# TETRAETHYLAMMONIUM CHLORIDE IN MULTIPLE SCLEROSIS

## *A Preliminary Report*

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DIRECT observation of the blood vessels in the central nervous system during sympathetic stimulation or after the injection of various drugs is the subject of a number of published reports. Most convincing are the observations made by Franklin and Brickner,[1] who have relieved retinal vasospasm and scotomas simultaneously by the use of amyl nitrite or intravenous papaverine. They postulate that lesions of multiple sclerosis result from, or are associated with, vasospasm, that scotomas in patients with multiple sclerosis are the result of vasospastic lesions in the retina, and that such disturbances apply with equal validity to any portions of the central nervous system.

Lyons *et al.*[2] have demonstrated that tetraethylammonium chloride is capable of relieving vasospasm in man by blocking the autonomic ganglia. If there is some truth to the assumption that the acute or the exacerbative symptoms of multiple sclerosis contain the element of vasospasm, tetraethylammonium chloride may produce a modifying influence upon these acute symptoms in perhaps the same fashion as do the injections of histamine by Horton, Wagener, Aita, and Woltman.[3]

Several recent articles on the treatment of multiple sclerosis have suggested that, irrespective of the underlying cause, one factor in the disease is some vascular disorder such as a venous stasis or change in vasomotor tone. Such hypotheses form the basis for the use of histamine and dicumarol.

In pursuance of this hypothesis tetraethylammonium chloride has been administered to a number of patients manifesting the acute and chronic symptoms of multiple sclerosis. All of the patients have a history of exacerbations and remissions of the disease.

The technic of administration consists of a deep intramuscular injection of tetraethylammonium chloride, 500-1200 mg. (Etamon*), three to six times per week. The immediate outstanding effects of the drug are an orthostatic hypotension and a loss of visual accommodation. The patient should remain in a supine position for one hour after treatment to avoid syncope and dizziness. Blood pressure readings are taken at five-minute intervals for one-half hour.

Fourteen patients who displayed the familiar acute manifestations of multiple sclerosis, such as transient scotomas, diplopia, numbness, paresthesias,

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weakness of the extremities, urinary incontinence, dysarthria, astereognosis, and ataxia, were treated. Continued treatment with tetraethylammonium chloride in all instances appears to have protected our patients so far from either relapses or further progression of symptoms. Intermittent scotomas were promptly relieved in 1 patient after injection of the drug. In this series the longest period of freedom from acute symptoms has been five months. In 1 patient who refused prolonged treatment there has been no evidence of relapse over a period of six weeks.

The pharmacologic action of tetraethylammonium chloride does not indicate that this drug would be of any benefit in preventing further relapses once medication has been discontinued. The small number of patients and brief period of observation does not offer convincing proof that the drug entirely controls the transitory symptoms of multiple sclerosis. Nevertheless, the fact that all 14 patients with acute symptoms began to show definite improvement of the most recently acquired manifestations within four days after onset of treatment seems significant. Furthermore, none of the members of this group became subjectively or objectively worse after therapeutic doses of tetraethylammonium chloride had been initiated.

The spontaneous and unpredictable remissive factor in multiple sclerosis is well known. Claim as to the value of the treatment, therefore, lies in the improbability that fourteen spontaneous remissions would have occurred within four days after onset of therapy.

The acute symptoms of multiple sclerosis responded to this therapy. Eight patients, whose chronic manifestations had been unvarying for six months or more prior to treatment, were not benefited. These studies indicate that the features of multiple sclerosis which have endured longer than two or three months are not relieved by injections of tetraethylammonium chloride. Therefore, early diagnosis appears to be of great importance if this type of therapy is to be of value.

The small series of patients and the brief time factor involved necessitate a cautious interpretation of the results. The experiences recorded, however, do suggest that the acute and newly-superimposed symptoms of multiple sclerosis may be subjectively and objectively modified by tetraethylammonium chloride. Therefore, it can be argued that the therapeutic value of this drug, like that of histamine and of dicumarol, is based on its ability to interfere with one of the pathologic features of multiple sclerosis.

## References

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3. Horton, B. T., Wagener, H. P., Aita, J. A., and Woltman, H. W.: Observations on treatment of multiple sclerosis by intravenous administration of histamine. Proc. Central Soc. Clin. Research **16**:23-24, 1943.