VIRGINIA
EPIDEMIOLOGY BULLETIN

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HUMAN EHRLICHIOSIS IN THE UNITED STATES*

Two emerging tick-borne diseases caused by *Ehrlichia* spp. have been recognized in the United States in the last decade: human ehrlichiosis due to *Ehrlichia chaffeensis*, identified in 1986, and human granulocytic ehrlichiosis (HGE), first diagnosed in 1993. Over 400 cases of human ehrlichiosis due to *E. chaffeensis* have been reported in 30 states, primarily in the southeastern and south central regions. To date, fewer than 100 cases of HGE have been confirmed in Connecticut, Massachusetts, Minnesota, Wisconsin and New York. Additional suspect cases are currently being investigated in Maryland, California, and Florida. HGE has been associated with four fatalities and *E. chaffeensis* infections have been associated with nine fatalities.

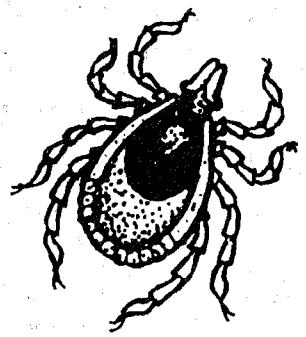
Etiology

Ehrlichiae are obligate intraleukocytic bacteria. Most members of this genus are veterinary pathogens. However, two species are known to cause human disease in the United States, *E. chaffeensis* and the yet-to-be-named etiologic agent of HGE. *E. chaffeensis* has been observed primarily in monocytes/macrophages but, occasionally in lymphocytes and neutrophils. The resultant disease is sometimes referred to as human monocytic ehrlichiosis (HME) to distinguish it from HGE. Human granulocytic ehrlichiosis is so named because the organism has been observed exclusively in granulocytes, primarily neutrophils. The causative agent of HGE was recently isolated by Dr. Jesse Goodman and his associates at the University of Minnesota, School of Medicine. This agent was found to be genetically distinct from *E. chaffeensis*, but closely resembles *E. equi*, which causes disease in horses.[1]

In This Issue:

Clinical Signs and Symptoms

The clinical signs and symptoms of both forms of human ehrlichiosis are similar.



Patients characteristically present with fever, headache (generally unresponsive to analgesic treatment), malaise, muscle aches, chills, sweating, and nausea and vomiting. Less commonly occurring signs and symptoms include cough, joint pains, confusion, and rash. The rash can occur anywhere on the body (not necessarily associated with the site of the tick bite) and is generally macular or papular (see Table, page 2).

Laboratory Findings

Common laboratory findings include thrombocytopenia, leukopenia, and elevated liver function tests. Anemia is noted in approximately half of the cases.

Pathology/Pathogenesis

The most commonly involved organs are the spleen, liver, bone marrow and lymph nodes. Occasional infection is observed in the pulmonary interstitium, adrenal glands, or kidneys. Unlike another common tickborne infection, Rocky Mountain spotted fever, ehrlichiosis is not associated with vasculitis. *E. chaffeensis* has been demonstrated in the cerebrospinal fluid.

Treatment

Antibiotic treatment should immediately be initiated when there is a strong suspicion of ehrlichiosis on the basis of clinical signs and supportive blood profiles. *Treatment should not be delayed until laboratory confirmation is obtained.* Fevers generally subside within 24-48 hours after treatment with doxycycline or other tetracyclines.

There are conflicting reports concerning the efficacy of chloramphenicol. Although chloramphenicol has been used to successfully treat suspected cases of ehrlichiosis, there are anecdotal reports of treatment failures and *in vitro* susceptibility testing of *E. chaffeensis* revealed resistance to chloramphenicol.[2,3] Elderly patients (>60 years old) are more likely to develop severe infections and have accounted for most fatalities. However, complications can occur in any age group, especially when prompt antibiotic treatment is not initiated within a few days after onset of the infection.

Laboratory Detection

The etiologic agent of HGE may occasionally be observed in cytoplasmic inclusions in peripheral granulocytes (especially neutrophils). These inclusions may be observed on routine examination of blood during differential blood counts. In contrast, *E. chaffeensis* is rarely detected by this method.

Infection with either disease is diagnosed more precisely by serologic or mo-

Comparison of HME and HGE[2]		
	HME (%) (n=156-211)	HGE (%) (n=12)
Fever	97	100
Malaise	84	100
Myalgia	68	100
Headache	81	100
Sweating	53	91
Nausea	48	50
Vomiting	37	50
Cough	26	25
Rash	36	8
Confusion	20	42
Percent with tick exposure	83	100
Percent with known tick bite	68	67
Etiologic agent	*E. chaffeensis*	Un-named, *E. equi*-like
Tick vector	*Amblyomma americanum, Dermacentor variabilis*	*Ixodes scapularis D. variabilis*

lecular techniques. Serologic assays for HGE generally use *Ehrlichia equi*, a closely related ehrlichial species, as surrogate antigen. Immunofluorescent assays are currently available at Centers for Disease Control and Prevention (CDC) for HGE and *E. chaffeensis*. Ideally, acute- and convalescent-phase serum specimens, drawn at least 4 weeks apart should be submitted for testing. All samples for testing at CDC should be submitted through the Virginia Division of Consolidated Laboratory Services (see page 3).

Molecular detection of the agent by using the polymerase chain reaction (PCR) can be done when the organism is circulating in the blood. The CDC laboratory currently performs this assay as a research tool, and prior approval by the laboratory is necessary before submitting samples.

Epidemiologic Features

HGE patients identified in the initial published report had evidence of exposure to, or bite by, *Ixodes scapularis* (deer tick) or *Dermacentor variabilis* (American dog tick). Infected *I. scapularis* have been identified by PCR assays in New York, Massachusetts, and Wisconsin. *I. scapularis* is also the vector of human babesiosis *(Babesia microti)* and Lyme disease *(Borrelia burgdorferi)*. HME infection with *E. chaffeensis* is associated with exposure to the lone star tick, *Amblyomma americanum* and possibly *D. variabilis*.

Tick season is approaching - Take precautions
Wear light-colored clothing, tuck pant legs into socks, use insect repellant and regularly check for crawling/attached ticks

The animal reservoir(s) of the HGE agent has not been identified. Naturally infected dogs have been found in areas of Minnesota and Wisconsin, but their role as potential reservoirs of the infection has not yet been determined. White-tailed deer or white-footed mice may also be involved, but further studies are necessary to clarify the natural life cycle of the HGE agent.

Both deer and dogs have been shown to be serologically positive for *E. chaffeensis*. In addition, *E. chaffeensis* has been transmitted from deer to deer by *A. americanum* (lone star tick). White-tailed deer that were experimentally infected were shown to have organisms in their blood for as long as two weeks yet were asymptomatic. The role of these species as potential reservoirs for *E. chaffeensis* has not been fully explored.

Prevention and Control

Because epidemiologic evidence indicates that both forms of human ehrlichiosis are tick transmitted, precautions to prevent tick bites, identical to those recommended for Rocky Mountain spotted fever or Lyme disease, should be taken. These precautions include, but are not limited to, wearing light-colored clothing to allow for greater visibility of crawling ticks, tucking pant legs into socks, regular body examinations, and using insect repellent. Attached ticks should be promptly removed using forceps; ticks should not be removed by hand since infection is possible through cuts in the fingers. An attached tick should be removed by pulling gently, but firmly, backward without twisting. Immediately clean the bite site with a disinfectant.

Current Research

CDC is actively involved in research on these emerging infectious diseases. Studies are under way to assess the distribution of

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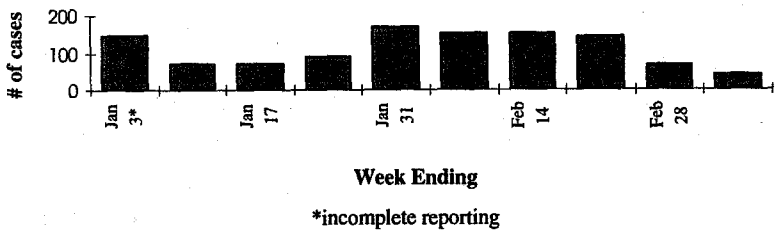
Influenza-like Illness, Virginia
Sentinel Surveillance 95-96



*incomplete reporting

The sentinel physician surveillance for the 1995-1996 influenza season is over. Reports of influenza-like illness have continued to declined since February 7. Influenza A was isolated from all regions of the state; one influenza B isolate was identified in March. The Office of Epidemiology would like to say "Thank You" to all persons who participated in the surveillance system.

human cases and infected ticks, and the natural reservoirs of both agents. Alternative methods for rapid diagnosis and accurate identification of both organisms are being investigated. Through cooperation with other institutions and health professionals, it is hoped that these new tick-borne illnesses can be better understood and dealt with effectively.

For More Information Please Contact:

Office of Epidemiology
Virginia Department of Health
(804)786-6261

Specimen Submission Information:

Samples for serologic testing:
At least 1 ml of serum from acute and convalescent bloods should be submitted for each test requested. Samples should be shipped refrigerated on ice packs to:

Division of Consolidated Laboratories
Virology/Immunology Lab
1 N. 14th Street
Richmond, Virginia 23219

Submission of samples for PCR testing requires prior approval by CDC. Inquiries should be directed to the Office of Epidemiology (804)786-6261. For PCR testing, submit a single EDTA blood sample (3-5 ml) from an acute-phase infection prior to antibiotic treatment. Specimens should be sent refrigerated on ice packs.

** Adapted from the publication "Human Ehrlichiosis in the U.S." Viral and Rickettsial Zoonoses Branch, CDC, 1995.*

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Virginia Ehrlichiosis

Human ehrlichiosis, whether HME or HGE, is not officially reportable in Virginia. We are interested in learning about cases, though, and have been collecting data on identified cases since 1986. Through 1995, 32 cases of human ehrlichiosis have been officially reported to the Office of Epidemiology, all caused by *Ehrlichia chaffeensis*. In addition, we have received anecdotal information regarding nine possible cases on the Eastern Shore. Cases have been identified in all regions of the state except the northern. The age range of cases was from 5 to 87 years, with 56% of cases over the age of 50. More males (25/32) than females were reported and cases were predominantly among whites (white=26, black=5, unknown=1).

Dr. Suzanne Jenkins, the public-health veterinarian in the Office of Epidemiology, has been interested in learning more about the role of dogs as reservoirs for *E. chaffeensis*. In 1991, a serological study was done on 73 dogs from animal shelters and kennels in Virginia. Serum antibodies that reacted to *E. chaffeensis* (34%) and *E. canis* (30%) were identified. Testing of whole blood by PCR revealed eight positives for *E. chaffeensis* and six positives for *E. ewingii* (the cause of canine granulocytic ehrlichiosis).[1]

In 1995, a person who worked in a kennel in southwest Virginia developed human ehrlichiosis. Twenty-five dogs that were associated with the case were tested for evidence of *Ehrlichia* infection. All PCR testing was negative but 21/25 were positive for antibodies to *E. chaffeensis* (titer range = 1:64 to 1:2048). These studies indicate that dogs may play a role in maintaining *E. chaffeensis* organisms in the environment, but more studies need to be done to more thoroughly elucidate this role.

We appreciate receiving reports of human ehrlichiosis cases. Although we have not yet received any reports of HGE, as testing for this disease becomes more common we expect that to change. If you have patients who present with signs and symptoms compatible with an ehrlichial illness and exposure to ticks, we recommend that you include both human monocytic and human granulocytic ehrlichiosis in your differential diagnosis.

Reference

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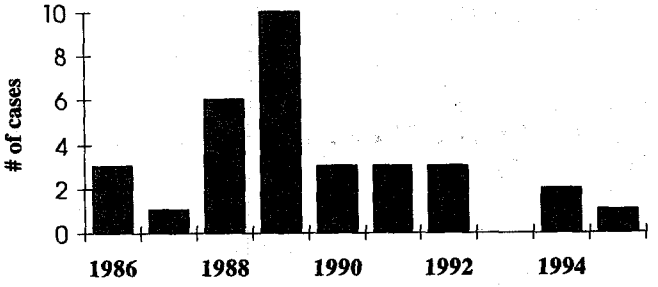
Human Monocytic Ehrlichiosis in Virginia



Cases of Selected Notifiable Diseases Reported in Virginia.*

Disease	Total Cases Reported, February 1996						Total Cases Reported Statewide, January through February		
		Regions							
	State	NW	N	SW	C	E	This Yr	Last Yr	5 Yr Avg
AIDS	95	16	30	8	15	26	149	154	150
Campylobacteriosis	26	12	5	5	4	0	49	59	53
Giardiasis	9	2	3	2	1	1	19	30	39
Gonorrhea	774	27	52	108	171	416	1563	1885	2159
Hepatitis A	8	1	2	3	0	2	10	33	25
Hepatitis B	13	0	4	4	3	2	17	12	24
Hepatitis NANB	1	0	0	0	1	0	1	0	4
HIV Infection	68	7	14	9	12	26	115	131	171
Influenza	36	30	0	2	0	4	162	719	508
Legionellosis	1	1	0	0	0	0	2	0	1
Lyme Disease	0	0	0	0	0	0	0	1	5
Measles	0	0	0	0	0	0	0	0	1
Meningitis, Aseptic	8	0	1	1	1	5	15	20	27
Meningitis, Bacterial†	5	0	2	3	0	0	8	20	18
Meningococcal Infections	8	2	5	1	0	0	11	10	9
Mumps	2	0	1	0	1	0	2	4	8
Pertussis	0	0	0	0	0	0	0	0	3
Rabies in Animals	32	7	5	7	5	8	56	44	40
Rocky Mountain Spotted Fever	0	0	0	0	0	0	0	0	0
Rubella	0	0	0	0	0	0	0	0	0
Salmonellosis	35	4	7	7	8	9	88	120	119
Shigellosis	20	1	10	0	1	8	38	26	39
Syphilis, Early‡	87	1	2	7	24	53	153	185	200
Tuberculosis	23	0	10	1	5	7	25	9	21

Localities Reporting Animal Rabies: Accomack 2 raccoons; Amelia 1 skunk; Appomatox 1 raccoon; Arlington 1 raccoon; Augusta 1 skunk; Bedford 1 skunk; Campbell 1 fox; Chesapeake 1 raccoon; Chesterfield 1 raccoon; Fairfax 2 raccoons; Fauquier 1 raccoon; Franklin County 1 raccoon; Frederick 1 raccoon, 1 skunk; Goochland 1 raccoon; Greene 1 raccoon; Greensville 1 skunk; Henrico 1 raccoon; Loudoun 1 cat, 1 raccoon; Middlesex 1 fox; Northampton 1 raccoon; Pittsylvania 1 cow, 1 skunk; Rockingham 2 skunks; Suffolk 1 raccoon; Tazewell 1 raccoon; Virginia Beach 2 raccoons.

Occupational Illnesses: Asbestosis 20; Carpal Tunnel Syndrome 46; Coal Workers' Pneumoconiosis 8; Lead Poisoning 1; Loss of Hearing 17; Mesothelioma 1.

*Data for 1996 are provisional.

†Other than meningococcal.

‡ Includes primary, secondary, and early latent.

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