

Narcolepsy and Streptococcal Infections

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WE READ WITH KEEN INTEREST THE PAPER BY ARAN AND COLLEAGUES READDRESSING THE ROLE OF STREPTOCOCCAL INFECTIONS IN THE ETIOLOGY OF narcolepsy.¹ Prior studies have, perhaps not surprisingly, yielded mixed results for antibody testing, given the lag between infection and neurologic symptom onset for some poststreptococcal complications, such as Sydenham chorea. Antibody titer levels drop after a streptococcal infection and can be normal by the time of diagnosis. Aran and colleagues showed that the association of narcolepsy with antibody titer levels was stronger the closer that the titer levels were determined in relationship to disease onset. In a population-based case-control study of narcolepsy in King County, Washington,² we found that 90.9% of 45 patients who were DQB1*0602 positive reported having had a strep throat infection, versus an estimated 75.9% of DQB1*0602-positive control subjects (n = 95). After adjustment for race and family income, the risk of narcolepsy in a person with a history of a physician-diagnosed strep throat before age 21 years was estimated to be 5.4-fold higher (95% confidence interval = 1.5, 19.1) than in individuals without such a history.³ In contrast, little or no association was found between narcolepsy and other childhood infectious diseases, such as mononucleosis, pneumonia, or hepatitis, or with vaccinations. These findings fit well with the observation from the same study that an increased risk of narcolepsy was associated with having lived with 2 or more household smokers before age 21 years (odds ratio = 5.1; 95% confidence interval = 1.6, 12.1).⁴

In children, exposure to environmental tobacco smoke through passive smoking is associated with serious bacterial infections and with altered immunity.⁴ In addition, neurologic disorders with a hypothesized autoimmune etiology have been known to follow streptococcal infections, specifically, Sydenham chorea and pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS).^{1,3,5} Finally, people with HLA DQB1*0602 handle streptococcal infections differently than do those without HLA DQB1*0602.^{1,3} HLA DQB1*0602 is strongly associated with narcolepsy, and the associations mentioned previously were seen in cases and control subjects who were all positive for HLA DQB1*0602.

These results support the hypothesis that genetically susceptible individuals develop narcolepsy as a complication of a streptococcal infection, which they are more likely to develop because of exposure to environmental tobacco smoke through

passive smoking. The streptococcal infection may then trigger an autoimmune response with selective destruction of the hypocretin (orexin) cells in the hypothalamus. Narcolepsy ensues, with the severity reflecting the degree of hypocretin (orexin) cell loss.⁶

We hope that future studies will address and refine this hypothesis about narcolepsy and streptococcal infections. Such studies should involve ascertainment of HLA DQB1*0602 status in both cases and control subjects so that comparisons can be made between genetically predisposed individuals. Establishing an etiology would be the essential first step in preventing this chronic and disabling disease.

DISCLOSURE STATEMENT

The authors have indicated no financial conflicts of interest.

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