

RELAPSING FEVER/LYME DISEASE MULTIPLE SCLEROSIS

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ABSTRACT

Lyme Disease and Relapsing Fever caused by *Borrelia burgdorferi* and *Borrelia hermsii*, respectively, have been generally considered curable if diagnosed early. However, it is becoming apparent that when these diseases are left undiagnosed and untreated they may cause severe problems for some people. They, in fact, may be one of the major causes of Multiple Sclerosis. These two *Borrelia* infections, when left untreated, are now known to be capable of causing neurological problems, cardiac problems, relapses as much as ten years later, increased IgG/albumin ratio and increased lymphocytes. These same things hold true for Multiple Sclerosis patients. This paper discusses the *Borrelia* spirochetes which cause Lyme Disease and Relapsing Fever and what correlation that may have with Multiple Sclerosis.

INTRODUCTION

The purpose of this paper is to see what relationship, if any, may exist between Multiple Sclerosis and spirochetal infections. The main spirochetes this paper will be addressing specifically are those from the Genus *Borrelia* which cause Relapsing Fever and Lyme Disease.

SPIROCHETES

The genus *Borrelia* consists of arthropod-borne spirochetes which have adapted to a rather complex set of ecological circumstances. *Borreliae* are transmitted by ticks or lice to vertebrate hosts (humans, birds, rodents) and cause diseases such as Relapsing Fever and Lyme Disease. Bergey mentions 28 different *Borrelia* species in his manual (2) and with *Borrelia burgdorferi* (the Lyme spirochete), there are now 29 different claimed species. Almost nothing is known about the physiology of the Lyme spirochete and relatively little has been done on *Borrelia* physiology.

The Borrelia causing Relapsing Fever have the interesting property of being able to undergo antigenic variation. There is evidence that the surface antigens of the organism shift and grow a new population with alternative antigens, which is the case with each relapse (8). During a relapse event, a Borrelia population consisting of a single serotype can change suddenly to a mixture of as many as seven serotypes. **Relapsing Fever Borrelia contain 30-40 periplasmic flagella (8). Borreliae have loosely coiled cells that measure 0.2-0.5 microns in diameter by 5-25 microns in length (8).**

The Lyme spirochete is quite different morphologically from other Borrelia (8). The tightly coiled cell morphology of the Lyme spirochete is more like that of the Treponemes than of Borrelia. The Lyme spirochete has flagellae, resembling Treponema, but it grows in modified Kelly's medium like Borrelia (5). Lyme disease spirochetes appear to contain 14 periplasmic flagella, similar to the 2 to 16 present in Treponemes (9).

The Lyme spirochete is able to induce various immunologic responses by phagocytic cells. The organism contains a potent lipopolysaccharide (endotoxin) which has the capacity to activate chondrocytes that results in cartilage degradation (5). This spirochete can also induce a proliferation of lymphocytes and the production of interleukin 1, probably very important for its induction of a vigorous immune response that leads to pathologic consequences (5).

Ticks Carrying Lyme Disease

With Lyme disease, the Ixodidae or hard ticks are implicated. The species of ticks implicated for Lyme Disease are: *Ixodes dammini* (located in North east and Midwest of U.S. and in Ontario), *I. pacificus*, (located in U.S. West Coast & Utah), *I. ricinus*, (located in Western Europe, Switzerland), *I. scapularis*, (located in U.S. East Coast, Southeast, and Texas), *Amblyoma americanum*, (located in New Jersey, and Southern U.S.), and *Dermacentor variabilis*, (American dog tick, located in Texas and other areas of U.S.); (the last three listed are suspected, but not proven to transmit Lyme) (5). What is interesting to note is that the species *D. variabilis* and *A. americanum* also transmit Rocky Mountain Fever.

Ticks Carrying Relapsing Fever

The known species of ticks that transmit Relapsing Fever are: *Ornithodoros hermsii*, *O. parkeri* and *O. turicatae*, all soft ticks or Argasidae (5). It is now known that three North American Borrelia: *B. hermsii*, *B. turicatae*, and *B. parkeri*, actually constitute a single species of spirochetes (8). *O. Hermsi* ticks are night-feeders and take blood meals lasting an average of 15 minutes, after which they detach themselves. The bite that transmits the disease is painless, but usually produces a 2-3mm pruritic eschar (5). *B. hermsii* have in all

instances been acquired in areas forested with ponderosa pine and Douglas fir--in Washington at an elevation of 3116 ft., in Idaho and Oregon at 3510 ft., in California between 4921 ft. and 8202 ft., in Arizona at 8384 ft., and in Colorado at 8858 ft.

RELAPSING FEVER - SYMPTOMS/DIAGNOSIS

After a seven day incubation period, the disease begins abruptly with a temperature between 103 - 105 degrees F. Muscle pain, extreme exhaustion, nausea, vomiting, diarrhea, perspiration, abdominal pain, shaking chills, headache, rash, sore throat, swollen glands and cough are early signs. **Tachycardia is present and the patient is sleepy and confused.** Lymphadenopathy (particularly affecting cervical nodes) may develop. Jaundice is uncommon in tick-borne disease but occurs in about one third of patients with louse-borne disease, usually late in the course. A majority of patients with louse-borne relapsing fever have agglutinins for Proteus OX-K (21).

The initial febrile attack lasts three to six days, ending abruptly. Spirochetes rapidly disappear from the peripheral blood at this time. After an afebrile period of six to 10 days, a febrile, symptomatic relapse occurs, but it is of shorter duration than the original episode. There is usually only a single relapse in louse-borne disease, but several additional relapses are common in tick-borne relapsing fever. A mild normocytic anemia is common. **The disease peaks in late June and early July, with sporadic cases persisting into August.** It is interesting to note that the peak periods for Multiple Sclerosis are similar to the incidence of Borrelia. The seasonal variation of Multiple Sclerosis in Arizona, Ohio and Switzerland all showed peaks from May through August (14). The significance of this correlation is not known at this time.

LYME DISEASE - SYMPTOMS/DIAGNOSIS

Peak incidence is in summer and early fall. Early signs are mainly malaise, fatigue and lethargy. Headache, fever and chills, stiff neck and lymph adenopathy are also common. In addition there may be mild encephalopathic changes, memory difficulty and unusual clumsiness. About twenty-five percent notice a papule that expands to a red annular lesion (ECM, erythema chronicum migrans), about one month prior to the onset of arthritis. The skin lesions last a median of one and one-half weeks and may be recurrent. Besides arthritic symptoms, neurologic abnormalities may develop as well as myocardial conduction abnormalities of the atrioventricular node (5).

Spirochetel organisms were found in synovial specimens at a recent study at Yale (5). The organisms seen were up to 35 microns long and resembled in every respect the cultured spirochetes from ticks and extraarticular sites from patients (5). The synovium in addition, was

rich in complement, immunoglobulin and fibrin deposition. However, cultures to date of synovial tissue have not yet revealed growth of the organism (5). Thus, it is not known whether the spirochete is alive in affected synovium (11). Therefore, it is still unclear whether Lyme arthritis results directly from the presence of live spirochetes in synovium or whether it is an indirect immune response triggered by previous spirochetal infection. Furthermore, it seems likely that the spirochete may be directly responsible for the microvascular injury, the most characteristic feature of Lyme synovia (11). The microangiopathic process seen in Lyme disease is reminiscent of syphilitic microangiopathic changes described in the 19th century (5). The broad spectrum of clinical manifestations of Lyme disease, which may mimic a large number of diseases that need to be considered in the differential diagnosis, has been emphasized. Eighty-five percent of patients with Lyme disease have erythema chronicum migrans (ECM), therefore fifteen percent without the antecedent skin rash, will become dependent on serologic testing to confirm the diagnosis in many patients (6). Diagnosis is now essential, not only in the acute phase when treatment is likely to prevent most chronic complications, but in the chronic phase when treatment may also be effective (10).

FACTUAL INFORMATION

The Immune System

When an invader (antigen) is detected, the immune system responds by releasing one or more of its specialized lymphocytes. Released T-cells multiply and surround the invader. B-cells can also be released; they then produce antibodies (immunoglobins) that stick to the invader, thereby increasing the likelihood of its ingestion by macrophages. Antibodies immunoglobulin M (IgM) and immunoglobulin G (IgG) circulate in the blood, while immunoglobulin A (IgA) circulates in saliva and fluids that bathe mucous membranes. At least one other antibody, immunoglobulin E (IgE) exists, but little is known about it (16).

In Multiple Sclerosis the IgG antibodies are always increased (7). The MS population also has elevated IgG/albumin ratio, oligoclonal bands present, an increase in immunoglobulin level and an increase in lymphocytes. The plaques in MS have their origin around veins in the Central Nervous System (7:170). Acute MS lesions show intense infiltration and perivascular cuffing by small lymphocytes (7:427). As stated earlier, the Lyme spirochete may be directly responsible for microvascular injury (11).

Geographic Distribution of MS

Before World War II no cases of Multiple Sclerosis were reported on the Faroe Islands, then a cluster of 24 cases arose between 1943 and 1960, after British troops were stationed there (4). There was a strict control in importing dogs on the Faroes, hence a limited dog population.

However, when the British troops arrived on the island, they brought their dogs along (1). In Iceland, MS appeared as an epidemic from 1945-1954. (1), and also in 1923-1944, after WW II and WW I, respectively (7:91).

The recent outbreak of MS on Key West Island at the tip of Florida has 40 times the expected number for MS in a given population. In Key West the rate is 100 per 100,000 (4), the expected occurrence is 4.2 per 100,000 . The Orkney and Shetland Islands have the highest prevalence rates of MS known in the world (as high as 300 per 100,000) (1). Also Australia, New Zealand, Canada and the Northern part of the U.S., Guam, Western Norway, and Alaska have a high incidence of MS.

Looking at the geographic distribution of Multiple Sclerosis, it appears the mean annual temperature may correlate better with MS frequency than does geographic latitude (3). **One of the necessary environmental factors for tick survival is temperature and altitude.** If we look at the incidence of MS, it is also likely that ticks thrive in these regions. Then when one considers dogs as the possible host for ticks, we have a possible explanation as to epidemics occurring when troops are brought in.

DISCUSSION

Some things to consider when looking at Multiple Sclerosis are: 1) There is no man to man transfer (19). 2) A particular environmental extrahuman reservoir of the disease agent is highly probable. 3) This extra human reservoir may be picking up disease variations and passing them on to humans. 4) Dogs or cats may be suspected as reservoirs of the agent, since many MS patients have had close contact with them. 5) Insect vectors as links in the chain of transmission may be significant or not.

Of research done in regard to diet, a trial involving 116 MS patients showed that patients receiving 23 grams of linoleic acid daily and increasing polyunsaturated fatty acid levels in their blood had shorter and less severe exacerbations, but the frequency of relapses was not altered (7:527). Since *Borrelia spirochetes* find Oleic acid to be the most favorable for growth (12). Since Central Nervous System (CNS) myelin is composed of the lipids: cholesterol, phospholipid and galactolipid in a molar ratio varying between 4:3:2 and 4:4:2, (13) the myelin may be supplying the *Borrelia* with a favorable growth medium.

SIMILARITIES

The following similarities are found in the Cerebrospinal Fluid of some Lyme patients (11) and MS patients (7): Elevated IgG/albumin ratio, oligoclonal bands present, increase in immunoglobulin level, and an increase in lymphocytes. It may be true that if one inspected the myelin, one may find *spirochetes*. Rose Ichelson in 1957 was able to cultivate organisms from spinal fluids of persons with multiple sclerosis similar in morphology to those described by Steiner (17). Steiner describes his findings as follows: "In their fully developed, not yet disintegrating forms the *spirochetes* appeared as screw-like

organisms. In addition to regularly coiled forms of individual spirochetes there were more or less straight, irregularly or only partially coiled forms indicating a marked flexibility of this organism. The shorter and straight forms were usually thicker than the regularly threaded spirochetes. **Knobs at one end were not unusual.** There were also loops in the center of the longitudinal axis or more toward the end. The spirochetes were completely detached from any tissue elements. Very often they were seen in a microvacuole or surrounded by a small empty halo, separating them very distinctly from any tissue elements. It is this appearance, which, like other well known spirochetes in tissues, accentuates the foreign body nature of the spirochetes" (18).

Steiner found these organisms in the parenchyma of the brain and spinal cord as well as in vascular walls. He named the organisms "spirocheta myclophthora", meaning myelin sheath destroying spirochete (18). Prostaglandins turn up the body's thermostat, causing fever. Aspirin can interrupt the cycle before prostaglandins are produced." (22). **What all organisms do need to survive is iron.** It is believed that the reason fever therapy works is that it lowers the blood iron levels so low that microorganisms cannot grow (22).

CONCLUSION

A small organization, founded in Arizona consisting of people interested in vector borne diseases, now numbers 42 people who have shown elevated titers for Borrelia and/or Lyme. There have also been found three cases in South Dakota who show titers. South Dakota is a state where neither Borrelia nor Lyme have been known to exist. So far this group has come up with twelve with neurological problems and six with diagnosed Multiple Sclerosis, all having possible exposure to Borrelia hermsii or Borrelia burgdorferi. Dr. Sibley in Tucson, AZ, did a test group of 8 MS patients and found that 2 of the MS patients had elevated antibody titers to these two Borreliae. A larger study, with a test group of 100 MS patients, would be interesting to see if twenty-five percent of the 100 MS patients have high antibody titers to these two Borreliae.

HYPOTHESIS

The hypothesis that many cases of Multiple Sclerosis may be the result of an undiagnosed tick bite carrying either Lyme or Relapsing Fever, seems highly plausible for the following reasons:

- 1) *Borrelia spirochetes* may be acting as the trigger in MS, setting off an autoimmune reaction in which patients produce antibodies that attack their own nerve fibers.
- 2) An increased IgG to albumin ratio and oligoclonal bands are found in Lyme patients and MS patients.
- 3) The organisms Steiner and Ichelson found in the brains and spinal fluid and vascular walls of MS patients is described as the same as the organisms found in patients with Lyme disease.
- 4) Relapses occur with *Borrelia* Infections, some relapses may be as much as ten years apart. Relapses also occur in MS patients.
- 5) *Borrelia spirochetes* find Oleic acid to be the most favorable for growth, the myelin sheath which is rich in lipids may be supplying the spirochetes with a favorable growth medium.
- 6) Many patients with Lyme Disease develop cardiac problems, many MS patients also have to be on pacemakers for a period of time and have cardiac involvement.
- 7) Mean annual temperature and altitude may correlate better with the distribution of MS than latitude. Temperature, altitude and moisture play an important role in the life of a tick, the vector for *Borrelia*.
- 8) A number of MS patients have been found to have highly positive titers to *B. hermsii* and *B. burdorferi*.

CLOSING STATEMENT

Since it is becoming apparent that the Lyme and Relapsing Fever *Borrelia spirochetes* can cause much the same damage as the spirochete causing syphilis, the following quote by William Osler seems appropriate. "Know syphilis and all its manifestations and relations, and all things clinical will be added unto you". (*Aequanimitas*, with other addresses, "Internal Medicine as a vocation." [1849-1919] (21).

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