Multiple sclerosis

A lifestyle disease?

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Chronic diseases are the primary cause of disability, morbidity, and death in Western developed countries. Many of these diseases are related to environmental influences including diet, smoking, and other lifestyle factors. Public health measures address some of these factors, and studies strengthening the links between environmental factors and health can be useful in this regard.

In this issue of *Neurology*®, Dr. Marrie et al.[1] present a successful quantification of the prevalence of comorbidity by type and sex in a large multiple sclerosis (MS) population in Canada at time of diagnosis. The major strengths of the study include the large number of cases (23,382 incident MS cases) and controls (116,638) and use of validated case definitions for the disease states. Overall, there were 19,861 cases of morbidity for patients with MS, but there was no mention in the article of the extent of multiple comorbidities for these patients. Clearly, information regarding lifestyle such as smoking status and biomarkers of health would have increased the interpretability of these results. Further, the noticeably high age at diagnosis in this cohort suggests a possible selection bias. Even though the estimates of relative prevalence of the comorbidities were age-adjusted, this questions the representativeness of this cohort for patients with MS in general.

Nevertheless, the finding of a higher occurrence of a number of chronic diseases among patients with MS relative to the general population begs the question of whether there are shared risk factors for MS and these comorbid diseases. If so, recognizing them could lead to recommendations that would reduce the risk of both MS and the comorbid diseases.

There are several important risk-modifying factors linked to lifestyle established for MS: ultraviolet radiation exposure and low 25-hydroxyvitamin D [25(OH)D] concentration,[2] obesity,[2] low omega-3 fatty acid intake,[3] and smoking.[2] A common link to all these factors, and many of the associated conditions, is inflammation. Reduced inflammation is associated with vitamin D supplementation[4] and omega-3 fatty acids intake,[3] while increased inflammation is associated with obesity through increased secretion of adipokines[5] and smoking, through any of a number of possible mechanisms related to the immune system, blood–brain barrier, toxins, or chronic respiratory infections.[2]

The table lists the comorbid diseases in order of relative risk as reported by Marrie et al.[1] along with percentages of those diagnosed with MS having each comorbid disease, and indicates which risk-modifying factors have been linked to these diseases. As can be seen in the table, low 25(OH)D concentration, obesity, low omega-3 fatty acid intake, and smoking are associated with most of the studied comorbid diseases. The comorbid diseases were present both 5 years prior to MS diagnosis as well at diagnosis: it appears, therefore, that the risk of MS and the comorbid diseases could be reduced in the general population by increasing 25(OH)D concentrations and omega-3 fatty acid intake; avoiding becoming overweight or obese by limiting sugar intake and not overeating; and not smoking, preferably starting early in life. There is also evidence that taking similar measures after development of MS can reduce the symptoms and slow disease progression.[2] There are many health benefits of vitamin D.[6] Most of the action of vitamin D occurs through the action of the hormonal version, 1,25-dihydroxyvitamin D, which, through specific vitamin D receptors, affects expression of hundreds of genes, upregulating some, downregulating others.

Marrie and colleagues also found that, relative to the general population, male patients with MS had higher rates of depression, diabetes, and hypertension, but no higher rates of anxiety and epilepsy. The interpretation of these findings is difficult and would probably require new studies including information on risk factors.

Such studies including information on lifestyle factors should also try to determine how much of the comorbidity is caused by shared etiology and how much is caused by other factors related to the presence of one of the diseases. The take-home message to physicians and patients from the findings by

See page 1279

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Table Crude prevalence of comorbidity in the multiple sclerosis population at diagnosis compared to matched controls[1] and which risk-modifying factors have been linked to the diseases

Disease	RR[a]	Percent[b]	Ultraviolet exposure and vitamin D	Obesity	Omega 3 fatty acid	Smoking
Multiple sclerosis		100.0	+[2]	+[2]	+[3]	+[2]
Epilepsy	2.18	1.9			+[c]	
Depression	2.04	19.1	+[6,7]	+[8]	+[3]	+[9]
Bipolar disorder	1.86	3.2		+[8]	+[3]	
Inflammatory bowel disease	1.68	0.6	+[6]		+[3]	
Anxiety	1.61	11.1	+[c]		+[c]	
Chronic lung disease	1.34	12.1	+[6]	+[8]	+[c]	+[9]
Schizophrenia	1.32	1.1		+[8]	+[c]	
Ischemic heart disease	1.30	6.5	+[6]	+[10]	+[3]	+[9]
Hypertension	1.17	15.2	+[6]	+[8]	+[3]	+[9]
Diabetes	1.17	5.7	+[6]	+[8]	+[c]	+[9]
Hyperlipidemia	1.03	6.9		+[8]		+[9]

[a] Relative risk (RR) of comorbid disease as given in Marrie et al.[1]
[b] Percentage of patients with multiple sclerosis with the specified comorbid disease.[1]
[c] Supporting reference not given.

Marrie and colleagues, and this editorial, is that many chronic diseases have similar underlying lifestyle risk factors, including low ultraviolet exposure and 25 (OH)D concentrations, poor diet leading to obesity, low omega-3 fatty acid intake, and smoking. Thus, patients, especially those presenting with any of the chronic diseases discussed, should be further motivated to modify a possibly unhealthy lifestyle.

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REFERENCES

1. Marrie RA, Patten SB, Tremlett H, et al. Sex differences in comorbidity at diagnosis of multiple sclerosis: a population-based study. Neurology 2016;86:1279–1286.
2. Ascherio A, Munger KL, Lünemann JD. The initiation and prevention of multiple sclerosis. Nat Rev Neurol 2012;8:602–612.
3. Simopoulos AP. Omega-3 fatty acids in inflammation and autoimmune diseases. J Am Coll Nutr 2002;21:495–505.
4. Cannell JJ, Grant WB, Holick MF. Vitamin D and inflammation. Dermatoendocrinol 2015;6:e983401.
5. Aleksandrova K, Nimptsch K, Pischon T. Influence of obesity and related metabolic alterations on colorectal cancer risk. Curr Nutr Rep 2013;2:1–9.
6. Hossein-Nezhad A, Holick MF. Vitamin D for health: a global perspective. Mayo Clin Proc 2013;88:720–755.
7. Armstrong DJ, Meenagh GK, Bickle I, Lee AS, Curran ES, Finch MB. Vitamin D deficiency is associated with anxiety and depression in fibromyalgia. Clin Rheumatol 2007;26:551–554.
8. Martin-Rodriguez E, Guillen-Grima F, Martí A, Brugos-Larumbe A. Comorbidity associated with obesity in a large population: the APNA study. Obes Res Clin Pract 2015;9:435–447.
9. Cunningham TJ, Ford ES, Rolle IV, Wheaton AG, Croft JB. Associations of self-reported cigarette smoking with chronic obstructive pulmonary disease and co-morbid chronic conditions in the United States. COPD 2015;12:276–286.
10. Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation 1983;67:968–977.