EXPERIMENTAL MEDICINE. – ***The histo–physio–pathological problem of multiple sclerosis.***

Report (*) by Mr. Paul Le Gac, presented by Mr. Jacques Trefouel.

[Abstract:] The major lesions of multiple sclerosis are vascular. In the form of various types of arteritis, endarteritis, and endothelitis, they cause anoxia of the nerve tissue. The nervous lesions are secondary. The innervation, which is part of the reticulo–endothelial system, manifests its phagocytic function through massive proliferation.

Among diseases of the nervous system, multiple sclerosis is undoubtedly the condition that has posed, and that continues to pose, the largest number of problems that have not yet been solved.

Various different theories (e.g., infectious, allergic, and viral) have successively been adopted as an explanation for this syndrome, but none of these theories has ever been proven. As for the histological lesions, their disparate characteristics and their lack of precision have always made impossible to confirm any single pathognomonic process.

A report presented on February 29 [1] stated that certain cases of multiple sclerosis had been shown to consist of complications of rickettsioses and neo–rickettsioses. Our report today addresses the histo–physio–pathological problem of these cases, and the conclusions that can be inferred from them.

The anatomo–pathological setting of multiple sclerosis contains three essential factors, i.e., the vascular lesions, the neural lesions, and the massive proliferation of the innervation.

a. Vascular lesions. – The work done by the first histologists who addressed this problem (including, in particular, Rindfleisch [2], in 1863) indicates that their observations, which at first were accurate, establish that multiple sclerosis was not a disease that began in the nerve tissue, a rather, very specifically, a condition that affects the nutritive vascular system, leading to a disturbance in the nutrition of the nerve tissue that depends on the injured vessels.

Dejerine [3] deserves most of the credit for having insisted on the preponderance of vascular lesions involving the medulla and the cerebellum (in the form of various types of arteritis, endarteritis, and endothelitis), and for having speculated that these lesions might be the ones that are primarily responsible for the genesis of multiple sclerosis.

Along with our mentor, Charles Anglade, we ourselves have often made the same observations in the Chateau–Picon Neural Histology and Pathology Laboratory (in Bordeaux). However, we were not able to interpret these observations in a useful way, because the major importance of these lesions was not properly recognized (due to the fact that, in spite of the infectious theory advanced by P. Marie [4], the etiology of these vascular lesions had not been confirmed). Thus, we turned to other hypotheses.

Today, the detection of the specifically angiotropic process that represents the rickettsial and neo–rickettsial infiltration of the vascular tunica (primarily of the adventitia) is restoring the significant value of the still–valid observations made by the first histo–pathologists who studied the lesions associated with multiple sclerosis.

b. Neural lesions. – Vascular lesions are the primary type of lesion, and are consistently present. However, they are not the only lesions that are present. As demonstrated by Charcot [5], Babinski [6], A. Thomas [7], I. Bertrand [8], and Marinesco [9], among many others, alterations in the nerve tissue are also always observed. These lesions consist of a more or less pronounced involvement of the axis–cylinders, whose myelin is the subject of extensive disturbances. However, generally speaking, these lesions are not definitive. In fact, it appears that the axis–cylinders that are involved can undergo a true anatomical restoration.

Although the cells do not appear to be involved to any great extent, they are nevertheless the subject of some changes (e.g., phenomena consisting of vacuolization, fatty degeneration, tigrolysis, etc.).

All of these lesions, which are secondary, can be attributed in part to innervative proliferation. However, they are also probably attributable to the anoxia and to the effect of the rickettsial and neo–rickettsial toxins, which can play an active role in the demyelinization process.

c. The role played by the innervation. – In multiple sclerosis, the innervation is the seat of intense proliferation. This major change is caused not by the innervation's acknowledged minor functions of support and filling. Rather, it is a result of the distinct phagocytic power that the innervation (as part of the reticulo–endothelial system) displays within the context of certain pathological processes. The radial arrangement of its sheath or covering, which methodically encircles the vascular structures that serve as the receptacles for the pathogenic agent, suggests an attempt at phagocytosis. We should also recall that in arteriosclerosis of the medulla and of the cerebellum (a process that is capable of replicating the entire clinical setting of multiple sclerosis), the reticulo–endothelial system is not stressed by the endogenous toxins, and therefore phagocytosis is not demonstrated. Consequently, proliferation of the innervation is not observed unless this type of arteriosclerosis is accompanied by another, coexisting infection.

In conclusion, therefore, on the histo–physio–pathological level, we can view multiple sclerosis as the result of a disturbance in the nourishment of the nerve tissue, secondary to the vascular involvement. This disturbance primarily affects the following two major elements: oxygen and glucose. This theory of anoxia in multiple sclerosis has the great value of being able to provide a plausible explanation for the very frequent remissions of this condition.

(*) Meeting of March 14, 1960.

[1] P. Le Gac, P. Giroud, and N. Dumas, in *Comptes rendus*, Vol. 250 (1960), page 1937.

[2] Rindfleisch, in *Virchows. Arch.*, Vol. 26 (1863).

[3] Dejerine, in *Rev. Med. Mens.*, Vol. 3 (1883), page 172.

[4] P. Marie, in *Progres Medical* (1884).

[5] Charcot, in *Bull. et Mem. de la Societe des Hopitals de Paris* (1866), page 79.

[6] Babinski (thesis) (Paris, 1885).

[7] A. Thomas, in *Rev. Neur.* (June 15, 1910), page 490.

[8] I. Bertrand, in *Reun. Neur. Internat.* (Paris, 1924).

[9] Marinesco, in *Rev. Neur.*, Vol. 14 (1909), page 957.

The Academy met, in closed session, at 3:30 p.m.