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Testing practices and volume of non-Lyme tickborne diseases in the United States

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ABSTRACT

Large commercial laboratories in the United States were surveyed regarding the number of specimens tested for eight tickborne diseases in 2008. Seven large commercial laboratories reported testing a total of 2,927,881 specimens nationally (including Lyme disease). Of these, 495,585 specimens (17%) were tested for tickborne diseases other than Lyme disease. In addition to large commercial laboratories, another 1051 smaller commercial, hospital, and government laboratories in four states (CT, MD, MN, and NY) were surveyed regarding tickborne disease testing frequency, practices, and results. Ninety-two of these reported testing a total of 10,091 specimens for four tickborne diseases other than Lyme disease. We estimate the cost of laboratory diagnostic testing for non-Lyme disease tickborne diseases in 2008 to be $9.6 million. These data provide a baseline to evaluate trends in tickborne disease test utilization and insight into the burden of these diseases.

1. Introduction

North American ticks transmit the agents of Lyme disease and several other tickborne diseases (TBDs) of humans. Although the geographic distributions of specific diseases vary, TBDs occur throughout the United States and collectively constitute a public health problem. Overall reports of TBDs have increased over the last decade, possibly reflecting greater exposure, increased awareness, improved diagnostics, changes in surveillance practices, changes in human activities, and variation in tick distributions and infection prevalence.

Laboratory testing can be central to establishing the correct diagnosis and guiding care for patients with TBDs, including those with atypical presentations. Alternatively, testing specimens from patients with a low disease probability can lead to misinterpretation of positive results and inflate medical costs (Ramsey et al., 2004). The number of Lyme disease tests performed in 1995 was estimated at 2.8 million using marketing data (MK Associates, 1993; Tugwell et al., 1997); however, the current volume of testing for Lyme and other TBDs is expected to be much higher (Hinckley et al., 2014).

In an effort to better understand TBD diagnostic testing practice and volume, a nationwide survey of large commercial laboratories was conducted, as well as hospital-based and other smaller laboratories in four states where Lyme and other tick-borne diseases are endemic. In addition, we used the reported volume to estimate the cost of non-Lyme disease TBD testing in the United States.

2. Materials and methods

TickNET is a network created in 2007 to foster collaboration on surveillance, research, education, and prevention for tickborne diseases. Collaborators include various divisions within CDC and key state and local health departments. CDC provides extramural funding to participating health departments and partners through the Epidemiology and Laboratory Capacity for Infectious Diseases cooperative agreement, to sustain and enhance surveillance for Lyme disease, and through the Emerging Infections Program (EIP), to promote applied research. There are EIPs are located within

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Connecticut, Maryland, Minnesota, and New York, and Lyme disease cases in these four states accounted for nearly 40% of all reported cases in the United States in 2008. In addition, 56% of HGA cases, 14% of HME cases, and 5% of RMSF were reported from these four states in 2008 (CDC, 2010). At the time of this study, *Babesia* infection was not nationally notifiable so the endemnicity of babesiosis compared to other US states could not be compared. However, in 2011, more than 50% of the 1124 confirmed and probable cases of babesiosis were reported from Connecticut, Minnesota, and New York (CDC, 2011). The etiologic agents of Lyme disease, HGA, and babesiosis are all transmitted by the blacklegged tick (*Ixodes scapularis*).

In an effort to better understand TBD diagnostic testing practice and volume, a survey of large commercial laboratories as well as hospital-based and other smaller laboratories was conducted in four TickNET states. A two-phased approach was used (Fig. 1). The catchment area for this study included laboratories that were likely to test patients in Connecticut, Maryland, Minnesota, and New York, as determined by state and national disease surveillance records. The survey included commercial laboratories (Phase 1) and smaller clinical and hospital-based laboratories (Phase 2) that were likely to test patients for TBDs, as determined by a review of state disease surveillance records.

2.1. Phase 1

The first phase of the survey was aimed at large commercial laboratories known to conduct TBD disease testing nationally. The following laboratories were contacted by email and telephone to ask for participation: ARUP, Clinical Laboratory Partners, Focus Diagnostics, Laboratory Corporation of America (LabCorp), Mayo Medical Laboratories, Quest Diagnostics, and Specialty Laboratories. These laboratories accounted for the majority of Lyme disease cases reported to health departments in the four endemic states (Connecticut, Maryland, Minnesota and New York) in 2008. Three additional laboratories known to provide alternative non-FDA approved methods of Lyme disease testing (IGeneX, MD Laboratories, Neuroimmunology Laboratory) were also contacted and asked to participate. The survey was sent to laboratories by email and returned by fax or email. Non-responding laboratories were contacted by phone and email by EIP or CDC research staff on a minimum of three occasions to request participation. Commercial laboratories were asked to report their national specimen testing volume for eight TBDs (Lyme disease, RMSF, babesiosis, HGA, HME, tickborne relapsing fever, Colorado tick fever, and Powassan virus); because single specimens may have been tested for multiple pathogens and single patients could have multiple specimens submitted, the number of specimens tested does not necessarily reflect the number of patients tested. In addition, it is possible that one specimen may have been tested for one pathogen by more than one assay.

2.2. Phase 2

The second phase of the survey targeted clinical, hospital, government, and small commercial laboratories in the four TickNET states. State health department surveillance records in Connecticut, Maryland, and Minnesota were reviewed to identify laboratories that were known to conduct TBD testing. In New York, all licensed laboratories were surveyed regardless of whether or not they were known to conduct TBD testing. Identified laboratories were asked to complete an emailed survey regarding the number of tests and types of assays performed by their laboratory in 2008 for eight TBDs. As with the Phase 1 survey, laboratories reported the total specimens tested. Therefore, because single specimens may have been tested for multiple pathogens and single patients could have multiple specimens submitted, the number of specimens tested does not necessarily reflect the number of patients tested.

Respondents to Phase 2 were asked to report the percent positive by diagnostic assay for residents of the four endemic study states (CT, MD, MN, and NY). The number of tests and percent positive by test type were aggregated across all laboratories. Assay types included serologic testing (for all pathogens), direct visualization (babesiosis, HGA, HME), and PCR (babesiosis and HGA).

Non-responding laboratories were sent two follow-up emails. If still no response was received, research staff from the EIP in each state contacted laboratory managers in their respective states by telephone to request participation and collected survey responses over the telephone. Both phases of this research effort were deemed exempt from IRB review (non-human subject research) by the Yale Human Investigations Committee and CDC.

Table 1
Testing volume for tick-borne diseases in the US, 2008.[a]

Tickborne disease	Specimens tested	%
Lyme disease	2,432,396	83
Ehrlichiosis (HME)	193,121	6
Rocky Mountain spotted fever	152,713	5
Babesiosis	85,323	3
Anaplasmosis (HGA)	59,943	2
HGA/HME[b]	3750	<1
Tick-borne relapsing fever	405	<1
Colorado tick fever	230	<1
Powassan encephalitis	0	0
Total	2,927,881	

[a] Data aggregated from seven U.S. commercial laboratories.
[b] One laboratory could not provide data specific to *Anaplasma* vs. *Ehrlichia* PCR testing.

2.3. Estimating the costs of tickborne disease testing

To estimate the direct cost of non-Lyme disease TBD testing nationally, the proportion of assay types used to diagnose specific TBDs reported by the Phase 2 laboratories (e.g., IFA, PCR, microscopy) was applied to the national specimen testing volume for each TBD reported by the Phase 1 laboratories. The national limit for reimbursement in the 2008 clinical diagnostic laboratory fee schedule (Centers for Medicare and Medicaid Services, 2008) was then used to estimate the cost of national testing for the following test types: *Babesia, Anaplasma* or *Ehrlichia* direct detection (microscopy) ($16.76), *Babesia* indirect fluorescent antibody ($17.32), *Babesia* or *Anaplasma* PCR ($49.04), *Anaplasma* or *Ehrlichia* indirect fluorescent antibody ($14.22), HGA/HME concurrent panel ($28.44), RMSF indirect fluorescent antibody ($27.05). Although tickborne relapsing fever and Colorado tick fever are not endemic to CT, MD, MN, and NY, the 2008 national limit for their diagnostic immunoassays were also applied to the total number of specimens tested nationally ($37.38 and $36, respectively).

3. Results

3.1. Phase 1

Six laboratories completed the entire survey: ARUP, Clinical Laboratory Partners, Focus Diagnostics, LabCorp, Quest Diagnostics, and Specialty Laboratories. One additional laboratory, Mayo Medical Laboratories, completed only the PCR and serology sections of the survey. All data were aggregated to protect the identity of each individual laboratory.

National TBD testing volume is reported in Table 1. Of the nearly three million specimens tested for tickborne pathogens in 2008, 83% of the specimens were tested for Lyme disease, followed by HME (6%), RMSF (5%), babesiosis (3%), HGA (2%), tick-borne