new review would not be duplicative of an existing product. We found no systematic review related to the scope of the nomination.
• Impact of a New Evidence Review
  A new systematic review may prove useful in the development of public health strategies to mitigate the impact of the growing threat of tick-borne diseases.
• Feasibility of New Evidence Review
  A new systematic literature review is likely feasible with some modifications to the selection criteria.
Tick-Borne Disease Working Group

Topic Development Brief Update
Diagnostic Tests for Tick-Borne Diseases
Tick-Borne Disease Working Group

Purpose of this activity

• Assess available literature related to the key question
• Determine whether a systematic literature review will have an impact, is feasible, and the potential value of the review
Tick-Borne Disease Working Group

Process

1. Develop a key question, guiding questions, and PICOTS

2. Conduct a literature search using EBSCOhost and Government websites
## Key Question and PICOTS

<table>
<thead>
<tr>
<th>Key Question and PICOTS</th>
<th>Topic Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Key Question</td>
<td>What are the current diagnostic tests available for tick-borne diseases, and what is the state of the tests?</td>
</tr>
<tr>
<td>Population</td>
<td>People at risk for or diagnosed with tick-borne diseases</td>
</tr>
<tr>
<td>Interventions/Indicators</td>
<td>All diagnostic tests available for tick-borne diseases; most utilized diagnostic tests available for tick-borne diseases</td>
</tr>
<tr>
<td>Comparators</td>
<td>Compare findings from interventions/indicators</td>
</tr>
<tr>
<td>Outcomes</td>
<td>A catalogue of the current state of all diagnostic tests available for tick-borne diseases</td>
</tr>
<tr>
<td>Timing</td>
<td>Last 20 years (1998-2019)</td>
</tr>
<tr>
<td>Setting</td>
<td>Not applicable</td>
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</tbody>
</table>
Tick-Borne Disease Working Group

Process – Guiding Questions

Key Question: What are the current diagnostic tests available for tick-borne diseases, and what is the state of the tests?

Guiding Questions

• What are the current and future diagnostic tests/assays for tick-borne diseases?
• What is the state of the science for diagnostic tests, including direct diagnostic tests (antigen, DNA, RNA), for tick-borne diseases?
• What are the technological challenges to the utilization and development of diagnostic tests?
  • Utilization: Identify key challenges/gaps with the current diagnostic tests/assays utilized for tick-borne diseases (accuracy, conflicting tests, other).
  • Technical: What are the biggest challenges when developing new diagnostic tests?
• What is the current range of clinical and economic diagnostic test practices for tick-borne disease diagnosis and treatment?
Process – Search Criteria

A literature search was conducted using EBSCOhost and Government websites.

Key words and exclusion criteria were derived from the criteria set forth in the PICOTS. Articles were excluded when:

- Full article missing or there was not enough information in the abstract
- Article not from a peer-reviewed scholarly journal
- Article not relevant to topic area
Tick-Borne Disease Working Group

Findings

A preliminary assessment of the literature provided information on the following areas:

• Limitations of diagnostic tests available for Lyme Disease
• Challenges hindering diagnosis of other Tick-Borne Diseases
• Ongoing and future efforts to overcome diagnostic challenges
Tick-Borne Disease Working Group

Summary of Findings

• Appropriateness and Importance
  This topic is both appropriate and important.

• Desirability of a New Review/Duplication
  A new systematic review would be partially duplicative of an existing product.

• Impact of a New Evidence Review
  The impact of a new systematic literature review is likely to be low.

• Feasibility of New Evidence Review
  A new systematic literature review is not feasible at this time.
Tick-Borne Disease Working Group

Topic Development Brief Update
Persistent Symptoms of Lyme Disease
Purpose of this activity

• Assess available literature related to the Key Question
• Determine whether a systematic literature review will have an impact, is feasible, and the potential value of the review
Tick-Borne Disease Working Group

Process

1. Develop a key question, guiding questions, and PICOTS
2. Conduct a literature search using EBSCOhost and Government websites
Key Question and PICOTS | Topic Information
--- | ---
**Key Question** | What are the causes of persistent symptoms of Lyme disease in the United States and globally?

**Population** | People diagnosed with Lyme disease exhibiting persistent symptoms

**Interventions/Indicators** | Adequate and timely treatment, autoimmune responses, other causes

**Comparators** | Compare findings from interventions/indicators

**Outcomes** | Identifiable causes of persistent Lyme disease

**Timing** | Last 20 years (1998-2019)

**Setting** | Not applicable
Tick-Borne Disease Working Group

Process – Guiding Questions

Key Question: What are the causes of persistent symptoms of Lyme disease in the United States and globally?

Guiding Questions

• What is the evidence for persisting symptoms of Lyme disease in treated and untreated patients?
• What is/are the cause(s) of persistent symptoms? (Persisting infection, inadequate treatment, autoimmunity, other potential reasons, or a combination of causes?)
• What is the epidemiology of persisting symptoms of Lyme disease?
Tick-Borne Disease Working Group

Process – Search Criteria

• A literature search was conducted using EBSCOhost and Government websites

• Key words and exclusion criteria were derived from the criteria set forth in the PICOTS. Articles were excluded when:
  • Full article missing or there was not enough information in the abstract
  • Article not from a peer-reviewed scholarly journal
  • Article not relevant to topic area
Tick-Borne Disease Working Group

Findings

A preliminary assessment of the literature identified several proposed causes of persistent symptoms of Lyme Disease:

• inadequate treatment,
• genomic differences among subspecies of $B.\ burgdorferi$,
• long-term persistence of the $B.\ burgdorferi$ spirochete,
• the presence of one or more co-infections,
• the immune response to infection with $B.\ burgdorferi$, and
• autoimmunity involvement
Tick-Borne Disease Working Group

Summary of Findings

• Appropriateness and Importance
  This topic is both appropriate and important.

• Desirability of a New Review/Duplication
  A new review would not be duplicative of an existing product. We found no systematic reviews related to the scope of the nomination.

• Impact of a New Evidence Review
  The impact of a new systematic literature review is likely to be low.

• Feasibility of New Evidence Review
  A new systematic literature review will have a low impact, but is feasible at this time and may provide some potential direction for future research studies.
Tick-Borne Disease Working Group

Public Comment

- Order of Public Comment is:
  - Laura Hovind
  - Dorothy Leland
  - Jennifer Platt
  - Lorraine Johnson
  - Deborah Olsen
  - Charlotte Meyer
  - Phyllis Mervine
  - Allison Caruana

- 30 minutes of public speaking today
- 8 speakers
- 3 minutes each

3 ways to engage:
- Verbal public comment at meetings
- Written public comment for meetings, available on website
- Email comments 24/7
  tickbornedisease@hhs.gov
Tick-Borne Disease Working Group

Meeting #10  |  September 12, 2019

Lunch
Quick Recap of the Morning
Tick-Borne Disease Working Group

Federal Inventory
Tick-Borne Disease Working Group

Rationale for the Federal Inventory

According to the 21st Century Cure Act the Tick-Borne Disease Working Group was created to

• Review all efforts within the US Department of Health and Human Services related to all tickborne diseases
• Ensure inter-agency coordination and minimize overlap
• Identify research priorities and gaps
Tick-Borne Disease Working Group

Agencies Surveyed by the TBDWG for 2018 Report

- Centers for Disease Control and Prevention
- National Institutes of Health
- US Food and Drug Administration
- Centers for Medicare and Medicaid Services
- Department of Defense (DoD)
- Department of Veterans Affairs
- US Department of Agriculture (USDA) (proposed to be surveyed for 2020 report)
Tick-Borne Disease Working Group

Intramural and Extramural Activities

• CDC, NIH and DoD managed more than 1500 tickborne disease projects from FY 2010 to 2018
• $554 million invested in tickborne disease related projects, activities, and research
• Resulting publications: 467 (CDC), 235 (NIH), 41 (DoD), 7 (FDA)
Tick-Borne Disease Working Group

Needs and Gaps in Research Identified by the 2018 TBDWG

- Improve early and accurate diagnosis and treatment
- Strengthen national surveillance
- Understand the immunological mechanism (for example, the pathogen-host interaction) of immune protection for Lyme disease and other tickborne diseases
- Develop new rapid and accurate laboratory tests
- Develop antibiotic combination and/or therapeutic options for treating acute and persistent illness
- Encourage the development of strategic plans for tick-borne disease Federal investments
- Dedicate funding to tick-borne diseases and evaluate related activities using performance indicators and clear metrics for success
- Characterize how tick-borne disease affects US national security, military readiness, and the health and readiness of active-duty Service members, Veterans, and their families
Tick-Borne Disease Working Group

Proposed Plan to Address the Federal Inventory for 2020 Report

- Update the information in the inventory since the 2018 TBDWG report
- Request report on progress toward the agencies’ strategic plans to address tickborne diseases
- Request report on progress toward addressing the unmet priorities identified in the 2018 report
- Create a TBDWG Federal Inventory Subcommittee to analyze the new Federal Inventory content for use in the 2020 Report with attention to anaplasmosis, ehrlichiosis, tickborne rickettsiae and viruses, babesiosis, alpha Gal sensitivity, as well as Lyme borreliosis and other borrelioses
Tick-Borne Disease Working Group

Next 2 Meetings

- Both in-person
- Meeting #11 – January 28-29, 2020 in Washington, DC
- Meeting #12 – March 3-4, 2020 in Philadelphia, PA
Tick-Borne Disease Working Group

Recap of Decisions Made

1. Babesia Name change
2. Training name change
3. Public comment SC members
4. Topic Development Briefs next steps
5. Federal Inventory
6. TBD
## Tick-Borne Disease Working Group

### Next Steps

<table>
<thead>
<tr>
<th>Subcommittee Deliverable</th>
<th>Due Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finalize and submit Background and Methods section to Working Group for review</td>
<td>October 1, 2019</td>
</tr>
<tr>
<td>Begin drafting Results and Potential Actions section</td>
<td>After October 1, 2019</td>
</tr>
<tr>
<td>Begin reviewing and discussing draft Results and Potential Actions as a group</td>
<td>October 1, 2019</td>
</tr>
<tr>
<td>Finalize and submit Results and Potential Actions section to Working Group for review</td>
<td>November 1, 2019</td>
</tr>
<tr>
<td>Begin compiling complete Subcommittee Report to the working group</td>
<td>After November 1, 2019</td>
</tr>
<tr>
<td>Begin reviewing and discussing the complete subcommittee report to the working group</td>
<td>December 1, 2019</td>
</tr>
<tr>
<td>Finalize and submit complete Subcommittee Report to the Working Group</td>
<td>January 10, 2020</td>
</tr>
</tbody>
</table>
Before We Adjourn . . .

Thank You!

to everyone who worked to make this meeting possible, and to everyone who has provided input and suggestions, and to those of you who have joined us today.