Respiratory Symptoms or Signs on the Day of the Study Alter Pulmonary Function in Teenagers†

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Pulmonary function variables (forced expiratory flows and vital capacity, static lung volume, alveolar N₂ slope, closing volume and closing capacity) were compared in a group of 10–16 year old children with (n = 65) and without (n = 440) symptoms or signs of mild acute respiratory infection ('common cold'). Symptomatic children had a significant impairment of forced expiratory vital capacity and flows, with no change in static volumes, alveolar N₂ slopes and closing volumes. The effect was present only in boys (in whom RV/TLC and phase III slope were borderline abnormal), was more evident in older children (13 to 16 years) and was independent of the smoking habits or the presence of chronic respiratory symptoms. The results are in favour of a predominant involvement of upper airways, but signs of lower airways dysfunction are present in boys and in children 13 to 16 years old.

Respiratory symptoms questionnaires and pulmonary function tests are basic tools in the epidemiology of non-specific respiratory diseases.¹ The association between the presence of chronic respiratory symptoms and pulmonary function impairment is a classical notion.² In contrast, the effect of the presence of acute respiratory symptoms on lung function measurements is less well documented, as acute symptoms are not recorded by the standard respiratory symptoms questionnaires. A 'common cold' causing cough on the day of the examination was recently reported to induce a significant decrease in one second forced expiratory volume in a group of otherwise healthy Paris workers by Neukirch *et al.*³ We report the effect of acute respiratory symptoms or signs on pulmonary function in a group of children and adolescents in Lorraine, France.

SUBJECTS

The French Social Security system offers its affiliates a free medical check-up every five years in a network of Centres of Preventive Medicine spread over the country. The Vandoeuvre-Nancy Centre, in oper-

ation since 1969, covers about three million inhabitants. Following a geographical rotating system, a letter is addressed to each family explaining the importance of a complete medical check-up for the detection of inapparent diseases in their early phase. For those accepting the offer, an appointment is arranged and questionnaires on health status are mailed for self-completion. The families (including children over four years old and adults up to 60 years) attend the Centre twice. At the first visit (lasting half a day) further questionnaires are completed with the aid of an interviewer, anthropometric measurements are obtained, clinical physiology (auditive, ocular, cardiovascular, respiratory) measurements are made and venous blood is drawn for laboratory tests. At a second visit, two weeks later, the families meet a Centre physician for a physical examination, comments on the biological tests and a general conclusion about their health status.

In order to study the determinants of pulmonary function in children and adolescents in north-eastern France, parents were offered supplementary pulmonary function testing for children* in the 10 to 16 year age range between May and November 1983. This six-month period was deliberately chosen as the invited population came from a region with no atmospheric

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* Pulmonary function was not included in the routine battery of tests for this age group.

pollution. We selected children in this age range since they were old enough to cooperate in a complex respiratory manoeuvre, but unlikely to have become active smokers. The names of the children were taken sequentially from the Centre of Preventive Medicine computer list with a limit of 10 children per half day; between 5 and 20 children were examined daily. The purpose of the study was briefly explained to the parents and to the children in order to obtain informed consent and optimal cooperation. The study protocol was approved by the Committee of Ethics in Medical Research of the University Hospital and Centre for Preventive Medicine. A total of 684 subjects were examined, but the results for the first 149 (seen between 20 May and 11 June 1983) had to be deleted because of repeated technical failure of the spirometric semi-automated module. Thereafter, a computerized spirometer was satisfactorily used. Of the 535 children seen between June and November 1983, 14 were excluded because of incomplete medical history or for various clinical reasons (obesity, epilepsy, neuromuscular disorders), leaving 521 children. Fifteen of these were unable to perform the forced expirogram correctly, so that 506 subjects were included in the study.

METHODS

The study protocol consisted of a questionnaire (filled in by interviewing one parent), a forced expiration test and a single-breath nitrogen (SBN₂) washout test. We used the Children's Questionnaire recommended by the American Thoracic Society Epidemiology Standardization Project⁴ which was designed for self-completion by a parent or for personal interview. Although no physical examination was done, at the time pulmonary function testing was performed the child was asked if he had had a 'cold' (running or blocked nose, sore throat, cough) during the last 2-3 days and the presence of respiratory signs (rhinorea, hoarse voice, cough) was noted. The child was further invited to cough and the observer noted the result as 'loose' or 'dry'.⁵

The forced vital capacity (FVC), one second forced expiratory volume (FEV₁), peak expiratory flow (PEF), maximal mid-expiratory flow (MMF) and the forced expiratory flows (FEF) at 75-50 and 25% (to be expired) FVC were measured with an electronic spirometer (SPIROMATIC, Constructions L. Martin SA). A Fleisch n° 3 pneumotachograph measured the expired flow; the output was electronically linearized to 16 l.s⁻¹; volume was obtained by integration. The flow and volume signals were fed into a micro-computer (Apple II, Cupertino, California) which stored

the results together with the subject identification data and computed the predicted values. The system met the ATS Standards on Spirometry; calibration was done twice daily with a 3 litre syringe. At least three flow-volume curves were obtained; the best values were recorded for FVC, FEV₁ and PEF, while the FEF were calculated on the curves with the largest sum FVC plus FEV₁. The results were expressed in ml BTPS and in % of the predicted values obtained from the equations of Zapletal *et al.*⁷

The SBN₂ test was done using a computerized assembly as previously described.⁸ The expired volume (Fleisch n° 1 pneumotachograph + integrator) and N₂ concentration measured at the mouth (Hewlett-Packard 47302 A analyser) were fed into a micro-computer (Apple II) which calculated the alveolar (phase III) nitrogen slope (P III, %N₂.l⁻¹), the closing volume, expressed in ml BTPS and in % of vital capacity (CV/VC, %), the total lung capacity (TLC) and residual volume (RV) from the alveolar dilution equation⁹ and the closing capacity (CC, sum of CV and RV, expressed in ml and in % of TLC). The pneumotachograph-integrator was calibrated twice a day with a 1-litre syringe. The N₂ analyser had its zero level set with pure oxygen, the upper point of the scale was set on ambient air FN₂ adjusting for temperature and humidity and the linearity was checked with high-precision N₂ + O₂ mixtures. The subject performed at least two trials, preceded by a full inspiration and separated by a three minute pause; the expired vital capacity had to be within 13% of the separately measured FVC^{10,11} and the expiratory flow was kept below 0.5 l.s⁻¹. The result reported is the arithmetic mean of 2 or 3 trials. The inspiratory and expiratory valves were driven by the computer program, the respiratory flows and volumes were displayed on a screen so that the technician giving the test could concentrate on coaching and encouraging the child. Despite this, the number of failures was notably larger than for the forced expiration, only 415 children satisfactorily completing the SBN₂ test.

STATISTICAL METHODS

The association between binary data was assessed by the χ^2 test. Analysis of variance and the Student 't' test were used for comparing means of different groups.¹²

RESULTS

The information on respiratory symptoms or signs at the time of the study was not recorded for one child, so that the results for 505 children (240 girls) are presented: 65 children had respiratory symptoms or signs when tested; 7 of them had symptoms (cough with

TABLE 1 Anthropometric data (mean $\pm$ standard deviation)

	Boys		Girls	
	Present (n = 46)	Absent (n = 219)	Present (n = 19)	Absent (n = 221)
Acute respiratory infection				
Age (years)	12.92 ± 1.55	13.07 ± 1.64	12.81 ± 1.78	12.97 ± 1.70
Height (cm)	153.9 ± 11.8	154.6 ± 12.4	151.4 ± 8.6	152.8 ± 9.6
Weight (kg)	42.65 ± 10.74	43.52 ± 11.17	43.71 ± 9.91	44.02 ± 10.32

sputum) or signs (loose cough, fever) of lower airways involvement, while in the other 58 the symptoms (nasal obstruction, nasal discharge, sneezing, sore throat) were limited to the upper airways, thus corresponding to an abortive or mildly severe 'common cold'.¹³ A preliminary analysis indicated no difference for functional indices (eg FVC 103.1 ± 6.5 versus $102.1 \pm 10.6\%$ predicted for children with lower and upper airway involvement) between the two subgroups and we decided to combine them.

Among the 65 children with an acute respiratory infection (ARI) at the time of the study 46 (ie more than two-thirds) were boys; the association between presence of ARI and male sex was significant ($\chi^2 = 10.01$, $p < 0.01$). Age, height and weight (Table 1) did not differ significantly between the two groups in either sex.

For the sake of brevity, only results expressed in per cent of predicted values are reported for spirometry and forced flows. Boys with ARI had significantly lower FEV, FEV₁, PEF, MMF and FEF_{50%} as compared to those without; no difference was found in girls (Table 2).

ARI did not influence static lung volumes, distribution of inspired gas or small airways closure, with the exception of a slightly significant increase in the RV/TLC ratio and phase III N₂ slope in boys (Table 3).

Looking for the influence of age, we separated the children in two subgroups at age 13 (Table 4); again, no anthropometric differences were found between children with and without ARI (Table 4).

When the results of ventilatory function variables of boys were analysed by age, although some effect was present in subjects under 13, the differences were larger and statistical significance was reached (for FEV_{1.0}, MMF and MEF) in boys aged 13 to 16 years (Table 5). MEF_{50%} was 15.3% lower than predicted in boys with ARI—a difference significant at the 1% level (Table 5).

A higher proportion of children with chronic respiratory symptoms among the subgroup with ARI could

have influenced the results. We therefore excluded the subjects with a history of chronic cough, sputum production or wheeze, and repeated the analysis of pulmonary function. Thirty-nine children had acute symptoms or signs being otherwise asymptomatic; the proportion of boys (27 versus 12 girls) was still significantly increased ($\chi^2 = 7.20$, $p < 0.007$). The ventilatory function was decreased again for children with ARI; the differences between the mean values of functional indices were the same, the lower number of subjects limited the statistical power.

Among the SBN₂ variables, only P III was just significantly altered in children with ARI after excluding children with chronic respiratory symptoms (1.19 ± 0.50 versus 1.05 ± 0.39 , $p < 0.05$).

Finally, we repeated the analysis after excluding the children who smoked; the results (47 children with ARI versus 301 children without) did not differ from those presented in Tables 2 and 3.

DISCUSSION

This study indicates significant impairment of pulmonary function in children with symptoms or signs of acute respiratory infection confirming and extending previous findings in children¹⁴ and adults.³ Standard questionnaires (practically all derived from the original British MRC Questionnaire on Respiratory Symptoms¹⁵) are used to define chronic bronchitis, asthma and related conditions.¹⁶ Only chronic symptoms are recorded, however, by these questionnaires; in epi-

TABLE 2 Spirometry and forced expiratory flows (% of predicted, mean $\pm$ SD)

	Boys		Girls	
	Present (n = 46)	Absent (n = 219)	Present (n = 19)	Absent (n = 221)
Acute respiratory infection				
FVC	99.8* ± 9.4	103.5 ± 10.2	108.1 ± 9.6	108.5 ± 11.2
FEV _{1.0}	100.5* ± 10.7	105.0 ± 11.0	106.2 ± 10.5	107.2 ± 12.3
FEV _{1.0} /FVC	100.7 ± 6.2	101.5 ± 5.8	98.4 ± 7.4	98.9 ± 5.8
PEF	100.4** ± 15.6	107.5 ± 16.0	114.3 ± 16.9	116.2 ± 18.1
MMF	91.5* ± 18.9	99.7 ± 21.2	101.5 ± 21.6	103.9 ± 20.8
FEF _{75%}	91.2 ± 15.1	96.6 ± 17.7	102.5 ± 16.9	107.9 ± 19.1
FEF _{50%}	86.5*** ± 18.5	97.8 ± 20.7	102.1 ± 20.9	105.8 ± 21.7
FEF _{25%}	86.3 ± 23.2	89.3 ± 24.2	102.8 ± 27.5	103.1 ± 26.7

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

TABLE 3 Lung volumes and intrapulmonary distribution of ventilation (mean $\pm$ SD)

Acute respiratory infection	Boys		Girls	
	Present (n = 42)	Absent (n = 482)	Present (n = 15)	Absent (n = 176)
TLC, ml	3740 ± 954	3948 ± 963	3609 ± 819	3546 ± 758
RV, ml	692 ± 197	692 ± 220	673 ± 229	662 ± 187
RV/TLC, %	18.6* ± 3.0	17.5 ± 2.8	18.4 ± 2.9	18.6 ± 3.0
Phase III, % N ₂ -I ⁻¹	1.16* ± 0.48	1.01 ± 0.39	1.02 ± 0.26	1.13 ± 0.43
CV, ml	183 ± 97	182 ± 73	137 ± 90	144 ± 71
CV/VC, %	5.93 ± 2.30	5.79 ± 2.07	4.54 ± 2.28	5.03 ± 1.95
CC, ml	848 ± 262	860 ± 245	749 ± 258	775 ± 220
CC/TLC, %	22.6 ± 3.5	21.8 ± 3.2	20.3 ± 3.3	21.8 ± 3.5

* $p < 0.05$

demiological studies on lung function acute respiratory symptoms should not be present at the time of study, although this is rarely specified.

Acute respiratory infections in children represent a most important public health problem.¹⁷ Practically all are of viral origin; with the exception of adeno- and herpes viruses (containing DNA) all the other viruses causing ARI contain ribonucleic acid (RNA).^{13,18} Although various viruses can elicit ARI of variable severity, the more severe forms of infection are due to influenza, respiratory syncytial and adenoviruses, while milder forms are mostly due to coronavirus, parainfluenza and rhinoviruses.^{13,18,19} Some authors divide ARI into upper and lower respiratory tract infections; we choose to follow Crofton and Douglas¹³ who recognize six clinical pictures (the coryzal, pharyngeal, pharyngoconjunctival, influenza, herpangina,

and croup syndromes) and four severity categories (abortive, mild, moderate, and severe colds).

The effect of acute respiratory infections on lung function was not the primary objective of our study; in fact, the survey was scheduled for summer and early autumn, with the hope of avoiding the viral epidemics of the cold season. As the first outbreak of infection occurred, we recorded the presence of symptoms in order to exclude these children for the analysis. When a second outbreak appeared we decided to analyse the subgroup with respiratory symptoms or signs as it comprised a considerable number of children. No attempt was made to identify the virus (viruses) responsible for the infection. However, in only 7 of the 65 children studied did the clinical picture correspond to a moderately severe 'common cold'.¹³ Various pulmonary function disturbances have been documented in moderate or severe ARI due to adenovirus,²⁰ respiratory syncytial or influenza viruses;^{21,22} for the sake of brevity the present discussion will be limited to the effects of less aggressive viruses. Also, we will mainly discuss the results of *naturally acquired infections in healthy children* or adults; the results of *experimental infections*, the consequences of *vaccinations* with live attenuated viruses, and those of ARI in *subjects with chronic lung diseases* will be only briefly mentioned.

Picken *et al*²³ were the first to report pulmonary function changes during an upper respiratory tract infection. The serial study of 12 healthy subjects suggested the involvement of 'small airways' (frequency-dependence of dynamic compliance) 4–8 weeks after the start of the infection, with a return to normal after an additional four weeks. In a follow-up study of 18 healthy adults Cate *et al*²⁴ recorded pulmonary function during 24 illness episodes caused by eight rhinovirus strains. While no consistent effects on ventilatory function were found, these authors noticed a significant decrease in steady-state diffusing capacity—a finding attributed by them to ventilation inhomogeneity due to bronchiolitis. The study by

TABLE 4 Anthropometric data by age group

Age group (years)	Boys				Girls			
	10–13		13–16		10–13		13–16	
Acute respiratory infection	Present (n = 26)	Absent (n = 101)	Present (n = 20)	Absent (n = 118)	Present (n = 11)	Absent (n = 112)	Present (n = 8)	Absent (n = 109)
Age (years)	11.71 ± 0.72	11.55 ± 0.83	14.48 ± 0.72	14.38 ± 0.84	11.44 ± 0.75	11.52 ± 0.88	14.71 ± 0.72	14.46 ± 0.84
Height (cm)	147.1 ± 8.0	145.6 ± 7.9	162.6 ± 10.1	162.2 ± 10.3	147.3 ± 5.9	146.7 ± 8.2	157.2 ± 8.4	159.1 ± 6.3
Weight (kg)	36.16 ± 6.16	36.51 ± 7.28	51.10 ± 9.50	49.52 ± 10.40	38.72 ± 7.06	37.77 ± 7.57	50.56 ± 9.15	50.45 ± 8.70

TABLE 5 Ventilatory function in boys, by age group (% pred., mean $\pm$ SD)

Age group	10-13 years		13-16 years	
	Present (n = 26)	Absent (n = 101)	Present (n = 20)	Absent (n = 118)
Acute respiratory infection				
FVC	99.8 ± 8.3	103.3 ± 9.5	99.8 ± 10.8	103.6 ± 10.7
FEV _{1.0}	101.9 ± 8.8	104.5 ± 10.5	98.6* ± 12.6	105.4 ± 11.3
FEV _{1.0} /FVC	102.1 ± 4.9	101.3 ± 5.8	98.9 ± 7.1	101.7 ± 5.7
PEF	99.0 ± 16.2	105.4 ± 14.2	102.3 ± 14.4	109.2 ± 17.1
MMF	92.7 ± 16.9	97.4 ± 20.4	89.7* ± 21.42	101.7 ± 21.6
FEF _{75%}	89.8 ± 11.3	96.4 ± 16.6	93.2 ± 19.1	96.8 ± 18.5
FEF _{50%}	87.9 ± 17.4	95.3 ± 19.9	84.6** ± 19.5	99.9 ± 21.1
FEF _{25%}	88.6 ± 21.9	85.2 ± 22.8	83.3 ± 24.4	92.8 ± 24.8

* $p < 0.05$; ** $p < 0.01$

Fridy *et al.*²⁵ included 52 subjects, 22 of whom returned for serial studies of pulmonary function during and after a mild viral respiratory illness. A complete battery of pulmonary function tests was used (static lung volumes, closing volume, air- and helium-flow-volume curves); the pulmonary function changes, suggesting peripheral airways obstruction, occurred only in smokers, and persisted for several weeks. Using experimental rhinovirus infection in healthy volunteers, Blair *et al.*²⁶ demonstrated the greater sensitivity of frequency-dependence of dynamic compliance which became abnormal when closing volume, maximal expiratory flows, specific conductance were unchanged. For Bush *et al.*²⁷ the most sensitive test was the volume of isoflow, and the methacholine response became positive in the three (out of seven) subjects developing lower airways and systemic symptoms. An increase in bronchial reactivity is in agreement with clinical data²⁸ showing that more than half of rhinovirus infection episodes are associated with wheezing in children and adults. Airway hyperreactivity may be the consequence of sensitization of airway epithelial receptors after mucosal cell damage, of a diminished adrenergic response of bronchial smooth muscle, or of histamine release secondary to virus infection.²⁹ The subject remains controversial, however, as negative results have also been recently reported.^{30,31}

The only study of pulmonary function in normal children with upper respiratory infections was done in Chapel Hill, North Carolina, by Collier *et al.*¹⁴ A total of 55 children aged 2.5 to 11 years were followed for a

mean duration of two years, yielding 617 'well' and 237 'illness' observations. Lung function tests comprised spirometry (including forced expiratory flows) and static lung volumes (helium dilution); the observed lung function values were adjusted (by sex) for height and clinical status (normal or upper respiratory illness). Adjusted mean values of FVC, FEV₁, PEF, MMF, and FEF_{50%} decreased during upper respiratory illness, the differences between the mean values of the 'illness' and 'well' observations were not significant in children over seven years of age. In younger children, FVC, FEV₁, PEF and FEF_{50%} showed significant difference in girls, while only FVC and PEF did so in boys. TLC and the functional residual capacity did not differ in any sex-age group. In the present study, age, height and weight were not significantly different in children with and without ARI allowing the comparison of absolute values of lung function results. The presence of an ARI was significantly associated with male sex, and pulmonary function was impaired in boys but not in girls.

This finding suggests that *male gender increases vulnerability* for respiratory disease not only in adults,³² but also in children. Most ventilatory function indices were decreased in boys with ARI. The differences between means ranged from 3-4% for FVC and FEV₁ to more than 10% for FEF_{50%} ($p < 0.001$). We were somewhat surprised to find a non-significant difference for FEF_{25%}, as this index is in principle more sensitive to early airflow limitation.³³ Our results confirmed the lack of sensitivity of this index for detecting abnormality during ARI in children^{14,21} and adults;³ this is attributable in part to the high coefficient of variation. In the children studied by us the differences in the whole group were exclusively due to impairment of lung function in boys. The sex difference observed was not due to statistical factors (lower inter-subject variability in boys) but to the absence of any effect of

TABLE 6 Spirometry and forced expiratory flows in children without chronic respiratory symptoms (mean $\pm$ SD, % of predicted)

	Acute respiratory infection		
	Present (n = 39)	Absent (n = 331)	Significance (p)
FVC	101.7 $\pm$ 10.6	106.1 $\pm$ 11.2	<0.02
FEV _{1.0}	102.4 $\pm$ 10.8	106.6 $\pm$ 11.7	<0.03
FEV _{1.0} /VC	100.8 $\pm$ 5.1	100.6 $\pm$ 5.6	ns
PEF	107.1 $\pm$ 15.6	112.8 $\pm$ 17.5	<0.05
MMF	96.0 $\pm$ 17.2	102.8 $\pm$ 20.3	<0.05
FEF _{75%}	97.1 $\pm$ 14.4	103.4 $\pm$ 19.2	<0.05
FEF _{50%}	92.1 $\pm$ 17.8	102.8 $\pm$ 21.0	<0.002
FEF _{25%}	90.9 $\pm$ 22.2	98.1 $\pm$ 35.9	ns

ns = not significant

infection in girls (Table 2). Our results differ from those of Collier *et al.*¹⁴ who reported significant differences in girls, but are in agreement with other studies indicating that airways are relatively narrower in young boys compared to those of girls.³⁴ Moreover, increased reactivity in the lung periphery of male as compared to female dogs was reported from the Johns Hopkins Medical Institutions.³⁵ A narrowing of airways is expected to have a greater effect on airway resistance or forced flows the smaller the baseline diameter is. Contrary to this prediction, and to the results of Collier *et al.*,¹⁴ we found the differences in ventilatory function to be significant in older boys (Table 5). Although we find no obvious explanation for this, it should be stressed that the comparison between this study and that of Collier *et al.* is limited by several important differences. First, their study was a prospective longitudinal one, each child having several measurements done; they were able to statistically validate minimal differences in pulmonary function (eg 50 ml or 50 ml s⁻¹). Second, their children were much younger than those studied by us (2.5 to 11 years old). Third, 66% of their children were black, and racial differences in the reaction to virus infection may exist.

In our study, lung volumes and distribution of ventilation were less influenced by ARI, confirming the negative results of Collier *et al.*¹⁴ There was one exception to this, however. In boys, a slight increase of the RV/TLC ratio accompanied a marginally significant increase of phase III slope (Table 3). Although minor, these changes are of interest because the same two variables were altered (borderline statistical significance) in a group of asymptomatic adults with a history of recent acute respiratory infection.^{36,37} An increase in RV and in P III slope was reported by Coates *et al.*³⁸ after experimental iv infusion of saline in man; this suggests that peripheral airway obstruction (revealed by hyperinflation and altered distribution of ventilation) accompanies minimal increases in interstitial lung fluid. Closing volume and closing capacity proved to be of no value in detecting abnormality, in agreement with a previous report on passive exposure to tobacco smoke.³⁹ The impairment of pulmonary function variables in children with ARI was not due to the presence of chronic respiratory symptoms, since the results were unchanged (with unavoidable loss of statistical significance) when the analysis was restricted to the 39 children without chronic symptoms (Table 6). Tobacco smoking did not interact with the influence of ARI since the exclusion of 18 children who smoked among the symptomatic group had no influence on the results. Atmospheric pollution is known to increase the incidence of respiratory infections in children;⁴⁰ this influ-

ence was excluded in the present study as the children came from a non-polluted area. Other factors, which were not controlled in this analysis, are represented by parental respiratory symptoms,⁴¹ parental smoking,^{41,42} socioeconomic and educational level⁴³ or housing conditions.⁴⁴

Can a mild ARI have consequences in the long term? In contrast to the severe infections due to aggressive viruses (respiratory syncytial virus, adenovirus) whose sequels are well known,⁴⁵ the reported regression of physiological disturbances over 3 to 6 weeks^{13,23} allows this question to be answered in the negative, at least for healthy subjects. The effect of repeated (even mild) 'insults' of the respiratory tract by 'benign' viruses in children with chronic respiratory disease remains to be assessed.

In conclusion, we have found consistent, statistically significant, impairment of ventilatory function in a group of 10–16 year old children with mild acute respiratory infection on the day of the study. Functional disturbances were present among boys, but not girls; they were more important in older children (13 to 16 years). The effect was independent of tobacco consumption and of the presence of chronic respiratory symptoms. Ventilatory defects did not fit the classical obstructive type, since both FEV₁ and FVC were decreased in equal proportions, the FEV₁/FVC ratio being unchanged. Taken as a whole, the tests of 'small airway dysfunction' were less sensitive as compared to spirometry in detecting abnormality due to ARI, with the exception of a borderline increase in the RV/TLC ratio and of phase III N₂ slope in boys. As functional signs of large (eg PFR, FEV₁) and small airways (RV/TLC, P III) co-exist, it can be concluded that the whole respiratory tract is functionally affected by an ARI.

The present results support the proposal of the GAP Conference Committee⁴⁶ that paediatric reference standards for lung function tests should be obtained on children with *no present acute respiratory symptoms and no history of an upper respiratory tract infection during the preceding weeks*.

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