Physical, Behavioral, and Cognitive Effects of Prenatal Tobacco and Postnatal Secondhand Smoke Exposure

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The purpose of this review is to examine the rapidly expanding literature regarding the effects of prenatal tobacco and postnatal secondhand smoke (SHS) exposure on child health and development. Mechanisms of SHS exposure are reviewed, including critical periods during which exposure to tobacco products appears to be particularly harmful to the developing fetus and child. The biological, biochemical, and neurologic effects of the small fraction of identified components of SHS are described. Research describing these adverse effects of both in utero and childhood exposure is reviewed, including findings from both animal models and humans. The following adverse physical outcomes are discussed: sudden infant death syndrome, low birth weight, decreased head circumference, respiratory infections, otitis media, asthma, childhood cancer, hearing loss, dental caries, and the metabolic syndrome. In addition, the association between the following adverse cognitive and behavioral outcomes and such exposures is described: conduct disorder, attention-deficit/hyperactivity disorder, poor academic achievement, and cognitive impairment. The evidence supporting the adverse effects of SHS exposure is extensive yet rapidly expanding due to improving technology and increased awareness of this profound public health problem. The growing use of alternative tobacco products, such as hookahs (a.k.a. waterpipes), and the scant literature on possible effects from prenatal and secondhand smoke exposure from these products are also discussed. A review of the current knowledge of this important subject has implications for future research as well as public policy and clinical practice.

Curr Probl Pediatr Adolesc Health Care 2014;44:219-241

Introduction

More than 1 billion people worldwide smoke tobacco products, and it is predicted that this remarkable number will reach 1.9 billion by 2025.[1] According to the World Health Organization (WHO), there are approximately 6 million deaths per year caused by tobacco, and the economic burden of increased tobacco-related morbidity and mortality runs in the hundreds of billions of dollars.[2] Many smokers, however, remain unaware of the harmful consequences of their tobacco use for themselves, their families, as well as for the larger public. Many others, although knowing about these consequences to themselves and others, still have profound difficulty in quitting because of the addictive nature of nicotine.[2]

There are several ways children and adolescents can be exposed to tobacco. Prenatally, this occurs through maternal smoking or maternal secondhand smoke (SHS) exposure. During childhood or adolescence, active smoking, SHS and thirdhand smoke are all possible means of exposure.

The first evidence statistically linking tobacco smoking with lung cancer appeared in the German journal *Der Tabakgegner* (The Tobacco Opponent) in 1912.[3] Doll and Hill[4] confirmed this finding in 1950 using elegantly developed epidemiologic techniques. These and other findings linking tobacco smoking and adverse health consequences became widely recognized worldwide by the 1964 publication in the U.S. of the seminal report entitled *Smoking and Health: Report of the Advisory Committee to the Surgeon General of the Public Health Service*.[5] It is now authoritatively recognized that there is

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; DNA, deoxyribonucleic acid; ETS, environmental tobacco smoke; 5-HT, 5-hydroxytryptamine (serotonin); IQ, intelligence quotient; PAH, polycyclic aromatic hydrocarbon; SHS, secondhand smoke; SIDS, sudden infant death syndrome; TSNA, tobacco-specific *N*-nitrosamines.

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Curr Probl Pediatr Adolesc Health Care 2014;44:219-241
1538-5442/$ - see front matter
Published by Mosby, Inc.
http://dx.doi.org/10.1016/j.cppeds.2014.03.007

no safe level of exposure to tobacco smoke. Despite dramatic decreases in rates of cigarette smoking, tobacco use continues to be the leading cause of preventable premature death worldwide.[6]

In addition to the widely recognized effects of tobacco use and exposure on adult health, literature regarding the prenatal and postnatal physical effects of tobacco exposure on children is extensive and continues to grow. Prenatal exposure to tobacco and postnatal exposure to secondhand smoke are the leading preventable causes of sudden infant death syndrome (SIDS),[7–9] have been linked with intrauterine growth restriction and decreased head circumference among newborns, and are associated with numerous physical health problems during childhood including lower respiratory tract infections, asthma, otitis media, dental caries, hearing loss, and the metabolic syndrome.

Recently, research has examined the cognitive and behavioral effects of prenatal and postnatal SHS exposure. Animal models have elucidated that prenatal exposure to nicotine results in neurotoxic and neuromodulatory effects on the brain that result in alterations of normal brain composition, causing impairments in learning, memory, hearing, and behavior. New studies are beginning to focus on dysregulation of specific genes and biochemical pathways by tobacco smoke exposure during the prenatal period, elucidating a novel mechanism that will be discussed in this article to explain the pathology.

In the words of Cuthbertson and Britton,[10] failure to protect children exposed to SHS "is potentially catastrophic" for their future health. Our estimates are that every day of practice, each primary care physician seeing children for well child care will encounter on average 3 children who will die prematurely of tobacco-related exposure (unpublished data). Growing numbers of individuals and groups are actively calling for measures such as smoking bans in households and in public places to ensure the elimination of children's exposure to SHS.[11]

Components of Secondhand Smoke

Secondhand smoke, also known as "environmental tobacco smoke" (ETS), refers to the smoke discharged from the lit end of a burned tobacco product as well as the smoke exhaled during active smoking.[12] There are more than 4000 chemicals present in SHS, and more than 250 of these are known to be carcinogenic or toxic in some other way.[13] Some of the toxic agents in SHS are as follows: "hydrogen cyanide (used in chemical weapons), carbon monoxide (found in car exhaust), butane (used in lighter fluid), ammonia (used in household cleaners), and toluene (found in paint thinner), arsenic (used in pesticides), lead (formerly found in paint), chromium (used to make steel), and cadmium (used to make batteries)."[14] There also are additional recognized carcinogens in SHS, including polycyclic aromatic hydrocarbons (PAHs), tobacco-specific *N*-nitrosamines (TSNA), and numerous other hydrocarbons, aldehydes, organic compounds, and metals, although these agents have been less rigorously studied.[6,12]

Measurement of SHS Exposure

The ideal biomarker for SHS exposure has yet to be identified. Currently, the same markers used to measure active smoking are used to measure SHS exposure.[15] Exposure to SHS is assessed indirectly by measuring the concentrations of carbon monoxide, thiocyanate, or nicotine metabolites such as cotinine.[16] Although carbon monoxide and thiocyanate can reflect SHS exposure, they are not specific because they are found in multiple sources and can be produced from exposures to agents other than SHS.[16]

Cotinine is a direct metabolite of nicotine that has a longer half-life and a high specificity for SHS exposure.[17] This chemical freely crosses the placenta and accumulates in fetal tissues.[18,19] Cotinine can be measured in saliva, blood, or urine, and indicates the amount of nicotine exposure over the past 3 days.[20] It is currently unclear whether measurement of cotinine in meconium reflects exposures over a more extended period of time.[21] After birth, breast milk is a potential source of nicotine exposure. Nicotine and cotinine can accumulate to concentrations two- to three-fold higher in breast milk than in plasma.[22]

New methods of postnatal cotinine detection, such as liquid chromatography–tandem mass spectroscopy, are being developed to quantitatively estimate exposure to SHS.[23]

Thirdhand Smoke

The term "thirdhand" smoke was coined in 2006, referring to residual matter from tobacco smoke that stays on surfaces and in dust.[24] While many components of thirdhand smoke are the same as those in SHS, there are additional biologically active chemicals formed from reactions between SHS particles with chemicals such as ozone and gaseous oxide.[24,25] Of great concern is that exposure to thirdhand smoke can occur in household with no active smokers. In fact,