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MULTIPLE SCLEROSIS: A FUNCTIONAL APPROACH

The Lancet has published several articles and letters between 1976 and 1978 reporting small bowel abnormalities in multiple sclerosis including increased inflammatory-cell infiltration [1] and loss of villous architecture [2, 3]. Several authors, including in *The American Journal of Gastroenterology*, linked cases of multiple sclerosis with intestinal malabsorption [2-4].

We still do not well understand the mechanisms underlying the initiation and progression of multiple sclerosis, but it has an autoimmune origin [5]. However, "unlike autoimmune conditions such as rheumatoid arthritis, systemic lupus erythematosus or myasthenia gravis, multiple sclerosis has no specific immunological marker" [6], despite the fact that the presence of at least two different antibodies - anti-myelin oligodendrocyte glycoprotein (MOG) and anti-myelin basic protein (MBP) - appears highly predictive of typical clinical events that establish the diagnosis of clinically definite multiple sclerosis [7].

Recently, more evidence accumulates about the link between autoimmune diseases and an abnormal intestinal permeability, a condition often named "*leaky gut syndrome*". An article published in *Science* (March 2005) suggests that a leaky gut barrier allows antigens to enter the lamina propria, leading to the disruption of the immune system [8]. Another paper that appeared soon after in *Acta Paediatrica* (April 2005) explained how leaky intestines could trigger an abnormal antigen exposure, itself enabling the cross-recognition of molecular structures shared between self and nonself, a phenomenon called "molecular mimicry" [9].

Fasano, the world-leading expert on cœliac disease, claims that "the loss of the protective function of mucosal barriers (mainly the gastrointestinal and lung mucosa) is necessary for autoimmunity to develop" [10]. He even suggests, "the autoimmune process can be arrested if the interplay between genes and environmental triggers is prevented by re-establishing intestinal barrier function" [10]. Actually, Crohn's disease as the other inflammatory bowel diseases corresponds to an autoimmune condition characterized by increased intestinal permeability [11]. Interestingly, "multiple sclerosis (MS) patients may have an increased risk of co-acquisition of Crohn's disease" and "a subgroup (5 among 20 patients enrolled in the study) of MS patients has increased intestinal permeability" [12].

Taking into account that "alcohol abuse impairs the function of the intestinal barrier" [13], and that ethanol is known to increase intestinal permeability [14], we underline how MS patients are well known to be at increased risk from alcohol excessive consumption [15]. Consequently, several paths may lead to the gut metabolism abnormalities seen in MS [16].

"Intestinal permeability is characteristically elevated in untreated cœliac disease" [17] as well as "intestinal permeability is altered in children with cow's milk allergy" [18]. In fact, impaired intestinal permeability seems to be present in all subjects with adverse reactions to food [19] and breast-feeding could favourably influence intestinal permeability [19]. Not surprisingly, dairy-free diet [20] and gluten-free diet [21] could show beneficial to MS patients, and they "were less likely than controls to have been breast fed for a prolonged period of time, another point [being] added to the long list of the benefits of prolonged breast feeding" [22]. We spot similar beneficial effects towards autistic patients [23, 24], while these patients also suffer from an abnormal intestinal permeability [25].

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