Chapter 10

PASSIVE SMOKING: ASSESSING THE HEALTH IMPACT ON CHILDREN

H. Moshammer[1], K. Polanska[2], W. Hanke[2,3] and M. Neuberger[1]

[1] Institute for Environmental Health, ZPH, Medical University of Vienna, Austria
[2] Nofer Institute of Occupational Medicine, Lodz, Poland
[3] Statistics Medical University, Lodz, Poland

ABSTRACT

Almost half of the child population is involuntarily exposed to environmental tobacco smoke (ETS). The problem starts before conception since active smoking reduces the sperm count and fertility. The fetus is affected if the pregnant woman is passively exposed to tobacco smoke but even more so if she herself smokes cigarettes. The infant and toddler cannot actively prevent his or her exposure and even school-age children are usually powerless against smoking adults. In adolescence active smoking is often perceived as a sort of initiation rite. Discos and other meeting places of youngsters range highest in nicotine concentrations. Numerous health effects of all these various exposures are well established. This paper sets out to summarize existing exposure data (focusing mainly on European studies) and established exposure-effect estimates. This allows to calculate attributable risks for low birth weight, respiratory illness, middle ear diseases and mortality.

Per 1000 live births in Europe there are to be expected approximately 5 births with low birth weight at term, intrauterine growth restriction, and preterm delivery due to smoking in pregnancy each. The attributable number of cases of stillbirth and sudden infants' death syndrome are about one magnitude lower.

Odds Ratios of children's diseases associated with passive smoking (ETS exposure) by their mothers are substantially lower. But since the number of exposed pregnancies are higher the number of attributable cases is in the same order of magnitude as for active smoking in pregnancy.

Postnatal exposure of children to parental smoking causes approximately 10% of respiratory and middle ear diseases.

INTRODUCTION

This paper sets out to assess the health impact of passive smoking (environmental tobacco smoke, ETS) on children. "Child" in this paper considers exposure from pre-conception till adolescence but concentrates on in utero and early life exposure. Environmental tobacco smoke (ETS) also known as Second Hand Tobacco Smoke (SHTS) refers to the mixture of exhaled smoke and smoke coming from the burning tip of the cigarettes, cigars and pipes. It is composed of over 4000 different chemical compounds and over 40 known carcinogens.

Smoking affects the non-smoking child even before conception as male smokers display a significant increase in sperm disomy [Robbins et al., 2005] and semen volume [Pasqualotto et al., 2006]. The smokers' seminal plasma causes oxidative damage in spermatozoa [Arabi and Moshtaghi, 2005], and smoking can cause erectile dysfunction [Peate, 2005]. Even worse the prenatal (passive) exposure to tobacco smoke reduces the sperm counts later in life [Jensen et al., 2005; Jensen et al., 2004]. But equally harmful to reproductive health is active and passive smoking by pregnant women [Windham et al., 2005; Barbieri et al., 2005; Wilks and Hay, 2004; Neal et al., 2005; Talbot and Riveles, 2005].

This paper will concentrate on the health effects of passive smoking on children starting with exposure during the prenatal period and continuing with the exposure after birth. In adolescents many effects get less visible because as youngsters grow up they also become more mobile so that misclassification of exposure increases. The own smoking behavior of the adolescents is influenced by role models in their family and in addition by the addictive influences of exposure during pregnancy [Buka et al., 2003], possibly by very early modification of cholinergic receptors in the developing brain by nicotine [Falk et al., 2005]. Prenatal nicotine might also prime the developing brain for depression [Law et al., 2003].

Smoking by adolescents still displays an upward trend in Europe [WHO, 2002] with an average prevalence now just below 30%. So the effects of active smoking tend to confound the persistent impacts of passive smoking when the kids grow older. Nevertheless long lasting effects of early ETS exposure have been demonstrated [Boffeta et al., 2000] as well as late consequences of early damage.

Some of the damage caused by ETS exposure will be estimated based on exposure and effect data discussed in the following chapters.

EXPOSURE

There are several ways to assess ETS exposure that are either based on questionnaire data or on measurements. Questionnaires can be directed to non-smokers asking them about their perceived exposure to ETS or to the smoking parents to state the number of smokers in the household and/or the number of cigarettes smoked at home or in the vicinity of the children per day. One interesting way would be to ask the parents about their smoking behaviors and cross-check this by asking the (young) children about their ETS exposure at home. In the study conducted in Linz we have interviewed more than 1400 children aged 6-9 years and their parents during their health exam at school. These data show that reports of children and

their parents on household smoking habits are in good accordance with each other with a kappa of 0.78 for the number of smokers in the household and a kappa of 0.45 for the number of cigarettes smoked at home per day (ordinal in 7 categories). There was no clear indication of underreporting by the parents or the children.

Table 1.Smoking in pregnancy, ETS exposure of infants and schoolchildren [Moshammer et al., 2006]

Study (abbreviation) *	all	Am	AT	DE	NL	HU	SK	CZ	PL
Number of study-areas	76	24	8	3	24	5	4	4	4
Year(s) of questionnaires	88-98	88-90	96-98	92/93	97/98	96	96	96	96
Number of children in study	35,390	15,053	4,155	2,018	2,065	3,721	3,038	3,478	1,862
Percentage of boys	51.4	51.0	53.3	50. 5	49.6	47.6	53.5	56.5	49.3
Percentage of children, age 6 – 8	11.6	-	86.7	19.6	10.3	-	-	-	-
Percentage of children, age 9 and 10	23.8	30.3	13.0	36.8	39.9	6.9	16.8	12.0	28.3
Percentage of children, age 11 and 12	64.6	69.7	0.3	43.6	49.8	93.1	83.2	88.0	71.7
Smoking during pregnancy	19.7	26.6	18.3	4.9	28.2	12.9	6.6	8.8	25.81
Smoking exposure during first 2 years	54.3	63.3	-	19.1	28.2	12.9	6.6	8.8	25.8
Current ETS exposure	55.6	50.3	63.4	46.6	57.6	59.0	54.0	60.1	68.2

* Abbreviation	Country (Study)	Reference
SK	Slovakia (CESAR study)	[Leonardi et al., 2002] (CESAR: Central European Study of Air Pollution and Respiratory Health)
CZ	Czech R (CESAR study)	
HU	Hungary (CESAR study)	
PL	Poland (CESAR study)	
DE	Bitterfeldt study, Germany	[Heinrich et al., 1999]
AT	Linz Study, Austria	[Neuberger et al., 2002]
NL	24 school study, Netherlands	[Janssen et al., 2003]
Am ‡	24 city study, North America	[Raizenne et al., 1996]

- :   no data
‡   Data from 18 communities in the US (approx. 80% of children) and 6 in Canada

According to Samet and Yang [2001] in Europe about 40% of the child population is involuntarily exposed to tobacco smoke at home. The number of adult smokers in Europe is showing a decreasing trend, however, it is also observed that the number of smoking women in reproductive age is not decreasing but even increasing. Large differences in smoking prevalence exist between countries and in different environments (urban versus rural, socio-economic classes, etc.). Although exposure to passive smoking has declined during the last 10 years in Europe [Janson et al., 2006] it still poses a vital health problem. We [Moshammer et al., 2006] have recently compiled data on ETS exposure of schoolchildren for a multicenter study (table 1) from European and North-American countries. On average 20% of all women smoked during pregnancy and more than 50% of all children were exposed to ETS at home in their first 2 years of life and during school-age.

Questionnaire results differ depending on the question „do household members smoke?" compared to „do household members smoke at home / in vicinity to the child?". Seifert et al. [2002] found higher urinary cotinine values in children at age of 3 months and older when parents also smoked at home. Delaimy et al. [2001] in their study of children aged 3 months to 10 years did not find significantly different hair nicotine levels whether parents declared they only smoked outside or also inside the home, while the levels in children of non-smokers were significantly lower. Ownby et al. [2000] showed that not only the smoking behavior of

the parents but also of other care persons influenced the urinary cotinine-creatinine ratio of infants prospectively followed up from bV̧th to age 2 years.

Questionnaire data can be interpreted using measurement data that link reported exposure to a range of concentrations [Wong et al., 2002], either in (indoor) air, documented by ambient or by personal monitoring, or as internal exposure, captured by biomonitoring. But agreement between questionnaire and urinary cotinine was moderate to poor with a correlation coefficient of 0.22 and a kappa coefficient of 0.09 in a study by Callais et al. [2003].

Among the thousands of substances emitted in (indoor) air from smoking only few are specific enough to serve as a marker of ETS exposure. Nicotine is certainly quite specific and therefore has been most widely used as a vapor-phase ETS marker. 3-ethinylpyridine has been proposed recently as another specific marker [Kuusimäki et al., 2006] but this paper will focus on nicotine data only. The marker of choice for biomonitoring is cotinine as a metabolite of nicotine [Parna et al., 2005; Repace et al., 2006].

Being exposed to ETS at home or at office workplaces translates into an average nicotine concentration in the range of several µg/m³ [Glasgow et al., 1998; Hammond, 1999; Heloma et al., 2000; Jenkins et al., 2001; Berman, 2003; own unpublished data]. Personal sampling of nicotine in the breathing zone of non smokers exposed to ETS at home or at the workplace revealed concentrations in the same range or slightly less [Hammond et al., 1993; O'Connor et al., 1995; Phillips et al., 1996; Phillips et al., 1998; Scherer et al., 1999; Jenkins et al., 2001; Eisner et al., 2001; Phillips and Bentley, 2001]. Compared to these figures the concentrations of nicotine found in discos and other public places where youngsters meet are alarming [Nebot et al., 2005]. The highest nicotine concentrations were encountered in Austrian discos with a mean level of 154 and a maximum of 487 µg/m³ [Moshammer et al., 2004].

The results of atmospheric exposure measurements translate well into biomarkers of exposure [Marbury et al., 1993; Repace et al., 2006] with concentrations of cotinine in plasma in the lower ng/ml range. The correlation of urinary cotinine with urinary cadmium has been attributed to ETS exposure (assessed by questionnaire) and increased pulmonary uptake in children with asthma [Willers et al., 2005].

HEALTH EFFECTS

Prenatal Tobacco Smoke Exposure Due to Maternal Exposure to Environmental Tobacco Smoke (ETS) During Pregnancy

There are several health effects described in children due to maternal exposure: increased fetal death, decrement in birth weight (measured as low birth weight - LBW), foetal growth restriction (measured as fraction of small for gestational age infants – SGA), and shortening of gestational age (measured as fraction of infants from preterm delivery i.e. < 37 age of gestation).

Increase of Fetal Death

There is some epidemiologic evidence that maternal ETS exposure may play a role in spontaneous abortion [Windham et al. 1992; Ahlborg and Bodin, 1991]. This association could reflect an effect of ETS exposure on the mother and fetus, but also a direct effect of smoking on the sperm (if losses are due to fetal abnormalities). Both studies reported 50% increase of risk of spontaneous abortion for mothers who were exposed to ETS, although in one study the association was observed only with workplace, not home exposure. This increase was higher than expected from the concentrations of pollutants affecting the child (compared to active maternal smoking). Remmer [1987] has suggested that enzyme induction of mono-oxygenase systems among active smokers leads to detoxification of toxic compounds and because such enzyme induction would probably not occur with the lower exposures of those exposed only to ETS, their fetuses are less protected. Two more recent studies confirmed the increased risk of spontaneous abortion [Venners et al., 2004, Kharrazi et al., 2004]. Venners et al. [2004] related heavy paternal smoking to early pregnancy loss. In the second study with biochemical assessment of ETS exposure from all sources an odds ratio of 3.4 for fetal death was found in the highest cotinine quintile (0.236-10 ng/mL), compared with the lowest quintile (<0.026 ng/mL).

Decrement in Birth Weight

The overall evidence suggests that exposure of pregnant women to ETS slightly reduces the mean birth weight of the foetus. Windham et al. [1999] concluded that the best studies show weight decrements from 25 to 100 grams and pooled weight decrement was 24,9 g (16,1 to 33,7 g). Slightly higher pooled weight decrements of 82 g (37 to 126 g) were found in three studies that were based on cotinine measurements (saliva, serum) and adjusted for at least one confounder [Rebagliato et al., 1995; Haddow et al., 1988; Eskenazi et al., 1995]. The effect is small compared with the effects of maternal active smoking. Nevertheless the birth weight distribution shifts down with exposure to tobacco smoke. At the population level this shift leads to an increase in the number of low birth weight infants. It also puts infants who are already compromised into even higher risk categories.

Dose-response evidence was found in several [Rubin et al., 1986; Martinez et al., 1994; Lazazaroni, 1990; Kharrazi et al. 2004] but not all studies [Rebagliato et al., 1995; Zhang and Ratcliffe, 1993]. Two studies noted that birth weight decrement in infants of women highly exposed to ETS (>5h/day or >20 cigarettes/day) were similar to those of infants of light smokers [Lazazaroni, 1990; Roquer et al., 1995].

Higher birth weight decrement was observed for infarnts born to women over 30 years of age exposed to ETS [Ahluwalia et al., 1997]. A greater effect among lower social classes might be attributable to poorer housing conditions and ventilation, leading to increased exposure. Poorer nutritional status before pregnancy may make it more difficult to compensate for the effects of tobacco smoke.

Foetal Growth Restriction

ETS exposure of pregnant women adversely affects foetal growth. The pooled OR for IUGR (Intra Uterine Growth Retardation) or LBW at term based on 11 studies was 1.2 (95%CI: 1.1-1.3) [California-EPA, 1997]. Kharrazi et al. found a linear dose-dependent effect of log cotinine on mean infant length (-0.84 cm) over a wide range of serum cotinine

concentrations, while body mass index declined with exposures above approximately 0.5 ng/mL.

Shortening of Gestational Age

An elevated risk of preterm delivery was suggested based on some studies [Windham et al., 2000; Jaakkola et al., 2001]. Higher risk was associated with greater number of hours (>7h/day) of ETS exposure [Windham et al., 2000]. However this association was limited to non-whites only. In another study in which exposure assessment was based on nicotine concentration in maternal hair sampled after delivery, the risk of preterm delivery (<37 weeks) was increased in the high- and medium-exposure categories compared with the low one [Jaakkola et al., 2001]. Kharrazi et al. [2004] found an odds ratio of preterm delivery of 1.8 in the highest cotinine quintile (0.236-10 ng/mL), compared with the lowest quintile (<0.026 ng/mL).

Poor intrauterine growth has a lasting effect on subsequent growth and development of children including an increased risk of emotional and behavioural problems and lowered cognitive abilities and hyperactivity [DiFranza et al., 2004]. Another paper [Matte et al., 2001] also indicated decrements in IQ associated with lower birth weight (< 2500 g). Low birth weight (LBW) is associated with several health effects in adulthood, such as an increase in the incidence of coronary heart disease, stroke, hypertension, type 2 diabetes mellitus, insulin resistance, serum lipids and premature pubarche [Barker et al., 1993].

ETS Postnatal Exposure from Smoking by Parents or Other Persons

Lower Respiratory Tract Infections in Early Childhood

Based on meta-analysis of 36 studies, increased risk of lower respiratory infections in early childhood was associated with children's ETS exposure due to either one of the parents smoking OR = 1.6 (95%CI: 1.4 –1.7). Similar risk estimates were found for maternal smoking OR = 1.7 (95%CI: 1.6 – 1.9) and other household members smoking OR = 1.3 (95%CI: 1.2 – 1.4) [Strachan and Cook, 1997].

The risk of lower respiratory tract infections is the highest in the first year of life, and remains elevated until about the age of 3 years [Strachan and Cook, 1997]. The effects of ETS on the susceptibility to infections can be prevented, at least to some extent, by breastfeeding the child for a lengthy period.

Chronic Respiratory Symptoms

Chronic respiratory symptoms like wheeze, chronic cough and chronic phlegm are more prevalent in populations of children exposed to ETS due to parental smoking as shown in a meta-analysis of 60 studies [Cook and Strachan, 1997]. The following pooled risk estimates were found for specific symptoms: wheeze (41 studies) - OR= 1.24 (95% CI: 1.17-1.31); chronic cough (34 studies) – OR= 1.40 (95% CI: 1.27-1.53); chronic phlegm (7 studies) – OR= 1.35 (95%CI: 1.13-1.62).

Reduced Pulmonary Functions

In the Harvard Six Cities study 8706 schoolchildren were followed annually between the age of 6 to 18 years [Wang et al., 1994]. Small reductions in FEV1 through adolescence were

associated with both current and pre-school exposures to maternal smoking (annual decrement of 3.8 ml, 95% CI: 1.2-6.4 ml). While the effects of prenatal and early life exposure on pulmonary flow rates are proven and most evidently so for the endexpiratory flows, an increase in airways responsiveness in infancy due to ETS exposure remains controversial [Stocks and Dezateux, 2003].

Passive smoking due to maternal smoking is a stronger determinant of poor lung function than the smoking of father or other household members, probably due to prenatal effect and closer contact of the child with the mother [Cook et al., 1998]. Follow-up of infants with reduced pulmonary function at birth found that by the age of 6 years they still had reduced pulmonary function but were no longer experiencing wheezing [Martinez et al., 1995]. In children aged 6 to 12 years associations of lung function impairments with current passive smoking were measureable, but weaker than associations with maternal smoking in pregnancy [Moshammer et al., 2006]. The prevalence of poor lung function increased with the number of smokers in the home [Neuberger et al., 1995].

Increased Sensitisation Rate to Allergens

While exposure to ETS increases the risk of sensitisation to food allergens in the first few years of life [Kulig et al., 1999] it does not appear to increase the sensitivity to inhalant allergens. The systematic review of the effects of parental smoking on immunoglobulin (IgE) levels, skin prick positivity, and allergic rhinitis or eczema in children was conducted by Strachan and Cook 1998b. Based on this meta-analysis they indicated that parental smoking, either before or immediately after birth was unlikely to increase the risk of allergic sensitisation in children. Also Gergen [2001] sugested that exposure to ETS is not associated with increase in IgE in children. Another study indicated that parental smoking was associated with a significant enhancement of expression of the most important markers of allergic sensitization in the children of smoking parents which was particularly evident for boys [Ronchetti et al., 1990].

Asthma and Exacerbation of Asthma Symptoms

Clinically diagnosed asthma was found to be associated with parental smoking in metaanalysis of 37 studies: OR = 1.44 (95%CI: 1.27-1.64) [California-EPA, 1997]. Similar results provided metaanalysis of 25 studies on relationship between asthma and either parent smoking OR = 1.21 (95% CI: 1.10-1.31) [Cook and Strachan, 1997]. Additional evidence has come from meta-analysis of 8 longitudinal studies which concluded that incidence of asthma or wheezing was related to maternal smoking [Cook and Strachan, 1997]. While maternal smoking had a greater effect than paternal smoking, the effect of paternal smoking alone was clearly significant suggesting that the postnatal effect is also important [Cook and Strachan, 1997]. The prevalence of asthma increases with the number of smokers in the home [Lewis et al., 2005]. Effect of ETS exposure on the risk of asthma was stronger for the first 5-7 years of life than during school age [Strachan and Cook, 1997]. Young females are at higher risk than young males for an increased rate of respiratory symptoms, a diminished level of lung function and a greater asthma medication use due to air pollution (including ETS). However, only one study had a longitudinal design with the assessment of individual exposure [Li et al., 2000]. Parental smoking increases the frequency of attacks, the number of emergency department visits and the risk of intubation [Strachan and Carey, 1995]. The severity of asthma decreases in children when exposure is reduced [DiFranza et al., 2004].

Sudden Infant Death Syndrome

(SIDS) is defined as a sudden, unexpected death of an infant, without evidence of any fatal illness at autopsy. After congenital anomalies, SIDS is the most common cause of death among infants between 1 month and 1 year old in the US, accounting for 5417 deaths in 1990 but with a declining trend over the years [CDC, 1996]. By 2002 the numbers have declined to 2295 cases [CDC, 2004].

Prenatal smoking is almost invariably associated with postnatal smoking. Therefore it is difficult to judge whether the effect is due to prenatal or postnatal exposure. Based on a systematic review conducted by Anderson and Cook [1997] the risk for SIDS was increased almost twice in children with postnatal parental exposure after controlling for prenatal maternal smoking (OR=1.94; 95%CI: 1,56-2,43). Studies were controlled for maternal factors (age, parity); infant factors (sex, birth weight, gestational age), socioeconomic status (ethnicity, social class, education), infant care practices (breastfeeding, sleeping position, wrapping), and prenatal maternal smoking. The fact that infants who died from SIDS had a higher nicotine concentration in their lung tissue compared with non-SIDS cases supports the statement that postnatal exposure is also related to SIDS [McMartin et al., 2002].

In England and Wales there are approximately 400 SIDS deaths per year and Cook and Strachan [1999] attribute 80 deaths to maternal smoking.

Recently also hospital admissions of infants with Apparent Life Threatening Events (ALTE) have been associated with smoking in pregnancy [Kiechl-Kohlendorfer et al., 2005].

Middle Ear Disease

Evidence across study types and outcome measures consistently indicates an increased risk for middle ear disease in children exposed to parental smoking. Pooled odds ratios for either parent smoke in a meta-analysis of 40 studies were 1.48 (95%CI: 1.08-2.04) for recurrent otitis media (9 studies); 1.38 (95%CI: 1.23-1.55) for middle ear effusion (5 studies) and 1.21 (95%CI: 0.95-1.53) for glue ear (9 studies) [Strachan and Cook, 1998a].

About 10% of surgical operations for glue ear are attributable to the effects of parental smoking. Giving the reported 60 000 operations per year in England this amount to an extra 6 000 operations per year. The number of attributable episodes of glue ear will be far greater [Cook and Strachan, 1999].

Neurodevelopmental and Behavioural Problems (Attention Deficit and Hyperactivity Disorder – ADHD and Reduced General Intellectual Ability)

Poorer academic performance in relation to paternal, maternal or household smoking was reported at the time of a follow-up during childhood [Eskenazi and Castorina, 1999]. Clear decrement in performance on a range of cognitive, perceptual, central auditory and linguistic abilities associated with postnatal exposure was observed in 3 out of six studies that controlled for prenatal maternal smoking. Children of mothers who smoked only after pregnancy performed somewhat worse than children of mothers who smoked only during pregnancy [Eskenazi and Castorina, 1999].

There is increasing evidence that ETS exposure is linked with intellectual impairment. The reported ETS effects are: problems in cognitive function and achievements such as early grade retention [Byrd and Weitzman, 1994] reduced vocabulary and reasoning abilities and cognitive and intellectual deficits [Bauman et al., 1991; Johnson et al., 1999; Johnson et al., 2000]. Several studies suggest the existence of a dose response relationship between

neurotoxicity and smoke exposure and some studies found that the decrement in cognitive test scores are higher at lower levels of exposition [DiFranza et al., 2004; Fergusson et al., 1993; Weitzman et al., 1992; Denson et al., 1975]. However, there is uncertainty on the dimensions of this association.

The mechanisms by which ETS may exert its effects on cognitive function are unknown. Research on the effects of nicotine and cotinine [Audesirk and Cabell, 1999] on neurite length, suggest that exposure to these substances during prenatal development, may affect the survival and growth of essential nervous system components even at very low levels of exposure, as it happens with lead exposure [Schneider et al., 2003]. Prenatal exposure to tobacco smoke has been found to affect neuron growth and neuron connections. In rats, in utero exposure to nicotine has been shown to have a teratogenic effect on neurodevelopment in the brain [Slotkin et al., 1987]. Prenatal exposure results in profound alternations in neurotransmitter disposition, which are more evident in specific neuronal pathways. More research is needed to explore the mechanism by which postnatal ETS affects cognitive ability [Yolton et al., 2005]. It appears that the detrimental neurobehavioral effects of tobacco exposure have no thresholds. Recent research indicates that the inverse relationship between ETS exposure and cognitive outcomes is particularly evident at extremely low levels of exposure with serum cotinine below 1 ng/ml) [Yolton et al., 2005].

Cancer

The results on exposure to paternal tobacco smoke (before or after birth) suggest a positive association with brain tumours in children RR = 1.22 (95%CI: 1.05-1.40) based on 10 studies and lymphomas RR = 2.08 (95%CI: 1.08-3.98); 4 studies [Boffetta et al., 2000]. The data are too sparse for the other neoplasms in children, although the results of a few large studies are compatible with a weak carcinogenic effect of paternal smoke.

Recent results of a nested case-control study within the EPIC study, suggested that frequent exposure to environmental tobacco smoke during childhood was associated with lung cancer in adulthood (risk ratio 3.67 - 95% CI 1.19-11.11, for daily exposure for many hours) [Vineis et al., 2005].

ETS is a known human carcinogen, based on epidemiological studies indicating a causal relationship between ETS exposure and increased risk of lung cancer [IARC, 2002; Boffetta et al., 2000; Boffetta et al., 1998]. Studies attempting to look for a relationship between perinatal or early childhood exposure to ETS and cancer in childhood or in later life have so far failed to produce conclusive results [Boffetta et al., 2000; Sasco and Vainio, 1999]. However, biomarker-based studies have provided clear evidence of the potential of ETS exposure of children to cause genotoxic damage which may be associated with carcinogenesis [Grant, 2005]. For example, increased levels of carcinogen-DNA adducts (some of which may reflect increased cancer risk) have been found in blood leukocytes of children of smoking mothers [Whyatt et al., 2001], while metabolites of tobacco-specific carcinogens have been detected in the urine of ETS-exposed children [Tang et al., 1999; Hecht et al., 2001]. Because ETS is a complex mixture of thousands of chemicals, the role of specific components in the induction of health effects and the associated mechanisms are not known with certainty. For carcinogenesis, it is thought that polycyclic aromatic hydrocarbons and nitrosamines may play major roles through mechanisms involving genotoxicity (induction of DNA damage) as well as pathways connected with the production of reactive oxygen species. Nicotine stimulates cell proliferation, inhibits apoptosis [Tsurutami et al., 2005] and may be

transformed in human metabolism to a potent lung carcinogen [Hecht et al., 2001], thereby contributing to carcinogenesis both as an initiator and a promoter [Heusch et al., 1998; Villablanca et al., 1998].

The levels of carcinogen-DNA adducts found in the cord blood DNA of newborns of smoking mothers, as well as in blood leukocyte DNA of children exposed to ETS, tended to be higher than those of their mothers, suggesting that the foetus and children may have increased susceptibility to the genotoxic effects of airborne PAHs [Tang et al., 1999].

There is experimental evidence that certain food components (e.g. some polyphenolics and thiocyanate esters) may counter carcinogenesis caused by ETS carcinogens such as PAHs and tobacco-specific nitrosamines [Chung, 2001; Yang et al., 1998]. However at this stage such evidence is not sufficient to form the basis of an intervention strategy. Certain studies have suggested that individuals with specific variants in certain genes which affect the metabolism of carcinogens present in ETS (e.g. cytochrome P450IA1, glutathione- S-transferase M and P) may be more susceptible to ETS-related lung carcinogenesis, as well as induction of related pre-carcinogenic DNA damage, however no firm conclusions can be drawn at the present time [Hung et al., 2003; Kiyohara et al., 2003].

Dose-Response Relationship

Dose-response relationship between SIDS and both prenatal and postnatal maternal smoking was found in most of the studies. The same was also observed for the relationship between the prevalence of asthma, wheeze, chronic cough and parental smoking [Chan-Yeung and Dimich-Ward, 2003]. For the risk of chronic respiratory symptoms the risk measures were lower for one parent smoking and higher for both parents smoking. The effect of maternal smoking was stronger than paternal smoking [Cook and Strachan, 1997]. There are no data to indicate that low levels of exposure to ETS are harmless [DiFranza et al., 2004].

Certain adverse health effects caused by maternal smoking are reversible. In humans, maternal smoking increases the likelihood for a child to be born with a small head circumference. Children who are born to smoking mothers experience catch-up growth in weight and partial catch-up growth in length, but the differences in head circumference persist to at least 5 years of age. No difference in head circumference measurements was found when women who are pregnant stop smoking before 32 weeks' gestation [Lindley et al., 2000; DiFranza et al., 2004]. However, in assessing the effects of in utero exposure to ETS it is important to have in mind that exposure during specific stages of foetal development may represent critical windows during which short-lived exposure may give rise to irreversible effects. Given that the mechanisms of the other effects of ETS are not known with certainty, their potential reversibility cannot be predicted.

In a study on lung function in children no evidence of a no-effect threshold of ETS exposure was observed [Corbo et al., 1996]. In view of the multiplicity of the health effects associated with ETS, it should also be kept in mind that different effects may have different dose-response relationships and no-effect levels: for example the effect of exposure can significantly change if the woman temporarily stopped smoking during a period of pregnancy critical for causing damage [DiFranza et al., 2004].

IMPACT ASSESSMENT

Infants of lower birth weight and gestational age are at increased risk for neonatal mortality and morbidity. Intrauterine growth retardation (IUGR) or low birth weight (LBW) might have also long term consequences. The increased risk of mortality associated with being born with LBW appears to continue through childhood. The longer the gestation for a given birth weight, the lower the infant mortality rate. Infants born preterm are also subject to a number of complications associated with physiological immaturity, including cerebral palsy, hyaline membrane disease, sepsis, and seizure disorders. For example, poor intrauterine growth has a lasting effect on subsequent growth and development of children including an increased risk of emotional and behavioural problems and lowered cognitive abilities and hyperactivity [DiFranza et al., 2004]. One paper also indicated decrements in IQ associated with lower birth weight in children born with weight > 2500 g [Matte et al., 2001].

Some data suggest that infants who experience symmetrical growth restriction are less likely to exhibit later "catch-up" growth and also appear more likely to have cognitive deficits and difficulties in school. Some data indicate that adults born with IUGR may have an increased risk of developing cardiovascular diseases (including hypertension), diabetes mellitus and hyperlipidaemia [Barker et al., 1993].

Maternal Active Smoking During Pregnancy

The population attributable risk in percent (PAR%) for five poor pregnancy outcomes (LBW at term, IUGR, preterm delivery, stillbirth and SIDS) related to maternal active smoking during pregnancy is shown in table 2. LBW at term is a proxy of IUGR and indicates infants with birth weight is smaller than 2500g born from pregnancy lasting at least 37 weeks. LBW is more often used in epidemiological studies as the diagnosis can be based on birth weight and pregnancy duration, while IUGR identification needs ultrasounds examination during pregnancy. PAR% is the percentage of disease or death in the population that is attributable to an given exposure (formula 1). Table 2 lists the relative risk estimates available from literature and the PAR% assuming that about 25% pregnant women smoke during pregnancy. As much as 27% of cases of LBW at term or 20% of cases of IUGR might be attributable to maternal active smoking during pregnancy. Taking into account that the prevalence rate of IUGR in European countries is about 2-3% of all live births we can assume that 5-8 infants per 1000 live births are born with this pathology due to maternal smoking. Since the prevalence values for health outcomes differ regionally, local data might be more appropriate for calculating the number of cases attributable to maternal smoking during pregnancy.

Formula 1: The population attributable risk in percent (PAR%)
(1) PAR% = [P (RR-1) X100] / [P (RR-1) +1] P = prevalence of exposure, RR = relative risks

In a similar way the numbers of cases of preterm delivery, stillbirths and SIDS were calculated. As all the examined infant pathologies often coexist, the estimated numbers of cases attributable to active maternal smoking should not be added.

Table 2. Summary of effects of maternal active smoking during pregnancy

Outcome	Range of RR or OR (95% CI) if meta-analysis data were available*	PAR% **	Prevalence of health outcome (in %)	Number of cases attributable to maternal smoking per 1000 live births
LBW at term [CDC, 2001]	2.5 (1.5-3.5)	27	2-3	5.4-8.1
IUGR [CDC, 2004]	2.0 (1.5-2.5)	20	2-3	4.0-6.0
Preterm delivery [ShahandBracken, 2000]	1.3 (95% CI 1.2-1.3)	7	6-8	4.2-5.6
Stillbirths[CDC, 2001]	1.4 (1.2- 1.6)	9	0.33	0.3
SIDS [DiFranza et al., 2004]	3.0 (95% CI 2.5-3.5)	33	0.1	0.33

* for purposes of this estimates it is assumed that the odds ratios are equivalent to relative risks.
** P assumed to be 0.25

The estimated percentage of pregnant women smoking (25%) is relatively high. In the study by Moshammer et al. [2006] this high percentage was only reported by the participants from North America and from Poland (table 1). Considering a lower percentage of 10% (which was more typical for many other European datasets) leads to a substantially lower PAR% of 13% for LBW at term, 9% for IUGR, 3% for preterm delivery, 4% for stillbirths, and 17% for SIDS.

Maternal Passive Smoking During Pregnancy

The same approach was used to calculate the number of infants born with IUGR or LBW at term as the results of maternal passive exposure to tobacco smoke. These were the only health outcomes with valid information about the risk estimates.

It was assumed that 38% of pregnant women are exposed to ETS. The prevalence values for health outcomes were just examples and local data might be more appropriate for calculations of number of cases attributable to maternal ETS exposure during pregnancy. The results (table 3) indicate that for each 1000 live births 1-2 cases of IUGR or LBW at term might be the result of maternal passive smoking exposure during pregnancy.

Table 3. Summary of effects of maternal passive smoking during pregnancy

Outcome	OR (95% CI)*	PAR%	Prevalence of health outcome (in %)	Number of cases attributable to ETS maternal exposure per 1000 live births
IUGR or LBW at term [California EPA, 1997]	1.2 (1.1-1.3)	7	2-3	1.4-2.1

* for purposes of this estimates we assumed that the odds ratios are equivalent to relative risks.

In this calculation the effect of ETS exposure of pregnant women was considered to be independent of their smoking status. Also if the woman is smoking herself she and her foetus are affected by ETS. The percentage of non-smoking women exposed to ETS (at home or at

work) is somewhat lower. In a questionnaire recently administerd to 1000 non-smoking adults in Vienna 28% of the women reported exposure to ETS (own unpublished data).

Because exposure to ETS (during pregnancy) is more prevalent than active smoking during pregnancy the number of attributable cases of IUGR or LBW at term are in the same order of magnitude. For active smoking during pregnancy with a prevalence of 10% 2 - 3 cases of IUGR per 1000 live births would be expected.

Parental Postnatal Passive Smoking

The prevalence of children (age 0-7 years) exposure to ETS originating from parental smoking children is estimated to be about 40%. Considering the findings from table 1 this is a rather conservative estimate. This value differs in a wide range as it is affected by socio-economic/educational level and cultural background of a given community. The ORs in table 4 were taken from the paper of Cook and Strachan [1999]. The highest values were noted for lower respiratory illnesses at age 0-2 (19%) and recurrent otitis media (16%).

Table 4. Summary of effects of parental smoking on health of children (P = 0,4)

Outcome	OR (95% CI)* or range of ORs/RRs	PAR%
Lower respiratory illnesses at age 0-2	1.57 (1.42-1.74)	19
Prevalence rates at age 5-16		
Wheeze	1.24 (1.17-1.31)	9
Cough	1.40 (1.27-1.53)	14
Phlegm	1.35 (1.13-1.62)	12
Breathlessness	1.31 (1.08-1.59)	11
Asthma (cross-sectional studies)	1.21 (1.10-1.34)	8
Asthma (case-control studies)	1.37 (1.15-1.64)	13
Middle ear disease		
Acute otitis media	range 1.0 to 1.6	11
Recurrent otitis media	1.48 (1.08-2.04)	16
Middle ear effusion	1.38 (1.23-1.55)	13
Referral for glue ear	1.21 (0.95-1.53)	8

* for purposes of this estimates we assumed that the odds ratios are equivalent to relative risks.

The estimates of the prevalence of selected health outcomes substantially differ from study to study. For this reason no number of cases attributable to smoking per 1000 live births is calculated.

CONCLUSION

Passive smoking is a serious threat to the health of the children with a lasting impact even until adult life. Both smoking during pregnancy and passive exposure of the pregnant woman are relevant, adversely affecting some per 1000 live births. Although the risk estimates of the

latter exposure scenario are less pronounced, the population effect is of a similar range because of the higher prevalence of this exposure.

The involuntary ETS exposure of the children causes approximately 10% of the total load of respiratory and middle ear diseases and is responsible for many other detrimental health effects. In spite of many targeted initiatives like the Framework Convention on Tobacco Control [WHO, 2003] many more efforts are necessary to fight the tobacco epidemic.

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