

The Effects Of Smoking On Pregnant Women

MEIR COHEN

ABSTRACT

Smoking during pregnancy is accepted as the most significant avoidable risk factor for an unsuccessful pregnancy result. Smoking is linked with fetal growth restriction, and increasing evidence also suggests that smoking can cause stillbirth, preterm birth, placental abruption, and possibly sudden infant death syndrome. Smoking during pregnancy is also associated with enhanced risks of spontaneous abortions, ectopic pregnancies, and placenta previa, and it might increase risks of behavioral disorders in childhood. Studies have shown with randomized controlled trials, that smoking intervention during pregnancy has had limited success. Smoking during pregnancy continues to be an important risk factor for maternal and fetal outcomes during pregnancy.

INTRODUCTION

The earliest cigarettes were mostly impossible to tell apart from their predecessor, the cigar. Cigarette smoking first began in Central America around the 9th century in the form of reeds and smoking tubes. The Aztec and the Maya tribes smoked tobacco and various drugs in religious rituals and regularly depicted priests and deities smoking on pottery and temple engravings. The cigarette and the cigar were the most common methods of smoking in the Caribbean, Mexico and Central and South America until recent times. In the South and Central Americas, plantation workers used various plant wrappers to wrap their tobacco in order to smoke it. In Spain, maize wrappers were introduced, which evolutionized into fine paper. The resulting product was called papalate. In France this product became known as the cigarette. British soldiers made smoking popular in the English-speaking world, after they saw Russian and Turkish soldiers use it. They brought this habit back home to Britain. It became a habit in Britain and later in the United States.

Cigarette smoking is the leading avoidable cause of death in many countries. Lung cancer is now a more frequent cause of death among U.S. women than breast cancer (U.S. Department of Health and Human Services [USDHHS], 2001b). The high occurrence of smoking among young women highlights not only smoking-related risks of adverse pregnancy outcomes, such as spontaneous abortions, stillbirth, preterm birth, and fetal growth restriction (USDHHS, 2001b), but also possible smoking-related long-term effects on infants, including neurodevelopmental disorders (Fergusson, et al, 1998) and cancers (Schwartzbaum, et al, 1991). Usually, pregnant women are concerned about fetal well-being, so a good time to stop smoking would be before attempting pregnancy. Smoking termination should diminish the mothers' pregnancy risks (infertility, spontaneous abortion, ectopic pregnancy, and placental disorders) and also the long-term risks of developing lethal diseases such as cancers and cardiovascular diseases that are caused by smoking.

Meir Cohen, BS '11 graduated Torou with a major in Biology. He's planning to attend medical school.

Time trends in smoking among women

Starting in 1935, all of the yearly estimates of smoking popularity in the United States were only made for commercial purposes. Among females, daily smoking increased steadily, from 20% in 1935 to around 50% in 1965 (USDHHS, 2001b). The increase was especially prominent during and after World War II.

The increase in smoking popularity among women is most likely due to a couple of reasons. First, smoking popularity among women increased significantly in the younger birth cohorts. For example, in the birth cohort of white women born in 1900–1904, around 10% smoked at age 25, while among women born in 1920–1924, 40% smoked at age 25 years (USDHHS, 2001b). During WWII there were more women in the workplace than there ever was before. They were needed to help out due to all the men who were out at war. This definitely contributed the increase of women smoking. Second, it appears that the tobacco industry's successful promotion of smoking as a fashionable thing to do, during and after World War II, influenced all age groups (Brandt, 1996; Ernster, 1985). A good example of this would be the successful marketing of the Marlboro Man. Therefore, in the 1900–1904 birth cohort, the prevalence of smoking continued to increase until age 50 years, when more than 20% of white women smoked, while in the 1920–1924 birth cohort, smoking prevalence peaked at around age 35 years, when close to 50% of all white women smoked (USDHHS, 2001b). This increase occurred among African-American women as well but it was less prominent than among the white women. Among Hispanics, the smoking prevalence rates were not as high and there was no real difference between birth cohorts (USDHHS, 2001b). Another big factor of the female smoking increase came through the cinema. Many actors and actresses smoked in the movies that they acted in.

After 1965, the National Health Interview Survey has provided yearly estimates of smoking prevalence in the United States among Whites and Blacks. In 1979 they started to give smoking prevalence rates for Hispanics, Asians or Pacific Islanders, Native Americans, and Alaskan natives as well. Since the sixties, the prevalence of smokers among women aged 18 years or older has been fairly constant at around 40% (USDHHS, 2001b).

However, the rate of current smoking altogether has dropped from 34% in 1965 (USDHHS, 2001b) to 21% in 2000 (Trosclair, et al, 2002). This drop is observed in most ethnic groups, including non-Hispanic Whites, Hispanics, non-Hispanic Blacks, and Asians or Pacific Islanders. Meanwhile, smoking prevalence has not decreased among Native Americans and Alaskan natives.

The decrease in smoking prevalence during recent decades is especially noticeable among women in their reproductive years. In 1965, 38% of women aged 18–24 years smoked, as did 44% of women aged 25–44 years. In 2000, corresponding figures were 25% and 23%, respectively (USDHHS, 2002). However, during the past decade, the reduction in smoking prevalence among young women in the United States appears to have leveled off.

Since the mid-1960s, the popularity of smoking has dropped in the United States in all educational groups. The decline has been most distinct among highly educated women. Among women who held a bachelor's degree or higher, 26% smoked in 1974. In 2000 however, only 10% smoked (USDHHS, 2002). The smallest drop in smoking was among women with only a high school education. In 1974 32% smoked, while 27% smoked in 2000. Smoking is also popular among women below the poverty line, compared with those at or above it (USDHHS, 2002).

Most smokers now quit smoking. In the United States, the percentage of ex-smokers among adult females (18 years or older) doubled from 20% in 1965 to 40% in 1998 (USDHHS, 2001b). There are a few possible reasons for the decrease. Society has been educated in the health issues

that smoking causes. The many preventive measures against smoking seem to have worked. Some of these measures include prohibiting indoor tobacco use at work or in restaurants, advertisements, age limits for buying cigarettes, and higher tobacco taxes (Wakefield and Chaloupka, 2000).

More than 80% of current smokers started smoking before age 18 years (USDHHS, 2001b). Also, smokers who start to smoke early are less likely to quit later. In the United States, current smoking among high school seniors decreased from 39% in 1976 to around 33% in 1998 (USDHHS, 2001b).

Smoking behavior during pregnancy

Estimates of smoking during pregnancy are usually dependent on self-reported information. Substantiation of this information is done with biochemical markers such as cotinine. These biochemical markers have also shown that pregnant women may conceal their smoking (Ford, et al, 1997; Klebanoff, et al, 1998). Therefore, self-reported information of smoking during pregnancy is probably underestimated. Since disapproving attitudes toward smoking during pregnancy are greater, the legitimacy of self-reported smoking information may be a concern.

A Swedish study investigated the connection between self-reported smoking in early pregnancy and the risk of small-for-gestational-age (SGA) births in the 1980s and early 1990s (Cnattingius, 1997). The frequency of self-reported smoking in early pregnancy declined from 30% in 1983–1985 to 24% in 1990–1992. The risks of a SGA birth were almost identical for pregnancies in 1983–1985 compared with 1989–1992. There were also no differences found in risks connected to moderate (1–9 cigarettes per day) or heavy (10 or more cigarettes per day) smoking between these time periods.

In the United States, the National Natality Survey reported that 40% of white pregnant women smoked in 1967, compared with only 25% in 1980, while corresponding figures among black women were 33% and 23% (Kleinman and Kopstein, 1987). Since 1989, the information on the prevalence of smoking during pregnancy is accessible from the U.S. Standard Certificate of Live Birth. Birth certificate data of live births show that in 1989 close to 20% of American pregnant women smoked. Smoking declined since then, and in 2000 only 12% smoked (USDHHS, 2002).

The decline in smoking during pregnancy is probably mostly due to a decrease in women smoking in general as opposed to an improvement of mothers quitting before or during pregnancy (Cnattingius, 1997; USDHHS, 2001b, Wisborg, et al, 1996).

Smoking during pregnancy is highly affected by the education given to the mothers. For example, in the United States, only 2% of college-educated women reported smoking during pregnancy in 2000, while 25% of women who attended but did not complete college smoked (Martin, et al, 2002). Smoking during pregnancy is most common among Native Americans and Alaskan natives (20% in 2000); also, 16% of non-Hispanic Whites, 9% of non-Hispanic Blacks, and 4% of Hispanics smoke (Martin, 2002). Heavy smoking during pregnancy has become less common in the United States (Cnattingius, 1997; USDHHS, 2001b).

Smoking cessation among pregnant women

Almost all pregnant women who stop smoking do so because of concerns about fetal and infant health. Observation studies reported that 20%–40% of smokers quit during pregnancy (Cnattingius, et al, 1992; Fingerhut, et al, 1990; Wisborg et al. 1996). Of those who stop smoking, the majority do so in early pregnancy (Cnattingius, 1992; Fingerhut 1990; Wisborg et al., 1996).

The risk for continued smoking during pregnancy is greater in women who have had previous pregnancies than women who are in their first pregnancy. Women who started smoking at a young age, heavy smokers, and women exposed to second hand smoke are also more likely to continue to smoke during pregnancy (Cnattingius, USDHHS, 2001a, Wisborg et al., 1996). Although the connection between smoking and cancer and cardiovascular diseases is well known, most women who quit smoking during pregnancy usually resume smoking within 6 months after giving birth (USDHHS, 2001b).

It has been suggested that pregnancy may be an ideal time for smoking intervention. Pregnant women are concerned about fetal well-being, and pregnant women also repeatedly visit prenatal care clinics during pregnancy. This can help end the mothers' smoking addiction habits.

In an intervention trial done in Holland, pregnant women who smoked at least 10 cigarettes per day were randomized to receive a nicotine patch or a placebo patch. Patches were used for 11 weeks, and smoking habits were evaluated using salivary cotinine. Observance was low in both groups, and the authors found no differences in cotinine values between the groups (Wisborg, et al, 2000A). So far, smoking intervention strategies during pregnancy have had little success, and no effective methods exist for cheap intervention in regular prenatal care.

Reproductive outcomes

Smoking has been reported to affect the ability to conceive and increases the risk of infertility, which is normally defined as the inability to conceive after 12 consecutive months of unprotected intercourse. Other risks are pregnancy termination during the first 3 months, either as a miscarriage or an ectopic pregnancy; the risk of placental complications; the risks of other harmful pregnancy outcomes, including fetal growth restriction, preterm birth, fetal or infant death, and congenital malformations; and the associations between smoking during pregnancy and subsequent risks to the child, including risks of hospitalization, behavioral problems, psychiatric diseases, and childhood cancers.

Delayed conception and infertility

Pregnancy rates over defined periods of time are lower among smokers than nonsmokers (Florack, et al, 1994; Olsen, 1991). However, conception rates among nonsmokers and former smokers appear to be comparable (Curtis, et al, 1997). In studies of women who are not very fertile and are going through in vitro fertilization treatment, smoking seems to be connected with reduced fertility as well (Hughes and Brennan, 1996). Smoking seems to have anti-estrogenic effects (Baron, et al, 1990). Ovarian stimulation studies have shown that smokers exhibit a lower peak serum estradiol levels than nonsmokers (Gustafson, et al, 1996). Nicotine and the toxic products of cigarette combustion also can interfere with the structure of a corpus luteum, tubal transportation, or implantation (Gindoff and Tidey, 1989).

Ectopic pregnancy

Approximately 10% of maternal deaths in the United States are because of ectopic pregnancies (Atrash, et al, 1986). An ectopic pregnancy, is a complication in which the pregnancy implants outside the uterine cavity. Almost all ectopic pregnancies do not work. It can cause internal bleeding which is extremely dangerous for the mother. Most ectopic pregnancies occur in the Fallopian tubes, but the implantation can also occur in other areas such as the cervix, ovaries, and abdomen. Pelvic inflammatory disease (PID) is one of the most important risk factors for ectopic

pregnancy. Cigarette smoking is known to increase the risk of PID, providing a rationale for the association of smoking and ectopic pregnancies (USDHHS, 2001b). However, there may be a greater risk of ectopic pregnancy without a connection to PID. Smoking is thought to damage the tubal transport of the ovum. This increases the risk of ectopic pregnancies in women who smoke (Phipps 1987).

Spontaneous abortions

While many studies have found a modest association between a mother smoking and the risk of spontaneous abortion, there are studies that did not show any connection at all between cigarette smoking and the risk of a miscarriage (USDHHS, 2001b). Cotinine is a metabolite of nicotine that can be assessed and measured in many human tissues. It is considered to be a more correct determinant of tobacco exposure than self-reported tobacco intake. Ness (1999) discovered that the risk of miscarriage related to smoking is considerably underestimated when using self-reports as opposed to the use of cotinine in hair samples. Smoking is not associated with any fetal anomaly where the fetus will have the wrong amount of chromosomes. Rather, the smoking-related risk of spontaneous abortion may occur mostly among spontaneous abortions with the normal fetal karyotype. This is supported in part by the findings of Kline et al. (1995).

Placental complications

Placental abruption, which is the premature separation of the placenta from the uterine wall, occurs in less than 3% of all pregnancies and is one of the most common causes of maternal and perinatal death, the latter being defined as fetal death occurring at 28 weeks or later or death within the first week of life (Kyrklund-Blomberg, et al, 2001; USDHHS, 2001b). In pregnancies with placental abruption, perinatal mortality rates range from about 10% to 25% (Kyrklund-Blomberg 2001). Smoking during pregnancy is consistently linked with placental abruption. Smokers face a twofold-increase in the risk of placental abruption, and the risk increases with amount smoked as opposed to nonsmokers (Ananth, et al, 1999; USDHHS, 2001b). The risks of placental abruption caused from smoking can apply to both single and multiple pregnancies (Ananth, et al, 2001). Women who stop smoking during pregnancy have a lower risk of placental abruption as opposed to women who continue to smoke (Naeye, 1980). In pregnancies complicated with placental abruption, there has been a connection to smoking increasing the risk of perinatal death (Kyrklund-Blomberg, 2001).

Smoking may raise the risk of placental abruption in numerous possible ways. There are degenerative and inflammatory alterations of the placenta that are found in maternal smokers (Rasmussen, et al, 1999). Women with placental abruption also have decreased levels of blood ascorbic acid, which is important in collagen synthesis. Plasma ascorbic acid levels are lower in smokers than in nonsmokers, which can affect the placenta to separate early in smokers (Faruque, et al, 1995). Smoking also is linked with the preterm rupture of the membranes, which can increase the risk of placental abruption (Kyrklund-Blomberg, 2001).

Placenta previa, which is defined as a placenta that covers the internal cervical os, occurs in around 5 per 1,000 deliveries (Iyasu et al., 1993). Women with pregnancies complicated by placenta previa are at increased risk for severe vaginal bleedings before or during delivery, preterm birth, and maternal death. The risk of perinatal death is increased as well. Cigarette smoking is connected with placenta previa. A smoker's level of carbon monoxide is increased at the expense of oxygen. Therefore, a smoker will have less oxygen attached to hemoglobin in the blood than nonsmokers.

Smoking-induced chronic hypoxemia has been suggested to result in placental enlargement, which increases the risk that the placenta reaches the cervical os.

Pregnancy-induced hypertensive diseases

Preeclampsia is defined as pregnancy-induced hypertension combined with proteinuria. If preeclampsia is complicated with seizures, the condition is called eclampsia. Preeclampsia is the leading cause of maternal mortality in the United States (Berg, et al, 1996) and can cause reduced fetal growth, placental abruption, and perinatal death (Cnattingius, 1997). One surprising and not very well understood findings is that smoking is inversely related to risk of preeclampsia, and most studies find no dose-response relationship between amount smoked and reduction in risk (USDHHS, 2001b). Compared with preeclampsia, gestational hypertension (pregnancy-induced nonproteinuric hypertension) is generally associated with lower maternal and fetal risks (Naeye, 1981; Seshadri and Venkataraman, 1997). It is not really known if smoking can also reduce the risk of gestational hypertension. Most, but not all, studies find a moderate reduction in the risk of gestational hypertension associated with cigarette smoking (Ros, et al, 1998).

McGillivray (1983) addresses the lowered risk of preeclampsia and/or gestational hypertension for smokers than for nonsmokers. He writes that there would be less extension of plasma volume in smokers than in nonsmokers. Cigarette smoke also includes thiocyanate, which has hypotensive effects (Klonoff, et al, 1993). Moreover, nicotine can restrain the production of thromboxane, which is a potent vasoconstrictor and a platelet aggregation stimulator (Ylikorkala, et al, 1985).

While smoking may reduce the risk of preeclampsia, once a smoker does develop preeclampsia, smoking may exacerbate the ill effects of the disease. Preeclampsia also may lead to a reduction in oxygen levels in placental tissue (placental hypoxia). In preeclamptic pregnancies, vasoconstriction leads to increased arterial blood pressure and uteroplacental resistance, which may cause placental hypoxia (Harris, 1988). If smokers develop preeclampsia, the placental hypoxia may be especially pronounced, leading to substantially increased risks of fetal hypoxia, placental abruption, and fetal death.

Fetal growth restriction

Simpson and Linda (1957) reported many years ago that infants born to mothers who smoked 10 cigarettes or more per day weighed 200 grams less than infants born to nonsmoking mothers. Recently, there have been studies that showed the smoking-related reduction in birth weight is caused primarily by fetal growth restriction (Kramer, 1987). We now know that there is a connection between smoking and fetal growth restriction. This connection between smoking and SGA births has been proven time and time again. The literature on this is solid. It is also proven that the risk of SGA births rises with the amount of cigarettes smoked. It has also been shown that when the mother stops smoking the fetal growth improves. Nordstrom and Cnattingius (1994) watched mothers' smoking habits in two births each. They noticed that for women who smoked during their first pregnancy and then stopped smoking during their second pregnancy, the second birth weight was similar to the women who never smoked. This was noticed as well in mothers who quit smoking early in the pregnancy. The birth weight of the baby in the mother who quit early was similar to that for the mothers who never smoked. (MacArthur and Knox, 1988). There are other factors that can combine with the effects of smoking to affect the fetal growth. For instance,

when a mother is older, smoking can affect the fetal growth and cause a SGA birth more than it would in a younger mother (Cnattingius, 1989; Fox, et al, 1994, Wen, 1990).

It is not known what causes the smaller birth weight. It is known that nicotine can cause contraction of the placental blood vessels (Suzuki et al., 1971). It is also known that carbon monoxide binds to fetal hemoglobin, which would result in fetal hypoxemia (Lambers and Clark, 1996). The mother's weight gain during pregnancy is also linked with fetal growth. Nonsmoking mothers gain more weight during pregnancy than mothers who do smoke. However, even though nonsmokers gain more weight than smoking mothers, smoking while pregnant will raise the risk of an SGA birth (Spinillo et al., 1994).

Preterm birth

Preterm birth is defined as a birth occurring at least 4 weeks before the estimated date of delivery. The major cause of neonatal mortality and morbidity is when the baby is born early. However, because of improvements in neonatal care, most deaths usually occur when the baby is born very early i.e. at 32 weeks (Berkowitz and Papiernik, 1993). There have been intervention programs, which try to prevent preterm births. These programs have not been successful (Goldenberg and Andrews, 1996). Smoking prevention might be a way to help lower preterm births.

Smoking has been linked to preterm birth and if there is less smoking it can help lower preterm birth (Chan, et al, 2001, Zeitlin, et al, 2001). Smoking is associated with the increased risk of intrauterine infection. It has also been shown that the mother's immunity is impaired when there is smoking (Naeye, 1978). Smoking can also increase the risk of preterm labor through greater production of prostaglandins in fetal membranes (Hoffman, et al, 1990).

Preterm premature rupture of membranes is when the amniotic fluid leaks before 37 weeks of gestation. This is the second most common cause of preterm delivery (Spinillo, Nicola, 1994). Smoking has consistently been associated with preterm premature rupture of membranes (Lee and Silver, 2001). Smoking reduces serum copper and ascorbic acid in blood plasma. These are important for collagen synthesis and maintenance (Hadley et al., 1990). A lack of serum copper and ascorbic acid might result in reduced elastic properties of the fetal membranes, but the smoking-related increased weakness to infections also may increase the risk of preterm premature rupture of membranes (Holt, 1987). The smoking-related risk of elective preterm delivery is mediated largely by other smoking-related risks. As stated previously, smoking increases the risk of placental abruption, placenta previa, and fetal growth disturbances, conditions that may require elective preterm delivery.

Although the smoking-related risk of preterm birth is relatively small, there are consistent findings that smoking might be associated with preterm birth. Also, women who stop smoking between pregnancies reduce the risk of preterm birth in the next pregnancy, to a point that it is comparable to that of nonsmokers in both pregnancies (Cnattingius, et al, 1999).

Perinatal mortality

Perinatal mortality is when there is a fetal death at 28 weeks or later in gestation. Smoking is consistently linked with an increased risk of perinatal mortality. There is an interesting twist where babies of smokers have a lower perinatal mortality rate than babies born to nonsmokers when the birthweight is less than 3 kilograms. However, the risk is switched in babies that are heavier than 3 kg. When looking at the overall picture, infants born to smokers have a greater risk of perinatal mortality in overall relative birth weights (Wilcox, 1993). There are two possible ways

that smoking affects perinatal mortality. The first is due to the fetal growth restriction and the other is that smokers have a greater risk of delivering very small preterm infants.

Stillbirth

Stillbirth is officially defined as fetal death at 20 gestational weeks or later. However, over 80% of stillbirths happen during the preterm period. This is between 20 and 36 weeks (Copper, et al, 1994). Even when stillbirth is considered as a fetal death at 28 weeks or later, the majority of stillbirths are preterm (Stephansson, et al, 2001). Stillbirth is relatively uncommon, and when defined as fetal death at 28 weeks or later, rates range from 3 to 8 per 1,000 in Europe and North America (Andersen, 2001).

Smoking has consistently been associated with the risk of stillbirth. A study found that smoking was foremost associated with risk of unexplained stillbirth (Froen et al., 2001). Although the smoking related risk of stillbirth is modest, most studies find that the risk increases with amount smoked (USDHHS, 2001b). Smoking appears to influence the risk of primarily preterm stillbirth (Stephansson, 2001), and the proportion of growth-retarded stillbirths also is larger among preterm compared with term stillbirths (Gardosi et al., 1998).

The smoking-related fetal hypoxemia and the increase in vascular resistance may explain the connection between smoking and reduced fetal growth and also may be part of the increased risk of placental abruption (Kramer, 1987; Kramer, et al, 1997). Another study also showed that the elevated risk of stillbirth in smokers was due mostly to high rates of placental abruption and placenta previa (Meyer and Tonascia, 1977). Likewise, in Sweden, a study showed that smoking was associated with a 40% increased risk of stillbirth, and this risk was shown due to the smoking-related risks of fetal growth restriction and placental complications only (Raymond, et al, 1994). Another study found that women who stopped smoking in early pregnancy reduced the risk of stillbirth to that of nonsmokers (Wisborg, et al, 2001).

Neonatal mortality

Smoking has been linked with the increased risk of early neonatal mortality. This is when a baby is born and then dies during the first four week of life. (USDHHS, 2001b). Meyer and Tonascia (1977) found that the increased risk of neonatal mortality coming from a mother smoking comes from the increased risk of an early delivery.

Congenital malformations

There is no conclusive evidence that smoking can cause congenital malformation. Most studies have not found a link between maternal smoking during pregnancy and the overall risk of congenital malformation (Malloy, et al, 1989; Shiono, et al, 1986, Van den Eeden, et al, 1990). There has been research in regard to maternal smoking associated with the risk of oral face clefts. The risk of oral face clefts in a baby is slightly higher when the mother smokes. However, the evidence is not strong enough. This was observed with both cleft lip with and without palate. However, the evidence that maternal smoking is linked with cleft lip or with any other congenital malformity such as missing limbs and cardiac defects are inconclusive (USDHHS, 2001b).

SIDS and childhood morbidity

Sudden Infant Death Syndrome or SIDS, is when the death of an infant is sudden and the cause of the death remains unknown after a postmortem examination. The diagnosis of SIDS

is usually restricted to unexpected deaths among infants aged 4 weeks to 1 year. Over the past ten years the rate of SIDS has declined in most modern countries. This decline has mostly been attributed to the change from prone to back sleeping position (Mitchell, et al, 1999, Willinger, et al, 1994). It appears that the prevalence of SIDS continues to decline. In the United States, SIDS prevalence rates fell by 7% from 1999 to 2000 (Martin, 2002; Mathews, et al, 2002).

Even though the rates of SIDS is declining, it remains the most common cause of post neonatal death in developed countries, and most SIDS deaths occur at 2–3 months of life (USDHHS, 2001b). In the United States, SIDS rates vary considerably by ethnicity. For example, in 2000, SIDS rates per 100,000 live births were 29.4 among Asians and Pacific Islanders, 51.8 among Whites, 120.0 among Native Americans, and 122.1 among Blacks (Mathews et al., 2002). When compared with U.S. Whites, U.S. Blacks and Native Americans face a twofold increased risk of SIDS, while the corresponding risk among Asians and Pacific Islanders is reduced substantially. The reasons for these differences are not fully understood, but lifestyle factors may play a role (MacDorman, et al, 1997).

Although the decline in SIDS rates during the 1990s has been attributed to change in infants' sleeping positions, the decline also coincided in many countries with declining rates of cigarette smoking during pregnancy. Smoking during pregnancy has been associated with SIDS, and dose-response relationships have been reported in studies from different populations (MacDorman, 1997; Murphy, et al, 1982). The risk of SIDS among infants of daily smokers is commonly doubled or tripled, when compared with non-smokers, and sometimes more than tripled risks have been reported (Malloy, et al, 1992).

The smoking related risk of SIDS might be explained by examining the other differences between smokers and nonsmokers. However, many studies have shown that the association between smoking and SIDS has remained essentially the same even when measures of socioeconomic status, education, or alcohol were included (Nordstrom, et al, 1993; Wisborg, Kesmodel, 2000b). However, Malloy, Kleinman, Land, and Schramm (1988) found that the smoking-related risk of SIDS was reduced after evaluating other lifestyle differences and factors.

A relationship between smoking and risk of SIDS is observed consistently across various study designs and populations. However, because most women who smoke during pregnancy continue to smoke after birth, it has been debated whether the smoking-related risk of SIDS is caused by either prenatal or postnatal smoking exposure or both. Anderson and Cook (1997) performed a systematic review of the connections between maternal prenatal and postnatal smoking and risk of SIDS. In this review there was no conclusive evidence shown. Sixteen studies were performed and four studies reported on postnatal smoking after controlling for prenatal smoking. There were three studies that reported that maternal postnatal smoking increased the risk of SIDS independent of prenatal smoking (Klonoff-Cohen, 1995; Mitchell et al., 1993; Ponsonby, et al, 1995; Schoendorf and Kiely, 1992), and one study found that the association between postnatal smoking and SIDS was not significant (Blair et al., 1996). Mitchell et al. (1997) reported that the risk of SIDS was increased among infants born to mothers who were smokers and also shared a bed with their infants, while bed sharing among non-smokers did not influence risk of SIDS. Similar results have been reported by Fleming et al., (1996), although a recently published U.S. study found no evidence of an interaction between smoking status and bed sharing with regard to risk of SIDS (Hauck et al., 2003).

Dwyer et al. (1999) performed a study of close to 10,000 infants in a high-risk population, of whom 53 infants died of SIDS. They found that the cotinine level in the infants' urine was re-

duced by half if smoking mothers did not smoke in the infants' room, which indicates that smoking in an infant's bedroom does influence the infant's exposure to passive smoke. However, this finding was not accompanied by a reduced risk of SIDS. In a study of findings at autopsy, cotinine concentrations in pericardial fluid were analyzed in 67 infants who died from SIDS. About 25% of the SIDS infants had cotinine concentrations exceeding 30 ng/ml indicating tobacco exposure prior to death (Rajs et al, 1997). Thus, the evidence to date is that both prenatal and postnatal smoking exposure influence risk of SIDS (Anderson and Cook, 1997; Fleming 1996).

Risks of hospitalization and respiratory disorders during infancy and childhood

During the first years of life, children whose mothers smoked during pregnancy have an increased risk of hospitalization (Harlap and Davies, 1974; Rantakallio, 1978; Taylor and Wadsworth, 1987; Weitzman, et al, 1990; Wisborg, et al, 1999). This is because the smoking is associated with a high risk of respiratory sicknesses (Harlap and Davies, 1974; Taylor and Wadsworth, 1987; Wisborg, 1999). A study has shown that the maternal smoking can increase the risk of childhood asthma. (Weitzman et al., 1990). It has also been shown that smoking can increase the risk of hospitalization from gastrointestinal or dermatologic symptoms. However, it is unknown if these symptoms are from smoking exposure before or after the birth of the child (Wisborg et al., 1999).

Behavioral diseases in childhood

Maternal smoking during pregnancy and fetal growth retardation have been associated with many childhood behavior disorders. For example, it was found that compared with infants born to non-smokers, infants born to smokers faced a much greater risk of attention-deficit/hyperactivity disorder (ADHD), and this positive association remained significant after adjusting for socioeconomic status, parental IQ, and parental ADHD status (Milberger, 1996). In another study, children exposed to maternal smoking in utero had higher psychiatric symptoms rates for conduct disorder, alcohol abuse, substance abuse, and depression (Fergusson et al., 1998). Although smoking during pregnancy was associated with other factors, including socioeconomic disadvantage, impaired childrearing behaviors, and family problems, the smoking-related risks of adverse outcomes is still statistically significant after adjustments for these factors. These effects of maternal smoking were more pronounced for male than for female adolescents (Fergusson et al., 1998).

Autistic disorders in children are manifested by impaired social interactions, communication deviance, and stereotypical behavioral patterns. The cause of these disorders is thought to be largely genetically determined (Bailey, 1995), but there have been studies that showed children with autism to have an increased frequency of pre- and perinatal complications (Burd, et al, 1999). In one study, it was found that SGA infants had an almost tripled risk of having autism (Hultman, et al, 2002). However, when smoking was included in multivariate analysis, SGA infants faced a doubled risk of developing infantile autism, and compared with infants born to nonsmokers, those born to women who were daily smokers during pregnancy faced a much higher risk of developing autism (Hultman, 2002). Although the results from this study suggest that smoking and fetal growth might influence the risk of autism, these findings require confirmation.

Childhood cancers

Tobacco-specific carcinogenics, such as benzene and nitrosamines, probably pass through the placental barrier to the fetus (Norman, et al, 1996). Animal experiments support the hypothesis that tobacco smoke exposure during pregnancy may increase an offspring's risk of developing

tumors and hyperplasias (Pershagen, 1989). Animal experiments have shown that nitrosamine exposure during pregnancy may cause cancer in the central nervous system among offspring (Rice and Ward, 1982).

In four studies on risk of childhood cancer, information about smoking during pregnancy was collected before onset of disease (Golding, et al, 1990; Klebanoff, et al, 1996; Neutel and Buck, 1971; Pershagen, et al, 1992). Only one of these studies, including 33 cases, found that maternal smoking was associated with an increased risk of childhood cancer (Golding et al., 1990).

Results from case-control studies of smoking during pregnancy and overall risk of childhood cancer contradict each other. In a case-control study, which had over 500 cases, McKinney and Stiller (1986) found no connection between maternal smoking and childhood cancer risk. John, Savitz, and Sandler (1991) examined over 300 cases and found that smoking during pregnancy was connected with a 30% increased risk of childhood cancer.

Schwartzbaum (1991) reported a positive association between smoking during pregnancy and the risk of childhood cancer in a study that had 1,270 cases.

Because tobacco smoke includes leukogenic substances, maternal smoking during pregnancy has been studied mostly with regard to risk of leukemia and other cancers in blood and lymphatic tissue. Most studies have not found that smoking is connected with increased risk of childhood lymphatic leukemia (Tredaniel, et al, 1994). Results from studies on maternal smoking and myeloid leukemia are inconclusive. However this is probably due to the low number of included cases (Cnattingius, 1995; Shu et al., 1988).

Similarly, the association between maternal smoking and risk of childhood non-Hodgkin's lymphoma needs to be addressed in larger studies (Adami, 1996).

Most studies have not found a connection between maternal smoking and risk of childhood brain cancer (Linnet, 1996; Norman, 1996).

CONCLUSION

The most well known effect of smoking with pregnant women is fetal growth restriction. However, there has been a lot of literature showing that maternal smoking is related to the risks of preterm birth, stillbirth, and placental abruption. Increased risks have been found in most studies. It also has been shown that the risks increase the more one smokes. For example, if a pregnant woman smokes half a pack a day (approximately 10 cigarettes) the risks will not be as great as those of a woman who smokes two packs or more a day (twenty or more cigarettes). It has also been suggested that babies who have mothers who smoke have a greater chance of dying from SIDS. However it is unknown whether the increased risks are from smoking before or after the baby is born (Anderson and Cook, 1997; Dwyer et al., 1999). It is possible that both can attribute to the increased risks. Many studies have shown that there is a definite connection between smoking and fertility problems, ectopic pregnancies, and placenta previa. There are some suggestions that smoking during pregnancy can cause changes in the way the future child behaves and it has even been suggested that maternal smoking can cause an increase in ADHD and other behavior disorders. However, I have not found enough literature to definitely say that this is the case.

Smoking in the United States has been on the decline for a long time now. This is the case as well in other industrialized countries. However, in many other countries smoking is becoming more and more popular among young women. This is similar to what happened to the United States in the fifties. In these countries, sixty years ago it was rare to see women in the work force.

Now it is a common sight to see young women in the work force. It is important that they receive proper education about the risks of smoking. Smoking is still one of the most important preventable risk factors for unsuccessful pregnancy outcomes.

REFERENCES

- Adami, J., Glimelius, B., Cnattingius, S., Ekblom, A., Zahm, S. H., Linet, M., and Zack, M. (1996). Maternal and perinatal factors associated with non-Hodgkin's lymphoma among children. *International Journal of Cancer*, 65(6), 774–777.
- Ananth, C. V., Smulian, J. C., and Vintzileos, A. M. (1999). Incidence of placental abruption in relation to cigarette smoking and hypertensive disorders during pregnancy: A meta-analysis of observational studies. *Obstetrics and Gynecology*, 93(4), 622–628.
- Ananth, C. V., Smulian, J. C., Demissie, K., Vintzileos, A. M., and Knuppel, R. A. (2001). Placental abruption among singleton and twin births in the United States: Risk factor profiles. *American Journal of Epidemiology*, 153(8), 771–778.
- Andersen, A. M. (2001). Commentary: Social inequalities in risk of stillbirth—the price of success? *International Journal of Epidemiology*, 30(6), 1301–1302.
- Anderson, H. R., and Cook, D. G. (1997). Passive smoking and sudden infant death syndrome: Review of the epidemiological evidence. *Thorax*, 52(11), 1003–1009.
- Atrash, H. K., Hughes, J. M., & Hogue, C. J. (1986). Ectopic pregnancy in the United States. 1970–1983. *Morbidity and Mortality Weekly Report*, 35(2SS), 29SS–37SS.
- Bailey, A., Le Couteur, A., Gottesman, I., Bolton, P., Simonoff, E., Yuzda, E., and Rutter, M. (1995). Autism as a strongly genetic disorder: Evidence from a British twin study. *Psychological Medicine*, 25(1), 63–77.
- Baron, J. A., La Vecchia, C., and Levi, F. (1990). The antiestrogenic effect of cigarette smoking in women. *American Journal of Obstetrics and Gynecology*, 162(2), 502–514.
- Berg, C. J., Atrash, H. K., Koonin, L. M., and Tucker, M. (1996). Pregnancy-related mortality in the United States, 1987–1990. *Obstetrics and Gynecology*, 88(2), 161–167.
- Berkowitz, G. S., and Papiernik, E. (1993). Epidemiology of preterm birth. *Epidemiologic Reviews*, 15(2), 414–443.
- Blair, P. S., Fleming, P. J., Bensley, D., Smith, I., Bacon, C., Taylor, E., Berry, J., Golding, J., and Tripp, J. (1996). Smoking and the sudden infant death syndrome: Results from 1993–5 case-control study for confidential inquiry into stillbirths and deaths in infancy. Confidential Enquiry into Stillbirths and Deaths Regional Coordinators and Researchers. *British Medical Journal*, 313(7051), 195–198.
- Brandt, A. M. (1996). Recruiting women smokers: The engineering of consent. *Journal of American Medical Women's Association*, 51(1–2), 63–66.
- Burd, L., Severud, R., Kerbeshian, J., and Klug, M. G. (1999). Prenatal and perinatal risk factors for autism. *Journal of Perinatal Medicine*, 27(6), 441–450.
- Chan, A., Keane, R. J., and Robinson, J. S. (2001). The contribution of maternal smoking to preterm birth, small for gestational age and low birthweight among Aboriginal and non-Aboriginal births in South Australia. *Medical Journal of Australia*, 174(8), 389–393.
- Cnattingius, S. (1989). Does age potentiate the smoking-related risk of fetal growth retardation? *Early Human Development*, 20(3–4), 203–211.
- Cnattingius, S. (1997). Maternal age modifies the effect of maternal smoking on intrauterine growth retardation but not on late fetal death and placental abruption. *American Journal of Epidemiology*, 145(4), 319–323.
- Cnattingius, S., Granath, F., Petersson, G., and Harlow, B. L. (1999). The influence of gestational age and smoking habits on the risk of subsequent preterm deliveries. *New England Journal of Medicine*, 341(13), 943–948.
- Cnattingius, S., and Haglund, B. (1997). Decreasing smoking prevalence during pregnancy in Sweden: The effect on small-for-gestational-age births. *American Journal of Public Health*, 87(3), 410–413.
- Cnattingius, S., Lindmark, G., and Meirik, O. (1992). Who continues to smoke while pregnant? *Journal of Epidemiology and Community Health*, 46(3), 218–221.
- Cnattingius, S., Mills, J. L., Yuen, J., Eriksson, O., and Ros, H. S. (1997). The paradoxical effect of smoking in preeclamptic pregnancies: Smoking reduces the incidence but increases the rates of perinatal mortality, abruption placental, and intrauterine growth restriction. *American Journal of Obstetrics and Gynecology*, 177(1), 156–161.
- Cnattingius, S., Zack, M., Ekblom, A., Gunnarskog, J., Linet, M., and Adami, H. O. (1995). Prenatal and neonatal risk factors for childhood myeloid leukemia. *Cancer Epidemiology Biomarkers and Prevention*, 4(5), 441–445.
- Copper, R. L., Goldenberg, R. L., DuBard, M. B., and Davis, R. O. (1994). Risk factors for fetal death in White, Black, and Hispanic women. Collaborative Group on Preterm Birth Prevention. *Obstetrics and Gynecology*, 84(4), 490–495.
- Curtis, K. M., Savitz, D. A., and Arbuckle, T. E. (1997). Effects of cigarette smoking, caffeine consumption, and alcohol intake on fecundability. *American Journal of Epidemiology*, 146(1), 32–41.
- Dwyer, T., Ponsonby, A. L., and Couper, D. (1999). Tobacco smoke exposure at one month of age and subsequent risk of SIDS a prospective study. *American Journal of Epidemiology*, 149(7), 593–602.

- Ernster, V. L. (1985). Mixed messages for women. A social history of cigarette smoking and advertising. *New York State Journal of Medicine*, 85(7), 335–340.
- Faruque, M. O., Khan, M. R., Rahman, M. M., and Ahmed, F. (1995). Relationship between smoking and antioxidant nutrient status. *British Journal of Nutrition*, 73(4), 625–632.
- Fergusson, D. M., Woodward, L. J., and Horwood, L. J. (1998). Maternal smoking during pregnancy and psychiatric adjustment in late adolescence. *Archives of General Psychiatry*, 55(8), 721–727.
- Fingerhut, L. A., Kleinman, J. C., and Kendrick, J. S. (1990). Smoking before, during, and after pregnancy. *American Journal of Public Health*.
- Fleming, P. J., Blair, P. S., Bacon, C., Bensley, D., Smith, I., Taylor, E., Berry, J., Golding, J., and Tripp, J. (1996). Environment of infants during sleep and risk of the sudden infant death syndrome: Results of 1993–5 case-control study for confidential inquiry into stillbirths and deaths in infancy. Confidential Enquiry into Stillbirths and Deaths Regional Coordinators and Researchers. *British Medical Journal*, 313(7051), 191–195.
- Florack, E. I., Zielhuis, G. A., and Rolland, R. (1994). Cigarette smoking, alcohol consumption, and caffeine intake and fecundability. *Preventive Medicine*, 23(2), 175–180.
- Ford, R. P., Tappin, D. M., Schluter, P. J., and Wild, C. J. (1997). Smoking during pregnancy: How reliable are maternal self reports in New Zealand? *Journal of Epidemiology and Community Health*, 51(3), 246–251.
- Fox, S. H., Koepsell, T. D., and Daling, J. R. (1994). Birth weight and smoking during pregnancy—effect modification by maternal age. *American Journal of Epidemiology*, 139(10), 1008–1015.
- Froen, J. F., Arnestad, M., Frey, K., Vege, A., Saugstad, O. D., and Stray-Pedersen, B. (2001). Risk factors for sudden intrauterine unexplained death: Epidemiologic characteristics of singleton cases in Oslo, Norway, 1986–1995. *American Journal of Obstetrics and Gynecology*, 184(4), 694–702.
- Gardosi, J., Mul, T., Mongelli, M., and Fagan, D. (1998). Analysis of birthweight and gestational age in antepartum stillbirths. *British Journal of Obstetrics and Gynaecology*, 105(5), 524–530.
- Gindoff, P. R., and Tidey, G. F. (1989). Effects of smoking on female fecundity and early pregnancy outcome. *Seminars in Reproductive Endocrinology*, 7(4), 305–313.
- Goldenberg, R. L., and Andrews, W. W. (1996). Intrauterine infection and why preterm prevention programs have failed [editorial]. *American Journal of Public Health*, 86(6), 781–783.
- Golding, J., Paterson, M., and Kinlen, L. J. (1990). Factors associated with childhood cancer in a national cohort study. *British Journal of Cancer*, 62(2), 304–308.
- Gustafson, O., Nylund, L., and Carlstrom, K. (1996). Does hyper androgenism explain lower in vitro fertilization (IVF) success rates in smokers? *Acta Obstetrica et Gynecologica Scandinavica*, 75(2), 149–156.
- Hadley, C. B., Main, D. M., and Gabbe, S. G. (1990). Risk factors for preterm premature rupture of the fetal membranes. *American Journal of Perinatology*, 7(4), 374–379.
- Harlap, S., and Davies, A. M. (1974). Infant admissions to hospital and maternal smoking. *Lancet*, 1(7857), 529–532.
- Harris, B. A., Jr. (1988). Peripheral placental separation: A review. *Obstetrical and Gynecological Survey*, 43(10), 577–581.
- Hauck, F. R., Herman, S. M., Donovan, M., Iyasu, S., Merrick Moore, C., Donoghue, E., Kirschner, R. H., and Willinger, M. (2003). Sleep environment and the risk of sudden infant death syndrome in an urban population: The Chicago Infant Mortality Study. *Pediatrics*, 111(5 Pt 2), 1207–1214.
- Hoffman, D. R., Romero, R., and Johnston, J. M. (1990). Detection of platelet-activating factor in amniotic fluid of complicated pregnancies. *American Journal of Obstetrics and Gynecology*, 162(2), 525–528.
- Holt, P. G. (1987). Immune and inflammatory function in cigarette smokers. *Thorax*, 42(4), 241–249.
- Hultman, C. M., Sparen, P., and Cnattingius, S. (2002). Perinatal risk factors for infantile autism. *Epidemiology*, 13(4), 417–423.
- Iyasu, S., Safflas, A. K., Rowley, D. L., Koonin, L. M., Lawson, H. W., and Atrash, H. K. (1993). The epidemiology of placenta previa in the United States, 1979 through 1987. *American Journal of Obstetrics and Gynecology*, 168(5), 1424–1429.
- John, E. M., Savitz, D. A., and Sandler, D. P. (1991). Prenatal exposure to parents' smoking and childhood cancer. *American Journal of Epidemiology*, 133(2), 123–132.
- Klebanoff, M. A., Clemens, J. D., and Read, J. S. (1996). Maternal smoking during pregnancy and childhood cancer. *American Journal of Epidemiology*, 144(11), 1028–1033.
- Klebanoff, M. A., Levine, R. J., Clemens, J. D., DerSimonian, R., and Wilkins, D. G. (1998). Serum cotinine concentration and self-reported smoking during pregnancy. *American Journal of Epidemiology*, 148(3), 259–262.
- Kleinman, J. C., and Kopstein, A. (1987). Smoking during pregnancy, 1967–80. *American Journal of Public Health*, 77(7), 823–825.
- Kline, J., Levin, B., Kinney, A., Stein, Z., Susser, M., & Warburton, D. (1995). Cigarette smoking and spontaneous abortion of known karyotype. Precise data but uncertain inferences. *American Journal of Epidemiology*, 141(5), 417–427.
- Klonoff-Cohen, H., Edelstein, S., and Savitz, D. (1993). Cigarette smoking and preeclampsia. *Obstetrics and Gynecology*, 81(4), 541–544.
- Klonoff-Cohen, H. S., Edelstein, S. L., Lefkowitz, E. S., Srinivasan, I. P., Kaegi, D., Chang, J. C., and Wiley, K. J. (1995). The effect of passive smoking and tobacco exposure through breast milk on sudden infant death syndrome. *Journal of the American Medical Association*, 273(10), 795–798.

- Kramer, M. S. (1987). Intrauterine growth and gestational duration determinants. *Pediatrics*, 80(4), 502–511.
- Kramer, M. S., Usher, R. H., Pollack, R., Boyd, M., and Usher, S. (1997). Etiologic determinants of abruptio placentae. *Obstetrics and Gynecology*, 89(2), 221–226.
- Kyrklund-Blomberg, N. B., and Cnattingius, S. (1998). Preterm birth and maternal smoking: Risks related to gestational age and onset of delivery. *American Journal of Obstetrics and Gynecology*, 179(4), 1051–1055.
- Kyrklund-Blomberg, N. B., Gennser, G., and Cnattingius, S. (2001). Placental abruption and perinatal death. *Paediatric and Perinatal Epidemiology*, 15(3), 290–297.
- Lambers, D. S., and Clark, K. E. (1996). The maternal and fetal physiologic effects of nicotine. *Seminars in Perinatology*, 20(2), 115–126.
- Lambers, D. S., & Clark, K. E. (1996). The maternal and fetal physiologic effects of nicotine. *Seminars in Perinatology*, 20(2), 115–126.
- Lee, T., & Silver, H. (2001). Etiology and epidemiology of preterm premature rupture of the membranes. *Clinical Perinatology*, 28(4), 721–734.
- Linnet, M. S., Gridley, G., Cnattingius, S., Nicholson, H. S., Martinsson, U., Glimelius, B., Adami, H. O., and Zack, M. (1996). Maternal and perinatal risk factors for childhood brain tumors (Sweden). *Cancer Causes and Control*, 7(4), 437–448.
- MacArthur, C., and Knox, E. G. (1988). Smoking in pregnancy: Effects of stopping at different stages. *British Journal of Obstetrics and Gynaecology*, 95(6), 551–555.
- MacDorman, M. F., Cnattingius, S., Hoffman, H. J., Kramer, M. S., and Haglund, B. (1997). Sudden infant death syndrome and smoking in the United States and Sweden. *American Journal of Epidemiology*, 146(3), 249–257.
- Malloy, M. H., Hoffman, H. J., and Peterson, D. R. (1992). Sudden infant death syndrome and maternal smoking. *American Journal of Public Health*, 82(10), 1380–1382.
- Malloy, M. H., Kleinman, J. C., Bakewell, J. M., Schramm, W. F., and Land, G. H. (1989). Maternal smoking during pregnancy: No association with congenital malformations in Missouri 1980–83. *American Journal of Public Health*, 79(9), 1243–1246.
- Malloy, M. H., Kleinman, J. C., Land, G. H., and Schramm, W. F. (1988). The association of maternal smoking with age and cause of infant death. *American Journal of Epidemiology*, 128(1), 46–55.
- Martin, J. A., Hamilton, B. E., Ventura, S. J., Menacker, F., and Park, M. M. (2002). Births: Final data for 2000. *National Vital Statistics Reports*, 50(5), 1–104.
- Mathews, T. J., Menacker, F., and MacDorman, M. F. (2002). Infant mortality statistics from the 2000 period linked birth/infant death data set. *National Vital Statistics Reports*, 50(12), 1–28.
- McGillivray, I. (1983). Preeclampsia: The hypertensive diseases of pregnancy.
- McKinney, P. A., & Stiller, C. A. (1986). Maternal smoking during pregnancy and the risk of childhood cancer. *Lancet*, 2(8505), 519–520.
- Meyer, M. B., and Tonascia, J. A. (1977). Maternal smoking, pregnancy complications, and perinatal mortality. *American Journal of Obstetrics and Gynecology*, 128(5), 494–502.
- Milberger, S., Biederman, J., Faraone, S. V., Chen, L., and Jones, J. (1996). Is maternal smoking during pregnancy a risk factor for attention deficit hyperactivity disorder in children? *American Journal of Psychiatry*, 153(9), 1138–1142.
- Mitchell, E. A. (1995). Smoking: The next major modifiable risk factor. In T. O. Rognum (ed.), *Sudden infant death syndrome: New trends in the nineties* (pp.114–118).
- Mitchell, E. A., Ford, R. P., Stewart, A. W., Taylor, B. J., Becroft, D. M., and Thompson, J. M. (1993). Smoking and the sudden infant death syndrome. *Pediatrics*, 91(5), 893–896.
- Mitchell, E. A., Thach, B. T., Thompson, J. M., and Williams, S. (1999). Changing infants' sleep position increases risk of sudden infant death syndrome. *New Zealand Cot Death Study. Archives of Pediatrics and Adolescent Medicine*, 153(11), 1136–1141.
- Mitchell, E. A., Tuohy, P. G., Brunt, J. M., Thompson, J. M., Clements, M. S., Stewart, A. W., Ford, R. P., and Taylor, B. J. (1997). Risk factors for sudden infant death syndrome following the prevention campaign in New Zealand: A prospective study. *Pediatrics*, 100(5), 835–840.
- Murphy, J. F., Newcombe, R. G., and Sibert, J. R. (1982). The epidemiology of sudden infant death syndrome. *Journal of Epidemiology and Community Health*, 36(1), 17–21.
- Naeye, R. L. (1978). Effects of maternal cigarette smoking on the fetus and placenta. *British Journal of Obstetrics and Gynaecology*, 85(10), 732–737.
- Naeye, R. L. (1980). Abruptio placentae and placenta previa: Frequency, perinatal mortality, and cigarette smoking. *Obstetrics and Gynecology*, 55(6), 701–704.
- Naeye, R. L. (1981). Maternal blood pressure and fetal growth. *American Journal of Obstetrics and Gynecology*, 141(7), 780–787.
- National Board of Health Denmark. (2002). Survey of smoking habits in Denmark 2002. Copenhagen: National Board of Health.
- Ness, R. B., Grisso, J. A., Hirschinger, N., Markovic, N., Shaw, L. M., Day, N. L., and Kline, J. (1999). Cocaine and tobacco use and the risk of spontaneous abortion. *New England Journal of Medicine*, 340(5), 333–339.
- Neutel, C. I., and Buck, C. (1971). Effect of smoking during pregnancy on the risk of cancer in children. *Journal of the National*

- Cancer Institute, 47(1), 59–63.
- Nordstrom, M. L., Cnattingius, S., and Haglund, B. (1993). Social differences in Swedish infant mortality by cause of death, 1983 to 1986. *American Journal of Public Health*, 83(1), 26–30.
- Nordstrom, M. L., and Cnattingius, S. (1994). Smoking habits and birthweights in two successive births in Sweden. *Early Human Development*, 37(3), 195–204.
- Norman, M. A., Holly, E. A., and Preston-Martin, S. (1996). Childhood brain tumors and exposure to tobacco smoke. *Cancer Epidemiology, Biomarkers and Prevention*, 5(2), 85–91.
- Pershagen, G. (1989). Childhood cancer and malignancies other than lung cancer related to passive smoking. *Mutation Research*, 222(2), 129–135.
- Pershagen, G., Ericson, A., and Otterblad-Olausson, P. (1992). Maternal smoking in pregnancy: Does it increase the risk of childhood cancer? *International Journal of Epidemiology*, 21(1), 1–5.
- Phipps, W. R., Cramer, D. W., Schiff, I., Belisle, S., Stillman, R., Albrecht, B., Gibson, M., Berger, M. J., and Wilson, E. (1987). The association between smoking and female infertility as influenced by cause of the infertility. *Fertility and Sterility*, 48(3), 377–382.
- Ponsonby, A. L., Dwyer, T., Kasl, S. V., and Cochrane, J. A. (1995). The Tasmanian SIDS Case-Control Study: Univariable and multi-variable risk factor analysis. *Paediatric and Perinatal Epidemiology*, 9(3), 256–272.
- Rajs, J., Rasten-Almqvist, P., Falck, G., Eksborg, S., and Andersson, B. S. (1997). Sudden infant death syndrome: Postmortem findings of nicotine and cotinine in pericardial fluid of infants in relation to morphological changes and position at death. *Pediatric Pathology and Laboratory Medicine*, 17(1), 83–97.
- Rantakallio, P. (1978). Relationship of maternal smoking to morbidity and mortality of the child up to the age of five. *Acta Paediatrica Scandinavica*, 67(5), 621–631.
- Rasmussen, S., Irgens, L. M., and Dalaker, K. (1999). A history of placental dysfunction and risk of placental abruption. *Paediatric and Perinatal Epidemiology*, 13(1), 9–21.
- Raymond, E. G., Cnattingius, S., and Kiely, J. L. (1994). Effects of maternal age, parity, and smoking on the risk of stillbirth. *British Journal of Obstetrics and Gynaecology*, 101(4), 301–306.
- Rice, J. M., & Ward, J. M. (1982). Age dependence of susceptibility to carcinogenesis in the nervous system. *Annals of the New York Academy of Sciences*, 381, 274–289.
- Ros, H. S., Cnattingius, S., and Lipworth, L. (1998). Comparison of risk factors for preeclampsia and gestational hypertension in a population-based cohort study. *American Journal of Epidemiology*, 147(11), 1062–1070.
- Schwartzbaum, J. A., George, S. L., Pratt, C. B., and Davis, B. (1991). An exploratory study of environmental and medical factors potentially related to childhood cancer. *Medical and Pediatric Oncology*, 19(2), 115–121.
- Schoendorf, K. C., and Kiely, J. L. (1992). Relationship of sudden infant death syndrome to maternal smoking during and after pregnancy. *Pediatrics*, 90(6), 905–908.
- Seshadri, L., and Venkataraman, I. (1997). Hypertension in pregnancy. Outcomes, proteinuric vs. nonproteinuric. *Journal of Reproductive Medicine*, 42(2), 88–90.
- Shiono, P. H., Klebanoff, M. A., and Berendes, H. W. (1986). Congenital malformations and maternal smoking during pregnancy. *Teratology*, 34(1), 65–71.
- Shu, X. O., Gao, Y. T., Brinton, L. A., Linet, M. S., Tu, J. T., Zheng, W., and Fraumeni, J. F., Jr. (1988). A population based case-control study of childhood leukemia in Shanghai. *Cancer*, 62(3), 635–644.
- Shiono, P. H., Klebanoff, M. A., and Rhoads, G. G. (1986). Smoking and drinking during pregnancy. Their effects on preterm birth. *Journal of the American Medical Association*, 255(1), 82–84.
- Simpson, W. J., and Linda, L. A. (1957). A preliminary report in cigarette smoking and the incidence of prematurity. *American Journal of Obstetrics and Gynecology*, 73, 808–815.
- Spinillo, A., Capuzzo, E., Nicola, S. E., Colonna, L., Egbe, T. O., and Zara, C. (1994). Factors potentiating the smoking-related risk of fetal growth retardation. *British Journal of Obstetrics and Gynaecology*, 101(11), 954–958.
- Spinillo, A., Nicola, S., Piazzzi, G., Ghazal, K., Colonna, L., and Baltaro, F. (1994). Epidemiological correlates of preterm premature rupture of membranes. *International Journal of Gynaecology and Obstetrics*, 47(1), 7–15.
- Stephansson, O., Dickman, P. W., Johansson, A., and Cnattingius, S. (2001). Maternal weight, pregnancy weight gain, and the risk of antepartum stillbirth. *American Journal of Obstetrics and Gynecology*, 184(3), 463–469.
- Suzuki, K., Horiguchi, T., Comas-Urrutia, A. C., Mueller-Heubach, E., Morishima, H. O., & Adamsons, K. (1971). Pharmacologic effects of nicotine upon the fetus and mother in the rhesus monkey. *American Journal of Obstetrics and Gynecology*, 111(8), 1092–1101.
- Taylor, B., and Wadsworth, J. (1987). Maternal smoking during pregnancy and lower respiratory tract illness in early life. *Archives of Disease in Childhood*, 62(8), 786–791.
- Tredaniel, J., Boffetta, P., Little, J., Saracci, R., and Hirsch, A. (1994). Exposure to passive smoking during pregnancy and childhood, and cancer risk: The epidemiological evidence. *Pediatric and Perinatal Epidemiology*, 8(3), 233–255.
- Trosclair, A., Husten, C., Pedersen, L., and Dhillon, I. (2002). Cigarette smoking among adults—United States, 2000. *Morbidity and Mortality Weekly Report*, 51(29), 642–645.
- U.S. Department of Health and Human Services. (2001a). Patterns of tobacco use among women and girls. In *Women and smoking: A report of the surgeon general* (pp.19–176). Rockville, MD: U.S. Department of Health and Human

- Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office of Smoking and Health.
- U.S. Department of Health and Human Services. (2001b). Health consequences of tobacco use among women. In *Women and smoking: A report of the surgeon general* (pp.177–450). Rockville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office of Smoking and Health.
- U.S. Department of Health and Human Services. (2002). *Health, United States, 2002, with chartbooks on trends in the health of Americans* (DHHS Publication No.1232). Hyattsville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics.
- Van den Eeden, S. K., Karagas, M. R., Daling, J. R., and Vaughan, T. L. (1990). A case-control study of maternal smoking and congenital malformations. *Pediatric and Perinatal Epidemiology*, 4(2), 147–155.
- Wakefield, M., and Chaloupka, F. (2000). Effectiveness of comprehensive tobacco control programmes in reducing teenage smoking in the USA. *Tobacco Control*, 9(2), 177–186.
- Weitzman, M., Gortmaker, S., Walker, D. K., & Sobol, A. (1990). Maternal smoking and childhood asthma. *Pediatrics*, 85(4), 505–511.
- Wen, S. W., Goldenberg, R. L., Cutter, G. R., Hoffman, H. J., Cliver, S. P., Davis, R. O., and DuBard, M. B. (1990). Smoking, maternal age, fetal growth, and gestational age at delivery. *American Journal of Obstetrics and Gynecology*, 162(1), 53–58.
- Wilcox, A. J. (1993). Birth weight and perinatal mortality: The effect of maternal smoking. *American Journal of Epidemiology*, 137(10), 1098–1104.
- Willinger, M., Hoffman, H. J., and Hartford, R. B. (1994). Infant sleep position and risk for sudden infant death syndrome: National Institutes of Health, Bethesda, MD. *Pediatrics*, 93(5), 814–819.
- Wisborg, K., Henriksen, T. B., Jespersen, L. B., and Secher, N. J. (2000 A). Nicotine patches for pregnant smokers: A randomized controlled study. *Obstetrics and Gynecology*, 96(6), 967–971.
- Wisborg, K., Henriksen, T. B., Obel, C., Skajaa, E., and Ostergaard, J. R. (1999). Smoking during pregnancy and hospitalization of the child. *Pediatrics*, 104(4), e46.
- Wisborg, K., Henriksen, T. B., Hedegaard, M., & Secher, N. J. (1996). Smoking among pregnant women and the significance of socio- demographic factors on smoking cessation. *Ugeskrift for Laeger*, 158(26), 3784–3788.
- Wisborg, K., Kesmodel, U., Henriksen, T. B., Olsen, S. F., and Secher, N. J. (2000 B). A prospective study of smoking during pregnancy and SIDS. *Archives of Disease in Childhood*, 83(3), 203–206.
- Wisborg, K., Kesmodel, U., Henriksen, T. B., Olsen, S. F., and Secher, N. J. (2001). Exposure to tobacco smoke in utero and the risk of stillbirth and death in the first year of life. *American Journal of Epidemiology*, 154(4), 322–327.
- Ylikorkala, O., Viinikka, L., and Lehtovirta, P. (1985). Effect of nicotine on fetal prostacyclin and thromboxane in humans. *Obstetrics and Gynecology*, 66(1), 102–105.
- Zeitlin, J. A., Ancel, P. Y., Saurel-Cubizolles, M. J., and Papiernik, E. (2001). Are risk factors the same for small for gestational age versus other preterm births? *American Journal of Obstetrics and Gynecology*, 185(1), 208–215.