TICKS - A PANDORA'S BOX

Willy Burgdorfer

Even in ancient times, ticks have been looked upon - in the words of Aristotle - as "disgusting parasitic animals" that adversely affect the well being of humans and their domestic animals. According to Pliny (77 AD) "...there is an animal living on blood with its head always fixed and swelling. Being of an animal which has no exit for its food, it bursts with over-repletion and dies from actual nourishment."

Ticks as potential sources and vectors of a pathogen was first established during an outbreak in 1868 of a disastrous epizootic that killed thousands of cattle in Illinois and Louisiana. For a quarter of a century, veterinary and medical scientists struggled with the mysteries of TEXAS FEVER as the disease was called. It was not until 1886 that Dr. Theobald Smith discovered the infectious agent, now known as Babesia bigemina in the erythrocytes of infected cattle. Shortly thereafter he and his associate Dr. Kilbourne solved the complex riddle of the transmission of this agent by the cattle tick, Boophilus annulatus.

A few years later medical attention was directed towards Western Montana where dozens of pioneers and settlers died of a mysterious disease referred to as "black fever", "black measles" or "spotted fever". To determine whether the causative agent had anything to do with the Texas Fever agent, Dr. Howard Taylor Ricketts was sent out to Western Montana to investigate. Ricketts could not confirm the Babesia theory but established that the wood tick, Dermacentor andersoni was the vector of an agent unknown to him. Although Ricketts examined *noninfectious* and infectious ticks, he was not able to differentiate symbiote-like bacteria from the causative agent. This was done 15 years later by Dr. Wolbach who, honoring Ricketts' work, named the agent of spotted fever Dermacentroxenus rickettsii, known today as Rickettsia rickettsii.

So - what are ticks?

According to acarologists and medical entomologists, ticks are classified as arthropods, a biological grouping of invertebrate animals with jointed legs, segmented bodies and external skeleton. Within the arthropod classification ticks are arachnids that include also spiders and mites. Most ticks require at

least 3 hosts to complete their life cycle which consists of 4 distinct developmental stages: the egg, larva, nymph and adult. Some ticks parasitize only one or two hosts. Each of the three parasitic stages i.e., larva, nymph and adult requires a blood meal for further development.

According to tick taxonomists, about 850 species have been identified. Of these about 100 have been shown capable of transmitting pathogens such as bacteria, viruses protozoa and toxin.

Although the distinctive biological and physiological properties of ticks and interactions between hosts permit them to act as reservoirs for several of these pathogens, there are many intrinsic and extrinsic biological factors that restrict or contribute to the success of a tick species to serve as an efficient vector. For instance, the long life cycle of ticks versus the short life span of small mammalian host is a biological phenomenon with epidemiological importance in the survival of infections in nature. Indeed, ticks are long-lived. Many if not most have life cycles that extend for years. Certain Ornithodoros species (vectors of relapsing fever spirochetes), for instance, have been known to survive for more than 30 years without a blood meal.

Other biological factors of important epidemiological implications include (a) transstadial development which is the passage of a pathogen from one developmental stage to another, and (b) transovarial transmission which is the passage of a pathogen via eggs of an infected female. This phenomenon is extremely important for the maintenance and distribution of a pathogen in nature. It has first been observed by Smith and Kilbourne for Babesia bigemina in the cattle tick, Boophilus annulatus and by Ricketts for the spotted fever agent in the wood tick, Dermacentor andersoni and, (c) venereal transmission which is the infection of female ticks and their eggs via pathogen-laden sperm cells of infected male ticks. This phenomenon occurs rarely and is not considered an important means for infecting tick females and their eggs in nature.

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Ticks are the most important biological vectors of human and animal disease agents including viruses, rickettsiae, spirochetes, protozoa and even microfilaria. The handout summarizes the tick-borne diseases in the United States. They are vectored by one or more species of ticks of the genera Dermacentor, Ixodes, Amblyomma, Rhipicephalus and Ornithodoros.

The infection of ticks with pathogens takes place during feeding on an infectious vertebrate host or in rare instances also through cannibalism i.e., the feeding of one tick on another.

The ingested host blood flows through the pharyngeal cavity and oesophagus into the midgut and its diverticula. There it is dehydrated and its fluid components are passed through the midgut epithelium into the hemolymph. The erythrocytes of the host blood are digested and the hemoglobin is crystallized. These crystals are then subjected to intracellular and extracellular digestion in the gut lumen as well as in epithelial cells.

Although practically every species of tick can receive infectious agents into its digestive tract, the capacity for survival and transmission for further developmental stages or to a vertebrate hosts is the property of certain specific tick species. This property has been claimed to be determined genetically in the course of the phylogenesis of certain ticks. On the other hand, successful and long-lasting infections of ticks often depend on concentrations of pathogens ingested. These concentrations should be large enough to establish a threshold infection necessary for the survival and development of pathogens. To give an example: Between 10 and 100 guinea pig infectious doses per 0.5 ml of blood are necessary to infect 50% of feeding larval Demacentor *andersoni* with Rickettsia rickettsii. Ticks feeding during periods of high rickettsemias have high infection rates whereas those feeding during periods of low rickettsemias have low rates or do not become infected at all.

When ingested in sufficient quantities, viruses, bacteria, etc. may overcome the midgut barrier and penetrate the gut wall into the hemocele where they are taken up by plasmatocytes or where they invade the hemocytes and tissues of the various organs including the salivary glands.

In many instances vector specificity - probably genetically determined - prevents the survival and development of a pathogen. A striking example is provided by the inability of ticks to become vectors of rabies virus which will survive in the gut lumen for only 14 days without further development. The typhus rickettsa, R. prowazekii to name another example is usually associated with the body louse, Pediculus humanus humanus. All attempts to infect ticks with this agent have failed. Transient midgut infections have

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been recorded but the rickettsiae were not able to invade and penetrate the gut epithelium.

Most tick-borne pathogens that survive the midgut barrier produce in their vectors a systemic or generalized infection, i.e. all tissues such as salivary glands, Malpighian tubules, central ganglion, hypodermal tissues and those of the genital systems (ovary, testes) become heavily infected and may remain so for the rest of the tick's life.

In contrast are infection patterns in certain species of Ixodes ticks that only recently (1981) had been shown to be efficient vectors of spirochetes causing Lyme disease. Never before had spirochetes been associated with Ixodes spp until your speaker discovered them in the midgut of Ixodes scapularis (= I. dammini) and identified them as the long sought cause of Lyme disease. One of the reasons that this organism now known as Borrelia burgdorferi had escaped attention by investigators is the fact that its initial distribution in more than 90% of infected ticks is limited to the midgut where it aggregates in pit-like structures between epithelial cells. Ingestion of blood initiates spirochetal development and penetration of the gut wall and subsequent distribution via hemolymph into various tissues including salivary glands and ovary.

Massive spirochetal infections have occasionally been recorded in ovarian tissues of infected I. scapularis females that, however, failed to oviposit or laid only small batches of eggs that did not develop. Electronmicroscopic examination of ovarian tissues from such females revealed massive spirochetal invasion of developing oocytes. As illustrated on the next slide numerous spirochetes may be present between the vitelline and oocyte membranes where they destroy the microvillar processes responsible for the formation and deposition of the egg cuticle. Eggs so affected fail to mature and prevent oviposition.

Nevertheless transovarial transmission of B. burgdorferi has occasionally been reported but appears to be of minor significance in the maintenance and distribution of infected ticks in nature.

All tick vectors with systemic infections transmit their pathogens via saliva during the early phase of the feeding process that may last from 3 to 30 minutes for ticks of the genus Ornithodoros (vectors of tick-borne relapsing

fevers) and from 2 to 8 days for all other tick species referred to in the handout.

Because the initial infection in the Lyme disease vectors is limited to the tick's midgut, the transmission of the causative spirochetes is delayed awaiting stimulation and multiplication by the tick's feeding. This will activate the spirochetes to migrate from the midgut through the gut wall into the hemolymph and eventually into the salivary glands from where they are injected via saliva into a host.

Because of this delay, tick bites of short duration have been considered noninfectious. This, in my opinion, is a false and risky conclusion in view of the many accounts of Lyme disease having been contracted after only a few hours of tick attachment and/or feeding. Indeed the offending tick may have a systemic infection prior to feeding or may transmit spirochetes by regurgitation of infectious gut material.

There is no such a thing as a "normal" tick. Every specimen regardless of species or geographical distribution harbors bacterialike symbiotes that may or may not affect the host.

Therefore, a tick attached to one's skin has to be removed without delay. To do this properly, use curved forceps or pointed tweezers - grasp the hypostome of the tick as close to the skin as possible and pull upward with steady pressure. Because a feeding tick is inserted into the skin by its hypostome whose posteriorly directed denticles firmly secure it, removal may require repeated attempts.

Do not twist the tick - it may break apart leaving it partly lodged in the skin.

Do not prick, crush or burn the tick - tick juices may contaminate the bite wound.

Do not apply petroleum jelly, mineral oil or fingernail polish - these products are ineffective in dislodging a tick.

Do not use bare fingers to remove the tick; if you must do so, protect your fingers with tissue papers. Be careful not to crush the tick.

Be sure to wash your hands and disinfect the bite wound. Once a tick is removed, it is placed into a pill box or other small container along with information about the person bitten, the date of the bite, and the location where the tick most likely had been contracted. The boxed tick should then be stored at a readily visible site to remind a person becoming ill within 2 to 3 weeks that the condition may be tick-associated and that it is time to consult a physician.

In concluding today's discussion, I would like to refer briefly to Human Ehrlichioses as a recently emerged new group of tick-borne diseases in the U.S.

Human monocytic ehrlichiosis (HME), discovered in 1986 is caused by Ehrlichia chaffeensis and is transmitted by the lone-star tick, Amblyomma americanum and the dog tick, Dermacentor variabilis.

A closely related disease is the Human granulocytic ehrlichiosis (HGE) whose agent as yet unnamed, is said to be transmitted by the black-legged tick, Ixodes scapularis and the American dog tick, Dermacentor variabilis.

Practically nothing is known about the development of these agents in their tick vectors and on their natural history. Intensive research on these subjects is in progress and undoubtedly will soon shed light on the pathogen/vector relationship of these agents.

Burgdorfer - Ticks: A Pandora's Box

Established tick-borne diseases of humans and/or animals in the United States

NAME	AGENT	TICK VECTOR(S)	GEOGRAPHIC DISTRIBUTION
Lyme disease	*Borrelia burgdorferi*	*Ixodes scapularis (=dammini)* *I. pacificus*	Northeastern and midwestern United States, California
	B. lonestari	*Amblyomma americanum*	Oregon, southern and southeastern U.S., southern and eastern U.S.
Rocky Mountain spotted fever	*Rickettsia rickettsii*	*Dermacentor andersoni* *D. variablilis* *A. americanum*	Throughout U.S. except Maine, Alaska, Hawaii
Tick-borne relapsing fever	*B. hermsii* *B. turicatae* *B. parkeri*	*Ornithodoros hermsi* *O. turicata* *O. parkeri*	Northwestern U.S., southern Canada, southwestern U.S. Western U.S.
Colorado tick fever	CTF virus	*D. andersoni*	Rocky Mountain region
Powassan encephalitis	*Encephalitis virus*	*D. andersoni* *Ixodes* spp.	U.S., Canada
Tularemia	*Francisella tularensis*	*D. andersoni* *D. variabilis* *A. americanum*	Throughout U.S., especially Missouri, Kansas, Tennesee, Kentucky, Arkansas, Oklahoma, Illinois, Texas, Colorado, Utah
Human babesiosis	*Babesia microti*	*I. scapularis* other tick spp.	Massachusetts, New York, Rhode Island, Wisconsin, Mexico
Tick paralysis	Toxin (unidentified)	*Dermacentor* spp.	Northwestern and eastern U.S., western Canada
Human monocytic ehrlichiosis (HME)	*Ehrlichia chaffeensis*	*A. americanum* *D. variabilis*	Southeastern U.S.
Human granulocytic ehrlichiosis	unnamed	*I. scapularis* *D. variabilis*	Midwestern U.S.
Canine ehrlichiosis	*E. canis*	*Rhipicephalus sanguineus*	Southern and Southwestern U.S.
Equine ehrlichiosis	*E. equi*	*Dermacentor* spp. *I. pacificus* *A. americanum*	California, Illinois, Colorado, Florida
Potomac horse fever	*E. risticii*	??	Throughout U.S.
Anaplasmosis	*Anaplasma marginale*	*Dermacentor* spp.	Western and southern U.S.
Epizootic bovine abortion	*B. coriaceae*	*O. coriaceus*	Western U.S.

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Willy Burgdorfer, PhD, MD (Hon.) 3/18/98

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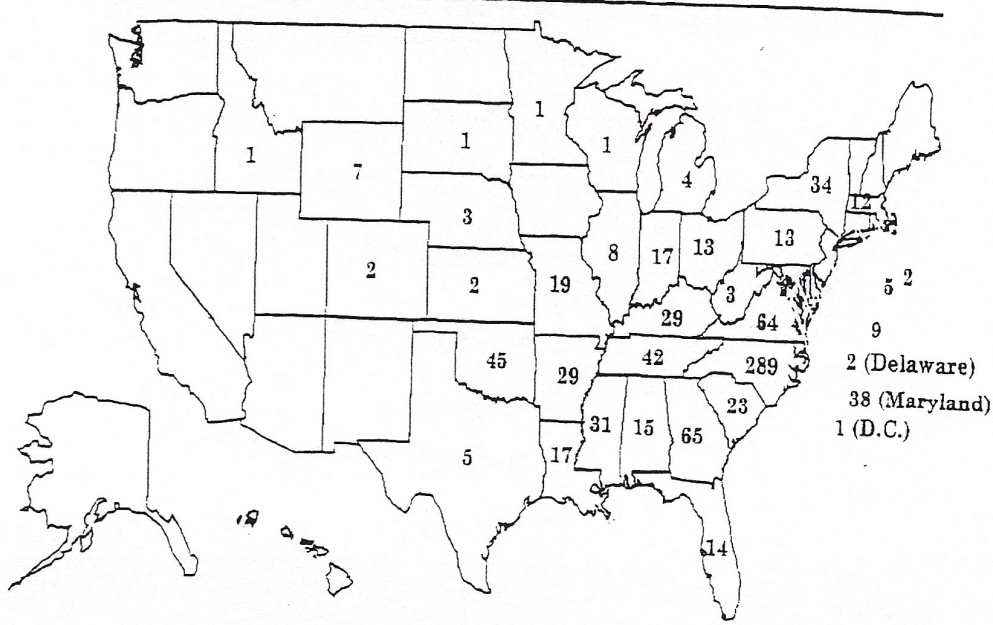
Lyme disease	*Borrelia burgdorferi* *B. lonestari*	*Ixodes scapularis (=dammini)* *I. pacificus* *Amblyomma americanum*	Northeastern & midwestern U.S., California, Oregon, southern & southeastern U.S., southern & eastern U.S.
Rocky Mountain spotted fever	*Rickettsia rickettsii*	*Dermacentor andersoni* *D. variablilis* *A. americanum*	Throughout U.S. except Maine, Alaska, Hawaii
Tick-borne relapsing fever	*B. hermsii* *B. turicatae* *B. parkeri*	*Ornithodoros hermsi* *O. turicata* *O. parkeri*	Northwestern U.S., southern Canada, southwestern U.S. Western U.S.
Colorado tick fever	CTF virus	*D. andersoni*	Rocky Mountain region
Powassan encephalitis	*Encephalitis virus*	*D. andersoni* *Ixodes spp.*	U.S., Canada
Tularemia	*Francisella tularensis*	*D. andersoni* *D. variabilis* *A. americanum*	Throughout U.S., especially Missouri, Kansas, Tennesee, Kentucky, Arkansas, Oklahoma, Illinois, Texas, Colorado, Utah
Human babesiosis	*Babesia microti*	*I. scapularis* other tick spp.	Massachusetts, New York, Rhode Island, Wisconsin, Mexico
Tick paralysis	Toxin (unidentified)	*Dermacentor* spp.	Northwestern & eastern U.S. western Canada
Human monocytic ehrlichiosis (HME)	*Ehrlichia chaffeensis*	*A. americanum* *D. variabilis*	Southeastern U.S.
Human granulocytic ehrlichiosis	unnamed	*I. scapularis* *D. variabilis*	Midwestern U.S.
Canine ehrlichiosis	*E. canis*	*Rhipicephalus sanguineus*	Southern & Southwestern U.S.
Equine ehrlichiosis	*E. equi*	*Dermacentor* spp. *I. pacificus* *A. americanum*	California, Illinois, Colorado, Florida
Potomac horse fever	*E. risticii*	??	Throughout U.S.
Anaplasmosis	*Anaplasma marginale*	*Dermacentor* spp.	Western & southern U.S.
Epizootic bovine abortion	*B. coriaceae*	*O. coriaceus*	Western U.S.

Vectors of Tick-borne Disease

Hard Ticks

Name	Location	Diseases
Amblyomma americanum (lone star tick)	southern, south-central states	ehrlichiosis, Lyme disease, RMSF tularemia
Dermacentor andersoni (Rocky Mountain wood tick)	western and mountain states	CTF, RMSF, tularemia
Dermacentor variabilis (American dog tick)	all U.S. except mountain states	RMSF, tularema
Ixodes pacificus (Western black-legged tick)	Pacific coast	babesiosis, Lyme disease, ehrlichiosis
Ixodes scapularis (black-legged tick)	Eastern U.S.	babesiosis, Lyme disease

Rocky Mountain Spotted Fever in the United States, 1996*



n = 831 cases in 41 states plus the District of Columbia

Rocky Mountain Spotted Fever / Spotted Fever Group Rickettsioses

- **Etiologic agents:** *Rickettsia rickettsii, Rickettsia* species
- **Vectors:** *Dermacentor* species, *Amblyomma* species
- **Reservoirs:** small mammals, ticks

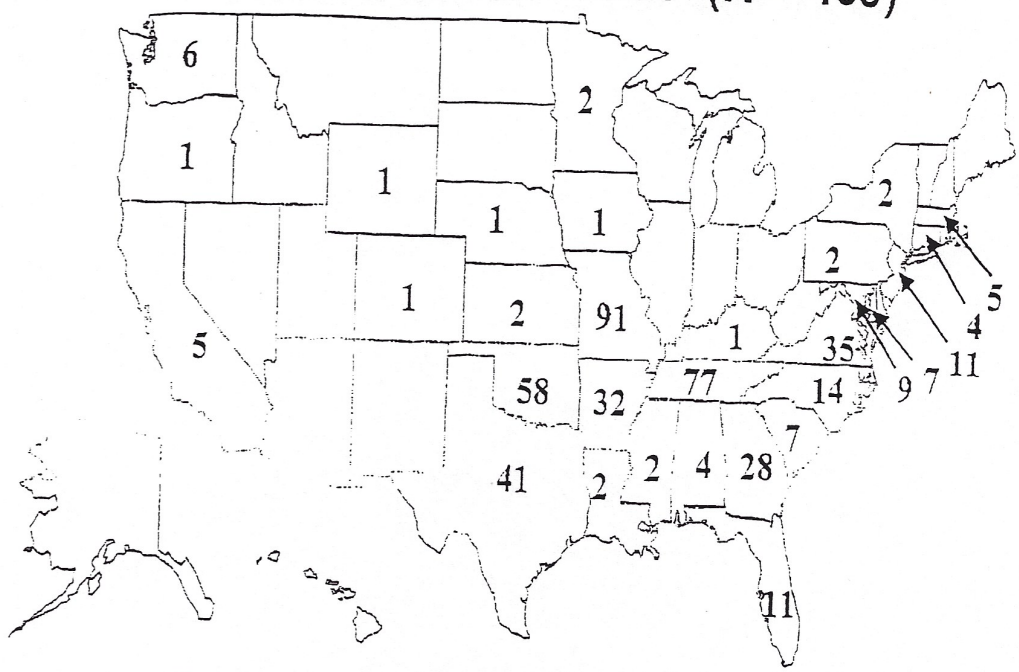
Rocky Mountain Spotted Fever / Spotted Fever Group Rickettsioses

Signs and symptoms*

- sudden onset of flu-like symptoms including high, spiking fever and headache
- maculopapular or petechial rash
- complications include pneumonitis, myocarditis, renal failure, encephalitis, gangrene of the extremities

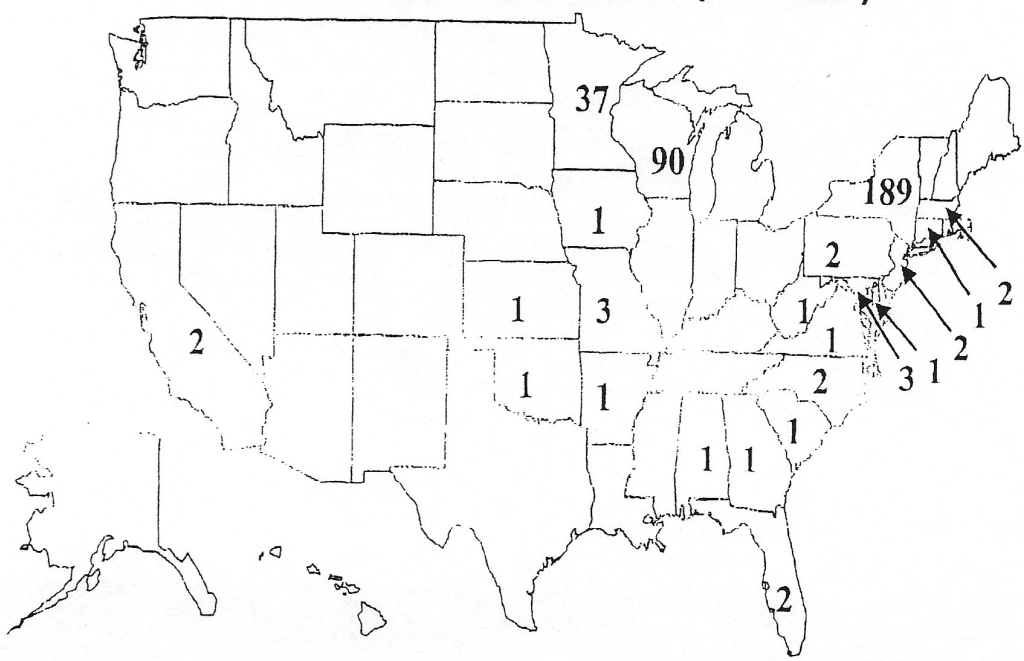
*incubation period: usually 5 to 7 days (range of 3 to 14 days)

Confirmed Cases of Human Monocytotrophic Ehrlichiosis, 1985-1996 (N = 469)



Data for states other than Texas contributed by CDC.

Confirmed Cases of Human Granulocytotrophic Ehrlichiosis, 1990-1996 (N = 344)



Data contributed by CDC, Drs. Bakken, Persing, and Wong

Ehrlichiosis

- **Etiologic agents:** *Ehrlichia chaffeensis, Ehrlichia* species
- **Vectors:** *Amblyomma americanum, Ixodes scapularis,* possibly other species
- **Reservoirs:** small-, medium-, and large-sized mammals

Ehrlichiosis

Signs and symptoms*

- sudden onset of high fever, headache, myalgias, malaise
- leukopenia
- thrombocytopenia
- elevated liver enzymes
- maculopapular or petechial rash may be present
- complications include ARDS, renal failure, liver damage, secondary opportunistic infections

*incubation period: about 10 days

Babesiosis

- **Etiologic agents:** *Babesia microti, Babesia* species
- **Vectors:** *Ixodes* species
- **Reservoirs:** white-footed mouse, other mammals

Babesiosis

Signs and symptoms*

- gradual onset of flu-like symptoms with irregular fever
- mild to severe hemolytic anemia
- severe infections in asplenic patients

*incubation period: 1 to 6 weeks.

Tularemia

- **Etiologic agent:** *Francisella tularenis*
- **Vectors:** *Dermacenter andersoni, D. variabilis, Amblyomma americanum;* also deerflies (*Chrysops discalis*)
- **Reservoirs:** rabbits, hares, rodents, ticks

Tularemia

Signs and symptoms*

- sudden onset of fever
- with tick-borne disease, regional lymphadenopathy with or with out ulcerated skin lesion
- complications include secondary pneumonia, mild hepatitis, pharyngitis

*incubation period: usually 3 to 5 days (range of 1 to 14 days)

Colorado Tick Fever

- **Etiologic agent:** double-stranded RNA virus
- **Vector:** *Dermacentor andersoni*
- **Reservoir:** small mammals

Colorado Tick Fever

Signs and symptoms*

- sudden onset of acute febrile illness with diphasic fever
- leukopenia
- thrombocytopenia
- complications include meningoencephalitis, hemmorhage, pericarditis, pneumonitis, hepatitis

*incubation period: 3 to 6 days.

Proper Tick Removal

- Remove tick as soon as possible.
- Use tweezers to grasp tick at attachment site as close to skin as possible.
- Without twisting, gently pull tick out using slow, steady pressure.
- If removal with fingers is necessary, use protective barrier to avoid contact with tick fluids.
- Do not apply hot matches, nail polish, petroleum jelly, or other chemicals to tick.
- Do not crush, squeeze, or puncture tick
- Carefully clean site with soap and water.
- Send ticks for identification and testing.

Prevention of Tick-borne Disease

- Wear light-colored clothing so ticks are more easily seen.
- Wear long-sleeved shirts and long pants; tuck shirts into pants and pants into socks.
- Use insect repellants and acaracides applied to the skin (i.e. DEET) or clothing (i.e. permethrin).
- Stay in the middle of trails.
- Periodically examine skin, clothing, hair.
- Inspect and remove ticks from pets frequently.

Prevention of Tick Bites around the House

- Mow grass often.
- Prune trees and remove shrubby overgrowth.
- Clear away wood, garbage, and leaf piles.
- Remove stone walls.
- Fence property.