EXPERIMENTAL TOXIC ENCEPHALOMYELOPATHY

(Diffuse sclerosis following subcutaneous injections of potassium cyanide)*

BY ARMANDO FERRARO, M. D.,
RESEARCH ASSOCIATE IN NEUROPATHOLOGY, OF THE NEW YORK STATE PSYCHIATRIC INSTITUTE AND HOSPITAL, NEW YORK, N. Y.

The problem of the etiology and pathogenesis of diffuse sclerosis and multiple sclerosis has been put forth in the last few years especially in connection with acute encephalomyelopathies following infectious conditions of childhood. The desire of reproducing experimentally these pathological conditions of diffuse or multiple sclerosis has been in the mind of numerous investigators, but unfortunately up to date, with the exception of very few reports, nothing definite has entered our current literature.

Diffuse sclerosis and multiple sclerosis are pathological conditions so closely related that I feel partly justified in applying to the etiology of diffuse sclerosis some of the knowledge we already possess in regard to multiple sclerosis.

The various theories concerning the etiology of multiple sclerosis relate to either infections or toxins. The theory of infectious origin of multiple sclerosis has particularly developed under Pierre Marie's influence. Later on, based on the work of Bullock, the possibility of a filtrable virus was considered. Besta and Ceni thought of aspergillus fungatis as one etiological factor. We all know in this connection the work of Chevassut and Purves-Stewart, which unfortunately has not been substantiated by further investigations of Carmichael, Tronconi, Arthur Weil, and others. On the other hand, Steiner thought the condition due to a spirochetais, a conception which, however, still lacks substantial proof.

The toxic theory has three groups of supporters: one following Marburg's idea that a ferment acts destructively on the myelin sheaths; a second one inspired by Strümpel and Müller's conception of an endogenous origin of the disease in the form of a primary involvement of the glia, and a third one believing the toxic

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factor to be an unknown endogenous substance which would primarily act on the myelin covering of nerve fibers.

Following Marburg's inspiration, Brickner again took up the lead and tried to establish that the process of demyelination is due to a lipolytic ferment (lipase) present in the blood of multiple sclerosis patients.

The theory of a primary disease of the glia elements does not seem to have found very numerous advocates with the exception, possibly, of Scholz, Collier and Greenfield, who feel this to be the case in diffuse sclerosis. Coenen and Mir in diffuse sclerosis also speak in terms of a primary disease of the oligodendroglia, while Wertham feels that neuroglia reaction may be set up irrespective of the process of demyelination.

Among the advocates of an endogenous origin related to an unknown toxin we can mention Hassin, A. Weil, Claude, and recently Putnam, who succeeded in reproducing the pathological lesions of multiple sclerosis following intraperitoneal injection of tetanus toxin in 2 out of 48 dogs. A. Jakob also feels that in diffuse sclerosis an endogenous metabolic toxin may be at the base of the pathological lesions.

Aside from such rather fragmentary reports I have been unable to find in the literature any investigation in which experiments carried on a large scale have given constant results in the reproduction of lesions which histopathologically can be classified either as multiple or diffuse sclerosis.

Following the lead of a supposed toxic origin of multiple sclerosis and because of the possibilities of diffuse sclerosis being also a toxic condition, I have tried to reproduce from an experimental standpoint the lesions characteristic of such conditions through the use of a substance, potassium cyanide, which, as we all know, interferes with the oxidizing power of the living cells. According to Warburg cyanide affects the respiratory enzymes and, therefore, inhibits the respiration of tissues. F. O. Schmidt and O. H. A. Schmidt have established that oxygen consumption of resting nerves of the green frog may be practically completely inhibited by cyanide and that the ability of cyanided nerve to conduct an