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Environmental pollution and asthma

S. BALDACCI, A. SCOGNAMIGLIO, G.VIEGI

Environmental Pulmonary Epidemiology Group, CNR Institute of Clinical Physiology, Pisa, Italy

INTRODUCTION

The current knowledge on epidemiology and epidemiological determinants of asthma is not yet complete. In particular, some of the study results are contrasting, mainly due to the lack of an exact definition by which morbidity for asthma can be identified and measured.

On the other hand, also the data on the mortality trends in different countries are a confirmation of the lack of a standardization of asthma-measurement criteria[1].

In the document "Bronchial asthma: the dimension of the problem", released on January 2000 by the World Health Organization on the Web page (http://www.who.int/inf-fs/En/fact206.htlm), it is reported that asthma deaths worldwide have reached the amount of over 180 000 per year. In Switzerland about 8% of the population suffers from asthma against the 2% of 25-30 years ago. In Germany

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about four million asthmatics are estimated, while in Western Europe, according to the UCB Allergy Institute in Belgium, asthma has doubled in the last 10 years. In the United States asthma has increased more than 60% since the early eighties and deaths have doubled up to 5 000 per year. In Japan there are about 3 000 000 asthmatics, of which 7% have severe and 30% moderate asthma. In Australia one child every six under age 16 suffers from asthma.

In the last years, the interest towards bronchial asthma by the scientific community in the respiratory disease field has increased. As a matter of fact, recent accomplishments lead to believe that the occurrence of asthma has been increasing in the developed countries, even if the range of prevalence rates described is quite broad[2].

Although it is diffcult to define asthma for epidemiological studies, the prevalence of asthma, assessed by the definitions reported by the questionnaire of "diagnosed asthma in life" and "wheezes lifetime", is already high and still increasing[2].

Despite many notions on the pathogenesis, the aetiology of the disease is not yet completely known and there is no unanimous consensus on how to justify the increase of disease cases reported in the last years and their different geographical distribution.

There are contrasting opinions also on the distribution and the meaning of some of the epidemiological determinants of the disease. It is not known if the asthma mortality rate is increasing everywhere or perhaps only in some countries (for example in New Zealand and in Australia where even an "asthma epidemic" has been mentioned) and if this increase is connected to an improper use of drugs or to an increasing prevalence of the disease. Recent studies seem to indicate an increase of the prevalence rates of asthma world-wide[2,3].

In 1996 the American Thoracic Society published a document on the health effects of outdoor air pollution which has allowed to draw a picture on the scientific knowledge regarding such issue[4,5]. This document has been somewhat updated in 1999[6]. Since the second half of this century, following three serious acute episodes that yielded an appreciable increase in the mortality rate of the population involved, air pollution has begun to be considered a serious problem of public health, and as such, it has become object of numerous epidemiological and experimental studies[7].

Most of the diseases that are affected by air pollution can also be caused by other factors such as cigarette smoking and by occupational exposure to dusts and fumes[8].

Therefore, the epidemiological branch that covers air pollution is specific as to variable of exposure but not as to kind of health effects. For obvious reasons, the respiratory system is the first target for health effects caused by air pollution.

The epidemiological field that is interested in air pollution has characteristics that distinguish it from other epidemiological fields, such as ubiquity of the exposure, difficulty in the evaluation of individual exposure and episodes of acute exposure.

Exposure to air pollution is ubiquitous since it cannot be avoided once the pollutants have been emitted or have been formed in the air. Thus, one of the problems in epidemiological studies is finding subjects that haven't been exposed and could represent the control group[9].

Also when the concentrations of outdoor environmental pollutants are more or less uniform through time and space (which rarely occurs), evaluation of individual exposure is made difficult by the fact that people spend most of their time in indoor environments (home, workplace and public areas). Therefore, in air pollution epidemiology, the knowledge of the sources of indoor pollution is particularly important for defining total human exposure[9].

The health effects provoked by air pollution can be acute or chronic. In some circumstances, there can be accidents (for example in industrial plants) with out-spills of large quantities of air-dispersed pollutants that can determine the exposure to high concentrations of outdoor air pollutants[10].

Unfavorable climatic conditions for the dispersion of airborne pollutants constantly emitted by sources such as vehicular traffic, industrial plants, and domestic heating, are among the most common causes of these episodes of high concentrations of air pollution in the outdoor environment. A period of high air pollution concentrations, due to adverse weather conditions, goes usually on for some days and is defined as an "episode of air pollution".

Episodes of air pollution can happen in winter or in summer and are characterized by different pollutants. High concentrations of photochemical pollutants, such as ozone, can happen during the summer. Pollution from increasing use of fossil fuels for heating is typical during the winter[9].

As mentioned above, aside from air pollution, other factors, such as tobacco smoke, occupational exposure to dusts or to irritant gases and exposure to indoor allergens, can cause respiratory diseases. Hence, it is necessary to pay special attention in controlling confounding factors[10].

In the last decades, the concentration of air pollution components such as SO_2 and total suspended particulate has decreased in many areas of Europe. This is due to the accomplishment of actions realized with the aim to reduce emissions and to variations in energy productions for industrial processes and heating. Instead, levels of other pollutants as NO_2, O_3 and fine and ultra-fine corpuscolate particles have increased during the same period, especially due to the vehicular traffic intensification. In the past, epidemiological studies in Europe evaluated the health effects produced by high concentrations of pollutants as SO_2, total suspended particulate, and "black smoke". More recent studies reported the effects of air pollution on respiratory symptoms and pulmonary function at lower levels, sometimes below the attention threshold set by regulations, suggesting the existence of atmospheric pollution effects below those levels so far considered safe for health[11].

ASTHMA AND "OUTDOOR" POLLUTION

Recent estimations indicate that in the whole world about 100 to 150 millions of people, roughly the equivalent of the people of the Russian federation, are affected by asthma and this number is increasing (http://www.who.int/inf-fs/en/fact206.htlm). There has been a generalized increase of the prevalence rates of respiratory problems among children in the whole industrialized world. In the 1983-1993 decade there has been a fivefold upraise of the number of English families that have asked for invalidity indemnity because of children affected by severe asthma[7].

Recently, increases in deaths and morbidity from asthma have been observed in the United States[12] and in other industrialized countries in which also an increase of the severity of the disease has been reported.

The exacerbations of asthma have been connected to the increases of environmental concentration of ozone[13] and of particles[7] with an estimated increase of 3% in asthma attacks associated to a $10\mu g/m^3$ increase in PM_{10} (Table I)[14].

A larger demand for medicines against asthma has been connected to the increased of the levels of particulate in a cohort of asthmatics in Utah and in a group of asthmatics in The Netherlands (panel study), with an estimated effect of a 2.9% increase in the use of bronchodilators associated to a $10\mu g/m^3$ increase in PM_{10}[14].

While individual predisposition towards developing atopy and asthma is genetically determined, the substantial geographical variations in the prevailing of such factors are due to environmental factors[15]: exposure to outdoor pollutants[7], exposure to indoor pollutants[16], tobacco smoke[7], alergens (in particular, the house-dust mite)[17]. Smoke of the mother during pregnancy has been connected to a reduced pulmonary development in children and to the persistence of asthma in adulthood[18]. Smoking adults are more frequently sensitized to new occupational allergens[7]. A recent survey conducted in

TABLE I

Combined effect estimates of daily mean particulate pollution

	% Change in health indicator per each 10μg/m^3 increase in PM_{10}
Increase in daily mortality	
Total deaths	1.0
Respiratory deaths	3.4
Cardiovascular deaths	1.4
Increase in hospital usage (all respiratory)	
Admissions	0.8
Emergency department visits	1.0
Exacerbation of asthma	
Asthmatic attacks	3.0
Bronchodilators	2.9
Emergency department visits*	3.4
Hospital admission	1.9
Increase in respiratory systems reports	
Lower respiratory	3.0
Upper respiratory	0.7
Cough	1.2
Decrease in lung function	
Forced expired volume	0.15
Peak expiratory flow	0.08

* One study only
From reference nº14

France, the National Adolescent Health Survey (NAHS), showed that prevalence rates of asthma were higher among boys while a more severe disease was associated with early onset and female sex. No association was found between this disease and puberty[19].

Recently, it is common belief that the increase of the prevalence rate of asthma is due to the variations in lifestyle throughout the last decades which could have led to a more susceptible population[3]. These variations include: changes in the diet, particularly a minor uptake of anti-oxidants that could enhance susceptibility to infections and inflammation of airways; reduction of the size of families with children exposed to a minor number of viral infections in early age, thus possibly being completely protected by infections to the extent of not enabling their immune system to develop correctly. Indeed, epidemiological evidence suggests that having older brothers or sisters is protective with respect to atopy and this seems to depend on the effect of the respiratory infections that detour the immune response from the pattern involving T helper lymphocytes subtype 2 (Th2) towards the one of Thl[15].

It seems unlikely that variations in reporting or diagnosing the disease could be responsible of the increased incidence of respiratory problems observed in recent years in all the industrialized world. Between 1976 and 1987, the severe asthma attacks have more than doubled in England and in Wales (from 10,7 to 27,1 every 100 000 patients a week), with the highest increase among children[7].

Other allergy diseases as hay fever are becoming more common in industrialized societies, particularly in the urban areas[20]. There is some evi-

dence indicating that hay fever symptoms are exacerbated when the concentration of pollutants are high[20] and that vehicular exhaust can enhance sensitivity towards pollen[21]. These observations suggest that atmospheric pollution plays a considerable role in the exacerbation of the disease in asthmatics, and that it can contribute to the overall morbidity due to asthma and to respiratory allergies[20]. A European multi-center epidemiological study is evaluating the short term effects on health using the methodic of time series (APHEA). From the results published so far it shows that, as in the Unites States, in the European cities participating to the study there is an association between the daily levels of particulate, NO_2 and SO_2 and exacerbation of asthma[22].

Contrasting evidence regarding the relationship between air pollution and respiratory disease is shown by three German cross-sectional studies to which about 9 000 adults (age 20-44, in the European study ECRHS) resident in Erfurt (East Germany) and Hamburg (West Germany), 8 000 school-age children (age 9-11) resident in Lipsia (East Germany) and in Monaco (West Germany), and about 2 000 children in preschool-age (age 6) resident in the polluted areas and in the control areas of East and West Germany[23,25], respectively, have participated. Higher prevalences of bronchitis, tonsillitis, recurring cold, and chronic cough have been estimated in East Germany characterized by higher pollution levels (high concentrations of particulate and SO_2). Instead, higher prevalence of asthma, rhinitis, allergic sensitivity and hyperresponsiveness have been observed in West Germany. However, wheezes have resulted to have a greater prevalence in West Germany considering the study on the adult population, while considering the study on children ages 9-11, they have shown to have a higher prevalence in East Germany. Vehicular emission concentrations have resulted greater in West Germany than in East Germany. However, it seems unlikely that this greater prevalence of allergic respiratory conditions is imputable to vehicular emission alone, but rather to other factors associated to the lifestyle of western societies that should be considered[3]. A population-based study realized by the SIDRIA Collaborative Group in children living in some areas of northern and central Italy has shown an increased occurrence of current respiratory symptoms in subjects exposed to the exhausts from heavy vehicular traffic[26].

Epidemiological investigations are little diffused because, beside the acquisition of a scientific standardized methodology, they also require a considerable expense of personal energies and of time. However, if accomplished, they would offer precious results both in terms of broadening scientific knowledge and of providing useful data for health and economical territory programming.

In Italy, two large perspective studies have been conducted: one in the rural area of Po Delta (3,289 subjects, aged 8-64, investigated from 1980 to 1982 in the first phase; 2,841 subjects aged 8-73, investigated since 1988 to 1991 in the second phase) and one in the urban area of Pisa (3,866 subjects, aged 5-90, investigated from 1985 to 1988 in the first phase; 2,841 subjects, aged 8-97, investigated from 1991 to 1993 in the second phase)[27].

When comparing air quality in the two areas, total suspended particulate and SO_2 reached higher levels in the urban area; indeed, in regard to the two second phases, the mean annual values of particulate and of SO_2 were 99 and 24 $\mu g/m^3$ in Pisa area, but 54 and 8 $\mu g/m^3$ in Po Delta area.

The results obtained up to date have shown a higher prevalence of respiratory symptoms and diseases (especially of rhinitis and wheezes) and of bronchial reactivity in the urban area of Pisa compared with that of Po Delta. Considering the two cross-sectional phases in the rural and urban areas, Fig.1 shows that there has been a general increase of respiratory symptoms/diseases in non smokers aged 25-64 and, in particular, of wheezes and rhinitis in the second studies; dyspnea has re-

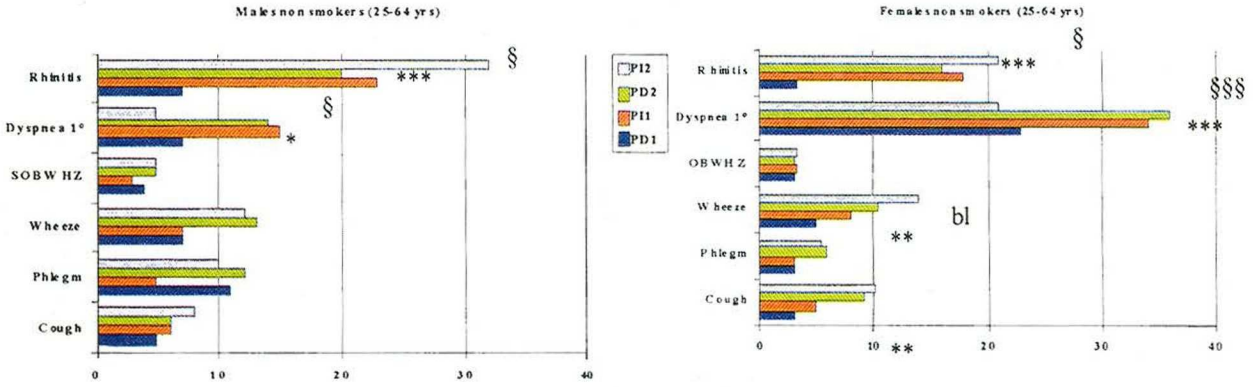

Fig. 1 – Cross-sectional comparison of prevalence rates of respiratory symptoms/diseases in non-smokers, 25 to 64 years, participating in the first and second surveys of Po Delta (PDl, PD2) and of Pisa (PI1, PI2). $^{*}p<0.05$; $^{**}p<0.01$; $^{***}p<0.001$ (PD1 vs PI2); § $p<0.05$; §§ $p<0.01$; §§§ $p<0.001$ (PD2 vs PI2).

markably increased only in Po Delta area. For what concerns the skin tests to the most common allergens, high frequencies and of the same entity (about 1/3 of population) have been shown both in Pisa and Po Delta areas[9]. As to the determination of the total serum IgE, in the Po Delta area mean values of 40KU/L have been found, together with a relationship to gender (higher values in males), positive skin test to common aeroallergens, active and passive smoking and work exposure to dusts, chemical compounds and gas[28]. In Latium, Forastiere et al have suggested that living in an area with higher pollution levels, also if within the standards of air quality, can increase bronchial reactivity independently from atopy, asthma and diameter of the airways[29]. Zwich et al[30] and Wang et al[31] have found a greater prevalence of bronchial hyperresponsiveness in children exposed to high concentrations of ozone and incinerator pollutants, respectively.

A common limit to most of the studies is represented by the fact that the studies cover large areas in which the individual level of exposure is defined by residence in the area. That, on one hand, leads to a potential misclassification of the subjects which reduces the power of the studies and the capability to spot risks that are not particularly high, and, on the other hand, it does not allow to put into evidence dose-response relations since all the residences in a given area are considered equally exposed. Therefore, there is a need for studies in which individual exposure can be defined with accuracy through complex geo-temporal elaboration of data from the monitoring of air quality. Moreover, there is a need to better identify the subjects affected by asthma, creating subgroups based on onset age, persistence of symptoms, pulmonary function in early months of life, sensitivity spectrum towards allergens. Indeed, it is possible that the relationship between disease and environment could be different in these subgroups and that these variations should be taken into account in the future studies.

In conclusion, epidemiologic evidences that support the existence of a relationship between en-

vironmental pollution and airways diseases are in agreement for what concerns bronchitic manifestations, while there are discrepancies for what concerns the relationship between environmental and asthma or symptoms and functional conditions correlated to asthma. There is, however, agreement in believing that air conditions and the concentration of some pollutants can be the cause of a worsening of the symptoms in asthmatic subjects. The relationship between the incidence of asthma in susceptible subjects, but still not ill, and the conditions of air pollution is yet to be clarified.

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O asmático e a escolha da profissão

MÁRIO CHAVES LOUREIRO*

INTRODUÇÃO

A asma brônquica (A.B.) é uma afecção de natureza inflamatória, complexa, repetidamente agudizada e autolimitada na maioria das vezes e outras (menos) potencialmente crónica.

Resulta da interacção entre o meio-ambiente e o epitélio respiratório, este "marcado" pela genética, e é mediada por reacção imunológica adequada a cada circunstância.

Sendo assim, natural é que o asmático deva acautelar o estilo de vida pessoal, familiar e profissional, evitando expôr-se aos factores ambientais, que sabe serem-lhe desfavoráveis. Mas, antes de analisar estes aspectos, visitem-se, sumariamente, as características patogénicas e clínicas da asma e da mediação imunológica, para se enquadrarem os aspectos antes focados. Clinicamente, após contacto com o estímulo indutor a reacção desencadeia-se entre 5 a 15 minutos, dura cerca de 1 hora, podendo autolimitar-se ou não. Secundariamente, pode instalar-se a chamada reacção tardia, que surge 2 a 6 horas após a exposição, podendo manter-se de 12 a 24 horas. Segue-se um período de hiperreactividade das estruturas brônquicas, que por reestimulação específica, inespecífica (irritantes) ou autónoma, pode manter a inflamação.

A reacção inflamatória é imunológica, maioritarimente IgE mediada, mas podendo não o ser, LT dependente ou não, mas sempre eosinofílica e dependente do perfil citoquímico Th_2 (IL_4, IL_5).

Independentemente dos agentes capazes de **induzirem** as crises asmáticas, outros há suficientemente agressivos, para **amplificarem** a reacção inflamatória ou até a desencadearem por mecanismo diverso e, outros ainda, denominados **irritantes**, só por si determinantes para provocarem pelo menos broncoconstrição.

E, sendo a "condição" asmática dificilmente

* Chefe de Serviço de Pneumologia
H.U.C.