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1993 CONSENSUS TREATMENT GUIDELINES

Dr. DeSilva is a practicing Internist in Edison, New Jersey. He is an attending staff member at Raritan Bay Medical Center and JFK Medical Center in Edison. He is a medical consultant for Hoechst-Roussel Pharm. Inc. on product line altase (ramapril). Dr. DeSilva is a member of the Lyme Disease Foundtion's Medical Advisory Board, American Heart Association, American Society of Internal Medicine, and the American Medical Association. His is Medical Director of Carbonudum Company in Keasbey, New Jersey (BP America affiliate), and is on the Medical Advisory Board of Physicians Computer Network in Lawrence Harbor, NJ. Dr. DeSilva is the weekly Host of *Med Line* (WCTC Radio) and has made appearances on CBS Morning Show, CBS Evening News, CNN Sonya Live.

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COUMARIN SUSCEPTIBILITY AND RESISTANCE IN THE LYME DISEASE AGENT

Dr. Samuels, PhD did his undergraduate education at Rensselaer Polytechnic Institute, Troy, NY and Colorado College in Colorado Springs, CO. He received his PhD in Molecular and Cellular Biology from the University of Arizona, Tucson. He did his dissertation research on the phosphorylation of DNA topoisomerase I in mammalian cells. Post-doctoral Fellow in the Laboratory of Vectors and pathogens (Claude F. Garon, Chief), at Rocky Mountain Laboratories. Current research on DNA-protein interactions, particularly the role of DNA gyrase whic is the molecular target of coumermycin A, in the Lyme disease agent, *Borrelia burgdorferi*.

Coumermycin A1 is an inhibitor of DNA gyrase, an enzyme that catalyzes super coiling of DNA and is required for bacterial DNA replication. We have recently shown that *Borrelia burgdorferi*, a spirochete and a causative agent of Lyme disease, is more susceptible than many other eubacteria to coumermycin, as well as novobiocin, another coumarin antibiotic; this contrasted with its relative resistance to the DNA gyrase inhibitors nalidixic acid, oxolinic acid, and ciprofloxacin. Coumermycin at 0.2 ug/ml inhibited growth (MIC) in BSK II medium and the slightest inhibitory dose of 0.003 ug/ml induced the

1993

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reversible relaxation of two negatively-super coiled circular plasmids within 2 hours (20% of the doubling time). Because there are very few *B. burgforferi* mutants of any sort derived from selection, we isolated 11 coumermycin-resistant clones from approximately 10^{10} cells. All had a MIC of at least 20 ug/ml and maintained coumermycin resistance after at least 30 generations in the absence of selection. Two variants produced proteins not found significant levels in parental cells. CR9B had an outer surface protein with a molecular mass of approximately 27 kDa and CR9C overproduced OspC, a 23 kDa protein that is coded for by the only gene mapped to a circular plasmid in *B. burgdorferi*. None of the variants appeared to have lost the circular plasmids. In the absence of coumermycin, three of the variants (CR8a, CR9C, and CR9E) maintained circular plasmid super coiling while the others had relaxed circular plasmids. Unfortunately, coumermycin is not a clinically useful anti microbial agent; we hope that further work on the coumarin drugs yields an effective treatment for Lyme disease.

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RHEUMATOLOGIC MANIFESTATIONS OF LYME BORRELIOSIS

Dr. Schwartzberg is a Rheumatologist at the Jersey Shore Medical Center. He also treats many Lyme disease patients on a daily basis at his private practice in Neptune, New Jersey.

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REHABILITATION THERAPY AS A SUPPORT TO TREATMENT

A significant number of patients with chronic Lyme Disease present in very poor physical condition. They complain of exhaustion, poor stamina, soreness of tendons, ligaments, and joints, and, especially of the neck. On exam, many have gained weight, have increased percentage of body fat, display generalized muscular weakness, loss of range of motion, and elevated resting heart rates, even in the absence of clinical myopathy or markers of inflammation, such as elevated CPK and sedimentation rates. Because of these