

## Ehrlichiosis and Anaplasmosis

*Ehrlichiosis/Anaplasmosis is a Class C disease. It must be reported to the state within five business days.*

Ehrlichiosis (previously called human monocytic ehrlichiosis, HME) and anaplasmosis (previously called human granulocytic ehrlichiosis, HGE) are emerging illnesses caused by tick-borne rickettsial organisms that are clinically indistinguishable - resulting in acute, influenza-like illness with fever, chills, headache, malaise and myalgia and nausea. They also frequently cause rash with leukopenia, thrombocytopenia, and elevated liver enzymes, mainly ALT. Ehrlichiosis and anaplasmosis, if left untreated or poorly managed, can also result in severe and even fatal complications such as acute respiratory distress syndrome (ARDS), meningitis/encephalitis and renal failure. The incubation period, before the onset of symptoms, is seven to 14 days after a tick bite or exposure.

### Epidemiology

Ehrlichiosis and anaplasmosis are caused by three related bacterial zoonotic pathogens that infect animal reservoir hosts and are transmitted by ticks to humans. Ehrlichiosis and anaplasmosis were first recognized as a disease of humans in the United States in the late 1980's and mid-1990's respectively before they were added to the national notifiable list as a reportable disease in 1999. The first case of HME was reported in a patient from Fort Chaffee, Arizona in 1991.

Ehrlichiosis, commonly referred to as human monocytic ehrlichiosis (HME) results from infection by *Ehrlichia chaffeensis* that occurs commonly in the southeastern and south-central United States, while *E. ewingii* infections have been reported mainly in immunocompromised people from Missouri, Oklahoma, Tennessee and Arkansas. Both the infections are transmitted by lone star ticks (*Amblyomma americanum*). Three states (Oklahoma, Missouri, Arkansas) account for 30% of all reported *E. chaffeensis*.

Anaplasmosis, previously described as human granulocytic ehrlichiosis (HGE) is caused by bacterium *Anaplasma phagocytophilum*. The agent was believed to be similar or identical to two old pathogens, namely *E. equi* and *E. phagocytophilia*. The disease is most frequently reported from the upper midwestern and northeastern United States that correspond with known geographic distribution of Lyme disease. The black-legged tick (*Ixodes scapularis*) is the principal vector of anaplasmosis in the upper midwestern and northeastern U.S., while the western black-legged tick (*Ixodes pacificus*) may transmit the pathogen along the West Coast. These tick species also transmit *Borrelia burgdorferi*, which causes Lyme disease and *Babesia spp.* that causes Babesiosis. Ninety percent of all reported anaplasmosis cases occur in six states (New York, Connecticut, New Jersey, Rhode Island, Minnesota and Wisconsin).

During 2000 to 2007, the reported incidence rate of *E. chaffeensis* and *A. phagocytophilum* increased from 0.80 to 3.0 cases per million persons per year and 1.4 to 3.0 cases per million persons per year respectively.

The gold standard serologic test for diagnosis of ehrlichiosis and anaplasmosis is the indirect fluorescent antibody (IFA) assay, performed on paired serum samples to demonstrate a

significant four-fold rise in antibody titers. PCR assays can also be used to determine the disease. Other methods include presence of morulae in leukocytes in peripheral blood (monocytes for *E. chaffeensis*; granulocytes for *E. ewingii* and anaplasmosis) and immunohistochemical staining of tissue. Despite the availability of highly sensitive and specific tests to diagnose the illness, some cases are difficult to diagnose due to the inability of the tests to delineate the causative agents, as seen with undetermined cases where laboratory evidence may not be conclusive enough to place cases in one of the categories.

No licensed vaccine providing immunity to ehrlichiosis and anaplasmosis is available. Limiting exposure to ticks is an important method of prevention. Since elimination of all activities resulting in tick exposure is impossible, protective measures such as wearing light-colored clothing, tucking pant legs into socks and applying appropriate repellents to clothing and skin should be employed. Prompt inspection and removal of ticks are also very important. As in many tick-transmitted diseases, the tick must be attached for several hours before transmission takes place, thus the importance of tick removal.

For surveillance purpose, four sub-categories of confirmed or probable ehrlichiosis/anaplasmosis should be reported:

- 1) Human ehrlichiosis (HME) caused by *E. chaffeensis*,
- 2) Human ehrlichiosis caused by *E. ewingii*,
- 3) Human anaplasmosis (HGE) caused by *A. phagocytophilum*, or
- 4) Human ehrlichiosis/anaplasmosis – undetermined. (Cases reported in the fourth sub-category can only be reported as “probable” because the cases are only weakly supported by ambiguous laboratory test results).

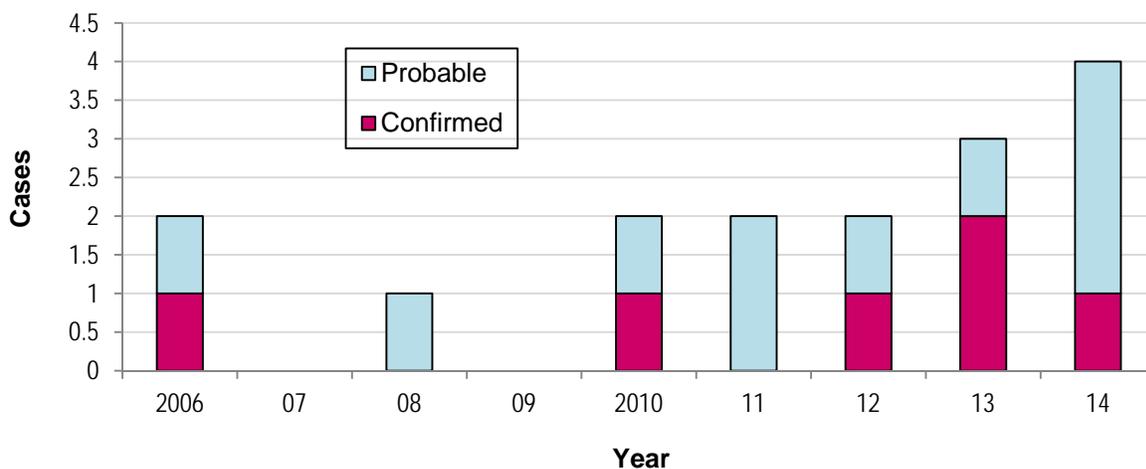
## Cases

As of 2013, the incidence of both ehrlichiosis and anaplasmosis in Louisiana were 0.02 cases per million each. Nationally, the number of cases of both the diseases has increased steadily since the disease became reportable in 1999, while case fatality rates has declined to 1.8% for ehrlichiosis and remained low, at less than 1% for anaplasmosis.

A total of 16 cases of ehrlichiosis/anaplasmosis have been reported in Louisiana since 2006, of which four cases occurred in 2014. Reported occurrence of ehrlichiosis/anaplasmosis in this state ranges from zero to two cases per year from 2006 to 2012. *E. chaffeensis* infections constitute the majority of these cases followed by ehrlichiosis/anaplasmosis-undetermined and *A. phagocytophilum*. Cases have been classified as confirmed or probable based on the level of diagnosis determined in each circumstance.

Nationally, the frequency of reported cases of anaplasmosis and ehrlichiosis is highest among males over 40 years of age and people over 50 years of age. There has been a rise of two-fold in cases since 2006. This increase reflects the national trend that is particularly influenced by increased numbers of cases reported from suburban areas, presumably due to human migration into naturally pristine or forested areas, and a combination of new diagnostic tests (Figure 1).

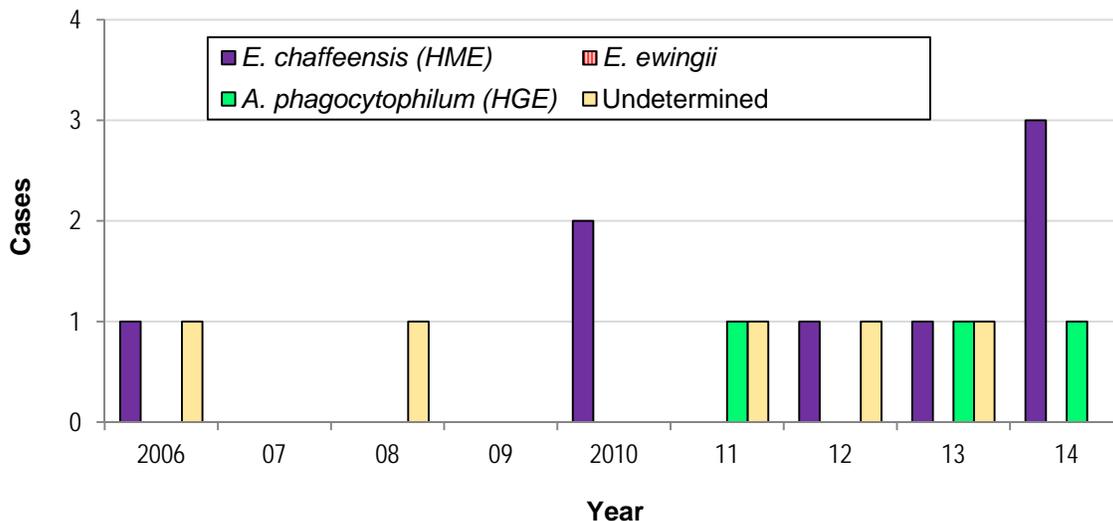
Figure 1: Ehrlichiosis/anaplasmosis reported cases (including both confirmed and probable), Louisiana, 2006-2014



Nationally, 80% of the *E. chaffeensis* cases were classified as probable cases. A majority of these probable cases (73%) were diagnosed using single acute-phase IgG titer by IFA with 11% of them demonstrating seroconversion, and were classified as confirmed cases. Also, 10% of the total cases were confirmed by PCR. Similarly, for *A. phagocytophilum*, 76% cases were classified as probable cases. 52% of the probable cases were reported with only single positive IFA, of which 8.3% showed seroconversion on IFA, and were classified as confirmed cases. Sixteen percent of the cases were confirmed by PCR.

In 2014, incidence rates of ehrlichiosis and anaplasmosis in Louisiana were **0.6** (0.2 in 2013) cases per million and **0.2** (0.2 in 2013) cases per million respectively.

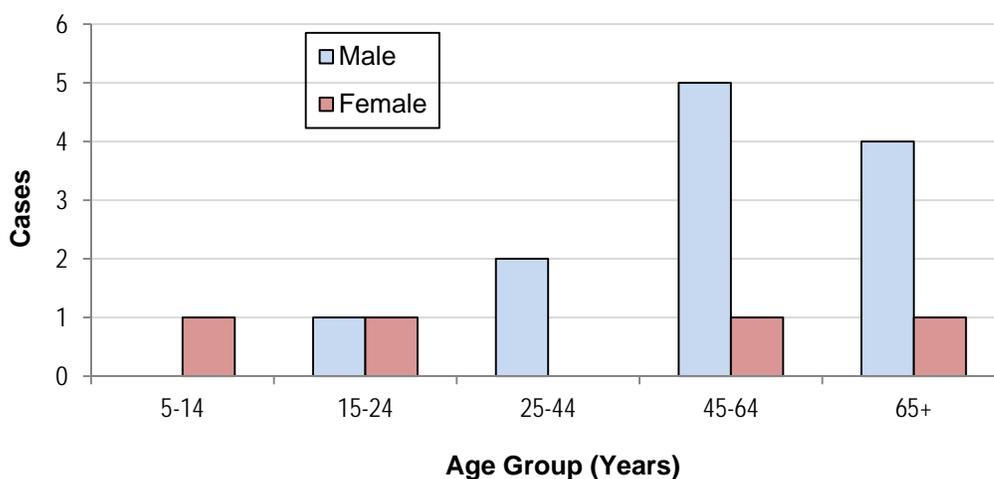
Figure 2: Ehrlichiosis/anaplasmosis case numbers for *E. chaffeensis*, *A. phagocytophilum*, *E. ewingii* and undetermined Louisiana, 2006-2014



## Gender and Age

Nationally, the frequency of both the disease is highest in males and people aged 50 years and older, while the highest incidence rates of ehrlichiosis and anaplasmosis was seen in the age group 60 to 64 years and the 65 and older group respectively. Overall, more cases were reported among males (75%) than females. Data also indicated a huge preponderance among males in the age group of 45 to 64 years old, followed by those aged 65 years and older. However, males and females in the 15 to 24 year old age group were equally affected (Figure 3).

Figure 3: Ehrlichiosis/anaplasmosis cases by age and gender (including both confirmed and probable), Louisiana, 2006-2014

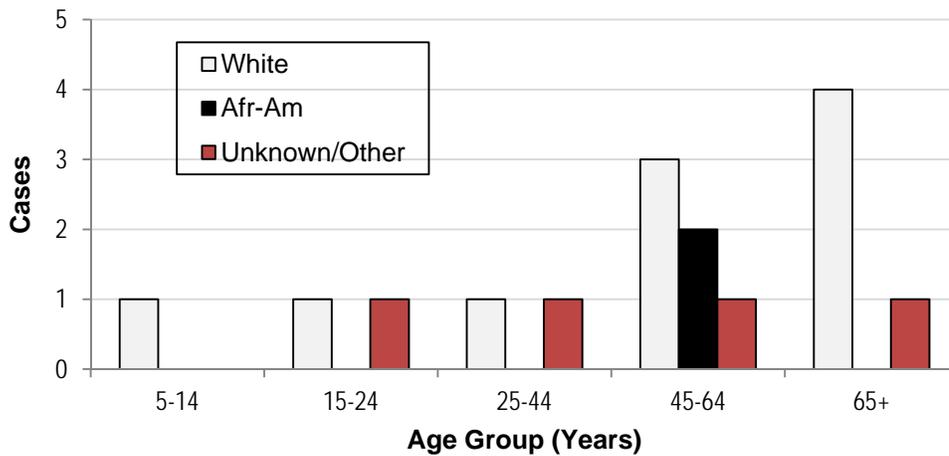


Those in the age group of 65 years and older reported the highest incidence of ehrlichiosis/anaplasmosis at 0.8 cases per 100,000 population when compared to other age groups.

## Race and Age

Nationwide, 92% cases occur in Whites and non-Hispanic ethnicity. In comparison, Whites comprised 63% of all reported cases in Louisiana; 13% were Black. All other cases were reported as other races or unknown from 2006 to 2014 (Figure 4).

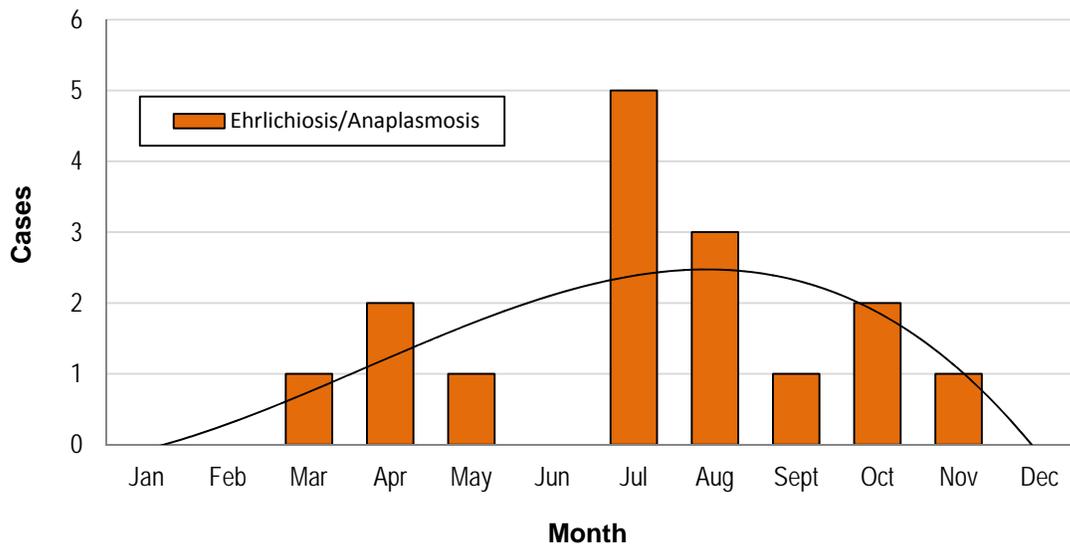
Figure 4: Ehrlichiosis/anaplasmosis cases by age and race (including both confirmed and probable) - Louisiana, 2006-2014



### Seasonality

In the United States, majority of cases are infected during summer months with a peak in the months of June and July. In Louisiana, 50% of all reported cases occurred between June and August, of which, 31% cases occurred in the month of July alone followed by 19% cases in August (Figure 5). Louisiana’s sub-tropical climate likely fosters a longer period of tick activity.

Figure 5: Ehrlichiosis/anaplasmosis reported cases (including both confirmed and probable) by month of onset - Louisiana, 2006-2014



## Hospitalization

In a 2011 report noting 2000 to 2007 data, national hospitalization rates were reported to be around 49% for cases of *E.chaffeensis* and 36% for *A.phagocytophilum*. Since 2000, rate of ehrlichiosis and anaplasmosis diagnosis in Louisiana hospitals was 6.2 cases per million hospitalized patients as per the Louisiana Hospital Inpatient Discharge Database (LAHIDD) database. Sixty-three percent of the total cases of ehrlichiosis and anaplasmosis in Louisiana that required hospital admission were males and approximately 43% of hospitalized patients were in the 45 to 64 years age group. LAHIDD data from 2000-2012 showed that 33.3% of all cases suffered at least one life-threatening complication.

The most frequently listed accompanying diagnoses with ehrlichiosis and anaplasmosis diagnosis in the LAHIDD database included fever and hyponatremia (20% each), neutropenia (20%) and thrombocytopenia (23%).

Also, the median number of days and treatment cost for people who were hospitalized with ehrlichiosis and anaplasmosis in Louisiana and associated complications or other accompanying diagnoses was 4.5 days and \$22,097 respectively.

## Case fatality

Nationally, case fatality rates (CFR) for *E. chaffeensis* and *A. phagocytophilum* during 2000-2007 were 1.9% and 0.6% respectively. CFR was highest among persons five to nine years of age (3.7%) and 70 years and older (3.5%) for *E. chaffeensis* and among age group 20 to 39 years (1.2%) for *A. phagocytophilum*. Median time between onset and death was 11 days (range 7 to 32 days) for *E.chaffeensis* and 8.5 days (range 2 to 36 days) for *A.phagocytophilum*. Patients with immunosuppressive conditions, including diabetes, cancer and arthritis had worse clinical courses and outcomes and death (RR = 3.7).

To date in Louisiana, no deaths have been reported to Department of Health and Hospitals' Infectious Disease Epidemiology section.

## Geography

The highest case counts of ehrlichiosis and anaplasmosis occurred in the Orleans, Caddo, Ouachita, Union and Washington parishes (Figure 6). With the exception of Union parish, the above mentioned parishes, in addition to St Tammany, Calcasieu, Lafayette and Livingston parishes also reported high incidence of Rocky Mountain Spotted Fever.

