Invited Commentary

Invited Commentary: Parental Smoking as a Risk Factor for Adult Tobacco Use: Can Maternal Smoking During Pregnancy Be Distinguished From the Social Environmental Influence During Childhood?

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Parental smoking is known to have prenatal health effects on developing fetuses, and postnatal exposure to secondhand smoke causes adverse health effects during childhood and beyond. Further, there is solid evidence that parental smoking during childhood is a potent risk factor for smoking in offspring. In this issue of the Journal, Rydell et al. (Am J Epidemiol. 2014;179(12):1409–1417) add to a growing body of evidence showing that maternal smoking during pregnancy is statistically associated with the long-term risk of tobacco use in offspring. The data revealed a strong signal between maternal smoking during pregnancy and tobacco use in young adulthood, an association that was largely concentrated in snus use but not cigarette smoking. This new study adds to a growing body of epidemiologic evidence that consistently points toward maternal smoking during pregnancy being associated with an increased risk of offspring tobacco use in later life. There is also evidence from animal models indicating that fetal exposure to maternal nicotine use in utero can have a durable impact on the neural pathways that affect lifetime sensitivity to nicotine. This is an important research topic that continues to yield a consistent signal despite an array of inferential challenges.

cigarette smoking; parental smoking; pregnancy; risk factors

Abbreviation: SHS, secondhand smoke.
determinants of youth smoking, but parental smoking behavior is more strongly associated with offspring smoking than are parental attitudes (13). The risk of smoking increases with the number of parents who smoke (5, 7) and is elevated in households in which only the mother or the father smokes (6). These associations extend into adulthood (14, 15). The influence of parental smoking on children’s smoking is also exerted through sibling smoking, as sibling smoking is also a strong risk factor for smoking that persists into adulthood (14).

**IS MATERNAL SMOKING DURING PREGNANCY AN INDEPENDENT RISK FACTOR FOR OFFSPRING TOBACCO USE?**

Against this backdrop, an emerging body of evidence suggests that maternal smoking during pregnancy may also contribute independently to offspring tobacco use. In this issue of the *Journal*, Rydell et al. (16) report the findings of a study in Sweden of maternal smoking during pregnancy in relation to the risk of smoking and snus use in young adulthood. In a cleverly designed study, the investigators measured smoking histories and parental smoking during childhood and adolescence through subject recall in a cohort of recently recruited young adults. Maternal smoking during pregnancy was measured via linkage to a national birth certificate registry. The predicted association was observed between maternal smoking during pregnancy and offspring tobacco use in young adulthood. After adjustment for parental smoking during childhood, the association with smoking virtually disappeared, but that for snus use remained. The nearly complete attenuation of the association with smoking after adjustment for parents’ postnatal tobacco use could be interpreted as evidence of childhood exposure to parental smoking being not only more proximal in the causal pathway between in utero exposure and adult smoking but also more important.

The association with snus but not cigarette smoking is potentially explainable by the secular changes in tobacco use that took place in Sweden during this time period, when cigarette smoking began to be supplanted by use of snus (17). This could also be interpreted as evidence that the association is specific to nicotine and that social modeling of parental behavior may not play such a critical role.

Overall, the results of the study by Rydell et al. (16) add to a body of evidence documenting that maternal smoking during pregnancy is statistically associated with subsequent tobacco use in late adolescence and adulthood (18–22). In a cohort of women and offspring (*n* = 608) who were followed over time, Cornelius et al. (18) observed that maternal smoking during pregnancy was associated with smoking and nicotine dependence in young adult offspring. Using data from the Providence, Rhode Island, site of the National Collaborative Perinatal Project, which recruited pregnant women from 1959 to 1966 and then followed-up offspring (*n* = 1,248; average age, 29 years) for smoking status, Buka et al. (19) found that exposure to maternal smoking, particularly smoking of 1 or more packs of cigarettes per day, was significantly associated with nicotine dependence in adult offspring. In smaller cohorts, maternal smoking during pregnancy was associated with smoking at 42 years of age in the New York City National Collaborative Perinatal Project site (*n* = 262) (22) and with smoking initiation when offspring were 16–21 years of age in the Ottawa Prenatal Prospective Study (*n* = 152) (20). These consistent findings in well-designed prospective cohort studies are unlikely to be attributable to chance. Further, other studies based on remote recall of smoking during pregnancy have also yielded similar results (23, 24).

**INFERENTIAL CHALLENGES**

A lingering question is whether these observed associations are merely due to maternal smoking during pregnancy serving as a proxy for exposure to parental smoking during childhood. For example, the likelihood of being free from exposure to parental smoking during childhood in the study of Rydell et al. (16) was 9-fold greater in those not exposed to maternal smoking in utero than in those who were exposed (55% vs. 6%). In another study, passive exposure to nicotine until age 15 years was 2.6 times greater in those who were exposed to maternal smoking during pregnancy than in those who were not exposed (20).

A cohort of mothers and offspring (*n* = 3,058) were followed-up from their pregnancies onward by Al Mamun et al. (21), with maternal smoking data collected before, during, and after pregnancy. A key finding was that the risk of offspring smoking was higher in those whose mothers smoked before, during, and after pregnancy than in those whose mothers smoked before and after but not during pregnancy. By isolating smoking during pregnancy, these results support the hypothesis that maternal smoking specifically during pregnancy could contribute over and above the social environment during childhood. Even for these findings, however, a concern is that mothers who continued to smoke during pregnancy have greater nicotine dependence and a higher prevalence of other risk factors for offspring smoking than do mothers who were smokers but quit smoking during pregnancy. Clear differences exist between expectant mothers who do and do not smoke during pregnancy; those who smoke are more likely to be younger, single, and of lower socioeconomic status, to drink alcohol or use other substances, and to have psychiatric comorbidities (25, 26), differences that were also seen by Rydell et al. (16). Each of these factors is associated with an increased likelihood of adult smoking. More importantly, these differences are also evident even when comparing mothers who smoke but not during pregnancy with mothers who did smoke during pregnancy (21, 27).

Thus, those exposed to maternal smoking during pregnancy represent a higher-risk group for smoking for many reasons other than maternal prenatal exposure to smoke. Mothers who smoke during pregnancy represent a select subset of all mothers, and even a select subset of mothers who smoke. As has been previously pointed out for maternal smoking during pregnancy in relation to a different outcome (delinquency) (28), the fact that smoking during pregnancy is a marker for such a complex constellation of inter-related risk factors makes it difficult to statistically adjust away these factors.

A separate issue facing the field is the need to more completely characterize parental—not just maternal—smoking over time. In 2-parent households, the possible exposure groups are no parental smoking, smoking by the father only, smoking by the mother only, and smoking by both parents. In
prior studies, paternal smoking during pregnancy was often not considered, and neither was paternal smoking when the offspring were children. This omission may result in misclassification and confounding due to mother and child exposure to paternal secondhand smoke and paternal modeling of smoking. Data from the Child Health and Development Study (29) illustrate the importance of this issue: father-only smoking during pregnancy was slightly more strongly associated with regular smoking in offspring at 17 of years age than mother-only smoking (relative risk = 1.6 vs. 1.4), with an even higher relative risk of 2.4 if both parents smoked (29). Using more detailed classification while accounting for transitions in parental smoking over time could yield valuable clues to assess the validity of the association with maternal smoking. For example, in households in which the father is a persistent never smoker, comparing offspring smoking in mothers who smoked during pregnancy and then quit in the offspring’s early life with those who smoked during pregnancy and persisted smoking thereafter would provide clues to the relative importance of maternal smoking during childhood versus during pregnancy. However, the stratum size in the former group in a single study is likely to be too small to yield meaningful inferences. This challenge could potentially be addressed by pooling data across studies; however, even this approach may not yield adequate stratum sizes for such rare transitions. Accounting for parental smoking—rather than just maternal smoking—and transitions in parental smoking over time may lead to a refined understanding of this association, but it will not surmount the central problem of confounding due to the important differences between mothers who smoke during pregnancy and those who do not.

**BIOLOGICAL PLAUSIBILITY**

When faced with the inferential challenges posed by attempting to tease apart the impact of prenatal exposures from that of exposure after birth, complementary evidence from the basic sciences to elucidate a biological mechanism assumes a critical role. As indicated by Rydell et al. (16), evidence from animal models does in fact support the notion that maternal nicotine exposure can have an effect on biological imprinting in ways that increase the offspring’s susceptibility to nicotine dependence by impacting responsiveness to nicotine. For example, prenatal nicotine exposure in rats and mice has been shown to negatively impact important neural pathways in the developing brain, resulting in impairments that include long-term changes in sensitivity to nicotine (30).

In addition to nicotine having a direct effect on nicotinic receptors in the fetal brain, it is possible that in utero tobacco exposure may impact the propensity to smoke through epigenetic alterations (31). Epigenetic markers have yet to be studied directly in relation to this topic, but compared with offspring who were not exposed to maternal smoking in utero, exposed offspring have detectable differences in specific DNA methylation markers at birth (32) and even into adulthood (33). In seeking to further clarify whether this association is causal, this field of research stands to benefit, as Rydell et al. (16) suggest, from the integration of biomarkers in future research that attempts to verify whether the findings from basic science research are relevant to human populations.

**SUMMARY AND CONCLUSION**

Attempting to pinpoint whether maternal smoking during pregnancy is genuinely associated with tobacco use in adulthood above and beyond the contribution of the social environment during childhood and adolescence is an important public health challenge. The current body of evidence, with an important addition by Rydell et al. in this issue of the Journal, has identified a clear statistical association. Despite the inherent challenges in measuring an impact of maternal smoking during pregnancy that is independent of the postnatal influence of parental smoking, the current body of basic science and epidemiologic evidence certainly opens up the possibility that this may be the case.

Parental smoking is a critical family health issue. Parents who smoke increase their personal risk of smoking-caused disease; expose other family members to the adverse health effects of SHS, and increase the risk that their children will smoke. All are powerful reasons for parents not to smoke cigarettes. As the evidence advances toward achieving resolution on the potential effect of maternal smoking during pregnancy on the risk of offspring smoking in later life, there is already strong evidence of the health benefits to the fetus of stopping smoking as soon in the pregnancy as possible. Successful smoking cessation interventions for parents and expectant parents could reap substantial public health benefits not only by directly enhancing the health of parents and children but also by disrupting the familial propagation of tobacco use and thus sparing future generations from the deleterious health effects of tobacco exposure.

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