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Analysis of the Known Synergistic Effects of the Exposure to Selected Air Pollutants

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New philosophy of the prognosis of adverse health effects due to the inhalation of air pollutants

(Jozef S. Pastuszka)

While trying to change the philosophy of the prediction of adverse health effects due to the inhalation of polluted air, it should be noted again that in a typical urban environment, the population is exposed to about 200 air pollutants or classes of air pollutants. Therefore, instead of investigating the unique effects of specific pollutants, it has been suggested that it might be more reasonable to assume that it is a mixture of pollutants that might be considered harmful to health (Dominici and Butnett 2003; Moolgavkar 2003; Stieb et al. 2002; Roberts and Martin 2006; Dionisio et al. 2013). Potential interaction among pollutants seems to be a fundamental problem indispensable for explaining the relations between the exposure of people to air pollutants and their

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health condition. However, before any analysis of this problem, some key terms should be precisely defined. According to U.S. EPA Guidance (2000), and supplemented by Mauderly and Samet (2009), the following terms may be introduced:

Additivity: effect of the combination equals the sum of individual effects.

Synergism: effect of the combination is greater than the sum of individual effects.

Antagonism: effect of the combination is less than the sum of individual effects.

Inhibition: a component having no effect reduces the effect of another component.

Potentiation: a component having no effect increases the effect of another component.

Masking: two components have opposite, cancelling effects such that no effect is observed from the combination.

For the prognostic reasons, the development of new models to concurrently estimate the adverse health effects of multiple air pollutants has been identified by statisticians, epidemiologists, and policy makers as an important topic of research (Dominici and Burnett 2003). Another new model provides for identification and estimation of a mixture of pollutants associated with adverse health effects has been also introduced by Roberts and Martin (2006).

Delfino et al. (2010) analyzed the role of the oxidative potential of particle mixtures containing probably hundreds of correlated chemicals. According to their opinion, oxidative potential likely depends on particle composition and size distribution, especially ultrafine particle concentration, and on the transition metals and certain semi-volatile and volatile organic chemicals. This problem needs, of course, advanced future studies using biomarkers of oxidative stress. Delfino et al. (2010) suggest to measure systematic inflammatory and thrombotic mediators in the blood as well as, simultaneously, clinical outcomes to assess the impact of air pollutant-related oxidative stress.

Mauderly and Samet (2009) reviewed selected published literature to determine whether synergic effects of combinations of pollutants on health outcomes have actually been demonstrated. They concluded that the plausibility of synergism among environmental pollutants has been established, although comparisons are limited, and most involved exposure concentrations were higher than typical of environmental pollutants.

Mauderly and Samet (2009) noticed that in the literature the term "synergy" is often used loosely and sometimes applied to any effect of a combination of pollutants that is greater than the effect of one of the components alone. Meanwhile it should be remembered that synergy is strictly defined as occurring if the effect of the combined exposure is greater than the sum of the effects of these two or more individual components of the mixture (see, for example, Mauderly and Samet 2009; USEPA 2000).

While analysing the synergy, another phenomenon should also be mentioned. It sometimes appears during the comparison of the low level of exposure to some air pollutants and unexpected strong health effects. Such phenomenon, related with an exposure to carbon dioxide and nitrogen dioxide has been recently reviewed by Delfino et al. (2010). They indicated that although epidemiologic studies have

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shown associations of cardiovascular morbidity and mortality with ambient CO and NO₂ (Brook et al. 2010; Bhaskaran et al. 2009), concentrations of these gases have been considerably lower in relation to levels causing effects in experimental studies and models. Therefore, Delfino et al. (2010) concluded that it is possible that these gasses serve as surrogates for other causal components from fossil fuel combustion. A recent review also reports a lack of consistent findings in time series studies for the relation of ozone to daily hospital data for myocardial infarction (Bhaskaran et al. 2009; Delfino et al. 2010).

Synergy and other interactions

Synergy and other interactions between human carcinogens

(Jozef S. Pastuszka)

It was mentioned in Chapter 5 that there is a significant synergy phenomenon between the exposure to asbestos and tobacco smoke. Generally, calculation of risk due to inhalation of some, different carcinogenic pollutants, is not easy. Kaldor and L'Abbé reviewed in 1990 the definition of interaction and the theoretical basis for different types of interaction in cancer causation. Actually, their analysis seems to still be absolutely relevant. They concluded that when a mixture of pollutants contains several carcinogens which fall within the same class (according to their physical and chemical properties), and if it appears that individual pollutants from this class have an effect on cancer risk, the carcinogenicity of the mixture could reasonably be expected to be the simple sum of the components' effects. However, if the mixture consists of pollutants from different classes of carcinogens, a multiplicative effect would provide a more appropriate representation of the overall carcinogenicity of the mixture (Kaldor and L'Abbé 1990).

Synergistic effects of biological particles and other air pollutants

(Aino Nevalainen, Martin Täubel and Anne Hyvärinen)

The major part of research that links outdoor biological particles to health are allergological studies connected with pollen and fungal allergens. Otherwise, health effects of exposures to airborne biological agents have mainly been studied in either occupational settings or in indoor environments. Although the research on health effects of atmospheric particulate matter has increased enormously during the last few decades (e.g., Cesaroni et al. 2014), it is evident that biological particles have had no major role in this paradigm. This is interesting, as many health effects have been linked with exposures to both PM and biological particles.

Microbial interactions between fungi and bacteria are a well-known phenomenon in, e.g., biocontrol research (Whipps 2001; Woo et al. 2002). While these interactions are recognized to be extremely complex by microbial ecologists, the paradigm of studies that would reveal the possibly health-relevant interactions is yet to be established. Furthermore, there is a limited amount of knowledge about synergistic health effects linking biological agents to other—non-biological—pollutants. One can expect that in the future, with improved DNA-based methodology for detection and

quantifying biological material, and for better understanding microbial physiology with approaches such as proteomics and lipidomics, this situation will change. As presented before, a causal relationship can only in a few cases be established between a health outcome and a defined biological agent. Usually there is a complex mixture of exposing agents that leads to health symptoms or disease with pathophysiological pathways that are not fully known. This applies, e.g., to indoor environments with damp and mold, where health effects are manifold while exposure levels often remain relatively low, as opposed to occupational settings with very intense exposures. Are such indoor situations examples of synergistic effects of various pollutants? This possibility is often mentioned in the literature but rather in a sense of frustrated discussion than in the form of vigorous efforts to experimentally study such effects.

Mycotoxins have been suggested to potentially cause or contribute to adverse health effects observed in occupants of moisture damaged indoor environments. Toxins are found in such environments but exposure levels are very low and difficult to differentiate from non-damaged indoor environments (Peitzsch et al. 2012). Human studies where exposure to airborne microbial toxins would have been linked to observed health effects are scarce (Kirjavainen et al. 2015; Cai et al. 2011; Zock et al. 2014) and clearly, more such studies are needed.

There is more data on toxins from experimental studies that have used *in vitro* approaches. Using spores and pure toxins of the fungus *Stachybotrys chartarum* and toxin-producing bacterium *Streptomyces californicus*, synergistic interactions were observed as shown with inflammatory markers and cytotoxicity (Huttunen et al. 2004). Kankkunen et al. (2009) concluded that human macrophages sense trichothecene mycotoxins as a danger signal, which activates a number of inflammatory reactions. The toxins gliotoxin and patulin acted synergistically in a so called MIXTOX model, while the combined effect with sterigmatocystin was antagonistic, with switch to synergism if the toxicity of the mixture was mainly caused by sterigmatocystin (Mueller et al. 2013). Neurotoxicity and inflammation caused by the mycotoxin roridin A and the potentiation of the effects by bacterial LPS was documented in a mouse model with intranasal instillation (Islam et al. 2007). As these examples demonstrate, microbial metabolites may have significant potential for adverse health effects both individually and as combinations with other agents. The role of microbial toxins in outdoor particulate exposures is totally unknown today; however, such toxins are also found in the outdoor air (Täubel et al. 2013).

Even if the details of the exposures and development of health effects are poorly known today, there is need for policies that aim to control the observed health effects of environmental stressors. One such stressor that can potentially be avoided is the exposure due to moisture and mold associated with indoor environments.

Recently, the WHO has stated in their guidelines on dampness and mould (WHO 2009) that while causative agents of adverse health effects in damp buildings have not been conclusively identified, excess level of various microbial agents, including mycotoxins, in the indoor environment need to be considered a potential health hazard. For this reason, it is of key importance to prevent or remove microbial growth in response to moisture problems in buildings, which implies excessive microbial proliferation and distribution of microbial spores and fragments, allergens,

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Other interactions between airborne microorganisms and particulate matter

(Jozef S. Pastuszka)

It is interesting that particle exposures also increase the risk for human infection. Recently Ghio (2014) indicated that one of the mechanisms for particle-related infections includes an accumulation of iron by surface functional groups of particulate matter (PM). Besides, air pollution can modify the concentration levels of bioaerosols, as well as their number size-distributions. This applies in particular to the interaction of bacterial aerosol with dust suspended in the air. It is estimated that about 80% of the microorganisms present in the air can be attached to dust particles, and lots of data points to the strengthening of an unfavorable, combined impact on the health of people exposed simultaneously to biological and dust aerosols (Seedorf et al. 1998; Haas et al. 2013). The phenomenon of the attachment of fine particles, including biological particles, to a coarse solid particle is illustrated in Fig. 12-1. This aggregate is surrounded by the bacterial colony developed from one bacterial particle (precisely: one colony forming unit—CFU) collected together with the airborne dust particle.

Recently, Brągoszewska et al. (2013) showed that in the atmospheric air in Gliwice, Poland, concentration of coarse bacterial particles (having the aerodynamic diameter $d_{ac} > 3.3 \mu\text{m}$) was highly correlated with the concentration of coarse

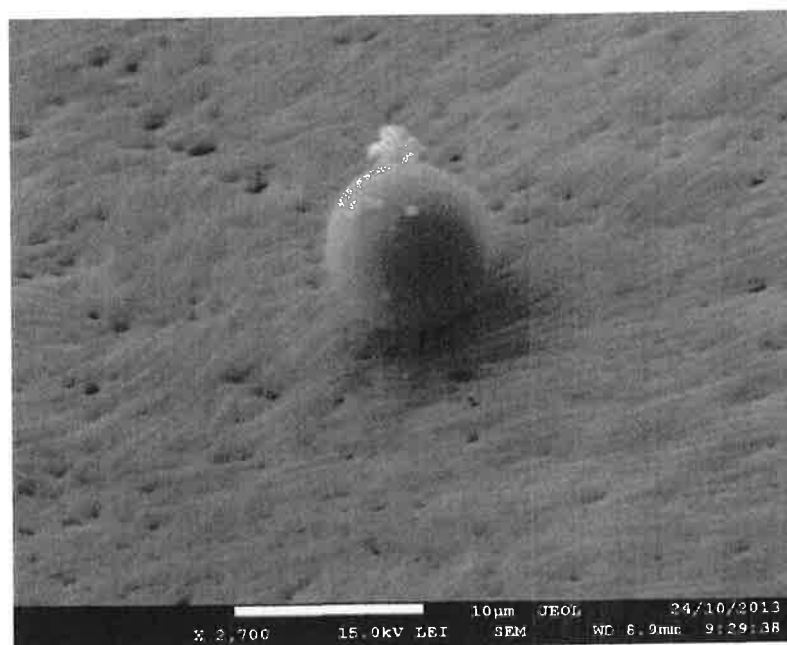


Fig. 12-1. Coarse solid particle collected together with airborne bacteria by using an Andersen 6-stage impactor. This particle is located in the center of a bacterial colony. Micrograph was taken by Ewa Talik, University of Silesia. With permission.

particles of atmospheric particulate matter (Fig. 12-2). Although the mentioned above phenomenon of the attachment of fine bacterial particles to a coarse solid particle can be responsible for this correlation, this problem needs future investigation. The equation of the regression line for the graph in Fig. 12-1 can be assumed as follows, $y = 0.0148 \cdot x + \text{const}$. At the significance level of 0.05, there is a relatively strong correlation between the concentration of coarse bacteria and dust equal to 0.79. It should be noted, however, that this relationship was a preliminary estimate only, and for the higher concentration levels of airborne dust—it probably will not be linear.

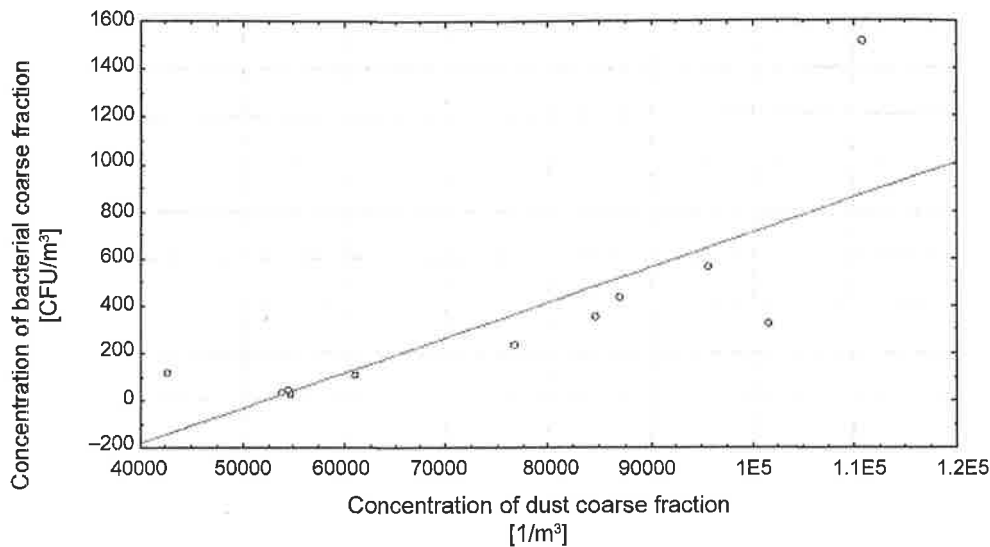


Fig. 12-2. Concentration of the coarse fraction of bacterial aerosol versus number concentration of coarse solid particles in ambient air in Gliwice (Bragoszewska et al. 2013).

Synergy and allergic symptoms

(Jozef S. Pastuszka)

Exposure to environmental substances triggering allergic symptoms of the respiratory tract

The number of registered allergy cases worldwide is increasing each year (Aas et al. 1997; IOM 2000). Although a relatively short time ago the problem of allergy occurred rather rarely, currently most of the population in many regions of the world suffers from it. Due to the fact that this drastic increase of morbidity occurred in a short period of time, genetic changes must be excluded as the reason of increasing cases of allergy, while environmental changes should be considered as one of the important causal factors. This hypothesis is confirmed, among others, by the large geographical variability of the common allergy based asthma symptoms. A map of these symptoms was created within the International Study of Asthma and Allergies (ISAAC). In the report of these studies (ISAAC 1998), the diversity of asthma symptoms in various countries was presented. In Western Europe, asthma occurs as

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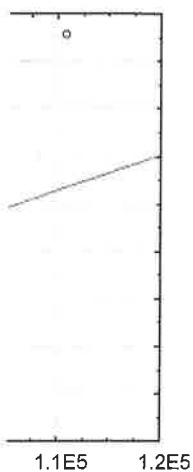
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much as ten times more frequently than in the eastern part of the continent, while the frequency of morbidity is higher in urbanized areas than in agricultural ones. The reason for this state of things is the subject of many speculations. It is assumed that the following factors may be important:

- 1) The so called "western lifestyle"
- 2) Infections during infancy
- 3) Type and range of immunization
- 4) Diet
- 5) Exposure to tobacco smoke (ETS)
- 6) Pets

Although all of the above mentioned factors seem to be important, and especially the exposure to tobacco smoke, or "passive smoking" (Wartenberg et al. 1994; Dayal et al. 1994), the greatest significance is attributed to the relation between the allergens and humidity at home (Bornehag et al. 2001).

The role of indoor air pollution (in rooms) in initiating and intensifying asthma symptoms has been widely discussed by the Institute of Medicine of National Academy of Sciences USA (IOM 2000). The review of this issue was concluded by the statement: "we still do not know whether or to what extent the reported increases in asthma can be attributed to indoor exposures". The authors of the report blame the existing literature data for the state of the art. Scientific articles usually do not discuss the issue of indoor environment (rooms) on an appropriate level and *vice versa*; scientific studies on the indoor exposure do not focus on asthma. As a result, the issues of asthma and the quality of the indoor environment are very poorly related. Because of this, the postulate of the above mentioned report is to initiate extensive interdisciplinary studies on asthma, which should involve not only clinicians, immunologists, and biologists but also engineers, architects, building materials specialists, and all the others who are responsible for the designing and functioning of the environment. This American point of view is confirmed in a number of other studies and reviews (Sundell and Kjellmam 1994; Sundell 1999; Andersson et al. 1997; Ahlbom et al. 1998; Bornehag et al. 2001; Wargocki et al. 2002).

Exposure to allergens is of, course, crucial to inducing allergy. The most significant sources of emission of allergens in the indoor environment are probably house dust, mites, and pets. It seems that less significant (in the scale of the issue), is exposure to formaldehyde and volatile organic compounds, although in certain cases they can be evidently related even to asthma (e.g., Wieslander et al. 1996). In a number of studies, the exposure to allergens such as airborne chemicals, microorganisms (Gravesen 1979) and their metabolites (Rylander 1996) and airborne dust (Koch 2000; Ezzati et al. 2000), or exposure to groups of select air pollutants (Bascom 1996; McConnel et al. 1999; Koenig 1999) are discussed.

Allergy to mites' deject is a common worldwide issue. Mites require moist environment and are therefore directly related to moisture and poor building ventilation. However, on the other hand, mites are scarce in some regions of the world where allergy cases are frequent. This situation occurs, for example, in northern Scandinavia (Sundell et al. 1995). The broadest studies on house dust mites in Poland were carried out by Solarz (1987). Horak and others (1996) studied the content of mites, bacteria,



and microscopic fungi in settled dust in apartments in Upper Silesia. The authors determined that in houses with residents suffering from asthma, the concentration of fungi in dust settled on beds was five times higher than in houses without residents suffering from asthma. The lack of presence of visible mould in any of the studied houses is also important. These studies support the hypothesis put forward by Pastuszka, that the intensification of asthma symptoms (or attacks) in people allergic to fungi occurs as a consequence of inhaling fungal aerosol from close sources of emission (Pastuszka et al. 2000; Pastuszka 2001).

The hypothesis that micro-flora in apartments is dominated by *Micrococcaceae*, mainly by *Micrococcus* and *Staphylococcus*, put forward in the 1990s by Finnish and British researchers, was confirmed also in other countries, including Poland (Pastuszka et al. 2000). Generally, the obtained results indicated that the occurring concentration levels of bacterial and fungal aerosol in Polish apartments are comparable with the concentration levels registered in apartments in other parts of Europe. Figure 12-3 shows colonies of such Gram-positive cocci obtained from the air samples collected recently in the same area in Poland, while the example of Gram-positive rods is illustrated in Fig. 12-4.

It is interesting that Gawel and others (1997) in their studies carried out in Rabka, Poland, did not find a correlation between the frequency of occurrence of specific antibodies IgE in children's blood sera and the concentration of pollen grains and spores of specific plant species in the atmosphere. The most frequent aeroallergens were

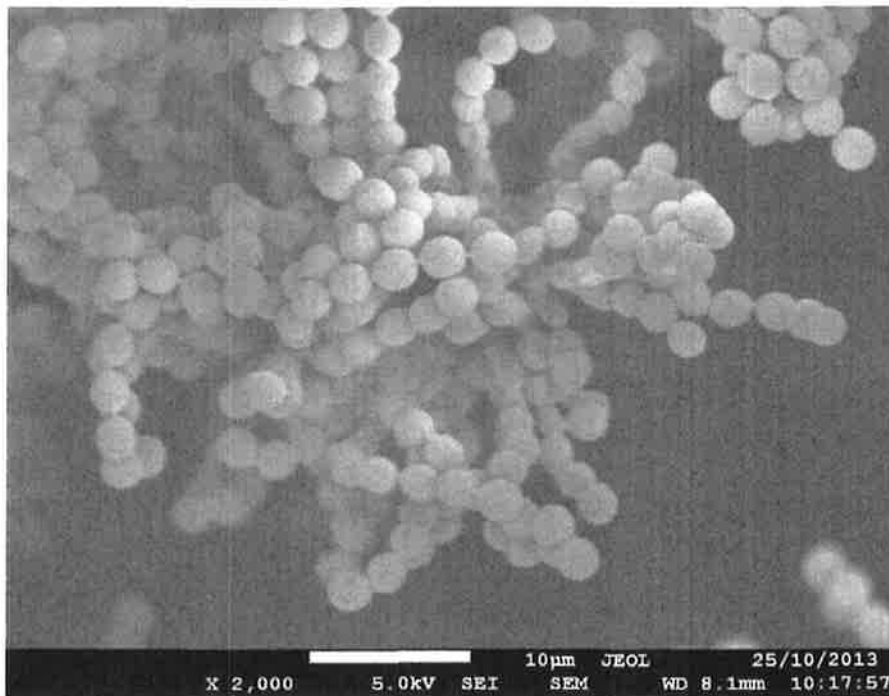


Fig. 12-3. Colonies of the bacteria (Gram-positive cocci) grown on the agar from the collected sample of airborne bacteria. Micrograph was made by Ewa Talik, University of Silesia. With permission.



Fig. 12-4. Gram-positive rods (bacteria). Micrograph was made by Ewa Talik, University of Silesia. With permission.

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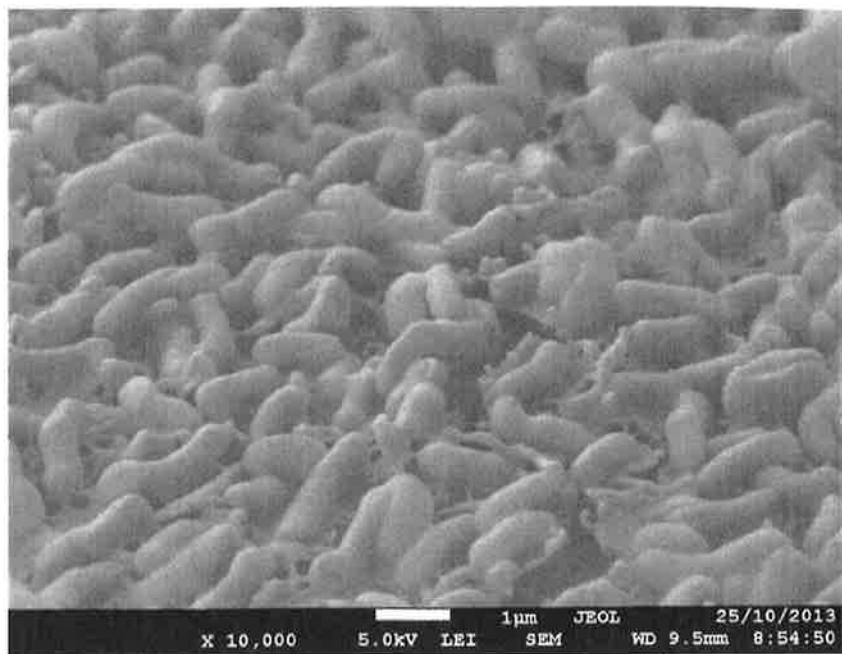


Fig. 12-4. Colonies of bacteria (Gram-positive rods) grown on the agar from the collected sample of airborne bacteria. Micrograph was made by Ewa Talik, University of Silesia. With permission.

spores, mainly *Cladosporium*, with relatively low frequency of increased concentration of specific antibodies IgE. Grass pollen, despite low year average concentration, resulted in the largest amount of increased concentrations of IgE.

In the study conducted in Germany (Nicolai and Mutius 1996), it has been determined that exposure of children aged 9–11 to high concentrations of sulfur dioxide and dust in the atmospheric air is related to the increased morbidity to bronchitis but is not correlated to asthma or hay fever.

Jędrychowski and Flak (1998) conducted epidemiological research on a population of over a thousand school children aged 9, attending schools in Cracow, Poland, with varied levels of atmospheric air pollution. The authors determined that only the occurrence of the symptom of chronic coughing was unrelated to the children's allergies but was related to atmospheric air pollution. Moreover, the risk of hay fever was related to the level of pollution and allergy, while the influence of moisture and mould was statistically significant in occurrence of hay fever, wheeze, and short breath.

The analysis of collected literature data indicates that the most significant environmental factors affecting the development of allergies in children are tobacco smoke and high humidity at home, often caused by poor ventilation. Moisture at home causes the increase of amount of a number of allergens, such as bioaerosols (Burge 1990), and especially microscopic fungi (e.g., Kemp et al. 2002), and mites, which can be causally related with occurrence or intensification of allergy. This conclusion directly supports the studies of Cuijpers and coworkers (1995).



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Example of case-study

Preliminary studies on potential influence of a few airborne allergens indoors on children's asthma were carried out by Pastuszka and co-workers (2003a). They measured the concentration of TSP, PM₅, fungi, bacteria as well as Gram-negative bacteria. They analyzed the selected air pollutants only and neglect other environmental factors promoting asthma, such as changes in the air temperature or different meteorological parameters (Hales et al. 1998). Aerosol particles were collected using the Casella samplers (TSP, PM₅) and the Harvard impactors (PM₁₀, PM_{2.5}). Samples have been taken during three months, mostly at the flats (apartments) in 4–10 story buildings. Additionally, in some homes the airborne particles were fractionated in a 10-stage Andersen impactor. To determine the relative contribution of the indoor and outdoor environment to the total exposure to the respirable fraction of the aerosol, the selected participants of the two-day exposure experiment (15 people/voluntaries) filled out an activity diary and a questionnaire about their homes and their surroundings during the course of the study.

Subjects for indoor environmental testing were identified from a population of asthmatic children seen in the Clinic of Environmental Medicine at the Institute of Occupational Medicine and Environmental Health in Sosnowiec, Poland. The measurements of the concentration of TSP and PM₅ as well as bacterial and fungal aerosol were carried out in two categories of homes in Sosnowiec: (A)—10 homes with asthmatic children, and (C)—15 control homes with healthy children. Airborne bacteria and fungi were collected using the 6-stage Andersen impactor. Microorganisms were collected on nutrient media (specific to either fungi or bacteria) in Petri dishes located on all impactor stages.

The results of this pilot cross-sectional study carried out in the homes with asthmatic children (A) and in the group of homes (C) are presented in Table 12-1. It can be seen that between the homes (A) and (C) the difference in the averaged concentration of airborne matter is for TSP only $14 \mu\text{g m}^{-3}$ while for PM₅, it is $28 \mu\text{g m}^{-3}$. It is interesting to note that although the visual inspection has not detected the fungal contamination in any home, the averaged concentration of airborne fungi in homes (A) was significantly higher than in homes (C). The level of airborne bacteria was also elevated in homes with asthmatic children in comparison with the control flats. Especially, the observed tendency to elevating the concentration of Gram-negative bacteria, which can be the sources of endotoxin, seems to be very important. Unfortunately, this problem is very difficult to discuss because of the generally very low level of these bacteria indoors.

This study confirms that in allergy based asthma, the interaction of various separately occurring allergens, even in low concentrations, is significant. Besides, several different pathways should be proposed that contribute to the asthmatic response and which could be amplified by the particulate matter exposure. This result agrees with a well-known phenomenon that particulate matter (PM) and endotoxins are able to trigger inflammatory responses in the lung. Unfortunately, most studies have focused on the components separately and on the identification of chemical components associated with PM.

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Particulate matte	TSP [μg]
	PM ₅ [μg]
Fungi total [CFU]	C
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Respirable fungi	C
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Bacteria total [C	C
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Gram-negative l	C
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Table 12-1. Concentration levels of different indoor aerosols in homes with asthmatic and healthy children in Sosnowiec, Poland. Results of the cross-sectional study (Pastuszka et al. 2003a).

Aerosol	Concentration in homes with asthmatic children	Healthy children
Particulate matter (Geometric mean)		
TSP [$\mu\text{g m}^{-3}$]	179	165
PM5 [$\mu\text{g m}^{-3}$]	123	95
Fungi total [CFU m^{-3}]		
Geometric mean	230	129
Median	179	104
Respirable fungi [CFU m^{-3}]		
Geometric mean	177	96
Median	147	62
Bacteria total [CFU m^{-3}]		
Geometric mean	881	703
Median	944	526
Respirable bacteria [CFU m^{-3}]		
Geometric mean	445	331
Median	391	274
Gram-negative bacteria (total) [CFU m^{-3}]		
Geometric mean	31	29
Median	39	24
Number of flats studied	10	15

Analysis of other recent data

Since biological components may represent around 20% of airborne PM, and endotoxins may reach concentrations as high as 30 EU/mg, some studies have focused attention on the characterization of endotoxins present in PM and health effects (for example, Górny and Dutkiewicz 1998). Review of the available literature made recently by Degobbi et al. (2011) has suggested that the endotoxin adsorbed in PM is able to elicit immunological responses associated with increase in pro-inflammatory cytokine expression. On the other hand, the obtained results confirm the hypothesis that the mass might not be the best metric for describing the harmful fraction of airborne particles (Donaldson et al. 2000). The total mass is usually dominated by larger secondary particles such as sulfates and nitrates, which are generally considered to be of low toxicity, whereas the mass contribution of fungi, bacteria, or endotoxins is much less than the inhaled mass of other pollutants.

Besides, allergens from animals are frequent in an indoor environment (Custovic et al. 1997; Ahlbom et al. 1998). Currently a related issue is being discussed, whether exposure to allergens during infancy constitutes a risk factor, or on the contrary, it prevents an allergy in the subsequent period of life. The dominating opinion seems to be that early exposure to allergens is a significant risk factor of allergy (Ahlbom et al. 1998).

Meantime, Peden (2002) reviewed available literature on the relation between air pollutants and asthma. He stated that most asthma exacerbations that result in hospitalization are associated with viral upper respiratory tract infections. However, a more recently appreciated cause of asthma exacerbation is exposure to pollutants, including ozone and various components of particulate matter (PM), including transition metals, diesel exhaust, and biological compounds such as endotoxins.

Takano et al. (2002) experimentally documented that diesel exhaust particles (DEP) enhance neutrophilic lung inflammation related to bacterial endotoxins. The enhancement is mediated by the induction of proinflammatory molecules, likely through the expression of Toll-like receptors and the activation of p65-containing dimer(s) of NF- κ B, such as p65/p50.

Finally, it should be mentioned that finding detailed conclusions on the air pollutants-asthma relationship is often very difficult. Caution for the analysis of asthma data obtained in developing countries is especially needed. For example, Brożek et al. (2010) analyzed a 15-year trend in the prevalence of allergic disorders and respiratory symptoms in children living in an urban area of Upper Silesia, Poland. Three cross-sectional studies (1993, 2002, and 2007) in children aged 7–10 showed a statistically significant increase in the prevalence of all physician-diagnosed allergic disorders (1993–2002–2007): asthma (3.4%–4.7%–8.5%); allergic rhinitis (9.1%–13.7%–17.4%); atopic dermatitis (3.6%–8.4%–8.9%); allergic conjunctivitis (4.3%–11.8%–14.9%); allergy to pollen (5.9%–12.3%–17.3%); allergy to food (5.5%–11.0%–17.0%). A simultaneous decreasing trend in the prevalence of coughing correlated with a significant improvement of ambient air quality. However, this rising trends could result from both increasing incidence and improved diagnosis of allergic diseases. The quickly improving diagnosis of allergic symptoms is really a fact in a number of countries now and may be a reason (although the “technical” reason only) of the rising number of cases of environmentally generated asthma documented in the literature.

Other kinds of interactions

It is very interesting that some interactions can be found not only between the airborne allergens but also between allergens suspended in the air (aeroallergens) and present in food (food allergens). An example is studies of Kasznia-Kocot and Sąda-Cieślak (1993), who found the allergic background of the disease in 95.3% of children suffering from obturative bronchitis. Hypersensitivity to both respirable and food allergens was dominant. It was determined that, apart from atopy in the family, too early introduction to solid food and exposure to environmental allergens such as tobacco smoke (ETS—passive smoking), house dust, plumage, hay dust are favorable to the development of an allergy. These data confirm the leading role of allergens occurring in indoor air of flats in the induction and intensification of allergies of the respiratory system in children.

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New tools in health care of the community exposed to air pollutants

(Jozef S. Pastuszka)

Aggregative risk index

Actually, there is well documented relation between human health, well-being, and air pollution levels. Therefore, some sanitary index which could be used to communicate information about the health risk as a consequence of air pollution in real-time and forecast of this health risk is needed. The first step in this direction was so called "air quality indices" but most of them are not accompanied by health advice on health protection. In the next step, the quality of outdoor air was classified according to the special index being an averaged concentration of some, arbitrary selected pollutants, and summarized together with the specific factors reflecting the generally assumed "toxicity" of these pollutants. The advanced formula of the air quality index is based on the exposure-response relationship (Cairncross et al. 2007; Pyta 2008) and defined in using the probability function for the occurrence of the specified health outcomes, on the assumption that there are no threshold concentrations which are safe for health (a risk based approach). Sicard et al. (2011, 2012) intensively worked on the new index associated with the corresponding daily risk increase, which was easy to understand and intuitive for the general public. They defined the Aggregative Risk Index (ARI), being the total attributable risk for simultaneous short-term exposure to several air pollutants, as follows (Sicard et al. 2011, 2012):

$$ARI = \sum_i (RR_i - 1) = \sum_i a_i C_i \tag{12-1}$$

where: the *ARI* index reflects the contribution of individual pollutants to total risk,

C_i —is the corresponding time-averaged concentrations (in $\mu\text{g m}^{-3}$)

a_i —is the coefficient proportional to the incremental risk values ($RR_i - 1$)

From the published RR_i values for each of i pollutants, it can be obtained the coefficients for the terms a_i in order to derive a numerical scale specific to each of the pollutants for the analyzed/studied area.

For each pollutant and pathology, the risk index coefficient a_i can be calculated using the following equation (Sicard et al. 2012):

$$a_i = \frac{4(RR_i - 1)}{10(1.120 - 1)} \tag{12-2}$$

Table 12-2 shows, prepared by Sicard et al. (2012), the arbitrary index scale used to facilitate risk communication. The index values may extend beyond 10 for highly polluted areas. It can be seen that the index has four bands indicating "Low, Moderate, High and Very High" risk of increase. The choice of percentage change is arbitrary.

It is important to mention that the health response varies between individuals, therefore the prognosis of the adverse health level can be made only for the exposed

Table 12-2. Arbitrary generic scale for the Aggregate Risk Index, associated risk increase, health advice, and information on the short-term effects for information and communication in the European regions (Sicard et al. 2012).

Index	Information level	Excess relative risk increase	Health messages	
			At risk population	General population
0 1 2 3	Low	Low risk of increase: 0–11.9%	Enjoy your usual outdoor activities. Follow your doctor's advice about exercise.	Ideal conditions for outdoor activities.
4 5 6	Moderate	Moderate risk of increase: 12.0–20.9%	If you have heart or lung problems, consider reducing strenuous physical outdoors activities, or reschedule to times when the index is lower. Follow your doctor's advice about exercise.	No need to modify your usual outdoor activities unless you experience symptoms.
7 8 9	High	High risk of increase: 21.0–29.9%	Children, the elderly, and people with heart or lungs problems should reduce physical exertion outdoors, particularly if they experience symptoms or reschedule to periods when the index is lower. Follow your doctor's usual advise.	Anyone experiencing discomfort such as coughing or throat irritation should consider reducing or rescheduling strenuous outdoor activities to when the index is lower.
10	Very high	Very high risk of increase:	Health warnings of emergency conditions.	Health alert: everyone may experience more serious health effects.

population (i.e., for the set of the organisms), not for the one, determined person. Such a prediction for the individual subject is possible but needs cooperation with a physician who can modify the general prediction to the individual patient, knowing his/her specific health condition.

Synergy of small doses of air pollutants

Current preventive hygiene and preventive medicine programs led to significant improvement of health of the people of the subpopulation occupationally exposed to air pollutants, as well as the health of the population in general. However, these successes concerned only people absorbing very large doses and usually exposed to concentration levels of air pollutants which today would be rated as extremely high. Nowadays, the focus of environmental scientists, industrial hygienists, and experts on environmental health is on the health effects of exposure to much lower concentrations of air pollutants. Analysis of the results obtained so far from epidemiological and toxicological studies on people absorbing relatively small doses of air pollutants reveal a complicated picture. On the one hand, it turns out that exposure to relatively

low pollutants' concentration distinctive, measurable negative particulates. One intriguing of airborne particles are print bronchitis, asthma, chronic o immune systems, and age o

As can be seen, prediction population to aerosol is very observed health effects and of a quantitative "dose-effect" when assessing the quality (Owen et al. 1992), which is in the interpretation of a gro obtained in the Upper Siles 1993, 1995, 2003b, 2010; J& 2013) confronted with the r exposed to specific air pol Pastuszka et al. 2000, 2003a, relating air quality with hea

Another example has be who found that a relatively n enormously increase the ca the example of exposure o n-dodecane is used to dilut potency although n-dodeca: carcinogenic. They also not low concentrations of the c:

It seems that at a rele individually studied, air p co-occurring pollutants beg synergism has already been doses of pollutants, especia so far. Meanwhile, it seem of air pollutants, synergism and absolutely cannot be i proposed as a new research indoor environment.

Concluding remark

The mechanism of synergy l Our scientific experience a synergic mechanism exists specific pollutants on huma is a significant synergy ph

low pollutants' concentrations, oftentimes lower than the current standards, implies distinctive, measurable negative health effects. The example is exposure to airborne particulates. One intriguing aspect of the epidemiological data is that health effects of airborne particles are primarily seen in people with predisposing factors, including bronchitis, asthma, chronic obstructive pulmonary diseases, pneumonia, compromised immune systems, and age over 65 years old (after Takano et al. 2002).

As can be seen, prediction of health effects of the exposure of the general population to aerosol is very difficult, especially because the direct correlation of the observed health effects and the absorbed dose of pollutants prevent the estimation of a quantitative "dose-effect" relationship. These issues are especially important when assessing the quality of indoor environment, especially home environment (Owen et al. 1992), which is dominates the daily exposure. The increasing difficulties in the interpretation of a growing collection of measurement data (including the data obtained in the Upper Silesia region, Poland, e.g., Pastuszka 1997; Pastuszka et al. 1993, 1995, 2003b, 2010; Jabłońska et al. 2001; Ćwiklak et al. 2009; Kozielska et al. 2013) confronted with the research data concerning the state of the health of people exposed to specific air pollutants, especially indoors (e.g., Pastuszka 1999, 2001; Pastuszka et al. 2000, 2003a, 2005) indicate the necessity to verify the basic hypothesis relating air quality with health effects.

Another example has been described a long time ago by Bingham and Falk (1969), who found that a relatively nontoxic substance, together with a known carcinogen, can enormously increase the carcinogenic potency of the known carcinogen. They give the example of exposure of mice to benzo(a)pyrene and benzo(a)anthracene when n-dodecane is used to dilute these chemicals. The result is a 1,000-fold increase in potency although n-dodecane itself is considered relatively benign and certainly not carcinogenic. They also noticed that the effect is greatest or at least most apparent at low concentrations of the carcinogen (Bingham and Falk 1969).

It seems that at a relatively low level of exposure to "basic", until recently individually studied, air pollutants, the inhalation of the whole composition of co-occurring pollutants begins to play a significant role. Although, the phenomenon of synergism has already been studied for some pollutants, the synergism of relatively low doses of pollutants, especially of non-carcinogenic substances, has not been studied so far. Meanwhile, it seems, at the exposure to relatively low concentration levels of air pollutants, synergism of the inhaled pollutants is one of the basic phenomena and absolutely cannot be ignored. Wherefore this direction of research should be proposed as a new research strategy, especially in reference to the research of the indoor environment.

Concluding remarks about the mechanism of synergy

The mechanism of synergy between air pollutants is, generally speaking, still unknown. Our scientific experience and available literature indicate that probably no universal synergic mechanism exists. It seems that each case of the common influence of some, specific pollutants on human health needs an individual explanation. For example, there is a significant synergy phenomenon between the exposure to asbestos and tobacco

smoke. It has been found that the cancer risk for smokers exposed to airborne asbestos is roughly ten times higher compared to non-smoking people exposed to asbestos of the same level (see Chapter 5). This synergy is probably due to carcinogenic compounds absorbed on the fibers. This hypothesis, if true, may be classified into the group of simple explanations related with very simple cases of synergy. Another example is synergy between gaseous pollutants and airborne bacteria when it is believed that the micro-damages of the respiratory tract made by toxic gases (SO₂, NO₂, or others) enable rapid penetration of inhaled live bacteria to the bloodstream.

Also much more complicated synergic phenomena are mentioned in this book. In our opinion, the synergy of airborne pollutants inhaled in very small doses, synergy of aeroallergens and food allergens, as well as, synergy between air pollutants and socio-economic factors seem to be especially difficult for a detailed, quantitative explanation and needs future interdisciplinary studies.

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Synergic Influence of Gaseous, Particulate, and Biological Pollutants on Human Health

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