

FOCUS

ON LYME DISEASE

UNITED STATES ARMY CENTER FOR HEALTH PROMOTION AND PREVENTIVE MEDICINE

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LETTER FROM THE EDITOR

'**FOCUS – ON LYME DISEASE**' is a periodic publication of the U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPM). It is designed to keep you informed about Lyme disease and other tick-borne diseases, as well as preventive measures, and to provide you with the tools to educate others. Material printed in this publication comes from a variety of sources including professional contacts; conferences; scientific literature; computer networks; USACHPPM Tick-Borne Disease Data Repository; Armed Forces Pest Management Board; federal, state and local health agencies; universities; press; and other organizations. Your comments, suggestions, and questions are welcome. Please contact me at the following: Sandra Evans, U.S. Army Center for Health Promotion and Preventive Medicine, ATTN: Entomological Sciences Program, 5158 Blackhawk Road, Aberdeen Proving Ground, MD 21010-5403; DSN 584-3613; Commercial (410) 436-3613; FAX – 2037; or E-mail: Sandra.Evans@apg.amedd.army.mil. The FOCUS is also accessible via the USACHPPM website: <http://chppm-www.apgea.army.mil/ento/>

*** TICK-BORNE DISEASE SUMMARY** From the MMWR (Morbidity and Mortality Weekly Report), Centers for Disease Control and Prevention, September 13, 1999, Vol. 48, No. 36: Cumulative 1999 Lyme disease cases reported for the United States, as of September 11, 1999 (36th week): 6,774 (as compared to 10,673 for 1998); for the same reporting period, 372 cases of Rocky Mountain spotted fever (RMSF), 26 cases of human monocytic ehrlichiosis (HME), and 107 cases of human granulocytic ehrlichiosis (HGE).

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New Serological Test for *B. burgdorferi*

In February 1999, a new serological test method for the diagnosis of Lyme disease was approved by the Food and Drug Administration (FDA). It is called PreVue™, and it was developed and is manufactured by Chembio Diagnostic Systems in Medford, New York (Tel: 516-924-1135). The product, which is distributed by Wampole Laboratories, Dist. (Division of Carter-Wallace, Inc., Cranbury, NJ 08512-0161, 1-800-257-9525 for orders or technical assistance), is used for the detection of IgG/IgM antibodies to *Borrelia burgdorferi* in human serum or whole blood. The product insert is lengthy and comprehensive, and states the following under the section entitled 'Intended Use': ***'The Wampole PreVue™ B. burgdorferi antibody detection assay is a single use, unitized immunochromatographic test that uses recombinant B. burgdorferi antigens for the qualitative presumptive (first step) detection of IgG and IgM antibodies to B. burgdorferi in human serum or whole blood. This test should be used only in patients with history, signs and symptoms that are consistent with Lyme disease. Equivocal or positive results should be supplemented by testing with a standardized Western-blot (second-step) procedure. Positive supplemental (second-step) results are supportive evidence of exposure to B. burgdorferi and can be used to support a clinical diagnosis of Lyme disease. The diagnosis of Lyme disease must be made based on history, signs (such as erythema migrans), symptoms, and other laboratory data, in addition to the presence of antibodies to B. burgdorferi. Negative results (either first- or second-step) should not be used to exclude Lyme disease.'***

The FDA approved the test, based on results of clinical studies conducted by the manufacturer: PreVue accurately detected Lyme disease in 72 percent of one group of 120 blood samples, and 95 percent of another group of 42 blood samples. The test incorrectly identified Lyme disease in three percent of 100 blood samples in which it

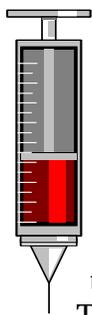
was not present. According to the FDA, this 'false-positive' rate is similar to that of other laboratory tests for Lyme disease. Details on these studies, as well as others, are provided in the product insert under the section entitled 'Performance Characteristics.'

PreVue uses recombinant *B. burgdorferi* antigens rather than whole cell *B. burgdorferi* preparations, and provides a preliminary, qualitative result within an hour at the point of care (the doctor's office). The test device operates on the following principle, as stated in the product insert: ***'A 5 µl sample of serum, or a 10 µl sample of whole blood, is added to the SAMPLE WINDOW. A diluent is then added to the SAMPLE WINDOW. The specimen and diluent dissolve color-labeled antibody binding proteins, and all the IgG and IgM antibodies in the sample become color-labeled. The color-labeled antibodies in the sample then migrate by capillary action to the antigen band that is impregnated in the TEST WINDOW. If B. burgdorferi-specific antibodies are present they will be captured by the recombinant B. burgdorferi antigens impregnated in the TEST WINDOW. Visualization of a colored line in the TEST WINDOW will occur only when B. burgdorferi-specific antibodies are present. As the color-labeled antibodies continue to migrate along the test membrane, they will bind to antibody-binding proteins located in the CONTROL WINDOW and will generate a colored band regardless of the presence of B. burgdorferi antibodies in the sample. Therefore, the presence of two colored bands, one in the TEST WINDOW and the other in the CONTROL WINDOW, indicates a positive result, while the presence of a colored band ONLY in the CONTROL WINDOW indicates a negative result.'***

PreVue became available commercially on June 16, 1999, and costs approximately \$200.00 for a kit that contains enough of the following items to perform 20 tests: TEST DEVICES; a

bottle of DILUENT; HIGH POSITIVE *B. burgdorferi* CONTROL; NEGATIVE CONTROL; and both 5 µl and 10 µl CAPILLARY TUBES. The kit insert indicates that good laboratory practice recommends positive and negative controls be run periodically in place of serum or blood samples in order to monitor proper kit performance.*

New Lyme Vaccine Licensed



On 22 December 1999, the Food and Drug Administration (FDA) licensed the first human Lyme disease vaccine. Developed and marketed by SmithKline Beecham under the tradename *LYMERix*[™], the vaccine consists of *Borrelia burgdorferi* outer surface lipoprotein A (OspA) which is adsorbed to an adjuvant (aluminum hydroxide).

The vaccine induces the body to develop antibodies that target the OspA of *B. burgdorferi* while the spirochetes are still inside the gut of a feeding tick, killing them before they have the chance to enter and infect the person. (For more details, see the previous issue of the FOCUS, No. 11, Fall 1998).

LYMERix requires a total of 3 inoculations over the course of a year in order to confer a final maximum immunity of 78 percent (the first injection is followed one month later by the second injection, after which the third injection is given at month 12). Approximately 50 percent immunity is achieved following the second injection. *LYMERix* is only licensed for use in individuals aged 15 years to 70 years, and is only

effective against North American strains of *B. burgdorferi*. It will not protect against other tick-borne infections, and the necessity and frequency of boosters has not yet been determined. The Centers for Disease Control and Prevention (CDC) published “Recommendations for the Use of Lyme Vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP)” in the Morbidity and Mortality Weekly Report (MMWR), June 4, 1999/Vol. 48/ No. RR-7. They are available in hard copy, or from the CDC’s website at: <http://www.cdc.gov>. Click on MMWR and download the .pdf format of the document for the best presentation (you will need Adobe Acrobat for this format). The document discusses clinical features of Lyme disease, epidemiology, prevention and control techniques, the vaccine and its mechanism of action, its performance (safety and efficacy), cost-effectiveness, assessing a person’s risk of acquiring Lyme disease, recommendations for use of the vaccine, and future considerations. The Appendix includes a National Lyme Disease risk map, which color codes the United States according to four categories of risk: high, moderate, low, and minimal/none. The methods that were used to create the map are also discussed. A summary table of the ACIP’s recommendations for use of the vaccine is included, and the major portion of that table is reproduced on the following page.

Currently, no specific Department of Defense guidance or policy has been promulgated regarding provision and use of *LYMERix* within the military.*

IN THE NEWS

Summary Table

Recommendations for Use of Recombinant Outer-Surface Protein A Vaccine for the Prevention of Lyme Disease, Advisory Committee on Immunization Practices, MMWR 1999;48(No. RR-7)

	Vaccination Recommendation
Persons who reside, work, or recreate in areas of high or moderate risk	
Persons aged 15-70 years whose exposure to tick-infested habitat is frequent or prolonged.....	Should be considered
Persons aged 15-70 years who are exposed to tick-infested habitat, but whose exposure is not frequent or prolonged.....	May be considered
Persons whose exposure to tick-infested habitat is minimal or none	Not recommended
Persons who reside, work, or recreate in areas of low or no risk	Not recommended
Travelers to areas of high or moderate risk	
Travelers aged 15-70 years whose exposure to tick-infested habitat is frequent or prolonged.....	Should be considered
Children aged <15 years.....	Not recommended
Pregnant women	
Health-care providers are encouraged to register vaccinations of pregnant women by calling SmithKline Beecham, toll free, at 1-800-366-8900, ext. 5231.....	Not recommended
Persons with immunodeficiency	No available data
Persons with musculoskeletal disease	Limited data available
Persons with previous history of Lyme disease	
Persons aged 15-70 years with previous uncomplicated Lyme disease who are at continued high risk.....	Should be considered
Persons with treatment-resistant Lyme arthritis.....	Not recommended
Persons with chronic joint or neurologic illness related to Lyme disease, and persons with second- or third-degree atrioventricular block.....	No available data
Other Recommendations	
Vaccine schedule	
Three doses administered by intramuscular injection as follows: Initial dose, followed by a third dose 12 months after the first dose	
Second dose (year 1) and third dose (year 2) administered several weeks before the beginning of the disease-transmission season, which is usually April	
Boosters	
Existing data indicate that boosters might be needed, but additional data are required before recommendations can be made regarding booster schedules	
Simultaneous administration with other vaccines	
Additional data needed.	
If simultaneous administration is necessary, use separate syringes and separate injection sites	

Reported Distribution of *Ixodes scapularis* and *Ixodes pacificus* (Acari: Ixodidae) in the United States*

Abstract. ‘Lyme disease, caused by infection with *Borrelia burgdorferi*, is the most frequently reported arthropod-borne disease in the United States. To develop a national map of the distribution of the vectors of *B. burgdorferi* to humans (*Ixodes scapularis* Say and *Ixodes pacificus* Cooley & Kohls ticks), we sent questionnaires to acarologists, health officials, and Lyme disease researchers; surveyed the 1966-1996 MEDLINE data base; and reviewed 1907-1995 National Tick Collection data. Tick collection methods cited included flagging and dragging, deer surveys, small- and medium-sized mammal surveys, CO₂ baiting, and receipt of tick submissions. A total of 1,058 unique, county-specific *I. scapularis* and *I. pacificus* records was obtained. Tick populations were classified as “reported” (< 6 ticks and 1 life stage identified) or “established” (≥ ticks or > 1 life stage identified). Established populations of *I. scapularis* were identified in 396 counties in 32 states in the eastern and central United States, whereas established populations of *I. pacificus* were found in 90 counties in 5 western states. Counties with established populations were most concentrated in the northeastern, upper northcentral, and west-coastal states but were also clustered in southeastern and Gulf-coastal states. A less concentrated distribution was found in the south-central states. Reports were notably missing from all but a few counties in Ohio, West Virginia, western Virginia and North Carolina, Kentucky, and Tennessee. They were absent in the Great Plains and Rocky Mountain regions and from large areas of western states east of the Cascade and Sierra Nevada cordilleras. These data are useful for identifying areas of Lyme disease risk, for targeting Lyme disease prevention strategies, and for monitoring trends in spatial distribution of Lyme disease vector ticks.’

This excellent article includes a map of the United States, delineated by county, and color coded according to the presence of “established” and “reported” vectors, as defined above. It also lists all counties by name in a separate table. The U.S. tick distribution map can ALSO be found on the internet at: <http://www.cdc.gov/ncidod/dvbid/tickmap.pdf>.

*Dennis, DT, TS Nekomoto, JC Victor, WS Paul, and J Piesman. September 1998. J. Med. Entomol. 35(5):629-638. ✱

STATE-OF-THE-ART CLINICAL ARTICLE: Rocky Mountain Spotted

Fever* [Comments contained within brackets are made entirely by the editor]

Abstract. ‘Rocky Mountain spotted fever (RMSF), a potentially fatal, tick-borne bacterium *Rickettsia rickettsii*, is endemic in parts of North and South America, especially the southeastern and southcentral United States. Although it was first recognized > 100 years ago, the disease remains difficult to diagnose because a rash does not appear until an average of 3 days into the illness, and does not manifest a petechial [a term used to describe flat, pinpoint-size, red spots caused by tiny hemorrhages beneath the skin] or purpuric [a more generalized term that describes both the tiny petechiae, as well as the larger ecchymoses, i.e. bruises or black and blue marks caused by more extensive hemorrhaging] character until later in the course, if at all. Common presenting symptoms include fever, headache, myalgias [muscular pains], and gastrointestinal disturbances. The mortality rate associated with RMSF is 20% to 25% if untreated, and 5% with appropriate antibiotic therapy (if not initiated early enough). Treatment with doxycycline may be preferable to chloramphenicol therapy, because the tetracyclines have been shown in a retrospective study to be associated with a higher survival rate. Physicians must maintain a high index of suspicion for RMSF in patients

IN THE LITERATURE

with febrile illness and a history of potential tick exposure who present in the spring through the fall.’

This is an excellent article that summarizes the history, epidemiology, pathogenesis, clinical manifestations, diagnosis, antibiotic treatment, and prevention of RMSF.

[Unlike its name would suggest, RMSF is now most common in the eastern half of the United States, with North Carolina generally reporting the greatest number of cases]. Its history began in the west, however, with the first case reported in 1896 by an army physician, MAJ Marshall H. Wood, in Boise, Idaho. Subsequently, in the first decade of the twentieth century, a large number of cases, including many deaths, occurred in the Bitterroot valley of Montana. Research continued in that location, with ground-breaking demonstrations by Howard Ricketts that RMSF could be transmitted to guinea pigs by ticks, and that the agent of RMSF was present in blood from infected humans. Effective antibiotic treatments were not discovered until the late 1940s.

Within the United States, the major vectors of *R. rickettsii* are the American dog tick, *Dermacentor variabilis*, in the eastern two-thirds of the country, as well as along the West Coast, and the wood tick, *D. andersoni*, in the Rocky Mountain states. Outside the U.S., the [brown dog tick], *Rhipicephalus sanguineus*, is the vector in Mexico, and the [cayenne tick], *Amblyomma cajennense*, in Central and South America. [*R. rickettsii* is a New World species, and is not found outside the Americas, although other species of *Rickettsia* cause varying degrees of pathogenicity in other parts of the world].

Transmission of *R. rickettsii* may occur in as little as 6-10 hours after an infected tick begins feeding, or may take up to 24 hours or more. Illness begins 2 to 14 days after the tick bite, with a mean of 7 days. The first symptom

is most often fever greater than 102°F, occurring in two-thirds of patients during the first 3 days of illness. [In about half the cases], a petechial rash begins 2-3 days after the onset of illness and starts on the ankles and wrists, then progresses over the trunk, palms, and soles. Nausea and/or vomiting is present in 56-60% of cases. Severe or fatal illness is associated with lack of history of tick bite, rash that appears late or not at all, presence of a glucose-6-phosphate dehydrogenase deficiency (in male African Americans), or presentation of nonspecific, atypical symptoms [= misdiagnosis].

Because RMSF progresses quickly, diagnosis must be based on history and clinical findings. Serology may be used to confirm a clinical diagnosis, but antibodies are generally not detectable until 7 to 10 days after the onset of symptoms. Serological diagnosis requires a four-fold rise in titer between acute and convalescent sera, and indirect fluorescent antibody assay (IFA) is the most sensitive method available (94%). Early treatment [which is important] may subdue the rise in titer. Rickettsiae can sometimes be observed by staining skin biopsies of patients who have a rash.



Petechial rash of RMSF on hand and wrist

Photograph courtesy of Dr. William A. Petri, Jr., Department of Medicine, Virginia School of Medicine, Charlottesville, VA 22908

Differential diagnosis in patients who initially present with fever, headache, and/or a petechial rash, includes a wide variety of bacterial and rickettsial infections such as ehrlichiosis, meningococemia, infectious mononucleosis, typhoid fever, typhus, leptospirosis, bacterial sepsis, even pneumonia, bronchitis, or gastroenteritis; enteroviral

infections; or vascular conditions that cause vasculitis [inflammation of blood vessels] or thrombotic thrombocytopenic purpura [a severe form of spontaneous subcutaneous bleeding].

*Thorner, AR, DH Walker, and WA Petri, Jr. December 1998. Clin. Infect. Dis. 27:1353-60. ✱

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***Ehrlichia ewingii*, a Newly Recognized Agent of Human Ehrlichiosis.** Buller, RS, M Arens, SP Hmiel, CD Paddock, JW Sumner, Y Rikihisa, A Unver, M Gaudreault-Keener, FA Manian, AM Liddell, N Schmulewitz, FA Storch. July 15, 1999. N. Engl. J. Med. 341(3):148-155.

Polymerase chain reaction (PCR) was used to test white blood cells in the blood from 413 patients with possible ehrlichiosis. In four of these patients, DNA was detected that matched that of *Ehrlichia ewingii*, an agent previously only found to infect dogs (canine granulocytic ehrlichiosis). The tests were negative for the organisms currently known to cause human ehrlichiosis in the U.S.: *E. chaffeensis* (causes human monocytic ehrlichiosis, HME) and the yet unnamed agent that causes human granulocytic ehrlichiosis (HGE). One of the patient's dogs also had positive PCR results for *E. ewingii*. In addition, morulae (clusters of ehrlichial organisms) were detected in granulocytes (a type of white blood cell) of two of the patients.

All four patients were from Missouri, and presented between May and August of 1996, 1997, or 1998 with fever, headache, and thrombocytopenia [abnormally small number of platelets present in the blood], with or without leukopenia [abnormally small number of white blood cells present in the blood]. All had been exposed to ticks, and three were immunocompromised because of medications they were taking for other chronic medical conditions; the other had previously been healthy. All four patients were successfully treated with doxycycline.✱

Ehrlichiosis – Ticks, Dogs, and Doxycycline

[An editorial in the same issue (July 15, 1999) of the New England Journal of Medicine as the previous article, above].

In this excellent editorial, Jesse L. Goodman, M.D., M.P.H., (University of Minnesota, Minneapolis, MN 55455), clarifies and discusses the implications of the findings presented in the report by Buller et al.

Dr. Goodman raises many questions and answers some: ‘Three of the four patients were immunocompromised. Does *E. ewingii* usually not infect immunocompetent humans, or does it produce in them an infection that is mild or asymptomatic? What are the clinical spectrum and natural history of the disease? In dogs, *E. ewingii* can cause arthritis and chronic infection. What are this organism's zoonotic hosts other than dogs? What is its geographic range? Given that *A. americanum* may also be the vector for *E. ewingii*, can coinfection with *E. chaffeensis* occur?...’

IN THE LITERATURE

‘...So, what does a clinician need to do? Most important is to remember that ehrlichial infections can be severe or even fatal if untreated. A diagnosis of ehrlichiosis must be considered in anyone who presents with an acute febrile illness after potential or documented exposure to ticks. Leukopenia, thrombocytopenia, elevations in aminotransferase levels, or a combination of these findings is usually present or soon develops in patients with ehrlichiosis...differential diagnosis is extensive. Diseases such as endocarditis, other forms of septicemia, vasculitis, and thrombotic thrombocytopenic purpura must be considered. The presence of inclusions in leukocytes in...blood smears should be sought, although their absence does not exclude the possibility of ehrlichiosis. The other tests currently available are primarily used to confirm a diagnosis and usually are not helpful when the patient presents for care.’ (i.e., serological testing of acute and convalescent serum samples, PCR analysis for ehrlichial agents prior to antibiotic therapy, and culture of ehrlichiae. In addition, some of these techniques are not widely available and are time-consuming). Patients usually respond to treatment with doxycycline within 24 to 48 hours.✱

FOR YOUR INFORMATION

*** Human Ehrlichiosis Now Nationally Reportable ***

As of January 1, 1999, 56 infectious diseases, including both human monocytic ehrlichiosis (HME) and human granulocytic ehrlichiosis (HGE), were designated as notifiable at the national level. Neither HME nor HGE are reportable in every state or territory, however, so the reported numbers of cases represent only the totals from states or territories in which the diseases are reportable. Statistics for the human ehrlichioses first began appearing in the Morbidity and Mortality Weekly Report (MMWR) with the June 4, 1999 issue (Vol. 48, No. 21).✱

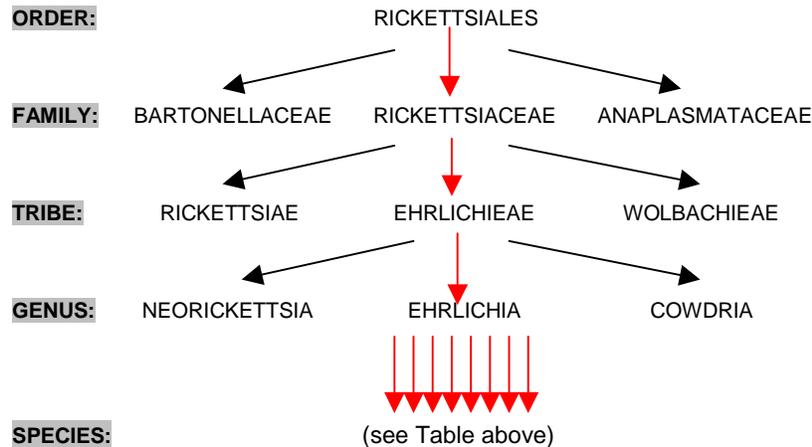
Ehrlichiosis – An Overview

WHAT IS EHRLICHIOSIS? Ehrlichiosis is a generic term for those tick-borne diseases of humans and other animals, known collectively as ‘ehrlichioses,’ that are caused by members of the bacterial genus *Ehrlichia*. Each species of *Ehrlichia* causes a different type of ehrlichiosis, and usually targets a specific host animal species.

TAXONOMY	
GENUS: EHRLICHIA	
SPECIES	TARGET
E. canis	DOGS (canine ehrlichiosis)
E. ewingii	DOGS (canine granulocytic ehrlichiosis)
E. risticii	HORSES (Potomac Horse Fever)
E. equi	HORSES (equine ehrlichiosis)
E. phagocytophila	SHEEP, CATTLE (tick-borne fever)
E. sennetsu	HUMAN (Sennetsu fever)
E. chaffeensis	HUMAN (human monocytic ehrlichiosis)
E. ?	HUMAN (human granulocytic ehrlichiosis)

FOR YOUR INFORMATION

Ehrlichiae are very small bacteria, very closely related to rickettsiae, the type of bacteria that cause Rocky Mountain spotted fever. A taxonomic chart follows:



Ehrlichiae invade, and live within (i.e., they are intracellular), white blood cells, thereby adversely affecting the immune system and lessening the body's ability to fight secondary infections. They reside in the cytoplasm outside the nucleus. Ehrlichiae are considered to be pleomorphic, meaning variable in shape (Figure 1), although they are most frequently spherical or ellipsoidal (Figure 2). While ehrlichiae are sometimes scattered singly throughout the cytoplasm, they are more often found clustered together as aggregates of many organisms. These clusters are berry-like in appearance and are called 'morulae' (singular 'morula') (Figures 1, 2, and 3). Ehrlichiae have a rippled outer cell wall, and an inner plasma membrane (Figure 3).

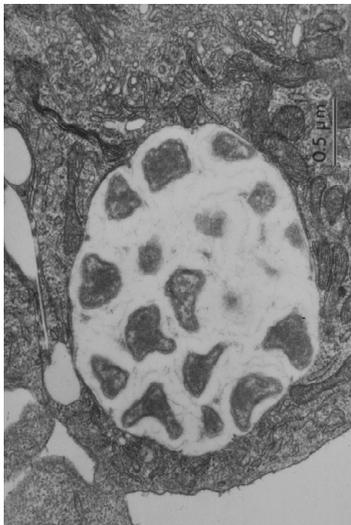


Figure 1: Cluster (morula) of *Ehrlichia chaffeensis*, exhibiting variable (pleomorphic) shapes. Courtesy of Jacqueline Dawson, CDC.

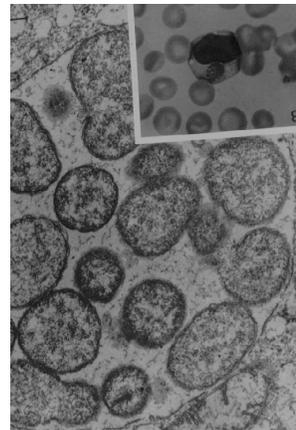


Figure 2. Cluster (morula) of *Ehrlichia canis* within the cytoplasm of an infected canine monocyte, exhibiting spherical and ellipsoidal shapes. Inset B, shows a large, dark morula of *E. canis* within a monocyte. The smaller spherical body within the monocyte is the nucleus. From: Bergey's Manual of Systematic Bacteriology.

FOR YOUR INFORMATION

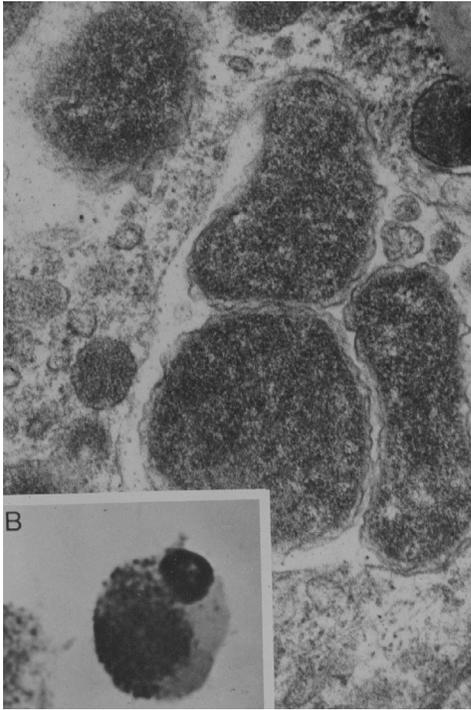


Figure 3. Small cluster (morula) of three individual *Ehrlichia sennetsu*. Each individual organism is surrounded by a plasma membrane and a rippled outer cell wall. Inset B shows numerous individual organisms scattered throughout the cytoplasm of a human monocyte. The smaller, solid dark spherical body within the monocyte is the nucleus. From: Bergey's Manual of Systematic Bacteriology.

HISTORY. Ehrlichiosis was first recognized in Africa (Algeria) in 1935, as a disease of dogs, caused by *Ehrlichia canis* and known as canine ehrlichiosis. In the 1960s, an outbreak of this disease struck a large contingent of military guard dogs stationed in Vietnam. Most of the dogs died due to hemorrhagic complications.

Ehrlichiosis in humans was first described in 1954 as a mononucleosis-like illness in Japan. This type of ehrlichiosis is called Sennetsu fever and it occurs in very limited areas of the Far East, primarily Japan. It is extremely rare, usually very mild, and no deaths have ever been reported. It is caused by *E. sennetsu*.

In the United States, the first diagnosed case of human ehrlichiosis occurred in 1986 in a 51-year-old man from Detroit who had been exposed to ticks in a rural area of Arkansas. At the time, this human case of ehrlichiosis was attributed to *E. canis*. In 1990, however, the agent of human ehrlichiosis was isolated from the blood of a US Army reservist training at Fort Chaffee, Arkansas. The new species of ehrlichiae was named *E. chaffeensis*, and the specific disease that it causes has been designated human monocytic ehrlichiosis (HME) because the pathogen primarily infects white blood cells known as monocytes (Figure 4).

In 1994, another type of human ehrlichiosis was recognized following a report of 12 cases of an ehrlichial illness, which occurred in Minnesota and Wisconsin from 1990 through 1993. Two of those patients died from complications and secondary infections. This ehrlichial illness has been designated human granulocytic ehrlichiosis (HGE) because white blood cells known as granulocytes, primarily neutrophils, are usually infected (Figure 4). The organism that causes HGE has not yet been conclusively identified, although it is very similar, or possibly identical to, the veterinary pathogens *E. equi* and *E. phagocytophila*. Currently, it is referred to simply as the 'agent of HGE', or 'aoHGE.'

Most recently, *E. ewingii*, a pathogen of dogs, has also been found to cause human illness. (See article on page 9).

SYMPTOMS. Symptoms of both HME and HGE begin in 1-21 days (average 7) days following infection, and they resemble those of Rocky Mountain spotted fever. Symptoms vary greatly in severity, ranging from an illness so mild that no medical attention is sought, to a severe, life-threatening condition. The most common symptoms are high fever, headache, chills, and muscular aches and pains, but may also include nausea, vomiting, loss of appetite,

Three types
of granulocytic
white blood cells.

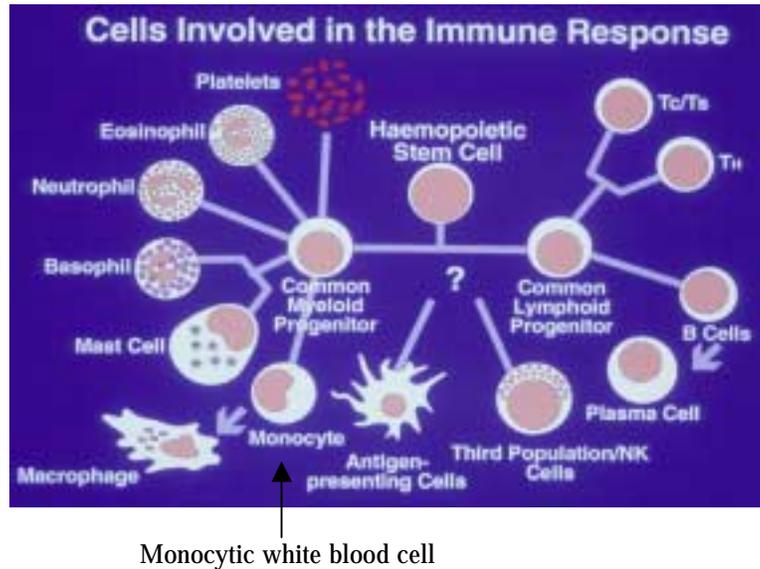


Figure 4. Different species of *Ehrlichia* infect monocytes and granulocytes
(Technical rendering by N. Pospisil, U.S. Army Center for Health Promotion & Preventive
Medicine, from an illustration in *Immunology*, 2nd ed., by Roitt, Brostoff, & Male, 1989,
Gower Medical Publishing, London, England.)

and an overall feeling of bodily discomfort (malaise). Rash is rare, but when present may resemble the spotted rash of RMSF, although usually less prominent and more variable in appearance and location. Since ehrlichiae invade white blood cells, the body's immune system is adversely affected. This lessens the body's ability to fight other infections, and complications can quickly arise. In the most severe cases, kidney or respiratory failure occurs. There have been a number of deaths associated with both HME and HGE.

DIAGNOSIS AND TREATMENT. In addition to evaluating clinical symptoms, a diagnosis of ehrlichiosis is confirmed by testing blood samples for antibody titers to different species of *Ehrlichia*, and by observing the bacteria in different types of white blood cells. Blood testing may also indicate thrombocytopenia, leukopenia, and elevated liver enzyme levels. The antibiotic doxycycline is very effective for treating both HME and HGE. Because human ehrlichiosis can be so severe, or even deadly, it is very important to obtain early diagnosis and treatment.

HOW IS EHRLICHIOSIS SPREAD? The ehrlichioses are tick-borne diseases. Ehrlichiae are transmitted to humans via the bite of infected ticks, which have picked up the pathogens while feeding on infected animal reservoirs. The vector of *E. chaffeensis* is the Lone Star tick, *Amblyomma americanum*. This tick is very common in the south central and southeastern United States, where the largest number of HME cases occur. The major vector of the agent of HGE is the black-legged tick (= deer tick), *Ixodes scapularis*. Likewise, the majority of HGE cases follow the geographic distribution of this tick species, occurring primarily in the upper Midwest and northeastern United States. The brown dog tick, *Rhipicephalus sanguineus*, is the most likely vector of *E. canis*.

INCIDENCE. According to the Centers for Disease Control and Prevention (CDC), from 1986 – 1997, 1,223 ehrlichiosis cases (HME plus HGE) were reported from 30 state health departments, to include 19 states in which ehrlichiosis was considered reportable as of August 1998, five states that routinely collected

FOR YOUR INFORMATION

information on cases, and six states that occasionally received reports of cases. Of these

cases, 742 were designated HME, 449 as HGE, and 32 as unspecified type.

States in which Human Ehrlichiosis is Reportable, with totals for each type, reported through 1997*

State	1 st year reportable	HME	HGE	Unspecified type	Total
Arizona	1997	1	0	0	1
Arkansas	1993	55	0	0	55
California	1996	2	3	0	5
Connecticut	1995	9	156	9	174
Florida	1996	21	0	0	21
Kentucky	1989	14	0	0	14
Maine	1996	0	0	0	0
Michigan	1993	---	---	2	2
Minnesota	1996	2	36	0	38
Missouri	Unknown	162	0	0	162
New Hampshire	1996	0	0	0	0
New Jersey	1995	35	4	0	39
New York	1996	28	195	0	223
North Carolina	1998	204	1	0	205
Pennsylvania	1992	1	1	1	3
Rhode Island	1996	0	2	0	2
South Carolina	1990	---	---	5	5
Tennessee	1996	---	---	7	7
Texas	1996	45	0	0	45
Totals		479	398	24	1001

* Data from the CDC: Published in Emerging Infectious Diseases, "The Human Ehrlichioses in the United States." McQuiston, JH, CD Paddock, RC Holman, and JE Childs, 5(5), Sep-Oct 1999.

States which have collected and reported some data on Human Ehrlichiosis, but which have not officially established reporting requirements*

State	HME	HGE	Unspecified Type	Total
Colorado	---	---	3	3
Illinois	5	1	2	8
Indiana	21	0	0	21
Louisiana	---	---	1	1
Maryland	6	0	1	7
Massachusetts	0	5	0	5
Mississippi	---	---	1	1
New Mexico	1	0	0	1
Oklahoma	76	0	0	76
Virginia	54	0	0	54
Wisconsin	0	45	0	45
Totals	163	51	8	222

* Data from the CDC: Published in Emerging Infectious Diseases, "The Human Ehrlichioses in the United States." McQuiston, JH, CD Paddock, RC Holman, and JE Childs, 5(5), Sep-Oct 1999.

Update From USACHPPM:

Results of USACHPPM's Department of Defense Tick Test Kit Service, Infection in Ticks Removed from Humans, 1998

Although worldwide, mosquitoes rank as the number-one vector of human disease (led by malaria), in the United States, ticks account for the bulk of arthropod-borne disease cases [led by Lyme disease (LD, 12,801 cases in 1997); followed by Rocky Mountain spotted fever (RMSF, 409 cases in 1997); as well as others, such as human monocytic ehrlichiosis (HME), human granulocytic ehrlichiosis (HGE), and babesiosis]. To help address this health concern, the Entomological Sciences Program (ESP) of the U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPM) provides a 'Tick Test Kit' service for the Department of Defense (DOD). This service is highlighted here:

To assist DOD health clinics, the ESP designed, assembles, and disseminates 'Tick Test Kits'. DOD health care personnel use these kits to submit ticks removed from tick-bite patients to the ESP laboratory for identification and analysis. Telephonic, followed by written, results are provided back to the clinic. Since different tick species are the vectors for different pathogens (or groups of pathogens), and since many tick-borne diseases have virtually identical early symptoms, knowledge of tick species and infection status is valuable to the physician in making diagnosis and treatment determinations. In addition, there is increasing evidence that, in some cases, ticks are infected with, and simultaneously transmit, more than one kind of pathogen. This situation can further complicate clinical presentation, diagnosis, and effective treatment.

The ESP uses polymerase chain reaction (PCR) to analyze ticks for infection with the agents of four diseases: LD (*Borrelia*



burgdorferi), RMSF (*Rickettsia rickettsii*), HME (*Ehrlichia chaffeensis*), and HGE (unnamed ehrlichia, closely related to *E. phagocytophila*, a pathogen of sheep and cattle, and currently designated 'agent of HGE' or 'aoHGE'). Specific tick species, therefore, are generally only analyzed for those pathogens for which they are known to be either a confirmed or potentially competent vector.

In 1998, 1774 ticks removed from humans were received from DOD health clinics (see Table). All were identified. Of these, 863 were alive, and subsequently tested for pathogens. A total of 397 Lone Star ticks (*Amblyomma americanum*) were tested for *E. chaffeensis* and *B. burgdorferi*: 3 (0.8%) contained *E. chaffeensis* and 15 (3.8%) contained *B. burgdorferi*. A total of 367 American dog ticks (*Dermacentor variabilis*) were tested for *R. rickettsii* and one (0.3%) was positive. Of 97 black-legged ticks (= deer ticks, *Ixodes scapularis*) tested, 21 (21.6%) contained *B. burgdorferi* and 4 (4.1%) contained the agent of HGE. Two (2.1%) of these 97 black-legged ticks were co-infected with both agents.

FOR YOUR INFORMATION

**USACHPPM'S TICK TEST KIT PROGRAM
Ticks Removed from Humans, 1998**

Species	Identified	Tested	Positive Results			
			Bb ¹	Rr ²	Ec ³	aoHGE ⁴
<i>Ixodes scapularis</i> (black-legged tick)	295	97*	21	---	---	4
<i>Ixodes pacificus</i> (western black-legged tick)	1	0	---	---	---	---
<i>Amblyomma americanum</i> (Lone Star tick)	978	397	3	---	15	---
<i>Amblyomma maculatum</i> (Gulf coast tick)	2	0	---	---	---	---
<i>Dermacentor variabilis</i> (American dog tick)	492	367	---	1	---	---
<i>Rhipicephalus sanguineus</i> (brown dog tick)	6	2	---	0	---	---
Totals	1774	863	24	1	15	4

¹ Bb (*Borrelia burgdorferi*, agent of Lyme disease)

² Rr (*Rickettsia rickettsii*, agent of RMSF)

³ Ec (*Ehrlichia chaffeensis*, agent of human monocytic ehrlichiosis)

⁴ aoHGE (agent of human granulocytic ehrlichiosis, currently unnamed)

* Two of these ticks were co-infected with Bb and aoHGE.

Approximately half of the ticks submitted through the tick test kit service are dead when they arrive at the ESP laboratory. This high rate of mortality is due in large part to trauma sustained by the ticks during the removal process (i.e. damage to their mouthparts), coupled with delay in the mailing procedure (shipping ticks by Federal Express, and sending them promptly following removal from the patient, helps to alleviate this second problem).

As soon as a tick dies, if it is not immediately preserved in some manner (for example by placing it into alcohol or by freezing it), its cells begin to degrade, thereby releasing digestive enzymes that can break down the cell's contents (including any pathogens that might be present). Analysis of dead, unpreserved ticks, therefore, yields equivocal negative results (positive results, on the other hand, are dependable). For this reason, we do not

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analyze the majority of dead ticks at this time; however, because of the higher infection rate (*B. burgdorferi*) associated with *Ixodes* ticks (= greater disease threat), we are analyzing all *Ixodes* ticks, both live and dead specimens. We are finding that the infection rate in dead *Ixodes* specimens is very similar to that for live specimens. As time and resources allow, we hope to start analyzing dead *Amblyomma* and *Dermacentor* ticks soon.

In the meantime, species identification continues to be performed for all ticks, whether

live or dead. This is important information because it is a preliminary indicator of the disease(s) that could be associated with each individual tick bite incident.

If you are a DOD health care provider, and would like your clinic to participate in the DOD Tick Test Kit program, contact Ellen Stromdahl or Sandra Evans at the USACHPPM [DSN 584-3613 or commercial (410) 436-3613] for details and kits. THIS SERVICE IS FREE! ✱

Factory-Treated Uniforms Available Soon - Order Now!

The Defense Logistics Agency has assigned stock numbers for permethrin-treated battle dress uniforms (BDUs). New, untreated uniforms will be factory-treated and assigned the proper stock numbers following treatment and prior to issue. The Defense Supply Center Philadelphia (DSCP) will contract to have the untreated uniforms factory-treated --- that is, once it receives enough orders from customers to make contracting economically feasible. To date, the DSCP has only received a small number of requisitions, and these are being held on backorder until a sufficient number of additional orders are received. So submit your requisitions now!

Factory-treated uniforms will provide protection against arthropod-borne diseases (such as malaria, dengue, tick-borne encephalitis, Lyme disease, and ehrlichiosis, etc.) **for the lifetime of the uniform!** A factory-treated uniform provides the same protection as a uniform that is treated with either the Individual Dynamic Application (IDA) kit (permethrin impregnation kit, NSN 6840-01-345-0237) or the two-gallon sprayer method (NSN 6840-01-334-2666), but **requires no effort on your part!** The treatment is available for woodland temperate BDUs (Type IX), woodland enhanced hot weather BDUs (Type X), and desert BDUs (Type XI). Stock numbers and FY 2000 pricing appears below. For further information on the status of uniform availability, contact James Kane, Defense Supply Center Philadelphia, DSN 444-5608.

Table 1

PERMETHRIN-TREATED BATTLE DRESS UNIFORMS	
Item	FY00 Price
Woodland Temperate (Trousers)	\$ 26.90
Woodland Temperate (Coat)	\$ 26.55
Woodland Enhanced Hot Weather (Trousers)	\$ 28.65
Woodland Enhanced Hot Weather (Coat)	\$ 25.90
Desert (Trousers)	\$ 28.65
Desert (Coat)	\$ 26.95

FOR YOUR INFORMATION

Table 2

PERMETHRIN-TREATED WOODLAND TEMPERATE BDUs (TYPE IX)						
Trousers			Coat			
Size	Length	NSN	Size	Length	NSN	
X-Small	X-Short	8415-01-458-9465	X-Small	X-Short	8415-01-458-8028	
	Short	8415-01-458-9495		Short	8415-01-458-8666	
	Regular	8415-01-458-9518		Regular	8415-01-458-8674	
Short	Long	8415-01-458-9523	Short	XX-Short	8415-01-458-9218	
	X-Short	8415-01-459-0012		X-Short	8415-01-458-8678	
	Short	8415-01-459-0030		Short	8415-01-458-8693	
	Regular	8415-01-459-0035		Regular	8415-01-458-8709	
	Long	8415-01-459-0048		Long	8415-01-458-8716	
	X-Long	8415-01-459-0058		X-Long	8415-01-458-8720	
Medium	X-Short	8415-01-459-0064	Medium	XX-Short	8415-01-458-9229	
	Short	8415-01-459-0132		X-Short	8415-01-458-9012	
	Regular	8415-01-459-0117		Short	8415-01-458-9017	
	Long	8415-01-459-0976		Regular	8415-01-458-9020	
	X-Long	8415-01-459-0940		Long	8415-01-458-9028	
	XX-Long	8415-01-459-0943		X-Long	8415-01-458-9033	
Large	Short	8415-01-459-0946	Large	X-Short	8415-01-458-9054	
	Regular	8415-01-459-0957		Short	8415-01-458-9092	
	Long	8415-01-459-0969		Regular	8415-01-458-9095	
	X-Long	8415-01-459-0981		Long	8415-01-458-9108	
	XX-Long	8415-01-459-0991		X-Long	8415-01-458-9113	
	X-Large	8415-01-459-0997		X-Large	Regular	8415-01-458-9141
	Regular	8415-01-459-1006		Long	8415-01-458-9163	
	Long	8415-01-459-1026				
	XX-Large	8415-01-459-1076				

Table 3

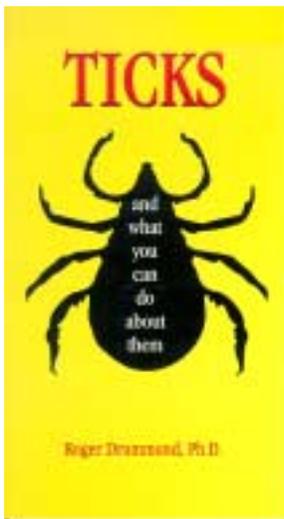
PERMETHRIN-TREATED WOODLAND ENHANCED HOT WEATHER BDUs (TYPE X)					
Trousers			Coat		
Size	Length	NSN	Size	Length	NSN
X-Small	X-Short	8415-01-453-4039	X-Small	X-Short	8415-01-453-7794
	Short	8415-01-453-4610		Short	8415-01-453-7802
	Regular	8415-01-453-4614		Regular	8415-01-453-7806
Small	Long	8415-01-453-4639	Small	Long	8415-01-453-7905
	X-Short	8415-01-453-4644		XX-Short	8415-01-453-7917
	Short	8415-01-453-4646		X-Short	8415-01-453-7963
	Regular	8415-01-453-4647		Short	8415-01-453-7995
	Long	8415-01-453-4692		Regular	8415-01-453-8012
	X-Short	8415-01-453-4700		Long	8415-01-453-8018
Medium	Short	8415-01-453-4712	Medium	X-Long	8415-01-453-8063
	Regular	8415-01-453-4785		XX-Short	8415-01-453-8067
	Long	8415-01-453-4830		X-Short	8415-01-453-8236
	X-Long	8415-01-453-4862		Short	8415-01-453-8284
	XX-Long	8415-01-453-5092		Regular	8415-01-453-8292
	Large	8415-01-453-5223		Long	8415-01-453-8300
	Regular	8415-01-453-5236		X-Long	8415-01-453-8304
	Long	8415-01-453-5245		XX-Long	8415-01-453-8610
	X-Long	8415-01-453-5251		Large	X-Short
X-Large	XX-Long	8415-01-453-5255		Short	8415-01-453-8625
	Short	8415-01-453-7735		Regular	8415-01-453-8636
	Regular	8415-01-453-7741		Long	8415-01-453-8642
	Long	8415-01-453-7748		X-Long	8415-01-453-8645
	X-Long	8415-01-453-7762		XX-Long	8415-01-453-8648
	XX-Long	8415-01-453-7772		X-Large	Short
				Regular	8415-01-453-8677
				Long	8415-01-453-8680

FOR YOUR INFORMATION

Table 4

PERMETHRIN-TREATED DESERT CAMOUFLAGE BDUs (TYPE XI)					
Trousers			Coat		
Size	Length	NSN	Size	Length	NSN
X-Small	X-Short	8415-01-453-2860	X-Small	X-Short	8415-01-453-1348
	Short	8415-01-453-3008		Short	8415-01-453-1393
	Regular	8415-01-453-3035		Regular	8415-01-453-1435
Small	Long	8415-01-453-3045	Small	Long	8415-01-453-1454
	X-Short	8415-01-453-3209		XX-Short	8415-01-453-1478
	Short	8415-01-453-3219		X-Short	8415-01-453-1496
Medium	Regular	8415-01-453-3226	Medium	Short	8415-01-453-2034
	Long	8415-01-453-3239		Regular	8415-01-453-2036
	X-Short	8415-01-453-3290		Long	8415-01-453-2047
Large	Short	8415-01-453-3306	Large	X-Long	8415-01-453-2054
	Regular	8415-01-453-3313		XX-Short	8415-01-453-2128
	Long	8415-01-453-3318		X-Short	8415-01-453-2135
X-Large	X-Long	8415-01-453-3322	X-Large	Short	8415-01-453-2153
	XX-Long	8415-01-453-3333		Regular	8415-01-453-2179
	Short	8415-01-453-3340		Long	8415-01-453-2298
X-Small	Regular	8415-01-453-3347	X-Small	X-Long	8415-01-453-2301
	Long	8415-01-453-3354		XX-Long	8415-01-453-2472
	X-Long	8415-01-453-3762		X-Short	8415-01-453-2482
Small	XX-Long	8415-01-453-3824	Small	Short	8415-01-453-2547
	Short	8415-01-453-3863		Regular	8415-01-453-2577
	Regular	8415-01-453-3869		Long	8415-01-453-2619
Medium	Long	8415-01-453-3873	Medium	X-Long	8415-01-453-2628
	X-Long	8415-01-453-3998		XX-Long	8415-01-453-2636
	XX-Long	8415-01-453-4024		X-Long	8415-01-453-2821
X-Large			X-Large	Short	8415-01-453-2821
				Regular	8415-01-453-2832
				Long	8415-01-453-2855

PUBLICATIONS



Ticks: And What You Can Do About Them

By Roger Drummond, Ph. D.

Paperback – 72 pages, 2nd edition (June 1998), ISBN 0899972225
 Wilderness Press (www.wildernesspress.com),
 2440 Bancroft Way, Berkeley, CA 94704 (800) 443-7227
\$4.95

Roger Drummond was a research scientist with the U.S. Livestock Insects Laboratory, U.S. Department of Agriculture for 30 years (10 years as Director), and now works as a consultant. He has written over 200 scientific articles on the biology and control of ticks and other pests. This is a concise, easy-to-read, handy pocket-sized book that presents practical information on different species of ticks found in the United States, including very useful **maps of their distributions**, discussions on the diseases they carry, how you can protect yourself, and how to control them.

UPCOMING EVENTS

1999

16-19 November 1999

162nd Meeting of the Armed Forces Pest Management Board (AFPMB)

Washington, DC. POC: COL Bob McKenna, AFPMB, Forest Glen Section, Walter Reed Army Medical Center, Washington, DC 20307-5001, (301) 295-7476; DSN 295-7476; FAX: -7473; <http://www-afpmb.acq.osd.mil>

28 November – 2 December 1999

48th Annual Meeting of the American Society of Tropical Medicine and Hygiene (ASTMH)

Washington Hilton and Towers, Washington, DC. POC: Visit the ASTMH website at: <http://www.entsoc.org>. Program Chair: Dr. William Petri, Jr., Room 2115, MR4 Bldg., University of Virginia HSC, Charlottesville, VA 22908, (804) 924-5621; FAX: -0075; E-mail: wap3g@virginia.edu

12-16 December 1999

Annual Meeting of the Entomological Society of America (ESA)

Hyatt Regency, Atlanta, GA. POC: Visit the ESA website at: <http://www.entsoc.org>. ESA, 9301 Annapolis Road, #300, Lanham, MD 20706, (301) 731-4535; FAX: -4538; E-mail: meet@entsoc.org

2000

28 January – 5 February 2000

40th Navy Occupational Health and Preventive Medicine Workshop

Norfolk, VA. POC: Ms. Carol Boston (757) 462-5508, DSN 253-5508; Mr. Richard John -5512; LCDR Sandy Wolff -5575. Or, dial a workshop information line at extension -5423, Navy Environmental Health Center (NEHC), 2510 Walmer Avenue, Norfolk, VA 23513-2617. Visit the NEHC website at: <http://www-nehc.med.navy.mil>, or E-mail: Workshop@nehc.med.navy.mil

19-23 February 2000

71st Annual Meeting of the Eastern Branch of the Entomological Society of America

Sheraton Springfield, Springfield, Massachusetts. POC: William Gimpel, (410) 841-5920; FAX - 5835; E-mail: gimpelwf@mda.state.md.us

24-26 March 2000

13th International Scientific Conference on Lyme Disease and Other Tick-Borne Disorders

Hartford Marriott Farmington, Farmington, CT. POC: Lyme Disease Foundation, Inc. (LDF), One Financial Plaza, Hartford, CT 06103-2601, (860) 525-2000; FAX: -TICK (8425); E-mail: Lymefnd@aol.com, or visit the LDF website at: <http://www.lyme.org>

26-29 March 2000

55th Annual Meeting of the North Central Branch of the Entomological Society of America

Radisson Hotel, Metrodome, Minneapolis. POC: Ted Radcliffe, Department of Entomology, 219 Hodson Hall, 1980 Folwell Avenue, University of Minnesota, St. Paul, MN 55108-6125, (612) 624-9773; FAX: (612) 625-5299; E-mail: radcl001@maron.tc.umn.edu

UPCOMING EVENTS

30 April – 3 May 2000

15th Meeting of the American Society for Rickettsiology (ASR)

South Seas Plantation, Captiva Island, FL. POC: Burt Anderson, Department of Medical Microbiology and Immunology, USF College of Medicine MDC10, 12901 Bruce B. Downs Blvd., Tampa, FL 33612, (813) 974-2608; FAX: -4151; E-mail: banderso@com1.med.usf.edu

25-28 June 2000

84th Annual Meeting of the Pacific Branch of the Entomological Society of America

Double Tree Hotel, Costa Mesa, CA. POC: Contact the ESA, 9301 Annapolis Road, #300, Lanham, MD 20706, (301) 731-4535; FAX: -4538; or visit their website at: <http://www.entsoc.org>

20-26 August 2000

XXI International Congress of Entomology

Iguassu Falls, Brazil. POC: XXI International Congress of Entomology, c/o Dr. Decio Luiz Gazzoni, P.O. Box 231, 86001-970 Londrina-PR, Brazil; website: <http://www.embrapa.br/ic>

3-7 December 2000

Annual Meeting of the Entomological Society of America

Hyatt Regency, Montreal, Canada. POC: ESA, 9301 Annapolis Road, Lanham, MD 20706, (301) 731-4535; FAX: -4538; or visit their website at: <http://www.entsoc.org>



REQUEST FORM

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Comments: _____

Mail or FAX this form to: U.S. Army Center for Health Promotion & Preventive Medicine
ATTN: Entomological Sciences Program/FOCUS On Lyme Disease
5158 Blackhawk Road
Aberdeen Proving Ground, MD 21010-5403
DSN 584-3613; Commercial (410) 436-3613
FAX: -2037; E-Mail: Sandra.Evans @apg.amedd.army.mil



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