Environment and Respiratory Diseases in Childhood:

The Italian Experience

CLAUDIA GALASSI, MD, ANNIBALE BIGGERI, MD, GIOVANNINO CICCONE, MD, FRANCESCO FORASTIERE, MD, AND THE SIDRIA PHASE 1 COLLABORATIVE GROUP*

To estimate the prevalence of respiratory disorders in children, and to investigate the roles of potential environmental risk factors, including exposure to outdoor air pollution, a large multicenter, population based survey (SIDRIA) was conducted in Italy in 1994–1995. The study enrolled more than 40,000 children. Results allowed international comparisons of the prevalences of asthma and allergies in childhood in the framework of the ISAAC (International Study of Asthma and Allergies in Childhood) study, and supplied further evidence of the adverse respiratory effects of many environmental factors. The methods and main findings of the SIDRIA study are presented, focusing on the role of outdoor risk factors. *Key words*: children/adolescents; respiratory disorders; bronchitis; asthma; air pollution.

INT J OCCUP ENVIRON HEALTH 2005;11:103-106

large multicenter, population-based survey, SIDRIA (Studi italiani sui disturbi respiratori L nell'infanzia e l'ambiente) [Italian Studies on Respiratory Disorders in Children and the Environment], was conducted in Italy in 1994-1995. The SIDRIA Collaborative Group was assembled to provide data on the prevalence of respiratory disorders and allergies in Italian schoolchildren for comparison with prevalences in other countries. The standardized methodology proposed by the International Study of Asthma and Allergies in Childhood (ISAAC)^{1,2} was used. SIDRIA contributed to the ISAAC study with a large sample of children, and widely extended the objective of ISAAC, since it was aimed at evaluating the effects of several potential environmental risk factors, including outdoor air pollution, on children's respiratory health.

The results of the SIDRIA project have been extensively published^{3–10}; in this paper, we summarize the main results, with emphasis on the associations we found between exposure to traffic pollution and respiratory disorders.^{3–5}

RESEARCH METHODS

The SIDRIA study was carried out between October 1994 and March 1995 in ten centers of Northern and Central Italy varying in size, latitude, climate, and level of urbanization. Prevalence and the role of air pollution were investigated in two separate phases of the study.

Prevalence

The study population consisted of a random sample of children aged 6-7 years and adolescents aged 13-14 years from ten areas of Northern and Central Italy. Each center was required to sample at least 1,000 subjects for each age group. Standardized self-administered questionnaires were used. In addition to the ISAAC items on asthma, rhinitis, and eczema, the health sections of the questionnaires elicited: 1) medical diagnosis of asthma; 2) occurrence of other respiratory symptoms; 3) medical history of episodes of respiratory diseases that had occurred during the first two years of life. The questionnaires also included other sections on many known or suspected risk factors for respiratory diseases, including passive smoking exposure, characteristics of the household, and exposure to road traffic. Questions about traffic included: 1) a subjective evaluation of the traffic density in the zone of residence (absent, low, intermediate, high); and 2) the frequency of passing buses and lorries in the street of residence. Separate validation studies of traffic indicators in two cities, using different approaches,⁴ supported the absence of an important reporting bias .

A questionnaire was distributed to the children and adolescents at school and filled in at home by their parents; a shorter questionnaire, mainly on current respiratory symptoms and on personal smoking habits, was filled in directly by adolescents at school.

The sample analyzed included more than 40,000 children and adolescents, from 547 schools. The response rate was very high, more than 90% in all centers (Table 1).

Address correspondence and reprint requests to: Giovannino Ciccone, MD, CPO Piemonte, ASO S. Giovanni Battista (Molinette) —Torino, Via Santena, 7, 10126—Torino, Italy; telephone: 011-6336857; fax: 011-6334664; e-mail: <gianni.ciccone@cpo.it>.

^{*}The members of the SIDRIA Phase 1 Collaborative Group are listed at the end of the article.

TABLE 1 Characteristics of the SIDRIA Centers and Response Rate by Respondent (Parents or Adolescents) and Age Group, Prevalence Study, 1994–1995*

						Questionnaires Completed by					
	Inhabitants (Thousands)		Schools with Children Aged		Parents of Children Aged				Adolescents		
					6–7 Yr		13–14 Yr		13–14 Yr		
			6–7 Yr	13–14 Yr	No.	(%)	No.	(%)	No.	(%)	
Torino	935	7,221	14	14	1,428	(96.9)	1,211	(95.0)	1,242	(97.5)	
Milano	1,383	7,611	30	35	3,616	(96.1)	3,349	(96.1)	3 <i>,</i> 373	(96.8)	
Cremona	155	188	23	24	1,392	(100.0)	1,198	(99.0)	1,201	(99.3)	
Trento	450	72	—	87			4,287	(91.4)	4,426	(94.4)	
Emilia Romagna	3,924	177	74	55	4,472	(98.2)	3,976	(98.0)	3,961	(97.7)	
Firenze-Prato	814	954	15	11	1,138	(96.2)	1,144	(94.5)	1,171	(96.7)	
Empoli-Fucecchic	221	249	22	12	1,434	(91.0)	1,016	(94.9)	1,046	(97.7)	
Siena	250	66	—	19			1,162	(95.9)	1,181	(97.4)	
Viterbo	125	75	13	12	1,230	(97.5)	886	(91.9)	922	(95.6)	
Roma	2,688	1,793	46	41	4,027	(94.5)	3,181	(90.2)	3,323	(94.2)	
Total			237	310	18,737	(96.3)	21,410	(94.3)	21,846	(96.2)	

*Modified from SIDRIA Collaborative Group.²⁹

†Inhabitants/km².

Air Pollution Study

To evaluate the association between mean annual levels of pollutants (NO_2 , SO_2 , and PM_{10}) and prevalence of respiratory symptoms, 10,106 children aged 6 to 11 years attending 46 primary schools located within 1 km from 29 air-pollution–monitoring stations were enrolled in the study. The 29 monitoring stations, located in 22 cities belonging to ten areas of Northern and Central Italy, routinely monitored a wide range of air pollutants. Mean levels of NO_2 were also measured using passive samplers placed in school yards. The survey was conducted in the same period as the prevalence investigation, applying the same method.² Symptomatic children were compared with a common reference group of children with a negative history of respiratory disorders.

ASTHMA AND ALLERGIES

The prevalences of asthma and asthmatic symptoms among Italian children are reported in Table 2. The observed prevalence of asthma of about 9% among both children and adolescents was one of the lowest among the countries participating to the ISAAC study. No large variations were observed among the different Italian areas. As regards the other allergic disorders, the prevalence of symptoms of eczema dermatitis was 6% for both age groups, while 6% of the children and 14% of the adolescents were found to have hay fever, again quite low prevalences compared with those observed in other countries.

RESPIRATORY HEALTH AND TRAFFIC AIR POLLUTION

The adverse health effects of exposure to air pollutants have been extensively described.¹¹ Although the pathogenic mechanism is still not completely understood, exposure to outdoor air pollution has been associated with both acute and chronic adverse health effects, including lung cancer.^{12–15} Particulate matter, ozone, and nitrogen oxides are at present the pollutants of most concern.

Children represent a population particularly at risk from air pollution, since they spend many hours outdoors, frequently performing intense physical activities, and because of a potential higher sensitivity during development.¹⁶ In the SIDRIA study,³ environmental data indicated that the highest concentrations for most pollutants were recorded in the three largest cities covered by the survey (Torino, Milano, and Roma), with average yearly concentrations of 50–70 µg/m³ for particulate matter with mean aerodynamic diameter < 10 µm (PM₁₀) and 80–100 µg/m³ for NO₂. It should be

TABLE 2 Prevalences of Wheezing and Asthma among Children 6–7 Years Old by Latitude and Level of Urbanization, SIDRIA Prevalence Study, 1994–1995

	Lati	tude	Urbanization			
	North Italy	Central Italy	Metropolitan Areas	Urban Areas	Rural Areas	
Wheezing (lifetime)	24.1	24.8	23.3	26.0	25.5	
Wheezing (last 12 months)	7.5	8.0	7.4	7.6	8.3	
Asthma (lifetime)	7.8	10.5	10.2	8.1	7.3	

noted, however, that mean annual levels of PM_{10} were, in the urban environments covered by the survey, frequently above the annual limit specified by the EU for PM_{10} , i.e., 40 µg/m^{3.17} On the other hand, SO₂ levels in the studied areas were very low.

A strong association between the prevalence of current persistent phlegm and mean annual levels of NO₂ was found, with an increase of 25% with an increase of 21 µg/m³ NO₂ (passive samplers), or 28% with an increase of 37.5 µg/m³ NO₂ measured by the monitoring stations. The frequency of persistent phlegm was also associated with PM₁₀, with a 66% increase for the higher quartile of exposure (60–101 µg/m³) compared with the lowest (20–35 µg/m³).³ Associations for NO₂ and PM₁₀ of the same magnitude were found among children reporting both current asthmatic and bronchitic symptoms: this finding suggests a greater susceptibility of these children (with more severe respiratory conditions) to the effects of air pollution.

An association between SO_2 exposure and asthmatic symptoms was found, but only at the highest levels of exposure (fourth quartile, 13–21 µg/m³).

In summary, mean annual levels of air pollution, measured by means of monitoring stations, were found to be associated with current adverse respiratory conditions of children, and particularly with the more severe conditions.

The use of estimates of exposure to air pollutants derived from monitoring stations, although common in epidemiologic studies, could lead to a misclassification of children's exposures, given the wide variations in time and activity patterns. Furthermore, the method used to measure suspended particles were not standardized across the different areas during the study. Thus, some degree of misclassification of exposures, especially to particulate matter, of the children enrolled in the air pollution study is probable; however, such misclassification would have biased the odds ratios toward the null value, and therefore the observed associations would be likely to be underestimated.

The effects of exposure to air pollution from road traffic was evaluated individually, by means of the information supplied by parental questionnaires regarding the perception of traffic in the area of residence.^{4,5} For children living in the largest cities, a strong and consistent association was found between the prevalences of several current respiratory disorders and the indicator of frequency of lorry traffic in the street of residence, while a weak association was observed for the generic indicator of "traffic" in the zone of residence; this finding suggests a specific and more dangerous effect of diesel exhaust (diesel is the fuel used in heavy vehicles in Italy). Other epidemiological studies have also found that chronic respiratory symptoms and reduced lung function in children are more strongly associated with lorry traffic rather than with automobile traffic, supporting the hypothesis of greater danger from

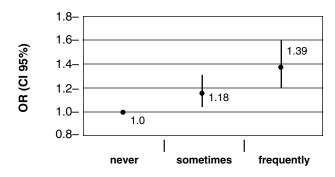


Figure 1—Truck traffic in the streets of residence in the three larger cities included in the SIDRIA-study (Torino, Milano, and Roma), and prevalences of both asthmatic and bronchitic symptoms (test for linear trend: p = 0,000). SIDRIA prevalence study, 1994–1995.

diesel exhausts.^{18–22} Emissions of fine particles are much higher in diesel exhausts than in gasoline exhausts.²³ Fine particles are considered to be toxic to the respiratory mucosa, causing inflammatory reactions and predisposing to infections of the lower respiratory tract,^{24,25} and experimental studies suggest that diesel particles may enhance immunologic responses to allergens.^{26,27}

As in the air pollution study, the strongest associations were found for current bronchitic symptoms (persistent cough or phlegm), and for the association of asthmatic and bronchitic symptoms (Figure 1), again supporting the hypothesis of increased susceptibility of the sicker children to environmental pollution.

An association was also found for respiratory disorders in the first two years of life, with a stronger effect on lower respiratory tract infections (bronchitis, pneumonia, bronchiolitis) rather than on asthmatic symptoms.

The results are concordant with the findings of recent investigations aimed at disentangling the effects on children of long-term exposures to air pollutants at the community level, which have shown consistent associations with the prevalence and/or incidence of bronchitis, cough, and deficit in lung function; these effects seem to be stronger in asthmatic children.

CONCLUSIONS AND FUTURE PERSPECTIVES

The results of the SIDRIA study confirm the findings of many other investigations, suggesting that air pollution from traffic, and particularly from heavy vehicles, even at the concentrations at present experienced in Western countries, is harmful to the respiratory health of children.

In 2002, a second population-based survey (SIDRIA Phase 2) was begun to improve national estimates of the prevalences of respiratory disorders, as well as to evaluate variations in time trends of the respiratory disorders in children and to identify environmental factors that may relate to such variations. Analysis of the data is ongoing, but preliminary results²⁸ have shown that the percentage of children living in areas of high traffic density is not substantially reduced compared with that found in the first phase of the study. From a public health point of view, the problem is particularly relevant, given the high proportion of children exposed, and supports the need for stricter regulation of traffic in residential areas.

The members of the SIDRIA Phase 1 Collaborative Group are: G. Ciccone, A. Camerlengo, M. Bugiani, P. Dalmasso, F. Faggiano, T. Fatur Volante, C. Magnani, P. Natale, P. Piccioni (Torino); L. Bisanti, V. Gianelle, F. Rusconi, S. Sideri (Milano); S. Piffer, F. Filippetti, E. Nava (Trento); M. Biocca, E. Canossa, B. Cavalchi, D. Cervino, S. Cattani, E. De'Munari, M. Deserti, S. Ferro, F. Fortezza, F. Frigo, C. Galassi, M. Martini, P. Mazzali, L. Paterlini, R. Sogni, M. Zanini (Emilia Romagna); E. Chellini, L. Agati, E. Barletta, A. Biggeri, G. Bini, M. Bini, L. Chetoni, D. Grechi, A. Seniori Costantini (Firenze); E. Renzoni, P. Sestini (Siena); G. Viegi (Pisa); F. Forastiere, N. Agabiti, G. Corbo, V. Dell'Orco, S. Mallone, C. Micera, P. Palermo, G. Pallotti, G. Piras, R. Pistelli (Roma); E. Salera (Frosinone); D. Argentini, G. Chiarucci (Latina).

References

- 1. ISAAC Steering Committee. Wordwide variations in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. Lancet. 1998;351:1225-32
- 2. ISAAC Steering Committee. Wordwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood. Eur Respir J. 1998;12:315-35.
- AAVV. SIDRIA. Studi Italiani sui Disturbi respiratori nell'Infanzia e l'Ambiente. Regione Emilia Romagna/CDS. Dossier n.45. Ravenna, Italy, 2000. [In Italian]
- Ciccone G, Forastiere F, Agabiti N, et al. Road traffic and adverse respiratory effects in children. Occup Environ Med. 1998;55:771-8.
- 5. Ciccone G; Gruppo collaborativo SIDRIA. Studi Italiani sui Disturbi Respiratori nell'Infanzia e l'Ambiente. [Features of traffic near houses and respiratory damage in children: the results of the SIDRIA (Italian Study on Respiratory Problems in Childhood and the Environment)]. Caratteristiche del traffico nei pressi dell'abitazione e tipo di danni respiratori in età pediatrica. I risultati di SIDRIA. Ann Ist Super Sanita. 2000;36:305-9. [In Italian]
- Agabiti N, Mallone S, Forastiere F, et al. The impact of parental smoking on asthma and wheezing. SIDRIA Collaborative Group. Studi Italiani sui Disturbi Respiratori nell'Infanzia e l'Ambiente. Epidemiology. 1999;10:692-8.
- SIDRIA Collaborative Group. Asthma and respiratory symptoms in 6-7 year-old Italian children: gender, latitude, urbanisation and socio-economic factors. Eur Respir J. 1997; 10:1780-6.
- Renzoni E, Forastiere F, Biggeri A, et al. Differences in parentaland self-report of asthma, rhinitis and eczema among Italian adolescents. SIDRIA collaborative group. Studi Italiani sui Disordini Respiratori dell' Infanzia e l'Ambiente. Eur Respir J. 1999;14:597-604.
- Rusconi F, Galassi C, Corbo G, et al. Risk factors for early, persistent, and late-onset wheezing in young children. SIDRIA Collaborative Group. Am J Respir Crit Care Med. 1999;160:1617-22.
- Forastiere F, Pistelli R, Sestini P, et al. Consumption of fresh fruit rich in vitamin C and wheezing symptoms in children. Thorax. 2000; 55:283-8.
- 11. Brunekreef B, Holgate ST. Air pollution and health. Lancet. 2002;360:1233-42.

- WHO. Regional Office for Europe, Copenhagen, Denmark. Air Quality Guidelines for Europe. Regional Publications, European Series, M. 91, 2000.
 Pope CA 3rd, Burnett RT, Thun MJ, et al. Lung cancer, car-
- Pope CA 3rd, Burnett RT, Thun MJ, et al. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. JAMA. 2002; 287:1132-41.
- Hoek G, Brunekreef B, Goldbohm S, Fischer P, van den Brandt PA. Association between mortality and indicators of trafficrelated air pollution in The Netherlands: a cohort study. Lancet. 2002;360(9341):1203-9.
- Nafstad P, Haheim LL, Oftedal B, et al. Lung cancer and air pollution: a 27 year follow up of 16 209 Norwegian men. Thorax. 2003; 58:1071-6.
- Gauderman WJ, Gilliland GF, Vora H, Avol E, Stram D, McConnell R, Thomas D, Lurmann F, Margolis HG, Rappaport EB, Berhane K, Peters JM. Association between air pollution and lung function growth in southern California children: results from a second cohort. Am J Respir Crit Care Med. 2002; 166:76-84.
- European Commission. Council directive 1999/30/EC of April 1999 relating to limit values for sulphur dioxide, nitrogen dioxide and oxide of nitrogen, particulate matter and lead in ambient air. Official Journal of the European Commission (26.6.1999). L 163/41-60.
- Weiland SK, Mundt KA, Ruckmann A, Keil U. Self-reported wheezing and allergic rhinitis in children and traffic density on street of residence. Ann Epidemiol. 1994;4:243-7.
- Duhme H, Weiland SK, Keil U, et al. The association between self-reported symptoms of asthma and allergic rhinitis and-self reported traffic density on street of residence in adolescents. Epidemiology. 1996;7:578-82
- Van Vliet P, Knape M, De Hartog J, Janssen N, Harssema H, Brunekreef B. Motor vehicle exhausts and chronic respiratory symptoms in children living near major freeways. Environ Res. 1997;74:122-32.
- Brunekreef B, Janssen NAH, de Hartog J, et al. Air pollution from truck traffic and lung function in children living near motorways. Epidemiology. 1997;8:298-303.
- Janssen NA, Brunekreef B, van Vliet P, et al. The relationship between air pollution from heavy traffic and allergic sensitization, bronchial hyperresponsiveness, and respiratory symptoms in Dutch schoolchildren. Environ Health Perspect. 2003; 111:1512-8.
- Hildeman LM, Markowsky GR, Cass GR. Chemical composition of emissions from urban sources of fine organic aerosol. Environ Sci Technol 1991; 25: 744-59.
- Committee of the Environmental and Occupational Health Assembly of the American Thoracic Society. Health effects of outdoor air pollution (part I). Am J Respir Crit Care Med. 1996; 153:3-50.
- Committee of the Environmental and Occupational Health Assembly of the American Thoracic Society. Health effects of outdoor air pollution (part II). Am J Respir Crit Care Med. 1996;153:477-98.
- Nordenhall C, Pourazar J, Ledin MC, Levin JO, Sandstrom T, Adelroth E. Diesel exhaust enhances airway responsiveness in asthmatic subjects. Eur Respir J. 2001;17:909-15.
- Diaz-Sanchez D, Penichet-Garcia M, Saxon A. Diesel exhaust particles directly induce activated mast cells to degranulate and increase histamine levels and symptom severity. J Allergy Clin Immunol. 2000;106:1140-6. ID: 89.
- Galassi C, Ciccone G, Forastiere F, Biggeri A, and Sidria-2 Collaborative Group. Exposure to environmental risk factors and respiratory disorders in children: preliminary results of a large survey in Italy (SIDRIA-2° phase). Epidemiology, 2003, 14(5 suppl), S82.
- SIDRIA Collaborative Group. La frequenza dell'asma pediatrico in diverse aree italiane. Epidemiol Prev. 1997;21:235-42. [In Italian]