

Interventions might offer a pregnant pause in addiction

Doctors have known for decades that cigarettes and alcohol harm developing babies. Now, because many pregnant women find it difficult to beat these addictions, research has begun looking for ways to minimize their damage to the fetus.

For instance, although governments recommend that pregnant women stop smoking, they don't usually recommend nicotine replacement therapy (NRT), owing to a lack of research on its safety and efficacy in pregnant women. Meanwhile, despite decades of warnings that smoking causes problems such as stillbirths and miscarriage, many pregnant smokers don't quit—17% of women smoke throughout pregnancy in Britain, for instance.

Preliminary studies have offered both good and bad news about nicotine replacement therapy in pregnant smokers. In 2000, a Danish group published the only large placebo-controlled trial on NRT to date in 250 women (*Obstet. Gynecol.* **96**, 967–971; 2000). Although NRT didn't help women stop smoking, the trial found that NRT users gave birth to heavier infants than those who did not receive the nicotine therapy.

Clouding the picture, a 2006 observational study found an elevated risk of birth defects due to NRT. But other studies have contradicted those results (*Obstet. Gynecol.* **107**, 51–57; 2006). And a study published in August found that pregnant women receiving NRT did not have higher rates of stillbirth than smokers who did not use NRT (*BJOG* **115**, 1405–1410; 2008). The study also found that women who used NRT had lower rates of stillbirth than those who smoked and did not use NRT, but the trend didn't reach statistical significance.

According to Tim Coleman of the University of Nottingham, the evidence so far suggests that NRT is safer than smoking for the fetus. But he adds that the picture remains incomplete. "It may well be safe to use nicotine to keep you away from cigarettes, because once you light a cigarette you expose yourself to all other sorts of horrible things," says Coleman, who is now recruiting 1,050 pregnant women for a placebo-controlled NRT trial sponsored by the UK's National Institute for Health Research Health Technology Assessment Programme. Meanwhile, a study published in September hinted that exercise might help women quit smoking during pregnancy (*BMC*

Public Health, doi:10.1186/1471-2458-8-328; 2008).

Alcohol has more wide-ranging effects on the fetus than tobacco. Drinking during pregnancy can result in fetal alcohol spectrum disorders, defined by symptoms including physical, cognitive and behavioral effects. Researchers reported this fall that a preliminary study found an association between heavy drinking in the first trimester of pregnancy and delivering a child with cleft lip (*Am. J. Epidemiol.* **168**, 638–646; 2008). And alcohol abuse in pregnancy is widespread—it is the top cause of preventable mental retardation in the US, for instance.

Over the past decade, researchers have been developing strategies for blocking alcohol's damage. Among the most promising has been the use of a nutrient called choline, found in foods such as eggs, nuts and liver and recently recognized as essential to normal brain development.

Neuroscientist Jennifer Thomas at San Diego State University in California has found that if given at the same time as alcohol to pregnant rats, choline lessens the learning deficits of their offspring (*Neurotoxicol. Teratol.* **22**, 703–711; 2000). More intriguingly, if given to baby rats during the brain development stage that corresponds to that seen in human infants and young children, choline still ameliorates hyperactivity and spatial learning deficits (*Behav. Neurosci.* **121**, 120–130; 2007). Thomas is not sure how choline works to ameliorate these deficits; the nutrient is a precursor to numerous molecules, including neurotransmitters, cell membrane components and signaling factors. But knowing the mechanism may not be essential, as choline is a nutrient, not a drug, and may therefore be less risky.

Moreover, the fact that choline might help after birth is seen as a huge plus, as many pregnant women don't disclose their drinking, making it unlikely that they can be treated during pregnancy.

Still, Thomas has already begun a study to look at the effects of supplementing pregnant women's diets with choline. Scientists have high hopes for the strategy: "It's one of the most promising approaches," says Kenneth Warren, acting director of the US National Institute on Alcohol Abuse and Alcoholism in Bethesda, Maryland. Warren, Thomas and others stress that women should, of course, try not to drink at all during pregnancy. But if they cannot, Thomas hopes her work may one day spare their children from this drug's devastating effects.

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Smoking for two: Several recent studies have looked at whether nicotine replacement might help