Tick Threats

New diseases brought to you by your neighborhood ticks

By TINA ADLER

Did you ever get the sensation, after pulling a tick off your skin, that another one was crawling unseen on your body? Scientists studying tickborne diseases feel rather like that these days. Just when they identify a new, potentially lethal organism that those bloodsuckers spread, a new one crops up.

The latest deadly tick disease, ehrlichiosis, is caused by *Ehrlichia*, a genus of bacteria in the family Rickettsiaceae. Another member of that genus causes Rocky Mountain spotted fever. Researchers first detected *Ehrlichia* in humans in the mid-1980s. In 1990, they identified the specific species doing the dirty work as *E. chaffeensis*. In the May ANNALS OF INTERNAL MEDICINE, investigators at the Centers for Disease Control and Prevention (CDC) in Atlanta published the largest case study of human ehrlichiosis to date. The report describes 237 patients, including three who died from the infection. Only 2 months earlier, another team announced it had discovered in six people from Wisconsin and Minnesota an *Ehrlichia* species never before seen in humans, granulocytic *Ehrlichia*. Two of the six people died.

"I think we are going to keep finding new species. . . .There is a lot of *Ehrlichia* out there," including what may be a new Venezuelan species, says James G. Olson of the CDC. In fact, the CDC now knows of at least 300 people who have developed ehrlichiosis, including nine who died of it. "There are undoubtedly many more" infected individuals whom the CDC has not heard about, he adds.

No one knows how many people have contracted ehrlichiosis. The disease fools physicians, masquerading as Rocky Mountain spotted fever, Lyme disease, a bad cold, even sepsis. Physicians who diagnose it don't necessarily tell the CDC. And not all individuals infected with *Ehrlichia* develop symptoms.

"Probably the vast majority don't get sick or have [only] a mild illness," says the CDC's Jacqueline E. Dawson. Why some people have no symptoms while others become quite impaired remains a mystery. Infections act that way oftentimes, explains E. Dale Everett of the University of Missouri Health Sciences Center in Columbia.

For those who do fall ill, quick treatment is crucial.

Since completing a study last year of 30 patients diagnosed with *E. chaffeensis*, "we've had two more deaths," says Everett. "There was a delay in diagnosis, so they weren't treated as early as we'd have liked," he explains. The dead men—one in his 30s, the other in his 60s—were first seen at hospitals outside Columbia.

Agricultural Research Service—USDA

Two ticks suspected of hosting E. chaffeensis: Ambylomma americanum, *or Lone Star tick, and* Dermacentor variabilis, *or American dog tick.*

Ehrlichia probably infected people prior to the 1990s, but nobody recognized it, researchers assert. Veterinarians have known for years that animals harbor a species of these bacteria. At first, investigators thought that dogs had shared their species, *E. canis,* with their human buddies.

CDC researchers first detected *Ehrlichia* in a man who encountered a lot of ticks while visiting Arkansas. He developed what his doctor originally diagnosed as Rocky Mountain spotted fever. Tests showed, however, that the Arkansas traveler never developed antibodies to the bacterium that causes the disease. But such antibodies don't always show up in people believed to have Rocky Mountain spotted fever, says J. Stephen Dumler of the University of Maryland School of Medicine in Baltimore.

In fact, the case would have received little attention if a pathologist had not noticed unusual aggregates of bacteria hidden in the man's white blood cells. When CDC investigators examined the blood sample, they discovered what seemed to be antibodies to *E. canis*.

The researchers then looked at the blood of other Rocky Mountain spotted fever patients who had not developed antibodies and again found what they thought was *E. canis*. It seemed that a bacterium thought to infect only dogs had crossed species and infected humans.

In 1987, the NEW ENGLAND JOURNAL OF MEDICINE published the first description of the new ailment. Symptoms included fever, headache, muscle pain, nausea, a low number of white blood cells, and poor liver function, among others. Some infected individuals showed no symptoms; others died from the infection. Most lived in the southern United States.

Then, in 1990, CDC researchers discovered subtle differences between the DNA sequence of *E. canis* and that of the bacterium plaguing humans. Since so few *Ehrlichia* infect cells, she and her colleagues had to use a technique known as polymerase chain reaction to grow more of the organisms' DNA to examine.

These findings didn't surprise Dumler, one of the discoverers of granulocytic *Ehrlichia*. "We know that the canine tick

doesn't like to bite humans," he asserts.

The CDC team had detected a new *Ehrlichia*, which they named *E. chaffeensis*. Laboratory tests suggest that deer are also susceptible to the bacterium.

In the MAY ANNALS OF INTERNAL MEDICINE, Daniel B. Fishbein and his CDC colleagues describe human cases of *E. chaffeensis* reported to the center from 1985 to 1990. In the same issue, Everett and his coworkers report on their prospective study of 30 people diagnosed with *E. chaffeensis* in Missouri. Everett's and the CDC's cases resemble each other closely. "The results came out pretty much the same," says Everett.

Individuals with granulocytic *Ehrlichia* have symptoms similar to those found in people infected with *E. chaffeensis*, Sheng-Min Chen of the University of Texas Medical Branch in Galveston and her colleagues report in the March JOURNAL OF CLINICAL MICROBIOLOGY.

All of these people felt sick enough to go to a doctor, so they represent worst-case scenarios of the disease; most were subsequently hospitalized. The patients generally fell ill between April and September. Most recalled having received a tick bite or being in a tick-infested area before becoming sick. According to the CDC report, their symptoms generally appeared about 9 days after the tick bite. Recovery took about 3 weeks.

The people described by the CDC came primarily from rural areas in 21 states. Oklahoma had 57 cases, the highest of any state. Other locales may have had as many or more ehrlichiosis cases but failed to diagnose or report them, the authors note.

Granulocytic *Ehrlichia*'s stomping grounds tend to be in the northern United States, in deer tick country, Chen says. In fact, Dumler and others suspect that the infamous deer tick — which transmits Lyme disease — will soon become even more notorious. They accuse it of carrying the granulocytic *Ehrlichia* as well.

Ehrlichia causes illness by taking up residence in white blood cells, leading to inflammation of blood vessels, Fishbein explains. This inflammation prevents blood from getting to the organs. "We can't really say" what actually kills some people, he acknowledges. Victims tend to develop multiple complications, including lung and kidney problems.

Ehrlichiosis proves tricky to diagnose because of its many, common symptoms, researchers warn. Only about 20 percent of the cases described in the CDC study were initially diagnosed as rickettsial illness. Instead, physicians thought most sufferers had upper respiratory disease, influenza, gastroenteritis, or some other ailment.

Dawson recommends that physicians start by asking patients if they have encountered a tick recently. "A very high percentage of patients do recall being bitten," she says. Researchers have yet to prove that ticks actually chauffeur the bacterium around, but the evidence strongly supports this theory.

Decreased leukocyte and platelet counts, seen in blood tests, differentiate this infection from Rocky Mountain spotted fever. However, "since *Ehrlichia* is potentially a fatal disease . . . the physician doesn't have time to wait for lab results" before beginning treatment, Dawson points out. Tetracycline cures ehrlichiosis, as it does most other tick-borne ailments, and has patients feeling better within 24 to 48 hours, the CDC report states.

Misdiagnosing the disease as Rocky Mountain spotted fever "is not a big problem" since the same antibiotics work for both illnesses, Olson says. "The real problem comes when patients are misdiagnosed as having Lyme disease," which requires different drugs.

"[Polymerase chain reaction] is a very powerful tool" for diagnosing ehrlichiosis, but it's too complicated and sensitive for use in a doctor's office, Dawson says.

Granulocytic *Ehrlichia* appears to act much like *E. chaffeensis*. However, researchers consider it a unique creature, in part because of where it dwells in the body. This pathogen enters the white blood cells called granulocytes, which combat bacteria, Chen and her colleagues point out. *E. chaffeensis* tends to get inside monocytes, white blood cells that help fight viral as well as bacterial infections.

"A remarkable feature was the restriction of the infectious organisms to granulocytes, a finding previously observed in several other patients from this geographic region but rarely in humans with *E. chaffeensis*," Chen and her colleagues write.

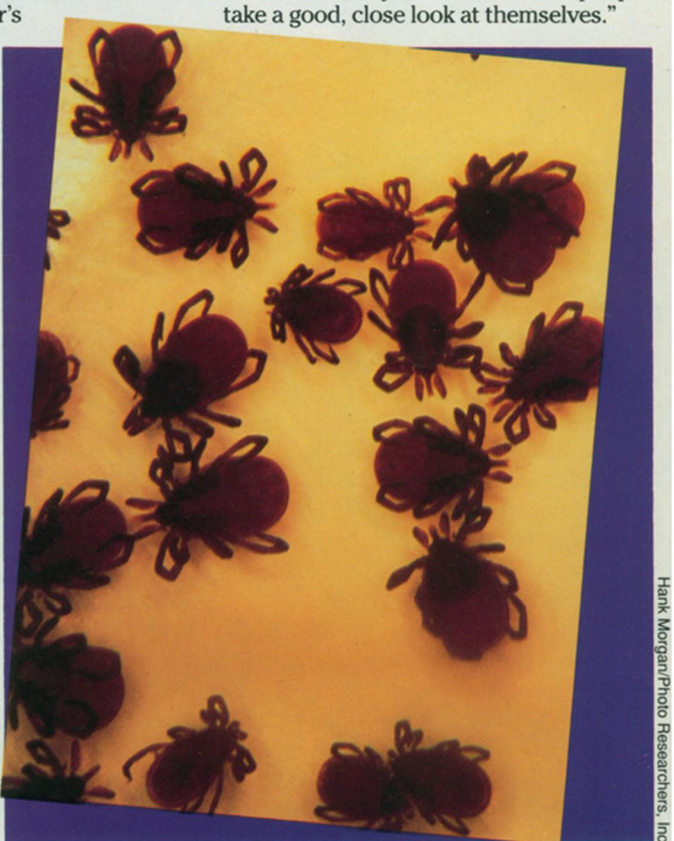
The DNA of this bacterium looks almost exactly like that of *E. phagocytophila*, which infects sheep and cattle, and *E. equi*, which attacks horses, the team finds.

"It is unclear whether all of these organisms are variant strains of a single species or whether they represent two or three *Ehrlichia* species," the investigators note. "The genetic data would suggest they are all members of the same species."

Being unable to grow granulocytic *Ehrlichia* in a cell culture prevented researchers from discovering it sooner, Dumler says. "We only found it because we looked at the DNA."

While tickborne diseases strike more often now than in the past, ticks probably are not carrying any more bacteria, Olson believes. People encounter the jaws of ticks more frequently these days because they spend more time hiking and doing other activities in areas where ticks abound, he and others suggest.

Outdoor enthusiasts can use insect repellents to deter ticks. What's more, "as best we can tell, the ticks have to be attached for about 24 hours to transmit these diseases, so early removal of ticks is very important," Everett advises. "At the end of their day, we recommend people take a good, close look at themselves."



Hank Morgan/Photo Researchers, Inc.

The tiny deer tick, known to cause Lyme disease, is now also a suspect in the potentially deadly granulocytic Ehrlichia.

During such evening grooming sessions, keep in mind Everett's comforting observation: "There are literally hundreds of tick bites for every person who develops a disease." And when contemplating what method of murder to use if you do find a tick, remember Olson's words: "The tick is an innocent reservoir." □