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Human Granulocytic Anaplasmosis - Connecticut, 2011-2014

Human granulocytic anaplasmosis (HGA), formerly known as human granulocytic ehrlichiosis, is a tick-borne disease caused by the bacterium *Anaplasma phagocytophilum*. In Connecticut, HGA is transmitted to humans through the bite of an infected *Ixodes scapularis* (deer tick or black-legged tick), the same tick that transmits Lyme disease and babesiosis (*1*).

The Connecticut Department of Public Health (DPH) used the anaplasmosis National Surveillance Case Definition (NSDC), which was established in 2009, to determine case status. The NSCD defines a confirmed case as a patient with clinically compatible illness characterized by acute onset of fever, plus one or more of the following: headache, myalgia, anemia, leukopenia, thrombocytopenia, or elevated hepatic transaminases; plus 1) a fourfold change in IgG-specific antibody titer to *A. phagocytophilum* antigen by indirect fluorescence assay (IFA) in paired serum samples, or 2) a positive polymerase chain reaction (PCR) assay, or 3) immunostaining of antigen in a biopsy or autopsy sample, or 4) isolation from a clinical specimen in cell culture. A probable case is a patient who has a clinically compatible disease plus 1) elevated IgG or IgM antibody, or 2) microscopic identification of morulae in neutrophils or eosinophils. To interpret serologic evidence, the Centers for Disease Control and Prevention uses an IFA IgG cutoff of >1:64 and does not use IgM results because of low specificity (*2*).

During 2011-2014, the DPH received 2,700 individual case-reports of *A. phagocytophilum*. Positive test results included 2,146 (80%) IgG serology, 483 (18%) PCR, 61 (2%) positive blood smears, 1 (<1%) culture, and 9 (<1%) tests identified as other. Of the reports received, 349 (13%) were classified as not a case, 250 (9%) were probable cases, and 239 (9%) were confirmed cases (Figure 1). The remaining 1,862 (69%) reports contained information that was insufficient for case classification (e.g. positive laboratory test only, lost to follow-up). Of the 2,146 positive IgG titers only, 7 (0.3%) were classified as a confirmed case after follow-up. During the same period, of the 483 positive PCR results received, 231 (48%) were classified as a confirmed case after follow-up.

Of the confirmed cases, date of onset of illness was reported for 190 patients; 158 (84%) occurred during April - July. The ages of patients ranged from 1-92 years (mean = 57.4). The age specific rates for confirmed cases was highest among those 70-79 years of age (6.3 cases per 100,000 population), and lowest for children < 9 years (0.3 cases per 100,000 population). Males accounted for 61% of cases.

Symptoms reported included fever (20%), malaise (17%), muscle aches (15%), headache (13%), thrombocytopenia (12%), elevated hepatic transaminases (10%), leukopenia (9%), and anemia (4%). A total of 49 case-patients were hospitalized

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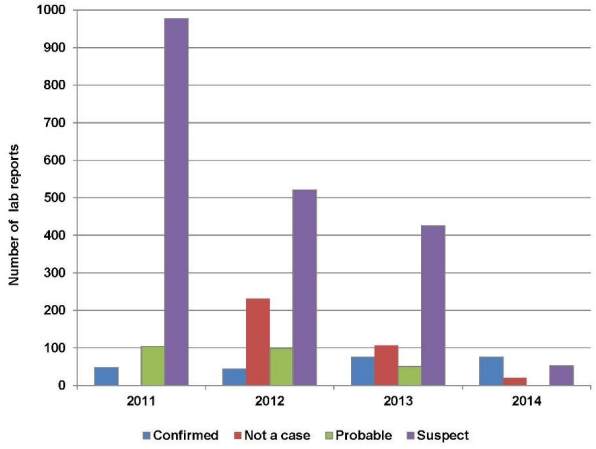
Figure 1. Number of *Anaplasma phagocytophilum* case reports-Connecticut, 2011-2014.



including 14 (29%) aged 70-79 years; no deaths were reported. Statewide, the average annual number of confirmed cases was 59 (range 44-72), and the average annual incidence was 1.6 cases per 100,000 population. Windham County had the highest average county rate with 9.3 cases per 100,000 population (Figure 2). The lowest rates were reported from Hartford and New Haven counties (0.2 and 0.3 cases/100,000 population respectively).

Reported by

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Editorial

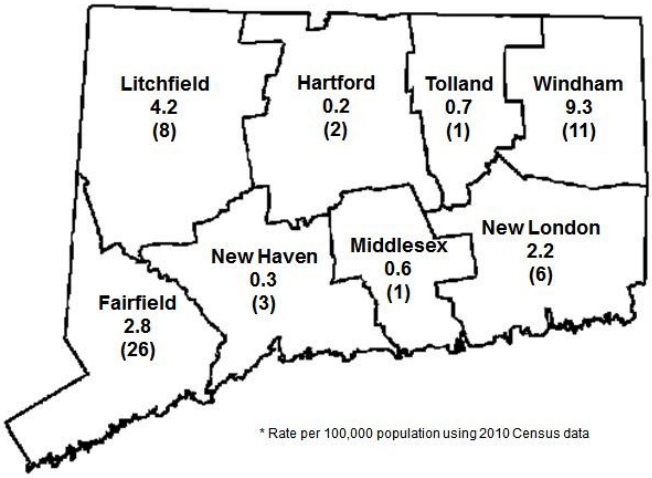
Connecticut has conducted surveillance for anaplasmosis since 1995, which has allowed the DPH to determine the epidemiology of this disease. As our data show, anaplasmosis is most frequently diagnosed in adults, and especially in patients over 60 years of age; the age group most likely to be hospitalized. During the past 20 years, incidence of anaplasmosis has remained relatively stable with yearly variation often seen with vector-borne diseases.

In 2014, the DPH made changes to anaplasmosis surveillance methods and the case definition. Healthcare providers are no longer required to report cases of anaplasmosis. The diagnosis of anaplasmosis is made based on clinical signs and symptoms, which can be vague. Because of this, physicians should not delay treatment. Confirmation is available through laboratory testing. Laboratories are required to report *Anaplasma* positive PCR test results only. All other testing, including serology results and smears are no longer reportable to the DPH. This should substantially reduce the burden of anaplasmosis reporting on laboratories and surveillance coordinators. Connecticut data indicate that very few (0.3%) confirmed cases were identified through positive serology.

Follow-up was conducted on all positive test results received, and involved sending supplemental reporting forms to the ordering physician. Included on the supplemental report form were questions concerning clinical findings that were necessary for case classification under the NSCD. From 2011-2014, less than one third of follow-up forms were returned. In 2014, follow-up was conducted on 85 positive PCR results only and all supplemental reports were returned. As of January 1, 2015, follow-up for anaplasmosis was discontinued. For the purposes of the DPH, all PCR positive *Anaplasma* test results will be defined as confirmed cases. These cases do not necessarily meet the NSCD.

Testing is readily available through commercial laboratories. Health care providers are urged to continue to include anaplasmosis in the differential diagnosis of acute febrile illnesses, especially during spring and summer months. For questions concerning anaplasmosis or to order the most current version of the Laboratory Report of Significant Findings form OL-15C, please contact the Epidemiology and Emerging Infections Program at (860) 509-7994 or visit our website at http://www.ct.gov/dph. Select "Forms" from the top navigation bar, and select the OL-15C fillable PDF.

Figure 2. Average annual number of *Anaplasma phagocytophilum* (cases) and rate by county, Connecticut, 2011-2014



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Babesiosis Surveillance — Connecticut, 2014

Babesiosis is a parasitic infection caused by several species of *Babesia*. In Connecticut, cases of babesiosis are generally caused by *Babesia microti*, and it is most often transmitted through the bite of infected *Ixodes scapularis* ticks. It is also possible to become infected through a blood transfusion; however this is not common. Babesiosis was first identified in Connecticut in 1988, and surveillance was initiated by the Connecticut Department of Public Health (DPH) in 1989 for physician reporting and 1990 for laboratory reporting. With the establishment of a national surveillance case definition (NSCD) in 2011, babesiosis became a nationally notifiable disease (*1*). Case classification for babesiosis using the national surveillance case definition incorporates both clinical and laboratory findings.

Laboratory criteria for diagnosis consists of confirmatory and supportive test results. Confirmatory laboratory findings detect active parasitemia and include: observation of the *Babesia* parasite on blood smear; DNA detection in whole blood by polymerase chain reaction (PCR); genomic sequences in whole blood by nucleic acid amplification (NAA); or confirmed infection through animal inoculation (infrequently used). Supportive laboratory results include: serology through Indirect Fluorescent Antibody (IFA): total immunoglobulin or IgG antibody titer≥ 1:256 for *B. microti* or *B. divergens* or ≥ 1:512 for *B. duncani*. These tests are considered supportive because they indicate an immune response to the parasite and cannot readily distinguish between current active infection or prior infection. Laboratories report positive results for confirmatory and supportive testing to DPH via the Laboratory Report of Significant Findings form OL-15C.

Clinical findings included in the surveillance case definition include objective signs (fever, anemia, thrombocytopenia) and subjective symptoms (chills, sweats, headache, myalgia, arthralgia). To determine case status, the NSCD requires both clinical and laboratory information, therefore the DPH conducts follow-up on all positive laboratory results. Supplemental reporting forms are mailed to the ordering physician or the Infection Control Department of the hospital performing testing with a request to complete and return. Healthcare providers can use the Reportable Disease Confidential Case Report Form PD-23 to report cases of babesiosis. Signs and symptoms can be included in the 'confirmatory information' section of the form.

A confirmed case is defined by the NSCD as a case that has confirmatory laboratory results and meets at least one of the objective or subjective clinical evidence criteria, regardless of the mode of transmission (can include clinically manifest cases in transfusion recipients or blood donors). A probable case is defined as a patient with a supportive laboratory result and at least one objective clinical finding. Blood donors or recipients who are epidemiologically-linked to a confirmed or probable case may also meet the probable case definition if: they have confirmatory laboratory evidence but no objective or subjective clinical signs; or have supportive laboratory evidence, do not have any objective clinical signs and may or may not have subjective clinical signs. A suspect case is defined as having a confirmatory or supportive laboratory result with insufficient clinical information for further classification (e.g., laboratory report only, no clinical information provided). Only confirmed cases are reported to the Centers for Disease Control and Prevention for inclusion in the national statistics.

During 2014, the DPH received 685 reports of babesiosis on patients who obtained a total of 834 positive laboratory tests. Laboratory reports received included 55% serology, 28% blood smear, and 17% PCR/NAA results. Of the 685 reports, there were 174 (25%) confirmed, 40 (6%) probable, 150 (22%) not a case, and 321 (47%) suspect cases.

Incidence rates were calculated using the 2013 population estimates. The 2014 statewide incidence for babesiosis was 4.8 cases per 100,000 population. As was observed from the 2011-2013 data, the highest incidence rates were recorded in Windham County (19.6 cases per 100,000 population) and New London County (22.3 cases per 100,000 population) (*2*). Cases from Windham and New London counties accounted for 48% of all confirmed cases state-wide (see table on page 20).

Among confirmed cases, the median age was 65 years (range of 3-93 years); 63% were male. Of the 149 cases for which race information was available, 143 (96%) were white, 4 were Black or

Table. Babesiosis Incidence Rates by County—Connecticut, 2014

County	Number of Confirmed Cases	Incidence Rate*
Fairfield	24	2.6
Hartford	12	1.3
Litchfield	11	1.2
Middlesex	15	9.1
New Haven	17	2.0
New London	61	22.3
Tolland	9	5.9
Windham	23	19.6
Unknown	2	--
Total	174	4.8

*Incidence rate calculated using the 2013 population estimates.

African-American, 2 Asian, and 2 other. Ethnicity was available for 109 (63%) cases; 5 were Hispanic. Among the 81 (49%) confirmed cases for whom information was available, 3 (4%) were recipients of blood, organ, or tissue products within the past year. No confirmed cases were identified among individuals identified as recent blood donors. History of blood donation within the past year was unknown in 76% of confirmed cases, suggesting this is not routinely collected in the setting of clinical care for active cases.

Among the 173 confirmed cases, 78 (45%) were hospitalized with a mean length of stay of 5 days (range 1-23 days). The following clinical syndromes were seen among confirmed case-patients: 132 (76%) had fever, 111 (64%) thrombocytopenia, 92 (53%) anemia, 87 (50%) myalgia, 86 (50%) chills, 81 (47%) headache, 65 (38%) sweats, and 63 (36%) arthralgia. For the 89 confirmed cases with known symptom onset date, 90% had onset during the summer months of June (28%), July (45%), and August (17%).

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Editorial

Eastern Connecticut has consistently reported the highest incidence of confirmed babesiosis. The increased incidence rates from these counties are consistent with previous years. High rates of babesiosis in eastern Connecticut may also be due in part to the high rate of infection in the wildlife reservoir, the white footed mouse (*Peromyscus leucopus*), and land use (*3*).

Babesiosis is preventable and treatable; however, it can be severe and life-threatening especially in persons without a spleen, elderly, or immunocompromised. Accurate, timely, and complete data are needed to help better determine the epidemiology of this disease in Connecticut. Providers are reminded to complete and return the Babesiosis Case Report Form. Tick control and personal protective measures are necessary to prevent this disease, as well as Lyme disease and anaplasmosis. When evaluating patients with fever and other symptoms suggestive of tick-borne illness, clinicians should consider babesiosis in the differential diagnosis, especially for those with potential tick exposures during the months of June–August.

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