I
n the 1960s, the US Surgeon General and American Heart Association issued reports warning of the dangers of smoking on fatal coronary artery disease.1–3 Since those early publications, 32 US Surgeon General reports and thousands of studies have been released exposing the harmful effects of cigarette smoking on cardiovascular health.4,5 Yet, more than a half a century later, the toxic legacy continues to unravel. Cigarette smoking is now well established as a causal risk factor for cardiovascular disease (CVD). Pooled data from almost 1 million people reveals that the risk of ischemic heart disease for current smokers is 2.6 times (95% confidence interval [CI], 2.4–2.7) higher for men and 3.0 times (95% CI, 2.8–3.2) higher for women compared with nonsmokers.6 Secondhand smoke (SHS) exposure has emerged as a significant risk factor for CVD among nonsmokers, demonstrating a dose-dependent relationship with higher risk of CVD among those with higher SHS exposure.7–9 In epidemiological studies, the risk of coronary heart disease among SHS-exposed nonsmoking adults is 1.25 times (95% CI, 1.17–1.32) higher than unexposed adults.10

Although the risks of concurrent SHS exposure are clear, the deleterious cardiovascular health effects of remote SHS exposure, especially from SHS exposure during childhood, have been more difficult to demonstrate. Clinicians and public health professionals have unanswered questions about how to reduce exposure to risk factors during childhood that increase the risk of adult CVD. Are adults exposed to SHS in childhood at higher risk of CVD compared with those with a smoke-free childhood? Does the vascular damage observed in healthy nonsmoking young adults exposed to SHS persist decades later?11,12 Can the residual risk of CVD events in excess of classic risk factors be partly explained by early life SHS exposure? Clearly, the immediate effects of SHS on children are overwhelmingly harmful. Increased respiratory illnesses and infections from childhood SHS exposure result in extra emergency department visits and medical expenditures.13,14 The detrimental health outcomes in childhood because of concurrent SHS exposure are sufficient to warrant action; however, the connection between remote SHS exposure in childhood and heart disease in adulthood remains poorly characterized. Previous studies have not been able to detect an association between self-reported cumulative lifetime SHS exposure and risk of myocardial infarction.15 Childhood may be an especially vulnerable period for lasting and permanent harmful cardiovascular effects of SHS.16 Incomplete pediatric exposure ascertainment likely limits the ability of previous studies to detect those outcomes in adulthood. To overcome the long observation period required to detect hard CVD outcomes from prospectively collected pediatric assessments, noninvasive and subclinical measures of CVD have been used as key clinically relevant biomarkers.17,18 In this issue of Circulation, West et al19 describe the long-term consequences of SHS exposure in childhood (aged 3–18 years) on subclinical atherosclerosis in early adulthood (mean age, 37 years) by studying the 26-year follow-up of 2448 children from the Cardiovascular Risk in Young Finns Study. The investigators examined childhood serum cotinine, a biomarker of tobacco exposure, in conjunction with parental report of smoking status as a proxy for parental smoking “hygiene” to determine whether the risk of developing ultrasound-detected carotid plaque in early adulthood differs by parental smoking hygiene in childhood.

The Cardiovascular Risk in Young Finns Study obtained baseline measurements in 1980 of children 3 to 18 years of age from 5 cities in Finland (Helsinki, Kuopio, Oulu, Tampere, and Turku). The investigators ascertained cigarette SHS exposure in 2 ways, by parental report of current or ever smoking at either of the 2 childhood exams in 1980 and 1983 and by measuring serum cotinine from stored frozen serum samples in a subset of the participants (n=1330). The outcome was carotid plaque, defined as a >50% protrusion of the vessel wall into the arterial lumen, and was measured at the 2001 or 2007 assessments at a mean age of 36.6 years (SD, 5.5 years). A total of 64 participants (2.6%) developed a carotid plaque at the end of the follow-up period. In regression models adjusting for confounders that cluster with parental smoking, including markers of socioeconomic status and the participants’ childhood and adulthood smoking status (model 3), the risk for the development of carotid plaque was 2.3 times (95% CI, 1.2–4.7) and 1.6 times (95% CI, 1.0–2.7) higher for participants exposed to parental smoking in childhood (ever and current parental smokers, respectively) compared with unexposed participants. Notably, further adjustment for participants’ childhood and adulthood blood pressure and lipids (model 5) did little to attenuate the relationship between parental smoking and the participants’ risk of carotid plaque. This suggests that the risk from SHS exposure during childhood may be independent and in excess of other CVD risk factors, such as blood pressure, lipids, and personal smoking status.

Further subdivision of the parental smoking category into hygienic parental smoker (nondetectable childhood serum

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cotinine) or nonhygienic parental smoker (childhood cotinine >0 and <3 ng/mL), revealed a graded response, with the highest level of risk among participants exposed to nonhygienic parental smokers (relative risk, 4.1 [95% CI, 1.3–12.9] and relative risk, 4.0 [95% CI, 1.7–9.8] associated with ever and current parental smokers, respectively) compared with nonexposed participants. The lower bounds of the CIs for the risk of developing carotid plaque among participants with good parental smoking hygiene crossed below 1.0, but the risk estimates remained elevated (relative risk, 1.9 [95% CI, 0.6–5.7] and relative risk, 1.6 [95% CI, 0.6–4.0] associated with ever and current parental smokers, respectively). Because of the relatively low number of carotid plaques at follow-up and only a subset of the full sample having cotinine levels, stratification of the study sample into parental hygiene subgroups further limits the power to detect a difference of this magnitude. The elevated risk estimates in the “good hygiene” parental smoking group compared with non-smoking parents are not definitive but do support current recommendations that there are no safe levels of exposure to SHS.4

This study demonstrates that childhood SHS exposure is associated with an important elevated risk of carotid plaque in early adulthood (approximately 2 times higher than unexposed). This study extends previous work done by this group and others demonstrating increased carotid intima media thickness and endothelial dysfunction in young adults exposed to SHS in childhood.20,21 The use of carotid plaque, which represents a more advanced atherosclerotic lesion and a more clinically relevant measure,22 as the outcome in the current study presents a strong argument for the adverse effect of childhood SHS on adult CVD. Inflammation has been proposed as a major mechanism underlying this process.21 In sensitivity analyses in the current study, an adjustment for childhood and adulthood C-reactive protein in a subset of participants with this measure attenuated the association by only 4%, suggesting that either additional factors may be involved or that 2 serum C-reactive protein measurements are an insufficient measure of inflammation to account for the underlying pathogenesis. Recent evidence from the Avon Longitudinal Study of Parents and Children has demonstrated that prenatal maternal smoking affects epigenetic changes in DNA methylation in the offspring, with persistence of the DNA methylation changes into adolescence.22 Although research in this area is in the early stages, the long-term impact of parental smoking on the offspring epigenome may underlie part of the atherogenic process.

Undoubtedly some residual confounding from CVD risk factors that cluster with parental smoking remains and contributes to the connection between parental smoking and offspring subclinical atherosclerosis. A wide range of CVD risk factors are found to be abnormal in youth exposed to parental SHS and parental smoking, some of which may not be causally related to parental smoking and may contribute to future atherosclerotic risk.23 The contribution from perinatal smoking exposure cannot be assessed directly in this study but likely contributes to the effect in both current and ever parental smokers. Misclassification may have occurred in multiple areas including from using serum cotinine as a short-term marker (=1 week) of SHS exposure and not fully capturing poor parental smoking hygiene, limitations in noninvasive imaging to detect carotid plaque, inaccuracies from self-reported parental smoking, and additional unmeasured sources of SHS exposure (10% of the participants recorded as having no parental smoking had detectable cotinine). Despite the study limitations, many of which would have made the associations more difficult to detect, the findings provide a major step forward in demonstrating a solid link between childhood SHS exposure and adult atherosclerosis.

Smoking rates have been decreasing in the United States and worldwide in large part because of public health campaigns and legislative action to reduce public smoking. Despite the tremendous progress, household SHS exposure very much remains a contemporary issue. The results of the Global Youth Tobacco Surveys of more than 350000 youth in 1999–2008 reveal that 30.4% were exposed to SHS inside their homes.26 Among households with 1 adult smoker in the United States in 2010–2011, a majority (54%) did not have smoke-free home rules to protect the health of children in the household.27 Children from ethnic minority and economically disadvantaged populations are disproportionately exposed to SHS.28 Legislative tobacco control measures remain an important route to reducing childhood SHS exposure. Policies on banning smoking in public places and workplaces have been widely implemented and have already been associated with decreases in CVD.29 Progress continues to be made as bans on smoking in cars with children have been enacted in at least 4 US states, 10 Canadian provinces, Australia, South Africa, Cyprus, England, and Wales.30 In 2009, the American Academy of Pediatrics called for children to have universal smoke-free home, car, school, work, and play environments, both inside and outside.31 It should be noted that SHS exposure in children and adolescents is involuntary, because they are unable to choose their own environments and leave smoke-exposed settings. In 2003, the Canadian Lung Association issued a controversial statement declaring that exposing children to SHS is tantamount to child abuse.32 Although this represents an extreme viewpoint, the cardiovascular community is beholden to support advocacy programs to reduce SHS exposure in children and translate the evidence, as presented here, into public health practice to reduce the premature onset of atherosclerosis. Clinically, unanswered questions for future research remain. Does SHS exposure modify the risk of CVD because of other CVD risk factors, such as dyslipidemia? Should treatment thresholds for blood pressure or lipids differ among individuals exposed to SHS, or should clinician efforts be focused on removing the SHS exposure? This study provides further evidence to support the efforts of practitioners, both adult and pediatric, to identify children exposed to SHS during clinical encounters and to make recommendations and referrals to support parental quitting and, in the interim, to follow hygienic smoking practices. Steps like these will help achieve the American Heart Association’s 2020 goals of improving cardiovascular health for all Americans.33

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