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The Frequency of Relapse in Multiple Sclerosis*
A Study Based on 245 Cases

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Summary. The authors analyze the course of 245 cases of multiple sclerosis. The mean annual frequency of attacks is 0.66 for all the patients (remittent forms and progressive forms). Although it is usually suggested that this frequency decreases with the years, this has not been found in our study. Our results also indicate that we would have to follow 590 patients over 1 year or 190 over 2 years before being able to attest the effectiveness of a treatment decreasing the frequency of attacks by 25%.

Key words: Multiple sclerosis — Relapses in multiple sclerosis.

Most trials of therapy of multiple sclerosis are based on a quantitative evaluation, measuring the degree of disability or the objective data of the physical examination or both.

The annual frequency of attacks has scarcely been taken into account. Indeed, it seems that use of the notion of the frequency of attacks involves many difficulties. It is generally thought that the frequency of attacks decreases with the years even though the disease goes on developing and the functional disability increases. There are also some progressive forms which worsen slowly, without obvious bouts; this type of development may be the only pattern of progression from the onset or

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follow a series of bouts (secondary progressive forms). But these forms are about 10% and in all other cases the disease develops with regressive bouts which can easily be identified and dated. Another obstacle, more difficult to overcome during trials of therapy, is the value for the average annual frequency itself, which is about 0.5 in the main reported studies. If an attack occurs every 2 years on average, a brief treatment lasting only a few weeks or months cannot retain this frequency criterion. This, practically, would demand an increased number of patients and a longer duration of treatment. Moreover, patients are frequently seen after a recent attack. If they are then included in a therapeutic trial, the observation period is very likely to coincide with a decline and a remission of the disease, since the next attack may not occur for 3 years. A drawback of this kind can also distort the trials in which a rating scale is used for evaluation of the functional disability or objective physical abnormalities, because the natural favorable course of an attack might be considered as a positive effect of the treatment being studied. A comparative study enables us to avoid this difficulty but also requires a large number of patients.

Hopefully, a more effective therapy will be discovered in the near future, which will be capable of slowing down or definitively stopping the regular occurrence of attacks and the development of the disease. To be valid, the trials of a therapy of this kind will have to use both the rating scales and the average annual frequency of the attacks. Further points for consideration are but how long the patients will have to be treated and kept under observation and how many patients will be required for a positive conclusion to be possible.

Is it sufficient to treat a few patients for a few weeks or months as is usually done? Too often the number of patients and the duration of the treatment are not decided in relation to the selected parameters but imposed by external circumstances, for example, the number of patients presenting at a medical center during the trial period or the toxicity of the drug used. In an attempt to answer these two crucial questions we have analyzed the frequency of attacks in 245 patients over a period giving a total of 2393 patient years.

Materials and Methods

The study was based on the analysis of 400 cases of multiple sclerosis been between January 1965 and October 1970 (in the Service de Neurologie et Néuro-psychologie, Hôpital de la Salpêtrière, Prof. F. Lhermitte). Only those patients who had no intellectual deterioration and no major psychiatric disorder and who were continuously supervised by a team of 2 neurologists (R.M. and J.G.) were accepted for inclusion. The cases which had no firm diagnosis of multiple sclerosis were excluded, i.e. the case of "possible" multiple sclerosis according to the criteria