SUMMER NEWSLETTER 2010



Highlights...

Scroll down to see these features and more!

- State Department of Public Health tick activities
- Letter from TIC-NC about Lyme disease published in medical journal
- TIC-NC featured in UNC Health Newsletter
- Letter in medical journal on efficacy of prophylactic treatment of tick bites for Lyme disease-- not a good idea
- YouTube video on Bartonella infections
- Severe Allergic Response Hours after Eating Red Meat; Antigens Stimulated by Tick Bites are Suspected Cause
- Stop getting ticks: send in your own clothes for Insect Shield treatment, form attached

Quote of the month... "The small tick in my armpit remained attached long enough for my body to mount an inflammatory response (itching, swelling and pain) before I noticed and removed it "

-- Ed Breitschwerdt, D.V.M

STATE VECTOR-BORNE DISEASE TASK FORCE MEETING **SCHEDULE**

In 2010 the remaining Vectorborne Task Force meeting dates are:

• Oct 22, Environmental Health Training Room, 1A 224 at 2728 Capital Blvd, Raleigh

Each meeting is on Friday and will meet from 10 AM until 12 PM. The meetings are open to the public.

The state has recently revised their tick-related brochures. Another revision is due soon. They can be accessed at: http://www.deh.enr.state.nc.us/phpm/brochures.htm

ROCKY MOUNTAIN SPOTTED FEVER IN A TICK RESEARCHER IN SPITE OF CAREFUL TICK CHECKS

A tick expert's bite June 7, 2010 News & Observer

RALEIGH I have studied tick-borne infectious agents for more than two decades - directing a vector-borne infectious disease diagnostic laboratory and a tick-borne disease research lab at N.C. State's College of Veterinary Medicine since 1982 - and I am very familiar with the potential outcomes of tick-transmitted diseases, which can include rapid onset illnesses or death or induction of chronic and insidious symptoms.

Consequently, I do "tick checks" after outdoor activity on my farm, but I recently missed one.

When I discovered the tick, I followed recommendation I've given to hundreds of individuals in lectures on tick-borne pathogens. I placed the parasite in a vial of alcohol and wrote the date of its removal on the label. This is an important step, as there are at least four tick species that attach to animals and people in North Carolina, and each species can transmit different bacteria that collectively cause a spectrum of diseases. Knowing the species can help the physician or veterinarian understand which infectious agent has been transmitted.

Tick size can be misleading. Each species has several life stages, so when someone says they found a small tick and presumes it is a "deer tick" (Ixodes scapularis, which transmits Lyme disease) this can be meaningless. Also, only female ticks become engorged (the big, fat, blood-filled tick frequently found on dogs, deer and other animals). Following a blood meal, the mother tick detaches and lays a few thousand eggs to produce larval ticks. So assuming that because a tick is small it did not feed long enough to transmit bacteria is a dangerous assumption.

The small tick in my armpit remained attached long enough for my body to mount an inflammatory response (itching, swelling and pain) before I noticed and removed it. Not initially feeling an attached tick is the norm, since ticks have evolved the ability to secrete chemicals that block pain and decrease the body's inflammatory response.

Symptoms develop in seven to 14 days following transmission of most tick-borne organisms. If a person is healthy two weeks after an attachment episode, it is unlikely that the stored tick transmitted an organism that would induce disease.

Nine days after removing my tick I developed severe chills. The next day my symptoms progressed to include fever, muscle pain and headache - classic symptoms of Rocky Mountain spotted fever and human granulocytic or monocytic ehrlichiosis, the three most serious and frequent tick-transmitted diseases of dogs and people in the southeastern United States.

Typical of the early stages of these diseases, my white blood cell count (the body's first line of defense) was low. My bone marrow responded by sending new white blood cells to fight the infection. After blood was obtained for diagnostic testing, antibiotic treatment was started immediately. This is of critical importance, as a delay in diagnosis and initiation of antibiotics for 24-48 hours greatly increases the severity of illness and the chances of death.

One major focus of our ongoing research at the College of Veterinary Medicine is the development of sensitive and rapid diagnostic tests for the detection of tick-transmitted infectious agents in patient samples (animals and human patients). While I received an antibiotic early in my illness, we still tested my blood for DNA evidence (i.e., detecting specific gene

targets of the infectious agents). Within hours we learned that both the tick and my blood contained Rickettsia DNA. This, in conjunction with the rash on my arms and legs, indicated Rocky Mountain spotted fever. In some instances ticks transmit more than one infectious agent, which complicates diagnosis and treatment. Fortunately for me, tests for other organisms were negative.

North Carolina, along with Oklahoma, generally reports the highest number of Rocky Mountain spotted fever cases each year. Approximately 6 percent of those who contract the disease die. When death occurs, it is usually due to a delay in medical care or because of a failure to recall and report a tick attachment. Unfortunately it is not unusual for a tick to bite, transmit an infectious agent and detach without the individual knowing that he or she was bitten.

As a veterinary internist, I took an oath to protect animal and human health. I appreciate the importance of One Health - how ecosystem health and health of wildlife, domestic animals and people are linked. I take ticks and the diseases they transmit very seriously.

This recent experience enhanced my belief that tick-transmitted diseases deserve respect and enhanced, comparative biomedical research. The next time you walk in the beautiful fields and valleys of North Carolina, apply a tick repellent and remember to check carefully for attached ticks when you return home. Ed Breitschwerdt, D.V.M., is professor of medicine and infectious diseases in the College of Veterinary Medicine at N.C. State University and adjunct professor of medicine at Duke University Medical Center.

FREE ACCESS ARTICLE ON ISSUES WITH CLINICAL PRACTICE GUIDELINES

The Infectious Diseases Society of America Lyme guidelines: a cautionary tale about development of clinical practice guidelines Lorraine Johnson and Raphael B. Stricker

Philosophy, Ethics, and Humanities in Medicine 2010, **5:**9doi:10.1186/1747-5341-5-9

Provisional Abstract: Flawed clinical practice guidelines may compromise patient care. Commercial conflicts of interest on panels that write treatment guidelines are particularly problematic because panelists may have conflicting agendas that influence guideline recommendations. Historically, there has been no legal remedy for conflicts of interest on guidelines panels. However, in May 2008, the Attorney General of Connecticut concluded a ground-breaking antitrust investigation into the development of Lyme disease treatment guidelines by one of the largest medical societies in the United States, the Infectious Diseases Society of America (IDSA). Although the investigation found significant flaws in the IDSA guidelines development process, the subsequent review of the guidelines mandated by the settlement was compromised by a lack of impartiality at various stages of the IDSA review process. This article will examine the interplay between the recent calls for guidelines reform, the ethical canons of medicine, and due process considerations under antitrust laws as they apply to the formulation of the IDSA Lyme disease treatment guidelines. The article will also discuss

pitfalls in the implementation of the IDSA antitrust settlement that should be avoided in the future. Link to entire article: http://www.peh-med.com/content/pdf/1747-5341-5-9.pdf

STATE TICK-BORNE DISEASE ACTIVITIES 2009 TO PRESENT

Much of the state's work was made possible through activities organized by DENR PHPM, particularly Marcee Toliver. The outstanding job of characterizing tick distribution in NC via environmental sampling and attachment studies and information on this work can be viewed at: http://www.deh.enr.state.nc.us/phpm/ticks_projects.htm. Additionally DENR has worked closely with the Vector Borne Disease Diagnostic Laboratory

(http://www.cvm.ncsu.edu/vth/ticklab.html) and they have presented results of their work at prior vector borne work group meetings. Below is a timeline of some Department of Public Health activities:

- On Aug 29th 2009 Dr Carl Williams participated with DENR staff to provide vector borne disease education to the public at the Fiesta del Pueblo health and fitness fair at the NC Fairgrounds.
- On Sep 16th 2009 Carl Williams, Jodi Reber, and Marcee Toliver gave and in-service on tickborne disease prevention, treatment and diagnosis and rabies risk assessment to providers and LHD staff, in Rockingham and Caswell counties.
- On Oct 14-15 2009 Carl and Jodi gave a presentation on diagnosis and reporting of LaCrosse encephalitis at Mission Hospitals pediatric grand rounds and subsequently gave a presentation on LaCrosse and tickborne diseases to Mission Hospital Infection Control Practitioners and to the Swain and Haywood County health departments.
- On Oct 21st Dr. Davies gave a presentation on tick borne disease prevention, diagnosis and surveillance at ECU pediatric grand rounds.
- On Nov 6th Dr. Williams presented on Lyme disease in companion animals and the utility of dogs as sentinels for Lyme disease at the annual North Carolina Veterinary Conference
- On Nov 13th Dr. Williams and Marcee presented an update on tickborne diseases in North Carolina at the Terrence Lee Memorial Symposium in Asheville at MAHEC/Mission Hospital.
- On Nov 16th Dr. Williams and Dr. Davies presented a Lyme disease and STARI update at Duke University grand rounds.
- On Feb 16th 2010 Jodi conducted an in-service for the Wake County Health Department CD staff. They were trained on case reporting and investigation of tick borne diseases
- On March 17th the DPH issued a press release to alert clinicians and citizens that Lyme disease can be acquired in NC. Recent cases in Wake county led to the designation of that county as endemic for Lyme disease for surveillance purposes (see: http://www.dhhs.state.nc.us/pressrel/2010/2010-3-17-wakelyme.htm).
- On Apr 7th Jodi provided a training session on tick borne diseases for UNC HealthLink staff. For reference UNC HealthLink is a free service of UNC Health Care. HealthLink provides quick, easy access to the resources and expertise of our doctors and staff.

- On April 20th the Chatham County Health Department hosted an educational symposium for health care providers in the county at a Pittsboro restaurant. Dr. Davies, Dr. Williams, and Dr. Paul Mead (from the CDC) presented on tickborne disease prevention, treatment, diagnosis and reporting.
- On May 1st Governor Perdue proclaimed May as Tick and Mosquito awareness month based on input from many parties including DPH and DENR (see: http://www.governor.state.nc.us/NewsItems/ProclamationDetail.aspx?newsItemID=1049
- On May 4th Dr. Davies, Secretary Freeman from DENR and Lt. Governor Walter Dalton announced the NC winners of the Fight the Bite poster contest (see: http://www.fightthebitecontest.org/). DPH and DENR staff worked to provide curriculum resources to the Department of Public Instruction and to encourage teachers to have their students participate in the contest.
- With DENR staff Marcee Toliver and Dr. Harrison, Carl participated in a Vectorborne disease and rabies awareness symposium at Camp Lejeune Naval Hospital on May 5th and 6th. Military medical providers and preventive medicine specialists were provided training on tick and borne and mosquito borne disease prevention, investigation and reporting. Also information was provided on rabies risk assessments.
- On May 12th the DPH issued two memos to providers detailing the importance of surveillance for tick borne rickettsial diseases, arboviral diseases, and Lyme disease.
- Dr Williams participated with DENR staff and served at a health fair on May 13-16 for the North Carolina National Guard Yellow Ribbon Program. Information was provided on Vectorborne diseases.
- On May 23rd Dr. Haskell participated with DENR staff to provide vector borne disease education to the public at the WRAL health and fitness fair at the NC Fairgrounds.
- Dr Williams conducted an in-service for the Albemarle Regional Health Services CD staff on June 17th. They were trained on prevention and investigation of tick borne diseases and rabies risk assessment.
- On Jun 23rd Jodi conducted an in-service for the Johnston County Health Department CD staff. They were trained on case reporting and investigation of tick borne diseases.

ARTICLE ON EFFECTIVENESS OF CERTAIN HERBS ON LYME DISEASE

In Vitro Effectiveness of Samento and Banderol Herbal Extracts on the Different Morphological Forms of Borrelia Burgdorferi

by Akshita Datar, Navroop Kaur, Seema Patel, David F. Luecke, and Eva Sapi, PhD Lyme Disease Research Group, University of New Haven

Abstract

A tick-borne, multisystemic disease, Lyme borreliosis caused by the spirochete Borrelia burgdorferi has grown into a major public health problem during the last 10 years. The primary treatment for chronic Lyme disease is administration of various antibiotics. However, relapse often occurs when antibiotic treatment is discontinued. One possible explanation for this is that B. burgdorferi become resistant to antibiotic treatment, by converting from their vegetative spirochete form into different round bodies and/or into biofilmlike colonies. There is an urgent need to find novel therapeutic agents that can eliminate all these different morphologies of B.

burgdorferi. In this study, two herbal extracts, Samento and Banderol, as well as doxycycline (one of the primary antibiotics for Lyme disease treatment) were tested for their in vitro effectiveness on several of the different morphological forms of B. burgdorferi (spirochetes, round bodies, and biofilmlike colonies) using fluorescent, darkfield microscopic, and BacLight viability staining methods. Our results demonstrated that both herbal agents, but not doxycycline, had very significant effects on all forms of B. burgdorferi, especially when used in combination, suggesting that herbal agents could provide an effective therapeutic approach for Lyme disease patients. Link to entire article: http://www.townsendletter.com/July2010/sapi0710.html

LETTER PUBLISHED IN THE JOURNAL OF THE AMERICAN ACADEMY OF PHYSICIAN ASSISTANTS, JULY 2010

Lyme disease rash is not always a bull's eye To the Editor:

Ms. Kruger has written a succinct and balanced article on Lyme disease (LD) ("On target with vector-borne infections: Understanding Lyme disease," May 2010). Unfortunately, the photo and description of the "classic" erythema migrans (EM) rash as a bull's eye can be misleading. In fact, most EM rashes do not have central clearing, especially early on. I have seen cases in which people did not seek treatment for a large solid EM rash thinking it was not the real thing. These unfortunate victims went on to develop late LD. Because the bull's-eye appearance of the EM rash has been widely promoted, it is incumbent upon medical providers to correct this misinformation by using photographs of solid EM rashes and educating the public about this pitfall.

Marcia E. Herman-Giddens, PA, DrPH

President, Tick-borne Infections Council of North Carolina, Inc REFERENCES

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UNC HEALTHCARE NEWSLETTER ARTICLE FEATURES TIC-NC, July 22, 3010

Tick Diseases on the Rise in North Carolina

Once attached to a host, ticks spend several days or weeks feeding and then drop off. However, before they go, they can infect the host with serious illnesses. This concerns Dr. Marcia Herman-Giddens, who has watched North Carolina's tick disease rates rising in recent decades. Dr. Herman-Giddens is president of the Tick-Borne Infections Council of North Carolina, which advocates for better education, research, and



control of the diseases. She is also adjunct professor of maternal and child health at UNC Gillings School of Global Public Health.



Dr. Herman-Giddens points to data on diseases such as Rocky Mountain spotted fever, which grew from 78 to 515 cases statewide between 2000 and 2008, according to the state Department of Health and Human Services. Rocky

Mountain spotted fever is a potentially fatal illness that can cause fever, chills, aches, nausea, and a rash.

Reported cases of Lyme disease have remained relatively steady since 1990. However, in March, state officials declared for the first time that the disease was a known threat in Wake County, NC. Similar declarations have been made in Wilkes, Wilson, Pitt, and Carteret counties.

Dr. Herman-Giddens blames the rise in tick diseases on growth in the state's population of white-tailed deer, a favorite tick host. Suburban development in central North Carolina has broken forest land into patches of borders and wooded areas where the deer thrive.

[Photo #1: An adult female lone star tick. Photo source: CDC]

[Photo #2: Dr. Marcia Herman-Giddens]

ARTICLE FROM THE WALL STREET JOURNAL-- THE MAJORITY OF TICKS BITES HAPPENS CLOSE TO HOME August 2, 2010

While most people worry about tick bites after outdoor activities like camping, hiking and golf, the majority of bites happen close to home.

The federal Centers for Disease Control and Prevention and the National Institute of Allergy and Infectious Diseases are investigating an alarming rise in several different types of tick-borne infections including Lyme disease, Rocky Mountain spotted fever and ehrlichiosis. Not only are more diseases being spread by ticks, but more species of ticks are transmitting disease, including some, like brown dog ticks, not previously considered a danger to humans. The blood-sucking parasites are the leading carriers of disease in the U.S. and second only to mosquitoes worldwide.

See for complete

BUT IF YOU VACATION ON MAINE ISLANDS...

Here is some not so happy information from Maine's Vector-borne Disease Laboratory:

Isle au Haut and Swan's Island have been important study sites of ours. In 2004 when we flagged 24 adult I. scap./hr, 23% infected on IAH. (Those are moderate rates as compared to south coastal Maine (~90/hr, 67% infected in Wells). At Swan's it was 8.7/hr, 43% infected in 2007. www.mmcri.org/lyme/lymehome.html

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J Antimicrob Chemother doi:10.1093/jac/dkq214

Comment on: Efficacy of antibiotic prophylaxis for the prevention of Lyme disease: an updated systematic review and meta-analysis

David J. Volkman*

SUNY, Stony Brook, NY, USA

*E-mail: volkmans@optonline.net

Keywords: anti-infective development, tick-bite prophylaxis, *Borrelia* spp.

Sir,

The recent article by Warshafsky et al. may encourage the use of single-oral-dose doxycycline for tick-bite prophylaxis, which in my opinion and in the light of other evidence, is likely to be ineffective. The recommendation for single-dose prophylaxis was first made by Nadelman et al.² in 2001 as a result of a randomized controlled trial in 482 patients and was included in the Infectious Diseases Society of America's (IDSA's) guidelines for the treatment of Lyme disease.3 Three of the authors of the Nadelman et al.² article were also authors of the IDSA guidelines. In their original article, Nadelman et al.² showed that their single-dose regimen was 87% effective in blocking both the erythema migrans (EM) and the appearance of anti-Borrelia antibodies expected with borreliosis, but they did not show that it blocked actual infection in the antibiotic recipients. This is analogous to observations made in the 1950s that low-dose penicillin blocked cutaneous lesions of syphilis in rabbits but not the infection.4 The study by Nadelman et al.2 did not comment on complaints of fever and flu-like illness and limited its follow-up to 6 weeks instead of the 1-2 years used in other studies and no normal control group was used to compare the incidence

of fever and flu-like illness with that of the treated/placebo groups.

However, investigators at the CDC in Fort Collins, Colorado, showed that 80% of newly infected mice treated with a comparable single oral dose of doxycycline developed persistent borreliosis, which was found by grinding up tissues and using culture and PCR for bacterial detection. The sera from these mice were discarded without testing for anti-Borrelia antibodies so we do not know if they remained seronegative despite proven infection.

Not surprisingly when the same criteria are used in the recent meta-analysis a similar result is obtained, i.e. a single oral dose blocks both EM and antibodies. By promoting this potentially flawed recommendation, the authors and the IDSA may actually promote persistent borreliosis that will be seronegative, and therefore difficult to diagnose.

Transparency declarations

None to declare.

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ARGUMENT AGAINST FOLLOWING IDSA TREATMENT GUIDELINES

Insufficient Evidence and Poor Outcomes: IDSA Treatment Recommendations Rightly Ignored, Elizabeth Maloney (10 July 2010)

Comments from IDSA president, Dr. Richard J. Whitley, suggest that he fully believes that the best defense is a good offense. Instead of addressing the shortcomings of the IDSA guidelines on Lyme disease, of which there are many, he assails Dr. Stricker and Ms. Johnson for not providing evidence that long-term treatments are valid.[1] He also tries to distract readers from considering the weak scientific underpinnings of the IDSA guidelines by raising the specter of unending courses of IV antibiotics and life-threatening drug-resistant superbugs; readers should not be fooled by such tactics.

Organizations which create treatment guidelines are obligated to prove the validity of their recommendations. This requires them to disclose the strength of their evidence so clinicians can use this information to judge the merits of the treatment recommendations. Because the IDSA Lyme guidelines issued 72 graded recommendations, it is easy for clinicians to lose sight of the fact that 54% of these, including 17 strong recommendations, were based on panel opinion.[2] Other guidelines developers, such as the American Academy of Pediatrics, require that the strength of a recommendation be matched to the strength of the underlying evidence;[3] unlike the IDSA, AAP would not restrict treatment options, via strong recommendations, purely on the basis of panel opinion.

The evidence strength ratings assigned by guidelines panels must be justifiable; even the pedestrian, IDSA-chosen review panel recognized that the strength of the supporting evidence had been stretched to reach the single-dose doxycycline prophylaxis recommendation.[4] And, evaluating the strength of an individual study requires more than a casual glance at the abstract and conclusion. When the article in question is written by a panelist on the 2006 guidelines, the examination should be especially vigorous so as to withstand charges of professional cronyism. This is also true when recommendations are issued to address areas of medical controversy.

This clearly did not happen with the IDSA guidelines. Consider the issue of treatment duration for erythema migrans, a contentious topic. The IDSA guidelines panel cited 8 prospective studies to support its recommendation; of these, only 2 investigated doxycycline regimens employing brief, 10 day treatment durations. In the study by Mazzarotti et al, the authors claimed the 10-day doxycycline arm had a 95% success rate.[5] However, of the 22 patients randomized to and completing this treatment, 7 were immediately retreated with doxycycline or amoxicillin and another patient later required IV ceftriaxone. Thus, 10 days of doxycycline failed to cure 36% of the patients, not 5%. One would think that such a gross overstatement of treatment success would have been caught by a diligent guideline panel; panelist Steere, as one of Mazzarotti coauthors, may have been best positioned to prevent the inclusion of this study in the guidelines. The other study, by guidelines panelist Wormser, had excessive drop-out rates.[6] At the study completion 49% of the subjects were unevaluable; at the earlier 12 month evaluation, 29% of the patients were already unevaluable. Biostatisticians warn against drawing outcome conclusions when drop-out rates exceed 20%;[7] thus, the panel also erred in citing the study by Wormser as supportive. If these studies are representative of what the IDSA considers sound scientific evidence, perhaps it is premature to be making recommendations in the first place.

After discovering a lack of support for the 10 day doxycycline regimen, I re-evaluated the data from the other 6 trials cited as supportive evidence for the early Lyme disease treatment recommendations.[8-13] During that process, I reanalyzed the outcome data using intent-to-treat methodology (ITT) as opposed to the complete-case(cc) or last-observation-carried-forward (LOCF) methods used in the original papers. ITT is the method preferred because CC and LOCF overstate treatment outcomes.[14] Differences in study designs and in the definitions of treatment success, improvement and failure make direct comparisons difficult but if success is defined as a return to the pre-morbid baseline without relapse during the observation period, then the overall success rates for doxycycline, amoxicillin and cefuroxime are roughly 65%. While this may seem incredulous to many, the review panel, which received my analysis in the course of its deliberations, suggested that future guidelines describe the first-line agents as "effective rather than highly effective.[4]

Dr. Whitley expressed concerns regarding the use of long-term antibiotics in patients with persistent symptoms. There can be no doubt that such approaches carry risks but those risks must be weighed in light of the situation for which they are employed; this is not a case of using sledgehammer to swat a fly. The disease burden in this group is quite high, as the retreatment trials demonstrated.[15-17]

The IDSA guidelines also prohibit retreatment for patients with late neurologic Lyme disease who remain symptomatic following 30 days of ceftriaxone. This restriction is based on scant evidence. The guidelines cite only 4 trials, with a total of 96 patients representing a limited disease spectrum, which can be analyzed in terms of neurologic outcomes.[18-21] In this very small cohort, treatment successfully restored health in only 7, 35% of the patients. Such a poor outcome is unacceptable for a patient group burdened with a disease causing a profoundly negative impact on the quality of their lives.

While physicians are cautioned to do no harm, it is clear that for the majority of patients with late neurologic Lyme disease, doing nothing more is harmful. To appease those looking for a scientific basis for additional antibiotic therapy, I suggest they read the 1999 study by Logigian et al.[21] In that open label trial using 30 days of ceftriaxone, one patient (who was well at the 6 month evaluation) reported a relapse, supported by a deterioration in his verbal and visual memory, 2 months later. Based on that information, the authors retreated him with 30 additional days of ceftriaxone and he demonstrated sustained improvement. Given that Steere served on the original guidelines panel and co-authored this paper, it is curious that the IDSA recommends against retreatment. Given the poor outcomes to shorter treatment durations and the disease burden, it is unconscionable.

Similarly detailed critiques can be made for the other major recommendations. Rather than shoot the messengers (Dr. Stricker and Ms. Johnson), Dr. Whitley should heed the message: the IDSA failed, in its initial and review efforts, to create impartial, conflict-free, evidence-based guidelines. Moreover, the errors of the guidelines panel were compounded by the review panel, which had an obligation to provide an unbiased review and right these transparent errors. Those of us who understand the situation lack mechanisms to resolve it. The duty remains with the IDSA members; physicians, heal thyselves.

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YOUTTUBE VIDEO BY OUR OWN DR. BREITSCHWERDT ON BARTONELLA

Bartonella / NC State video : http://www.youtube.com/watch?v=g5g_PVSIA_0 by Dr. Ed Breitschwerdt, professor of internal medicine at North Carolina State School of Veterinary Medicine. Ticks and other insects have been implicated in the transmission. | May 04, 2010 .

BEEF, PORK, AND LAMB ALLERGY RELATED TO TICK BITES

New Research from UVA Health System Describes Delayed Anaphylaxis, A Notion That May Alter Conventional Food Allergy Paradigm

Patients in Study Suffered Severe Allergic Response Hours after Eating Red Meat; Antigens Stimulated by Tick Bites are Suspected Cause

CHARLOTTESVILLE, Va., May 14, 2009 - Spring is here and more of us are heading outside to enjoy jogging, hiking, gardening and camping. Wherever our outdoor adventures lead, there is a good chance that we'll come in contact with one of nature's most notorious hitchhikers, the tiny seed tick.

New NIH-funded research from the University of Virginia Health System suggests that it is wise to be wary of the seed tick because its bite may set off a cascade of events that not only defy current thinking about food allergies, but also create serious health risks for people with certain blood types.

In a paper published in the February 2009 *Journal of Allergy and Clinical Immunology*, UVA researchers describe a novel and severe allergic response, which they call delayed anaphylactic shock. The reaction occurs three to six hours after patients eat beef, pork or lamb. Symptoms begin with itching that intensifies as hives develop on the skin's outer and deeper layers. Itching quickly escalates to swelling, intestinal irritation and the alarming, life-threatening symptoms of anaphylaxis: airway constriction, chaotic heart beat, a rapid drop in blood pressure and loss of consciousness.

"Our conventional understanding is that anaphylaxis happens within seconds or minutes of exposure. The notion that it can be delayed for several hours is a paradigm altering discovery," says senior study investigator, Thomas Platts-Mills, M.D., Ph.D., Professor of Medicine and Microbiology at UVA and head of the Division of Allergy and Clinical Immunology.

The researchers found that the delayed response is being triggered by an IgE antibody that binds to a sugar molecule known as galactose- α -1,3-galactose (alpha-gal). The antibody was found in the serum of all 24 adults assessed in the study and in more than 100 other individuals, including six children, now being tracked by the UVA study team.

"Alpha-gal is an unexpected culprit," explains lead author, Scott Commins, M.D., Ph.D., an allergy and immunology fellow at UVA who will join its medical faculty in July. "Today's textbooks tell us that allergic reactions are caused by proteins in food, pollen, dander and venom. They are not supposed to be caused by sugars like alpha-gal."

UVA researchers are still determining what triggers the production of alpha-gal antibodies. So far, evidence strongly suggests that tick bites are the cause. "Eighty percent of our study cohort reported being bitten by ticks either weeks or months before symptoms began. When we consider all the patients in our database, more than 90 percent had tick bites," Commins notes.

"We are continuing to investigate this link by gathering patient information from a network of allergists around the U.S. and in four other countries."

"In our findings, we refer to 'seed' tick, which is the generic term for the larval form of ticks. Ticks such as dog tick, deer tick, Lone Star, etc. are the adult forms. We believe all types of ticks can trigger this reaction," Commins explains.

Blood typing performed at UVA indicates that individuals with Type B or AB blood seem protected from developing IgE to alpha-gal. Commins is concerned that people with other blood types may be unaware of the risks posed by tick bites. "A lot of people suffer symptoms for years without knowing the cause. We worry that the number of undiagnosed or potential cases of alpha-gal sensitivity may be on a dramatic rise," Commins says. "However, we'll need more data to make formal projections."

The UVA study yielded other paradigm-challenging findings. First, the allergist's key diagnostic tool, the skin prick test, proved ineffective in detecting red meat allergy in study patients. (As part of the UVA research effort, Commins developed a skin testing technique to identify this allergy.) Second, most patients began experiencing symptoms as adults, defying the common belief that food allergies rarely develop after childhood.

According to Commins, the study is prompting new thinking about food allergies as well as continued investigation. "Our observations have turned a lot of conventional wisdom upside down while raising a number of important questions," he notes. "We still need to figure out what triggers production of IgE to alpha-gal, why some blood groups are protected and why the allergic reaction is delayed and so severe."

On a practical note, Commins advises quick removal of hitchhiking ticks and monitoring of bite sites. "People who develop the red meat allergy often report they experienced significant itching and redness around the bites," he explains. "Anyone who is concerned about developing the alpha-gal antibody after tick bites should have a screening test. It's far safer than waiting for an allergic reaction to occur."

In addition to Platts-Mills and Commins, the UVA study co-authors were *Shama M. Satinover*, MS, Jacob Hosen, BS, Jonathan Mozena, MD, Larry Borish, MD, Barrett D. Lewis, MD, Judith A. Woodfolk, MBChB, PhD.

More information about ongoing alpha-gal research at UVA can be obtained from Commins via email (spc7w@virginia.edu) or by phone (434.982.3958 or 434.924.5917).

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