Maternal Smoking and Infant Cardiovascular Physiology
A Mechanism of Early Cardiovascular Disease Development?

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For many years, smoking has been linked to detrimental outcomes in pregnancy, with an increased risk of preterm and still births. There is now also a growing body of evidence that prenatal smoke exposure is linked with longer-term health problems for the offspring, including neurological, respiratory, and, in particular, cardiovascular disorders. Maternal smoking has been associated with increased cholesterol levels, body mass index, blood pressure, and carotid wall thickening in the offspring. The key intervention is to help mothers give up smoking. However, for those offspring who have already been exposed to smoke as children, it is of clinical importance to try and understand underlying mechanisms for the increased cardiovascular risk to provide optimal primary prevention advice. Increasingly, more direct mechanistic insults to the vasculature during fetal and infant development are being explored with, for example, endothelial functional integrity and the role of NO coming under scrutiny (Figure).

Autonomic Function in Infancy and Tobacco Smoke Exposure
In this issue of Hypertension, Cohen et al. highlight an important potential physiological mechanism, namely that tobacco exposure in critical stages of fetal and infant development “reprogram” autonomic blood pressure control mechanisms. The work develops previous observations by the authors that infants exposed to nicotine during fetal life have a “hyperreactive” autonomic system in the first few weeks of postnatal life. They now show that these infants also have different parasympathetic and sympathetic control at 1 year of age, which results in abnormal blood pressure control on tilt testing. These results are consistent with those of Browne et al., who demonstrated an alteration in autonomic function in tilt testing between smoke-exposed and control infants, finding the same hyperreactivity in the early days of life. Viskari-Lahdeoja et al. also found that infant autonomic response were altered on side motion, showing a reduced elevation of heart rate and blood pressure in children aged 10 to 16 weeks old. The careful experimental approach of Cohen et al. and others, has provided unique insights into autonomic function development during the first year of life, which is complex to study in humans. As a result, we now know there are clear differences in vascular physiology between smoke-exposed and control infants.

Relation Between Smoke Exposure and Development?
What reasons could there be for this difference in physiology during the first year? One possibility may relate to the recent observation that children born to mothers who smoked during pregnancy also had differences in neurological development. Offspring of smokers are ~2 times more likely to show signs of developmental delay at 12 months of age. Accurate developmental data are difficult to collect, and Cohen et al. do not report the developmental stage of the infants exposed to smoke. Development of orthostatic control is likely to be interrelated with the progression of the infant from lying to sitting and then to standing, as they become more dependent on appropriate orthostatic responses. Programmed differences in autonomic control may complicate the ease with which infants can learn to stand and ultimately walk. An alternative interpretation is that the differences in autonomic control merely reflect this slower development. More prolonged follow-up will be able to determine whether these differences disappear in the infant as they mobilize fully.

Long-Term Cardiovascular Reprogramming?
Could differences in autonomic control during the first year of life be a causal pathway in the development of cardiovascular disease in later life? It is possible that abnormal cardiovascular responses accelerate underlying cardiovascular disease during fetal and infant life sufficiently to account for a later increased cardiovascular risk. However, it is more likely that a long-term impact on cardiovascular disease development will result from long-term differences in vascular responses over many years. Therefore, it will be helpful to investigate in future studies whether there is true “reprogramming” of cardiovascular responses. Cohen et al. emphasize that the children exposed to tobacco smoke during pregnancy were still exposed to tobacco smoke in the home during the first year of life. This makes it difficult to discern whether the effects seen are a long-term reprogramming because of previous exposure in utero or whether the changes reflect ongoing tobacco exposure. The question is raised: if the infants are taken out of the smoking environment would the differences correct themselves?

Conclusions
The significance of this article lies in its ability to undertake complex physiological studies in infants and demonstrate...
SMOKING IN PREGNANCY
Exposes mother, fetus and placenta to:
- nicotine
- free radicals
- carbon monoxide
- other toxins

A
IN UTERO
- placental damage: change in structure and integrity of function
- umbilical circulation changes
- direct effects on fetal circulation e.g. fetal hemoglobin saturation
- direct effects on fetal vascular cells

INTRAUTERINE GROWTH RESTRICTION
PERTERM BIRTH
STILLBIRTH
REDUCED BIRTHWEIGHT

B
POSTNATAL
- Classical CVD risk factors
- Endothelial function
- Structural vascular changes
- Autonomic control

- BMI
- lipid profile
- blood pressure
- decreased NO bioavailability
- decreased activity of eNOS
- Increased intima-media thickness in vessels
- Changes in sympathetic and parasympathetic tone
- Hyperreactive state at birth
- Lower heart rate
- Lower response to stress in infant life

INCREASED CARDIOVASCULAR DISEASE

Figure. Relation of maternal smoking during pregnancy and in utero (A) and postnatal (B) impacts on the cardiovascular system of the offspring that may lead to increased incidence of cardiovascular disease in later life. The oval in box B highlights the potential mechanism of programmed changes in autonomic control observed by Cohen et al.7
differences in response to stress in those exposed to smoke during fetal and infant life. The findings firmly establish loss of homeostatic control as a potential mechanism in an association between early tobacco exposure and later cardiovascular disease development. Follow-up into childhood will provide opportunities to understand whether the differences demonstrated at the end of the first year of life are independent of developmental stages. Furthermore, if, in those infants who are no longer exposed to tobacco smoke, the differences in cardiovascular response persist, then these observations will be confirmed as an example of reprogrammed physiology with the potential to influence the emergence of cardiovascular risk factors and disease.

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None.

References
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