Correspondence

Letter Regarding Article by Weitzman et al, "Tobacco Smoke Exposure Is Associated With the Metabolic Syndrome in Adolescents"

To the Editor:

Weitzman et al[1] found a relationship between exposure to tobacco smoke and risk of developing metabolic syndrome among adolescents. They speculate that tobacco smoke exposure may increase the risk of insulin resistance, which in turn may contribute to an increased risk of developing metabolic syndrome. Other studies may lend some insights into this process.

Recent studies indicate that epigenetic mechanisms may be involved in metabolic syndrome and type 2 diabetes.[2–4] There is growing evidence that variations in DNA methylation patterns may play a role in insulin resistance.[3] The promoters of key genes involved in glucose metabolism display differential DNA methylation. It has been suggested that alterations in DNA methylation patterns might explain how developmental programming during the prenatal period influences the risk of developing metabolic syndrome later in life.[2] Diabetes is often a part of syndromes involving aberrant imprinting. Age-associated epigenetic drift of methylation patterns parallels an increased risk of various pathological conditions, including insulin resistance.[2,3]

Smoking has been associated with aberrant DNA methylation patterns.[5] The inactivation of key genes through promoter hypermethylation is believed to be one of the mechanisms by which tobacco smoke promotes the development of lung cancer.

As more is learned about the epigenetics of metabolic syndrome, it might be worth looking at the impact of tobacco smoke on the methylation of genes related to that condition.

Disclosures

None.

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Response

We thank Celia Ross for her very interesting letter. She proposes that our findings reported earlier in this journal[1] of a strong, dose-response association between second-hand smoke exposure, as assessed by cotinine levels, and the metabolic syndrome among adolescents may be explained by findings from a related literature. That literature, she points out, suggests that DNA methylation patterns may play a causative role in the development of insulin resistance, type 2 diabetes, and the metabolic syndrome.

Although we recognize the need for additional epidemiologic studies that confirm (or do not confirm) our findings, we believe that her suggestion is potentially important for 2 distinct reasons. First, the identification of a plausible underlying biological mechanism to explain these epidemiologically observed phenomena creates opportunities for assigning causality with the subsequent possibility of more effective disease prevention and treatment strategies.[2] Second, she also raises the possibility that the association we reported, to a degree that is currently entirely unclear, may reflect not so much concurrent or earlier childhood exposure to secondhand smoke but rather prenatal exposure. Difficulties inherent in distinguishing the effects of prenatal from postnatal tobacco smoke exposure have arisen not only in this area of study but also in terms of parental smoking and children's risks of asthma, ear infections, sudden infant death syndrome, and neurobehavioral development,[3,4] and her suggestion may aid work in these related areas as well.

Disclosures

Dr Daniels is a consultant/advisory board member of Abbott Laboratories. The other authors report no conflicts.

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