



Harmful effects of smoking in pregnancy

Exposure of the fetus to cigarette smoke is an important, dose-related and preventable risk factor in the quest for optimal pregnancy outcome. It is therefore essential that all health care workers and mothers are fully aware of these adverse effects.

Nicotine, the dominant alkaloid in tobacco smoke, easily crosses the placenta, leading to fetal plasma concentrations on average 15% higher than those of the mother.¹ Nicotine also concentrates in placental tissue, amniotic fluid and breast-milk. Amniotic nicotine levels in the mid-trimester are up to 54% higher than those in maternal serum. The swallowing of amniotic fluid therefore increases fetal intake of nicotine. The consequence is that fetuses of mothers who smoke are exposed to relatively higher levels of nicotine than their mothers. Further risks are added neonatally by maternal smoking during lactation as the plasma/breast-milk nicotine ratio is 2.9:1. Therefore, it is not surprising that nicotine has extensive effects on: (i) maternal and fetal cardiovascular systems; (ii) uterine, umbilical and cerebral blood flow; (iii) the developing cerebral cortex; (iv) developing respiratory epithelium; and (v) fetal growth.

The adverse effect of nicotine is through its vasoconstrictive effects on the uterine and potentially also on the umbilical artery.¹ It is of great concern that nicotine can activate nicotine receptors in the fetal brain as this may affect brain development and smoking patterns later in life.²

As we know today, the endothelium plays a much greater role in health and disease than was ever thought to be the case 10 years ago. It has been shown that the free radical components of cigarette smoke cause much of the damage.³ Even passive smoking is associated with abnormal endothelial function.⁴ The risk of passive smoking is comparable with that of a light smoker in pregnancy.¹

As far as the specific effect on the endothelium is concerned, it seems that smoking during pregnancy is associated with reduced cellular fibronectin and increased intracellular adhesion molecule-1.⁵ In addition, it has been found that cigarette smoking is associated with increased circulating levels of lipid peroxidation products, which may contribute to endothelial damage.

Carbon monoxide in cigarette smoke inhibits release of oxygen to fetal tissues by creating carboxyhaemoglobin, which induces relative tissue hypoxia.⁶ Microscopic examination of placental tissue of smokers reveals thickening of the trophoblastic membrane, hypertrophy and calcifications — evidence of the response to hypoxia.⁷ At microvascular level, delayed neutrophil transit has been described, which gives rise to structural lung damage because of accumulation of cells in the interstitium and bronchialveolar spaces. Lackman *et al.*⁸ showed transplacental fetal exposure to two tobacco-specific carcinogens, isolated from the urine of *in utero* exposed neonates. The effects of the other components of cigarette smoke, e.g. hydrogen

cyanide, thiocyanates and hydrocarbons, will not be addressed here.

The harmful effects of fetal nicotine exposure are evident in all trimesters of pregnancy.¹ In the first trimester there is a 33% increase in incidence of spontaneous abortion. In the second trimester there is a dose-dependent increase in preterm labour and prematurity,⁸ and in the third trimester a doubled risk of low birth weight.

In their five meta-analyses of the adverse effects of maternal smoking, Castles *et al.*⁹ found a statistically significant increase in the risks of abruptio placentae, placenta praevia, ectopic pregnancy and preterm prelabour rupture of membranes. In addition, maternal cigarette smoking has also been implied in the aetiology of congenital defects, e.g. cleft lips and palates,¹⁰ neural tube defects, congenital cardiac defects, limb reduction defects⁶ and anencephaly.¹ Furthermore, smoking is associated with an increase in childhood malignancies, including brain tumours, leukaemia and lymphoma.¹¹

The complications associated with maternal cigarette smoking during the neonatal period include doubling the risk of sudden infant death syndrome (SIDS)¹² and restriction of pulmonary maturation, leading to increased incidence of asthma and upper respiratory infections in children.¹ Follow-up of children who suffered *in utero* cigarette smoke exposure showed negative long-term cognitive outcomes, including behavioural disorders, cognitive impairment relating to linguistic skills and comprehension.¹ Physical manifestations include decreased head circumference in comparison to smoke-free controls.

According to a recent study conducted at Tygerberg Hospital,¹³ 39% of pregnant women smoked (in contrast to the 22% of pregnant women in a developed country such as the USA¹⁴). The 1995 South African national survey found an increase in the general smoking population of 1% per annum.¹⁵ The rate of increase was noted to be highest among the coloured population. Smoking prevalence in the coloured population (59%) is notably higher than among Indians (36%), whites (35%) and blacks (31%). It is of great concern that in an era of preventive medicine the smoking population in South Africa is growing, escalating the adverse effects pointed out in the text.

Decreasing the prevalence and initiation of smoking in pregnancy would be the most effective method of reducing the adverse effects of smoking in pregnancy,⁷ in this way directly improving perinatal outcome.

Elbie Viljoen

Department of Obstetrics and Gynaecology
Stellenbosch University
Tygerberg, W Cape

Corresponding author: E Viljoen (jevill123@yahoo.co.uk)



EDITORIAL

1. Lambers DS, Clark KE. The maternal and fetal physiological effects of nicotine. *Semin Perinatol* 1996; **20**: 115-126.
2. Hellstrom-Lindahl E, Nordberg A. Smoking during pregnancy: a way to transfer addiction to the next generation? *Respiration* 2002; **69**: 289-293.
3. Pittilo MR. Cigarette smoking, endothelial injury and cardiovascular disease. *Int J Exp Pathol* 2000; **81**: 219-230.
4. Puranik R, Celermajer DS. Smoking and endothelial function. *Prog Cardiovasc Dis* 2003; **45**: 443-458.
5. Lain KY, Wilson JW, Crombleholme WR, Ness RB, Roberts JM. Smoking during pregnancy is associated with alterations in markers of endothelial function. *Am J Obstet Gynecol* 2003; **189**: 1196-1201.
6. Salafia C, Shiverick K. Cigarette smoking and pregnancy II: Vascular effects. *Placenta* 1999; **20**: 273-279.
7. Ashmead GG. Smoking and pregnancy. *J Matern Fetal Neonatal Med* 2003; **14**: 297-304.
8. Lackmann GH, Salzberger U, Tollner U, Chen M, Camella SG, Hecht SS. Metabolites of a tobacco specific carcinogen in the urine of newborns. *J Natl Cancer Inst* 1999; **91**: 459-465.
9. Castles A, Adams EA, Melvin CL, Kelsch C, Boulton ML. Effects of smoking in pregnancy. *Am J Prev Med* 1999; **16**: 208-215.
10. Wyzynski DF, Duffy DL, Beaty TH. Maternal cigarette smoking and oral clefts: a meta analysis. *Cleft Palate Craniofac J* 1997; **34**: 206-211.
11. Sasco AJ, Vainio H. From in utero exposure to parental smoking to childhood cancer: a possible link and need for action. *Hum Exp Toxicol* 1999; **18**: 192-201.
12. Anderson H, Cook DG. Passive smoking and sudden infant death syndrome: review of the epidemiological evidence. *Thorax* 1997; **52**: 1003-1009.
13. Odendaal HJ, Van Schie DL, De Jeu RM. Adverse effects of cigarette smoking on preterm labour and abruptio placentae. *Int J Gynaecol Obstet* 2001; **74**: 287-288.
14. Surgeon General's Report on Women and Smoking: Marketing Cigarettes to Women. www.cdc.gov/tobacco/sgr_forwomen/index.htm (2001).
15. Steyn K, Yach D, Stander I, Fourie JM. Smoking in urban pregnant women in South Africa. *S Afr Med J* 1997; **87**: 460-463.