Physician Bulletin:

Smoking & Fertility

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Most patients are aware of the general health risks of smoking, the risks of smoking in pregnancy, and most smokers consider smoking cessation once pregnant. However, fewer patients understand the effect of smoking on their fertility.

Based on their meta-analysis, Augood et al.\(^1\), estimated that up to 13% of infertility may be related to smoking. Their meta-analysis of 12 studies compared 10,928 smoking women with 19,128 non-smoking women and calculated an odds ratio (OR) of 1.60 [95% confidence interval (CI) 1.34–1.91] for risk of infertility in women smokers versus non-smokers. They also looked at the effect of smoking on IVF specifically, and in a meta-analysis of 9 studies, they found an OR of 0.66 (95% CI 0.49–0.88) for pregnancies per IVF cycle in smokers versus non-smokers.

It appears that menopause occurs 1 to 4 years earlier in smoking women compared to non-smoking women\(^2\) and so it may be that smoking accelerates the rate of follicular depletion. Studies show that basal FSH\(^3\) levels are higher and AMH\(^4\) levels are lower in active smokers compared to non-smokers. Both of these are markers of ovarian reserve. Studies also show higher miscarriage rates in smokers.\(^1\) This may be related to the mutagenic effects of cigarette smoke\(^5\) or it may be related to the known vasoconstrictive and antimetabolic properties of some components of cigarette smoke. These substances, such as nicotine, carbon monoxide, and cyanide, may lead to placental insufficiency and embryonic and fetal growth restriction and demise.

The effect on male fertility is less clear. While sperm concentrations, motility, and morphology often are reduced in smokers compared to non-smokers, they often remain within the normal range.

Getting patients to quit is challenging and can be time resource intensive. However, when patients are considering their fertility this may be a time when they can be more motivated to quit once they understand the impact of smoking on their fertility. A Family planning study did show a return to normal fecundity in those who quit and so this is encouraging.\(^6\) Fertility treatment can become expensive and so patients may also be economically incentivized to quit if they understand that treatments are more likely to succeed if they quit. Smokers are likely to require twice the IVF attempts as non-smokers to be successful.\(^6\) A five-step approach to aid in smoking cessation is recommended: 1) Ask about smoking at every opportunity; 2) Advise all smokers to stop; 3) Assess willingness to stop; 4) Assist patients in stopping (including the use of pharmaceuticals and carbon monoxide monitoring); and 5) Arrange follow-up visits. Medical adjunctive therapy for smoking cessation has not been studied extensively in infertile women. A Cochrane review\(^7\) of smoking cessation treatments in pregnant patients showed that nicotine replacement therapy (NRT) was not effect in placebo RCTs but was shown
to be effective in non-placebo RCTs. The usefulness is therefore not clear and more study is required. Bupropion has not been well studied in infertility or pregnant patients. Bupropion is a category B drug while Nicotine gum carries a category C classification and the nicotine patch is a category D agent.

The likelihood of achieving smoking cessation appears to increase with each attempt and so patients need to be encouraged to keep trying. Hopefully, by understanding the effects of smoking on fertility, patients can be further motivated to quit smoking.