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Ecological Havoc, the Rise of White-Tailed Deer, and the Emergence of *Amblyomma americanum*-Associated Zoonoses in the United States

C. D. Paddock[1] (✉) · M. J. Yabsley[2]

[1]Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA
cdp9@cdc.gov
[2]Southeastern Cooperative Wildlife Disease Study, College of Veterinary Medicine, University of Georgia, Athens, GA, USA

Abstract Two infectious diseases, and one presumably infectious disease, each vectored by or associated with the bite of the lone star tick (*Amblyomma americanum*), were identified and characterized by clinicians and scientists in the United States during the 1980s and 1990s. These three conditions—human monocytic (or monocytotropic) ehrlichiosis (HME), *Ehrlichia ewingii* ehrlichiosis, and southern tick-associated rash illness (STARI)—undoubtedly existed in the United States prior to this time. However,

the near-simultaneous recognition of these diseases is remarkable and suggests the involvement of a unifying process that thrust multiple pathogens into the sphere of human recognition. Previous works by other investigators have emphasized the pivotal role of white-tailed deer (*Odocoileus virginianus*) in the emergence of Lyme disease, human babesiosis, and human granulocytic anaplasmosis. Because whitetails serve as a keystone host for all stages of lone star ticks, and an important reservoir host for *Ehrlichia chaffeensis*, *E. ewingii*, and *Borrelia lonestari*, the near-exponential growth of white-tailed deer populations that occurred in the eastern United States during the twentieth century is likely to have dramatically affected the frequency and distribution of *A. americanum*-associated zoonoses. This chapter describes the natural histories of the pathogens definitively or putatively associated with HME, *E. ewingii* ehrlichiosis, and STARI; the role of white-tailed deer as hosts to lone star ticks and the agents of these diseases; and the cascade of ecologic disturbances to the landscape of the United States that have occurred during the last 200 years that provided critical leverage in the proliferation of white-tailed deer, and ultimately resulted in the emergence of these diseases in human populations.

1 Introduction

> The American white-tailed deer (*Odocoileus virginianus*) is the oldest deer species alive. It is an expert in surviving predation of diverse forms and, like other old North American indigenous mammals, adjusts remarkably well to human activity, to cities, and to agriculture. It is a deer of ecological havoc, a survival virtuoso. . .
>
> Valerius Geist 1998

Five tickborne infectious diseases—babesiosis, Lyme disease, human monocytic (or monocytotropic) ehrlichiosis (HME), human granulocytic anaplasmosis (HGA), and *Ehrlichia ewingii* ehrlichiosis—were identified and characterized by clinicians and scientists in the United States during a relatively short span of three decades between 1969 and 1999 (Scrimenti 1970; Western et al. 1970; Steere et al. 1978; Maeda et al. 1987; Bakken et al. 1994; Buller et al. 1999). A sixth, as-yet etiologically uncharacterized syndrome, southern tick-associated rash illness (STARI), was also discovered during this period (Schulze et al. 1984; Masters et al. 1994, 1998). The appreciation of these previously unrecognized infections and subsequent discoveries of the varied pathogenic agents that caused these conditions effectively doubled the number of distinct, North American, tick-transmitted diseases and expanded considerably the recognized magnitude of tick-borne infections in the United States. Until the early 1980s, Rocky Mountain spotted fever was the most commonly recognized tick-borne disease in the United States. During 2003, passive surveillance identified approximately 1,100 cases of this disease; however, approximately 320, 360, and

21,300 cases of HME, HGA, and Lyme disease, respectively, were also reported during this same interval (Centers for Disease Control and Prevention 2005). None of these last three diseases had been identified three decades earlier.

It is extremely unlikely that one or more of the pathogens that cause these illnesses arrived in North America during the last half of the twentieth century. For example, DNA of *Borrelia burgdorferi,* the causative agent of Lyme disease, has been detected in archival specimens of New England deer mice and black-legged ticks collected during the 1890s and 1940s, respectively (Persing et al. 1990; Marshall et al. 1994). As outlined in other chapters of this book, multiple factors over time and space contributed to the appreciation of these ecologically and etiologically diverse zoonoses in human populations. Nonetheless, the near-simultaneous recognition of these varied diseases is remarkable and suggests the involvement of a unifying process that thrust these pathogens into the sphere of human recognition.

Several compelling arguments describe the pivotal role of white-tailed deer in the emergence of Lyme disease and babesiosis in the northeastern and upper midwestern United States (Piesman et al. 1979; Wilson et al. 1985; Spielman et al. 1993; Spielman 1994). While this chapter borrows insights provided by these arguments, it focuses primarily on various environmental and ecological imbalances that were introduced to white-tailed deer by a cascade of human interventions during the nineteenth and twentieth centuries and how these combined to create the emergence of three diseases—HME, *E. ewingii* ehrlichiosis, and STARI—each of which is associated with the lone star tick (*Amblyomma americanum*) (Fig. 1).

2
The Natural History of *A. americanum*-associated Zoonoses

The role played by white-tailed deer in the recognition of multiple zoonoses transmitted by *A. americanum* can be linked to several sources of data that implicate deer as the keystone host for lone star tick populations and as an important natural reservoir for the pathogens that cause these diseases.

2.1
White-Tailed Deer as Hosts for *A. americanum*

A. americanum is a widely-distributed, hard tick that obtains its blood meals from a variety of ground-nesting birds and medium-to-large-sized mammals. White-tailed deer support all parasitic stages of *A. americanum* and are

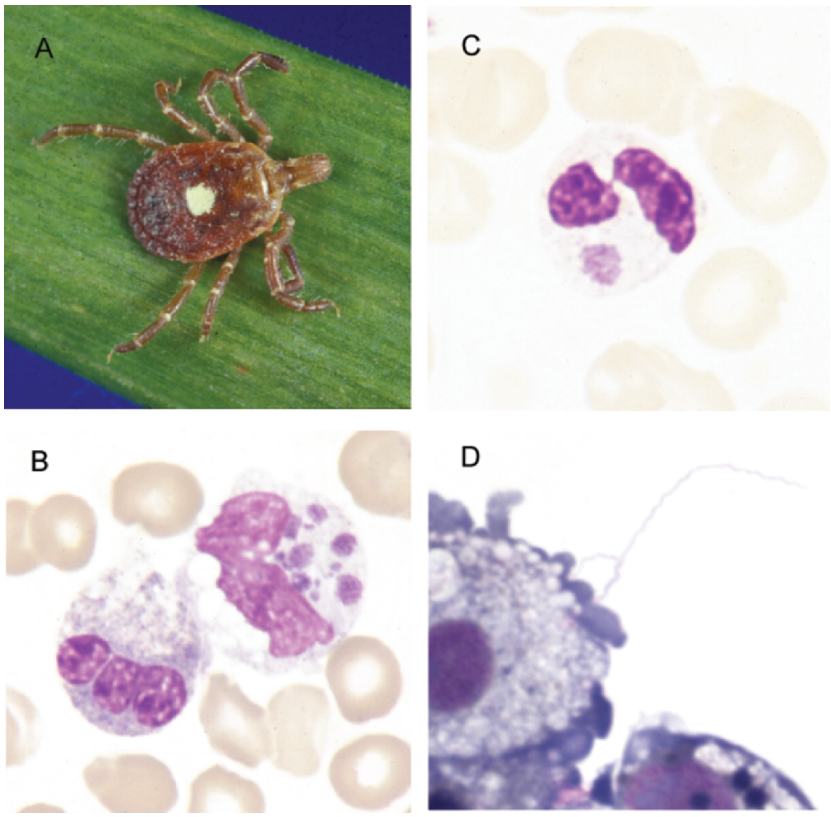

Fig. 1 **A** Adult female lone star tick, *Amblyomma americanum* (photograph provided by Jim Gathany). *A. americanum* is the most frequently encountered human-biting tick in the southeastern and lower midwestern United States (Merten and Durden 2000). **B** Morulae of *Ehrlichia chaffeensis*, the causative agent of human monocytic ehrlichiosis (HME), in the cytoplasm of a mononuclear cell from the peripheral blood of a hospitalized patient (modified Wright's stain). Each morula measures 1.0–6.0 μm in greatest dimension and consists of a cytoplasmic vacuole containing 1 to more than 40 small, coccoid to coccobacillary bacteria that stain dark blue to purple with eosin-azure stains (Paddock and Childs 2003). **C** Morula of *Ehrlichia ewingii* in a neutrophil from the peripheral blood of a patient with *E. ewingii* ehrlichiosis (modified Wright's stain). Morulae of *E. ewingii* are morphologically similar to *E. chaffeensis* but are tropic for neutrophils and occasionally eosinophils of infected hosts (Paddock et al. 2005). **D** *Borrelia lonestari*, the putative agent of southern tick-associated rash illness (STARI), in ISE6 tick cell culture (Giemsa stain). Cultured spirochetes measure 11–25 μm in length and approximately 0.25 μm in width and generally display a flat, wavelike shape with widely variable wavelengths (1.50–2.36 μm) and amplitudes (0.45–0.53 μm). (Varela et al. 2004a)

regarded as the principal wildlife host of lone star ticks (Bishopp and Trembley 1945; Clymer et al. 1970; Bloemer et al. 1986; Kollars et al. 2000). Lone star ticks will perish rapidly of desiccation if isolated from microclimates with high humidity (Hoch et al. 1971). In this context, the abundance of *A. americanum* is influenced primarily by host availability and physiographic variables, which include the degree of ambient moisture, the temperature, the number of daylight hours, and the preferred vegetation type, namely dense understory vegetation in young, second-growth woodland habitats (Hair and Howell 1970; Patrick and Hair 1978). White-tailed deer maintain a dual role in the survival and proliferation of lone star ticks by serving as a preferred food source and as a vehicle for transport and localization within the preferred habitat. In favorable environmental settings, white-tailed deer support enormous numbers of *A. americanum*: in western Kentucky and Tennessee, mean half-body infestations of deer during March through November were as high as 205 adults, 479 nymphs, and 1,150 larvae (Bloemer et al. 1988). As many 2,550 ticks per ear were recorded in an area of Arkansas (Goddard and McHugh 1990).

Environmental and host-related determinants of tick distribution and abundance characteristically vary over time; however, the linkage between the number of white-tailed deer and numbers of lone star ticks has been demonstrated by mathematical models and by deer exclusion studies in various locations. A computer simulation integrating development rates for various stages, fecundity of engorged females, survival of life stages regulated by habitat and climatologic variables, host finding rates, and density-dependent survival rates on hosts demonstrated a linear relationship between the density of deer and of *A. americanum* in a wildlife ecosystem (Mount et al. 1993). Exclusion of white-tailed deer from a 71-ha plot of oak-hickory hardwood forest and reverting fields in western Tennessee during 1985–1988 resulted in a mean percent reduction of larval-, nymphal-, and adult-stage lone star ticks by 88%, 53%, and 51%, respectively, when compared with tick numbers in adjacent control plots where deer were allowed free access during the 4-year interval (Bloemer et al. 1990) (Fig. 2). Similarly, exclusion of white-tailed deer from two approximately 1-ha exclosures in woodland tracts on Fire Island, New York, reduced densities of nymphal-stage *A. americanum* by approximately 48% during the 4 years of post-treatment as compared with pretreatment values (Ginsberg et al. 2002).

2.2 *A. americanum* as Vectors of Ehrlichiae and Borreliae

Ehrlichia chaffeensis and *E. ewingii* are acquired by *A. americanum* ticks from an infective blood meal from a vertebrate host and are subsequently passed transstadially in the tick vector (Anziani et al. 1990; Ewing et al. 1995). *E. chaffeensis*

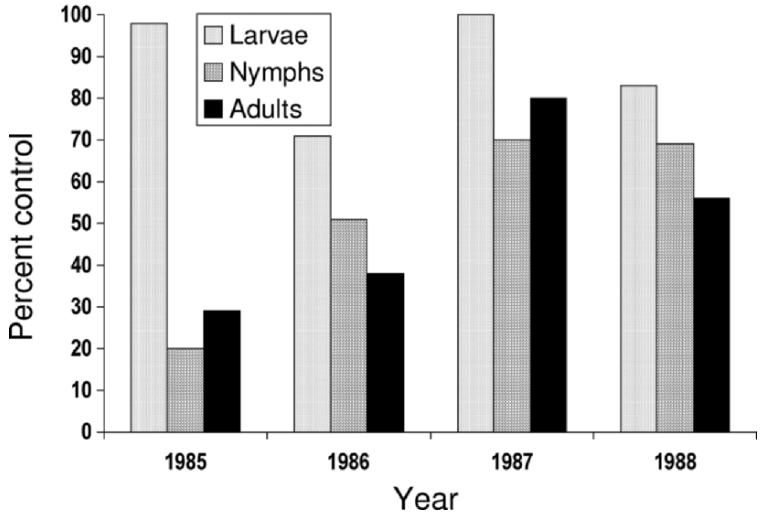

Fig. 2 Percent control of *Amblyomma americanum* larvae, nymphs, and adults (defined as (1–[mean number of ticks per life-stage in deer-excluded plots/mean number of ticks per life-stage in deer-accessible plots] × 100%) during 1985–1988, following exclusion of white-tailed deer from recreational areas at Land Between the Lakes in Kentucky and Tennessee. (Data from Bloemer et al. 1990)

and *E. ewingii* have been detected in adult- and nymphal-stage ticks collected in many southeastern, lower Midwest, and northeastern states (Paddock and Childs 2003; Mixson et al. 2004; Paddock et al. 2005; Schulze et al. 2005; Mixson et al. 2006; Sirigireddy et al. 2006). Because ehrlichiae are not vertically transmitted from adult female ticks to their progeny (Groves et al 1975; Long et al 2003), vertebrate hosts represent important natural reservoirs for *E. chaffeensis* and *E. ewingii*. Infection of *A. americanum* with *B. lonestari* was first reported in 1996 (Barbour et al. 1996; Armstrong et al. 1996) and has been described throughout the range of the lone star tick (Burkot et al. 2001; Stromdahl et al. 2003; Clark 2004; Varela et al. 2004b; Schulze et al. 2005; Taft et al. 2006; Mixson et al. 2006; Schulze et al. 2006). In addition to nymphs and adults, infections have been reported in larval-stage *A. americanum* ticks (Stromdahl et al. 2003), suggesting that transovarial transmission may occur; however, this has not been evaluated experimentally.

Infection prevalences of adult ticks with these agents have been evaluated by using various PCR assays (Table 1). Estimates provided by these studies may not be generalizable over time and space; in addition to extrinsic factors, including

Table 1 Prevalence of infection with *Ehrlichia chaffeensis*, *Ehrlichia ewingii*, and *Borrelia lonestari* in adult lone star ticks in selected areas, as determined by PCR analysis

Agent, state of tick collection	Year(s) of tick collection	No. of ticks tested (% infected)	Reference
E. chaffeensis			
GA	1993–1995	50 (12.0)	Lockhart et al. 1997a
MO	1995	48 (23.0)	Roland et al. 1998
GA	NS	250 (5.2)	Whitlock et al. 2000
CT	1996–1998	106 (7.6)	IJdo et al. 2000
RI	1992	52 (11.5)	IJdo et al. 2000
MO	2000	579 (9.8)	Steiert and Gilfoy 2002
FL	1998	323 (13.6)	Paddock and Childs 2003
NY	1998, 2003	473 (12.5)	Mixson et al. 2004
GA	2001–2003	398 (2.0)	Varela et al. 2004b
NJ	2003	121 (12.3)	Schulze et al. 2005
E. ewingii			
NC	1995, 1998	462 (0.6)	Wolf et al. 2000
FL	1996–1999	121 (1.6)	Sumner et al. 2000
MO	2000	579 (5.4)	Steiert and Gilfoy 2002
TX	NS	66 (7.6)	Long et al. 2004
GA	2001–2003	398 (4.8)	Varela et al. 2004b
NJ	2003	121 (8.2)	Schulze et al. 2005
B. lonestari			
NJ	NS	50 (6.0)	Barbour et al. 1996
NY	NS	318 (3.1)	Barbour et al. 1996
MD	1995	199 (2.0)	Armstrong et al. 1996
AL	1999	19 (10.5)	Burkot et al. 2001
VA	2000	299 (4.3)	Stromdahl et al. 2003
FL	1999–2000	142 (2.8)	Clark 2004
GA	2001–2003	398 (1.0)	Varela et al. 2004b
NJ	2003	121 (9.1)	Schulze et al. 2005

NS Not specified

geographic location, that may influence prevalence estimates, these figures may also vary depending by sample size and DNA detection techniques used by different investigators. For example, a study of *A. americanum* collected from several regions on Long Island, New York, during 2003 revealed *E. chaffeensis* in 0%–27% of adult ticks from five different sampling sites (Mixson et al. 2004). Most studies evaluating individual adult lone star ticks by PCR demonstrate an average prevalence of infection with *E. chaffeensis* of approximately 5%–15% (Lockhart et al. 1997b; Roland et al. 1998; IJdo et al. 2000; Whitlock et al. 2000; Steiert and Gilfoy 2002; Paddock and Childs 2003; Mixson et al. 2004; Varela et al. 2004b; Schulze et al. 2005) and with *E. ewingii* and *B. lonestari* of approximately 1%–10% (Armstrong et al. 1996; Barbour et al. 1996; Wolf et al. 2000; Sumner et al. 2000; Burkot et al. 2001; Steiert and Gilfoy 2002; Stromdahl et al. 2003; Clark 2004; Long et al. 2004; Varela et al. 2004b; Schulze et al. 2005; Mixson et al. 2006; Schulze et al. 2006). Infection prevalences of nymphal-stage ticks are generally lower than prevalences observed in adult *A. americanum* (Paddock and Childs 2003; Mixson et al. 2004). Occasional co-infections of adult lone star ticks with *E. chaffeensis* and *E. ewingii, E. chaffeensis* and *B. lonestari*, or *E. ewingii* and *B. lonestari* have been described (Steiert and Gilfoy 2002; Schulze et al. 2005; Mixson et al. 2006). Simultaneous infection of individual adult ticks with two distinct genetic variants of *E. chaffeensis* has also been reported (Mixson et al. 2004).

2.3 White-Tailed Deer as Reservoirs of Ehrlichiae and Borreliae

The current understanding of the epizootiology of HME indicates that white-tailed deer are the principal reservoir host for *E. chaffeensis*. Antibodies reactive with *E. chaffeensis* antigens have been detected at high prevalences in deer populations from many locations in the southeastern and south-central United States (Lockhart et al. 1996; Mueller-Anneling et al. 2000; Yabsley et al. 2003a). Confirmation of deer as reservoirs has been provided by molecular detection and culture isolation from individuals sampled from multiple serologically positive deer populations (Lockhart et al. 1997a, 1997b; Yabsley et al. 2002, 2003a; Arens et al. 2003) (Table 2). However, deer density alone does not represent a significant predictor of risk for HME (Yabsley et al. 2005); instead, densities of *A. americanum* influence the prevalence of infection of *E. chaffeensis* in white-tailed deer, because deer populations are not naturally infected with *E. chaffeensis* unless infested by lone star ticks (Lockhart et al. 1995, 1996; Yabsley et al. 2003a) (Table 3).

Co-infections with *E. chaffeensis* and *E. ewingii* and simultaneous infection with two distinct genetic variants of *E. chaffeensis* in a single white-tailed deer have been described (Yabsley et al. 2002, 2003b). Recent investigations have also

Table 2 Prevalence of infection with *Ehrlichia chaffeensis*, *Ehrlichia ewingii*, and *Borrelia lonestari* in white-tailed deer in selected areas, as determined by PCR analysis

Agent, state of deer collection	Years of deer collection	No. of deer tested (% infected)	Reference
E. chaffeensis			
GA	1993–1995	28 (54.0)	Lockhart et al. 1997a
AR	1996–2001	26 (7.7)	Yabsley et al. 2002
KY	1996–2001	15 (6.7)	Yabsley et al. 2002
NC	1996–2001	9 (22.2)	Yabsley et al. 2002
MO	2000–2001	217 (23.0)	Arens et al. 2003
E. ewingii			
AR	1996–2001	26 (3.8)	Yabsley et al. 2002
KY	1996–2001	15 (6.7)	Yabsley et al. 2002
NC	1996–2001	9 (11.1)	Yabsley et al. 2002
MO	2000–2001	217 (20.3)	Arens et al. 2003
B. lonestari			
AR, FL, GA, KY, LA, MS, NC, SC	1996–2000	80 (8.7)	Moore et al. 2003

demonstrated that primary infection of deer with *E. chaffeensis* does not confer immunologic protection against subsequent infection with a genotypically different strain of *E. chaffeensis* (Varela et al. 2005; Varela-Stokes et al. 2006).

White-tailed deer are the main reservoir responsible for maintenance of the enzootic cycle of *E. chaffeensis* in nature; however, several other vertebrate species are experimentally susceptible, naturally infected, or have evidence of exposure to *E. chaffeensis*. Serologic, molecular, or culture-based evidence of natural infections has been documented for domestic dogs, domestic goats, coyotes, lemurs, rabbits, foxes, and raccoons in the United States (Lockhart et al. 1997b; Davidson et al. 1999; Comer et al. 2000; Dugan et al. 2000; Kocan et al. 2000; Liddell et al. 2003; Yabsley et al. 2004) and in marsh deer (*Blastocercus dichotomus*) in Brazil (Machado et al. 2006).

Comparatively less is known about the natural histories of *E. ewingii* and *B. lonestari*; however, available evidence suggests that deer are also important reservoirs of these two agents. Natural infection of deer with *E. ewingii* has been reported from several locations throughout the distribution of the lone star tick (Yabsley et al. 2002; Arens et al. 2003) (Table 2). Although *E. ewingii* has not been isolated in cell culture, it has been successfully transmitted from naturally infected deer to naïve fawns by blood inoculation (Yabsley et al. 2002). Domestic dogs are

Table 3 Temporal associations between lone star tick infestations and the appearance of antibodies reactive with *Ehrlichia chaffeensis* in white-tailed deer populations in various locations in the United States (from Lockhart et al. 1995; Yabsley et al. 2003b)

Location, year	No. of deer evaluated	Percentage of deer infested with ticks	Percentage of deer with antibodies
Clarke County, GA			
1981	10	0	0
1982	10	0	0
1983	10	10	0
1986	15	47	7
1987	38	87	21
1988	10	80	100
1991	5	100	100
1992	24	100	100
Concordia Parish, LA			
1986	5	0	0
1991	12	67	38
1999	5	100	60
Haywood County, TN			
1989	5	0	0
1994	6	0	0
1998	5	60	20

also common hosts of *E. ewingii* and may represent important natural reservoirs of this agent (Goodman et al. 2003; Liddell et al. 2003; Ndip et al. 2006). White-tailed deer naturally infected with *B. lonestari* have been reported from multiple southeastern states (Moore et al. 2003) (Table 2), and deer have been shown in experiments to be susceptible to infection by inoculation with a culture isolate of this *B. lonestari*, and capable of developing a viable spirochetemia for at least 12 days (Moyer 2005; Moyer et al. 2006). Attempts to infect rodents, domestic dogs, and calves with *B. lonestari* have been unsuccessful (Moyer 2005).

Because white-tailed deer can be naturally infected with multiple, antigenically similar pathogens (e.g., *E. chaffeensis, E. ewingii*, *A. phagocytophilum*, and a nonspeciated *Anaplasma* sp. [i.e., the "white-tailed deer agent"]) and can also be infected with or exposed to *B. lonestari* and *B. burgdorferi*, the potential for serologic cross-reaction is an important consideration in serologic surveys

(Lockhart et al. 1997b; Yabsley et al. 2002; Arens et al. 2003). More specific serologic tests (e.g., Western blot), molecular-based assays, or culture isolation should be considered when evaluating for various tick-borne infections in white-tailed deer.

No single assay is ideal, because the level of bacteremia may be lower than the level of detection, even by highly sensitive nested PCR assays. As an example, PCR failed to amplify *E. chaffeensis* or *E. ewingii* DNA from whole blood specimens of deer from Jones County, Georgia; however, when blood from these animals was inoculated into naïve fawns, ehrlichiae were later detected in the inoculated fawns (Yabsley et al. 2002). Despite its limitations, PCR has proven to be a useful field surveillance tool, and several studies have used this technique to document the prevalence of infection with *A americanum*-associated ehrlichiae by using molecular assays (Lockhart et al. 1997b; Yabsley et al. 2002; Arens et al. 2003) (Table 2). The limited availability of fresh sterile blood samples, which need to be obtained from deer while these pathogens are in the peripheral circulation, markedly hampers attempts at cell culture isolation of ehrlichiae and Borreliae from wild deer. In addition, white-tailed deer are also nearly ubiquitously infected with a flagellated protozoan parasite (*Trypanosoma cervi*) that often hinders attempts to isolate in culture ehrlichiae and borreliae from naturally infected wild deer. Multiple isolates of *E. chaffeensis* have been obtained in cell culture from wild deer (Lockhart et al. 1997a; Yabsley et al. 2003a); however, *E. ewingii* has not been cultivated from any host, and *B. lonestari* has only recently been isolated from field-collected *A. americanum* (Varela et al. 2004a).

3
Ecological Havoc and White-Tailed Deer Populations

The ability of white-tailed deer to use ecologically disturbed environments to its advantage has contributed considerably to the extraordinary expansion of this animal in the eastern United States during the twentieth century. However, the near-exponential growth of whitetails was not the result of one disastrous human intervention but rather the culmination of various environmental imbalances created during a course of more than 200 years.

3.1
The Fall and Rise of Eastern Forests

As settlers in the United States advanced westward from the Atlantic coast during the 1700s and 1800s, mature forests in the east were felled to provide lumber for local construction and fuel, and for export to Europe. New England

forests were harvested particularly for naval stores (e.g., turpentine, tar, and pitch), tannin, ship masts, fences and shingles and as fuel for early industry and domestic purposes; it is estimated that more than 260 million cords of firewood were burned in New England between 1630 and 1800 (Cronon 1983). Large volumes of wood were also consumed to produce charcoal for glassmaking and for smelting iron ore (Spielman 1994). Perhaps more importantly, timbered regions were cleared extensively to provide land for crops and pasturage. Colonial farmers soon recognized that certain tree species were associated with certain types of soil. Hickory, maple, ash, and beech generated rich black humus from centuries of accumulated leaf litter, and settlers identified the presence of these particular trees as indicators of prime agricultural land. Less desirable were the acidic and sandy soils typically associated with hemlock, spruce, and pines (Cronon 1983). In this context, hardwood forests were often the first to disappear to create cultivable acreage. By 1860, woodlands occupied less than 15% of the total land area of New England, having largely been replaced by cleared tracts for farming and agriculture. Farmland comprised approximately 75% of the total land area of Connecticut and New York by 1860 and 1880, respectively (Severinghaus and Brown 1956; Thomson 1977). Deforested landscapes resulted in profound changes in regional microclimate, hydrology, and soil mechanics. Cleared land became sunnier, drier, windier, hotter, and colder (Cronon 1983), changes that are particularly inhospitable to the survival of lone star tick populations.

Vast numbers of eastern farms, fields, and previously harvested forests that were abandoned during the westward expansion of the 1800s and early 1900s became reforested by gradual encroachment of successional trees and shrubs. This transition from farmlands back to forests extended well into the twentieth century. Forest surveys conducted in Virginia in 1940 and 1957 identified an 8.6% increase in forested land in the state during this 17-year period, which occurred almost entirely in agricultural areas that had been abandoned and allowed to revert to second-growth, predominantly hardwood, stands. During this interval, croplands decreased from 6.0 to 3.2 million acres, while hardwood forests increased by 1.4 million acres (Atwood et al. 1965).

Prior to the early twentieth century, the longleaf pine (*Pinus palustris*) dominated much of the forested regions of the southeastern United States. The longleaf forest originally comprised an unbroken belt 100–200 miles wide that covered an estimated 30–60 million acres from southern Virginia to central Florida and westward to central Texas. The longleaf pine was prized in naval architecture for keels, beams, and sideplanks of sailing vessels. It was also valued as structural timber for posts, piles, and joists for bridges, trestles, and warehouses. It was considered a superior wood for wharf construction, and wharves in almost every port from New Orleans to New York were built primarily from longleaf lumber. Longleaf pines were also worked extensively

for oleoresin (gum) that was collected and processed to produce turpentine, pitch, and tar (Wahlenberg 1946). In 1880, the annual cut of longleaf pine was estimated at 2 billion board feet and increased steadily to a peak of 13 billion board feet in 1907; by 1946, the longleaf belt was reduced to one-third to one-half of its original area. In extensively harvested regions, longleaf forests were replaced partly or entirely by mixed pines and hardwoods, particularly scrub oak (Wahlenberg 1946). This was accompanied by vigorous growth of formerly suppressed understory flora, creating ecotones comprised of smaller trees and more abundant surface vegetation.

In this context, extensive logging of virgin longleaf pine forests of the Southeast, and the abandonment of farmland in the Northeast, both occurring during the late nineteenth and early twentieth centuries, eventually created extensive tracts of land dominated by young, second-growth woodlands and forests that provided favorable microclimatic conditions for tick survival and an optimum habitat for deer (see below).

3.2
The Fall and Rise of White-Tailed Deer Populations

Prior to and during the early nineteenth century, white-tailed deer were widespread throughout the eastern United States and were important to American Indians and European settlers as an item of trade and as a source of food and clothing. However, unregulated year-round harvests of deer, often aided by packs of dogs, night hunting with fire torches, or hunting from boats, coupled with extensive habitat losses during the mid to late 1800s, led to a dramatic decrease in the number of deer. Deer hunting achieved its zenith with the widespread availability of repeating rifles after the Civil War. In addition, profit motives for market hunters were encouraged by the expansion of the US railway system, which occurred during this same period (Severinghaus and Brown 1956; McCabe and McCabe 1984). By the end of the nineteenth century, an estimated 300,000–500,000 deer remained in North America (Downing 1987). Remnant deer populations were small, isolated, and typically confined to mountainous areas, coastal marshes and swamps, and river bottoms that were inaccessible to hunters.

As early as the mid-1600s, hunting regulations had been established in some areas of the Northeast; however, these laws were not enforced. By the early 1900s, most states had established substantive hunting restrictions to alleviate dramatic population declines. During the mid-1900s, several southeastern and midwestern states began to restock deer populations by translocating large numbers of deer from remnant deer populations. Translocated deer originated primarily from several southeastern states, Wisconsin, and Texas. Increased

protection and intensive restocking contributed to a resurgence of white-tailed deer in the United States to an estimated 18 million animals by 1992 (McDonald and Miller 1993) (Fig. 3).

Several biological characteristics of white-tailed deer contribute to rapid and prodigious population growth when food is abundant and natural predators are absent or noncontributory:

1. Relative longevity (6 years or longer)
2. Early reproductive maturation
3. High reproductive rate
4. High fawn survival
5. Social tolerance
6. Relatively indiscriminate food preferences (Leopold et al. 1947; Geist 1998)

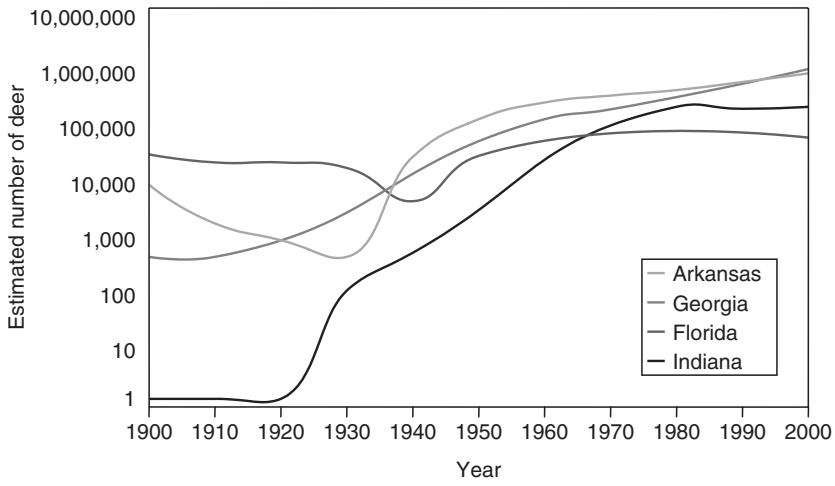

Fig. 3 Approximate number of white-tailed deer in Arkansas, Florida, Georgia, and Indiana during the twentieth century. Precolonial estimates are not available, but deer were widespread and abundant in each of these states. Deer numbers dramatically decreased in Arkansas, Georgia, and Indiana following European settlement of these states and reached the nadir during the late nineteenth century. The principal decrease in Florida deer populations occurred during the 1930s and 1940s following an aggressive deer control program designed to eradicate the tick vector of cattle fever, *Boophilus annulatus*

Whitetails readily consume leaves, twigs, and buds from approximately 100 species of woody plants. Because deer can eat only what they are able to reach—the "browse-line" for white-tailed deer is 6 ft or lower—these animals typically do not flourish in mature forests with sparse understory vegetation. In this context, whitetails thrive best in mosaic habitats where immature, second-growth woods are interspersed with open fields and meadows that provide an ample assortment of accessible foliage (Iker 1983). In addition, white-tailed deer, unlike most other mammalian wildlife species, are notable for their lack of movement from areas with excessive deer densities (i.e., social tolerance) (Leopold et al. 1947).

When situated in environments with abundant low foliage, a white-tailed deer population can potentially double in number every 2 years. For example, the George Reserve in Michigan was stocked with two male and four female whitetails in 1927; within 5 years, the population had increased to an estimated 220 animals. When this same population was thinned to ten deer in 1975, it again increased rapidly to 212 animals by 1980 (McCullough 1984). In Indiana, where deer had been entirely eliminated, 35 whitetails were introduced in 1934; by the early 1980s, that population had multiplied to approximately 100,000 (Iker 1983). The extraordinary growth of white-tailed deer populations is reflected in tabulations of deer-vehicle collisions in the United States. In 1974, a comprehensive listing of road-killed deer compiled by wardens and other game officials amounted to 146,229 animals (Rue 1978). Indiana recorded 34,000 deer kills resulting from automobile collisions in 1 year alone (1987) (Whitaker and Hamilton 1998).

Other ecological disturbances created by humans are likely to have compounded increasing densities of white-tailed deer that occurred during the twentieth century. Natural predators, particularly wolves and cougars, were extirpated from much of the natural range occupied by white-tailed deer. The eastern forest wolf, *Canis lyacon*, was once distributed from Florida to southern Ontario and Quebec, and westward from the Atlantic coast to Oklahoma. In the eastern United States, removal of large carnivores from this region occurred largely during the nineteenth century and often coincided with irruptive growth of deer. Wolves and cougars disappeared from Mount Desert Island in Maine during 1845–1880 and from the Adirondack Mountains in New York between 1882 and 1897. As a result, deer populations expanded considerably in number at these locations (Leopold et al. 1947).

Almost 60 years ago, some wildlife biologists already recognized the problem of deer overabundance in many areas of the United States. In 1947, Aldo Leopold and co-workers wrote, "Prior to the turn of the century, the prevalent population problem in deer was scarcity. Since that time, about a hundred herds of deer . . . have pyramided their numbers to the point of presenting a problem." These authors also mentioned that "there is only one region without deer troubles: the Southeast. Here screw worm and hound dog seem to perform

the regulatory functions elsewhere delegated, often without success, to legislatures or conservation commissions. Many parts of the Southeast could support more deer to the advantage of all concerned."

The primary screwworm, *Cochliomyia hominovorax,* caused substantial mortality in domesticated animals and various wildlife species in the southern United States prior to a coordinated control program that used the Sterile Insect Technique during the 1950s and 1960s, which effectively eradicated the screwworm from North America (Krafsur et al. 1987; Baumgartner 1988). The results of this intervention, viewed in context with the observations by Leopold and colleagues (Leopold et al. 1947), might then suggest that human activity aimed at eliminating a deleterious ectoparasite of livestock also eliminated a natural cause of mortality in white-tail deer, particularly in a region of the United States (i.e., the Southeast) that could accommodate greater numbers of these animals.

3.3
Historical Abundance and Range of *A. americanum*

Accurate and quantifiable data that describe *A. americanum* numbers over broad geographic expanses and long intervals of time are limited by the lack of long-term longitudinal studies using controlled methods. However, despite obvious biases and limitations, tick-bite records provide surrogate, albeit crude, regional estimates of lone star population densities. Early twentieth century entomologists commented that in most eastern and southern states, humans were more frequently bitten by *A. americanum* than by any other species of tick (Hooker et al. 1912), and contemporary records seem to support this observation (Merten and Durden 2000). In addition, *A. americanum* was implicated more frequently than any other species in 410 tick-bite records for Air Force personnel from 30 states from 1989–1992 (Campbell and Bowles 1994). The lone star tick accounted for 758 (83%) of 913 ticks removed from 460 persons in Georgia and South Carolina during 1990–1995, and 63 (53%) of 119 ticks recovered from 73 persons in Mississippi during 1990–1999 (Felz et al. 1996; Goddard 2002). In surveys encompassing more restricted geographic areas, the predominance of lone star ticks may be even more pronounced. From a recent study examining the perceived risk of Lyme disease among residents of Gibson Island, Maryland, 1,098 (71%) of 1,556 ticks submitted by residents of during 1994–1996 were *A. americanum* (Armstrong et al. 2001). Although these reports indicate the continuous presence of an aggressive human-biting tick, some anecdotal and prospective evidence indicates that the number of lone star ticks has increased during the last several decades in regions of the southeastern and northeastern United States (Ginsberg et al. 1991; Felz et al. 1996; Ginsberg and Zhioua 1996; Means and White 1997; Mixson et al. 2004; Schulze et al. 2005).

More objective data have documented recent range extensions of the lone star tick within and at the margins of historically established boundaries (Bishopp and Trembley 1945; Cooley and Kohls 1944; Mock et al. 2001). The current distribution of *A. americanum* extends from west-central Texas eastward to the Atlantic Coast, and encompasses the entire southeastern quadrant of the United States, much of the lower Midwest, and parts of coastal New England (Childs and Paddock 2003). Recent studies have identified the appearance of lone star ticks in previously noninfested deer populations from several regions of the southeastern United States during the 1980s (Lockhart et al. 1995; Yabsley et al. 2003b). Importantly, the arrival of *A. americanum* in these populations is clearly associated with subsequent serologic evidence of infection with *E. chaffeensis* or closely related ehrlichiae in these animals (Table 3).

Contemporary range extensions of the lone star tick have become particularly evident in the northeastern United States. In 1754, *A. americanum* became the first North American tick species to be formally described by European naturalists, an event that in all likelihood reflected its relative abundance in the eastern United States during the mid-eighteenth century; however, by 1870 lone star ticks were considered extinct in many parts of New England. Consider the description by New York entomologist Asa Fitch of a "flattened, obovate, chestnut red tick, having a white spot on the end of its scutel, and a whitish ring on its knees:"

> The most common tick of our country, called the wood tick from its inhabiting the woodlands, though formerly abundant throughout the northern and middle states, has now become nearly or quite extinct. The Swedish naturalist Kalm, in passing through the east part of our state 120 years ago, when crossing the Hudson River to Lake Champlain, speaks of the discomfort he experienced from the wood ticks with which the forests there abounded. At this day, along the route he pursued, not one of these insects can probably be found . . . becoming thus extinct with the settlement of the country and the clearing off of its forests. . . In those sections of the country which were settled little over a century ago, tradition still speaks of the annoyances which our American wood ticks were . . . so abundant that if one sits down on the earth or on the trunk of some fallen tree, his clothes and even his body soon gets covered with them (Fitch 1870).

Tick surveys conducted on the southeastern region of Long Island in 1971 identified small, but established, populations of *A. americanum* where none of this species had been recovered during extensive collections approximately 25 years earlier (Collins et al. 1949; Good 1973). Lone star ticks were first documented from Fire Island, New York, in 1988 (Ginsberg et al. 1991) and within several years became the predominant tick from that location (Ginsberg and Zhioua 1996; Ginsberg et al. 2002). Established populations of lone star ticks now exist across Long Island (Mixson et al. 2004).

4
The Emergence of *A. americanum*-Associated Infections in Human Populations

The recognition of *A. americanum*-associated zoonoses can be linked to many factors peculiar to the 1980s and 1990s that occurred independently of the varied environmental disturbances discussed previously. These factors include the development of sensitive and robust molecular diagnostics and the expansion of an immunosuppressed, sentinel patient cohort that was particularly susceptible to the ehrlichioses (Childs and Paddock 2003; Paddock and Childs 2003).

4.1
Human Monocytic Ehrlichiosis

The first documented case of HME occurred in mid-April 1986, when a medical intern at a hospital in Detroit, Michigan, identified unusual intraleukocytic inclusions in a peripheral blood smear of a critically ill patient. The patient, a 51-year-old man, had sustained several tick-bites approximately 2 weeks earlier while planting trees in rural northern Arkansas. Investigators subsequently recognized these inclusions as clusters of bacteria belonging to the genus *Ehrlichia*, a group of organisms previously recognized in the United States solely as veterinary pathogens (Maeda et al. 1987; Fishbein 1990).

During the next several years, clinicians and scientists identified a novel species, *E. chaffeensis*, as a newly recognized agent causing moderately severe to fatal tick-borne disease throughout much of the southeastern, lower midwestern, and mid-Atlantic regions of the United States (Anderson et al. 1991; Fishbein et al. 1994). The identification and characterization of this pathogen was facilitated by isolation of the agent in cell culture (Dawson et al. 1991) and by broadening use of polymerase chain reaction (PCR) technology (Anderson et al. 1992b). During the 1990s, several cases of life-threatening HME were identified among patients with immune systems compromised by neoplasia, corticosteroids, or human immunodeficiency virus (Paddock et al. 2001; Paddock and Childs 2003), and these cases accentuated public health concern regarding *E. chaffeensis*.

Two initial studies that summarized national data for HME during 1986–1997 (742 cases reported by 17 states) (McQuiston et al. 1999) and 1997–2001 (503 cases reported by 23 states) (Gardner et al. 2003) were limited by the lack of a uniform case definition and by inconsistencies in reporting requirements by individual states during the intervals examined. This is reflected by erratic counts in some states (e.g., 54 cases were reported in Virginia during 1986–1997 but only one during 1997–2001). However, some identifiable trends, including consistently

high numbers of cases in Arkansas, Missouri, North Carolina, and Oklahoma were identified from these data (McQuiston et al. 1999; Gardner et al. 2003).

Subsequent efforts have been assisted by a uniform case definition for surveillance, which was adopted by state health departments in 1996 and revised in 2000, and by the inclusion of the ehrlichioses in 1999 in the National Electronic Telecommunications System for Surveillance (NETSS). The number of states reporting cases of HME has increased steadily (from three states in 1990 to 48 states by 2003) and the total number of reported cases has risen from 24 cases reported by two states in 1997 to 319 cases reported by 26 states in 2003 (Table 4) (Satalowich 1997; McQuiston et al. 1999; Gardner et al. 2003; Centers for Disease Control and Prevention 2005; Demma et al. 2005). Future estimates of HME incidence are likely to more accurately portray temporal changes in magnitude as the national surveillance system matures. Estimates of regional incidence determined by active surveillance indicate that the frequency of HME may be considerably higher than indicated by passive surveillance in some areas where the disease is endemic. For example, mean incidence rates of 5.2 and 6.8

Table 4 Summary of national case counts and estimated annual incidence of human monocytic ehrlichiosis (HME) in selected states, by year of occurrence, during 1997–2003 (from Satalowich 1997; McQuiston et al. 1999; Gardner et al. 2003; Centers for Disease Control and Prevention 2005; Demma et al. 2005)

	1997	1998	1999	2000	2001	2002	2003
No. of states that report HME (no. reporting >1 case to NETSS)	18 (2)	19 (7)	33 (13)	37 (18)	41 (18)	48 (24)	48(26)
Total reported US cases	24	32	115	196	145	219	319
Estimated annual incidence per million population							
Arkansas	8.7	5.5	8.6	8.2	0.0	6.6	7.0
Missouri	0.0	1.5	8.6	10.5	4.8	8.6	6.0
Maryland	NR	NR	NR	NR	0.4	4.9	9.2
New York	0.0	0.0	0.1	0.2	1.2	0.7	0.6
North Carolina	NR	0.3	1.6	1.2	1.3	2.0	3.2
Oklahoma	NR	NR	3.3	3.5	6.9	3.7	9.4
Tennessee	0.0	0.0	0.2	8.4	3.5	4.8	5.3

NETSS National Electronic Telecommunications System for Surveillance; *NR* HME was not reportable in the given year

per million persons were obtained from passive surveillance in Missouri during 1997–2001 and 2001–2002, respectively (Gardner et al. 2003; Demma et al. 2005); however, active surveillance in southeast Missouri and southwest Illinois during 1997–1999 revealed an incidence of 20–47 cases per million persons (Olano et al. 2003).

4.2 *E. ewingii* Ehrlichiosis

In May 1996, investigators at Washington University Medical Center in St. Louis, Missouri, used a broad-range PCR assay to amplify DNA sequence of *E. ewingii* from a blood sample from an 11-year-old boy from southern Missouri who was assumed to have HME. The child had been exposed to ticks and was subsequently hospitalized with fever, headache, myalgia, and a stiff neck. He had also received a kidney transplant at 27 months of age and was receiving immune-suppressing medications at the time of his illness. During the next 3 years, these same investigators identified other cases of disease caused by *E. ewingii* in two additional immune-suppressed patients and one immune-intact patient. In contrast to findings in patients with HME, morulae were identified in the neutrophils, and occasionally eosinophils, of the patients with *E. ewingii* ehrlichiosis (Buller et al. 1999).

This pathogen had been first identified approximately 25 years earlier as a "new" strain of *Ehrlichia canis* when veterinarians identified morulae in peripheral blood granulocytes of an ill dog from Arkansas in 1970 (Ewing et al. 1971). Investigators subsequently used molecular tools to characterize this ehrlichia as a novel species that they named *E. ewingii* (Anderson et al. 1992a). Following the initial report of human ehrlichiosis caused by *E. ewingii* in 1999 (Buller et al. 1999), cases were identified in Oklahoma and Tennessee in persons co-infected with human immunodeficiency virus (Paddock et al. 2001). Through 2001, 17 patients with *E. ewingii* ehrlichiosis were diagnosed and 12 (70%) had underlying medical conditions causing immune suppression (Paddock et al. 2005).

Cases of disease caused by *E. ewingii* are not identified specifically by NETSS (www.cste.org/ps/2000/2000-id-03.htm). Data examining the relative prevalence of *E. chaffeensis* and *E. ewingii* in canine or deer populations and in lone star ticks in areas where both diseases are endemic suggest that *E. ewingii* occurs in reservoir and vector populations at frequencies similar to or, in some cases, greater than infection with *E. chaffeensis* (Tables 1 and 2) (Yabsley et al. 2002; Steiert and Gilfoy 2002; Arens et al. 2003; Liddell et al. 2003; Long et al. 2004; Varela et al. 2004b; Schulze et al. 2005); however, confirmed cases of disease caused by *E. ewingii* are uncommon relative to cases of HME: investigators at Washington University Medical Center confirmed approximately 200 cases of ehrlichiosis during 1994–2003, of which 89% were caused by *E. chaffeensis* and 11% were caused by *E. ewingii* (Liddell et al. 2003). It has been

suggested that *E. ewingii* causes a milder illness than *E. chaffeensis*, particularly in persons without preexisting immune suppression, and that fewer *E. ewingii*-infected patients seek medical attention and confirmatory laboratory evaluation (Paddock et al. 2005).

4.3 Southern Tick-Associated Rash Illness

STARI, also known as southern Lyme disease or as Masters' disease for the physician who identified and described many cases of this illness among patients in southeast Missouri during the late 1980s (Masters et al. 1994, 1998), is a Lyme disease-like condition associated with the bite of *A. americanum* ticks and described in the southeastern and lower midwestern United States. Cases were first documented in the early 1980s (Schulze et al. 1984), and since then more cases have been described from Georgia, Kentucky, Maryland, Missouri, North Carolina, and South Carolina (Masters et al. 1994, 1998; Kirkland et al. 1997; Felz et al. 1999; James et al. 2001; Armstrong et al. 2001; Haddad et al. 2005).

The etiologic agent of STARI has not been definitively identified, although several lines of evidence suggest that a *Borrelia* sp. transmitted by the lone star tick may be a cause of this illness. The clinical presentation of STARI resembles a borreliosis and patients with STARI develop an expanding circular rash at the site of the tick-bite similar to the erythema chronicum migrans rash observed in patients with Lyme disease. Generalized fatigue, headache, and fever may also be present (Kirkland et al. 1997; Masters et al. 1998). *B. burgdorferi*, the causative agent of Lyme disease, has been isolated from rodents and ticks in the southeastern United States (Oliver et al. 1992; Clark 2004); however, the number of confirmed Lyme disease cases in the Southeast is low relative to the number in the Northeast and upper Midwest, and STARI cases are associated with bites of lone star ticks rather than blacklegged ticks (the principal vector of *B. burgdorferi* in the United States) (Schulze et al. 1984; Kirkland et al. 1997; Masters et al. 1998). These observations, and the detection DNA of *B. lonestari* from a rash biopsy specimen from one STARI patient (James et al. 2001), suggest that the etiology of STARI is distinct from *B. burgdorferi*. However, a recent evaluation of 30 STARI patients in Missouri failed to detect *B. lonestari* or *B. burgdorferi* DNA in any of 31 skin biopsy specimens obtained from rash lesions of patients with a clinical diagnosis of STARI; these data suggest that one or more agents other than *B. lonestari* might also contribute to this syndrome (Wormser et al. 2005).

Because the signs and symptoms of STARI closely resemble those of Lyme disease and because the distribution of *A. americanum* and *Ixodes scapularis* are often sympatric, particularly in the mid-Atlantic states, unrecognized cases of STARI may be embedded among cases of presumptively diagnosed Lyme

disease (Masters et al. 1994; Armstrong et al. 2001). In this context, an accurate impression of the magnitude of STARI awaits further assessment.

4.4
Other *A. americanum*-Associated Pathogens or Potential Pathogens

Natural infections of lone star ticks with other recognized pathogens and with agents of undetermined pathogenicity have been identified throughout the range of *A. americanum*. These pathogens include *Francisella tularensis* (the causative agent of tularemia) (Hopla and Downs 1953; Calhoun 1954; Hopla 1955), *Coxiella burnetii* (the causative agent of Q fever) (Parker and Kohls 1943; Philip and White 1955), *Rickettsia parkeri* (the cause of a newly recognized, eschar-associated spotted fever rickettsiosis in the United States) (Goddard and Norment 1986), *Rickettsia amblyommii* (a potential agent of spotted fever rickettsiosis) (Burgdorfer et al. 1981; Dasch et al. 1993; Mixson et al. 2006), and lone star virus (an incompletely characterized arbovirus isolated from a lone star tick collected in western Kentucky) (Kokernot et al. 1969).

The most recently discovered bacterium associated with *A. americanum* is the Panola Mountain *Ehrlichia* (PME). This as-yet unnamed *Ehrlichia* species, first identified in lone star ticks collected near Atlanta, Georgia, in 2005, shows close genetic similarity to *Ehrlichia ruminantium*, the agent of heartwater in ruminants (Loftis et al. 2006). The PME has also been detected in *A. americanum* ticks collected in Missouri, and in the blood of naturally infected white-tailed deer in Arkansas, North Carolina, and Virginia (M.J. Yabsely, unpublished observations). *A. americanum* ticks maintain the PME transstadially and are able to transmit this agent to goats and deer in experimental settings; however, the role of the PME as a pathogen of humans requires further investigation (Loftis et al. 2006; M.J. Yabsley, unpublished observations). The impact of various ecological influences on the distribution and abundance of lone star ticks and the resulting frequencies of these agents in human or animal populations has not been explored.

5
Other Zoonoses Associated with White-Tailed Deer

Several investigators, notably Andrew Spielman and co-workers at Harvard University, previously identified the explosive growth of white-tailed deer populations in the United States during the twentieth century as a crucial epizootiological determinant in the emergence of Lyme disease, human babesiosis, and HGA (Piesman et al. 1979; Wilson et al. 1985; Spielman et al. 1993, Spielman 1994;

Thompson et al. 2001). The primary US vector of the pathogens that cause each these diseases is the blacklegged tick, *I. scapularis.* Although deer are an important host for adult blacklegged ticks, the natural histories of *I. scapularis*-associated pathogens are distinct from those described for *A. americanum*-vectored agents in two important ecologic features. First, small rodents, not deer, are the principal hosts for larval- and nymphal-stage *I. scapularis* (Spielman et al. 1993; Spielman 1994). Second, in most regions of the eastern United States, the main vertebrate reservoir host for *B. burgdorferi*, *B. microti*, and *A. phagocytophilum* is the white-footed mouse, *Peromyscus leucopus* (Piesman and Spielman 1982; Donahue et al. 1987; Telford et al. 1996).

Blacklegged ticks can acquire *B. burgdorferi* from experimentally infected deer (Oliver et al. 1992), but disparities between these data, the rarity of recovery of viable spirochetes from deer, and low infection rates of *I. scapularis* ticks collected from whitetails in nature indicate a relative incompetence of white-tailed deer as a reservoir of *B. burgdorferi* (Loken et al. 1985; Telford et al. 1988; Lacombe et al. 1993). White-tailed deer are also refractory to infection with *B. microti* (Piesman et al. 1979). These data suggest that deer serve a minimal role, if any, as reservoirs for some or all of these agents. White-tailed deer are experimentally susceptible to infection with *A. phagocytophilum* (Tate et al. 2005), and a recent study identified molecular evidence of infection with *A. phagocytophilum* in 73 (16%) of 458 deer from 19 states in the southeastern and south-central United States. These studies suggest that white-tailed deer may also be an important sentinel animal for this pathogen (Dugan et al. 2006).

6
Conclusion and Prospectus

> The rapid changes in most environments of the world brought about by the population explosion and socioeconomic events of modern civilization are causing natural enzootics of tickborne infectious agents to change in intensity, distribution, and relation to public health.
>
> Harry Hoogstral 1981

Why were babesiosis, Lyme disease, HME, HGA, *E. ewingii* ehrlichiosis, and STARI not formally described until the last few decades of the twentieth century? Although robust molecular methods were eventually needed to characterize and define the pathogens responsible for each disease, the initial discoveries depended only on astute clinicians and traditional laboratory methods (Western et al. 1970; Fishbein 1990; Bakken 1998), and these resources existed in abundance in the United States for many decades prior to documented recognition of these six tick-borne diseases. The conspicuousness of an expanding,

erythematous, targetoid exanthem (i.e., the erythema migrans rash of Lyme disease and STARI) during routine physical examination and the unusual and characteristic appearance of intraerythrocytic babesiae and intraleukocytic ehrlichiae in standard blood smears suggests that descriptions of these tick-borne infections would have appeared earlier and with greater frequency in the medical literature had they been as prevalent in preceding decades as they were during the 1970s and 1980s (Spielman et al. 1993). It can be reasonably assumed that morulae and erythema migrans were identified in a few patients prior to the formal descriptions of the associated disease entities but that a connection of these features to ehrlichiosis or borreliosis was missed or not investigated. The environmental and ecologic imbalances created by human intervention described in this chapter did not create novel tick-borne zoonoses; rather, these events amplified the incidence of the diseases in human populations to a threshold of recognition (Paddock and Childs 2003).

Multiple lines of evidence support the hypothesis that exaggerated growth of white-tailed deer populations provided critical leverage in the emergence of *I. scapularis*- and *A. americanum*-transmitted zoonoses (Spielman et al. 1993; Childs and Paddock 2003; Paddock and Childs 2003). In the case of lone star tick-associated diseases, these changes resulted in (1) expansion of a reservoir pool for ehrlichiae and borreliae, (2) expansion of a keystone host for the vector tick, and (3) range extensions for both tick and pathogen as deer populations were reestablished throughout the eastern United States. Nonetheless, it is also likely that other distinct ecologic disturbances contributed to the emergence of one or more of these diseases.

Several investigators have suggested that rebounding populations of wild turkey (*Meleagris gallopavo*) in the United States might also contribute to recent range extensions of the lone star tick. *A. americanum* has also been called the turkey tick because in its immature stages these ticks are often found attached to *M. gallopavo*, and several studies have identified this bird as an important host of *A. americanum* (Means and White 1997; Kollars et al. 2000; Mock et al. 2001). The fall and rise of wild turkey populations in the eastern United States approximates that of white-tailed deer. Loss of woodland habitat and unrestricted hunting resulted in extirpation of wild turkeys throughout most of their ancestral range. The last recorded observations of native turkeys in Connecticut, New York, and Massachusetts were in 1813, 1844, and 1851, respectively, and by 1907, wild turkeys had also vanished from Kansas, Ohio, Illinois, Indiana, and Iowa (Kennamer et al. 1992). By the early twentieth century, only small populations existed in remote, inaccessible areas. Restoration programs, aided largely by trap-and-transplant programs initiated during the early 1950s, resulted in remarkable population growth and range extensions of wild turkeys. During 1959–1990, the estimated number of eastern wild turkeys

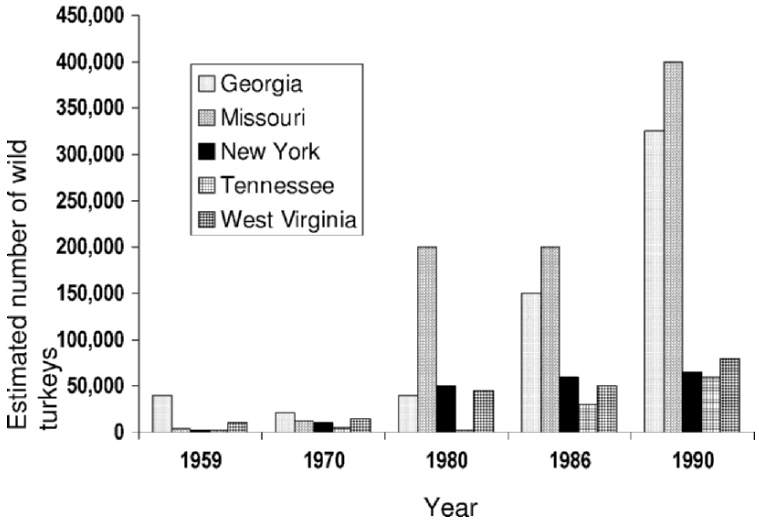

Fig. 4 The estimated number of wild turkeys (*Meleagris gallopavo*) in selected states, 1959–1990 (data from Kennamer et al. 1992). Wild turkeys were nearly extirpated from most of the eastern United States, but populations rebounded considerably during the last half of the twentieth century. This large gallinaceous bird is often a host to larval and nymphal stages of the lone star tick

swelled from approximately 239,000 to over 2,550,000 (Kennamer et al. 1992) (Fig. 4). Increased wild turkey densities have also been suggested as a factor in the recent range extension of *A. americanum* into areas of eastern Kansas (Mock et al. 2001). Population increases of other potential hosts or reservoirs, including coyotes, have also been suggested as contributing to the emergence of *A. americanum*-associated zoonoses (Kocan et al. 2000; Childs and Paddock 2003).

The range of *A. americanum* is increasing, often extending into regions occupied by deer populations not previously infested by lone star ticks (Keirans and Lacombe 1998; Lockhart et al. 1995; Yabsley et al. 2003a). By use of logistic regression modeling, several climatic and landcover variables have been associated with the presence of *E. chaffeensis*-reactive antibodies in deer, a finding that is highly associated with *A. americanum* infestation (Yabsley et al. 2003a, 2005). These models also predict several geographic areas that appear to have suitable tick habitat but where no evidence of ticks or infections of *E. chaffeensis* in deer exists currently (Fig. 5). These regions represent areas of potential spread and should be closely monitored. If *A. americanum* becomes established in these regions, human inhabitants of these areas are placed at risk for disease caused by any of the several pathogens vectored by the lone star tick.

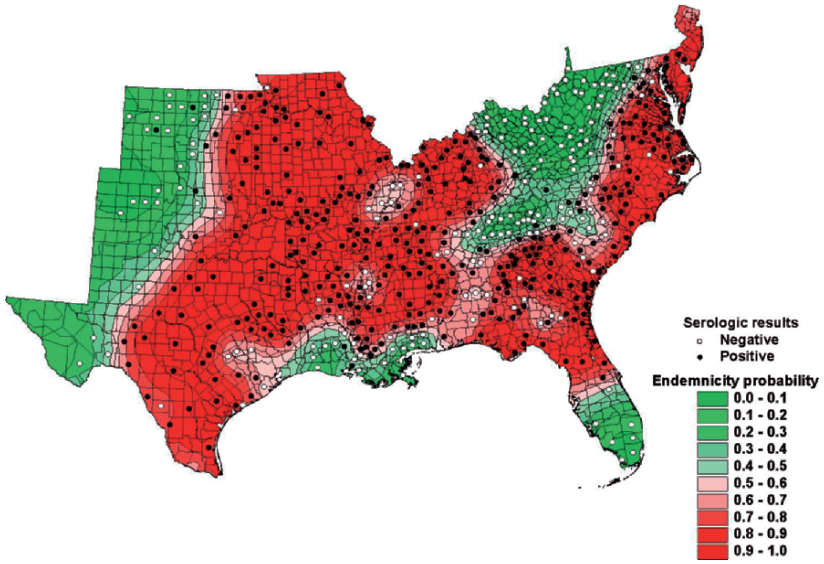

Fig. 5 A Kriging map identifying the endemic probabilities for *Ehrlichia chaffeensis* as determined by geospatial analyses (Yabsley et al. 2005). *Solid circles* represent areas populated by deer with antibodies reactive with *E. chaffeensis*; *open circles* represent areas with seronegative deer (Yabsley et al. 2003b). Increasing probabilities correspond with an increased chance of deer populations that are infected with *E. chaffeensis*

Despite decades of human influence, the natural histories of multiple *A. americanum*-associated diseases in the United States have only recently been unveiled (Childs and Paddock 2003). What will be the prevalence of these pathogens in vector and reservoir populations and the incidence of these diseases in human populations in years to come? It is unlikely that whitetail populations or the incidence of these diseases will continue to climb unrestricted. Valerius Geist, commenting on the recent expansion of whitetails, states that, "This 'weed species' specializes in exploiting opportunities, not at competing for resources through local contests or scrambles." In many aspects, as Geist suggests, the successful adaptation of whitetails to the evolving landscape of the eastern United States parallels the proliferation of weedy plant species that adapt well to disrupted or drastically altered environments. "Weeds" typically flourish because of adverse conditions created by human intervention (e.g., pollution, cultivation, trampling, or herbicide spraying); in this context, "weeds" do not exist in natural environments (Vessel and Wong 1987).

Because disrupted environments require continued intervention to maintain disequilibrium, these landscapes are not stable; for example, a weed-infested lot does not remain weedy indefinitely. Unless continued, the various environmental disturbances and imbalances of the last two centuries that established ideal biotypes for white-tailed deer will not maintain a landscape that allows large numbers of these animals to perpetuate. Over time, whitetail populations can stabilize or diminish as second-growth forests succeed to mature stands. Nonetheless, whitetails have a remarkable propensity to exist in regions despite diminishing food resources; thus downward trends in deer or lone star tick populations are not likely to occur soon. As with white-tailed deer and lone star ticks, the ehrlichioses and STARI are firmly established in North America. Intelligent control and management practices of white-tailed deer populations offer the best hope of stemming further influx of these zoonoses into human populations.

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