Smoking in pregnancy
Shane Higgins

This update discusses the evidence to link maternal smoking during pregnancy with adverse pregnancy outcome, and also the potential long-term effects on health of in-utero exposure to tobacco smoke. Smoking cessation strategies will also be considered. Curr Opin Obstet Gynecol 14:145–151. © 2002 Lippincott Williams & Wilkins.

Introduction
Prevalence studies suggest that 20–50% of women in developed countries report smoking at the onset of pregnancy [1**,2**]. International data do not indicate a clear trend towards reduced smoking in pregnancy in these countries.

When considering the effects of smoking in pregnancy, we must consider not only the short-term immediate effects on pregnancy outcome (miscarriage, low birth-weight, preterm birth and perinatal death) but also the long-term effects on the health of mothers (subfertility, malignancy), children (congenital abnormalities, childhood respiratory and behavioural problems) and adults (ischaemic heart disease, hypertension, insulin-dependent diabetes, obesity, obstructive lung disease and cerebrovascular accidents).

With the proposal by Barker [3] on the fetal origins of adult disease and an acknowledgement that smoking is one of the few preventable factors associated with adverse pregnancy outcome, much of the recent published work concentrates on smoking cessation strategies.

This review focuses on articles published since September 2000.

Subfertility and implantation failure
Hull et al. [4], in a retrospective population-based study involving 8515 couples with a planned pregnancy, identified factors that were associated with achieving a conception within a defined period (6 or 12 months) and leading to the birth of a baby (>24 weeks). A self-completed questionnaire was used to identify smokers. Using a logistic regression model they demonstrated that women who actively smoked had an increased risk of failing to conceive within 6 months [adjusted odds ratio (OR) 1.23, 95% confidence interval (CI) 0.98–1.49] or 12 months (OR 1.54, 95% CI 1.19–2.01). Active smoking by the male partner was also associated with reduced failure to conceive within 6 months, but the data failed to demonstrate a significant difference in conception rates at 12 months, except when the heaviest smokers were considered alone (OR 1.34, 95% CI 1.04–1.73). Non-smoking women exposed to environmental tobacco smoke (ETS) alone were more likely to fail to conceive within 6 months than non-exposed women (OR 1.17, 95% CI 1.02–1.37), but no significant effect on conception was found at 12 months (OR 1.14, 0.92–1.42). The unreliability of self-reporting as a measure of smoking
status and the quantity smoked is an important issue that may lead to measurement errors and an inability to identify true effects.

In a case–control study, Ness et al. [5] found an independent and significant association between smoking in pregnancy and spontaneous abortion (OR 1.8, 95% CI 1.3–2.6). An objective assessment of smoking habits of the participants was undertaken adding a greater degree of reliability to the result.

**Congenital anomalies**

In a retrospective cohort study involving 18016 births, Woods [6] examined the association between smoking during pregnancy and the occurrence of congenital anomalies. Self-reporting identified 1943 (11%) smokers at entry to the study. Using a logistic regression analysis to control for age, race and diabetes, only congenital anomalies of the cardiovascular system were significantly higher in the smoking population ($P<0.01$). However, in a retrospective study of this nature limitations relate to under-reporting the exposure history and quantifying the number of cigarettes smoked thus potentially incorrectly classifying women, and such studies are notoriously prone to recall bias.

In keeping with the inconsistencies of reporting an association between cigarette smoking and congenital anomalies, a further retrospective study by Chung et al. [7*] identified all cases of isolated cleft lip/palate from the US National Centre for Health Statistics 1996 Natality database. A total of 2207 cases was identified and compared with 4414 randomly selected controls born without congenital anomalies. The number of cigarettes used was stratified into none, one to 10 per day during pregnancy, 11–20 and 21 or more. The adjusted OR for having a baby born with a cleft lip/palate in women with a history of cigarette smoking compared with women who never smoked during pregnancy was 1.34, 95% CI 1.16–1.54. The risk remained statistically significant when cases were stratified according to the number of cigarettes smoked, with OR of 1.32, 95% CI 1.12–1.57 (1–10 per day), 1.28, 95% CI 1.01–1.63 (11–20) and 1.69, 95% CI 1.14–2.50 (21 or more), demonstrating what appears to be a dose-response relationship. It may be that the inconsistency of previous reports is related to small sample sizes that lacked statistical power to detect this association rather than the lack of a true association.

**Fetal growth restriction, low birthweight, preterm birth**

Smoking during pregnancy is associated with placental insufficiency, low birthweight and preterm birth. Lindley and colleagues [8*,9] investigated the effect of continuing or stopping smoking during pregnancy on five infant anthropometric indices. Using a subpopula-

...tion of all Swedish births from 1991 to 1992, on whom data were prospectively collected on smoking habits at both the first antenatal visit and again at the 32 week visit, the authors compared the anthropometric measurements of infants born to women who reported smoking at the first antenatal visit and the 32nd week visit with those born to women who reported smoking at the first antenatal visit but who had ceased smoking by 32 weeks with infants born to non-smokers. Data concerning smoking habits at 32 weeks were available for 15% of the population, collected on a convenience sample rather than a random sample. The outcome measures compared were birthweight, crown–heel length, head circumference and two measures of infant body proportionality, ponderal index and brain : body-weight ratio (BBR). All five indices were corrected for confounding variables. The proportionality scores were also corrected for infant birthweight $z$ score. This is a measure of the degree of growth restriction, and thereby allows comparison of the proportionality of infants with the same degree of growth restriction who differed in only one aspect of their exposure, i.e. whether or not their mothers smoked or not during pregnancy.

The authors demonstrated an association between continued smoking and reductions in birthweight, crown–heel length and head circumference, the effects being more severe with heavier smoking ($P<0.001$). Stopping smoking between the booking antenatal visit and 32 weeks appeared to result in the complete elimination of the smoking-associated deficits in birthweight and head circumference but not the deficit in crown–heel length ($P<0.01$).

With respect to the indices of proportionality, continued smoking was associated with a reduction in BBR ($P<0.001$), however quitting smoking before 32 weeks was sufficient to eliminate the smoking-associated deficits in the BBR. The ponderal index was elevated among the infants of women who smoked throughout pregnancy ($P<0.001$) and was not overcome when smoking was ceased before 32 weeks ($P<0.01$). It would appear therefore that the length stunting that had occurred during early pregnancy was not overcome when the mother was identified as a non-smoker by 32 weeks.

The results of the study should be viewed with caution as the subjects of the analysis were not chosen at random, and were therefore not necessarily representative of the smoking population. This potential selection bias may have led to the over or underestimation of the association between smoking and the anthropometric indices measured. Other concerns relate to the possible confounding variables that were not considered (socio-economic status and maternal use of alcohol and drugs) and the gestation at which smoking cessation occurred,
as these variables may have affected the outcomes measured.

Wong and Koren [10**] in a prospective study demonstrated that women whose delivery is complicated by fetal distress under-report their smoking habits ($P=0.04$). It is likely that maternal guilt associated with the adverse outcome together with the acknowledgement of the diminished social acceptance of smoking during pregnancy may lead to under-reporting.

Chan et al. [2**] examined the 1998–1999 perinatal data from South Australia to study the effect of maternal smoking on preterm birth, the incidence of small for gestational age (SGA) and low birthweight births among Aboriginal and non-Aboriginal births. Data were available on smoking habits at the first antenatal visit and the average number of cigarettes smoked per day compared with non-Aboriginal women. There was a lower rate of quitting smoking among Aboriginal women.

The relative risk was elevated among Aboriginal women of having a preterm (OR 1.64, 95% CI, 1.51, 1.80), SGA (OR 2.28, 95% CI, 2.14, 2.43) and low birthweight (OR 2.52, 95% CI 2.29, 2.76) baby. The population-attributable risk (defined as the proportion of a disease in the population that would theoretically disappear if exposure to the risk factor was eliminated) expressed as a percentage demonstrated that when comparing non-Aboriginal with Aboriginal births, approximately 11 versus 20% of preterm births, 21 versus 48% of SGA births and 23 versus 35% of low birthweight births were attributable to maternal smoking. The paper acknowledged the urgent need for education to the dangers of smoking and smoking cessation strategies among Aboriginal women.

The associations between maternal smoking and childhood disorders published within the review timeframe are considered.

Sudden infant death syndrome

In a prospectively collected dataset involving 24,986 births, Wisborg et al. [16] demonstrated that among the 20 sudden infant deaths that occurred, the children of smokers had more than three times the risk of sudden infant death syndrome (SIDS) (OR 3.5, 95% CI 1.4, 8.7) compared with children of non-smokers, and the risk of SIDS appeared to be dose related ($P<0.05$). The smoking-related data were collected prospectively and therefore could not be biased by the parents’ knowledge about the death of their child.

Pollock [17] demonstrated a similar association between smoking and SIDS based on data from the 1995 USA birth register. The author also examined the cost effectiveness of a smoking cessation programme. On the basis of the economic model of Marks et al. [18], with an estimated reduction of 11.7% of SIDS deaths within the smoking-exposed group, the estimated cost per averted SIDS death for a typical cessation programme was US$210,500 (95% CI US$119,200, US$224,400).

Browne et al. [19**] postulated that SIDS may be partly caused by subtle alterations in the autonomic mediation of cardiorespiratory control. The authors set out to test the hypothesis that maternal smoking in pregnancy alters autonomic function in infants. Fifty infants (26 infants of non-smokers and 24 of smokers) were assessed using
blood pressure responses to a passive head-up tilt on days 2–3 and again at 3 months of age. At 2–3 days the systolic pressure response to tilt was significantly different between the groups. In the infants of smokers, systolic pressure decreased by a mean (SE) of 7.1 (1.1) mmHg, whereas in control infants it remained unchanged. At 3 months systolic pressure in the infants of smokers remained unchanged but increased in control patients by 6.2 (2.1) mmHg (P<0.05). Such altered autonomically mediated cardiovascular control may reflect an increased susceptibility to SIDS in the infants of smokers.

**Childhood behavioural and psychiatric illness**

For many years research has questioned whether the potential association between smoking during pregnancy and behavioural and psychiatric problems was direct or resulted from other maternal social and lifestyle factors related to both smoking and childhood behaviour. It has been suggested that biological factors including smoking during pregnancy may be involved in the development of childhood negativity, behavioural and psychiatric problems. Brook et al. [20] conducted a survey consisting of a structured questionnaire to mothers of 2-year-old children. The subjects were selected on the grounds of their having smoked during pregnancy or having stopped smoking during pregnancy or having started smoking after pregnancy. The scale of negativity was a composite of three subscales of toddlers’ troublesome behaviours assumed to be precursors of later unconventionality and lessened emotional control: impulsivity, risk taking, and rebelliousness. Logistic regression analyses were undertaken, controlling for parental personality/behaviour/attitudes, perinatal variables, demographic variables and parenting behaviour. The effect of maternal smoking during pregnancy increased the odds of childhood negativity, and was found to be independent of the controlled variables (chi-square 5.60, P < 0.05). Wasserman et al. [21] examined the effects of smoking during pregnancy on childhood behaviour problems. Observations of behaviour problems in 199 children between the ages of 4 and 5 years were considered when complete data on potential covariates were available. Assessments were undertaken of the quality of the home environment, child behaviour problems (Child Behaviour Checklist questionnaire) and blood lead levels measured 6 monthly from birth to the age under consideration. Adjusting for age, sex, birthweight, ethnicity, maternal education and home environment, smoking was associated with worse scores on the following subscales of the Child Behaviour Checklist questionnaire: aggressive, delinquent, attention problems, social problems and externalizing factor. Daughters of smokers received significantly higher scores on somatic complaints compared with non-smokers. The lead concentration was associated with small increases in the delinquent subscale.

Although the authors controlled for several confounding variables they did not control for genetic risk. It may be argued that the offspring of mothers who smoke during pregnancy may be those more likely to inherit genotypes for antisocial behaviour.

**Childhood blood pressure**

Blake et al. [22**] explored the association between birthweight and childhood blood pressure taking into account smoking during pregnancy. In a prospective study data on 1708 women enrolled at 16–18 weeks were analysed (1042 non-smokers and 666 smokers). Pregnancy outcome data and subsequent follow-up assessment data on the children at ages 1, 3 and 6 years were recorded. There was an 80% follow-up rate to age 6 years. The authors demonstrated that smoking during pregnancy and lower birthweight were positively associated with higher childhood blood pressure. The average systolic blood pressure (SBP) of children aged 6 years whose mothers smoked during pregnancy was 4.2 mmHg (95% CI 0.0, 2.3) higher than that of children born to mothers who did not smoke during pregnancy. For those mothers who smoked more than 20 cigarettes per day the observed increase in SBP at age 6 years was 3.4 mmHg (95% CI 0.5, 7.4). Among the children of mothers who never smoked an inverse relationship was observed between SBP and birthweight; in children whose mothers smoked there was an observed but not statistically significant increase in SBP associated with increasing birthweight. Their finding of a positive relationship between birthweight and blood pressure in early childhood in the offspring of mothers who smoked during pregnancy contradicts the previously held theory that the relationship between maternal smoking and blood pressure is explained by maternal smoking causing a uniform decrease in birthweight, which subsequently increases blood pressure due to the known inverse relationship with birthweight.

**Childhood respiratory disorders**

A number of published studies investigated the relationship between maternal smoking in pregnancy, environmental tobacco smoke exposure and chronic childhood respiratory problems. Gilliland et al. [23] demonstrated among 3357 school children a reduction in a number of lung function tests (peak expiratory flow rate –3.0%, 95% CI –4.4, –1.4; mean mid-expiratory flow –4.6%, 95% CI –7.0, –2.3; forced expiratory flow –6.2%, 95% CI –9.1, –3.1), in those exposed *in utero* to maternal smoking, adjusting for various confounding variables. Adjusting for household ETS exposure did not significantly change the results. The study involved a self-administered questionnaire completed by the parents of the children. In a further study carried out by the same group [24] a self-response questionnaire was used to ascertain children with wheezing or physician-diagnosed
asthma. Lifetime exposure to tobacco smoke was determined from responses to questions regarding smoking histories of household members and any history of maternal smoking during pregnancy. In-utero exposure to maternal smoking without childhood ETS exposure was associated with an increased prevalence of physician-diagnosed asthma (OR 1.8, 95% CI 1.1, 2.9), a lifetime history of wheezing (OR 1.8, 95% CI 1.2, 1.6) and persistent wheezing (OR 3.1, 95% CI 1.6, 6.1). Current or previous ETS exposure was not associated with an increased prevalence of childhood asthma, but was consistently associated with childhood wheezing [24].

Breast cancer risks
In a matched case–control study Innes and Byers [25] evaluated the association of smoking during a woman’s first pregnancy, a period of pronounced growth and differentiation of breast tissue, and her subsequent risk of breast cancer. In their study they identified 319 women aged between 26 and 45 years who had completed their first pregnancy at least one year before the diagnosis of breast cancer was made. A total of 768 matched controls was identified. Information on smoking status was obtained from the case record of each patient. Smoking during pregnancy was associated with an increased risk for early-onset breast cancer (crude OR 2.7, 95% CI 1.1, 6.3). Adjustment for maternal age, subject age, race and education appeared to strengthen the association (OR 4.8, 95% CI 1.6, 14.6).

Smoking cessation strategies
Women who smoke are more likely to be younger, caucasian and from the lower socioeconomic strata of society and thus less educated (25–30% of women in these categories smoke) [26•]. The numbers who commence smoking are highest and the rates of cessation lowest among low socioeconomic strata women for some or all of the following reasons. Younger smokers are less concerned about the long-term ill effects and are more vulnerable to the effects of image advertising by the tobacco industry. Some women appear to be attracted to some unique benefits of smoking (weight and affect management), and believe that smoking assists them to cope with stress and the multiple demands related to the competing roles of mother, homemaker and employee. The subpopulation of pregnant smokers represents a group that would be more resistant to cessation pressures and in whom any cessation programme would need to be potent and multifaceted [26•].

Women who smoke may follow any one of a number of paths in dealing with their smoking as they embark upon pregnancy. Some women will stop smoking before becoming pregnant. The exact proportion of such women is unknown, but a recent estimate of self-reported smoking rates on entry to obstetric care was reported as 13.6%, which is lower than population rates [27]. These patients are classified as ex- or non-smokers and are not offered any intervention. They are usually highly motivated and dedicated to becoming smoke free not only for the pregnancy but also for life.

Spontaneous quitters discontinue smoking as soon as they learn that they are pregnant. The numbers vary, with dramatic demographic differences between the spontaneous quitters and those who continue to smoke in terms of race, educational level, income and employment status. The strength of nicotine addiction as measured by the years of smoking and cotinine concentrations and having a partner who smokes are seen as important factors that influence whether a woman will be a spontaneous quitter. A total of 80–85% of spontaneous quitters will maintain smoking cessation for the duration of the pregnancy, but as many as 70% will be smoking again by 6 months after delivery. The challenge with spontaneous quitters would appear to be to shift the emphasis from the baby to self during the latter stages of the pregnancy, and to initiate specific interventions designed to prevent relapse, interventions that are largely lacking at present.

Women who continue to smoke during pregnancy display even greater differences in demographic details when compared with non-smokers or spontaneous quitters. They also tend to have more psychosocial problems, less support and fewer financial resources, more family problems and less residential stability. The successful institution of a smoking cessation programme for this subpopulation poses a significant challenge. Earlier interventions (<24 weeks) have been able to help some women to quit; however, in one study [28] none of the women recruited between 24 and 32 weeks quit or significantly reduced their smoking.

In a further self-recruiting randomized controlled trial [29], in which 82 patients recruited to the study before 30 weeks’ gestation were randomly assigned to receive usual antenatal care or usual care plus a videotape programme to help quit smoking, the rates of abstinence were found not to differ between the groups. In a secondary analysis of literature reviews and a meta-analysis of published work, Melvin et al. [30•] recommended a brief cessation counselling session of 5–15 min, which when delivered by a trained provider with the aid of pregnancy-specific self-help materials significantly increased rates of cessation among smokers (relative risk 1.7, 95% CI 1.3, 2.2). The effect was less obvious with more addicted smokers. The authors
recommended the use of the Agency for Health Care Policy and Research’s clinical practice guideline treating tobacco use and dependence, a clinical practice guideline which uses the ‘ask, advise, assess, assist and arrange’ steps. Other authors [31] demonstrated a significant difference in quit rates during pregnancy among patients randomly assigned to receive financial incentives and social support ($P<0.0001$). Some might question the approach of external rewards as causing the subjects to lose the inherent motivation to modify behaviour over the long term.

Few intervention strategies exist to assist women who are spontaneous quitters from relapsing after the birth of their baby. A randomized controlled trial, project PANDA [26], targeted women in the final weeks of pregnancy with mailed videos and newsletters, and demonstrated a significant reduction in relapse rates over the follow-up period for the intervention group participants. However, another randomized controlled trial [32] targeting women for postpartum relapse prevention intervention found no difference in the relapse rates between women in the intervention and control groups. The variables found to be associated with relapse were low confidence for maintaining cessation, less encouragement from family and friends to refrain from smoking, and a greater number of smokers among family and friends.

Partners who smoke appear to make a critical contribution both to the woman’s continued smoking during pregnancy and the relapse rate postpartum for spontaneous quitters. Partner involvement in protecting the baby from exposure to tobacco smoke during the pregnancy and postpartum period and assisting the pregnant woman to quit smoking is of vital importance requiring worthwhile interventions and evaluation research.

In a Cochrane meta-analysis of 34 randomized and quasi-randomized trials of smoking cessation programmes implemented during pregnancy [1**] a significant reduction in smoking was demonstrated in the intervention groups (OR 0.53, 95% CI 0.47–0.60), an absolute difference of 6.4% women continuing to smoke, with better results seen in the trials with high intensity intervention.

**Nicotine replacement therapy**

There remains concern regarding the safety, efficacy and effectiveness of the use of nicotine replacement therapy (NRT) during pregnancy. In animal models nicotine administered by osmotic pump to simulate transdermal patch application can reduce fetal growth and produce some neurological abnormalities secondary to disturbances of neuronal maturation and neuronal cell death. The impact of nicotine is related to the time in pregnancy when it is administered, the dosage level and whether it is given continuously or intermittently [33]. In a randomized controlled trial, Wisborg et al. [34] assigned patients who were smoking more than 10 cigarettes at the end of the first trimester to receive nicotine patches or placebo patches in conjunction with cessation counselling. There was no difference in the number of women from the treatment group who quit smoking when compared with the placebo group; however, the overall quit rate among participants was much higher than expected. No serious adverse effects were noted. Among women in the treatment group who were non-smokers throughout pregnancy the mean birthweight was 509 g higher than those in the placebo group, a finding difficult to explain. The lack of a definitive answer suggests a need for further studies in this area.

**Conclusion**

There is a growing body of epidemiological data to support the profound negative effect maternal smoking during pregnancy has on intrauterine fetal wellbeing, an effect that has lasting and widespread consequences. Much of these data are drawn from studies with retrospective reporting of smoking habits. This method of data collection has been shown, in the presence of an adverse outcome, to lead to under-reporting of the habit. This may as a consequence lead to an under-estimation of the strength of association between maternal smoking during pregnancy and the outcome under investigation. This problem identifies a need for better prospective data collection with more objective assessments of smoking habits used.

There remains a strong association identified between continued smoking and daily consumption and social disadvantage, high parity, low income, being without a partner and receiving state-funded maternity care [1**].

Smoking cessation has been shown to be an effective intervention in antenatal care. Intervention strategies employed should focus on the subgroups within the smoking population least likely to quit smoking during pregnancy and most likely to relapse after delivery.

Healthcare providers are well placed to provide quit smoking intervention information to smokers, and antenatal staff appear more likely to provide counselling than other healthcare providers. Training and institutional support can build on this platform [35].

This review details only the effects of smoking that have been reported over the past 12 months.
References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

• of special interest
** of outstanding interest

A systematic meta-analysis of smoking cessation strategies.

Identifies the serious smoking problem that exists among the indigenous Australian population and the impact of such on fetal health.


A sufficiently powered study to demonstrate an association between a congenital birth defect and smoking.

Acknowledges that smoking cessation during pregnancy can benefit anthropometric indices.


Clearly identifies a need for more objective and unbiased methods of identifying smokers to validate potential associations between smoking and various pregnancy outcomes.


Highlights the association between placental pathologies and smoking.


Postulates a pathophysiological mechanism by which smoking, through its effect on autonomic nervous system, might cause SIDS.


Demonstrates a relationship between smoking in pregnancy and childhood blood pressure.


A good overview of smoking habits and smokers’ intentions during pregnancy.


A detailed review of a successful smoking cessation strategy.


