

CHAPTER 4

Smoking and the lung

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Extensive research has been conducted to investigate the effects of exposure to environmental tobacco smoke (ETS) on respiratory diseases throughout childhood. Involuntary tobacco smoke exposure can begin in the earliest period of life, by the developing foetus, through an active smoking mother or by ETS exposure of nonsmoking females during pregnancy, which may continue through childhood. Active smoking by children and adolescents adds to the risk later in life. Many researchers have aimed to separate the effects of *in utero* and postnatal exposure, as well as exposure during infancy and later childhood, as potentially different time windows of susceptibility. However, patterns of smoking are tightly connected and exposures overlap critical time periods. Therefore, the health effects assessed in different developmental stages may be related to current and past exposures in most studies. There is no doubt that exposure to passive and active smoking is detrimental to the respiratory system, particularly during lung growth and development. In this chapter, patterns and predictors of tobacco exposure, predominant respiratory health effects in different life stages, as well as important public health issues will be considered.

Patterns and predictors of exposure to environmental and active tobacco smoke in childhood and adolescence

The primary response to active smoking is inflammation of the airway epithelium which has been shown in studies using bronchoalveolar lavage (BAL) techniques [1, 2]. Since the examination of lavage fluids is an invasive method, ethical constraints prevent BAL studies among children. However, experimental animal studies suggest that passive smoking is associated with inflammation of the airways in a similar manner to active smoking [3]. Patterns and predictors of passive and active tobacco smoke exposure are important because they are related to a child's risk for adverse respiratory health effects.

Environmental tobacco smoke

The mixture of sidestream smoke, which emanates from the burning end of the cigarette, and exhaled mainstream smoke both contribute to ETS [4]. Levels of indoor pollutants like respirable suspended particles (RSP), polycyclic aromatic hydrocarbons, carbon monoxide, and nitrogen dioxide increase with the number of smokers present [5]. One-half of the total amount of RSP ($120 \mu\text{g}\cdot\text{m}^{-3}$) from an indoor environment in which smoking was allowed, originated from tobacco [6]. In the homes of 951 smokers an average concentration of $49 \mu\text{g}\cdot\text{m}^{-3}$ RSP were found, in comparison to $22 \mu\text{g}\cdot\text{m}^{-3}$ in 905

nonsmokers' homes [7]. These "real" concentrations of ETS have been shown to cause inflammatory effects after short-term exposure in healthy adults [8] as well as in pre- and postnatally exposed rats [3, 9].

A child's exposure to ETS results from the contact to ETS air contaminants at specific concentrations for given time periods. Since infants and small children spend most of their time at home [10], their exposure to parental smoking can be substantial. A Dutch study including personal measurements for particulate matter with a diameter less than 10 μM (PM₁₀) and time activity patterns among schoolchildren (aged 10–12 yrs), showed that in an average day 14.9 h were spent at home, 5.7 h at school, and 2.7 h outdoors. In this study, children of smoking parents were exposed to a mean of 123.3 $\mu\text{g}\cdot\text{m}^{-3}$ PM₁₀ (range: 80.1–195.4 $\mu\text{g}\cdot\text{m}^{-3}$) compared to a concentration of 84.0 $\mu\text{g}\cdot\text{m}^{-3}$ (56.9–126.4 $\mu\text{g}\cdot\text{m}^{-3}$) for children with nonsmoking parents [11]. Many earlier reports have shown consistently that parental self-reported smoking is a valid and reliable marker of a child's exposure to passive smoke [12–15]. In fact, questionnaire information on smoking habits may be a more valid estimate of the relevant (average) long-term ETS exposure than urinary measurements [12–15], because the half-life of cotinine is short in children (6–54 h) and reflects only short-term exposures [16]. Thus, the variability of urinary measurements may be high.

In North America, the average smoking rates have declined roughly from one-half to one-third of the total population in the last three decades [17], whereas in most European countries smoking rates were still high during the 1990s. In females aged 20–44 yrs, *i.e.* the time when people usually have children, rates ranged from 9.1–49.1% in Portugal and Denmark, respectively [18]. The corresponding rates among males ranged from 31.9–64.2% in Sweden and Spain, respectively [18]. These rates relate to the parental smoking prevalence found in studies about childrens' respiratory health indicating that up to 50% of children may be exposed to ETS during childhood [19–24] (table 1). A study using salivary cotinine measurements in children ($n=2,727$) aged 5–8 yrs, showed that 53.0% of children were exposed to ETS and mean cotinine concentrations rose from 0.52 $\text{ng}\cdot\text{mL}^{-1}$ in the highest social class to 1.36 $\text{ng}\cdot\text{mL}^{-1}$ in the lowest social class ($p<0.001$) [25]. Low levels of education as an indicator of socioeconomic status were also shown to be a risk factor for smoking in males and females across Europe [18] and in the USA [19], further suggesting a particularly high risk for children with a low socioeconomic status to be exposed to ETS. This notion was confirmed by the authors' own findings in Munich and Dresden. Children with a low social status ($n=2,618$), assessed as low parental education, had twice as much exposure to both general ETS and heavy ETS compared with children from a high social class ($n=2,686$; fig. 1) [26].

The predominant location for ETS exposure of young children is the home although other indoor environments such as in vehicles, at school, and other public places add to the child's ETS exposure. The Canadian human time-activity pattern survey using 24-h time activity recall diaries has shown that among children aged 0–11 yrs ($n=105$), the relevant locations contributing to the total exposure to ETS were the living room (22.3%), outdoors (14.4%), the bedroom (12.6%), the kitchen (8.4%), and the car (8.4%) [27]. In adolescence, public places may become more relevant exposure determinants as has been shown for adults [27].

Active tobacco smoking

The use of tobacco among children and teenagers shows different patterns in different parts of the world. In the USA, smoking rates among high school students decreased from 38.8% in 1976 to ~28% in the late 1980s, but rose steeply in the late 1990s almost to the level observed three decades ago [28]. Similar rates and trends were observed in

Table 1. – Examples of respiratory health studies reporting children's exposure to environmental tobacco smoke (ETS) and parental smoking rates in different countries

Country and year of study	Subjects n	Age group yrs	Study design and data	Definition of exposure to ETS [#]	ETS exposure rates
USA enrolment 1980–84 [19]	847	0–1.66	Prospective birth cohort	Smoking during entire first year of life	Maternal: 25% Paternal: 29.6%
UK enrolment 1989–90 [20]	1456	0–4	Prospective birth cohort	Maternal smoking between 0–4 yrs Any paternal smoking	Maternal smoking: 25.2% Paternal smoking With family history of atopy: 36.7% Without family history of atopy: 40.0%
Australia enrolment 1987–91 [21]		0–1		Interview questionnaire Smoking at 1 month of life	Maternal: F 35%; M 28% Paternal: F 36%; M 43%
Finland enrolment 1991–95 [22]	4578	16	Retrospective birth cohort	Maternal smoking ever	47.5%
USA (California) 1993 [23]	3357	10–16	Cross-sectional	Any past or current household exposure Maternal smoking during pregnancy	Household ETS: 41.5% <i>In utero</i> exposure to maternal smoking: 19.3%
Italy 1994–95 [24]	18737	6–7	Cross-sectional	Either parent smoking currently	54.2%
	21068	13–14			51.9%

F: females; M: males. [#]: smoking prevalence was elicited confidentially *via* self-administered questionnaires unless otherwise stated.

Canada [29]. Observed and estimated average smoking rates in the population age-group of 14–19 yrs in Germany, demonstrated an increase among females from 1.9% in 1920–1924 to 21.9% in 1990–1994 with a peak in the late 1970s (40.8%), while rates among males in 1994 were almost on the same level as in 1920 (25.6% *versus* 26.2%, respectively) with a rise in 1975–1979 (49.2%) [30]. Data from a recently repeated cross-sectional survey among seventh graders in Eastern Germany showed a temporary increase in

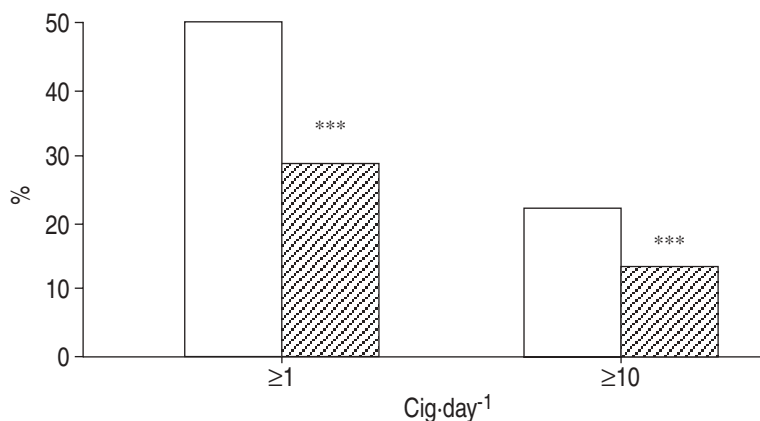


Fig. 1. – Exposure to environmental tobacco smoke in children's homes in relation to social status in Germany. A high social status (▨): parental education at least a high school degree (n=2,686); low social status (□): all lower education (n=2,618); cig-day⁻¹: cigarettes per day. ***: p<0.001 *versus* low social status [26].

smoking rates in the late 1990s (1993: 9.2%; 1997: 17.6%; 1999: 10.8%) [31]. A falling age of onset has been observed repeatedly in North America [32] and in Europe [33]. In Germany, in April 1999, the average age of smoking initiation in the age-group 10–15 yrs was 13.4 yrs, while at the same time among the group aged 15–20 yrs, it was 15.9 yrs [33], indicating that today, children are at risk of taking up smoking even before becoming teenagers [32, 33].

Individual smoking behaviour among adolescents has been investigated in several studies (table 2). In follow-up studies about the development of lung function, initiated in the USA during the 1970s, rather low smoking rates were found among children aged 10–14 yrs. However, smoking rates increased with age during follow-up [34, 35] which is in accordance with the findings of cross-sectional studies [36, 37] (table 2). Several demographic factors can be considered as predictors for the uptake of regular smoking in adolescence. Socioeconomic status, related to the rate of adult smoking throughout Europe [38] and children's exposure to ETS [19, 26], is also related to the risk for uptake of regular smoking among teenagers. In the study by WEILAND *et al.* [36] in Germany, 32.8% of adolescents aged 13–15 yrs with low social status smoked, in comparison to 23.1% among teenagers with high social status. However, in a study from the United Arab Emirates, an inverse association was suggested. The highest level of a father's education was related to the highest smoking rates among young males (University: 24.3%; illiterate: 12.6%; table 2) [39]. These differing findings may reflect the influence of the specific cultural background in different countries and ethnic groups on teenage smoking behaviour. The most important predictor of children's smoking may be parental smoking or living in a household with a smoker, which has been suggested by findings from several studies, where the smoking prevalence almost doubled among children of smoking parents compared with children from nonsmoking homes [24, 36] (table 2). Within an average population, sex is related to smoking rates in youths, with females smoking less than males (in 1999, aged 10–15 yrs: males 1.6%, females 1.3%; aged 15–20 yrs: males 27.8%, females 21.4%) [33]. However, the findings of some studies suggested that the prevalence of smoking among female teenagers is almost as high as among teenage males, or even higher, but heavy smoking may be more common among young males [34, 36]. Sex-specific smoking rates among adolescents are most probably related to country and cultural background as suggested by sex differences in smoking rates among adults [18].

Development through pre-adolescence, early adolescence, middle adolescence, and late adolescence is characterized by psychosocial factors [40] which may relate to the vulnerability of adolescents to take up smoking and develop nicotine addiction. Such factors may involve risk-taking as a conspicuous process to define the self and relationships with peers [40], the increasing intensity of peer group identification, feelings of omnipotence which may be characterized by intellectual recognition of the possibility of death from smoking-related diseases [39], and emotional denial [41, 42]. A critical role of psychosocial syndromes in the onset of cigarette dependence has been suspected but studies among children and adolescents are rare. Recently, in a 4-yr follow-up of the Early Developmental Stages of Psychopathology Study in subjects (n=3,021) aged 14–24 yrs, social anxiety was identified as a potential predictor of onset of nicotine dependence among baseline nonusers (odds ratio (OR): 3.85; 95% confidence interval (CI): 1.34–11.0) and nondependent users (1.5; 1.01–2.23) [38]. In a study among high school males (n=1,486), aged 15–19 yrs in a developing country, 33% of the smokers reported stress as being the most important factor for smoking [39]. These findings indicate that tobacco use is a socially accepted behaviour that relieves anxiety and stress in social situations [38, 39].

However, smoking rates among teenagers are increasing in the USA and in many Western countries and the age of onset is going down. The reduction in smoking rates

Table 2. – Examples of studies reporting smoking rates among children and adolescents in different countries

Country and year of study	Subjects n	Age group yrs	Study design and data	Definition of smoking [#]	Rates of active smoking
USA recruitment 1974–79 [34]	10060	10–14 15–18	Follow-up	Cig-day ⁻¹	0–4 cig-day ⁻¹ : F 2.5%; M 2.1% 5–14 cig-day ⁻¹ : F 0.9%; M 1.0% 0–4 cig-day ⁻¹ : F 9.1%; M 6.4% 5–14 cig-day ⁻¹ : F 6.1%; M 6.8%
USA recruitment 1974 [35]	669	10–14 15–19	Baseline follow-up	Smoking assessed during lung function measurement Smoking yes \geq 1 cig-day ⁻¹	Time trends over 8 yrs Stable: F 0–8.8%; M 1.6–4.5% Decrease trend: F 61.5 to 36.4%; M 37.2 to 10.2%
Germany 1991 [36]	2050	13–15	Cross-sectional	Cig-day ⁻¹	1–10 cig-day ⁻¹ : F 11.8%; M 8.4% >10 cig-day ⁻¹ : F 4.1%; M 5.2%
Germany 1993 [37]	2392	12–16	Cross-sectional	Regular, occasional or exsmoking	In relation to parental smoking: 1–10 cig-day ⁻¹ : yes 13.1%; no 4.9% Regular smoking: 6.1% Occasional smokers: 9.4%
USA (California) 1993 [23]	3357	10–16	Cross-sectional	Private interview during lung function testing Any smoking Report of any smoking	Exsmokers: 8.3% Total sample: 3.0% Children with current exposure to household ETS: 6.0%
Italy 1994–95 [24]	21068	13–14	Cross-sectional	Report of any smoking	Total sample: 8% In relation to parental smoking: yes 9.7%; no 5.6%
Germany 1995 [38]	3021	14–24	At baseline follow-up	Computer-assisted personal interview Regular smoking: daily use for at least 4 weeks Nicotine-dependence: DSM-IV criteria Regular or exsmoking	Regular smoking: F: 18.5% M: 18.9% Nicotine dependence: 18.7% Regular smokers: 19.0% Exsmokers: 28.2%
United Arab Emirates 1995 [39]	1486	15–19	M only, cross-sectional	Regular or exsmoking	

Cig-day⁻¹: cigarettes per day; F: females; M: males; ETS: environmental tobacco smoke; DSM-IV: the Diagnostic and Statistical Manual of Mental Disorders, fourth edn.
#: smoking prevalence was elicited confidentially via self-administered questionnaire unless otherwise stated.

was found to result more from people giving up smoking than from fewer people taking it up [43, 44]. Socially accepted forms of risk behaviour are an attractive way of coping with typical demands and problems during adolescence [45]. Relevant stresses may be particularly high among young asthmatics [42]. It has been suggested further that the iconic status of smoking and the outlaw ("tough guy") behaviour among teenagers contributes to the successful recruitment of new smokers [17]. The perception of health threats later in life is outweighed by the potential social benefits from current risk behaviour. And last but not least, nicotine is an addictive drug, effective in the release of stress mechanisms [46] which makes prevention of tobacco use a drug-dependency issue. Most smokers know very well about their own health risk from smoking but mechanisms which are related to the addictive nature of nicotine keep smokers from quitting their addiction [17].

Lung development and involuntary smoking pre- and postnatally

The foetus may be exposed to toxins that cross the placental barrier by an active smoking mother or as a result of the mother's involuntary exposure to tobacco smoke. Mothers who smoke during pregnancy commonly continue to do so afterwards, and maternal exposure to ETS during pregnancy is very likely to relate to the infant's ETS exposure after birth. Therefore, adverse health effects particularly from *in utero* exposure are difficult to disentangle from the impact of postnatal exposure. However, there is sound evidence that maternal smoking during pregnancy affects the growth of the foetus and the maturation of the foetal lung, leading to decrements in airway function after birth [47–49] which may have continuing adverse effects on lung function throughout life [23, 50]. In an Australian study, reductions in lung function were found to be associated with maternal smoking in 450 newborns, 2 days after birth [47]. In a longitudinal study, prenatal, maternal, cigarette smoking was related significantly to reduced forced expiratory flow values in 80 healthy infants tested shortly after birth (mean±SD: 4.2±1.9 weeks), when controlling for postnatal exposure to ETS between birth, the time of lung function testing and other confounding factors [51]. In a Scandinavian cohort study (n=803) measuring lung function 2–3 days after birth, tidal flow/volume ratios in both sexes, and compliance in females only, were related to maternal smoking during pregnancy after controlling for reduced body size, which is also affected by prenatal smoke exposure [52].

The adverse effects on lung function were shown to persist over the first 18 months of life [48] and until later in childhood [49]. These results were confirmed by a recent prospective birth cohort study (n=237) [53]. In this study, males had consistently lower expiratory flow values at functional residual capacity (FRC) than females, but maternal smoking during pregnancy was linearly associated with a significantly lower FRC (-14.24 mL·s⁻¹) in both sexes compared with unexposed infants throughout the first year of life [53]. Another study investigating the respiratory mechanics in early infancy supported the hypothesis that intra-uterine smoke exposure during lung development causes smaller airways, as well as alterations in the growth or maturation of passive mechanical properties of the respiratory system in infants [54], possibly predisposing them to the occurrence of wheezy illness during the first year of life [55]. In infants who died from sudden infant death syndrome, the inner air walls were significantly thicker in the heavily exposed infants compared with nonexposed subjects, suggesting a contribution of involuntary tobacco exposure to exaggerated airway narrowing [56]. Recently, a community-based study in London showed that perinatal smoke exposure increased airway resistance, but not the specific airway conductance, at a mean age of

7.7 weeks in 44 exposed infants compared with 57 subjects whose mothers did not smoke before and after pregnancy [57]. The authors suggested that the differences viewed in the literature with respect to lung function impairments and maternal smoking very early in life, were due to the timing of measurements and maturational changes in the modulation of expiratory flow during the first 2 months of life [57, 58].

Lung function and passive and active smoking in childhood and adolescence

After beginning very early in life, adverse effects of exposure to ETS on lung function may be continued throughout childhood and adolescence. Lung growth may be diminished further by children and teenagers actively smoking. Therefore, maximum levels of lung function in early adulthood may be reduced due to passive and active smoking before the completion of lung growth.

A recent quantitative meta-analysis of 21 cross-sectional studies, in school-aged children exposed to ETS, showed an average reduction of forced expiratory volume in one second (FEV₁) of 1.4% (95% CI: 1.0–1.9), of mid-expiratory flow (MEF_{25%–75%}) rate of 5.0% (3.3–6.6) and of end-expiratory flow rate of 4.3% (3.1–5.5) [59]. The results of the few longitudinal studies are heterogeneous. The greatest effects were estimated in the East Boston study (n=633, aged 6–19 yrs) based on an autoregressive model. In nonsmoking children of currently smoking mothers the rate of growth in FEV₁ was reduced to 93% of the maximum rate over a 5-yr period [60]. The analogous effect of the child's active smoking was a growth reduction to 76.2% of the maximum rate. Passive and active exposure to tobacco smoke was expected to be additive in these models [60]. In contrast, in the Tucson, USA, cohort no effect on lung function or lung growth was found in relation to ETS exposure [61]. Findings from the large Harvard six cities study which followed 8,706 children aged 6–9 yrs for 12 yrs, suggested small but highly significant reductions of lung growth associated with maternal smoking in children aged 6–10 yrs: forced vital capacity, -2.8 mL·yr⁻¹ (range: -5.5–0.0); FEV₁, -3.8 mL·yr⁻¹ (-6.4–-1.1); MEF_{25%–75%}, -14.3 mL·yr⁻¹ (-29.0–0.3) [62]. In older children the effects were attenuated and no influence of parental smoking during the first 5 yrs of life was found in this study [62]. However, two other recent reports showed a significant reduction in pulmonary function caused by very early life exposure to tobacco smoke in adolescents [23] and adults [50], independent of exposure to passive and active smoke later in life. An Italian study using urinary cotinine measurements to assess smoke exposure among 317 nonsmoking adolescents (aged 12–15 yrs) living in nonsmoking households showed a significant trend for a reduced lung function in relation to occasional exposure to ETS from outside the home only [63]. A longitudinal study among subjects aged 15–40 yrs found no adverse impact of exposure to ETS on pulmonary function which was assessed from the beginning of the study [64]. These observations may underline the role of exposure to passive smoke earlier in life.

Few studies have examined the effects of active smoking among children and adolescents prospectively. In a further analysis of the East Boston study in the age-group of 15–19 yrs, a reduction in growth of FEV₁ of 92% of the maximal rate, was estimated in association with relatively small amounts of smoking (≤ 1 cigarette per month) starting at age 15 yrs [35]. GOLD *et al.* [34] followed a cohort of 5,158 males and 4,902 females from 10–18 yrs of age with yearly measurements of pulmonary function in the USA six cities study. The yearly growth of FEV₁ in smokers compared with nonsmokers (≥ 5 cigarettes per day *versus* never smoking) was 1.09% (95% CI: 0.70–1.47) slower in females and 0.20% (-1.16–0.56) slower in males, and the growth of forced mid-expiratory flow

(FEF_{25%-75%}) was 1.25% (0.38–2.13) slower in females and 0.93% (0.21–1.65) in males. Nonsmoking females reached a plateau in pulmonary function at ~18 yrs of age whereas those that smoked had a decline of FEV₁ and FEF_{25%-75%}. Furthermore, the adverse effects were shown clearly to be dose-dependent [34].

A "healthy smoker effect" has been suggested [65], *i.e.* individuals who may have particularly good respiratory health may tend to take up regular smoking more often or earlier than individuals with respiratory restrictions, resulting in an underestimation of the real effects of smoking on lung function in adolescence. Studies of the natural history of asthma have noted that decrements in lung function in young asthmatics are associated with a higher severity of asthma symptoms and persistence in adulthood [66], suggesting that any factor causing low levels of lung function among children with asthma may also worsen the prognosis of the disease. A Dutch study following up 119 asthmatics between the ages of 5–14, 22–32, and 32–42 yrs showed significant associations of FEV₁ between the three examinations in the different age-groups [67]. Interestingly, in smokers who quit smoking before one of the following examinations the decrease in lung function had slowed down. Asthmatics who continued to smoke did not have a steeper annual decline in lung function compared to nonsmoking asthmatics; the authors suggested that those subjects in particular who are not susceptible to the effects of smoking, continue to smoke indicating a "healthy smoker effect" [67].

It has been speculated whether subgroups of individuals might be particularly vulnerable toward the effects of inhaled toxicants [68], though biological determinants have not been characterized. Only recently, in random samples of schoolchildren ($n=3,526$) within the framework of the German International Study of Asthma and Allergies in Childhood (ISAAC) Phase II studies, a subgroup of children with low plasma levels of α_1 -antitrypsin ($\leq 116 \text{ mg}\cdot\text{dL}^{-1}$) was identified. These children had a significantly increased risk to develop decrements in lung function, particularly mid- to end-expiratory flow values, if they were exposed to ETS, compared to children with normal levels of α_1 -antitrypsin [26, 69]. The mean \pm SE % predicted in both groups were: MEF_{50%}, 79.4 ± 7.2 versus 99.0 ± 1.5 ; MEF_{75%}, 67.4 ± 10.0 versus 100.3 ± 2.9 ; maximal MEF, 73.7 ± 8.6 versus 99.9 ± 1.7 , respectively. Given the hazardous effects of exposure to ETS in these susceptible children, active smoking would be likely to result in clinically severe decrements in pulmonary function.

In conclusion, most studies indicate that exposure to ETS very early in life as well as exposure to passive and active smoke occurring throughout childhood and the teenage years, contribute to a continued reduction in growth of pulmonary function. The observed inconsistencies of the effects of exposure to both passive and active smoke, may, however, be due to factors associated with variability of normal growth and development particularly during puberty. The effects of exposure to ETS on lung function in childhood are relatively small on average and therefore may be obscured by other factors influencing the growth of lung function. In addition, self-selection for taking up smoking among adolescents, based on their respiratory health status, may attenuate the results towards a no effect level.

Respiratory tract illness and exposure to environmental tobacco smoke in infancy and early childhood

Several studies have considered the adverse effects of ETS and lower respiratory tract illness (LRTI), like pneumonia and bronchitis, in young children, while only a few authors have reported an impact on upper respiratory tract illness. The USA Environmental Protection Agency (EPA) has concluded a causal association between

LRTI and exposure to passive smoke, predominantly in infants and young children, in a review on adverse effects of ETS [70]. The findings of the British Child Health and Education study (n=12,743) suggested that maternal smoking during pregnancy determines the risk for LRTI in the first year of life while postnatal ETS exposures become less relevant [71]. However, since pre- and postnatal exposure cannot be separated in this study the results have to be regarded with caution. In the large birth cohort in Tucson, USA, the relationship between maternal smoking and LRTI was studied further [19]. Wheezing and nonwheezing LRTI were diagnosed by paediatricians and cotinine levels were measured in the umbilical cord, in addition to questionnaire assessment of maternal smoking. In the first year of life, the OR of developing LRTI was significantly increased in infants whose mothers smoked ≥ 20 cigarettes per day in comparison to children of non- or lightly smoking mothers (OR: 1.82; 95% CI: 1.13–2.94). Furthermore, infants who were exposed to smoke before and after birth showed a higher prevalence of respiratory symptoms than children who were exposed only after birth (46.2% versus 36.4%, respectively; $p < 0.03$) [19]. In the British community study conducted by DEZATEUX *et al.* [57], 45% of infants whose mother's smoked (n=44) were found to have more than one wheezy episode in the first year of life while this was reported for only 14% of the offspring of nonsmoking mothers (n=57). Infants of smoking mothers were also significantly more likely to develop wheezing at any given age in the first year compared with those of nonsmoking mothers, after adjustment for a family history of asthma and specific airway conductance (proportional hazards ratio: 3.2; 95% CI: 1.3–7.9; $p = 0.013$) [57].

The risk for LRTI was also increased in the first 3 yrs of life if children (with nonsmoking parents) were exposed to ETS in daycare centres [72] demonstrating an effect of ETS exposure after birth, regardless of prenatal exposure. The risk for LRTI was increased further when children were exposed to ETS at home and in daycare, in addition to regular contact with more than three children during daycare time (OR: 3.57; 95% CI: 1.21–10.54) [72]. In Italy, a significantly increased risk for at least three episodes of bronchitis or pneumonia was shown in children of smokers in the first 2 yrs of life compared with children of nonsmoking parents (1.7; 1.10–2.70) [73]. A dose-dependent effect was indicated in a Polish study. The rate of lung infections was increased in 32% of children with light ETS exposure and in 74% of heavily exposed children in comparison to nonexposed children [74]. Another study from the USA confirmed the adverse effects of involuntary smoking on infections, however, a dose-dependence was not observed in this study [75]. In a Norwegian study a dose-response gradient was reported for smoking by the father, in particular, and not the mother [76]. The strongest risk of parental smoking for bronchitis, pneumonia and respiratory symptoms was found in the first 2 yrs of life, compared with > 2 yrs of age in a study from New Zealand. A 2.5–3.5% increase per five daily cigarettes was found, which also suggested a dose-response relationship [77]. Recently, a meta-analysis of 13 studies on the association between ETS and the prevalence of LRTI in infancy and early childhood was conducted by LI *et al.* [78]. The authors reported a pronounced effect on LRTI in children ≤ 2 yrs of age (combined OR: 1.71; 95% CI: 1.66–2.25) compared to the effect for the age-group 3–6 yrs (1.25; 0.88–1.78). The combined OR for hospitalization for LRTI in infancy and early childhood was 1.93 (1.66–2.25). These results are in accordance with the results of the meta-analysis conducted by COOK and STRACHAN [79–81] who concluded that the overall risk of early LRTI was increased by a factor of ~ 1.6 if either parent smoked and by ~ 1.7 if the mother was a smoker. If only the father smoked the risk was increased 1.3-fold. These investigators found that the risk of parental smoking was largely independent of assessed confounding variables, suggesting that residual confounding by unmeasured factors is unlikely to be important [79].

In contrast to the consistent results on the association between LRTI and ETS in

infancy and childhood, the relevance of exposure to passive smoke and the upper respiratory tract, *e.g.* tonsillitis or sinusitis, is less clear. For example, no relationship was found between parental smoking and hospital admissions [82] or consultations with the general practitioner [83] due to upper respiratory illness, but children of smokers reported a sore throat more often than children of nonsmokers [84]. However, specific effects of exposure to ETS on upper respiratory tract illness may be difficult to identify, since many prevalent factors are known to affect the development of these very common illnesses in childhood.

Impact of environmental tobacco smoke on the development of wheeze and asthma from infancy to childhood

In several cross-sectional studies an association of wheeze and asthma with any exposure [24, 85, 86] and heavy exposure [24, 87] to ETS was demonstrated from early-to-late childhood. The strong link between *in utero* exposure to maternal smoking and impairments in infant pulmonary function with subsequent wheezing LRTI in the first years of life, may predominantly indicate the increase in risk for benign transient viral-associated wheeze in early infancy, rather than an increased risk for the development of asthma later in childhood. However, in the Tucson birth cohort study, exposure to ETS was related to both transient early wheeze and persistent wheeze at ≤ 6 yrs of age which may be regarded as equivalent to a doctor's diagnosis of asthma. The risk of children whose mothers smoked ≥ 10 cigarettes per day and had ≤ 12 yrs education was increased 2.5-fold (OR: 2.5; 95% CI: 1.42–4.59) compared with children of nonsmoking mothers at the same level of education. At a higher level of education no association was found [88]. Maternal smoking was not only related to the incidence of wheezing and nonwheezing illnesses but also to an earlier manifestation of these disorders in this birth cohort study [19]. A register-based study from Sweden has shown an increased risk for hospital admission for asthma, at least once, in relation to any maternal smoking during pregnancy in children aged 2–6 yrs (risk ratio: 1.3; 95% CI: 1.2–1.5) [89]. In a case-controlled study of children aged 7–9 yrs, an approximate two-fold increased risk to develop asthma and wheeze in relation to exposure to maternal smoking *in utero* was reported (OR: 1.9; 95% CI: 1.2–2.8). Interestingly, each additional household member added significantly to the risk (1.15; 1.0–1.3) suggesting that not only prenatal but also postnatal exposure to ETS increases the risk for asthma in childhood [90]. In a large British birth cohort study ($n=9,670$), a 14% increase in wheezy bronchitis was observed in children aged 10 yrs whose mothers smoked ≥ 4 cigarettes per day, and a 49% increase was related to maternal smoking of >14 cigarettes daily [91]. An association with asthma was not reported, however, a clear distinction between asthma and wheezy bronchitis was not made in this study. Two other studies found no association between parental smoking and the development of early childhood asthma [92, 93].

Among children who already had asthma, however, consistent evidence was found that passive smoke exposure is positively related to the severity of the disease [87, 94, 95]. In the review of the USA EPA, small but significant dose-dependent reductions in lung function, and an increased severity and excess of symptoms, among children with asthma, were found to be causally linked to ETS [70].

However, since the relationship between LRTI in infancy and asthma later in childhood is uncertain, LRTI, wheezy illness, and asthma should be considered separately. In the meta-analysis of COOK and STRACHAN [79–81], 10 studies focusing specifically on illness, associated with wheezing, were identified among 21 studies of LRTI. The authors reported a similar effect of either parent smoking for wheezing and

nonwheezing illness but maternal smoking had a stronger association with wheezing than with nonwheezing illness. Parental smoking seemed to be more a causal factor for "wheezy bronchitis" than for asthma in this meta-analysis [79–81], although a diagnostic bias with children of smokers being less likely to receive the label of doctor-diagnosed asthma [96], cannot be excluded. COOK and STRACHAN [79] calculated an increased overall risk of either parent smoking for asthma (OR: 1.21; 95% CI: 1.11–1.34), wheeze (1.24; 1.17–1.31) and cough (1.40; 1.27–1.53). The authors concluded further from their quantitative meta-analysis based on four longitudinal studies that the incidence of asthma or wheezy illness after the first year of life was weakly but significantly associated with maternal smoking (OR: 1.13), notably less than the risk for wheezing illness in infancy (2.08). In four cohort studies they found intermediate results, the risk estimate for maternal smoking being 1.31 [79–81].

The study of bronchial responsiveness as an objective measure of features closely related with asthma may help to understand the effect of exposure to ETS further. In an Italian cross-sectional survey of 1,215 children (aged 7–11 yrs), a dose-response relationship was found between the number of cigarettes smoked by the mother and bronchial hyperresponsiveness (BHR) to a methacholine challenge among females [97]. Maternal and paternal smoking were strong predictors of BHR in less educated families and overcrowded homes, indicating a modification of the smoking effect related to living conditions, which was also suggested in recent studies on asthma [89, 98, 99]. In another Italian study, a strong relationship between BHR and carbachol was found, however, the adverse effect was larger for young males than for young females, and the strongest association was found for children with asthma [100]. Diurnal peak flow variability was associated with maternal smoking in asthmatic nonatopic and nonasthmatic children in an Austrian survey [101]. However, in several other studies these findings were not confirmed, where maternal smoking was not related to BHR to a methacholine challenge [102, 103] or to hyperventilation of cold, dry air [104]. A recent meta-analysis of 19 studies using challenge tests in schoolchildren showed an overall positive association between ETS and BHR in the general population (OR: 1.29; 95% CI 1.10–1.50) [105].

In conclusion, the strongest evidence for an association between exposure to ETS and the onset of asthma or BHR in children was found for heavy exposure to tobacco smoke with an indication of a modifying effect by living conditions such as low socioeconomic status or crowding. This may either reflect a higher total "ETS dose", due to more smokers living closer together, or the additive effect of different adverse environmental influences, particularly occurring in surroundings of children with low social class. Some authors reported stronger effects on the prevalence of wheezy bronchitis than asthma. This may correspond to an underdiagnosis of asthma, reporting bias or smoking cessation by parents of children with doctor-diagnosed asthma. Furthermore, an increased prevalence of infectious diseases of the upper and lower respiratory tract, such as recurrent otitis media [106, 107], middle ear effusion [108], bronchitis and pneumonia, was found in association with exposure to ETS from infancy to school-aged children. This may indicate that the adverse impact of ETS is particularly strong for viral-induced asthmatic symptoms.

Effects of passive and active smoking on the prevalence and prognosis of asthma in adolescence

The association between parental or own smoking and the prevalence or prognosis of asthma in teenage years presents a controversial feature of the effects of smoking. While an association between maternal smoking and asthma or wheezy illness in childhood, up

to 6 yrs of age, was found in most studies, such a relationship was not seen in many studies investigating children in later childhood or in adolescence [66, 109–111]. Furthermore, few reports have been published on the influence of taking up active smoking by adolescents on the persistence, late-onset or exacerbation of asthma.

STRACHAN and COOK [109] found inconsistent results in the meta-analysis of eight studies of the prognosis of asthma or wheezing illness in relation to parental smoking. In younger children the prognosis was reported to be worse if either parent smoked, whereas persistence of symptoms into teenage years and the twenties was less prevalent in smokers' offspring. A follow-up study of wheezy infants ($n=92$) from Sweden suggests that changes in parental behaviour may explain these findings. The presence of asthma at 10 yrs of age was more common in children exposed to smoking at home in infancy (82% *versus* 59%) but not associated to current smoking (53.5% *versus* 51.5%), indicating that parents of children with asthma gave up smoking [112]. In a recent large cross-sectional study ($n=39,805$) from Italy, an increased risk for current wheeze (OR: 1.31; 95% CI: 1.11–1.56) and current asthma (1.29; 1.06–1.56) was found in subjects aged 13–14 yrs if both parents were current smokers regardless of parental smoking during pregnancy [24]. In this study, parental smoking was associated with an increased risk for asthma among children aged 6–7 yrs. Interestingly, in adolescents, parental smoking was more strongly related to wheezing without reported asthma than to asthma, suggesting that parents of children who were labelled as asthmatic tended to give up smoking eventually. Furthermore, the risk of maternal smoking during pregnancy was strongly related to asthma and wheeze in children aged 6–7 yrs, while the effect was only small for the older age-group [24], which may relate to the natural history of the remission of asthma from childhood to adolescence [113] or, alternatively, may indicate that mothers report their smoking habits in pregnancy inaccurately 14 yrs later, thereby introducing recall bias. In a recent analysis of the prospective British birth cohort study including 7,249 teenagers at age 16 yrs, a significant dose-dependent increase in wheeze at age 16 yrs of ~1.4-fold in relation to maternal smoking of ≥ 15 cigarettes per day either during pregnancy (1.35; 1.15–1.59) or currently (1.41; 1.22–1.62) was found, independent of birth weight [98].

Only a few studies have investigated the effects of active smoking in addition to the impact of exposure to ETS for asthma in adolescence. Findings from a retrospective twin study comprising 2,550 families suggested an association between ETS exposure at <7 yrs of age and the lifetime prevalence of a diagnosis of asthma at age 16 (OR: 1.59; 95% CI: 1.09–2.31), while no adverse effect of a teenager's own smoking was found [22]. In a follow-up study in the UK the natural history of respiratory symptoms and asthma was investigated in subjects aged 14–16 yrs ($n=2,289$), who had been studied previously when aged 6–8 yrs [114]. Significantly, any current exposure to passive smoke evoked ~1.5-fold increases in the risk for late-onset of wheeze, doctor-diagnosed asthma, current wheeze, current cough, and a more than two-fold increased risk for persistent cough in males and females. Children's active smoking was specifically associated with persistent wheeze (4.35; 1.20–14.3) in males only, and further with late-onset wheeze (1.68; 1.17–2.42), late-onset cough (1.91; 1.12–3.25), and current cough (1.71; 1.21–2.43) in both sexes. The stronger affect on symptoms in males who were on average smoking less than females (6.3% *versus* 8.5%, respectively) may reflect the adverse influence on the small airways calibre of males beginning earlier in life and continuing throughout childhood [114]. An approximate two-fold increase in risk for asthma symptoms and cough in relation to daily active smoking by children aged 12–14 yrs was found in the UK ISAAC study ($n=25,393$), while parental smoking was only associated with a relatively small increase in risk for respiratory symptoms [115]. In the Italian ISAAC study, active smoking among adolescents (aged 13–14 yrs, $n=21,068$) was associated with an increased risk of current asthma (1.59; 1.30–1.94) and current wheeze (1.97; 1.67–2.31) [24]. Neither of these two ISAAC surveys reported differences between males and females [24, 115].

Findings of two longitudinal studies have shown decreased smoking rates among symptomatic adolescent asthmatics compared with asymptomatic asthmatics giving further evidence to the suggested "healthy smoker" effect which may result in an underestimation of the hazardous effects of active smoking among teenagers with asthma [110, 116].

Overall, there is some evidence that the conflicting results on current and past exposure to passive smoke on the incidence and persistence of wheeze and asthma in adolescents may at least, in part, be due to methodological problems such as recall bias or changes in parental smoking behaviour. Alternatively, many factors may be involved in the natural history of asthma overlapping the effects of passive smoke. Active smoking is likely to contribute to the persistence and new onset of asthma symptoms and cough in adolescence.

Public health measures of prevention

The summarized evidence that exposure to passive and active smoke is causally related to many severe respiratory health outcomes, such as LRTI, onset and worsening of asthma, reduced lung function and growth, and that the adverse effects may be initiated very early in life, is striking. Therefore, there is a public health need to reduce tobacco exposure of children from the beginning of their lives. The reduction of the smoking prevalence is subject to an extensive body of literature, including aspects of risk communication [17, 117], health-related behaviour changes [118], and policy legislation [119]. Although the implementation of measures and legislation to prevent smoking and ETS exposure has not been undertaken in most European countries, a worldwide tendency of tobacco litigation for transforming the prospects for tobacco control has been noticed [120]. The World Health Organization has expressed that legislation is needed to ensure that public places frequented by children are free from smoke, and further suggested educational interventions to promote reduced ETS exposure in homes [119, 121].

The change in parental smoking behaviour at home has been considered as a more achievable aim than parental smoking cessation. However, few investigators have used objective measures of children's ETS exposure to test the effects of self-reported smoking restrictions at home. In the Massachusetts' tobacco telephone survey of 1,606 adolescents, the self-reported restriction of residential smoking policies was associated to the decrease of exposure to ETS, measured as self-reported hours of exposure [122]. In the Nordic countries, within the framework of a 3-yr intervention measure to reduce young children's ETS exposure (n=3,547), the extent to which parents tried to protect their children from ETS was investigated [123]. Of current smokers, 82% reported some efforts to change their smoking behaviour, and of all parents 75% introduced rules to limit ETS exposure in their homes [123]. However, a measurable reduction in children's ETS exposure was not evaluated in this study. In a randomized intervention trial (n=501), parents of asthmatic children aged 2–12 yrs belonging to the intervention group were informed at baseline about the effects of ETS on asthma and the potential benefits to the child when exposure was avoided [124]. Furthermore, advice was given on how to seek help to stop smoking, not to smoke in the presence of their child, and to discourage visitors from smoking in the home. Children's ETS exposure was controlled by salivary cotinine measurements. No significant reduction in salivary concentrations was found 1 yr after the baseline visit, 98% of parents were still smoking and there was even a tendency for parents in the intervention group to report more smoking at follow-up [124].

The results of the few intervention studies aimed at a reduction of children's involuntary tobacco smoke exposure gives further evidence to the impression that

rational format-based risk message delivery has failed in the case of smoking cessation programmes. COVELLO [117] has pointed out that resulting from the failure of most previous health-risk information campaigns a "significant long-term ETS related attitude and behaviour change is most likely to occur when the ETS campaign is based on a 15-point programme". According to COVELLO [117] the campaign should 1) be itself long-term; 2) be based on multiple, reinforcing communication channels and media; 3) be accompanied by a carefully designed educational and instructional programme; 4) be targeted to the information needs and concerns of highly specified groups; 5) be designed to include opportunities for fact-to-face communication; 6) be coordinated with community organizations; 7) use interpersonal networks and support groups to reinforce message; 8) use positive incentives and rewards; 9) use messages that are vivid, interesting and arousing; 10) involve leaders from community and other groups in programme design and implementation; 11) involve existing organizations and networks in the dissemination of information; 12) use empirical information informed through surveys and other means to identify credible and trustworthy campaign spokespersons; 13) use empirical information to identify preferred channels of communication; 14) include plans for extensive pretesting; and 15) set out with modest objectives. Further, the author recommended continuous message delivery, including "dramatic material" through channels that are attended by the target group regularly, and efforts to help adults and children understand the methods and assumptions underlying ETS risk calculations [117]. However, to date the implementation of such programmes on a widescale basis has not been undertaken. Efforts are needed to bridge the gap between theory and practice of prevention. In practice, nicotine substitution has been shown to lead to an overall doubling in smoking cessation rates among adults compared to *e.g.* brief advice only (5.5% *versus* 2.1%) [125], with each replacement product (gum, patches, nasal spray, inhaler) being similarly successful [126]. Bupropion, a nontricyclic antidepressant, is the first non-nicotine agent approved by the USA Food and Drug Administration for smoking cessation. Based upon the current data, PROCHAZKA [126], suggested that it makes sense to use bupropion in those persons who have failed or are unable to tolerate nicotine replacement therapy. However, success rates of smoking cessation using single-drug therapy are not high, which points out that an additional behavioural therapy is needed. For healthcare providers the following recommendation according to PROCHAZKA [126] may be suggested: 1) identify all smokers and diagnose nicotine dependence; 2) provide self-help smoking cessation brochures; 3) provide brief, tailored advice to all smokers; 4) refer problematic smokers to specialized clinics or practices; 5) use nicotine replacement and/or bupropion in combination with brief counselling and active follow-up.

The success in the USA of reducing the smoking rates by banning smoking from public places shows that a change in socially acceptable behaviour results in changes in individual behaviour. However, the age of onset of smoking was observed to be falling and rates of smoking among young people are still high today in Europe and the USA [32, 33, 43, 44]. In reducing the onset of smoking the comprehensive social influence (SI) programmes, including decision-making components, designed and applied particularly for different educational tracks were suggested to be most successful [127]. According to this model, SI, attitudes, and self-efficacy expectations predict the nonsmoking behaviour [127, 128]. The effectiveness of an SI approach containing boosters was evaluated in a randomized, smoking prevention trial in 52 high schools in the Netherlands [129]. In this approach, two intervention groups received SI training in small peer-led activity groups coordinated by teachers. One of the two intervention groups were given boosters in the form of magazines discussing information similar to the SI programme. The training consisted of several video- and manual-based lessons including reasons why people do or do not smoke, the effects and dangers of smoking, skills for the resistance of peer

pressure, how to react when bothered by smoke, and finally, focused on alternatives for smoking and a commitment to nonsmoking behaviour. In the first lesson the steps towards making a decision were discussed. The most successful approach was the SI programme with boosters resulting in a significantly lower increase in smoking rates than in the control group after 12 months (5.6% *versus* 12.6%, respectively) and 18 months (9.7% *versus* 14.9%, respectively) [129]. DIJKSTRA *et al.* [129] recommended the implementation of SI programmes containing boosters on the national level. Community action programmes and the implementation of nonsmoking policies based on the results of the community action [130] may be another way of delivering smoking prevention measures to children and adults at the community level.

Conclusion

In conclusion, as an initial practical step, healthcare providers should apply brief counselling to smoking parents, adolescents, and children, and offer the possibilities of nicotine replacement therapy to the adults. Particular target groups may be families with asthmatic children and young asthmatics, relatively less advantaged segments of the population, and potentially susceptible subgroups and individuals. For the future, specific training material for healthcare providers should be developed and distributed. In addition, more evaluation studies are needed to control and enhance the success and effectiveness of preventative actions. On a legislation level, the banning of smoking in public places throughout Europe should be promoted intensively. Although joint effort is needed to reduce involuntary and voluntary smoking, it is likely that direct, indirect, and intangible costs will be reduced over the long term.

Summary

In North America the population average smoking rates have declined roughly from one-half to one-third of the total population in the last three decades, but in most European countries smoking rates are still high. It can be estimated that up to 50% of children may be exposed to environmental tobacco smoke (ETS) during childhood. Smoking rates among teenagers are increasing in the USA and in many Western countries and the age of onset is going down. Low socioeconomic status predicts involuntary smoking among children and voluntary smoking among adults. Parental smoking is a strong risk factor for taking up smoking among teenagers.

Overall, associations between ETS and small albeit significant decrements in lung function in early infancy and throughout childhood and adolescence were shown in most studies. Asthmatics and susceptible individuals may be particularly at risk. Lower respiratory tract illness in infants and young children was consistently associated to ETS exposure. Several studies indicate that heavy parental smoking is related to the development of wheeze, asthma, and bronchial hyperresponsiveness from early-to-late childhood, and furthermore, among children who already have asthma, there is conclusive evidence that ETS exposure is positively related to the severity of the disease. The picture of effects of past and current exposure to passive smoke on the incidence and persistence of wheeze and asthma in adolescence is less clear. This may, at least in part, relate to changes in parental smoking behaviour, recall bias, and other methodological limitations or the natural history of asthma overlapping the effects of passive smoke. Active smoking is likely to contribute to the persistence and new onset of asthma symptoms and cough in adolescence.

For the reduction of active and passive tobacco exposure an initial practical step is to apply brief counselling to smoking parents, adolescents, and children, and to offer the possibilities of nicotine replacement therapy to adults. For the future, the banning of smoking in public places throughout Europe should be promoted intensively.

Keywords: Asthma, children, epidemiology, public health, respiratory health, smoking.

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