Drug Abuse

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Substance abuse in pregnancy is generally believed to be on the increase in many of the developed countries of the world. Pregnant women who expose themselves to toxic substances are at risk for adverse outcome. However, it is not entirely clear to what degree any one specific substance abused may affect either the mother or the baby during the course of pregnancy. In any one individual noted to be a substance abuser, there may be several "drugs" used at different stages or indeed at the same stage of gestation in pregnancy. The exact adverse outcome related to the toxicity of any substance is unclear, as lifestyle and socioeconomic factors also play an important role. Additionally, the role played by prescribed drugs is seldom considered.

This review considers, in three sections, substances that are known to be abused in pregnancy and for which there is some evidence of a mechanism that could lead to a poor outcome. Specifically, opiates (heroin and methadone), cocaine, amphetamines, marijuana (cannabis), and alcohol are discussed. Tobacco smoking with its known adverse effects, a problem for about 35% of pregnant women who smoke, is considered in a separate chapter. The first section of this chapter examines what is known about the extent of the problem, the numbers of pregnant women abusing "drugs," and the problems of ascertainment of drug abuse in pregnancy. The second section considers the general principles of placental handling of drugs, and how each specific drug affects placental function and transport of nutrients. The final section looks at assessment of fetal nutrition, and in particular the growth of the baby.

THE EXTENT OF "DRUG" ABUSE IN PREGNANCY

Obtaining reliable information about obstetric populations in this field is extremely difficult. Although some substances (e.g., alcohol) are freely available, others (e.g., cocaine) are illegal in the majority of countries, including the European nations and the United States. Underreporting of the use of illicit substances is likely for fear of reprisal, and for drugs that are readily obtained (both legal and illegal), feelings
of guilt about potential harmful effects on the unborn child may lead women to deny their use. There are certain methodologic considerations in examining the nature of the prevalence of substance abuse in pregnancy. Ascertainment of abuse can be either by questionnaire accompanied by an interview or by a laboratory assessment of the drug or a metabolite. Difficulties encountered by both of these approaches have been summarized (1). Questionnaires, either self-completed or backed up by interview, tend to have a reporting bias because of memory problems and an unwillingness to report accurately the use of illegal substances. Laboratory measures, although giving a degree of accuracy, do not always provide a broader picture of the history, pattern, dosage, and timing of use. Zuckerman et al. (2) reported that just over half of "identified" cocaine or marijuana users would have been picked up by urinalysis. Additionally, an accepted biochemical marker of drug abuse may itself alter in pregnancy because of physiologic adaptation and change with gestation. Screening for alcohol abuse in pregnancy is known to be problematic. Barrison et al. (3) showed that in pregnancy neither mean cell volume nor γ-glutamyl transpeptidase were reliable indicators of alcohol abuse.

It has also been suggested that pregnant women attending for antenatal care may alter their pattern of substance abuse before clinic visits, knowing that they will be asked for a sample of urine. In addition, opiates, for example, may be prescribed in pregnancy as antidiarrheal agents or for pain relief.

As a result, few good epidemiologic studies of substance abuse in pregnancy have been published, and many tend to identify the frequency of use in high-risk populations in inner-city areas, where drug abuse is known to be rife. Table 1 summarizes the incidence of drug abuse in pregnancy in several countries of the world for the specific substances included in this review.

PLACENTAL FUNCTION

With respect to the transfer of drugs from mother to fetus, the placenta should be considered as a lipid membrane. Passive diffusion is the mode of transfer for the majority of drugs, as their molecules are small and lipid-soluble. Maternal, placental, and fetal factors may affect placental transfer (4). Maternal factors include drug disposition during pregnancy, which is affected by changes in body weight, body composition (in particular fat content), and alterations in plasma volume, cardiac output, renal function, steroid hormone levels, and plasma protein concentrations. Secondly, blood flow to the uterus and fetoplacental unit influences the transfer of drugs to the fetus. With respect to placental factors, the permeability of the placenta to drugs depends on molecular size and lipid solubility, and on the surface area and thickness of tissue layers between the capillaries and the blood, which are known to change with gestation. The placenta contains enzyme systems that are involved in the metabolism of certain drugs (e.g., barbiturates) (5). However, its capacity may readily be overwhelmed and is likely to be less than that of either the fetal or the
maternal liver. It has been suggested that the human fetal liver is capable of metabolizing drugs, with well-developed enzyme systems from early in gestation. The degree of protein binding and the pH of the fetal circulation relative to that of the maternal circulation, which change throughout gestation, should also be considered. Additionally, placental transfer of drugs would be affected by timing and dosage. This information is particularly difficult to obtain from illegal drug abusers (6). The following subsections examine placental handling and how transport of nutrients is affected by specific substances.

**Opiates (Heroin and Methadone)**

Opiates, in particular heroin, readily cross the placenta, and morphine and its metabolites have been found in neonatal urine and meconium. Animal studies in sheep have confirmed rapid transfer of all opiates, with fetal levels being lower than those of the mother (7). The elimination half-lives of the opiate drugs was similar in maternal and fetal plasma, and the authors concluded that elimination from the fetus was mainly by placental clearance. Recently, work in humans examining maternal and neonatal plasma methadone levels found a significant relationship between them, but neonatal levels were consistently lower (8). Lower levels of opiates in the fetus relative to the mother could also be explained by high fetal tissue (liver and brain) uptake (8) or accumulation of significant amounts of opiates as nontransferable conjugates in amniotic fluid (7). There are no studies of the effects of opiates in other aspects of placental function.

**Cocaine**

Although many of the reported effects on the fetus of cocaine may be attributable to uterine vasoconstriction (9), a more active role for the placenta has been postulated. Studies in animals (9,10) show enzymes in the placenta capable of metabolizing cocaine and thus limiting the transfer of cocaine to the fetus. With respect to the human placenta (11), perfusion studies of isolated cotyledons confirm that the placenta could serve as a depot for cocaine, offering a degree of fetal protection; that fetal exposure might be prolonged by slow release of cocaine and its metabolites from a placental store; and that one of the major metabolites of cocaine, benzoylecgonine, does not cross the placenta as readily as cocaine. Increasingly, evidence is emerging from animal work that cocaine limits transplacental transfer of other substances to the fetus (9) and that this may not simply be related to flow, but a direct effect of cocaine on cellular uptake of nutrients. Results of work on human placental cells in tissue culture, both from human placental brush border membrane and from choriocarcinoma cells, suggest that the placenta itself is a direct target for cocaine, which affects transporter systems within the placenta, in particular noradrenaline and serotonin transporters (12). Such actions of cocaine may limit the transfer of essential nutrients to the developing fetus.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Opiates</th>
<th>Cocaine</th>
<th>Amphetamines</th>
<th>Marijuana</th>
<th>Multiple drug use</th>
<th>Alcohol</th>
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<td>6 Sacramento, USA</td>
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<td>37 Cleveland, USA</td>
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<td>Belfast, UK</td>
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<td>Heavy 35%</td>
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<td>34</td>
<td>Dundee, UK</td>
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<td>32</td>
<td>US Review</td>
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<td>1–2% Abusers</td>
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* Numbers in groups.
Amphetamines

It has generally been accepted that the mechanism underlying the harmful effects of amphetamine overuse in pregnancy is similar to that of cocaine—namely, decreased uterine blood flow as a result of vasoconstriction and thus a limited transfer of oxygen and nutrients to the fetus. Using methodology akin to that of their cocaine studies, the group from Augusta, Georgia, has shown that amphetamines also inhibit serotonin and norepinephrine transport in the human placenta (13). Although both drugs inhibit both transporter systems, amphetamines inhibit the norepinephrine transporter to a relatively greater degree, whereas cocaine preferentially inhibits the serotonin transporter. Such placental mechanisms would affect the concentrations of these vasoconstrictive substances in the intervillous space and could thus potentially limit transfer of many nutrient substances.

Marijuana (Cannabis)

Compounds derived from the hemp plant, known as cannabinoids, have been detected in neonatal urine and meconium, although once again levels in umbilical cord blood have been shown to be lower than those in the mother (7). Animal studies have suggested rather slow transfer of tetrahydrocannabinol, perhaps attributable to its extensive binding to maternal plasma proteins. Little is known about whether cannabinoids affect other placental functions, such as nutrient and oxygen transport, other than by the already known effects of tobacco smoking.

Alcohol

Alcohol and its major metabolite, acetaldehyde, both freely cross the placenta, and it is generally agreed alcohol affects fetal development and growth by direct toxicity rather than by any specific effect of either component on placental transport. Although there have been isolated reports in animals of alcohol interfering with active transport of amino acids across the placenta (14) by inhibition of amino acid transporter systems, others have shown that ethanol has significant fetal effects even when nutrition is well controlled (15).

FETAL NUTRITION

The assessment of fetal nutrition in the outcome of pregnancy in substance abusers has been examined only by consideration of the standard indices of fetal growth. Many workers have simply looked at birth weight without any control of confounding variables. Drugs may alter the length of gestation; for example, cocaine may down-regulate β-adrenergic receptors in the myometrium (7), thereby increasing the likelihood of early delivery. Other measurements of the newborn (e.g., birth length, head
circumference, skin fold thickness, arm circumference) that reflect fetal nutrition should be undertaken in an attempt to identify different patterns of poor growth related to specific drug abuse. Ultrasonic assessment of fetal growth has not been used but could in the future provide more insight into this problematic area. Importantly, several studies are now considering long-term outcome, including the growth of infants born to mothers who abuse drugs in pregnancy.

Before the impact of specific substances on fetal growth and development can be detailed, several general points must be considered. The first is the selection of cases for review. As a result of the difficulties of identifying women who abuse substances during pregnancy, many researchers have studied women attending specialized substance abuse centers. Such women, who are likely to be the subset of heavy or addicted users, may not be representative of population use, and this may therefore lead to a rather biased picture of outcome. Study designs often lack a suitable control or comparison group, and in this regard many other factors that influence fetal growth are often not considered in the selection of controls. Drug abuse is a marker of a different lifestyle, and other adverse factors, such as prostitution and sexually transmitted disease (in particular HIV infection), may be as important for outcome as the abuse of drugs.

Another major problem encountered in many studies is the recognized use of more than one substance during a pregnancy and the compounding effects of tobacco smoking. It has been suggested (16) that after controlling for environmental factors, many of the effects attributable to substance abuse disappear. For example, it has been postulated that dietary intake in women who are abusing drugs in pregnancy may be worse than in those who are not abusers. Evidence cited to support this hypothesis (17) includes serum levels of folate and ferritin, which themselves are poor markers of maternal nutritional status in pregnancy. Well-conducted, prospectively planned research is therefore needed to determine on a sound basis the effect of substance abuse on fetal nutrition and growth.

In the following sections, each drug is reviewed separately for its effects on fetal growth.

**Opiates (Heroin and Methadone)**

Opiates have in general been associated with fetal growth retardation and preterm delivery. In Liverpool (18), birth weight, head circumference, and body length were all reduced in the babies of heroin users compared with controls selected by taking the link before and after the index one. Similar findings from the United States have been summarized (19), and differences in outcome compared between heroin and methadone use. A decrease in birth weight in opiate abusers on average is ± 80 g. This review also detailed the proportion of infants that were small for dates and of low birth weight, concluding that there is an increased incidence of small-for-dates babies in heroin users (18%) in comparison with methadone users (12%) (compare
the 5% incidence of small-for-dates infants in drug-free populations). In Amsterdam (20), an increase in low birth weight, an increase in gestational age of less than 37 weeks, and a higher proportion under the 10th centile of birth weight for gestational age was confirmed in infants of heroin or heroin and methadone users. Further follow-up of these Dutch infants found that the differences in weight, height, and head circumference between the groups of children decreased as they became older. When the children were ages 4 to 12 years, no difference remained in the offspring of opiate users compared with those of nonusers other than in height, which was only marginally significant. Swedish workers have proposed that there may be fetal brain imprinting with heroin use in pregnancy and labor that might lead to altered behavior patterns in later life.

Cocaine

Although there are sound pathophysiologic mechanisms (see above) whereby cocaine might affect intrauterine growth, relatively recent reviews of the topic have come to very different conclusions (9,16,19). The group from Rochester, New York, claims that cocaine use leads to reduced birth weight and birth length, intrauterine growth retardation, and early gestation at delivery (9,19). Early delivery may result from abruption of the placenta, a recognized complication of cocaine use, or from the previously mentioned effects on the myometrium (7), confirmed recently in an intact animal (the baboon). On the other hand, the group from Pittsburgh, Pennsylvania (16), has concluded that when other risk factors correlated with cocaine exposure are considered, few studies show any effect of prenatal cocaine exposure on growth. Zuckerman et al. (2) used multiple regression analysis to control for confounding variables and found that many of the differences in neonatal growth indices in the offspring of cocaine users (either confirmed by urine assays or self-reported) either disappeared or became less significant. This group further examined neonatal body proportions (21). They found that after controlling for other potentially confounding variables, cocaine use, as detected by assays of maternal urine, was associated with a decrease in subscapular fat and of arm fat, but not of arm muscle circumference. They found no association between ponderal index or ratio of arm circumference to head circumference and cocaine abuse. They suggested that these findings would be consistent with the hypothesis that cocaine impairs nutrient transfer to the fetus. Prenatal care alone had a significant impact in decreasing the proportion of infants of low birth weight among cocaine users (22), adding to the belief that there is more involved in the impairment of fetal growth than substance abuse itself. A recent prospective multicenter study from the United States (23) has confirmed that cocaine use is relatively uncommon and not related to adverse birth outcome, with no increase in the frequency of preterm babies or babies of low birth weight. It was concluded that tobacco smoking was much more common and more likely to be related to poor fetal growth than either cocaine or marijuana use. Acceleration of fetal lung maturity,
suggested as being associated with cocaine use (24), has important implications for the management of obstetric complications if confirmed in further work.

Amphetamines

There are few reports of amphetamine abuse in pregnancy. Although there are theoretical reasons (see above) for amphetamine abuse to affect fetal growth, as for cocaine, few data are available. A Swedish survey (25) identified 69 women who were all known to have abused amphetamine in the course of pregnancy. A greater proportion of early deliveries and of babies of low birth weight was found compared with the Swedish population in general. These children were born in 1976/77 and have subsequently been followed up for 10 years. Mean body weight and length at 1 and 4 years were below those of a comparison group, but differences were statistically significant only for girls. At 8 and 10 years of age, weight and length of girls were similar to those of the comparison group and Swedish standards, whereas weight and length of the boys were above. The follow-up study of the Swedish workers identified behavioral differences in the children of amphetamine users, and they concluded that although social and environmental factors appear to have less influence on a child’s growth, exposure to amphetamines seems to be more influential on a child’s behavior pattern in later life. The impact of multiple drug use, assessed by intrapartum urine screening in Sacramento, California (6), found only very small differences in birth weight and head circumference, and no effect on neonatal length with amphetamine use. The effects of amphetamine use in this study were less than those of cocaine and multiple drug use. Previous reports from San Diego, California, and Dallas, Texas (26,27), showed decreased birth weight, birth length, and head circumference in association with amphetamine abuse.

Marijuana

In Ottawa, Fried et al. (28) found no reduction in birth weight, either raw or adjusted for confounding variables such as nicotine, alcohol, parity, maternal weight before pregnancy, and sex of the infant, in marijuana users. They did conclude, however, that heavy marijuana use was associated with significantly decreased length of gestation compared with moderate or irregular use or with non-use. Zuckerman et al. (2) found a negative effect on birth weight and length from marijuana use demonstrated by urinalysis, but not from self-reported use. In a review, Richardson et al. (16) concluded that it was unclear whether marijuana use affected intrauterine growth during pregnancy. There are only a few studies of growth in infancy, and no consistent effect of marijuana has been demonstrated. Recently, Shiono et al. (23), in an extensive multicenter study, reported that marijuana use is relatively common and is not related to adverse pregnancy outcome, but they considered only the proportion of preterm infants and infants of low birth weight. In a detailed neonatal assessment of body composition, Frank et al. (21) concluded that like
tobacco smoking, marijuana depresses lean body mass by leading to prolonged fetal hypoxia.

Alcohol

Although it is generally recognized that excessive drinking during pregnancy gives rise to the fetal alcohol syndrome, there is debate as to how much social or moderate drinking affects fetal growth. Fetal alcohol syndrome is a combination of growth retardation, mental retardation, facial abnormalities, and other possible systemic anomalies. Although fetal alcohol syndrome may be diagnosed in the neonate, it may not be recognized until there is postnatal growth retardation accompanied by developmental delay. A spectrum of effects of alcohol abuse in pregnancy, ranging from impaired fertility and early fetal wastage through birth defects and growth retardation to behavioral problems or a "normal" outcome, has been proposed. It is likely that there is a gradation of toxic effects depending on the amount and timing of alcohol use. It is widely debated whether there is a safe limit of alcohol consumption in pregnancy. If indeed there is a spectrum of effects of alcohol in pregnancy, it is perhaps not surprising that different levels of "safe" consumption have been defined. An increased risk for fetal alcohol syndrome has been associated with a daily alcohol intake exceeding 80 g (8 units per day), and fetal growth compromise with as little as 4 units per day. Earlier work in London indicated increased fetal growth retardation (percent birth weight less than the 10th centile) when women consumed more than 100 g of alcohol per week. In a population-based cohort study from Dundee, Scotland, there was no detectable effect on the outcome of pregnancy of alcohol consumption below 100 g/wk, whereas at higher levels of intake there was impairment of fetal growth (birth weight, length and head circumference) and shorter gestational age. After adjustment for the effect of smoking, social class, maternal size, and other confounding factors, only the relationship with shorter duration of pregnancy remained. In Finland, Halmesmaki demonstrated a dose-dependent alcohol effect on ultrasonically assessed fetal growth and suggested there was potential to limit growth retardation by counseling women and helping them reduce or stop their alcohol intake. This strategy is as yet unproven. The fetal alcohol syndrome is characterized by poor growth postnatally. The workers in Dundee followed up the offspring of their population-based study of alcohol consumption in pregnancy at the age of 18 months, and even at levels in excess of 100 g/wk they found no adverse outcome when both mental and physical development was assessed.

CONCLUSIONS

Although it is accepted generally that there is an increase of substance abuse in pregnancy, the exact magnitude of such an increase is poorly defined. Ascertainment
of drug use in pregnancy is difficult. A change in attitude toward such problems, coupled with improved laboratory screening, may be the way ahead in this area.

Animal studies can further help to elucidate mechanisms whereby such drugs might affect placental function and thereby fetal nutrition. However, hypotheses generalized from animal work need to be supported by properly conducted studies in the human.

The assessment of fetal nutrition mainly depends on measurements of the neonate. Improved means of assessing fetal nutrition in the infants of drug abusers should be sought. Properly conducted epidemiologic studies of drug abuse and its affect on pregnancy outcome are needed, based on population screening rather than selection of high-risk cases, with all the problems relating to adverse outcome resulting from a poor lifestyle and multiple drug abuse.

REFERENCES


**DISCUSSION**

**Dr. Battaglia:** The fetal alcohol syndrome, in the United States at least, is really confined to alcohol abuse as defined by the Diagnostic and Statistical Manual—III of the American Psychiatric Association, and those children with fetal alcohol syndrome are certainly severely developmentally handicapped, but again I don’t know of any one who has followed them through to adolescence. Do you know of any long-term follow-up?

**Dr. Doris Campbell:** No, I don’t know of any long-term follow-up directly on fetal alcohol syndrome. Fetal alcohol syndrome is the end of a spectrum ranging from normal growth, and
we really don’t know whether we are missing something more subtle with people who drink moderate amounts.

Dr. Talamantes: I wonder whether the effect of the fetal alcohol syndrome on development is not really a nutrition deficiency problem.

Dr. Stuart Campbell: I think not, because there are morphologic features in the fetus that wouldn’t be caused by undernutrition.

Dr. Doris Campbell: There is animal work to suggest that there are direct effects of alcohol, when you maintain nutrition artificially. But in the human, we just don’t know much about dietary intake coupled with heavy alcohol abuse in pregnancy.

Dr. Battaglia: I think there is a distinction between the baby who may have some effects of alcohol, which, I agree, could be nutritional, and the baby with effects that are clearly teratogenic. For example, this description of the hypoplasia of the middle part of the facies is a true teratogenic effect, and I don’t think that has much to do with maternal nutrition. Of all the compounds Dr. Campbell reviewed, alcohol is the only one in animal studies that is clearly teratogenic, and it is a very interesting teratogen in that it acts beyond embryogenesis and has clear effects on fetal development in animals. So that makes it very interesting to get good neurologic and developmental studies in children, because you have effects at a time when the brain is moving cells around in late fetal life, and remodeling at that stage could have some important effects. The Institute of Medicine has just published a study reviewing fetal alcohol syndrome (National Academy Press, 1996), and one issue discussed was whether there is a specific behavioral disorder associated with classic fetal alcohol syndrome beyond simply a marked reduction in IQ. Some people believe that there is such a characteristic behavioral pattern; they seem to be children who as they get older can’t assess risk, which gets them into a lot of problems in the school setting. But that isn’t clear yet.

Dr. Doris Campbell: The Dundee group did not come up with any differential effect that could be ascribed to increasing the amount of alcohol, but they did point out that the numbers taking over 120 g/wk were very small, and the numbers taking over 120 g/wk in the third trimester were different from the numbers drinking over 120 g/wk in the first trimester. So there is not only the amount to take into account, there is also the changing pattern through pregnancy that could have differential effects.

Dr. Talamantes: It would be very interesting to look at the Japanese population, which does not have the enzyme to metabolize alcohol, and to look at what would happen in those children born from women who consume alcohol in Japan. That would be to me a very interesting study.

Dr. Grahnquist: What about twin studies and alcohol fetopathy?

Dr. Doris Campbell: I have not seen anything relating to twins.

Dr. Grahnquist: My reason for asking this is because I came across twins, and one of them had a clear alcohol fetopathy but the other one didn’t, and the mother was a heavy drinker.

Dr. Doris Campbell: Abnormalities in twins are usually discordant and not concordant, so the distribution of blood to each twin comes into the picture as well, and even with monozygotic twins it is very uncommon to get concordance for abnormality.

Dr. Haschke: Any limit for daily alcohol consumption is questionable. Are there any data in relation to the drinking behavior of mothers? There are some mothers who drink continuously during the day, which results in a certain alcohol level in the body, and there are mothers who have periods of very heavy drinking, resulting in very high alcohol concentrations in the body, and then they slow down for a certain period. So there are different drinking types.

Dr. Doris Campbell: The only evidence that I saw relating to binge drinking was on
teratogenicity in early pregnancy, when alcohol might be having a direct effect on the fetal cells developing at that time (1). I found no data relating to binge drinking later on in pregnancy.

Dr. Battaglia: That has important public health implications. Health education aimed at reducing drinking in pregnancy works very well for casual drinkers, but they are not the women producing babies with the fetal alcohol syndrome. Those are the very heavy drinkers who are often binge drinkers, and our evidence in the United States shows that you are not going to get anywhere with a public health message with that group. You have to have a different approach, but we don’t know what. I don’t know about Europe, but in the United States we could really criticize government agencies that support research, because there is a huge amount of money spent on men’s drinking and how to treat it and there is very little spent on women’s drinking and how to treat it.

Dr. Doris Campbell: There is another variable with alcohol use, and that is the type of drink and whether it is spirits, wine, or beer. Many drinks have contaminating substances that might also be involved.

Dr. Stuart Campbell: The relative reduction in the biparietal diameter related to alcohol intake was clearly important in the Finnish study (2). Did they measure other fetal variables? If there is a small head circumference related to the abdominal circumference, then that is of great significance, but if it is just intratuerine growth retardation, it may be of less significance.

Dr. Doris Campbell: No, they didn’t measure any other parameters.

Dr. Battaglia: What would you hypothesize you would find on fetal velocimetry in the smoking mother, given the data that were presented on the development of the fetal capillary bed?

Dr. Stuart Campbell: It fits in with the work by John Kingdom, in which they found a decrease in the number of capillaries in the terminal villi. I suspect that it is related to impaired perfusion caused by the nicotine in the smoking, and that impaired perfusion eventually causes attrition of the capillaries in the tertiary villi and ultimately causes fetal hypoxia and centralization of flow to the fetal brain.

Dr. Soothill: We have shown a more than doubling of carboxyhemoglobin in the fetus, so I think oxygen delivery to the tissues is probably more relevant than transport across the placenta.

Dr. Doris Campbell: Some of the studies on smoking might explain the differences between smokers and non-smokers, but I wonder how you would explain the difference that has been found in birth weight when people stop smoking part way through the pregnancy?

Dr. Stuart Campbell: That would fit in with the carboxyhemoglobin story.

Dr. Soothill: Carboxyhemoglobin does seem to be trapped in the fetal circulation—it is more than double the maternal—and this has been shown in neonatal studies as well, presumably because of the high affinity of the fetal hemoglobin. It should be washed out over a period of a week or two, and therefore if oxygen delivery to the fetal tissues is reducing the growth, then that is one possibility.

Dr. Godfrey: With regard to alcohol, there are data from rats suggesting paternal effects of alcohol exposure before conception (3). And on the smoking data, there are very well-described differences in diet between smokers and non-smokers (4). Studies are currently in progress to address whether some of the effects of maternal smoking on fetal growth may be mediated through changes in the mothers’ dietary intakes.

Dr. Doris Campbell: Studies in pregnancy have not found major differences in dietary intake between smokers and non-smokers (5,6).
REFERENCES


