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Re: Ambient air pollution and early manifestation of type 1 diabetes.  
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Air pollution, infections and type 1 diabetes in children

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To the Editor:

We read with great interest the letter by Beyerlein et al. that reported an association between exposure to high levels of PM$_{10}$ and NO$_2$ and early manifestation of type 1 diabetes (T1D) in Bavaria, Germany. The authors had hypothesized a role for infections in such an association, based on an earlier study in which they had found an association between respiratory infections in the first year of life and islet autoimmunity among children at risk of T1D, and research suggesting that ambient air pollution may exacerbate inflammation and promote respiratory diseases in young children.

We have previously reported in *Epidemiology* that T1D at ages 0-14 years shows long-term (6-year) cyclical variation in northeast England. Other research we have conducted in this part of England found evidence of space-time clustering and of temporal clustering, i.e. an irregular (non-seasonal) temporal distribution of cases. We interpreted our findings principally with regard to the possible involvement of an infectious agent; in particular, one that occurs in “mini-epidemics”. The idea that ambient air pollution might be linked to T1D in children through the promotion of respiratory infections is intriguing. Nevertheless, there are reasons for caution in interpretation.

First, Beyerlein et al. did not find any clear associations between inflammatory markers and PM$_{10}$ exposure levels. This may suggest that any mechanism by which air pollution might affect T1D does not involve inflammation, at least based on the markers considered. Second, the effect found by Beyerlein et al. was specific to the 10$^{th}$ percentile of the age of diagnosis, corresponding in the whole dataset to ages less than 4 years, while no association was found for higher percentiles, corresponding to older ages at diagnosis. In contrast, Muirhead et al. found that the evidence for temporal clustering of T1D was more marked at ages 5-14 years than at younger ages. When discussing possible links with the hygiene hypothesis, we highlighted previously the importance of timing of exposure, in that certain viruses might provoke autoimmunity when given late but be protective when given very early. We also noted that the time between exposure to virus infections and disease might vary between individuals and that our findings of temporal clustering at ages 5-14 years would be consistent with infection(s) acting on the immune system of susceptible individuals and leading to clinically observable disease in some of these individuals shortly thereafter.

These findings, taken together with an analysis reporting differences in autoimmune characteristics between children diagnosed with T1D before 5 years of age and those diagnosed at a later age, may suggest different mechanisms – and possibly different risk factors - for childhood T1D at different ages. Nevertheless, it would be valuable to see whether the results of Beyerlein et al. can be
replicated elsewhere and whether there is further evidence to link together air pollution, infections and T1D in children.

REFERENCES