0021-7557/08/84-06/495
**Jornal de Pediatria**




# Risk factors for wheezing in the first year of life

**Herberto José Chong Neto,[1] Nelson Augusto Rosário,[2]**
**Grupo EISL Curitiba (Estudio Internacional de Sibilancias en Lactantes)[3]**

**Abstract**

**Objective:** To assess risk factors for wheezing in infants in southern Brazil.

**Methods:** Cross-sectional study using a standardized and validated questionnaire (Estudio Internacional de Sibilancias en Lactantes, EISL, or International Study of Wheezing in Infants). Parents of infants aged 12-15 months who attended 35 of 107 health centers between August 2005 and December 2006 for regular immunization were interviewed. The association between wheezing and factors studied was made using a prevalence ratio (PR) and confidence interval of 95% (95%CI) to perform a univariate analysis. Factors associated with wheezing in the bivariate analysis were studied using Poisson regression.

**Results:** Three thousand and three parents of infants filled out the questionnaire. The risk factors were male gender (PR = 1.14; 95%CI 1.05-1.24), history of asthma in the family [mother (PR = 1.18; 95%CI 1.04-1.33); father (PR = 1.20; 95%CI 1.05-1.39); siblings (PR = 1.23; 95%CI 1.08-1.42)], other pets in the home during pregnancy (PR = 1.28; 95%CI 1.07-1.53), age when child started daycare [0-3 months (PR = 1.15; 95%CI 0.98-1.34); 4-6 months (PR = 1.39; 95%CI 1.24-1.55); 7-12 months (PR = 1.20; 95%CI 1.07-1.35)], six or more episodes of cold (PR = 1.32; 95%CI 1.21-1.44), personal history of dermatitis (PR = 1.09; 95%CI 1.003-1.19), and mold in the home (PR = 1.14; 95%CI 1.04-1.24). Up-to-date immunization (PR = 0.79; 95%CI 0.63-0.98) and bathroom in the home (PR = 0.83; 95%CI 0.68-1.01) were protective factors.

**Conclusions:** Independent risk factors for wheezing in the first year of life are also known risks for asthma in children and adolescents. These data are useful to predict the diagnosis of asthma and to promote its prevention (when applicable).

*J Pediatr (Rio J). 2008;84(6):495-502:* Epidemiology, infant, wheezing, asthma, risk factors.

## Introduction

Infant wheezing is a determining factor for asthma in children and adolescents. Risk factors for asthma have been identified even before birth.[1] However, little is known about factors associated to wheezing episodes among infants in Brazil.

Maternal conditions and habits during pregnancy are related to the onset of wheezing among infants, just as children born of asthmatic mothers have higher risks of developing asthma.[2] Mothers who smoked during pregnancy gave birth to children with higher risks of wheezing and asthma. These children had high levels of IgE and IL-13 with low levels of of IL-4 and IFN-γ in cord blood and decreased airway caliber, with lower pulmonary function.[3-5]

During the perinatal period or the first four months of life, exclusive breastfeeding may be a protective factor for wheezing. However, other studies do not support that hypothesis.[6,7]

Respiratory viruses, such as respiratory syncytial virus (RSV), *Rhinovirus*, *Metapneumovirus*, *Parainfluenza* virus

1. Doutorando, Medicina Interna, Hospital de Clínicas, Universidade Federal do Paraná (UFPR), Curitiba, PR, Brazil.
2. Professor titular, Pediatria, Hospital de Clínicas, UFPR, Curitiba, PR, Brazil.
3. Grupo Estudio Internacional de Sibilancias en Lactantes (EISL) Curitiba: Bruno Guimarães Tannus, Leônidas Gustavo Tondo, Larissa Bollmann, Fernanda Valdameri Scapinello, Thaís Hissami Inoue, Francisco Emilio Ottmann, Arieno Cit Lorenzetti, Hugo Daniel Welter Ribeiro, Ricardo Pin, Luciana França Kalache, Renata Pimpão Rodrigues, Leonardo Dudeque Andriguetto, Emerson Rodrigues Barbosa, Kelly Cristina Vieira, Henrique Lopes, Cristine Secco Rosário, Dirceu Solé e Javier Mallol.

No conflicts of interest declared concerning the publication of this article.

**Suggested citation:** Chong Neto HJ, Rosário NA; Grupo EISL Curitiba (Estudio Internacional de Sibilancias en Lactantes). Risk factors for wheezing in the first year of life. J Pediatr (Rio J). 2008;84(6):495-502.

Manuscript received Jun 23 2008, accepted for publication Sep 03 2008.

doi:10.2223/JPED.1835

type 3 and *Influenza* virus, are associated to higher risks of wheezing among pre-school children.[8,9] Among low-income populations, pneumonia has been associated to recurrent wheezing.[10]

The risk of developing wheezing in early life is higher for males, for infants who attend daycare, those exposed to secondhand smoke, those in contact with high levels of endotoxin and room air allergens, such as those produced by mites, cockroaches and animal epithelium.[11-17]

In the KOALA study, immunized infants who followed the local immunization program did not have higher chances of developing wheezing than those who did not follow the recommended immunization schedule.[18]

Even though some risk factors for infant wheezing and asthma in children and adolescents are known, little is known about risk factors linked to wheezing in the first 12 months of life. The goal of the present study is to identify risk factors for wheezing among infants in Southern Brazil.

## Methods

The present study was performed as part of project EISL (Estudio Internacional de Sibilancias en Lactantes, or International Study of Wheezing in Infants), a multicenter, international, cross-sectional initiative developed to verify the prevalence of recurring wheezing, its clinical features, risk factors and association with respiratory infections among infants in the first 12 months of life in Latin America and some European countries. Like ISAAC (International Study of Asthma and Allergies in Childhood), EISL uses standardized case definitions and methodology, which increases the value of comparing data from centers from different countries and facilitates international collaboration.

The questionnaire was translated into Portuguese, back-translated into Spanish and validated among the local population.[19] The tool showed that parents or caretakers were able to identify wheezing episodes in their infants with high levels of agreement ($\kappa = 0.79$). Figure 1 shows the EISL questionnaire.[20]

In the 17 months of the study, the City Health Department had 107 health units, 35 of which were randomly selected and pro-rated to the population served by the units in the city. This method allows higher homogeneity in population samples, since the city is triangle-shaped and has an uneven demographic distribution.

The parents or legal representatives for infants aged 12-15 months who consecutively attended the health units for routine immunization between August 2005 and December 2006 were approached and had the study explained to them. If they agreed to participate, they filled out the informed consent form and the written questionnaire. The parents were also given guidance by 16 medical school students, who collaborated in collecting the material and answering 95% of questions in the tool, preventing any form from having blank answers. The interviewers were present at the health units once a month and in different days. The sample was a convenience sample, chosen to reach project goals.

The present study was approved by the Universidade Federal do Paraná (UFPR) Human Research Ethics Committee.

### *Statistical analysis*

Employing the same methodology as ISAAC, considering a prevalence of wheezing of 30% and 25% in two difference centers, the study is powerful within 95% and has a 1% significance level for this sample.[21]

Gross and adjusted prevalence ratio estimates, with a 95% confidence interval (95%CI), were calculated using Poisson regression with robust error variance in bivariate analyses and multivariate analysis, respectively. Covariables which had $p < 0.10$ were considered using Poisson multiple regression (multivariate analysis). An interactive procedure was determined, initially considering all covariables with $p < 0.10$ in a multiple regression model. Next, the covariable with the largest value of p was removed from the model and it was recalculated. At each subsequent step, the least statistically significant covariable (largest value of p) was removed until all covariables had a value of $p < 0.10$, thus determining the final model. All significant probabilities presented (values of p) are bilateral, and values smaller than 0.05 were considered statistically significant. Statistical analysis was done using the SAS 9.1.3 (Statistical Analysis System, Cary, NC, USA) application.

## Results

Three thousand and three infants participated in the study, consecutively, with 45.4% of them presenting one or more wheezing crises within the first 12 months of life.[22] Table 1 shows the demographic characteristics of the population assessed.

Bivariate analysis did not find any association between wheezing in the first year of life and history of rhinitis and dermatitis in the family (mother, father, siblings), smoking by other family members, daily consumption of industrial food by the infant, cooking with gas, wood or other chemicals, air conditioning in the home, presence of cats in the home during pregnancy, presence of dogs, cats or other pets (such as birds, rabbits, etc.) in the home during the interview, carpeting in the home, kitchen inside the house, having a telephone, low maternal education, living in low-pollution locations, number of siblings, working mothers and ethnic differences.

Table 2 presents the association between wheezing in the first 12 months of life and the variables, as well as the statistical significance used in bivariate analysis.

## International Study of Wheezing in Infants

Questionnaire about respiratory symptoms during first year of life

**Dear Mom (Dad or caretaker): Please answer (fill out) the questionnaire below about the respiratory problems your baby had during his/her first year of life (from the day he/she was born to his/her first birthday). We ask that you do NOT leave any question unanswered.**

Person who will fill out data: ☐ Mother ☐ Father ☐ Other _____

Child's name _____

AGE: _____ (months) SEX: ☐ Female ☐ Male

Adress: _____

Current date _____ Phone number _____

Date of birth: _____ (day-month-year / example 15-11-03)

Birth weight _____ kilograms _____ grams (example 3 kilograms 100 grams)

Current weigh _____ kilograms _____ grams

Birth height _____ cm Current height _____ cm

In what country was your baby born? _____

Please write an X next to the space corresponding to your answer.

1. Has your baby had wheezing in the chest or bronchitis or whistling during his/her first 12 months of life? ☐ YES ☐ NO
**If you answered NO, please go directly to question 12**
2. How many episodes of wheezing in the chest (bronchitis or whistling) did your baby have during the first year?
☐ None ☐ Less than 3 episodes ☐ 3 to 6 episodes ☐ More than 6 episodes
3. At what age did your baby first have an episode of wheezing in the chest (first bronchitis)? At months
4. Has your baby been treated with inhaled medications to relieve chest wheezing (bronchodilators) via nebulizers or inhalers (sprays)?
(For example: Salbutamol®, Aerolin®, Berotec®, Brycanil®) ☐ YES ☐ NO ☐ DON'T KNOW
5. Has your baby been treated with inhaled corticosteroids (cortisones in spray form)? (For example: Symbicort®, Flixotide®, Seretide®, Clenil®, Beclosol®, Budesonide®, Busonid®, Pulmicort®, Beclometasone®, Fluticasone®, etc.) ☐ YES ☐ NO ☐ DON'T KNOW
6. Has your baby been treated with antileukotrienes (Singulair®)? ☐ YES ☐ NO ☐ DON'T KNOW
7. During the last 12 months, how many times have you woke up during the night because your baby was coughing or had a wheezing chest?
☐ Never ☐ Rarely (less than once a month)
☐ Sometimes (some weeks of some months) ☐ Frequently (2 or more nights per week, almost every month)
8. During the last 12 months, has the wheezing (whistling) in your baby's chest been so strong that you have had to seek emergency services (Hospital, Clinic or Health Center)? ☐ YES ☐ NO
9. During the last 12 months, has the wheezing (whistling) in your baby's chest been so intense that you have felt it caused great difficulty in breathing (shortness of breath)? ☐ YES ☐ NO
10. Has your baby been admitted to the hospital for bronchitis? ☐ YES ☐ NO
11. Has a doctor ever told you your baby has asthma? ☐ YES ☐ NO
12. Has your baby ever had pneumonia? ☐ YES ☐ NO
13. Has your baby ever been admitted to the hospital for pneumonia? ☐ YES ☐ NO
14. Does anyone smoke inside your house (father, mother, grandparents, uncles)? ☐ YES ☐ NO
15. Do you smoke? ☐ YES ☐ NO
16. Did the mother of your baby smoke during pregnancy? ☐ YES ☐ NO
17. Does your baby have any family members with asthma? ☐ YES ☐ mother ☐ father ☐ siblings ☐ NO
18. Does your baby have any family members with hay fever or allergic rhinitis? ☐ YES ☐ mother ☐ father ☐ siblings ☐ NO
19. Does your baby have any family members with skin allergies (allergic dermatitis)? ☐ YES ☐ mother ☐ father ☐ siblings ☐ NO
20. Was your baby delivered by cesarean section? ☐ YES ☐ NO
21. Has your baby attended daycare this year? ☐ YES ☐ NO
22. How old were your baby when he started daycare? Months
23. How often do you feed your baby any of the following products (not home-made): yogurt, pudding, chips, chocolate, soda, fruit juice in bottle or box, artificial jam.
☐ Never ☐ Once a week ☐ Once a month ☐ Every day of the week
24. What type of heating do you use at home?
☐ None ☐ gas heater ☐ electric heater ☐ wood ☐ coal ☐ paraffin ☐ other
25. What type of fuel do you use to cook at home?
☐ Piped gas ☐ LPG cylinder ☐ electricity ☐ coal ☐ wood ☐ other
26. Do you have air conditioning at home? ☐ YES ☐ NO
27. Did you keep any pets (dog, cat, bird, rabbit) at home when your baby was born?
☐ YES ☐ dog ☐ cat ☐ others ☐ NO
28. Do you currently keep any pets at home? (dog, cat, bird, rabbit) ☐ YES ☐ dog ☐ cat ☐ others ☐ NO
29. Do you have carpeting at home? ☐ YES ☐ NO
30. Do you have a bathroom with sink, shower and toilet inside the house? ☐ YES ☐ NO
31. Is your kitchen (or the place where food is prepared) located inside the house? ☐ YES ☐ NO
32. Do you own a telephone (cell phone or landline)? ☐ YES ☐ NO
33. Please choose your level of education
☐ Basic or primary education, or none (8 years of schooling or less)
☐ Complete primary or incomplete secondary education (nine to 11 years of schooling)
☐ Complete secondary education and college (12 years of schooling or more)
34. For how many months did you only breastfeed your baby (without giving juices, baby food or any other kind of milk)? months
35. How many colds (episodes of sneezing, coughing and nasal discharge with or without fever) did your baby have during his first year of life? (write the number in the space) ☐ episodes
36. How old was your baby when he/she got his/her first cold? (write age in months in the space) ☐ months
37. Did your baby have or does he/she still have any skin allergies during his/her first year of life (itchy red spots on the skin, allergy to diaper, allergy to mosquito bites, to food, metals, etc.)? ☐ YES ☐ NO
38. Do you think the place where you live has atmospheric pollution (factory smoke, road traffic, etc.)?
☐ YES ☐ a lot ☐ moderate ☐ a little ☐ NO
39. Are there mold (mildew) or humidity stains in your house? ☐ YES ☐ NO
40. Is your baby's immunization up-to-date (corresponding to the first year)? ☐ YES ☐ NO
41. How many siblings does your baby have?
42. How many people (adults and children) currently live at your home?
43. Do you (the mother) currently have paid work? ☐ YES ☐ NO
44. What is your baby's ethnicity? ☐ White ☐ Black (mulatto, mixed race) ☐ Asian (Japanese and Chinese) ☐ Other
45. Has your baby been treated with oral corticosteroids (Predsim®, Prelone®, Decadron®) ? ☐ YES ☐ NO ☐ DON'T KNOW

Adapted from Dela Bianca et al.[20]

**Figure 1** - EISL questionnaire

**Table 1** - Demographic characteristics of population assessed

| Variables | Wheezers n (%) | Non-wheezers n (%) | p |
|---|---|---|---|
| Gender | | | |
| Male | 746 (54.7) | 776 (47.3) | 0.0001 |
| Female | 618 (45.3) | 863 (52.7) | |
| Birth weight, kg (mean ± SD) | 3.1±0.6 | 3.2±0.5 | 0.007 |
| Current weight, kg (mean ± SD) | 10.5±1.6 | 10.5±1.5 | 0.08 |
| Birth height, cm (mean ± SD) | 47.9±3.1 | 48±2.8 | 0.0001 |
| Current height, cm (mean ± SD) | 75.4±3.3 | 75.7±3.4 | 0.17 |
| Age of onset of wheezing in months (mean ± SD) | 5.5±3.1 | | |
| Ethnicity | | | |
| White | 1,134 (83.9) | 1,397 (85.5) | 0.21 |
| African-Brazilian | 199 (14.7) | 215 (13.2) | 0.22 |
| Asian | 8 (0.6) | 10 (0.6) | 1 |
| Others | 11 (0.8) | 11 (0.7) | 0.66 |
| Parental education | | | |
| Primary | 413 (30.7) | 467 (28.8) | 0.26 |
| High school | 440 (32.7) | 472 (29.1) | 0.03 |
| College | 491 (36.6) | 681 (42.1) | 0.002 |

SD = standard deviation.

In multivariate analysis, being male, family history of asthma, attending daycare, presence of other pets in the home during pregnancy, more than 6 episodes of cold, atopic dermatitis and mold stains in the home remained independent risk factors associated to wheezing in the first year of life, while up-to-date immunization was a protective factor. Attending daycare before 3 months of age and having a bathroom inside the home tended to be associated to infant wheezing. The variable "age of first cold" was excluded due to the large number of blank answers (n = 237) (Figure 2).

## Discussion

Antenatal and postnatal factors are responsible for wheezing in very young children. Identifying risk factors for wheezing in infants is crucial for preventing asthma during their growth.

In this population, male infants tended to develop wheezing more than female ones, a finding also seen in other studies. However, it is known that that relation becomes inverted as children grow and become adolescents. However, the causal relation still has not been established.[11,23]

In a cohort of 849 infants, those whose mothers had been diagnosed as asthmatic had greater chances of presenting wheezing in the first year of life, which was not seen when the fathers were asthmatic.[2]

In our assessment, those whose parents and siblings, separately, had histories of asthma had greater chances of having wheezing crises in the first 12 months of life than those who had no family history of asthma, pointing towards genetic factors prevalent in the development of wheezing among infants.

Infants which attended daycare or were exposed to a high number of older siblings during the first months of life were protected from asthma or recurring wheezing from 6 to 13 years-old. The same was not seen when infants turned 2 years-old.[12] In our sample, 0-3 months-old infants who attended daycare tended to have more wheezing crises, and those 4-12 months-old who remained in daycare had higher chances of wheezing. This was also seen among children ranging from 6 to 59 months of age in Sao Paulo in a study of a low-income population.[24] Checking the number of people who live in the same home, four or more, bivariate analysis showed an association with wheezing, but that number was not an independent risk factor after adjusting for potential factors in multivariate analysis, unlike what was seen in Tucson, AZ, USA.[12]

The presence of pets during pregnancy and after birth seems to be a protective factor against wheezing in early life. Children exposed to one or more dogs in the home after birth

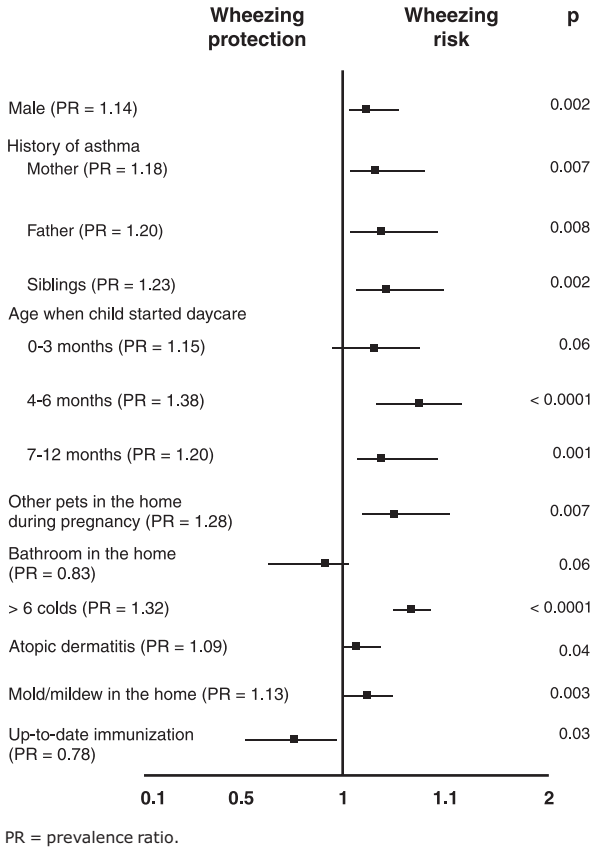
**Table 2** - Factors associated to wheezing in first 12 months of life in bivariate analysis

| Factors | PR | 95%CI | p |
|---|---|---|---|
| Male | 1.17 | 1.08-1.27 | < 0.0001 |
| Pneumonia | 1.87 | 1.74-2.01 | < 0.0001 |
| Hospital admission for pneumonia | 1.96 | 1.82-2.12 | < 0.0001 |
| Secondhand smoking | 1.09 | 1.007-1.17 | 0.03 |
| Maternal smoking during pregnancy | 1.11 | 1.001-1.23 | 0.04 |
| Asthma in the family | | | |
| Father | 1.34 | 1.20-1.50 | < 0.0001 |
| Mother | 1.39 | 1.22-1.59 | < 0.0001 |
| Siblings | 1.45 | 1.27-1.64 | < 0.0001 |
| Age when child started daycare | | | |
| 0-3 months | 1.32 | 1.14-1.53 | 0.0002 |
| 4-6 months | 1.47 | 1.33-1.63 | < 0.0001 |
| Industrial food | | | |
| Weekly | 1.21 | 1.008-1.47 | 0.04 |
| Monthly | 1.52 | 1.24-1.86 | < 0.0001 |
| Pets in the home during pregnancy | | | |
| Dog | 1.07 | 0.98-1.16 | 0.08 |
| Others | 1.28 | 1.07-1.53 | 0.006 |
| Bathroom inside the house | 0.79 | 0.65-0.95 | 0.01 |
| Higher maternal education | 0.89 | 0.80-0.98 | 0.02 |
| Exclusive breastfeeding | | | |
| 4-6 months | 0.88 | 0.80-0.95 | 0.003 |
| 7-12 months | 0.82 | 0.72-0.93 | 0.002 |
| ≥ 6 episodes of cold | 1.47 | 1.36-1.59 | < 0.0001 |
| Age of first cold | | | |
| 4-6 months | 0.84 | 0.77-0.92 | 0.0001 |
| 7-12 months | 0.57 | 0.51-0.64 | < 0.0001 |
| Atopic dermatitis | 1.24 | 1.14-1.34 | < 0.0001 |
| Lives in very polluted location | 1.13 | 1.01-1.26 | 0.02 |
| Mold/mildew in the home | 1.23 | 1.14-1.33 | < 0.0001 |
| Up-to-date immunization | 0.81 | 0.64-1.02 | 0.07 |
| More than four people in the home | 1.11 | 1.03-1.21 | 0.006 |

95%CI = 95% confidence interval; PR = prevalence ratio.

had less wheezing at early ages. That observation was valid for infants whose parents had no history of asthma, but not for the children of asthmatic parents.[17] The same was seen for cat allergens. Children of asthmatic parents had the same risk of wheezing in the first year of life regardless of whether there was environmental control for cat allergens or not. For children who had low risk of asthma, the chance of wheezing was lower, showing that exposure to that environmental factor was not important.[16]

The presence of dogs or other pets in the home during pregnancy (birds, rabbits, etc.) was a risk factor for wheezing in the population, according to the bivariate analysis. However, only the presence of other pets during pregnancy remained an independent variable associated to wheezing in the first twelve months. The presence of pets in the home at the time of the interview was not associated to infant wheezing.




PR = prevalence ratio.

**Figure 2** - Result of multivariate analysis (Poisson regression) between factors assessed and wheezing in first 12 months of life

The protection from having pets in the home during pregnancy remains controversial and requires further studies. The questionnaire did not specify exactly what other animals were found in the interviewees' homes, nor did it request that they be specified; it only mentioned, as examples, "birds and rabbits," which might have induced positive answers from parents. In any case, this is a relevant piece of information which requires further study.

Despite the fact that the mechanism is still unknown, children exposed to house fungi antigens (*Penicillium, Cladosporium, Aspergillus*, and *Alternaria*) during the first year of life had increased relative risk of croup, pneumonia, bronchitis and bronchiolitis.[25]

In the population described in the present study, the presence of mold and/or mildew in the home was an important factor for wheezing in the first year of life, probably due to the high relative humidity common in the city.

Having a bathroom inside the home is a factor associated to economic status in Brazil. The rate of wheezing infants in the low-income population was 80%, twice as much as the rate in the sample.[10] The same could be seen in a cross-sectional study of children under 5 years-old from low-income families in Sao Paulo, where living conditions were associated to higher risks of wheezing, though with a lower prevalence (12.5%) than that found in the city of Curitiba (in the Southern state of Paraná, Brazil).[24] In Curitiba, per capita income is higher than the national average, and the unemployment rate is among the lowest in the country. This might have been a determining factor for having a bathroom inside the home become a protective factor with marginal statistic significance. The prevalence of wheezing in developed countries is lower than that found in the present study, showing that economic conditions might be a protective factor.[15]

Stein et al. showed a direct correlation between wheezing and RSV. For 66% of wheezing infants, the associated virus was identified by culture or direct immunofluorescence and RSV was the most frequent finding.[9] In the Brazilian population, having 6 or more colds is considered a factor associated to wheezing. In Curitiba, the viral season is well-defined and must have contributed to that association.[26]

Atopic dermatitis is a predictive factor for infant asthma and the first manifestation of atopy.[27] In the present study, infants with atopic dermatitis had higher risk of wheezing in the first 12 months of life.

In a cohort of 2,545 families in the Netherlands, children who had completed the local immunization schedule (77%) were compared to 393 children with incomplete immunization (15%) and 182 children who were never immunized in their first 6 months of life (7%). No difference was seen in the rates of wheezing among infants in the first 12 months of life.[18] In the present study, children with updated immunization had lower risk of wheezing in the first year of life, a data point which contradicts the hygiene hypothesis, which states that immunized children have fewer infections and, consequently, more allergic diseases.[18]

These risk factors found for infant wheezing are different than those found for asthma risk in adolescents in Rio de Janeiro, except for atopic dermatitis, also found by written questionnaire.[28] Clarifying a possible correlation between risk factors for wheezing and/or asthma between different age groups requires the performance of a longitudinal study to check the temporal relation and association between asthma and wheezing factors.

The questionnaire is an acceptable research tool in epidemiological inquiries. However, the various centers must participate as much as possible so that there can be a broad overview of the objective at hand. It is simple, requires few resources and can be self-applicable. The tool must be applied in such a way as to differentiate the ill from the non-ill, which is done by validating it and calculating sensitivity and specificity coefficients.[29]

The sensitivity and specificity of this tool were high,[19] but the material was collected in 16 months, spanning some viral and climate seasons twice, which may have interfered with prevalence and produced some form of bias. The sample of 3,003 infants was also a convenience sample, chosen to reach study goals, which cannot be a determining factor for the rate of participation from the population.

In conclusion, some risk factors (male gender, family history of asthma, attending daycare, number of colds and personal history of dermatitis) are common to other populations from previous assessments. However, there are other factors (presence of other pets during pregnancy and mold/mildew in the home) which should be unique to the sample in the present study. Identifying risk factors for wheezing in the first year of life contributes to the diagnosis of asthma. Some factors are intrinsic, such as gender, family history of asthma and atopic dermatitis, which cannot be avoided. But some are extrinsic, such as attending daycare, mold stains in the home, colds and the presence of other pets (such as birds and rabbits), which can be avoided. Intervening on some of these factors, mainly those which are not intrinsic to the individual, could decrease the number of wheezing infants and, consequently, the number of asthmatic children as well.

**Acknowledgments**

We would like to thank the Curitiba Municipal Health Department for the authorization and release for performing this study in the public healthcare network.

**References**

1. Arruda LK, Solé D, Baena-Cagnani CE, Naspitz CK. Risk factors for asthma and atopy. Curr Opin Allergy Clin Immunol. 2005;5: 153-9.
2. Belanger K, Beckett W, Triche E, Bracken MB, Holford T, McSharry J, et al. Symptoms of wheeze and persistent cough in the first year of life: associations with indoor allergens, air contaminants, and maternal history of asthma. Am J Epidemiol. 2003;158:195-202.
3. DiFranza JR, Aligne CA, Weitzman M. Prenatal and postnatal enviromental tobacco smoke exposure and children's health. Pediatrics. 2004;113:1007-15.
4. Noakes PS, Holt PG, Prescott SL. Maternal smoking in pregnancy alters neonatal cytokine responses. Allergy. 2003;58:1053-8.
5. Gilliland FD, Berhane K, Li YF, Rappaport EB, Peters JM. Effects of early onset asthma and in utero exposure to maternal smoking on childhood lung function. Am J Respir Crit Care Med. 2003;167: 917-24.
6. Hanson LA, Korotkova M, Telemo E. Breast-feeding, infant formulas, and the immune system. Ann Allergy Asthma Immunol. 2003;90:59-63.
7. Sears MR, Greene JM, Willan AR, Taylor DR, Flannery EM, Cowan JO, et al. Long-term relation between breastfeeding and development of atopy and asthma in children and young adults: a longitudinal study. Lancet. 2002;360:901-7.
8. Illi S, von Mutius E, Lau S, Bergmann R, Niggemann B, Sommerfeld C, et al. Early childhood infectious diseases and the development of asthma up to school age: a birth cohort study. BMJ. 2001;322:390-5.
9. Stein RT, Sherrill D, Morgan WJ, Holberg CJ, Halonen M, Taussig LM, et al. Respiratory syncytial virus in early life and risk of wheeze and allergy by age 13 years. Lancet. 1999;353: 541-5.
10. Mallol J, Andrade R, Auger F, Rodríguez J, Alvarado R, Figueroa L. Wheezing during the first year of life in infants from low-income population: a descriptive study. Allergol Immunopathol (Madr). 2005;33:257-63.
11. van Merode T, Maas T, Twellaar M, Kester A, van Schayck CP. Gender-specific differences in the prevention of asthma-like symptoms in high-risk infants. Pediatr Allergy Immunol. 2007; 18:196-200.
12. Ball TM, Castro-Rodriguez JA, Griffith KA, Holberg CJ, Martinez FD, Wright AL. Siblings, day-care attendance, and the risk of asthma and wheezing during childhood. N Engl J Med. 2000;343:538-43.
13. Holberg CJ, Wright AL, Martinez FD, Morgan WJ, Taussig LM. Child day care, smoking by caregivers, and lower respiratory tract illness in the first 3 years of life. Group Health Medical Associates. Pediatrics. 1993;91:885-92.
14. Park JH, Gold DR, Spiegelman DL, Burge HA, Milton DK. House dust endotoxin and wheeze in the first year of life. Am J Respir Crit Care Med. 2001;163:322-8.
15. Gold DR, Burge HA, Carey V, Milton DK, Platts-Mills T, Weiss ST. Predictors of repeated wheeze in the first year of life: the relative roles of cockroach, birth weigth, acute lower respiratory illness, and maternal smoking. Am J Respir Crit Care Med. 1999;160: 227-36.
16. Custovic A, Simpson BM, Simpson A, Kissen P, Woodcock A; NAC Manchester Asthma and Allergy Study Group. Effect of environmental manipulation in pregnancy and early life on respiratory symptoms and atopy during first year of life: a randomised trial. Lancet. 2001;358:188-93.

17. Remes S, Castro-Rodriguez JA, Holberg CJ, Martinez FD, Wright AL. Dog exposure in infancy decreases the subsequent risk of frequent wheeze but not atopy. J Allergy Clin Immunol. 2001;108:509-15.

18. Kummeling I, Thijs C, Stelma F, Huber M, van den Brandt PA, Dagnelie PC. Diphtheria, pertussis, poliomyelitis, tetanus, and Haemophilus influenzae type b vaccinations and risk of eczema and recurrent wheeze in the first year of life: the KOALA Birth Cohort Study. Pediatrics. 2007;119:e367-73.

19. Chong Neto HJ, Rosario N, Dela Bianca AC, Solé D, Mallol J. Validation of a questionnaire for epidemiologic studies of wheezing in infants. Pediatr Allergy Immunol. 2007;18:86-7.

20. Dela Bianca AC, Wandalsen GF, Miyagi K, Camargo L, Cezarin D, Solé D, et al. Prevalência de sibilância em lactentes: proposta de protocolo internacional de estudo. Rev Bras Alergia Imunopatol. 2007;30:94-100.

21. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Matinez F, et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. Eur Respir J. 1995;8:483-91.

22. Chong Neto HJ, Rosário NA, Solé D, Mallol J. Prevalence of recurrent wheezing in infants. J Pediatr (Rio J.). 2007;83: 357-62.

23. Fagan JK, Scheff PA, Hryhorczuk D, Ramakrishnan V, Ross M, Persky V. Prevalence of asthma and other allergic diseases in an adolescent population: association with gender and race. Ann Allergy Asthma Immunol. 2001;86:177-84.

24. Benício MH, Ferreira MU, Cardoso MR, Konno SC, Monteiro CA. Wheezing conditions in early childhood: prevalence and risk factors in the city of São Paulo, Brazil. Bull World Health Organ. 2004;82:516-22.

25. Stark PC, Burge HA, Ryan LM, Milton DK, Gold DR. Fungal levels in the home and lower respiratory tract illnesses in the first year of life. Am J Respir Crit Care Med. 2003;168: 232-7.

26. Tsuchiya LR, Costa LM, Raboni SM, Nogueira MB, Pereira LA, Rotta I, et al. Viral respiratory infection in Curitiba, Southern Brazil. J Infect. 2005;51:401-7.

27. Castro-Rodríguez JA, Holberg CJ, Wright AL, Martinez FD. A clinical index to define risk of asthma in young children with recurrent wheezing. Am J Respir Crit Care Med. 2000;162: 1403-6.

28. Kuschnir FC, Alves da Cunha AJ. Environmental and socio-demographic factors associated to asthma in adolescents in Rio de Janeiro, Brazil. Pediatr Allergy Immunol. 2007;18: 142-8.

29. Anderson, HR, Bailey PA, Cooper JS, Palmer JC, West S. Medical care of asthma and wheezing illness in children: a community survey. J Epidemiol Community Health. 1983;37:180-6.

Correspondence:
Herberto José Chong Neto
Av. República Argentina, 2964
CEP 80610-260 - Curitiba, PR - Brazil
Tel.: +55 (41) 3360.1800, ramal 6216
Fax: +55 (41) 3363.0436
E-mail: h.chong@uol.com.br