Pregnancy,
Prenatal Exposure & Parenting
PREGNANCY, PRENATAL EXPOSURE & PARENTING

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Normal fetal development requires both mother and fetus to supply appropriate levels of thyroid hormone at different times.

Brain abnormalities found in children exposed to abnormally low concentrations of thyroid hormone during fetal development are similar to those found in children exposed to alcohol in utero.

Researchers have found that alcohol consumption during pregnancy can alter thyroid function in both the mother and fetus.

In order to assure normal fetal development, mother and fetus must both – at different times during gestation – contribute appropriate levels of thyroid hormone. If not, brain defects can result, some of which resemble those found in children suffering from fetal alcohol syndrome (FAS). Due to these commonalities, some researchers speculate that alcohol may mediate alcohol-related birth defects (ARBDs) by inducing hypothyroid conditions in utero. A study in the January issue of *Alcoholism: Clinical and Experimental Research (ACER)* investigates if alcohol consumption during the equivalent of the third trimester in sheep results in an alteration of fetal or maternal thyroid function.

“The thyroid hormone system plays important roles in growth, development and in the function of other hormone and organ systems,” explained Timothy A. Cudd, associate professor of physiology at Texas A&M University and lead author of the study. “Both mother and fetus must contribute thyroid hormone for normal fetal development. Early in development, before the fetus is capable of producing thyroid hormone, maternal thyroid hormone crosses the placenta to influence fetal development. Later in development, when higher concentrations are required for normal fetal development, a fetal contribution is required to create sufficient concentrations.”

Cudd and his co-authors knew that brain abnormalities found in children who were exposed to abnormally low concentrations of thyroid hormone during fetal development are similar to brain abnormalities found in children exposed to alcohol in utero. “From a behavioral standpoint,” said Cudd, “children born to hypothyroid mothers score less well on intelligence, attention, language, reading ability and school performance measures compared to children born to mothers with normal thyroid function. These deficiencies are similar to those in children with ARBDs. From an anatomical perspective, hypothyroidism and fetal alcohol exposure both affect the development of the hippocampus and the cerebellum.” Knowing these similarities, the study authors investigated if ARBDs are, in part, a result of alcohol-mediated thyroid hormone system dysfunction.

Researchers gave pregnant ewes alcohol doses of 0.75, 1.25, 1.5 or 1.75 g/kg or saline through catheters beginning on day 109 of gestation (a full term for sheep is 145 days). The ewes received alcohol or saline on three consecutive days, followed by four days without expo-
ALCOHOL CONSUMPTION DURING PREGNANCY ALTERS THYROID FUNCTION

sure, thereby mimicking a pattern of binge drinking. Fetal and maternal blood samples were collected on days 118 or 132.

“The administration of alcohol to sheep during the equivalent of the third trimester of pregnancy resulted in altered thyroid function in both the mother and fetus,” said Cudd. “This is an important study because even today so little is known regarding the mechanisms through which alcohol intake by pregnant mothers is bad for their fetuses,” said Catherine Rivier, a professor of neuroendocrinology/neurosciences at the Salk Institute. “In addition, the sheep is a good model for the human because the thyroid system of both species develops similarly during gestation. Prior to this study, we knew that, in general, fetal brain development requires thyroid hormones to grow normally and build all the right connections. These results show us that alcohol given to a pregnant mother lowers thyroid hormones in both the fetus and the mother. This finding gives investigators the rationale for doing additional experiments to see if these changes in thyroid hormones participate in defects due to alcohol.”

Cudd believes that the study’s findings do indeed support the hypothesis that alcohol might mediate ARBDs by altering thyroid function in the fetus and/or in the mother. “Nonetheless,” he said, “further studies are necessary to conclude that this is the case in humans. Clearly, abstaining from alcohol use during pregnancy is the safest course. However, if our findings are proven to hold in humans, then it may be possible to monitor thyroid function and even correct abnormal thyroid function in mothers to potentially mitigate the actions of alcohol on the fetal brain.”

Article is based on the following published research:

ALCOHOL, WOMEN AND PREGNANCY

- Pregnant women who drink moderate to heavy amounts place their offspring at risk for developmental deficits.
- Previous research suggests that alcohol exposure later in pregnancy may be particularly damaging.
- A new study has found that moderate alcohol exposure during early pregnancy may be just as damaging to neurobehavioral development as continuous or late exposure.
- Neurodevelopmental deficits caused by early exposure were more obvious than growth impairments.

There is little question that women who drink heavily during pregnancy place their children at risk of developing fetal alcohol syndrome (FAS), characterized by growth retardation, craniofacial anomalies and mental retardation. However, women who drink moderate amounts of alcohol may also place their children at risk of developing less severe deficits (once known as fetal alcohol effects but now called alcohol-related neurodevelopmental disorder), characterized by a lower IQ, attention deficits, learning deficits and reduced social competence. A study in the August issue of *Alcoholism: Clinical and Experimental Research (ACER)* has discovered that a crucial factor for the developing fetus may be when a woman drinks. Researchers found that moderate alcohol exposure during early pregnancy may be just as damaging to neurobehavioral development as continuous or late exposure.

“Previous research has found that alcohol exposure later in pregnancy is strongly associated with problems in growth and behavioral development,” said Mary L. Schneider, professor of occupational therapy and psychology at the University of Wisconsin–Madison and lead author of the study. “Yet women who report drinking late in pregnancy have usually consumed alcohol throughout and so it is hard to disentangle early drinking from late drinking. In addition, while animal studies have established that high doses cause numerous impairments, many questions remain regarding the issue of moderate fetal alcohol exposure. Since many women of childbearing age drink alcohol regularly, it is likely that some offspring are exposed to alcohol before pregnancy is detected. These are just some of the reasons for why I felt it was important to examine the effects of moderate drinking at different times during pregnancy.”

Study subjects were rhesus monkey infants whose mothers consumed a moderate dose of alcohol either continuously or during the human equivalent of the first or last two trimesters of pregnancy. (Moderate drinking in humans is defined as seven to 14 drinks per week or one to two drinks per day.) Schneider explained that not only do primate studies allow greater generalization to humans than rodent studies because of similarly complex social and cognitive abilities and brain development, but they are also less complex than “real life.” Among humans, she said, alcohol consumption can be confounded with cigarette smoking, less-than-adequate prenatal care, stress and other drug use,” all of which can have negative effects on fetal development. In addition, researchers can use adapted human tests such as the Brazelton Newborn Assessment Scale to assess early neurobehavior in monkeys.

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“We found that early gestation alcohol exposure was related to noteworthy reductions in infant attention and motor maturity in rhesus monkeys,” said Schneider. “Yet there were no significant growth impairments. Thus, it appears that behavioral effects can be detected under circumstances in which growth was not affected. We also found that early exposure was as harmful as exposure throughout pregnancy in these monkeys. To the extent that these data generalize to humans, it suggests that subtle neurodevelopmental effects could be induced before pregnancy is detected.”

“There are at least four very important aspects to this research,” noted Joanne Weinberg, professor of anatomy at the University of British Columbia. “The primate model is very powerful in this case because it allows researchers to carry out sophisticated neurobehavioral tests, comparable to tests used in humans, to see what the effects of alcohol are. Another important aspect concerns the moderate levels of alcohol exposure. There are very few physical problems in these animals, you don’t see deficits in growth, and yet functionally they’re not normal. This finding probably has relevance for a more substantial percentage of the population. The third aspect is one of timing. I think it’s really critical to know when alcohol has its effects on fetal brain development because this gives us clues as to how and why these effects occur. Finally, the data from this study clearly separate early exposure from continuous exposure. This relates back to the advantages of animal research, where you can target drinking to specific times during pregnancy instead of asking people to self report on their drinking behavior.”

For Schneider, the study’s findings have a clear message. “Women of childbearing age should abstain from consuming alcohol if they are considering pregnancy,” she said.

Weinberg concurs. “We need to see more education for both the general public and physicians about the fact that alcohol can be harmful,” she said, “and that we really don’t know what a safe level of drinking during pregnancy would be. Although the public is now more aware of FAS, they know much less about the more subtle effects that alcohol can have on a developing fetus. Even some pediatricians and obstetricians are not very well informed about the effects of moderate levels of fetal alcohol exposure, although they may know about FAS. The bottom-line message is that, “if you’re pregnant or thinking of becoming pregnant, we don’t know what a safe level for drinking is and you’re better off not drinking at all.”

Article is based on the following published research:

PREGNANCY, DRUGS AND ALCOHOL, EMOTIONAL INSTABILITY: WHAT NIGHTMARES ARE MADE OF

- Psychopathology is the study of emotional, behavioral and psychological problems.
- Pregnant women with co-occurring alcohol and drug dependencies have a unique psychopathology.
- They have more symptoms of depression, anxiety, impulsivity, aggression and suspiciousness.
- Drug-dependent women who are also alcohol dependent have special treatment needs.

The majority of alcohol research to date has focused primarily on men, or on combined samples of men and women. Even fewer psychopathological studies – which examine emotional, behavioral and psychological problems – have focused exclusively on women with drug dependencies. Of those that have, the focus has been on single substances of abuse, such as cocaine. A study in the July issue of *Alcoholism: Clinical and Experimental Research (ACER)* examines the psychopathology of pregnant women with co-occurring alcohol and drug dependencies.

“Pregnant drug-dependent women present for treatment with a variety of medical, psychosocial and emotional problems,” said Donna R. Miles, postdoctoral fellow in the Department of Pharmacology and Toxicology at Virginia Commonwealth University and lead author of the study. “Rates of homelessness, poverty, unemployment and prostitution are high in this patient population. Many of these women have histories of emotional, physical and sexual abuse. Yet societal stigmatization typically prompts pregnant women to conceal substance use, which makes identification and intervention difficult. In fact, many alcohol- and drug abusing women avoid prenatal care altogether. Furthermore, in many states, delivery of a drug-positive infant results in legal sanctions that include termination of parental rights and criminal prosecution.”

“Pregnancy can have multiple effects on alcohol/drug-dependent women,” added Roy W. Pickens, associate vice president for research and professor of psychiatry at Virginia Commonwealth University. “On the one hand, concern about the effects of alcohol/drug use may cause a pregnant woman to be more willing to seek and complete treatment. On the other hand, pregnancy adds to the unfounded social stigma of being alcohol/drug dependent, which may keep a woman from entering treatment.”

In the study, the psychopathology of 170 pregnant women in treatment for drug dependency was measured using the Minnesota Multiphasic Personality Inventory-Revised (MMPI-2). The MMPI-2 uses 567 self-report items to measure different aspects of psychopathology, including depression, anxiety, impulsivity, aggression and suspiciousness. The majority of the women (79%) were drug dependent only; less than one quarter (21%) were both alcohol and drug dependent.

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“Our findings show that cocaine- and/or heroin-dependent pregnant women who also have problems with alcohol come into treatment with more psychological problems than those who don’t also have alcohol problems,” said Miles. “Specifically, they had more symptoms of depression and anxiety as well as problems controlling impulsivity and aggression. They were also more likely to misinterpret life experiences and react in atypical ways to their environment. These findings emphasize the need for universal screening for alcohol problems in drug-using pregnant women and, for those who screen positive, to make sure treatment is offered and tailored to meet their needs.”

“These findings illustrate that all drug-dependent individuals are not the same,” agreed Pickens. The study suggests that alcohol dependence, in particular, is a factor related to psychiatric/personality disorders in the drug dependent individual. This difference needs to be recognized by treatment providers, the individuals’ relatives and the general public.”

U.S. Department of Health and Human Services 1996 data reveal that 5.5 percent of women used illicit drugs during pregnancy, while 18.8 percent reported alcohol use during pregnancy. Pickens said a more recent study found that a similar proportion (5 to 6%) of women had used illicit drugs during pregnancy, while a greater proportion (25%) had used alcohol. Because research shows that alcohol use during pregnancy is the leading known cause of mental retardation, said Miles, its use should not be overlooked, even when women are using other drugs.

Prior to the creation of the Baltimore Center for Addiction and Pregnancy (CAP), where this research was conducted, less than five percent of pregnant drug abusing women followed through with an initial referral to standard drug treatment. (CAP uses what is considered an intensive approach: residential treatment followed by 6.5 hours per day of outpatient treatment for the duration of pregnancy.) Subsequent to CAP’s establishment, Miles estimated that approximately 50 percent of the pregnant, drug-dependent women referred to CAP actually followed through with the referral.

“The women seeking treatment at CAP have severe cocaine and/or opiate dependence as well as limited financial, family/social and medical resources,” said Miles. “They are also older women with several previous pregnancies.” Most of the women were also single (75%), African American (80%) and had a mean age of 29 years. “This kind of program is often so focused on illicit drug use,” Miles continued, “that alcohol problems often go undetected or receive less emphasis. Yet this study found that alcohol seems to be uniquely associated with greater psychopathology.”

Article is based on the following published research:

EXPLORING THE COMPLEXITIES OF PRENATAL ALCOHOL EXPOSURE

- Children prenatally exposed to alcohol demonstrate distinct deficits in social and adaptive behavior.
- Researchers have found that children in psychiatric treatment who were not prenatally exposed to alcohol have the same deficits.
- As prenatally exposed children age, however, their social difficulties become more pronounced.

Prenatal alcohol exposure is the leading cause of mental retardation of known origin in the industrialized world. Children prenatally exposed to alcohol are less likely to consider consequences to their actions, lack appropriate initiative, can be unresponsive to subtle social cues and often lack reciprocal friendships. They also have increased behavioral and learning difficulties during adolescence, and frequently exhibit hyperactivity, attention deficits and/or concentration difficulties. Similar deficits have been described in clinical samples of children who are in psychiatric treatment, but were not prenatally exposed to alcohol. A study in the July issue of Alcoholism: Clinical and Experimental Research (ACER) compares these two groups of children.

“Our study is the first to compare prenatally exposed children to clinically referred children with no prenatal exposure,” said Shannon E. Whaley, assistant research psychologist at the UCLA Neuropsychiatric Institute and lead author of the study. “Multiple studies have provided clear evidence that children prenatally exposed to alcohol show distinct social and adaptive behavior deficits as compared to normal children of the same age. If these deficits are unique to the prenatally exposed children, then they are important not only for the diagnosis of fetal alcohol syndrome (FAS) or the more common alcohol-related neurodevelopmental disorder (ARND), but also for the course of treatment. If, however, these behaviors are not unique to prenatally exposed children, they remain crucial for intervention but are less useful for specific diagnosis.”

The study found that the behavior deficits of the prenatally exposed children are not particularly different than those exhibited by children with other psychiatric difficulties. However, as prenatally exposed children become older, their difficulties with socialization skills in particular (making and keeping friends, understanding social cues, behaving appropriately in social situations) become more pronounced.

“It is vitally important to examine social and adaptive functioning among these children because any attempt to help them will be shaped by their problems,” said Marian Sigman, professor of psychiatry and psychology at UCLA School of Medicine. “If children exposed to alcohol prenatally are not getting along with others, adults need to find ways to help them with their social relationships. Adaptive functioning reflects a broader set of abilities, such as the capacity to take care of one’s basic needs and communication skills. The finding that the adaptive deficits were similar across both groups is important because it means that adap-

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EXPLORING THE COMPLEXITIES OF PRENATAL ALCOHOL EXPOSURE

tive deficits are not unique to children prenatally exposed to alcohol, but [instead] characterize children with a variety of problems. The fact that social deficits became more significant with age may mean that these children might have more serious social deficits when they are older. We need to understand what can be done to stop this developmental pattern.”

The study used the Vineland Adaptive Behavior Scales, a widely used measure of adaptive functioning, to test the children. Both groups demonstrated distinct difficulties across three domains of age-appropriate functioning: basic daily living skills, communication and socialization behavior. Daily living skills included tasks like helping to put things away, feeding and dressing one’s self completely without assistance, knowing the date, reading the clock and knowing the value of money. Communication skills included reading and writing, paying attention at school, articulating clearly and expressing ideas in more than one way. Socialization skills included making friends, following rules, initiating activity and carrying on socially appropriate play and conversation. Unlike previous studies, researchers found that none of the deficits in these three domains were attributable to deficits in intellectual functioning.

“In the early years,” summed up Whaley, “social deficits of prenatally exposed children are likely to look similar to those exhibited by other children referred for psychological/psychiatric treatment. In fact, the lack of differences in social and adaptive behavior exhibited by the two groups of children shows how easy it is for prenatally exposed children to ‘blend in’ to clinical settings.” Whaley said that during the critically important examination that doctors and clinicians make to determine potential contributors to social deficits, prenatal exposure is often missed and thus, not addressed.

“As prenatally exposed children become older,” she added, “their difficulties with social skills are likely to become more pronounced than those exhibited by clinically referred children who were not prenatally exposed. Thus, after about age six or seven, prenatally exposed children show more difficulty than clinically referred children with the social skills required of older children and early adolescents. This includes things like making and keeping friends, having a group of friends, responding appropriately to strangers, controlling hurt feelings when they don’t get what they want, initiating conversations, refraining from asking questions that might hurt or embarrass others and responding to hints or indirect cues in conversation. This is an interesting finding, and particularly important for intervention with these children.”

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**Article is based on the following published research:**

**DRINKING DURING PREGNANCY: INFORMATION MAY NOT BE ENOUGH**

- In most Western countries, the medical and official position on drinking during pregnancy has been to recommend abstention.
- A Danish study shows that few pregnant women actually discuss drinking with their medical advisors.
- A majority of the women considered some alcohol during pregnancy to be acceptable.

Numerous studies have clearly shown that heavy drinking during pregnancy is the largest preventable cause of birth defects and mental retardation in the United States. Among most Western countries, the medical and official position on drinking during pregnancy has been to recommend abstention. However, research has shown that information about the potentially harmful effects of drinking alcohol during pregnancy does not necessarily lead to knowledge of the issue, nor do information and knowledge necessarily affect a pregnant woman’s attitude toward drinking. A study in the October issue of *Alcoholism: Clinical and Experimental Research (ACER)* examines where a group of pregnant Danish women obtained their information about drinking during pregnancy, their knowledge of the subject and their attitudes toward it.

“Several studies have suggested that passive receipt of information may possibly – but not necessarily – influence awareness and knowledge, but not attitudes or behavior,” said Ulrik Kesmodel, associate professor of epidemiology and social medicine at the University of Aarhus and lead author of the study. “Yet it seems that many politicians and people working with public health believe that just more information will help people change their lifestyle. In reality, information is just one element in changing attitudes and behavior. Knowledge, previous experiences, social influences, current health habits and underlying possibilities of change are the key determinants of change in attitudes and motivation and, eventually, health habits. The current policy of informing each pregnant woman when she presents herself for prenatal care may affect her knowledge, at best, but none of the other elements are targeted.”

In Denmark, all pregnant women are offered and most take advantage of free prenatal care at centers run by midwives. For this 1998 study, researchers recruited and interviewed 439 pregnant, Danish-speaking women who were seeking prenatal care at 15 to 16 weeks of gestation. The women were asked about their sources and levels of information about drinking during pregnancy, their beliefs about and knowledge of drinking during pregnancy, as well as their attitudes toward drinking during pregnancy.

Only one third of the women had discussed drinking during pregnancy with their general practitioner (GP) or midwife. Most of their information was gleaned from the mass media (65%) and relatives (40%). A majority of the women (76%) considered some alcohol during pregnancy to be acceptable, mostly on a weekly level. However, 85 percent regarded binge drinking as harmful. The women’s attitudes toward drinking during pregnancy appeared to exist independent of their knowledge of the subject.

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“It is true that only one third said they had discussed alcohol in pregnancy with their GP or a midwife,” said Kesmodel, “however, some pregnant women had probably forgotten discussing this, so the figures are likely higher. Still, this number is quite low, and seems to suggest two things: first, that GPs and midwives could probably do more to get the message across, and second, that health authorities should not rely on this method alone of getting the message across.”

“The mass media is a powerful medium for providing information to the general public,” said Kesmodel, “including the families of pregnant women. In addition, we know that pregnant women judge the information they receive from health personnel according to information available from the media, education, friends and family. Furthermore, by targeting the media and family as sources of information, health authorities may also affect social influences on pregnant women, a key determinant of change in attitude.”

“We see many studies of risk factors,” said Jørn Olsen, professor and head of the Danish Epidemiology Science Centre at the University of Aarhus, “and too few studies of how we could best handle health promotion. We need to track what kinds of effects different health information strategies have.”

“What is the evidence,” he asked, “that alcohol consumption of a few drinks per month or even per week, as opposed to daily intake, may be harmful in pregnancy? If there is no consistent data to suggest that an occasional drink is harmful, it is possible that a large proportion of pregnant women and health personnel will not be convinced by repeated statements that total abstinence is necessary during pregnancy. Many obstetricians in the U.S. do not appear to believe that a few drinks per week in pregnancy does harm to the fetus. If health professionals cannot reach a consensus on the issue, how can we expect pregnant women to follow an official recommendation?”

Kesmodel said that it’s important to ask some tough, albeit unpopular, questions. “There are many women who drink small amounts of alcohol [during] pregnancy, and many of them seem to be told by doctors and midwives that an occasional drink is all right. If the only official recommendation is to not drink, [then] these women are not told that there is a limit, nor approximately what the limit is. So we need to ask the question: Where is the limit? Reaching a consensus on this would allow us to standardize information for these women.”

**Article is based on the following published research:**

DRINKING DURING PREGNANCY: AMERICAN INDIANS AND AFRICAN AMERICANS

- Most health campaigns recommend abstinence from alcohol during pregnancy.
- Some women nonetheless continue to drink at relatively high levels while pregnant.
- This study examines two groups considered most at-risk: American Indians and African Americans.

Public health campaigns that recommend abstinence from alcohol during pregnancy have been, for the most part, successful. There are, however, some women for whom the “Just Say No” approach to drinking during pregnancy does not resonate. In an effort to better understand this anomaly, a study in the August issue of Alcoholism: Clinical and Experimental Research (ACER) closely examined the exposure and response to health warnings among two groups considered most at-risk for Fetal Alcohol Syndrome (FAS): American Indians and African Americans.

“We wanted to look at how some women interpret the messages they’re receiving,” said Lee Ann Kaskutas, a research scientist with the Alcohol Research Group at Berkeley and author of the study. “We wanted to discover what misconceptions women might have about the risk of drinking during pregnancy, what drinking habits they might have during pregnancy, and we also wanted to look very carefully at their drink size.”

As many people are aware, heavy drinking during pregnancy can cause FAS, which is the largest preventable cause of birth defects and mental retardation in the United States. Lighter drinking during pregnancy can lead to Fetal Alcohol Effects (FAE), such as low birthweight, slower postnatal growth and even spontaneous abortion. The Centers for Disease Control and Prevention (CDC) has found that about 15 percent of women consume alcohol during their pregnancies, and 2.1 percent consume alcohol frequently. The CDC also found that both alcohol use and frequent use of alcohol during pregnancy – after a decrease in the early 1990s – has lately increased.

Kaskutas said that some estimates have placed the cost of treating just some of the FAS disorders that occur at more than $321 million per year. An alternative method of estimation is to look at the cost of taking care of mentally retarded people in one year (approximately $11.7 billion), multiplying that by 11 percent (believed to be due to FAS), for an amount that exceeds one and one quarter billion dollars per year. Some ethnic groups seem to be more at risk than others, and Kaskutas’ study looked at the two groups with the highest rates of FAS: American Indians (2.97 per 1,000 births) and African Americans (0.6). Other rates are as follows: Whites (0.09 per 1,000 births), Hispanics (0.08) and Asians (0.03).

“Health campaigns that are directed at pregnant women have had a long reach,” observed Kaskutas, “and most women are abstaining just like the messages have said to do. Most of these women have seen the warning label on alcohol containers, most have seen an advertisement about drinking while pregnant, more than half have seen a sign at a liquor store or

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restaurant, and the vast majority said they have had a conversation on the topic. Furthermore, all but 10 percent said that they understood and believed the messages.”

“Those women who continued to drink while pregnant,” explained Kaskutas, “were more likely to say that these messages made them feel negatively toward themselves. This can, in turn, contribute to a negative self-esteem spiral of drinking and lack of proper care.”

“Health campaigns may need to be part of a larger attempt to change social norms,” added Ernestine Vanderveen, director of the National Institute on Alcohol Abuse and Alcoholism’s Alcohol Research Centers Program, “such as consumption behavior that involves harmful substances like alcohol, nicotine and caffeine.” One of the obstacles that researchers and public health officials still face, she noted, is a basic lack of understanding of human behavior. “We still don’t fully know how one’s behavior relates to one’s state of health and well-being, nor do we really understand the difference between health-enhancing and health-compromising behaviors. “That’s why,” she continued, “we really don’t know a lot about women’s drinking.”

“This study has relevance because it attempts to get at information that is very difficult to extract,” Vanderveen said. “In general, we probably need more work in terms of finding out from real people what their behaviors are, and how those relate to their health and well-being.”

Kaskutas said, “When you consider the income of these women, then the higher rate for FAS that we see by ethnicity disappears. So some of this disease is about poverty.” Kaskutas said she chose to focus on urban women because most of the research on American Indians has been carried out on reservations, and the few studies on Black urban women have not included American Indian urban women.

“Fewer than one in five of these women realize that it helps to cut down any time during pregnancy; African Americans and heavier drinkers are the most likely to feel this way,” she continued. “We also found that some women think certain beverages are safer than others. ... In addition, the women who drank more often also tended to have larger drinks.”

Kaskutas continued, “Probably the two most important findings have to do with message content and determination of risk. We need to make it clear that it does help to cut down at any time during the pregnancy. We’ve also got to pay attention to drink size when we study drinking during pregnancy.”

Article is based on the following published research:

GENETIC PROTECTION AGAINST FETAL ALCOHOL SYNDROME?

- Fetal Alcohol Syndrome (FAS) may be influenced by genetic factors in both the mother and child.
- Allelic variations of the alcohol dehydrogenase (ADH2) gene influences alcohol metabolism.
- Researchers have found that the ADH2*2 allele is more common among the normal population than among FAS children and their mothers.
- The ADH2*2 allele may confer protection against and/or resistance to developing FAS.

Fetal Alcohol Syndrome (FAS) is the most common cause of preventable mental retardation among children in the world today. Scientists believe that the development of FAS following excessive alcohol exposure is likely influenced by genetic factors in both the mother and child. Mixed-ancestry children in the Western Cape Province of South Africa have the highest frequency of FAS in the world. Knowing that allelic variation influences alcohol metabolising genes, researchers in the December issue of Alcoholism: Clinical and Experimental Research (ACER) examine what role polymorphisms of the alcohol dehydrogenase (ADH2) gene might have among this population.

“The socioeconomically deprived mixed-ancestry population of the Western Cape has a prevalence of FAS amongst school-entry children of 40-70 per thousand,” explained Denis Lowe Viljoen, head of the Department of Human Genetics at the National Health Laboratory Service and University of the Witwatersrand Faculty of Health Sciences. Viljoen, also the study’s lead author, uses “mixed-ancestry” to refer to descendents of the original Khoisan inhabitants and colonizing Europeans. Some farm laborers in these communities have received part of their wages in the form of alcohol for close to 300 years.

“This prevalence contrasts,” he continued, “with approximately 0.33 - 2.2 per thousand for the United States, eight per thousand amongst birth cohorts for North American Indians between 1970-1980, and 2.29 per thousand for selected inner-city African Americans.”

“The incidence of FAS in the Western Cape is frighteningly high, particularly if one considers two factors,” said Amanda Krause, researcher and associate professor at the National Health Laboratory Service and University of the Witwatersrand Faculty of Health Sciences. “One, these are minimum estimates, looking at children who reached school entry. Some FAS children may never reach school entry because of major birth defects. Two, FAS is the tip of the iceberg. Thus, the number of school children with fetal alcohol effects is likely exceedingly high.” The term fetal alcohol effects (FAE) is used to describe individuals known to be exposed to alcohol before birth who have discernible health anomalies, yet do not have the facial features characteristic of FAS.

“There is some good scientific evidence to suggest that FAS, like virtually all diseases, has some genetic and some environmental influences,” said Krause. “There is a small amount of data pointing to the obvious candidate genes, that is, genes involved in the body’s handling of continued ~
alcohol.” ADH is one of two enzymes that act sequentially to metabolize alcohol in the liver. ADH converts alcohol to acetaldehyde. Aldehyde dehydrogenase (ALDH) subsequently converts acetaldehyde to acetate. Acetate is then metabolized by tissues outside of the liver.

“We evaluated all isozymes of the ADH2 gene following the findings of a previous study that demonstrated protection of the ADH2*3 allele against alcohol-related birth defects,” said Viljoen. “The latter allele was no different in the mothers and FAS children than in the ethnically similar control population in our study, nor was the ADH2*1 allele. However, there was a significant, protective difference between FAS children and the controls regarding the ADH2*2 allele.” Viljoen noted that the ADH2*2 allele, like the ADH2*3 allele, has a high “Vmax,” which results in a more rapid breakdown of alcohol to acetaldehyde than would occur with the ADH2*1 allele (which has a low Vmax).

“The inference is that the metabolism of alcohol by individuals from the control group would proceed more rapidly than in the mothers and FAS children, and result in lower blood alcohol levels than the latter subjects. Alternatively, the presence of such an allele may discourage the control persons from drinking as heavily as the latter subjects. However, this was not tested as the controls were anonymous participants.”

Krause calls the study’s findings “one piece in a large puzzle of undefined size, with many missing pieces. The exact factors or genes involved,” she said, “are still poorly understood. The individual role of each factor and how they interact with each other requires a great deal of future research.”

“This is the first study to find any connection between a gene and FAS,” said Viljoen. “Presumably, many genes are working in concert within each person to provide either susceptibility to or protection from the effects of alcohol. Should these ‘major’ genes be found, they would provide a means of screening at risk persons for having a child with FAS. Also, the pathogenesis of FAS could become clearer. This raises the real possibility of treating high-risk, alcohol abusing pregnant women, thereby reducing the risk of producing a baby with FAS.”

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Article is based on the following published research:

LIGHT TO MODERATE DRINKING DURING PREGNANCY CAN AFFECT ADOLESCENT GROWTH

- Children with Fetal Alcohol Syndrome (FAS) commonly have growth deficits.
- Growth deficits also exist among children prenatally exposed to alcohol but without FAS.
- Researchers have found significant growth deficits among non-FAS children 14 years after birth.
- The deficits have a dose-response relation to gestational exposure, and are evident at consumption levels less than one drink per day.

Growth deficits are common among children with Fetal Alcohol Syndrome (FAS), affecting their height, weight and head circumference. Growth deficits have also been found among offspring exposed to alcohol during gestation but who have not developed FAS. Studies have, however, differed in this finding. Furthermore, few studies have followed these offspring beyond their early and middle childhoods. A study in the October issue of *Alcoholism: Clinical and Experimental Research (ACER)* examines the effects of alcohol exposure during gestation on the size of non-FAS offspring at 14 years of age.

“*The Maternal Health Practices and Child Development (MHPCD) project began in 1982,*” said Nancy L. Day, professor of psychiatry and epidemiology at the University of Pittsburgh School of Medicine and lead author of the study. “*Its purpose has been to study the effects of prenatal exposure to alcohol, marijuana, tobacco and other illicit drugs on the growth and development of the offspring. At numerous intervals, we have measured demographic status; the psychological, social and household environment; maternal and paternal substance use and substance use of the male partner in the household. We have also assessed the children’s cognitive, behavioral, academic and physical status. Furthermore, at ages 10, 14 and 16, we have additional measures of the children’s pubertal maturity, neuropsychological status, cognitive and behavioral development, affect, academic performance, psychiatric status, delinquent behaviors, substance use and the substance use of their friends.*”

For this study, part of the MHPCD project, women in their fourth month of pregnancy were recruited from an outpatient prenatal clinic between May 1983 and July 1985. The women were interviewed in their fourth month of pregnancy (n=1360), seventh month and at delivery (n=763). The MHPCD project evaluated the women (or current caregiver) and their children at eight and 18 months, three, six, 10 and 14 years of age. Data for this study were gathered when the children (n=565) were 14 years of age.

“This study population represents a light to moderately exposed group of children and is in contrast to most studies that have recruited only heavily exposed subjects,” said Day. “*The former group, however, represents the most common pattern of alcohol and other substance use during pregnancy.*”

Despite only light to moderate exposure, researchers identified significant growth deficits among the offspring. The adolescents were smaller in terms of their weight, height, head circum-

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Light to Moderate Drinking During Pregnancy Can Affect Adolescent Growth

The growth deficits had a dose-response relation to gestational exposure and, furthermore, significant effects were found at consumption levels less than one drink per day. The researchers also evaluated the effects of pattern of use. They found that growth was affected by a continuous exposure to alcohol and not by concentrated or binge drinking. The frequency of heavy or binge drinking (drinking four or more drinks/occasion) did not predict growth.

“It is notable that growth effects of prenatal alcohol can be detected in children more than 14 years after exposure,” said Sandra W. Jacobson, professor in the Department of Psychiatry and Behavioral Neurosciences at Wayne State University School of Medicine. “Moreover, the deficits were related to low-level alcohol exposure and a dichotomous measure of binge drinking during the first trimester, and were not found only among heavy drinkers or women who were alcoholic. The finding that growth effects can be related to first trimester drinking has very important implications for prevention and the need to identify women at risk earlier. Although the relatively small effects on head circumference and growth found at these low levels of exposure are unlikely to have any functional significance for the child, they suggest that there apparently was damage to the brain, particularly during sensitive fetal and early infant developmental periods. This damage may have serious implications for later cognitive and behavioral development.”

“In a dose-response relation, there is a direct association between the amount of exposure and the size of the effect. Those with a small exposure will have very small growth deficits; those with a large exposure will have much larger growth deficits. Exposure below the critical level will not have an effect, but exposure at or above that level will lead to the growth deficit. Our results have shown that the association between prenatal alcohol exposure and growth is one of dose-response. This is important for clinical and public health reasons because it means that even very small levels of alcohol exposure can affect the developing fetus. This means that there is no safe level for alcohol use during pregnancy. Women should abstain during these important months,” said Day.

Jacobson concurs. “However,” she said, “it is important to note that, although frequency of binge drinking was not statistically associated with reduced growth, the investigators reported that a dichotomous measure of bingeing was. Based on animal evidence, it is possible that these low level alcohol-related deficits may reflect maternal drinking on only a few days per week rather than drinking at very low levels every day.”

**Article is based on the following published research:**

LIGHT TO MODERATE DRINKING DURING PREGNANCY MAY LEAD TO LEARNING AND MEMORY DEFICITS IN ADOLESCENTS

- Heavy drinking during pregnancy can cause major impairments in the developing child.
- New research indicates that light to moderate drinking may also interfere with learning and memory as late as adolescence, particularly in the auditory/verbal domain.
- Most of the drinking in this study occurred during the first trimester.

Many people know about the dangers of prenatal alcohol exposure, particularly the damaging effects that heavy drinking can cause to a child’s cognitive development. A study published in the March issue of *Alcoholism: Clinical and Experimental Research (ACER)* has found that even light to moderate drinking during pregnancy may interfere with learning and memory during adolescence.

“We have known for a long time that drinking heavily during pregnancy could lead to major impairments in growth, behavior and cognitive function in children,” said Jennifer Willford, assistant professor of psychiatry at the University of Pittsburgh School of Medicine and the study’s first author. “This paper clearly shows that even small amounts of alcohol during pregnancy can have a significant impact on child development.”

“Learning and memory are cornerstones for success in school and in everyday life,” added Sarah Mattson, assistant professor in the Department of Psychology, and associate director of the Center for Behavioral Teratology at San Diego State University. “Disruption of the ability to learn and remember new information jeopardizes the job of children, that is, to go to school. The inability to learn new information in the verbal or nonverbal domain will interfere with a child’s ability to achieve alongside his or her peers.”

The data examined in this study were collected as part of the Maternal Health Practices and Child Development Project (MHPCD), an ongoing longitudinal study of 580 children and their mothers. The MHPCD examines the effects of prenatal exposure to alcohol, marijuana, tobacco and other illicit drugs on the growth, behavioral and cognitive development of the offspring. Researchers measure demographic status, maternal psychosocial characteristics, household environment and substance use at numerous intervals. They also assess the children’s growth, and behavioral, neuropsychological and academic status from birth onward.

For this study, mothers were assessed during each trimester of their pregnancies, and again with their children at regular intervals from birth to 16 years of age. Adolescent memory function was evaluated at 14 years of age (n=569) using the Children’s Memory Scale, an assessment tool that measures learning and immediate and delayed memory function in the verbal and visual-spatial domains.

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LIGHT TO MODERATE DRINKING DURING PREGNANCY MAY LEAD TO LEARNING AND MEMORY DEFICITS IN ADOLESCENTS

“We chose measures that would help us understand the types of learning and memory difficulties experienced by adolescents who were prenatally exposed to alcohol,” explained Willford. “We assessed verbal/auditory and visual/spatial abilities because each of us learns through a combination of verbal and nonverbal abilities. We also examined learning and memory to determine whether subjects were having difficulty with initial learning, remembering information for a short time or after a long period of time.”

“During the first trimester,” said Willford, “45 percent of the women drank, on average, less than one drink per day.” Despite these relatively low levels of alcohol consumption, researchers found an association with subtle difficulties with learning and memory in the offspring at 14 years of age, specifically in the auditory/verbal domain. “This indicates that drinking during the first trimester of pregnancy ... has long-term effects on development. Many women do not realize they are pregnant and/or seek prenatal care during this critical time,” said Willford.

“These types of deficits have already been demonstrated in studies with much higher levels of exposure,” added Mattson, “and thus, these data extend the continuum of effect to include lower levels of exposure. Another important finding is that the effects of alcohol exposure on memory for verbal information were mediated by verbal learning, a finding that has also been documented following higher levels of exposure. This finding is relatively novel in the field and thus the replication in a lower exposed sample suggests that this effect is specific to alcohol exposure.”

Yet another finding concerns growth deficits among those children exposed to light to moderate drinking during gestation. “These findings parallel earlier reports of continued growth deficits among those children exposed to light to moderate drinking during their mothers’ pregnancy,” said Willford. “This shows us that prenatal alcohol exposure can lead to deficits in multiple domains.”

“There is no safe level of drinking during pregnancy and there is no safe time to drink during pregnancy,” said Willford. “Women need this information before pregnancy recognition and their first visit to an obstetrician so that they may make better choices about drinking if they are planning to become, or think that they may be, pregnant.”

Article is based on the following published research:

**The Power of the Mother-Child Bond**

- An infant is extraordinarily sensitive to its mother’s behavior.
- Baby rats nursed by their intoxicated mothers exhibit greater overall distress and aversion to alcohol.
- The infants’ distress and aversion seem dependent on maternal reaction to alcohol.
- Alcohol’s effects on maternal behavior may have long-lasting consequences for the infant.

It’s no secret that a baby’s survival, under normal circumstances, is dependent on the mother’s behavior. Nourishment, appropriate body temperature, protection from harm—these are the basics. Yet researchers are also beginning to determine, as shown in a study in the April issue of *Alcoholism: Clinical and Experimental Research (ACER)*, that a mother’s behavior, altered by alcohol, can have powerful and enduring effects on her infant’s subsequent memories.

“Infants are exquisitely sensitive to maternal behavior,” said Norman E. Spear, distinguished professor of psychology at Binghamton University and one of the study’s lead authors. “If the mother’s behavior deviates just a little bit from the norm, the infants notice and it’s not a pleasant experience for them.”

“Specific memories may be generated in relation to alcohol,” added Juan Carlos Molina, co-author, professor of psychology at the University of Cordoba, and senior research scientist at the Instituto de Investigacion Medica Mercedes y Martin Ferreyra in Argentina.

In the study, baby rats were nursed by intoxicated mother rats. When compared with baby rats that nursed from alcohol-free mothers, the alcohol-exposed pups later demonstrated higher ultrasonic vocalizations (a traditional distress signal), greater motor activity during isolation (which is what rats do when they’re disturbed), and aversion to a texture (sandpaper) that had been matched through smell with alcohol. Spear believes that the mother’s alcohol-altered behavior, rather than the pup’s reaction to the alcohol itself, is what caused their distress and related behavior.

“The effects of the alcohol on the mother’s behavior are very subtle,” he explained, “but enough to make the experience aversive for the rat pup. There are some aspects of maternal behavior that are poorer in mother rats that have had alcohol. For example, retrieval behavior—when a mother retrieves a baby rat that has wandered away from the nest—is inhibited by alcohol. Another effect of alcohol on the mother is a decrease in body temperature; it may be a drop of only one and a half degrees centigrade, but the pups may detect the difference in warmth.”

“The animal model and the human literature are telling a similar story,” said Julie A. Mennella, biopsychologist at Monell Chemical Senses Center. “Memories are not only formed as a result of early sensory experiences with alcohol in the context of the mother, but they’re also retained for a considerable time span. This study is telling us that the presence of alcohol odor is capable of supporting some type of conditioning, such as aversion, when it’s paired with a new stimulus, such as sandpaper.”

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The Power of the Mother-Child Bond

Mennella said that Spear and Molina’s study is part of a growing body of research that speaks to the relevance of early learning. “Other research has shown that elementary-school-aged children of alcoholics were more likely to report more negative experiences about alcohol than children from non-alcoholic homes,” she said. “Some of the early learning about alcohol appears to be based on sensory experience and the context in which alcohol is experienced.” Indeed, Mennella believes this study speaks to the power of odor associations.

“Odors are often thought to provide us with the best memory cues,” she said. “Some of our oldest and most emotionally laden memories are associated with odors.” Mennella described a study conducted at her institution in which children were asked to complete a difficult task in a room that was scented with a particular odor. None of the children completed the difficult task. Shortly afterwards, the children were divided into three groups, all were given the same simple task to complete, but each were placed in three different rooms with different odors.

The group of children located in the room scented with the same odor as the room of the preceding difficult task performed worse that the other two groups. Mennella said that exposing rat pups to a sandpaper texture and children to a difficult task could both be classified as “arousing, emotionally salient” situations. The emotional context in which children or infants experience an odor can influence their subsequent behaviors, likes, dislikes and conditioning to alcohol.

A related area of study is what Mennella calls the “folklore” of alcohol consumption by lactating women. This refers to beliefs, brought to America by various immigrant groups, that alcohol consumption might increase milk production, facilitate milk release, relax the mother, increase the infant’s milk intake and/or help the baby sleep. Yet apart from possibly helping the mother relax, said Mennella, “there’s no scientific evidence that supports the folklore, in fact, it’s the opposite.”

“Some doctors today still recommend drinking before nursing,” observed Spear, “but there is still so much that is unknown. In addition, there are a lot more days during a human infant’s nursing period (up to two or three years) than a baby rat’s (21 days). Perhaps there is a cumulative effect.”

“The most important contribution about our study,” he said, “is simply to indicate that breastfeeding potentially represents a source of generating alcohol-related memories.” He nonetheless noted that cumulative studies “emphasize the need to avoid alcohol exposure during prenatal, neonatal and early postnatal periods of development.”

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Article is based on the following published research:

A recent study has found that the absence of a parent as role model can be stressful for infants.

Concentrations of cortisol, a principal stress hormone, can indicate levels of stress.

Cortisol may serve as an early biological marker of future alcohol consumption.

Adult absence during infancy has long-term psychobiological consequences.

A study in the May issue of Alcoholism: Clinical and Experimental Research (ACER) has found a link among the rearing environment (how a child is raised), sensitivity to stress and subsequent alcohol consumption. “It’s pretty clear that parents are the crucial role models and crucial shapers of their offspring’s behavior,” said J. Dee Higley, research psychologist at the National Institute of Child Health and Human Development and lab director of the experiment. “Adults are very good at helping youngsters to understand that ‘this is dangerous, this is not dangerous.’ In the absence of that kind of adult influence, children don’t have any kind of certainty about what to fear or enjoy, what is good or bad. Adults are also very good at cueing into whether their offspring are aroused or anxious, and then helping them to calm themselves down.”

Higley’s study looked at rhesus monkeys, which share between 90 to 95 percent of their genetic material with humans. These monkeys also have a similar adrenal system which, for the purposes of this study, means that they respond to stress like humans do. In addition, primates have very complex societies; they create social groups, they have rules about social behavior and they are (under normal circumstances) trained from youth to learn and use appropriate social skills. The monkeys used in this study were part of an ongoing longitudinal study investigating genetic and environmental influences on neurobiology, behavior and alcohol consumption.

The monkeys were divided into two groups for the first six months of their lives. The first group was “peer-reared,” meaning that group members were raised without the presence of their mothers or other adults, but surrounded by same-aged peers. Members of the second group were raised normally, in the presence of their mothers. At six months of age, all of the monkeys were separated from their groups for portions of a four-week period. Stress levels were assessed during this time by examining concentrations of cortisol, a principal stress hormone. At 50 months of age (roughly equivalent to young adulthood), the monkeys were allowed access to alcohol for five to seven weeks.

“This study very clearly showed that early life experiences can have a dramatic effect on subsequent development of alcohol consumption,” noted Larissa A. Pohorecky, professor of neuropharmacology at the Center of Alcohol Studies at Rutgers University. “It helps elucidate the mechanisms involved in stress/alcohol interaction.” She added that most of the other alcohol research, including her own, has focused on rodents. “So these are particularly important findings because these primates are the closest animal species to humans,” she said.

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The study found that infant monkeys from both groups, peer-reared and mother-reared, were stressed by their separation from the group (as evidenced by cortisol concentrations), although the peer-reared monkeys more so. In addition, those infant monkeys (from both groups) who were highly stressed as a result of their group separation, later consumed more alcohol (as young adults) than their less-stressed peers did.

“We may have found a biological marker,” he said, “which can be obtained very early in life and may predict future alcohol consumption. This is probably the strongest marker we’ve found so far in the non-human primate that predicts alcohol consumption.” He added that, “to the extent that this can be generalized to humans, we may have identified a biological predictor of future alcohol problems.” Higley said another implication is that “early-rearing experiences that increase anxiety – as measured by cortisol output – also increase subsequent alcohol consumption.”

In this experiment, separation from the group was what induced stress, but the monkeys’ peer-rearing environment may have ‘set them up’ for experiencing a greater level of stress. “The peer-reared monkeys had all the opportunities to socialize that mother-reared monkeys did – they could play with other-aged mates, form strong friendships, they could even fight, they could do all sorts of socially appropriate and inappropriate things – but what was lacking in their environment was an adult,” explained Higley. “These monkeys showed emotional instability, they were more fearful, they were much more reactive to the stimuli around them, and they did not have an adult around to calm them down. So what you have is a monkey who is chronically anxious and chronically fearful.”

Adult absence during infancy appears to have had other long-term psychobiological consequences, noted Higley. “As young teenagers, the peer-reared monkeys still showed infant-like fearfulness and anxiety that was absent in the mother-reared monkeys.” Indeed, other studies have found that prolonged stress in infancy (and a peer-rearing environment among monkeys is regarded as a stressor) may permanently alter the hormonal stress response and subsequent reactions to new stressors.

“These findings speak to the importance of how society handles children who have problems, families with parenting problems, general parenting issues and orphans to name a few,” she said. “We may not be paying enough attention to the importance of parenting roles and how they can affect children’s lives,” said Pohorecky.

**Article is based on the following published research:**