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# Epidemiology of passive smoke: a prospective study in 589 children

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**Abstract. – *Background:* Several studies have found that in children of smoking parents there is an increased incidence of respiratory illnesses and diminished pulmonary function. In infants of smoking atopic parents IgE levels are higher, atopic symptoms start earlier, and children are more likely to wheeze if the mother smokes than if she does not. Maternal smoking of 0.5 packs or more/day was identified as a risk for asthma developing in the 1st year of life. Among the environmental measures of our prevention program there is an absolute prohibition of smoking in the house of a "at risk" baby.**

***Materials and Methods:* We have studied 289 atopic children, 169 males and 120 females, aged 3.5 to 7.5 years, attending our Division because affected by respiratory allergy. We have asked their parents if they smoked and if there were smoking relatives in their homes, independently of the number or the packs of cigarette smoked. The parents of 300 children comparable for age and sex visiting our outpatient clinic for non respiratory disease served as controls.**

***Results:* Smokers were 175 fathers and 109 mothers of the asthmatic children and 153 fathers and 89 mothers of the controls.**

***Discussion:* Analysis of data shows that passive smoking is significantly associated with the development of asthma in atopic children, and that males are more at risk than females. We stress that a high number of asthmatic children have atopic, and asthmatic parents. Cigarette smoke is not only a triggering factor of respiratory allergy in babies at risk of atopy, but especially an additional genetic factor, since asthma can be more easily provoked if an atopic parent smokes (more if both parents smoke), and even in children of not atopic, smoking parents.**

*Key Words:*

Passive smoke, Childhood asthma, Genetic factors, Smoking fathers and mothers.

## Introduction

Infants and children at risk of atopy (that is with at least an atopic parent), are exposed to environmental tobacco smoke (ETS) in 54.7% of cases, caused by 48.3% of fathers and by 43.9% of mothers, as results from the data of 10 countries, summarized by Tables I and II[1-8].

A large body of epidemiological evidence has documented that the offsprings of smoking parents suffer earlier and more frequently from atopic disease than the children of nonsmoking parents and that cigarette smoke elicits or aggravates asthma in a substantial rate of children[9,10]. Several authors studying the relationships between cigarette smoking and serum IgE antibody levels have reported higher IgE concentrations in adult smokers and their offsprings compared to nonsmokers and to controls, respectively[11-13]. In high-risk babies the effects of parental smoking on IgE serum levels from their birth to three years of age were evident: the IgE concentrations were higher in children from households with smoking parents, and there was a significant difference at 9 and 36 months[11]. It has established that respiratory tract infections afflict these children more frequently than the children of nonsmoking parents[10,14-16]. The bulk of studies that have examined the relationship of maternal cigarette smoking to wheezing illnesses and asthma episodes in infancy have found a positive association: in children of a mother smoking only 10 cigarettes/day there is a higher risk of subsequent asthma and a reduced pulmonary function at one month of age[16-19]. Infants of smoking mothers were four times more likely to develop wheezing illnesses in the first year of life[16].

**Table I.** Diffusion of passive cigarette smoke in infants/children.

| Region/Nation | % | Ref |
|---|---|---|
| Latium (polluted zones) | 67 | 1 |
| Latium (not polluted zones) | 69 | 1 |
| Denmark | 66 | 2 |
| France | 35.5 | 3 |
| England | 53 | 4 |
| Poland | 50 | 5 |
| Poland | 55 | 6 |
| Sweden | 34 | 6 |
| Turkey | 74 | 7 |
| USA | 43 | 8 |
| Mean | 54.7 | |

Maternal smoking can be associated with asthma development in the first year of life[20] and a decreased lung function is possible[11] especially in boys[21].

Passive smoke has an enormous environmental impact on the early development of infantile asthma: the adverse negative effects are observed particularly in young children who spend 60% to 80% of their time indoors, and are exposed more than older children to products of adult smoke (75% of smoke is released in the environment)[22].

Numerous and not wholly known are the mechanisms through which cigarette smoke could act. Exposure to ETS has also been proposed to increase the risk of a direct action on the immune system with an increase in CD4+ cells and changes in CD4+/CD8+ ratio, independently of IgE-mediated mechanisms[23]. Adequately documented is another smoke mechanism of action, consisting of its capacity of damaging the bronchial mucosa, thus compromising the integrity of the intercellular junctions and altering the epithelial permeability. The ensuing penetration of allergens and infectious agents might facilitate the damage of these cells. Alveolar macrophages from the lungs of a heavy smoker have been found to be laden with dense "smokers' inclusions" which include particulate matter arising from tobacco smoke. Such cells also have an abnormally smooth surface when compared to normal alveolar macrophages. Macrophages can hang out in the lungs of smokers long after they kick their habit, and so the damage can likely go on for years. Smoke acts by impairing the ability of alveolar macrophages to initiate immune reactions as accessory cells and to secrete the cytokines necessary to T-cell proliferation[24].

**Table II.** Smoke diffusion in the parents.

| Smokers (Ref) | Fathers | Mothers |
|---|---|---|
| 5 | 56.9 | 43.8 |
| 6 (Poland) | 59 | 51 |
| 6 (Sweden) | 30 | 37 |
| Mean | 48.6% | 43.3% |

Although the relationship between ETS and increase of respiratory allergy in children at risk of atopy is widely demonstrated, and in several countries the governments and the authorities caring for public welfare have undertaken actions to reduce smoking by seriously ban or move tobacco advertising away from schools[25], the ETS world diffusion is not reduced, at the point that children not exposed to cigarette smoke at home may be equally sensitized by outside careers[4].

In a study in preparation on 225 children (124 males and 101 females) aged 3 to 15 years with a median age of 7 years + 5 months, sensitized to cat allergen in 37.7% of cases, 58.6% of children were exposed to passive smoke.

In this paper we report the data of a study done in a cohort of 289 children aged 3.5 to 7.5 years attending our Division because affected by respiratory allergy. At the first visit, their parents were questioned by the physician as to the smoking habits in the family homes, in particular whether the parents smoked or there were smoking relatives in their homes to evaluate a possible relation between exposure to passive smoke of atopic children and the presence of atopic disease in their offsprings.

The control group included 300 nonatopic children comparable for age and sex recruited during the same period from our outpatient clinic.

## Materials and Methods

This study included 289 children,169 males and 120 females, aged between 3.5 and 7.5 years, consecutively visited at the Allergy and

Immunology Division, Department of Pediatrics, University of Rome "La Sapienza"[26]. The diagnosis of respiratory allergy (asthma and/or allergic rhinitis) in the children was done according the following criteria: clinical history, physical examination and positive skin prick tests (SPTs) and/or RAST to the most common inhalant allergens.

### Skin Prick Test

Appropriate emergency equipment and medications were available on site. Parents were required to discontinue all oral/topical corticosteroids during the trial, antihistamines for 7 days, and all ß-agonists for 12 hr before SPT application. Skin testing was done at baseline by the prick method by a doctor trained in allergy with the co-operation of a qualified nurse. The skin was marked with a ballpoint pen for the allergens to be tested. The babies were then tested with: histamine hydrochloride (1 mg/ml) as a positive control and isotonic saline as a negative control. We continued with a battery of food and inhalant allergens, including *Dermatophagoides pteronyssinus, Alternaria alternata, Lolium perenne, Olea europea and Parietaria officinalis* (Lofarma, Italy). The diagnostic extract of each in-dividual allergen was placed on the volar surface of the forearm as drops through which the skin was superficial-ly pricked with a straight pin for one second. A new pin was used for each prick test and then discarded, and the drop of the extract was then wiped off about one minute after the prick[27].

SPTs were read 20 minutes after the test was finished and considered positive as follows:

+ when the wheal was the half of the histamine wheal;
++ when the wheal was equal to the histamine wheal;
+++ when the wheal was two-fold the histamine wheal;
++++ when the wheal was more than two-fold the histamine wheal[28].

We took for positive only children with a +++ or ++++ reaction, that is a wheal ≥ 3 mm with an area = 7 $mm^2$ (cut-off) So we considered as positive only the children with a mean wheal diameter of 3 mm or larger than the negatve (saline) control. A positive (histamine) control was performed to ensure the absence of any antihistamine drug interference[29].

### Specific IgE

Specific IgE antibodies determination was done by radioallergosorbent test (Phadezym RAST, Pharmacia Diagnostics). RAST results are expressed in "RAST Units" (PRU = Phadebas Rast Unit) as follows:

1st class = IgE levels < 0.35 IU/ml,
2nd class = IgE levels > 0.35 IU/ml and lesser than 0.7 IU/ml,
3rd class = IgE levels between 0.7 IU/ml and 17 IU/ml,
4th class = IgE levels higher than 17 IU/ml.

Only RAST results > 0.35 IU/ml were considered positive.

### Study Trial

We have asked the parents of the 589 children whether they smoked or there were relatives living in their home who smoked, independently from the number or the packs of cigarette smoked.

### Control Group

The parents of 300 healthy children recruited during the same period from our outpatient clinic with no history of atopy of comparable age and sex formed the control group.

### Informed Consent

All parents have given their informed consent.

### Statistical Analysis

Data were analyzed using the X2 method.

## Results

### Study Group

Regarding symptoms, 180/289 (62.5%) study children manifested only asthma and 109 (37.5%) asthma and rhinitis. The sensitizations were divided as follows: *Der p* 205 (70.9%); *Lolium perenne* 69 (23.8%); *Parietaria officinalis* 20 (6.9%). No child was positive to *Cynodon dactylon* and *Olea europaea.*

The RAST results showed a scarce concordance with SPT results: *Der p* 205/219, *Lolium perenne* 69/59; *Parietaria officinalis* 20/5: $p = 0.0006$.

The analysis Der p vs pollens showed also a very high statistical difference: $p = 0.0001$.

### Control Group

Only a low proportion of these children (9%) was reported to suffer from frequent wheezing. Only 13 tested positive for inhalant allergens and 9 had positive RAST results. But no child had positive SPT and RAST results.

### Study Trial

The results are shown in Table III.

The statistical analysis shows surprising results:

Fathers vs mothers $p = 0.0036$, Study fathers vs mothers $p = 0.0196$,

Control fathers vs mothers $p = 0.0387$, study fathers vs control fathers $p = 0.0001$, study mothers vs control mothers $p = 0.0001$.

It is very significant the number of couples smoking together.

In the home of the 300 nonatopic controls we have found a very high, unexpected number of smokers 153 fathers and 89 mothers (mothers vs fathers $p = 0.0001$).

The statistical analysis revealed high statistically differences between fathers and mothers of the study group versus the parents of the controls, $p = 0.0196$ and $p = 0.0387$, respectively. In addition, the statistical analysis: fathers vs mothers is also highly significant ($p = 0.0036$) at variance withthe above studies.

Another data is above all significant: in 64.5% of cases both par-ents smoked (93 couples) in the homes of children in study vs 48.6% (73 couples) in the home of controls, with a statistical significant difference ($p = 0.0059$).

A statistical very significant difference was found between male and female children of the study group ($p = 0.0001$).

## Discussion

This study evidently stresses that a high number of parents, atopic parents, yet they themselves asthmatic are smoking parents of asthmatic sons and daughters. Particularly worrying is another finding: the high proportion of both parents smoking in the homes of study children vs the couples in the home of controls, with a statistical significant difference. The statistical analysis: fathers vs mothers is highly significant and this is at variance with the previously alluded to studies (Table III). The low number of other household members probably depends on the smaller housings prevailing in Italy. Such data demonstrates in an unequivocal manner that cigarette smoke should be considered as a triggering factor of respiratory allergy. Therefore in babies at risk of atopy cigarette smoke should be regarded as an additional genetic factor[26] since asthma is more easily transmitted if an atopic parent smokes (even more if both parents smoke), however cigarette smoke is able to provoke asthma even in children of not atopic parents[4]. Evidence is already accumulating that there is a connection between parental smoking habits and atopic symptoms in children, notably the daily exposure in their own house: in a recent study 58% of allergic children with severe wheezing (aged 12-45 months) was exposed to passive smoking compared with 37% of not allergic babies[20].

It has been consistently been found that environmental tobacco smoke exposure is associated with morbidity, increased cough,

**Table III.** Number of people smoking in the home of 289 children and 300 controls.

| Smokers | Study children | | Controls | |
|---|---|---|---|---|
| | *Number* | *%* | *Number* | *%* |
| Fathers | 175 | 60.6 | 153 | 51 |
| Mothers | 109 | 37.7 | 89 | 29.7 |
| Others | 15 | 5.2 | 25 | 8.3 |
| Fathers and Mothers | 93 | 64.5 | 73 | 48.6 |

wheezing respiratory illness, bronchospasm, airway responsiveness, and increases in the number of emergency room visits[15,30-32]. The odds ratio (OR) for wheezing children of smokers was 1.36, and it was higher in babies under the age of two[31].

Time ago it was demonstrated that the offsprings of smoking parents show an increased prevalence either of positive SPTs to aeroallergens or bronchial hyperreactivity (BHR), suffer earlier and more frequently from atopic disease than those of nonsmoking parents, therefore ETS triggers or aggravates asthma in a great proportion of children[33-40]. The effect on the offsprings of maternal smoking 20 cigarettes is directly measurable and dose-dependent, as shown by mean decrement of 5-6% of both Peak Flow and $FEF_{25-75}$ (maximal midexpiratory flow[35]. Passive smoke can therefore represent the more important environmental factor with a causal relationship to an increased earlier onset of infantile asthma[36,38] and immediate consequence on the genetic transmission of atopy, as demonstrated by this study.

A crucial share of children have ETS exposure both during gestation and after birth. Young et al[33] have underlined that normal babies aged 4.5 weeks (mean) of mothers smoking during pregnancy may exhibit an increased level of BHR. Apparently healthy infants may show an altered respiratory function in 8% of cases[28] and other healthy infants aged 4.2 ± 1.9 weeks a significant FRC (functional residual capacity) reduction[41], later turning into respiratory illnesses with wheezing[21]. In this context, maternal smoking (even of only 10 cigarettes/day) may be associated with asthma developing in the first year of life (OR 2.6, $p = 0.0006$), use of asthma medications (OR 4.6, $p = 0.006$) and increased numbers of hospitalizations[17], which may adversely affect the normal development of respiratory tract[42]. A study on lung function in over 3000 schoolchildren elucidated an independent association between in utero exposure to maternal smoking and decreased small airway flow[16] in accordance with the greater risk of developing asthma in children with abnormalities of lung function[43] highlighted by the greater risk of children with pre-existing abnormalities[36]. Lung function during the first year of life is adversely affected by in utero passive tobacco smoke exposure[21]. The risk factor has been quantified: children of mothers with 12 or fewer years of education and who smoke at least 10 cigarettes/day are 2.5 times more likely to develop asthma and have < 15.7% MEF than children of mothers with the same education level who did not smoke or limit their smoking to 10 cigarettes/day[35].

The suggestion that passive exposure to tobacco smoke might influence allergic sensitisation in children was first made in 1981[11]: Strachan and Cook have meta-analyzed 36 related papers and concluded that there is little evidence that parental smoking, either before or immediately after birth, has an effect allergic sensitisation in children44. However, 22/165 (13.3%) high risk children followed-up to the age of 7 years were regularly exposed to ETS, strongly suggesting that smoking in the household had a significant impact on aeroallergen sensitisation (OR 2.9, 95% CI 1.1 to 7.7) and on atopic disorder increased risk (OR 1.7, 95% CI 0.7 to 4.4)[45].

In the US it is estimated that as much as 34% of cases under 17 years of age is the target of maternal smoke[46]. Forastiere et al propose the identity of the true smoker47, the mother (in 52% of males and 49% of females) who smokes 20 cigarettes/day. Although high OR were found for girls[47] and the smokers in the 2 groups were comparable[39], negative effects have been related mainly to maternal smoke and not with paternal smoke (excepted 47). This key feature is commonly related to a greater maternal inclination for her sons, a wider availability of time and a higher intimacy between mother and son in the first months of life[22].

Another concern is the report that urinary cotinine concentrations were 10-fold higher in breastfed children than those who were bottle-fed, in whom cotinine levels were even higher than those of adult passive smokers[39]. Interestingly, certain effects may derive from in utero exposure to tobacco components and metabolites[48].

Two more serious effects of maternal smoke: mothers smoking in pregnancy are less likely to choose to breastfed their babies[49], and smoke decreases EGF (epidermal growth factor) levels in breast milk[50], postponing in prospective “gut closure”.

Therefore the evidence till yet documented on the risks related to ETS suggests the ur-

**Table IV.** Quantitation of pediatric morbidity associated with household smoking.

| Condition | Pooled risk | % of at risk children |
|---|---|---|
| Asthma | 1.43-1.46 | 8-13 |
| Respiratory hospitalization | 1.55-2.41 | 15-23 |
| Lower respiratory tract infections | 1.46-2.50 | 12-20 |
| Cough | 1.36 | 10-16 |
| Middle-ear disease | 1.19-1.58 | 2-13 |
| Tympanostomy | 1.60 | 1-26 |
| Adenoidectomy tonsillectomy | 1.20-2.06 | 16-24 |

Notes: Pooled risk is a relative risk for cohort studies (first figure) and an odds ratio for case-control studies (second figure when present); a value > 1 shows a high risk of disease. All the results show a statistical significance between $p = 0.01$ and $p = 0.0001$.
Data from reference 10.

gency of strongly advising against maternal smoke during pregnancy and subsequently. As frequently suggested, parents, relatives, guests, regular carers who cannot stop smoking, must leave child's house, closing the main entrance. Smoking far from children, or in another room, open the window or the fan are wholly deceptive steps. On the other side, it has been convincingly demonstrated that significantly influencing infant exposure to ETS in the household is unproductive[18,51]. Everywhere there is no incentive to label smoking in the presence of children heralds potentially serious health consequences. Above all, kids and teenagers are to be protected, being the more exposed to ETS in all senses; it is hitherto intriguing the proposal of assessing the companies which diffuse promotional messages to recruit children as new smokers, exempting the companies which accept to revise their marketing[52].

Smoking should be banned wherever children are present due to the pediatric morbidity associated with household smoking (Table IV)[10]. Additional measures are required to reduce the level of passive smoking. It is important that interventions should restrict smoking in public places in addition to promoting a smoke-free environment in the home[53]. However, parents when questioned in conjunction with an illness of their children, tended to understate, or even withhold the truth about, passive smoke exposure, thus in children with bronchial asthma, the number of passive smokers as assessed by their parents were lower by 65% and 29% respectively when compared to the findings obtained from measurements[54].

Smoking during adolescence has been associated with increased risk of persistence or relapse of symptoms, as demonstrated by the 33-year[55] and the 25-year[56] follow-ups of children born in 1958 in England or recruited in a school survey in Melbourne, respectively.

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