Effect of Passive Smoking on Frequency of Respiratory Illnesses and Serum Immunoglobulin-E (IgE) and Interleukin-4 (IL-4) Concentrations in Exposed Children

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Summary
We studied the relationship of serum immunoglobulin-E (IgE) and interleukin-4 (IL-4) concentrations, eosinophil counts, and frequency of respiratory illness with passive smoking in 70 randomly selected children of smoking parents. Fifty randomly selected age-matched children of non-smoking parents served as controls. Children of smoking parents had higher frequency of respiratory illnesses per year (P<0.01), significantly higher total leukocytic and eosinophil counts, higher percentage of eosinophils (P<0.01), and higher serum IgE and IL-4 concentrations (P<0.05) compared to the control group. Serum IgE level was correlated positively with the average number of smoked cigarettes/day, number of siblings, and total leukocytic count. Interleukin-4 concentrations were significantly correlated with the number of smoked cigarettes and IgE levels. Although IgE levels were higher in children of smoking parents (587 ±359 IU/ml) compared to controls (189 ±21 IU/ml), they did not differ significantly between children with and those without frequent respiratory illnesses (605 ±365 and 557 ± 354 IU/ml, respectively). Interleukin-4 concentrations were significantly higher in children of smoking parents with frequent respiratory illness (1.8 ±0.5 pg/ml) vs. those without frequent respiratory illnesses (1.3 ± 0.45 pg/ml). Multiple logistic regression analysis revealed that the overall positivity of the risk factors predisposing to respiratory diseases in the study children was 79 per cent, and the highest odds ratio was that for IL-4 (OR = 5.15). In conclusion, there is a significant increase in IL-4 and IgE concentrations, high eosinophil count and frequent respiratory symptoms in children of smoking parents. It remains that the current state of knowledge on health risks associated with passive smoking warrants that strong preventive action be promoted.

Introduction
Passive smoking is a risk factor for childhood respiratory health. It is found to increase the incidence of night cough, snoring, respiratory infections, bronchial asthma, and otitis media in children in different reports. Parental smoking is associated with a significant enhancement of the expression of many markers of allergic sensitization including higher eosinophil count and IgE concentrations. The synthesis of IgE is regulated by cytokines such as interleukin-2 (IL-2), IL-4, and gamma interferon. IL-4 increases both numbers of IgE secreting cells as well as IgE production. The serum concentration of IL-4 is elevated in many allergic disorders, including atopic dermatitis, bronchial asthma, and anaphylaxis, and correlates with serum IgE concentration. However, there is no data about the effect of passive smoking on serum IL-4 concentrations in children.

Our aim was to study serum concentrations of IL-4 and IgE, and eosinophil count in relation to the frequency of respiratory illnesses/year, in children of smoking parents (n = 70) in a rural Egyptian area (Kalyoubeya) and compare them with those for children of non-smoking parents (n = 50) living in the same environment.

Subjects and Methods
Seventy randomly selected Egyptian school children of a smoking parent, with a mean age of 10.2 ± 1.9 years and 50 randomly selected age-matched children of non-smoking parents with a mean age of 9.8 ± 2.1 years, from a rural area (Kalyoubeya) were the subjects of this study. Informed consent for the study was obtained from the parents of each participant.
procedure was taken from all parents and children before including in the study. Environmental factors were evaluated through a questionnaire which included housing conditions, number of siblings and number of cigarettes smoked by the parent/parents at home per day. Thorough history-taking and physical examination were done, and children with family history of atopy or allergic disorder were excluded from the study. All children were followed regularly, every 3 months, for 1 year and any respiratory illness (upper or lower respiratory tract infection, wheezy chest, or middle ear disease) was recorded during this period. Respiratory illnesses frequency equal or more than three times per year was considered 'frequent'. During the second clinic visit, laboratory investigations were performed. A fasting venous blood sample was withdrawn from each child for determination of total leucocytic count (TLC), eosinophil count (EC), and percentage by Coulter counter, IL-4 concentration using the immunoenzymatic assay kit (Medgenix) and IgE levels using enzyme immunoassay test kit (Medix Biotech Inc).

Statistical analysis was performed using ANOVA test to compare among the study groups. Significance was accepted at \( P < 0.05 \). Results were expressed as mean ± SD.

### Results

Table 1 presents a comparison between children of smoking parents, with and without frequent respiratory symptoms, and children of non-smoking parents. No significant difference in age, sex, number of siblings, or housing conditions was detected among children of smoking (\( n = 70 \)) and non-smoking (\( n = 50 \)) parents. The frequency of respiratory illnesses, affecting both upper and lower respiratory tract, was significantly higher in children of smoking parents (3.4 ± 0.8/year) compared to children of non-smoking parents (1.2 ± 0.6/year). The TLC, EC, and IgE and IL-4 concentrations were significantly higher in children of smoking parents compared to controls. Serum IgE concentrations were correlated significantly with IL-4 levels (\( r = 0.56, P < 0.01 \)), TLC (\( r = 0.42, P = 0.02 \)) and number of smoked cigarettes at home/day (\( r = 0.36, P = 0.03 \)). Comparison between children of smoking parents with and those without frequent respiratory symptoms revealed that children with frequent respiratory symptoms had significantly higher IL-4 concentrations, and increased TLC and EC. However, IgE concentration and the mean number of smoked cigarettes by parents/day did not differ significantly among these two groups.

### Discussion

In this study a significantly higher incidence of respiratory illnesses per year, and increased IL-4
and IgE concentrations and eosinophil count have been demonstrated in children of smoking parents, studied prospectively for 1 year, compared to children of non-smoking parents living under the same environmental conditions. These findings are in agreement with other reports incriminating passive smoking in the development of various respiratory symptoms in children. ²,¹⁶⁻¹⁸

The marked increase of IL-4 concentrations in children of smoking parents especially those with frequent respiratory illnesses compared to controls, and the significantly higher concentrations of IL-4 in children of smoking parents with frequent respiratory illnesses compared to those with less frequent respiratory symptoms denote that IL-4 is an important mediator in the process of respiratory inflammation. The significantly increased IgE concentrations in children of smoking parents and the significant correlation between IL-4 concentration, on the one hand, and the EC and IgE concentration, on the other, suggest that passive smoking stimulates IgE synthesis possible via an enhanced production of IL-4. This can modulate the allergic reactivity of the exposed children and make their airways more susceptible to respiratory disorders. In addition, this effect might be more pronounced in children with allergic disorders with subsequent greater effect on their respiratory health. ⁶,¹⁸,¹⁹

Contrary to the findings of other investigators, neither the serum IgE concentration nor the frequency of respiratory illnesses differed between girls and boys of smoking parents. This indicates that passive smoking is an important risk factor in the development of respiratory diseases in both sexes. ¹⁸,²⁰ Although IgE concentration was correlated significantly with the mean number of cigarettes smoked by parents at home/day, no significant correlation was detected between the number of smoked cigarettes/day and the frequency of respiratory illnesses/year in their children (r = 0.21, P = 0.08). However, other investigators reported a higher prevalence of respiratory illnesses with increasing number of smoked cigarettes. ¹⁷ The significantly higher IL-4 concentrations in children of smoking parents with frequent respiratory diseases vs. those with less frequent respiratory illnesses, despite having similar IgE levels, suggests that in studying the effect of passive smoking measurement of IL-4 might be a more sensitive allergic/inflammatory marker than IgE. In support of this view, multiple logistic regression analysis including all the potential risk factors that might predispose to respiratory illness (age, sex, number of siblings, housing conditions, number of smoked cigarettes/day, IL-4, IgE, and EC) revealed an overall positivity of 79 per cent, with the highest odds ratio was that of IL-4 concentration (OR = 5.15), while that of IgE was 0.01.

In summary, this study shows that passive smoking increases the frequency of respiratory symptoms as well as allergic markers (IL-4, IgE, and EC) in exposed children. It appears that the current state of knowledge on health risks associated with passive smoking warrants that strong preventive action be actively promoted.

References


