

Babesia Updates in Treatment and Diagnosis and Education

I will soon be publishing a book as a small supplement to my 2006 Babesia Textbook which discusses some dose adjustments and other new information. We feel we might understand why many folks with Babesia relapse and why routine dosing fails.

Here is some new basic updated information and other abstracts some have enjoyed with some inserted comments.

1: Clin Infect Dis. 2008 Feb 1;46(3):370-6.

Persistent and relapsing babesiosis in immunocompromised patients.

Krause PJ, Gewurz BE, Hill D, Marty FM, Vannier E, Foppa IM, Furman RR, Neuhaus E, Skowron G, Gupta S, McCalla C, Pesanti EL, Young M, Heiman D, Hsue G, Gelfand JA, Wormser GP, Dickason J, Bia FJ, Hartman B, Telford SR 3rd, Christianson D, Dardick K, Coleman M, Giroto JE, Spielman A.

Division of Infectious Diseases, Connecticut Children's Medical Center, and

Department of Pediatrics, University of Connecticut School of Medicine,

Farmington, Connecticut 06106, USA. PKrause@ccmckids.org

BACKGROUND: Human babesiosis is a tickborne malaria-like illness that generally resolves without complication after administration of atovaquone and azithromycin or clindamycin and quinine. Although patients experiencing babesiosis that is unresponsive to standard antimicrobial therapy have been described, the pathogenesis, clinical course, and optimal treatment regimen of such cases remain uncertain.

METHODS: We compared the immunologic status, clinical course, and treatment of 14 case patients who experienced morbidity or death after persistence of Babesia microti infection, despite repeated courses of antibabesial treatment, with those of 46 control subjects whose infection resolved after a single course of standard therapy. This retrospective case-control study was performed in southern New England, New York, and Wisconsin.

RESULTS: All case patients were immunosuppressed at the time of acute babesiosis, compared with <10% of the control subjects. Most case patients experienced B cell lymphoma and were asplenic or had received rituximab before babesial illness. The case patients were more likely than control subjects to experience complications, and 3 died. Resolution of persistent infection occurred in 11

patients after 2-10 courses of therapy, including administration of a final antimicrobial regimen for at least 2 weeks after babesia were no longer seen on blood smear.

CONCLUSIONS: Immunocompromised people who are infected by B. microti are at risk of persistent relapsing illness. Such patients generally require antibabesial treatment for ≥ 6 weeks to **achieve cure, including 2 weeks after parasites are no longer detected on blood smear.** [WE HAVE A BABESIA BLOOD IMAGES TEXTBOOK PENDING ON THE VAST NUMBERS OF BABESIA FORMS MISSED BY SINCERE HARD WORKING TECHS WHO ARE READING SLIDES. THEY MISS BABESIA ALMOST ALWAYS].

PMID: 18181735 [PubMed - indexed for MEDLINE]

2: Clin Infect Dis. 2007 Dec 15;45(12):1588-90.

Treatment of refractory Babesia microti infection with atovaquone-proguanil in an HIV-infected patient: case report.

Vyas JM, Telford SR, Robbins GK.

Division of Infectious Diseases, Department of Medicine, Massachusetts General Hospital, Boston, MA 02114, USA. jvyas@partners.org

A patient with acquired immune deficiency syndrome presented with babesiosis 6 months after presumed tick exposure. Despite initial treatment with azithromycin and atovaquone, followed by quinine and clindamycin, he experienced an increasing parasite load. Finally, red blood cell exchange transfusion, anti-Babesia therapy, and the addition of atovaquone-proguanil to the treatment regimen led to symptomatic improvement and elimination of parasitemia. Low-level parasitemia recurred 20 weeks later and was eradicated by administration of atovaquone-proguanil monotherapy. **Atovaquone-proguanil appears to have activity against babesiosis and should be studied as a potential therapy for patients with refractory babesiosis. [IN A PENDING TEXT WE SUGGEST STANDARD DOSING LEADS TO RELAPSE].**

PMID: 18190320 [PubMed - indexed for MEDLINE]

3: Exp Parasitol. 2007 Oct;117(2):115-23. Epub 2007 Apr 3.

Babesia gibsoni: detection during experimental infections and after combined atovaquone and azithromycin therapy.

Jefferies R, Ryan UM, Jardine J, Robertson ID, Irwin PJ.

Australasian Centre for Companion Animal Research, Division of Health Sciences, Murdoch University, WA 6150, Australia.

Babesia gibsoni is a protozoan parasite of dogs worldwide yet both an effective treatment and a reliable method for detecting subclinical cases of this emerging infection remain elusive. Experimental B. gibsoni infections were established in vivo to investigate the efficacy of combined atovaquone and azithromycin drug therapy and to determine the detection limits of a nested-PCR, IFAT and microscopy during various stages of infection. While atovaquone and azithromycin produced a reduction in parasitaemia, it did not eliminate the parasite and drug resistance appeared to develop in one dog. **[PERHAPS DUE TO FLAWED DOSING]**. Polymerase chain reaction was found to be most useful in detecting infection in the pre-acute and acute stages, while IFAT was most reliable during chronic infections. Microscopy is suggested to be only effective for detecting acute stage infections. This study **also describes the detection of B. gibsoni in tissue samples during chronic infections for the first time, suggesting possible sequestration of this parasite. [SO A RED BLOOD CELL PARASITE CAN ENTER TISSUES – AN AMAZING FIND]**.

PMID: 17543304 [PubMed - indexed for MEDLINE]

4: Int J Med Microbiol. 2007 Jun;297(3):197-204. Epub 2007 Mar 12.

First case of human babesiosis in Germany - Clinical presentation and molecular characterisation of the pathogen.

Häselbarth K, Tenter AM, Brade V, Krieger G, Hunfeld KP.

Department of Internal Medicine II, Hegau-Bodensee-Medical Center, Singen, Germany.

Babesiosis is a common infection of animals and is gaining increasing attention as an emerging tick-borne zoonosis of humans in Europe. Here we report on the first case of human babesiosis in Germany in a 63-year-old splenectomised German patient with a relapse of nodular lymphocyte-predominant Hodgkin's lymphoma. After treatment with a chimeric anti-CD20 antibody preparation (Rituximab), the patient was hospitalised because of anaemia and dark urine from haemoglobinuria.

Presumptive diagnosis of babesiosis was made based on piriform parasitic erythrocytic inclusions in peripheral blood smears and confirmed by Babesia-specific 18S rDNA PCR. Sequence analysis revealed a >99% homology of the amplicon with the recently described EU1 organism clustering within the Babesia divergens/Babesia odocoilei complex. Despite treatment with quinine and clindamycin the patient relapsed and developed chronic parasitaemia requiring re-treatment and long-term maintenance therapy with atovaquone before he eventually seroconverted and the parasite was cleared. Our findings suggest that human babesiosis occurs in Germany and can take a chronic course in immunocompromised individuals.

PMID: 17350888 [PubMed - indexed for MEDLINE]

5: Acta Neurol Scand. 2007 Feb;115(2):129-31.

Motor neuron disease recovery associated with IV ceftriaxone and anti-Babesia therapy.

Harvey WT, Martz D.

Rocky Mountain Chronic Disease Specialists, L.L.C., North Circle Drive, Colorado Springs, CO 80909, USA. wth928@aol.com

This report summarizes what we believe to be the first verifiable case of a significant and progressive motor neuron disease (MND) consistent with amyotrophic lateral sclerosis that resolved during treatment with i.v. ceftriaxone plus oral atovaquone and mefloquine. The rationale for use of these antibiotics was (i) positive testing for Borrelia burgdorferi and (ii) red blood cell ring forms consistent with Babesia species infection. The patient has continued to be free of MND signs and symptoms for 15 months, although some symptoms consistent with disseminated Borreliosis remain.

PMID: 17212618 [PubMed - indexed for MEDLINE]

6: Expert Rev Anti Infect Ther. 2005 Apr;3(2):155-65.

Lyme disease: point/counterpoint.

Stricker RB, Lautin A, Burrascano JJ.

California Pacific Medical Center , 450 Sutter Street, Suite 1504, San Francisco, CA 94108, USA.
rstricker@usmamed.com

Lyme disease represents a growing public health threat. The controversial science and politics of Lyme disease have created barriers to reliable diagnosis and effective treatment of this protean illness. Two major clinical hurdles are the absence of a therapeutic end point in treating *Borrelia burgdorferi*, the spirochetal agent of Lyme disease, and the presence of tickborne coinfections

with organisms such as *Babesia*, *Anaplasma*, *Ehrlichia* and *Bartonella* that may complicate the course of the disease. From a pathophysiologic standpoint, the affinity of *Borrelia burgdorferi* for multiple cell types and the presence of nonreplicating forms of the Lyme disease spirochete have contributed to persistent infection and failure of simple antibiotic regimens. Newer approaches to the treatment of Lyme disease should take into account its clinical complexity in coinfecting patients and the possible need for prolonged combination therapy in patients with persistent symptoms of this potentially debilitating illness. The optimal antibiotic regimen for chronic Lyme disease remains to be determined.

PMID: 15918774 [PubMed - indexed for MEDLINE]

7: Am J Clin Pathol. 2003 Oct;120(4):554-9.

Babesiosis. Two atypical cases from Minnesota and a review.

Setty S, Khalil Z, Schori P, Azar M, Ferrieri P.

Department of Laboratory Medicine and Pathology, University of Minnesota Medical School, Minneapolis, MN, USA.

We present 2 atypical cases of babesiosis and a review of babesiosis. The first patient was a 72-year-old man with an intact spleen, who had marked intravascular hemolysis. His RBCs were parasitized heavily with trophozoites of *Babesia*, and he had a large number of extracellular aggregates of *Babesia*. The infection did not respond to oral antibiotic therapy, and he required an RBC exchange transfusion.

The second patient was a 29-year-old man who had undergone splenectomy and who had multiple episodes of fever and gastrointestinal symptoms for 4 months, with partial response to antibiotics. **Thin smears revealed both intraerythrocytic and extraerythrocytic forms [SO BABESIA IS ALSO OUTSIDE RED BLOOD CELLS. THIS IS ACTUALLY NOT A ROUTINE UNDERSTANDING FOUND IN PARASITE BOOKS AND HEMATOLOGY BOOKS].** in very low numbers. The infection responded promptly to clindamycin and quinine therapy. The varying clinical manifestations, from acute to chronic, at a wide range of ages and often the difficulty of detection by routine blood smears make it necessary that a high index of clinical suspicion be present for prompt diagnosis. With increasing numbers of cases of transfusion-transmitted babesiosis being reported, protection of the blood supply is essential.

PMID: 14560566 [PubMed - indexed for MEDLINE]

8: N Engl J Med. 1998 Jul 16;339(3):160-5.

Persistent parasitemia after acute babesiosis.

Krause PJ, Spielman A, Telford SR 3rd, Sikand VK, McKay K, Christianson D, Pollack RJ, Brassard P, Magera J, Ryan R, Persing DH.

Department of Pediatrics, Connecticut Children's Medical Center and University of Connecticut School of Medicine, Hartford 06106, USA.

BACKGROUND: Babesiosis, a zoonosis caused by the protozoan *Babesia microti*, is usually not treated when the symptoms are mild, because the parasitemia appears to be transient. However, the microscopical methods used to diagnose this infection are insensitive, and few infected people have been followed longitudinally. We compared the duration of parasitemia in people who had received specific antibabesial therapy with that in silently infected people who had not been treated. **METHODS:** Forty-six babesia-infected subjects were identified from 1991 through 1996 in a prospective, community-based study designed to detect episodes of illness and of seroconversion among the residents of southeastern Connecticut and Block Island, Rhode Island. Subjects with acute babesial illness were monitored every 3 months for up to 27 months by means of thin blood smears, *Bab. microti* polymerase-chain-reaction assays, serologic tests, and questionnaires. **RESULTS:** Babesial DNA persisted in the blood for a mean of 82 days in 24 infected subjects without specific symptoms who received no specific therapy. Babesial DNA persisted for 16 days in 22 acutely ill subjects who received clindamycin and quinine therapy ($P=0.03$), of whom 9 had side effects from the treatment. Among the subjects who did not receive specific therapy, symptoms of babesiosis persisted for a mean of 114 days in five subjects with babesial DNA present for 3 or more months and for only 15 days in seven others in whom the DNA was detectable for less than 3 months ($P<0.05$); one subject had recrudescence after two years. **CONCLUSIONS:** **When left untreated, silent babesial infection may persist for months or even years. Although treatment with clindamycin and quinine reduces the duration of parasitemia, infection may still persist and recrudescence and side effects are common. Improved treatments are needed.**

PMID: 9664092 [PubMed - indexed for MEDLINE]

9: Clin Infect Dis. 1996 May;22(5):809-12.

Babesiosis in patients with AIDS: a chronic infection presenting as fever of unknown origin.

Falagas ME, Klempner MS.

Department of Medicine, New England Medical Center, Boston, Massachusetts 02111, USA.

Babesiosis is a malaria-like, tick-transmitted zoonosis caused by protozoa of the family Piroplasmorida, which includes Babesia and Theileria species. In the United States, the infection is endemic in the Northeast and upper Midwest, although cases have recently been described in Northern California and Washington State. We report a case of babesiosis in a patient infected with HIV who presented with a prolonged fever of unknown origin; the patient had not undergone splenectomy. Parasitemia persisted despite initial clinical improvement after treatment with quinine and clindamycin. **Babesiosis was controlled with a maintenance regimen consisting of clindamycin, doxycycline, and high-dose azithromycin, but the infection was not eradicated.** Babesiosis should be considered in the differential diagnosis of HIV-infected patients with fevers and/or anemia in areas where the infection is endemic. HIV-infected patients who are severely immunosuppressed, even those without a history of splenectomy, may present with severe manifestations of babesiosis and develop a chronic infection, which may require therapy to prevent relapse of disease.

PMID: 8722936 [PubMed - indexed for MEDLINE]

10: JAMA. 1996 Jun 5;275(21):1657-60.

Concurrent Lyme disease and babesiosis. Evidence for increased severity and duration of illness.

Krause PJ, Telford SR 3rd, Spielman A, Sikand V, Ryan R, Christianson D, Burke G, Brassard P, Pollack R, Peck J, Persing DH.

Department of Pediatrics, University of Connecticut School of Medicine, Farmington 06030, USA.

OBJECTIVE--To determine whether patients coinfecting with Lyme disease and babesiosis in sites where both diseases are zoonotic experience a greater number of symptoms for a longer period of time than those with either infection alone.

DESIGN--Community-based, yearly serosurvey and clinic-based cohort study.

SETTING--Island community in Rhode Island and 2 Connecticut medical clinics from 1990 to 1994.

STUDY PARTICIPANTS--Long-term residents of the island community and patients seeking treatment at the clinics. MAIN OUTCOME MEASURES—Seroreactivity to the agents of Lyme disease and babesiosis and number and duration of symptoms.

RESULTS--Of 1156 serosurvey subjects, 97 (8.4%) were seroreactive against Lyme disease spirochete antigen, of whom 14 (14%) also were seroreactive against babesial antigen. Of 240 patients diagnosed with Lyme disease, 26 (11%) were coinfecting with babesiosis. Coinfecting patients experienced fatigue ($P = .002$), **headache** ($P < .001$), sweats ($P < .001$), chills ($P = .03$), anorexia ($P = .04$), **emotional lability** ($P = .02$), nausea ($P = .004$), conjunctivitis ($P = .04$), and splenomegaly ($P = .01$) more frequently than those with Lyme disease alone.

Thirteen (50%) of 26 coinfecting patients were symptomatic for 3 months or longer compared with 7 (4%) of the 184 patients with Lyme disease alone from whom follow-up data were available ($P < .001$). Patients coinfecting with Lyme disease experienced more symptoms and a more persistent episode of illness than did those ($n = 10$) experiencing babesial infection alone. Circulating spirochetal DNA was detected more than 3 times as often in coinfecting patients as in those with Lyme disease alone ($P = .06$). CONCLUSIONS--Approximately 10% of patients with Lyme disease in southern New England are coinfecting with babesiosis [**WHAT TEST IS SOLID ENOUGH TO ACTUALLY GIVE STRONG CERTIANTY THAT SOMEONE DOES NOT HAVE BABESIA?**] in sites where both diseases are zoonotic. The number of symptoms and duration of illness in patients with concurrent Lyme disease and babesiosis are greater than in patients with either infection alone. In areas where both Lyme disease and babesiosis have been reported, the possibility of concomitant babesial infection should be considered when moderate to severe Lyme disease has been diagnosed.

PMID: 8637139 [PubMed - indexed for MEDLINE]

11: Trends Parasitol. 2003 Feb;19(2):51-5.

Babesiosis: persistence in the face of adversity.

Allred DR.

Dept of Pathobiology, College of Veterinary Medicine, University of Florida, Gainesville, FL 32611-0880, USA. allredd@mail.vetmed.ufl.edu

Many babesial parasites establish infections of long duration in immune hosts. Among different species, at least four mechanisms are known that could facilitate evasion of the host immune response, although no one species is (yet) known to use them all. This update strives to illustrate the ramifications of these mechanisms and the interplay between them.

PMID: 12586467 [PubMed - indexed for MEDLINE]