Air pollution and respiratory diseases – a problematic risk factor

Poluarea atmosferică și bolile respiratorii – un factor de risc problematic

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Abstract

Pollution was a neglected factor for years in all the research that took in the viewfinder was examined in the risk factors in of respiratory diseases. Considering the concerns of politicians, scientists, doctors, which have intensified upgraded especially after the last climate "summit", "summit" climatological we found it necessary to have a review of the effects of pollution, pathogenic mechanisms of interaction, and some diseases strongly influenced by pollutants such as COPD, asthma, bronchialand bronchial and lung cancer.

Keywords: ***air pollution, respiratory diseases, risk factor***

Rezumat

Poluarea a reprezintat un factor neglijat ani întregi în toate cercetările care au avut în vizor factorii de risc în bolile respiratorii. Având în vedere reluarea preocupărilor politicienilor, oamenilor de știință, a medicilor, actualizate mai ales după ultimul „summit" climatologic am considerat necesar să trecem în revistă efectele poluării, mecanismele patogenice de interacțiune și unele afecțiuni puternic influențate de factorii poluanți precum BPOC-ul, astmul bronșic și cancerul pulmonar.

Cuvinte-cheie: ***poluarea atmosferică, bolile respiratorii, factor de risc***

Air pollution, or "self-pollution" for that matter (people being the main cause of pollution) and its relationship with respiratory and heart diseases is indisputable. Analyzed as a risk factor for respiratory diseases it is second on the list. The epidemiological and therapeutic connections of pollution, as well as the influences as a risk factor, were studied and analyzed much later compared to the main cause of respiratory disease, smoking. In these circumstances a positioning is necessary in relationship with respiratory diseases and also in the Romanian pneumology, especially since several medical associations (most recently the SPLF - the French Language Society of Pneumology, *Société de Pneumologie* de Langue Française), impressed by the great event that took place in Paris (the 21th climate conference of December 10th, 2015), published entire issues in specialized magazines.

General data

Pollutants come from various sources and take different forms, from particles to gases[1]:

1. The particulate matter (PM) (a blend of solid particles and liquid drops floating in the air, emitted by a specific source or formed in complicated chemical reactions in the atmosphere) taken into consideration is the one fluctuating between 0.1-2.5 μm. Some particles are produced by a specific source, while others are formed in complicated chemical reactions in the atmosphere. The range of particulate matter is extremely diverse – fine particles <2.5-0.1 μm; large particles, above 2.5-10 μm; the so-called total particles >15 μm (originating from soil erosions, oceans, volcanoes, forest fires, industrial or household combustion, incinerators, traffic) –, with norms required by the WHO of annual mean concentrations of 10 μg/m^3 for PM_{10} and 10 μg/m^3 for $PM_{2.5}$; and of daily mean concentrations of 50 μg/m^3 for PM_{10} and 25 μg/m^3 for $PM_{2.5}$.
2. SO_2, a colourless gas originating from volcanoes, the industrial or household combustion of fossil material, with an annual level of 24 μg/m^3 or a 10 minute-mean of 500 μg/m^3
3. NO_2, another gas with oxidising properties coming from urban areas, emitted mainly by cars in traffic, with an annual accepted level of 40 μg/m^3 and an accepted 1-hour level of 200μg/m^3
4. O_3, a dangerous oxidising agent released in photochemical reactions between hydrocarbons and nitric oxide with an 8 hours–mean of 100 μg/m^3

The connection between respiratory symptoms and pollutants

An attempt to review all studies conducted over a period of 16 years made by Simon and Chapin[1] began to outline a number of features of the relationship between respiratory symptoms and different pollutants, despite some assessment difficulties related to the multitude of symptomatic evaluation questionnaires used. For the particulate matter, the relationship appears for $PM_{2.5}$ (recognized to penetrate into the small airways), but it is much more evident for PM_{10} when permitted levels are exceeded[2,3]. Newborns and toddlers under two years of age are more sensitive, as are the atopics[4,5,6].

Regarding NO_2, there is a relationship with respiratory symptoms, especially in high traffic areas and areas with petrochemical industrial pollution[7]. The increase of NO_2 levels increases the risk of allergy to domestic animals and of sensitization to pneumoallergens[8].

For ozone things are not as obvious as for other pollutants[1]. Reports show that an increase of ozone level of

50ppb is linked to an increased prevalence of symptoms by 5%, especially in children[9]. It is said that ozone has a paradoxical protective effect, but it seems that this is due more to the reverse connection between NO_2 and ozone, and less to the genuine biological effects of ozone[10].

For SO_2 things are more obvious. The symptoms are much more prevalent in the industrial petrochemical areas[11], with a 40% increase in allergic people, one day after the increase of the level with 40 μg per m^3, and a 125% increase after 5 days of exposure in children with bronchial hyperreactivity and high IgE[12].

Evolution of respiratory pollutants

In 2010 the authors [1] noticed a change in the profile of the pollutants for the last two decades, with decreases of SO_2 and CO, and increases of particulate matter and NO_2 which are in fact markers of car traffic. In 2015[13] an increase of pollutants originating from heating systems (especially PM_{10}), and from exhaust pipes was noticed. Car traffic is still the main source of NO_2 pollution, which was previously decreasing[13].

2/3 of the studies [1] are mainly interested in the effects on children, this concern being generated by the fact that 80% of the pulmonary alveoli are formed after birth, and the lung develops in adolescence, and the prolonged outdoor exposure due to the time spent doing physical activity, often combined with hyperventilation. All of this was to the detriment of the studies done in elderly and adults, which are much fewer.

The evolution of pollution levels in different countries

In developed countries there is a tendency of decrease and slow improvement of the pollutant levels regarding the fine particulate matter $PM_{2.5}$, but the levels are still not within the limits required by the WHO[14]. On the other hand, the global warming will increase the level of ozone during summer, but it will also increase the level of the pollutants due to the increase of forest fires[15]. A rise of the global temperature by 1 degree between 1950 and 2003 resulted in a 2-6 times increase of the risk of forest fires[16]. To that is added the excessive use of air conditioning, and indeed of the electricity often produced in coal plants. Up to 339,000 premature deaths per year are attributed to particulate matter pollution, especially from forest fires[17]. The optimistic prediction on the rise in global temperature due to the greenhouse effect at the end of the century is of 2-3.5 degrees if a decrease of the current emissions level will be achieved, and the pessimistic prediction is of 4-6 degrees, if the emissions levels rise[18].

Pathophysiological mechanisms of action of the pollutants on the respiratory system

The effect occurs mainly on diseases like bronchial asthma, COPD and lung cancer, these being the most studied, but also on outdoor and indoor home exposure. In outdoor exposure, the main reported mechanisms, genetically mediated, are the response to the oxidative stress (with enzymatic changes, cell damage, DNA mutations, alterations of receptors, circulating lipoprotein oxidation), the remodeling phenomenon (with sub-epithelium fibrosis and irreversible bronchial obstruction), the involvement of inflammatory mechanisms with bronchial epithelium injuries and sensitization to allergens (e.g. pollen associated with diesel particles, with ozone, NO_2, SO_2, favors bronchi penetration)[19]. In contrast, in case of indoor exposure the ones that are acting are the allergens, endotoxins, chemicals and especially biomass combustion. The last one acts like the cigarette smoke, inducing the fibronectin production and fibrosis by fibroblasts (causing the non-smoker`s COPD). Actually, in case of bronchial asthma the mechanisms that are boosted by pollution are the ones associated with oxidative stress, whereas in COPD these are secondary and we are talking more about immunological changes[19].

Immediate and remote respiratory effects of pollutants

In recent years they were assessed by new statistical methods and by considering weather conditions (light wind and temperature inversion are conditions favouring the pollutants stagnation in the place where they were produced). The conclusions of the studies were various when it was noticed what is happening on ***short-time***:

- There is a relationship between cough, thoracic crackles, bronchitis and gas pollutants fluctuations, especially in newborns[20], and also with the infectious pathology (bronchitis, bronchiolitis, pneumonia, rhino-sinusitis) in children up to 4 years of age.
- There is a 2-6% increase of the risk of asthma exacerbation when the particulate pollution level increases by 10 μg/m^3. A 6% FEV1 decrease is noticed after 2 hours walks in polluted areas of London[20,21]. In COPD the risk factors related to pollutant presence contribute to hospital admissions due to exacerbations in a percentage of 2% in USA and 1% in China[22].
- There are risk groups with additional mortality induced by pollutants, such as elderly over 65 years, with increases of 1-3% in mortality at the rise of $PM_{2.5}$ levels by 10 μg/m^3, with a 24-48 hours onset delay[23].

On the **long-term**, for outdoor exposure there are more studies regarding the chronic effects, although it is hard to draw a boundary between acute and chronic, and it is even more difficult to define the long-term effects in terms of their visualization[24]. Living in certain French urban areas with high levels of $PM_{2.5}$, NO_2 and SO_2 leads to an increased risk of exercise-induced asthma, allergic rhinitis, allergic sensitization of children[25], and of chronic bronchitis in case of elderly people over 65 years[26]. There is also a risk for people living close to high traffic roads, where a 15-30% increase of asthma cases in children and COPD in adults is recorded[26].

Mortality

According to several studies, a 10 μg/m^3 increase of exposure to PM leads to a 9% increase of the risk of death due to cardio-vascular disease, and a 15-21% increase of the risk of death due to lung cancer[24,27].

Long-term indoor exposure, except for passive smoking, is linked to PM_{10} and $PM_{2.5}$ produced by wood and coal combustion, to NO_2 (gas heating), to volatile organic compounds (household products), and to other products (phtalates, halogen, organic pollutants, polychlorinated biphenols, DDT, dioxins, furans). All of these induce respiratory symptoms, respiratory infections, asthma crisis in children, etc.[24,28], and also approximately 3.4 millions of deaths in adults and children due to respiratory infections, COPD, lung cancer (especially in women exposed to biomass combustion)[24].

The relationship between COPD and different pollutants

Two important factors are outlined here. In developing countries the biomass combustion leads to indoor concentrations high above the values accepted by the WHO of 150 µg/24h, reaching 3000 µg in exposed areas[29]. Thus, 50% of deaths due to COPD and 75% in case of women are caused by this exposure[30]. The effects of these combustions are increased by active smoking, which increases the relative risk in women vs. men by 2.73, even 2.44 in a meta-analysis (4.39 in smokers and 2.66 in non-smokers)[31].

Related to the environment, it has been found that in industrial areas the pollution level is linked to climate fluctuations, the sulphates level, SO_2 (through multiple actions of reducing the respiratory functions, and through defense mechanisms impaired by photochemical oxidants), ozone, and environment temperature[32,33]. Mortality is determined by sulphuric acid levels[34]. Pollution-induced exacerbations are more common in winter, because of the interplay of pollutants and viral infections, because of the pro-inflammatory and bronchoconstrictor effect of pollutants, and because ozone is itself a strong oxidant.

Special attention should be paid to the connection between diesel motor emissions and COPD. The main components of the gas phase of the diesel engine emissions are CO, CO_2, NO, NO_2, aldehydes, SO_2, and aliphatic and aromatic hydrocarbons. Particles are under 0,1 µg. There is a worsening of symptoms, such as cough and chronic expectoration, without evidence of impairment of respiratory function due to methodological limitations of the studies[35]. However, the connection with COPD mortality is demonstrated by two recent studies performed on American railroad employees[36,37]. After adjustments for smoking and ethnicity a significant risk was found. The risk is also linked to the duration of exposure (number of cumulated working years) (relative risk of 1.61-1.67) and increases by 2.5% in each working year.

The relationship between pollutants and lung cancer

The relative risk for the association between diesel particles and lung cancer is 1.5[38]. Two effects, studied in experiments and also reported in humans, are at the origin of that risk: the genotoxic effect and the carcinogenic effect. Chromosomal abnormalities were found in workers exposed to diesel particles[39]. The polycyclic aromatic hydrocarbons (PAH) and nitro-PAH found in the soluble organic fraction of the diesel emissions are producing the genotoxic effect[35,39]. Although enough evidence was found in animal experiments, those proofs are limited in humans. In 1989, the International Cancer Research Center (CIRC – Centre International de Recherche sur le Cancer) placed diesel particles emissions in the 2A category (probable carcinogens for humans)[40]. Things changed in 2012, when CIRC placed the diesel particles in category 1, with certain carcinogenic effect for humans[39], based on recent studies, of which the last was published in 2011[41]. After adjustment for another associated factor, smoking, the relative risk was 1.31[41], but the most important finding of this last study was the reference linked to the dose-response ratio, the exposure duration, and the cumulative exposure index.

The relationship with bronchial asthma

It seems that diesel particles affect and play a role in the occurrence of asthma by two well studied mechanisms (potentiating of allergic response and of the proinflammatory effects)[35]. There is a synergy with respiratory allergens in stimulating the production of IgE by the B lymphocytes[42]. The inflammatory effect materializes in an increased number of inflammatory agents such as neutrophils, platelets in the peripheral blood[43], B lymphocytes, inflammatory mediators (histamine, fibronectin) in the bronchoalveolar lavage fluid and endothelial adhesion molecules in bronchial biopsies. Most of the epidemiological studies are performed on newborns and confirm a 1.3-1.56 relative risk of asthmatic bronchitis[44,45], and 1.59 relative risk of allergic rhinitis.

Conclusions

They are extremely well defined, also as future objectives, in Professor Charpin's article[46], which highlights that in the future we should keep in mind the following aspects:

1. Regarding *measurements:* we need their modeling versus direct multiplication (patient's address, the history and duration of exposure are extremely important).
2. For the *assessment of air quality* in the future we will have to widen the range of measurements for all man-made pollutants, even if some have decreasing levels (SO_2, lead, CO), because their list is extremely long.
3. In the field of *health effects* a change in strategy is required, starting from emissions restrictions of the big polluters in the 70's and focus towards vehicle emissions, with surveillance not only of the short-term effects, but also of the long-term ones, which slowly become more and more important (the relationship with lung development, COPD and lung cancer risk, influence on survival duration).
4. In the *political area* investments in reducing the particulate matter are necessary (the standard for 2020 is the 25 µm particle), with direct effects on the number of productive life years, the mortality levels, etc.

There is also a general issue which should be a primary concern for the coming years. A rigorous epidemiological and metrological methodology is necessary for the next studies, to deepen the knowledge of the relationship between air pollutant exposure and respiratory symp-

toms. The best evidence for this is the over 300,000 participants in the ESCAPE study, which, due to some limitations, did not show a rise of mortality by non-malignant respiratory disease[47]. An important final message about the relationship between pollution and respiratory diseases and more is to never forget that over 50% of the urban population is exposed to notable levels of pollutants, due to the fact that they live at less than 150 metres of roads circulated daily by more than 10,000 vehicles. This generates 15-30% of the new cases of child asthma, and chronic obstructive and coronary diseases in adults over 65 years of age[48]. Perhaps future urban planners and decision makers in urban politics will take in consideration how to reduce exposure in our country. One thing is already certain as it is shown by all the studies: various indispensable measures are urgently required to cover urban planning, transport, energy production, industry, construction and heating of buildings. ■

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