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Tobacco and pregnancy

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Synthesis

How important is it?

Prenatal cigarette smoke exposure (PCSE) is the leading preventable cause of several negative birth outcomes, and affects 600,000 live births in North America every year. Although more and more women quit when they find out they are pregnant, 10 to 15% continue to smoke. It is estimated that of those who ceased to smoke during pregnancy, most will start again after giving birth. The incidence of smoking during pregnancy has been dropping in the last two decades but remains high particularly among adolescent and low-income women. Eradicating PCSE would allow health care systems to save millions of dollars in neonatal costs.

What do we know?

Negative outcomes

Smoking during pregnancy is linked to several negative health outcomes, including *ectopic pregnancy*, miscarriage, *placenta previa* and premature labor. Newborns with prenatal cigarette smoke exposure (PCSE) are at risk of having a low birthweight, chronic *ischemia*, *hypoxia*, and excessive tonicity and startle response. Perinatal mortality is also more likely among infants exposed to cigarette smoke. Medical problems continue to be associated with PCSE in infancy and childhood. For instance, the proportion of babies who are victims of Sudden Infant Death Syndrome (SIDS) is higher among those who were exposed to cigarette smoke in utero. Children who had PCSE are also at risk for infantile colic, ear infections and respiratory problems, including asthma, coughing, and wheezing.

The negative outcomes associated with PCSE extend to the behavioural and developmental realms. Babies who were prenatally exposed to cigarette smoke tend to be more irritable and inattentive, and less responsive to inanimate auditory stimuli (ex. a rattle). In early childhood, PSCE has been linked to excess weight, language delay, Attention Deficit Hyperactivity Disorder (ADHD), conduct problems and externalizing problems, such as acting out and aggression. The detrimental outcomes associated with PCSE sometimes persist in adolescence and adulthood. This has been observed for externalizing problems, criminal behaviours, substance abuse, conduct disorder, ADHD, excess weight and the thinning of the orbitofrontal cortex, a brain

region linked to emotion-regulation and the reward system. Gender differences are to be taken into consideration when examining the negative consequences of PCSE. For instance, males who had PCSE seem to be particularly at risk for conduct disorder whereas for females substance abuse is the most frequent outcome.

Potential confounds

The major problem with assuming that PCSE causes these detrimental outcomes is that there is a number of confounding factors that might account for the association. Given that it would be highly unethical to ask women to smoke or not to smoke during pregnancy, it is nearly impossible to remove the possibility that other variables might cause the negative outcomes associated with PCSE. Factors such as parental education, family income, stressful life events, parenting style, poor mother-child relationship, peer influence and genetic predispositions are all related to both PCSE and negative health and behavioural outcomes. For example, the link between PCSE and child behaviour problems had been explained by the mother's own childhood background of conduct problems, arguably leading to both maternal smoking and child behaviour problems.

In addition, the nature of the association between PCSE and child outcomes is not always straightforward, and rather varies as a function of genetic background.

Creative approaches, such as quasi experimental research designs, have been taken to try to eliminate confounding factors and isolate the link between PCSE and negative outcomes. Animal research, twin studies, sibling-comparison design, in vitro fertilization cross-fostering design have all been used to account for genetic factors and eliminate potential environmental causes. Overall these studies show that:

1. The link between PCSE and child behaviour problems cannot be fully explained by heritability passed down from parents to offspring. Studies that examine mechanisms such as gene x environment interactions suggest a biological pathway.
2. There is an independent association between PCSE and certain negative birth outcomes, including prematurity and low birth weight, as well as infant mortality rates.
3. Behaviour genetic research suggests that PCSE may not be causally related to cognitive and behavioural deficits. Rather, PCSE may serve as a marker for other risk processes that contribute to developmental psychopathology and other adaptational problems.

What can be done?

Problems related to prenatal cigarette smoke exposure (PCSE) in children can be prevented by encouraging women of child-bearing age to quit smoking. Their multiple contacts with health-care systems and other service providers (ex. schools and daycares) should be taken as opportunities to expose them to smoking cessation support programs. Pregnant mothers in particular should know that, although quitting early in pregnancy is best, cessation or smoking reduction at any stage is beneficial to the growing fetus. Those who are reluctant should be given a brief intervention to increase their motivation to quit. Nicotine replacement therapies should be used only when the pregnant woman is unable to quit. In these cases, doses should be kept low and be administered intermittently (gum) rather than constantly (patch).

Extensive psychosocial interventions that go beyond a physician’s advice to quit have been used to increase cessation rates. Interventions that include multiple components, such as the "5-A" approach (Ask, Advise, Assess, Assist and Arrange), have been applied successfully to help pregnant mothers quit smoking.

To maximize the likelihood of quitting, it is also useful to identify and target psychosocial obstacles faced by some women. For instance, depressed women who smoke are more likely to have low income, live through stressful circumstances and live with partners who smoke. These factors make it even more difficult for women to quit and should be addressed to increase cessation rates. For instance, quitting can be encouraged by providing the help needed to treat depression. In addition, financial obstacles can be overcome by ensuring that smoking cessation treatments are covered by health insurance. Providing both mothers and their partners with treatment cannot only help decrease direct PCSE, but can also reduce exposure to second-hand smoke.

The public health sector has an important role to play in reducing the occurrence of the psychosocial problems associated with PCSE. Both prevention and intervention strategies need to be developed to address this issue. Since many women who quit smoking for pregnancy resume smoking within one year postnatally, stronger connections between prenatal and pediatric care services can also help maintain smoking abstinence in the long term. Finally, children’s health can also be improved by expanding and reinforcing policies on smoke-free environments.

Tobacco Consumption During Pregnancy and its Association with Psychosocial Child Development

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November 2023, 3e éd. rév.

Introduction

Self-report studies reveal that 7 to 25% of women of childbearing age in the United States endorse current smoking, including the use of electronic nicotine delivery systems (ENDS), which have recently increased in popularity.[1-2] Meta-analyses suggest that maternal tobacco consumption during pregnancy is associated with negative child behavioural and mental health outcomes, including attention deficit hyperactivity disorder, conduct problems, mood disorders, and schizophrenia.[3-6] Given the fact that almost half of the women who consume tobacco prior to pregnancy continue to do so throughout pregnancy,[7] these tobacco–behavioural linkages may have far-reaching implications for development and mental health in children.

Subject

Studies have linked maternal tobacco consumption during pregnancy to a number of adverse medical outcomes. Meta-analytic reviews report significant associations between maternal tobacco use in pregnancy and negative child health outcomes including low birthweight, sudden infant death syndrome, asthma, and obesity.[8] As noted above, the deleterious effects of maternal prenatal smoking on child development appear to extend to the psychosocial realm as well. This report reviews the evidence for the connection between maternal tobacco consumption and psychosocial child development and discusses relevant implications for interventions and public health policy.

Problems

The study of maternal tobacco consumption and its effect on child behavioural or psychosocial outcomes is fraught with methodological problems. The most serious methodological concern is the difficulty in establishing a causal connection due to the potential role of confounds in this process.[9] Research in this area is quasi-experimental. For obvious ethical reasons, women are not

randomly assigned to smoke or not to smoke during pregnancy. However, the factors identified with women who do smoke typically differ from those of women who do not in a number of different areas, including genetic and cultural background, childhood history of antisocial behaviour, socioeconomic status, mental health, personality traits, parenting styles, and exposure to stressful life events. These factors, in turn, are associated with greater risk for problematic child psychosocial development. However, no single study has been able to control for all of these potential confounds. Another methodological concern is the common use of retrospective rather than prospective reports of maternal smoking. The finding that maternal self-reports of smoking during pregnancy are highly correlated with direct biochemical measures [10] alleviates major concerns about the exclusive use of self-reports of maternal smoking in this research area. However, there remains a lingering concern regarding the capacity of self-report to detect exposure from various sources (i.e., second-hand exposures). Recent findings indicate that self-reported data should be supplemented with biological measurements of exposure. These data find that integrative assessments, that combine multiple measures of use, better reflect overall exposure and are most proficient in identifying the behavioural consequences associated with substance use.[11]

Research Context

Maternal prenatal smoking and its relationship to child psychosocial outcomes has been examined in both cross-sectional and longitudinal studies, and in both clinical and community samples. Animal studies have examined the effect of nicotine exposure on behavioural outcomes and brain functioning and neurobiological deficits have been suggested as a likely mediator for negative behavioural outcomes.[12] Human studies support this contention, noting associations between maternal prenatal smoking and reductions in frontal lobe volumes in infants,[13] decreased cortical thickness in children,[14] and a thinning of the cerebral and, potentially, orbitofrontal cortices in adolescents.[15] Nevertheless, there remains disagreement in the field concerning the relative importance of the direct effects of prenatal tobacco smoking, its associated familial background factors, and potentially moderating environmental or genetic vulnerabilities in the prediction of negative child behavioural outcomes.

Key Research Questions

The key research questions in this area are as follows:

- Is maternal tobacco consumption during pregnancy associated with deleterious behavioural outcomes in youth? And, if so:
- Can potential methodological confounds account for this association? And, if not:
- Are these risks specific to particular behavioural outcomes?
- Are these risks moderated by other factors including genetics, the biological sex of the child, co-exposures, or the environmental context of development?

Recent Research Results

Maternal prenatal smoking has been associated with increased risk for Attention Deficit Hyperactivity Disorder, oppositional behaviour, aggression, conduct disorder, problematic language and cognitive development, and substance misuse outcomes in youth.[16-21] A majority of studies suggest that statistical control for a range of potential confounds, including parental criminality, maternal mental health, parenting behaviour, socioeconomic status, prenatal exposure to drugs and alcohol, and other perinatal complications, does not change the general pattern of results. However, a few studies have found that the maternal prenatal smoking child outcome relationship is no longer significant when maternal background characteristics (e.g., childhood history of conduct disorder) and mother-child relationship qualities are taken into account.[22-24] Although evidence from twin studies suggests that the relationship between maternal smoking during pregnancy and child behaviour problems cannot be entirely accounted for by genetic influences,[22,25] recent studies using innovative design strategies have suggested that genetic or familial background factors may be essential components of the prenatal smoking and child externalizing behaviour association.[26,27]

The noted maternal prenatal smoking child behaviour outcome association appears stronger for externalizing or acting out behaviours; results from studies examining the associations between maternal prenatal smoking and child internalizing problems have been mixed.[9,28-30]

In addition, offspring biological sex appears to moderate the effects of maternal prenatal smoking on child psychosocial outcomes. Specifically, results are stronger for males in terms of the outcomes of conduct disorder, and stronger for females in terms of the outcome of substance misuse.[20,31] Family and socioeconomic context has been shown to moderate the effect of maternal prenatal smoking on child outcomes.[16,32,33] Gene by environment interaction studies also suggest that several distinct genetic polymorphisms, (including one that effects the

metabolism of smoking-related carcinogens), may moderate the association between maternal prenatal smoking and child externalizing behaviour.[34-36] Furthermore, maternal genetic profiles have been associated with the reduction or spontaneous quitting of smoking during pregnancy.[37] Epigenetic processes have also been identified as potential mechanisms through which maternal prenatal smoking may confer risk for vulnerabilities in child development. For instance, maternal smoking can affect embryonic DNA methylation which, in turn, can impact gene expression, phenotyping, and ultimately offspring behaviour later in life.[38] Moreover, DNA methylation has been found to mediate outcomes such as offspring neurodevelopment, memory, cognition, and attention, all of which can influence psychosocial development.[39-42] Further study of maternal psychosocial and genetic characteristics associated with cessation of smoking during pregnancy is needed to more effectively design intervention programs focused on pregnant women.

Conclusions

There are several possible mechanisms or explanations for the noted relationship between maternal prenatal smoking and behavioural problems in offspring. One possible explanation is that prenatal exposure to this teratogen increases the risk for child externalizing problems, but only in genetically or otherwise environmentally vulnerable individuals. Alternatively, maternal prenatal smoking may serve as a marker for other environmental effects that increase the risk of externalizing problems in children. For example, maternal prenatal smoking may be an indicator of a passive, neglectful parenting style. It may not reflect abuse or overt parental hostility but rather a subtle disruption in the parent-child relationship that is difficult to measure via questionnaires or short-term observations, but that nevertheless increases the risk for externalizing problems in children. An additional possibility is that maternal cigarette smoking may set off a chain of transactional biological and environmental factors that act together to increase risk for deleterious child development. Our understanding of this transactional process is rudimentary at this time.

Implications

Not all children whose mothers smoked during pregnancy will manifest deficits in behaviour or developmental outcomes. Future studies aimed at assessing the potentially moderating risk and protective factors in this process would be useful in designing effective prevention and intervention programs. A public health approach calls for prevention and intervention strategies designed to reduce the known risk factors for these deleterious psychosocial outcomes in

children. Maternal prenatal smoking is a relatively modifiable perinatal risk factor. Smoking cessation programs for pregnant women,[43] which may include novel mobile phone-based interventions,[44] financial incentives,[45] short-term and long-term nicotine replacement therapies,[46,47] and even low-intensity counselling interventions by general practitioners,[48] have been found to reduce or eliminate maternal smoking during pregnancy. An examination of the behavioural profiles of the children whose mothers successfully completed such programs would help provide important experimental evidence concerning the potentially causal role of maternal prenatal smoking on child behaviour problems.

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Prenatal Cigarette Smoke Exposure: Effects on Offspring

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March 2011

Introduction

Over 20% of North American and Canadian adults smoke despite the fact that cigarette smoking is the leading cause of preventable morbidity and mortality.[1,2] Tobacco is also the most commonly used substance during pregnancy;[3] 13.8% of pregnant American women smoke[4] and 10.5% of pregnant Canadian women smoke[5] affecting more than 600,000 live births per year.

Subject and Research Context

The scientific literature is replete with findings of adverse prenatal cigarette smoke exposure (PCSE) effects on offspring. More recent studies have improved on earlier methodologies with prospective designs, biological measures and statistical control of confounders. Many of these studies also use more sophisticated measures including objective *neurobehavioural test batteries*, *neuroimaging techniques* and assessment of *genotypic variability*. This brief synopsis will focus on studies published since the previous report on this topic by Peter Fried.[6]

Recent Research Results

The evidence is clear about PCSE's causal effects on neonatal morbidity and mortality,[7] and its effects on neurobehaviour is a recent focus in the infancy literature. PCSE is associated with infant irritability, inattention, decreased response to inanimate auditory stimuli,[8] *increased hypertonicity*[9] and more problematic temperament.[10] Key et al.[11] found that PCSE infants discriminated fewer syllables and processed them more slowly than non-exposed infants. Similarly, Golub and colleagues[12] demonstrated that exposed nonhuman primates showed less novelty preference in visual recognition.

Studies on the effects during childhood continue to show that PCSE is a consistent predictor of higher rates of problems such as language delay in preschoolers,[13] externalizing and internalizing

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behavioural problems such as acting out or withdrawal in 2-year-old children,[14] child aggression in 17- to 42-month olds,[15] and externalizing in early childhood that persists to age 18.[16] Studies have also considered the effects of both prenatal and postnatal tobacco smoke exposure and have demonstrated an independent effect of PCSE on childhood behaviour problems at ages 6[17] and 10.[18,19] In a large multinational study, Brion et al.[2] reported a direct relation between PCSE and offspring conduct and externalizing problems. In a clinical sample of children with ADHD, hyperactive-impulsive symptoms and conduct disorder symptoms were significantly higher among those with PCSE.[21] Others have found a relation between PCSE and conduct disorder symptoms.[22,23] Murray and colleagues[23] found that this relation between PCSE and conduct disorder symptoms in childhood extended to criminal behaviours when the offspring were ages 30-34. PCSE also has long-term effects on physical health in offspring. Johansson et al.[24] found timing effects in offspring wheezing, sleeping difficulties, excessive crying, and use of bronchodilating drugs depending on whether exposure was prenatal only, postnatal only, or both. Gilman et al.[25] examined over 52,000 children from birth to age 7 and found that low birth weight and a higher odds for being overweight were associated with PCSE. In two meta-analyses,[26,27] PCSE was significantly related to offspring obesity and overweight, respectively. Rooney et al.[28] also found that PCSE was a significant predictor of obesity in a birth cohort during adolescence and adulthood.

Recent studies on the effects of PCSE on risk for smoking in offspring have replicated and extended earlier reports. Menezes et al.[29] found this relation in early adolescence. Agrawal and colleagues[30] demonstrated that PCSE was associated with earlier age of initiation as well as earlier regular smoking. O'Callaghan and colleagues[31] reported this relation with nicotine dependence in young adulthood. Lotfipour and colleagues[32] reported an interactive effect between in utero tobacco smoke exposure *polymorphism* in the *nicotinic acetylcholine* receptor that influences smoking and other drug use. Underscoring these findings in an animal model, Slotkin et al.[33] noted that both prenatal and adolescent nicotine exposures resulted in permanent changes in synaptic function, and prenatal exposure sensitized females to the subsequent effects of nicotine.

With the development of faster genetic mapping techniques, more studies have incorporated genetics into their designs, documenting interaction effects of PCSE and genetic liability on outcomes. One such design found a dampened response to novelty among PCSE infants with genetic variability in the *DRD2* gene.[34] In another study,[35] 15-year-old males with PCSE who

were *homozygous* for the DAT1 dopamine transporter gene had higher rates of hyperactivity and impulsivity than all other groups.

Similarly, Neuman[36] found that the odds of a *DSM-IV* Attention Deficit Hyperactivity Disorder (ADHD) diagnosis were 2.9 times greater in twins with the *DAT1 allele*, 2.6 times greater in those with the *DRD4* seven-repeat allele, and 9.0 for offspring with PCSE and both alleles. Wakschlag and colleagues[37] tested the effects of a polymorphism of the enzyme *monomine oxidase* (MAOA) and PCSE on antisocial behaviour in adolescents demonstrating that *MAOA genotype*, PCSE and gender interact to predict antisocial behaviour in exposed male offspring.

Brain imaging studies have also advanced our knowledge about the mechanisms that may drive PCSE effects. Rivkin[38] examined the brain volume in a*magnetic resonance imaging (MRI)* study of 10- to 14-year-olds. PCSE was associated with significant reduction in cortical gray matter and total *parenchymal* volumes and head circumference. In another MRI study, Toro et al.[39] found that orbitofrontal, middle frontal, and *parahippocampal* cortices were thinner in the PCSE-exposed adolescents. Jacobsen et al.[40] used MRI and *diffusion tensor imaging (DTI)* to examine effects of prenatal and adolescent tobacco exposure on structure of brain white matter and found that both white matter microstructure and auditory processing were affected indicating that nicotine-induced disruption of the auditory *corticofugal fibers* may lead to reduced efficiency in auditory processing. In another study by Jacobsen and colleagues,[41] PCSE and exposure during adolescence was found to exert gender-specific deleterious effects on auditory and visual attention *fMRI (functional magnetic resonance imaging)*.

Research Gaps

Despite the mounting body of evidence linking PCSE to problems for offspring, several recent studies have not found significant associations.[42,43,44,45,46] These results suggest that it is important to consider factors that may account for the explained variance in outcomes, many of which are also related to smoking during pregnancy, such as lower education and income. Several review articles have synthesized PCSE effects,[47,48,49] with some reviews including non-human data.[50,51,52] One recent review[53] of the long-term consequences of fetal and neonatal nicotine exposure highlights concerns about the safety and utility of nicotine replacement therapy during pregnancy. Suggestions from reviews to address current gaps in the literature include: considering multiple factors in explaining the nature of attention hyperactivity disorder and behavioural problems; attaining an unbiased estimate of the magnitude of the association

between exposure and outcome, and more comprehensive study designs that involve the gene-environment interplay.

Conclusions

The large majority of recent studies have built upon the evidence of the last five decades that smoking during pregnancy is deleterious for multiple offspring outcomes and that these effects can be detected from infancy through adulthood. However, based on some of the studies with negative findings, it is apparent that there is a need for adequate control of potential confounds that may also contribute to these outcomes. Establishing causal links requires replication of findings across large numbers of studies with varying study populations. Part of the difficulty in concluding causal effects is due to the inability to separate prenatal exposure effects from other confounding environmental and genetic factors. New research examining genetic liability suggests that PCSE may interact with genes to produce effects. Animal models offer added support for linkage by supporting biological plausibility for such relations. Imaging techniques provide visible effects of exposure on brain structure and function. Although the mechanisms of PCSE's effects on the developing brain are not completely understood, newer research informs us that the mechanisms are multifactorial, involving biological effects, genetic susceptibility, and environmental factors.

Implications for Parents, Services, Policy

Since 1957 a plethora of studies have implicated PCSE with multiple adverse outcomes in offspring from birth through adulthood.[54] It is encouraging that rates of smoking during pregnancy have decreased in the past decade, but the prevalence is still too high, especially for specific groups that are already at higher risk for fetal problems such as teenagers and women of low-economic status. Public health efforts that have proved to be efficacious in reducing smoking should continue to receive support. With evidence of nicotine vulnerability among those prenatally exposed, stopping exposure in the first place, will not only prevent neurotoxicological effects in the offspring, but will prevent continuing smoking exposure in succeeding generations. There is now notable evidence that preventing PCSE may help prevent smoking uptake during adolescence in offspring. Based on what we do know, it is clear that women who are pregnant or who may become pregnant should abstain from smoking and nicotine exposure.

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Association Between Prenatal Exposure to Maternal Cigarette Smoking and the Brain and Behaviour of Adolescent Offspring

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Introduction

Approximately 10-15% of mothers smoke during pregnancy in Canada and the United States.[1,2] Given the high prevalence of maternal cigarette smoking, our group has initiated one of the largest studies to date evaluating the effects of developmental exposure to cigarettes on adolescent offspring brain and behaviour.[3] This review discusses a subset of the findings of our study and provides preclinical evidence for the hypothesized cause-and-effect relationships reported.

Subject

Maternal cigarette smoking can have significant impacts on the offspring. During the period of pregnancy or shortly after birth, reported consequences include smaller birth weight, sudden infant death syndrome and *placenta previa*.[4-6] In late childhood and early adolescence, subjects exposed to maternal cigarette smoking have higher incidents of attention deficit hyperactivity disorder,[7] substance use,[8] and intra-abdominal[9] and overall obesity.[4,10] In the current review, we focus on whether in utero exposure to cigarettes increases substance use behaviour in an adolescent population (12-18 years of age), and describe whether selective brain regions and/or genetic underpinnings could act as mediating factors influencing these associations.

Problems

In human studies, the causal relationship between maternal cigarette smoking and brain and behaviour is difficult to determine. Confounding factors include parental education, family income, stressful life events, peer influence and genetic predispositions, to name a few. Research using animal models, which does not have the same limitations, has assisted in elucidating the causality vis-à-vis these relationships as well as the mechanisms underlying the early and late-

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onset deficits seen in the human population.[11-13] In particular, animal models have demonstrated that developmental exposure to nicotine, believed to be the major psychoactive constituent in tobacco smoke, mediates many of the same associations seen in humans, including modifications in the reinforcing properties of nicotine[14] and cocaine,[15] as well as increased locomotor hyperactivity and changes in *cholinergic* and *catecholaminergic* neurotransmitter systems.[11,12,16] These results have provided supportive evidence that gestational nicotine exposure can be harmful to the developing fetus.[11,12]

Research Context

Based on clinical and preclinical evidence, we have set out to evaluate the consequences of maternal cigarette smoking in the adolescent brain and behaviour. The study encapsulates a population of nearly 800 adolescents (12-18 years of age), with a projected total population of 1,000 participants, half of whom have been exposed to maternal cigarette smoking; exposed adolescents were matched to the non-exposed by maternal education and the school attended.[3]

Key Research Question

Does prenatal exposure to maternal cigarette smoking influence adolescent brain and behaviour associations through underlying genetic factors, particularly associated with cognition and substance use?

Recent Research Results

Our study on the effects of maternal cigarette smoking on the brain and behaviour of adolescent offspring was first published in 2007.[3] We demonstrated that in utero cigarette exposure influenced the cortical thickness of adolescent offspring,[17] a finding also observed in animal models evaluating the consequences of gestational nicotine exposure.[18] In our human adolescent population, the region of the brain most influenced was the orbitofrontal cortex (OFC), a structure that regulates emotion and reward processing.[8] Given the importance of emotional regulation and reward processing in the adolescent brain, our subsequent studies tested whether modifications in this region of the brain could influence substance-use behaviour.[8] Our results illustrated that the thinning of the OFC significantly correlated with lifetime history of experimenting (at least once) with cigarettes, alcohol and other illicit substances in exposed adolescents, while a thicker OFC is associated with greater lifetime history of such experimentation in non-exposed adolescents, suggesting an experience-induced plasticity. For

exposed adolescents, we hypothesized that prenatal cigarette smoking induced an insult in the OFC, thus leading to thinning in the structure and thereby predisposing adolescents to substance-use behaviour. These findings are in line with preclinical studies that demonstrate gestational nicotine influences substance use behaviour[14,15] and cortical thinning.[18] For non-exposed adolescents, we hypothesized that experience-induced plasticity may influence the structure of the OFC through drug-taking behaviour. We provided evidence for this hypothesis by demonstrating that a *single nucleotide polymorphism* in the brain-derived neurotrophic factor (BDNF) gene, an important regulator of brain plasticity, could modify the OFC thickness based on lifetime history of drug experimentation in the non-exposed population.[8] In the exposed adolescents, BDNF polymorphisms had no effect on brain structure, which suggested that the BDNF gene has an absent function in this population. In support of this speculation, we demonstrated that maternal cigarette smoking increased *epigenetic* modifications of the BDNF gene, namely enhanced methylation of *cytosine-guanosine* repeats found in the DNA of the blood of the exposed adolescents.[19] These findings are consistent with data from an earlier study demonstrating that maternal cigarette smoking is associated with global increases in DNA methylation in exposed subjects.[20] Such mechanisms have been shown to influence BDNF expression,[21] thereby having potentially critical consequences on the structure of the brain.[22,23] Taken together, the results suggest that the OFC is susceptible to modifications by maternal cigarette smoking and is associated with changes in substance use behaviour; significant effects which are modified by the BDNF genotype.

Our most recent studies have started to evaluate sub-cortical effects induced by maternal cigarette smoking. We have been particularly interested in *striatal regions* of the brain, which receive rich *dopamine* projections that are quite likely important for mediating reward and addiction.[24] It is well known that nicotine, binding to nicotinic receptors, can induce dopamine release in striatal regions, a hallmark of drug reward.[25] Prenatal exposure to nicotine can reduce dopamine levels in striatal regions[16] and nicotine-induced dopamine release.[26] In humans, reductions in dopamine levels in striatal regions have been proposed to result in a larger striatal size.[27] In animal models, an attenuated dopaminergic system could influence reward-related behaviour, including increased cocaine self-administration observed at higher doses[15] and nicotine self-administration after withdrawal.[14] Such effects may be due to an overcompensation [26] and mediated through a nicotinic-receptor system.[11,12,24] We tested this hypothesis using a polymorphism in the alpha6 nicotinic receptor subunit, recently shown to be critical in the modulation of (i) nicotine-induced dopamine release in the *striatum*[28,29] and (ii) quit attempts in

smokers.[30] Our results demonstrated that increased substance-use behaviour and larger striatal size was only present in a subset of adolescents who were exposed to maternal cigarette smoking and had a particular version of the alpha6 gene.[24] Overall, the findings demonstrate long-term consequences of maternal cigarette smoking on a reward-related brain region and substance-use behaviour, with the variant of a nicotinic-receptor gene playing a significant role.

The above effects are present despite the fact that maternal cigarette smoking does not influence how our adolescent population performs on cognitive tasks.[31] Accessing 33 different measures of cognitive function, related to verbal, visual-spatial memory, processing speed, resistance to interference and motor dexterity, no differences were observed between adolescence that were exposed versus those non-exposed to maternal cigarette smoking. These findings suggest that maternal cigarette smoking is associated with selective brain-behaviour modifications in adolescent populations, particularly related to reward-seeking behaviour, but not with global cognitive modifications. It is also possible that subtle cognitive “deficits” are present at an early stage[32] but may diminish through subsequent (beneficial) effects of education.

Research Gaps

1. Which nicotinic receptor subunits are critical for mediating the consequences of prenatal cigarette exposure?
2. Which stages during pregnancy (or post pregnancy) are most critical for the consequences of maternal cigarette smoking?
3. Do similar effects occur through second hand-smoke exposure or through nicotine replacement therapies?
4. What strategies can be used to prevent emergence of delayed consequences of maternal smoking during pregnancy on the offspring behaviour?

Conclusions

Our findings demonstrate that prenatal exposure to maternal cigarette smoking can have long-lasting consequences on the brain and behaviour of adolescent offspring. While our results do not suggest cognitive differences between the exposed and non-exposed offspring, significant associations are observed for reward related behaviour. Genetic factors appear to be critical players in mediating this behavioural phenotype and its underlying neural mechanisms. In

particular, striatal and frontal cortical regions are sensitive to the influences of maternal cigarette smoking. Furthermore, maternal cigarette smoking has significant associations with modifications in the methylation of genes important for brain development, such as BDNF. These findings need to be taken in parallel with animal models that demonstrates prenatal nicotine exposure can have developmental consequences on the brain and behaviour of offspring, also with important changes on BDNF expression in the brain.[33]

Implications for Parents, Services and Policy

The implications of our findings are important to pregnant mothers who smoke or live in an environment where they are continuously exposed to cigarette smoke. On the positive side, not all children of women who smoked during pregnancy differ from those who were not exposed; thus, robust mechanisms must exist that protect the fetus from this adverse intra-uterine environment. On the other hand, data from both clinical and preclinical studies suggest that maternal cigarette smoking could have long-lasting consequences on the brain and behaviour of offspring. Impacts that may influence critical genes involved in brain development and brain structures related to reward related behaviour. Renewed services need to be provided for women who smoke and are planning on becoming pregnant. Further research is needed in order to determine the best smoking cessation therapies for pregnant mothers who are smoking. Given the preclinical evidence, further consideration is needed as to whether nicotine replacement therapies are the best smoking cessation medication available. Policies need to be developed to promote smoke-free mothers and further assist in reducing second hand cigarette smoke exposure in work and home environments.

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Causal Modeling of Prenatal Smoking Effects

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Introduction

Maternal smoking during pregnancy (SDP) is associated with increased risk for various offspring developmental problems, included pregnancy-related problems,[1] cognitive deficits,[2] unhealthy physical traits,[3] and later social and behavioural difficulties.[4] Research over the past two decades has focused on understanding the mechanisms through which SDP influences development. Most research has suggested that fetal exposure to the chemicals in cigarettes specifically causes developmental problems.[1,4] But, maternal SDP does not occur in isolation; SDP is correlated with many risks that may influence both maternal SDP and cause problems in the offspring. Questions, therefore, remain about the degree to which maternal SDP actually causes developmental problems in offspring or whether maternal SDP is a marker for other causal influences. A number of recent studies have used advanced methodological designs[5-6] to rigorously test alternative explanations for the association between SDP and developmental outcomes.[7]

Subject

Social science research should play a large role in directing public policy initiatives, especially those targeting families, by identifying modifiable causal risk factors for developmental problems.[8-12] When research identifies modifiable causal risk factors, interventions can help reduce exposure to those risks. If, in contrast, basic research rules out a causal inference from a putative risk factor, then subsequent research can identify the true causal influences and open up the possibility of new and more successful interventions.[7] Rigorous research on maternal SDP, therefore, will help influence public policy decisions by identifying true causal risk factors.

Problems

The problems with examining the causal effects of maternal SDP stem from the difficulties researchers have studying risk factors that cannot be experimentally manipulated. Because

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random assignment in human populations is the only scientific method that permits researchers to make definitive causal inferences, researchers must rely on alternative research designs to help rule out all plausible alternative explanations for the associations between risk factors and outcomes.[5,8-9] As such, research on SDP must take into consideration correlated environmental factors. Women who smoke while pregnant are more likely to use other substances while pregnant, use and abuse substances after pregnancy, have psychological problems, receive less education, and live in poorer neighbourhoods, to name a few examples.[2] And, research must take into consideration the role of possible confounding genetic factors. Because behaviour genetic research has found that genetic factors influence maternal SDP,[13-14] genetic factors that are passed down from parents to their children could account for the increased risk of problems in offspring exposed to SDP.

Research Context

Most research has suggested that SDP causes problems during pregnancy and psychosocial problems.[1,4] The association between SDP and offspring problems are (a) generally robust to the use of statistical controls for measured risks that are correlated SDP, (b) found across various studies, and (c) generally consistent with basic research on SDP conducted in animals.[15] But, questions remain about the generalizability of findings from animal studies to humans and the ability of the existing human research to adequately account for all possible alternative environmental and genetic explanations.[4,13,16-18]

Key Research Questions

The key research questions concern the degree to which SDP (a) specifically causes later developmental problems or (b) is merely a marker for other risk factors that cause later developmental problems. If maternal SDP does not have a causal influence on developmental problems, subsequent research will need to specify the correlated risk factors that are responsible for the increased problems found in offspring exposed to SDP. Such questions require researchers to use many different research designs, especially *quasi-experimental designs*, methods that can pull apart risk factors that typically co-occur.[5-6]

Recent Research Results

Researchers recently have used a number of quasi-experimental designs to study maternal SDP.[7] A number of studies have used the sibling-comparison design, the comparison of siblings who

were differentially exposed to SDP.[19-21] Researchers also have utilized the children of twins approach,[13,22] a comparison of differentially exposed offspring of adult twins. Some studies have used a novel *in vitro* fertilization (IVF) cross-fostering design[23] that include offspring who are not genetically related to their birth mother. Each of the designs help account for genetic factors passed down from parents to children, as well as environment confounds.

Recent sibling comparison, children of twins, and IVF cross-fostering studies have found that SDP is independently associated with adverse birth outcomes, such as early gestational age/preterm birth and low birth weight.[1,7,13,24-25] A recent sibling comparison study also found that SDP is independently associated with increased risk for infant mortality.[26] The results are consistent with a specific causal association because the designs helped account for correlated genetic and environmental factors that could otherwise explain the associations between SDP and pregnancy-related problems.

A number of recent quasi-experimental studies strongly suggest SDP does not cause later cognitive and psychosocial problems, however. Sibling comparison studies of offspring childhood conduct problems,[24,27] adult criminality,[28] intellectual abilities,[29-30] academic achievement[31] and adolescent obesity[3] found that family background factors (genetic and/or environmental factors shared by siblings) account for the association between SDP and each trait. These findings also are consistent with recent results from IVF cross-fostering studies of childhood conduct problems[25] and attention-deficit/hyperactivity disorder,[32] as well as a children of twins study of offspring ADHD problems.[33] The findings strongly suggest that risk factors that are correlated with SDP cause these later developmental problems, not the *teratogenic* effects of SDP.

Research Gaps

Most of the quasi-experimental studies on SDP have been based on large epidemiological studies, which have not used precise measurement of SDP or developmental outcomes. Future research, thus, will need to use combine rigorous quasi-experimental methods with more precise assessments. Because the recent quasi-experimental research on the association between SDP and later psychosocial development is not consistent with findings from animal studies[15] more translational research is necessary to better understand the discrepancies between the two research approaches. And, most of the quasi-experimental research only has ruled out a causal influence of SDP on later cognitive and psychosocial outcomes; future research will need to identify the true causal influences. Finally, most of the quasi-experimental research has focused

on understanding the main effect of SDP on development. There is also a great need to explore whether particular individuals are more susceptible to the effects of SDP.[34]

Conclusions

Research focused on identifying the causal processes through which SDP influences offspring development needs to use methods that can delineate possible teratogenic effects of SDP from correlated environmental and genetic factors. Research using various quasi-experimental designs suggests that maternal SDP is independently associated with pregnancy-related problems, such as shortened gestational age and low birth weight. Because the results have been replicated in numerous samples and with various research methods, each with their own strengths and weaknesses, a strong causal inference can be drawn with respect to these outcomes. One sibling comparison study, which will need to be replicated, also found that SDP is robustly associated with increased risk for infant mortality. The statistical association between SDP and later developmental difficulties, such as behavioural and academic problems, however, do not appear to be due to the specific effects of maternal SDP on the developing fetus. Rather, environmental and genetic factors that are correlated with maternal SDP are responsible for the increased risk of later problems in offspring exposed to maternal SDP.

Implications for Parents, Services and Policy

First and foremost, the results of the recent research on SDP emphasize that the reduction of maternal SDP remains a major public health priority. Again, recent studies strongly suggest that SDP causes increased pregnancy-related problems and (perhaps) infant mortality. Pregnant women, as well as women of childbearing age who are sexually active, should strive to reduce or eliminate their smoking. Service providers and policy makers should help implement empirically supported smoking cessation programs in these populations.

Second, the recent research on SDP emphasizes the need for policy makers and service providers to understand how social science research can and should direct policy initiatives.[8-9] In particular, the recent research suggests that reducing maternal SDP probably will not reduce many of the later problems that have been associated with SDP. Maternal SDP is correlated with many risks, and the recent findings from quasi-experimental designs strongly suggest that comprehensive interventions with pregnant women and young families, which target multiple risk factors,[35] are required to help offspring of women who smoke during pregnancy.

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Treating Tobacco Use Among Pregnant and Parenting Smokers

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Introduction

Since 1975, a growing volume of research has demonstrated the effectiveness of clinically proven interventions in achieving long-term or even permanent abstinence from tobacco use for all smokers.[1,2] Achieving cessation is especially important for pregnant and parenting smokers whose use of tobacco is a threat to their own health, and that of their pregnancies and offspring. Cessation of tobacco use, prevention of secondhand smoke exposure and prevention of relapse are key clinical intervention strategies during pregnancy and early childhood.[3] Given the harm associated with exposure to secondhand smoke (SHS), both parents and caregivers of young children should receive treatment to achieve cessation. Generally speaking, treatment for smokers also applies to parenting smokers but special considerations regarding treatment need to be made for pregnant women.

Subject

To date, intervention trials for pregnant women have focused on

- how to achieve higher rates of cessation during pregnancy
- how to prevent postpartum relapse
- the effect of cessation on birth outcomes.

Few intervention trials have specifically targeted pregnant and parenting smokers in an effort to reduce secondhand smoke exposure among young children. However, interventions designed for smokers as a group may also be used to achieve cessation for parents and, with some modification, for pregnant women. Increased cessation and abstinence rates will lead to reduced secondhand smoke exposure rates for pregnant women, infants and children.

Problems

The key problems in this area of investigation are as follows:

1. *Identifying all smokers, especially pregnant smokers*
   People who smoke are often reluctant to discuss their tobacco use with caregivers and to be labelled as smokers.[4] Given social pressure to abstain from smoking during pregnancy, pregnant women may be more reluctant to disclose their smoking status and may frequently be misclassified as non-smokers. Several trials have found high percentages of deception (28% and 35%) when self-reported smoking status is biochemically confirmed among pregnant women.[5,6,7]Although biochemical validation of self-reported smoking status remains the gold standard for identifying smokers, the associated expense and ethical issues generally consign its use to clinical trials. A structured, multiple-choice question to assess tobacco use among pregnant women increases the likelihood of accurate self-report by as much as 50%.[4] The choices in this question allow women to rate their smoking status under “never smoke,” “recently quit” (upon learning they were pregnant or while trying to get pregnant), and “continue to smoke” (although they may have reduced their smoking since learning of their pregnancy). These categories allow women to visualize their smoking behaviour in the context of their pregnancy and are designed to exclude responses that could paint pregnant women smokers as being irresponsible. Despite the improvement in disclosure observed with this technique, new approaches to ascertain smoking status are needed for both pregnant and other smokers.
2. Quantifying the exposure of pregnant women, fetuses, infants and young children to secondhand tobacco smoke and measuring its effect on maternal morbidity, fetal and infant outcomes and childhood morbidities. Methods for accurately quantifying ETS exposure that are accurate, non-intrusive and economical are needed for use in settings where pregnant women, infants and children are present.
3. Establishing linkages between exposure to varying levels of secondhand smoke and maternal outcomes, including miscarriage and infant and child outcomes.

Research Context

All of the studies included in meta-analyses to determine best practices for achieving cessation among pregnant smokers and smokers have in general, been conducted as randomized, controlled trials. These meta-analyses are summarized in Treating Tobacco Use and Dependence: A Clinical Practice Guideline (2008 update)[2] and various Cochrane Collaboration reviews.[8,9]

Key Research Questions

The following topics regarding treatment for pregnant smokers will require additional research:

- Ethical issues associated with the routine use of
    1. Biochemical validation of smoking status
    2. Biochemical feedback to increase the likelihood of cessation
    3. Incentives for pregnant smokers to remain smoke-free.
    - Understanding the motivation of spontaneous quitters.
    - Efficacious treatments for highly dependent smokers, spontaneous quitters and women who quit smoking during pregnancy.
    - The most efficacious amount of contact time, number of sessions and duration for smoking cessation interventions with pregnant women.
    - The efficacy of various counselling and behavioural therapies and motivational interventions (e.g., the physiological feedback of adverse impacts and the benefits of quitting).
    - The safety and efficacy of tobacco dependence pharmacotherapy during pregnancy with regard to the woman and fetus and to the woman and child during nursing.
    - The effects of smoking with the concomitant use of tobacco dependence pharmacotherapies.
    - The efficacy of targeted or individualized interventions during pregnancy.
    - Strategies for linking pre-conception, pregnancy and postpartum (including pediatric) interventions.

The primary research needs with regard to reducing parental secondhand smoke exposure are as follows:

- Mechanisms for accurate, economical and non-intrusive biochemical assessments of secondhand smoke exposure.
- Methods for establishing the relationship of secondhand smoke exposure to various health and behavioural outcomes while accounting for confounding variables and identifying

underlying mechanisms that explain observed linkages.

- Approaches to targeting smoking cessation messages and treatments to parents and caregivers to reduce the exposure of children to secondhand smoke.

Recent Research Results

The effects of smoking

Smoking remains the single most important preventable cause of poor birth outcomes. An estimated 5-8% of preterm deliveries, 13-19% of term deliveries of infants with low birth weight, 23-34% of cases of sudden infant death syndrome (SIDS), and 5-7% of preterm-related infant deaths can be attributed to prenatal maternal smoking.[3] Cigarette smoking by pregnant women has been shown to cause adverse fetal outcomes, including intrauterine growth restriction, *placenta previa*, abruptio placenta, decreased maternal thyroid function,[10,11] preterm premature rupture of membranes,[12] low birth weight, perinatal mortality,[10] and ectopic pregnancy.[10]

The risks of tobacco use during pregnancy extend beyond pregnancy-related complications. Children born to mothers who smoke during pregnancy are at an increased risk of asthma, infantile colic and childhood obesity.[13,14,15] Infants born to women who use smokeless tobacco during pregnancy have a high level of nicotine exposure, low birth weight and shortened gestational age as compared to mothers who smoke during pregnancy.[16,17] Women smokers are less likely to breastfeed their infants.[10]

The effects of maternal exposure to secondhand smoke

The evidence is sufficient to infer a causal relationship between maternal exposure to secondhand smoke and SIDS, and a small reduction in birth weight; and is suggestive but not sufficient to infer a causal relationship to preterm delivery, childhood cancer, childhood leukemia, childhood lymphomas and childhood brain tumors.[18]

The effects of secondhand smoke exposure from parental smoking

The evidence is sufficient to infer a causal relationship between secondhand smoke exposure from parental smoking and lower respiratory illnesses in infants and children; middle ear disease in children (including acute and recurrent otitis media and chronic middle ear effusion); cough, phlegm, wheeze and breathlessness among children of school age; ever having asthma among

children of school age, the onset of wheeze illnesses in early childhood; persistent adverse effects on lung function across childhood; and a lower level of lung function during childhood.[18]

The effectiveness of interventions for smokers

The literature on tobacco treatment supports the widespread adoption of screening for tobacco use and treatment for all tobacco users.[2]

The five major components (the “5 A's”) of a brief intervention in the primary care setting are Ask, Advise, Assess, Assist and Arrange. It is important for a clinician to ask the patient if he or she uses tobacco, advise him or her to quit, and assess willingness to make a quit attempt. The first three components of the 5A’s should be delivered to each tobacco user, regardless of his or her willingness to quit. If the patient is willing to quit, the clinician should assist him or her in making a quit attempt by offering medication and providing or referring for counseling or additional treatment and arrange for followup contacts to prevent relapse.[2] If the patient is unwilling to make a quit attempt, the clinician should provide a motivational intervention and arrange to address tobacco dependence at the next clinic visit.[2]

These intervention components constitute the core elements of a tobacco intervention, but they need not be applied in a rigid, invariant manner. For instance, the clinician need not deliver all elements personally. One clinician (e.g., a medical assistant) may ask about tobacco use status; and a prescribing clinician (e.g., physician, dentist, physician assistant, nurse practitioner) may deliver personal advice to quit, assess willingness to quit and assist with medications, but then refer the patient to a tobacco intervention resource (e.g., a tobacco cessation quitline, health educator) that would deliver additional treatment to the patient. Evidence indicates that full implementation of the 5 A's in clinical settings may yield results that are superior to partial implementation.[2]

Clinicians should support patients willing to quit by

- Helping the patient develop a quit plan.
- Recommending the use of approved medication, except when contraindicated or with specific populations for which there is insufficient evidence of effectiveness (i.e., pregnant women, smokeless tobacco users, light smokers and adolescents).[2] The first-line medications include: bupropion SR, nicotine gum, nicotine inhaler, nicotine lozenge, nicotine nasal spray, nicotine patch and varenicline; second-line medications include:

clonidine and nortriptyline.

- Providing practical counselling (problem solving/skills training, such as learning from past quitting experiences, anticipating triggers or challenges in quitting, and dealing with other smokers in the household).
- Providing social support as part of treatment.
- Providing supplementary materials, including information on quitlines.[2]

Treatment for pregnant smokers

Given the serious risks of smoking to the pregnant smoker and fetus, whenever possible pregnant smokers should be offered person-to-person psychosocial interventions that exceed minimal advice to quit. Although abstinence early in pregnancy will produce the greatest benefits to the fetus and expectant mother, quitting at any point during pregnancy can yield benefits. Therefore, clinicians should offer effective smoking cessation interventions to pregnant smokers at the time of the first prenatal visit and throughout the course of a woman's pregnancy.[2]

The use of a structured question to improve disclosure is also recommended. Pharmacotherapies should be considered only when the pregnant woman is otherwise unable to quit, and when the likelihood of quitting, with its potential benefits, outweighs the risks of pharmacotherapy and potential continued smoking. If nicotine replacement therapies are chosen, the clinician should consider using medication doses that are at the low end of the effective dose range, and consider choosing delivery systems that yield intermittent, rather than continuous, drug exposure (e.g., nicotine gum rather than the nicotine patch).[2] Because none of these medications has been tested in pregnant women for efficacy in treating tobacco dependence, the relative ratio of risks to benefits is unclear.

A five-step counselling approach adapted to meet these recommendations for pregnant smokers has been developed (see below).[3,19] This "5-A" approach works equally well with women of various ethnic and racial groups but is less effective with pregnant women who smoke heavily (i.e., more than one pack per day).[20]

The Five A's[3]

1. Ask the woman about her smoking status using a multiple-choice question to improve disclosure. The patient should choose the statement that best describes her smoking status:
    A. I have NEVER smoked or have smoked LESS THAN 100 cigarettes in my lifetime.
    B. I stopped smoking BEFORE I found out I was pregnant, and I am not smoking now.
    C. I stopped smoking AFTER I found out I was pregnant, and I am not smoking now.
    D. I smoke some now, but I have cut down on the number of cigarettes I smoke SINCE I found out I was pregnant.
    E. I smoke regularly now, about the same as BEFORE I found out I was pregnant.
2. Advise the patient who smokes to stop by providing advice to quit with information about the risks of continued smoking to the woman, fetus and newborn.
3. Assess the patient's willingness to attempt to quit smoking at the time.
4. Assist the patient who is interested in quitting by providing pregnancy-specific, self-help smoking cessation materials. Support the importance of having a smoke-free space at home and seeking out a "quitting buddy," such as a former smoker or non-smoker. Encourage the patient to talk about the process of quitting. Offer a direct referral to the smoker's quitline (1-800-QUIT NOW) to provide ongoing counseling and support.
5. Arrange follow-up visits to track the progress of the patient's attempt to quit smoking. For current and former smokers, smoking status should be monitored and recorded throughout pregnancy, providing opportunities to congratulate and support success, reinforce steps taken towards quitting, and advise those still considering a cessation attempt.

Conclusions

There is solid epidemiological evidence that maternal smoking during pregnancy can result in adverse outcomes in pregnant women, fetuses, infants and children. Women who quit smoking before or during pregnancy reduce the risk of seeing adverse reproductive outcomes. Children who live in smoke-free environments are also less likely to succumb to mortality and morbidity.

Smoking cessation programs based on current research findings are effective for both pregnant smokers and smokers in general. The most recent review indicates that extended or augmented psychosocial interventions exceeding minimal physician advice to quit smoking nearly tripled cessation rates among pregnant smokers.[2] Counselling and pharmacotherapeutic intervention

with smokers also resulted in a doubling or tripling of long-term abstinence.[2]

Despite these promising findings, abstinence achieved during pregnancy is not maintained for most women and clinical trials testing interventions to prevent relapse have not produced significant results. Similarly, little success in long-term abstinence has been reported from cessation programs for mothers of young children.[10,21,22] The lack of effectiveness in these areas indicates that infants and young children are at risk of developing conditions related to exposure to secondhand smoke and that these women are likely to expose fetuses to tobacco smoke during future pregnancies.

Despite these limitations, existing evidence-based approaches for treating pregnant and parenting smokers should be widely implemented. At least 35% of women who quit smoking while pregnant remain smoke-free, improving not only their own health but also the health of their children and other family members.[23] The return on investment for health care systems is significant and visible in the short term.

Implications for Policy and Services

Effective treatments exist and should be implemented for pregnant and parenting smokers. The health and economic benefits for individuals, families and society are significant and cost effective. If smoking cessation programs are properly and universally implemented, fewer children will die in the first year of life and will experience fewer smoking-related morbidities and other conditions throughout infancy and childhood.

Institutional policies facilitating the adoption of tobacco treatment interventions include:

- Implementing a tobacco user identification system in every clinic.
- Providing training, resources and feedback to ensure that providers consistently deliver effective treatments intervention.
- Dedicating staff to provide tobacco dependence treatment and assessing the delivery of this treatment in staff performance evaluations.
- Promoting hospital policies that support and provide tobacco dependence services.
- Monitoring and improving the quality of services delivered.
- Including tobacco dependence treatments (both counselling and pharmacotherapy) identified as effective in this Guideline as paid or covered services for all subscribers or

members of health insurance packages.[2]

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Tobacco Cessation Programs for Pregnant Women and Mothers of Young Children

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Introduction

Healthy People 2020 has set a goal for the United States of having no more than 12% of adults who smoke by 2020.[1] Current trends suggest that cessation rates among pregnant women are increasing.[2] Evidence also suggests that mothers of young children may be especially responsive to smoking cessation interventions.[3] Unfortunately, 19% of women of childbearing age (18 to 44) continue to smoke and few women maintain pregnancy-related cessation beyond pregnancy.[4] Intensive and targeted intervention efforts are needed to take full advantage of the parenting life stage for promoting smoking cessation and achieving reductions in the prevalence of smoking.

Subject

Pregnant women and mothers of young children, in particular those with low income and education, are a critically important target group for smoking cessation efforts because their smoking rates are highest and cessation offers health benefits for them and for their children.[5] In addition, women in the childbearing stage of life have multiple contacts with health-care systems and other service providers (e.g. schools and daycares) that could encourage and support smoking cessation.

Problems

- **Among the sizeable proportion of women who quit smoking for the duration of pregnancy, the rates of postpartum relapse are disappointingly high.** Pregnancy and parenting provide a powerful inducement for many women to quit smoking. Indeed, population surveys indicate that almost half of pregnant women report having quit smoking during pregnancy.[2,6] These cessation rates are substantially higher than those achieved by formal interventions with non-pregnant adults. Unfortunately, the majority of women who

quit smoking for pregnancy will relapse after the child's birth.

- **An intimate partner's smoking undermines smoking cessation and maintenance among pregnant and parenting women.** Living with an intimate partner who smokes has been a consistent predictor of continued smoking during pregnancy and postpartum relapse.[7,8,9] Moreover, partners' smoking has been shown to influence the type and level of support provided.[10] Despite evidence to suggest the possible benefits of conjoint cessation and that partner's efforts to quit along with the woman are viewed as important supportive behaviour, partner cessation has not been emphasized.

- **Effective cessation interventions are lacking for heavily nicotine-dependent pregnant smokers and for those with multiple social-psychological barriers to cessation.** Important questions remain concerning the optimal over-the-counter nicotine replacement therapies (now including the gum, the patch and lozenge) and how to encourage compliance to facilitate smoking cessation during pregnancy. The available delivery systems have different advantages and limitations related to fetal nicotine exposure and maternal compliance. Yet the scientific evidence base suggests that over-the-counter nicotine therapies maintain or even lower fetal exposure to nicotine, avert carbon monoxide exposure and could enhance maternal cessation.[11] Lacking are clinical guidelines for counselling women regarding use of over-the-counter nicotine replacement therapies for smoking cessation during pregnancy and early postpartum.
  Evidence also suggests that psychosocial barriers to cessation may cluster for some groups of women.[7,12,13] For example, women with depression are likely to have other co-occurring barriers, such as partners who smoke, low income and stressful lifestyles that may make cessation particularly difficult.[7] These women may need more intensive interventions and ongoing support. The clinical linkages between obstetric and pediatric care could be capitalized on to provide ongoing cessation support services to pregnant women and new mothers. Systems are needed for tracking women through this transition and providing intervention. Despite the potential benefit of this approach for helping women maintain long-term abstinence, few cessation programs that bridge obstetric and pediatric care are operational.[14]

- **Family-based approaches that link parents' smoking to child health and smoking initiation have had little attention**. Up to 40% of children in the U.S. and Canada are exposed to environmental tobacco smoke (ETS).[15,16] Moreover, parental smoking is a consistent predictor of youth experimentation and initiation of smoking.[17] Evidence

suggests that parents do not want their children to start smoking and concerns about children motivate smokers to consider cessation.[18] Intervention programs that address smoking as a family problem are needed, particularly for households in which one or both parents are smokers themselves. A noteworthy challenge for these interventions will be to incorporate them into existing service systems so they can be maintained.

- **Sustainable clinical systems for identifying pregnant women and mothers of young children who smoke and counselling them for cessation are not widespread**· Cessation support services have not been integrated consistently into clinical care settings, particularly those that serve low-income populations.[14] New models for providing ongoing support services that are appropriate for resource-poor settings, such as public-health clinics, may need to be considered.

Research Context

Despite the significant potential public-health benefit of reducing rates of smoking among this important target group, there has been surprisingly little research to identify optimal smoking cessation or relapse prevention interventions for pregnant women and mothers. Meta-analyses of pregnancy and postpartum cessation intervention trials[19] have been conducted, but no equivalent summary analyses are available for interventions targeting mothers of young children.

Despite the promise of nicotine replacement therapies, their use with heavily nicotine-dependent pregnant women and new mothers has been evaluated in only a few small trials. Similarly, few evaluations of couple- and family-based interventions have been conducted to date.

Key Research Questions

- How do we incorporate efficacious cessation/maintenance interventions into obstetric and pediatric care settings?
- What is the optimal way to involve intimate partners and other household smokers in cessation/maintenance interventions? And how might these interventions be incorporated into existing service systems (e.g. health-care settings, schools, etc)?
- How do we maintain women’s prepartum levels of motivation for cessation into postpartum, and can health service linkages facilitate this process?

- What information is essential for women to make informed decisions regarding use of nicotine replacement therapies during and immediately after pregnancy?
- How do we communicate information about the link between adult smoking and child health outcomes (e.g. environmental tobacco smoke exposure) in ways that motivate adult smoking cessation and deter children from starting to smoke?

Recent Research Results

Pregnant women: Consistent with clinical practice guidelines,[20] multi-component interventions are most effective and typically include provider advisement, print self-help materials, and telephone counselling.[21,22,23] However, a recent meta-analysis of cessation trials targeted to pregnancy and/or postpartum indicates that there has been substantial variability in the intensity of interventions evaluated.[19] Interventions have been provided during pregnancy[21,22] and in some cases intervention activities have been extended to[23] or exclusively focused on postpartum.[24]

Most interventions have shown improvements over usual care for cessation during pregnancy. However, most of these programs have been evaluated in managed-care settings.[21,23,24] Evaluations of programs provided in low-income public-health clinic settings[22,25,26] have not found consistent benefits above usual care. Intervention benefits also have been shown in improved birth outcomes.[19] Unfortunately, interventions have not shown significant benefits in relapse prevention.[19]

Mothers of young children: Interventions targeted to mothers who smoke have been focused on encouraging smoking cessation as a strategy to reduce children's exposure to environmental tobacco smoke (ETS) exposure.[27,28,29,30] Parents of children with asthma have frequently been the target groups for these studies.[29,30] While most have shown improvements in self-reported smoking topography, e.g. not smoking in the same room as the child, these interventions have had mixed success in increasing cessation rates.[27,29] It has been suggested that the somewhat contradictory message that ETS exposure can be reduced by limiting the proximity of smoking may undermine cessation efforts.[27] Most recently, a community organization approach was used to reduce smoking among low-income women of childbearing age[31] and showed promise by reducing overall smoking prevalence by 2 percentage points and reducing daily cigarette consumption among women in intervention communities.

Conclusions

Promoting smoking cessation among pregnant women and mothers is needed to reduce the overall population prevalence of smoking and related health harms. Currently, the context of pregnancy and postpartum, a time when women who smoke are receptive to smoking cessation encouragement, is not being capitalized on fully to encourage permanent smoking cessation. Additional consideration should be given to developing interventions that address smoking as a family issue and include intimate partners and children in the household to eliminate smoking within the family. Health-care system and community resources should also be brought to bear on this important public-health problem. Forging linkages between prenatal and pediatric care merits greater attention and would make it possible to provide ongoing services and support that will be needed to sustain smoking cessation in the long term. However, community involvement to influence social norms regarding smoking cessation will also be important.

Implications

Eliminating smoking among pregnant women and mothers has substantial importance for several areas of child development policy. Reducing exposure to tobacco smoke by the fetus and growing child will reduce low birth weight, sudden infant death syndrome, and morbidity. Smoking-attributable neonatal costs are appreciable and estimated at $367 million annually in the United States.[32] Reduction of environmental tobacco smoke will improve children's health in the short and long terms and reduce children's likelihood of becoming cigarette smokers themselves. Because children do not have the power to negotiate smoke-free households for themselves, indoor air policies should be strengthened and broadened wherever possible to reduce exposure in public settings and daycares and reinforce non-smoking as a normative behaviour. Pediatric organizations should consider sponsoring public-health campaigns aimed at families to increase awareness of and shift norms towards the importance of smoke-free households for family well-being. Lastly, as recommended by others,[33] health-insurance coverage is needed for smoking cessation treatments to overcome any cost barriers to their use.

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