

'Smogging kills' – Effects of air pollution on human respiratory system

Anna Grzywa-Celińska^{1,A-D,F}, Adam Krusiński^{1,B-E}, Janusz Milanowski^{1,E-F}

¹ Chair and Department of Pneumology, Oncology and Allergology, Medical University, Lublin., Poland
A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation,
D – Writing the article, E – Critical revision of the article, F – Final approval of article

Grzywa-Celińska A, Krusiński A, Milanowski J. 'Smogging kills' – Effects of air pollution on human respiratory system. *Ann Agric Environ Med*. doi: 10.26444/aaem/110477

Abstract

Atmospheric pollution suspended in humid air is popularly known as 'smog'. It is composed of dust particles of different sizes, as well as non-metal oxides, organic compounds, and heavy metals. Exposure to harmful substances suspended in the air – apart from, for example – smoking cigarettes, one of the modifiable factors leading to the development of respiratory diseases. There are six types of substances present in the air that have a negative impact on public health and result in significant consequences: ozone, particulate matter (PM) of different diameters – PM_{2.5}, PM_{2.5–10}, PM₁₀, nitrogen dioxide, sulphur dioxide, carbon monoxide and lead. Particular attention is given to small dust particles (PM₁₀ and PM_{2.5}) because they can penetrate into the lower respiratory tract. Apart from describing the composition of smog and sources of air pollution, the article also discusses the impact of atmospheric pollutants on both development and aggravation of the symptoms of such respiratory tract diseases as asthma, chronic obstructive pulmonary disease, respiratory infections and lung cancer. Some of legal measures applied in different countries aimed at reducing exposure to noxious air pollutants are reviewed. The authors believe that the increased focus on risks arising from inhaling toxic air pollution may be a first step for developing systemic solutions aimed at resolving or, at least, decreasing those risks.

Key words

air pollution, particulate matter, respiratory system, lung disease

INTRODUCTION

Severe atmospheric pollution suspended in the humid air is popularly known as *smog*. In Europe, including Poland, a major problem is an autumn-winter period smog, historically described as smog of the London type; it is composed of dust particles of different sizes, as well as non-metal oxides, organic compounds, and heavy metals. Air pollution typical for warmer seasons of the year is characterised by different composition. In this type of smog – called photochemical smog or Los Angeles smog – predominates ozone which is harmful to the human health. Exposure to harmful substances suspended in the air is one of the modifiable factors leading to the development of respiratory diseases.

OBJECTIVE

The aim of this study is to present the impact of noxious substances suspended in the air on the human organism. The influence is described of atmospheric pollutants on both the development of certain respiratory tract diseases and aggravation of their symptoms. Some of the legal measures (anti-smog resolutions, fuel tax policies, etc.) applied in different countries aimed at reducing exposure to toxic air pollutants are reviewed. The increased focus on risks arising from breathing air pollution may be a first step to develop the systemic solutions seeking to resolve such risks.

Smog composition. Winter smog plaguing Polish society shows a complex composition. A general division of the solid matters suspended in the fog as *dusts of different sizes* has been introduced. The United States Environmental Protection Agency (EPA) identifies six types of substances present in the air that have a detrimental effect on public health and result in negative environmental consequences; these comprise: ozone, particulate matter (PM) of different aerodynamic diameters – PM_{2.5}, PM_{2.5–10}, PM₁₀, nitrogen dioxide, sulphur dioxide, carbon monoxide, and lead [1]. Particular attention is paid to dust particles of 10 micrometres (PM₁₀) and 2.5 micrometres (PM_{2.5}); the first-mentioned are too large to penetrate deep into the respiratory tract although the correlation between its levels and exacerbation of cardiovascular and pulmonary diseases is known [2]. In the large dust particles, heavier contaminants (e.g. organic compounds and heavy metals) are suspended – mainly hydrocarbons, such as benzopyrene and fluorinated compounds, and heavy metals: cadmium, nickel, arsenic, and lead [3].

Dusts between 10 – 2.5 μm are mostly caught in the upper respiratory tract; however, sometimes a so-called respirable dust fraction is distinguished, i.e. particles smaller than 5 μm which penetrate to the alveolar air spaces [4].

PM_{2.5} are much more dangerous to health because of greater ability to penetration into the lower respiratory tract, and according to some sources – even deeper – the into alveoli [2, 5]. PM_{2.5} are composed of inorganic ions, i.a. nitric and hydrochloric acids residues, as well as alkaline metals, including potassium and sodium cations, ammonium ions, organic carbon and elementary carbon [3].

Smog is also composed of dust particles smaller than one micrometer – PM₁. These are so small that they pass

Address for correspondence: Anna Grzywa-Celińska Chair and Department of Pneumology, Oncology and Allergology, Medical University, Lublin., ul. Jaczewskiego 8, 20–954, Lublin, Poland
E-mail: acelin@op.pl

Received: 16.05.2019; accepted: 04.07.2019; first published: 29.07.2019

through the blood-air barrier, penetrate into the blood vessels, and may thereby have negative effects on the direct mechanism [2].

The other relevant elements of smog are non-metal oxides, mostly oxides of nitrogen and sulphur. Nitric oxide II (NO) – although harmful itself – due to its perishability is of importance as the nitric oxide IV (NO₂) precursor [6], which is one of the most harmful air pollutants.

Sources of air pollution. Heating installations – most of all traditional heaters adapted for the combustion of all kind of components, including wastes – are a major and difficult to manage source of air pollution. In Europe, transportation, especially road transport, is a source of 57% of nitric oxide emitted into the atmosphere; it also generates nearly 22% of carbon monoxide and 20% of PM_{2.5} [7]. Transportation is also a source of polycyclic aromatic hydrocarbons (PAHs) whose concentrations increase especially in winter. These are detrimental to health, both as isolated compounds and as a component of dust [8]. Diesel engine exhaust fumes are particularly critical which – besides PAHs rich in nitro groups – contain carbon and metals [2]. In Europe, industry (industrial processes and product use) remains the main producer of PAHs and accounts for 41% of PAHs production [9].

In Poland, industry is the predominant source of all basic air pollutants, followed by households. Industry is a major source of nitrogen oxides (emits 710 389 tonnes of NO₂-equivalent). Industry is also responsible for the production of most ozone precursors – 1,379,262 tonnes of non-methane volatile organic compounds (NMVOC) equivalent. In the case of dusts, the difference between industry and households is not as large; for example, in 2016, PM_{2.5} was emitted by industry in the amount of 87,910 tonnes of pollutants, while households emitted the amount of 59,764 tonnes of pollutants [10].

Under appropriate conditions, substances typical for winter smogs may become substrates for ozone which is the key component of photochemical smog. Ozone, i.e. trioxigen, is generally perceived as a human-friendly compound. This conviction is associated with the role of the protective layer that shields the earth's atmosphere from harmful ultraviolet radiation. Indeed, the stratospheric ozone layer stops carcinogenic UVB radiation; damage to this layer – called the ozone hole – constitutes a serious risk to human health. However, ozone as a chemical compound is harmful owing to its high chemical reactivity. When ozone is present in our immediate surroundings, i.e. in the troposphere, it acts as a damaging factor and an irritant [6]. Tropospheric ozone precursors include volatile air pollutants, such as nitrogen and carbon oxides, as well as simple organic compounds – hydrocarbons [11]. When air temperatures exceed 28 °C and high nitrogen dioxide concentration in the ambient air is observed, chemical reactions take place which result in the production of the final product, e.g. ozone [6].

Legal regulations. Polish law concerning controlling the concentration levels of different types of air pollutants and permissible concentrations of numerous substances, i.a. ozone, PM₁₀, PM_{2.5}, total suspended particulates (TSP), and oxides. An example of this is the Regulation of the Minister of the Environment issued in 2012 which states that the national PM_{2.5} emission reduction target is expected to be 18 µg/m³ by 2020 [12]. Regulations also stipulate the norms

of the composition of petrol and gas oils, as well as regulation emission levels of pollutants caused by fuels in waterborne transport and aviation fuels [13, 14, 15].

Additionally, the government envisages short-term activities aimed at reducing the level of pollutants on an *ad hoc* basis. Those activities include i.a. a ban on burning in home fireplaces and replacing this method with alternative sources, or promoting the use of free public transport instead of private cars. Another idea concerns outside urban traffic diversions for trucks, temporary suspension of construction works, and the wet cleaning of city streets [16].

Air pollution is also a matter of concern for the international law – this relates primarily to conventions and directives of the European Union (EU). They stress the role of cooperation between Member States, indicating the transboundary nature of such substances as ozone [17]. The EU, in many matters envisages individual targets for Member States, e.g. in Poland, the increase in the share of renewable sources within energy production is to be 15% by 2020 [18].

General impact of air pollution on population health. It is pointed out that of all the components of smog, PM_{2.5}, nitrogen dioxide, and ozone have the most serious effect on health. On the basis of data from 2005, it is estimated that exposure to PM_{2.5} shortens the lives of the EU citizens, on average, by 8 months, which means that annually it deprives them of a total of 3.6 million years of their lives [19]. Globally, it is a fifth-rank risk factor for death [20]. Nitrogen dioxide occupies second place in terms of health risk, followed by ozone which may lead to 21,00 deaths in the EU annually [19]. Similar statistics come from Poland, and according to data published in 2012, the annual numbers of deaths attributed to exposure to PM_{2.5}, nitrogen dioxide, and ozone were 44,600, 1,600, and 1,100, respectively [21]. It was proved that each 10 µg/mm³ increase in fine PM leads to a 4% increase in all-reasons mortality, 6% increase in cardiopulmonary mortality, and an 8% increment in lung cancer mortality [22].

Penetration of smog compounds into the respiratory system. Although it has been revealed that smog has a negative impact on many organs and systems of the human body, the most sensitive target – together with the cardiovascular system – is the respiratory tract. None of the components of smog are neutral for the respiratory tract and the lungs, and the mechanisms of their actions are differentiated – from direct tissue damage to complex immunomodulatory mechanisms. Large dust particles with a size range of 10 – 2.5 µm, are blocked at the level of the upper respiratory tract and have allergenic and irritating effects, while smaller particles, such as PM_{2.5}, reach the lower respiratory tract [2]. Although they are harmful *per se*, they are additionally carriers of other air pollutants, such as heavy metals and hydrocarbons [3]. Low molecular weight gases, nitrogen and sulphur oxides, and ozone, can pass more easily into the lungs. Hence, small particles, as well as the PM₁ fractions, have the ability to penetrate from the lung alveoli into the microcirculation. The rules of gaseous diffusion, such as Graham's law and Fick's law, state that particles of low-density, low-molar-mass, and high solubility in water, can overcome the alveolar barrier more easily. Similarly, in the lungs, the processes of diffusion are supported by a large surface area of the gas exchange, and low thickness of the alveolar-capillary membrane of barely 1 µm [23].

A basal pathomechanism leading to the development of numerous lung diseases associated with air pollutants results in direct damage of epithelial cells, which in turn leads to the formation of the inflammatory process. Additionally, reactive oxygen species (ROS) are additionally responsible for the irritating effect and destruction of the epithelium layer; they arise as a result of the presence of ozone, nitrogen oxides, *diesel smoke*, dusts, and phagocytic cell activation [2]. In general, inflammation is characterised by intensification of cellular response manifested by infiltrations consisting of neutrophils and macrophages which secrete pro-inflammatory cytokines. Xu et al. have shown that exposure of rats to PM_{2.5} leads to increase in the concentration of pro-inflammatory cytokines, such as tumour necrosis factor (TNF α) and interleukins: 6 (IL6) and 8 (IL8) [5]. TNF α , as well as interferon gamma (INF γ), activate the expression of the iNOS gene that results in nitric oxide synthesis, which is another source of free oxygen radicals [24]. However, Sarkar et al. demonstrated that in patients exposed to diesel exhaust, impairment of cell-mediated immunity was observed which manifested itself as decreased expression of the above-mentioned cytokines [25]. One of the mechanisms responsible for the weakening of this immunity may be an accumulation of dust-borne iron ions [26].

Influence of PM exposure on exacerbations of obstructive pulmonary diseases and respiratory infections. Epithelial damage and associated inflammatory activation lie at the origin of chronic obstructive pulmonary disease (COPD). Although tobacco smoke remains the main culprit, there are several similar substances in polluted air. Neutrophils and macrophages accumulated in the lungs initially produce cytokines, as detailed above, and subsequently release proteases, mainly elastases. On the other hand, ROS utilize antiproteases, including alpha-1 antitrypsin. This results in a shift in the balance towards proteases, which leads to emphysema.

The second component of COPD is chronic bronchitis in which neutrophils, macrophages and also CD8+ T-cells are involved. Additionally, compounds such as sulphur and nitrogen oxides chronically irritate the epithelium covering the lower airways, leading to their rebuilding with metaplastic changes in the secretory cells, and to the proliferation of goblet cells in the superficial layers of the bronchial walls. The consequence of this process is hypersecretion of mucus responsible for some of the pathological symptoms, as well as for promoting the development of bacterial infections [24].

There is reliable evidence confirming the influence of air pollution on the course of COPD. Ko et al. examined the effects of air pollution on hospitalization rates for exacerbations of chronic obstructive pulmonary disease. They found that all examined pollutants (NO₂, SO₂, O₃, PM₁₀, and PM_{2.5}) had a positive impact on hospital admissions for acute exacerbations of COPD [27]. These findings are confirmed by the study of Pothirat et al. [28]. Another study examining the impact of the PM₁₀ during a seasonal smog period on quality of life in COPD patients, showed a significant decrease in the quality of life measured during the high PM₁₀ period, particularly in the form of chest tightness and sleep disturbance [29].

Another common obstructive pulmonary disease is asthma. Smog can be a direct cause of asthma morbidity, as demonstrated in individuals with prior exposure to high doses

of ozone [6]. But what appears more often is that atmospheric pollutants intensify asthma symptoms in asthmatic patients. The studies conducted by Kowalska and Zejda in Silesia, south-western Poland, provide evidence of growth in the number of asthma-related ambulatory visits from the first day of deterioration in air quality [30]. Exacerbations are mostly due to irritancy, which explains the correlation between exposure to ozone and sulphur dioxide, and exacerbations of intrinsic asthma. It has also been demonstrated that smog has effects on allergic asthma exacerbations. This is related to the late cellular response causing secretion of, i.a. TNF α [24]. It has also been noted that asthmatic children who were exposed to nitrogen dioxide and ozone had a poorer reaction to the short-acting β -agonists (SABAs) expressed as a lower increase in FEV₁ [31].

The respiratory system in children – due to a dynamic growth and development of the lungs, fast minute ventilation, the immaturity of the immune system, and spending long hours outdoors – is much more sensitive to harmful particles. Based on the analysis of results of thirteen studies assessing the impact of ambient air pollution on children's health, Koranteng noticed that high air levels of NO₂, PM₁₀, CO and SO₂ were associated with higher rates of asthma hospitalizations [1]. The historical data concerning the impact of the Great Smog in London in 1952 proved that the rates of asthma in children born around the time of this environmental disaster were considerably higher [32].

Smog also has an impact on the incidence of the lower respiratory tract infections. Irritation of Goblet cells results in the mucus secretion promoting the development of pneumonia or bronchitis [24]. There is a known association between RSV infection (the cause of bronchiolitis typical for newborns) and smog. Interestingly, this correlation was demonstrated with regard to large particles PM₁₀ that should not enter the lower airways [33]. Bacterial infections are promoted by modulation of cellular immunity. While excessive cellular response could result in emphysema or chronic bronchitis, the weakened immunity increases the risk of infections, especially infections with tubercle and non-tubercle mycobacteria.

Smog and lung cancer. The role of ambient air pollution in pathogenesis of lung cancer is undeniable. This is due to the similarity regarding the chemical composition of smog and tobacco smoke, and the potential for inhaling them in the immediate vicinity of the bronchial epithelium. The apparent tobacco-induced histological types of cancer are: squamous cell carcinoma and small-cell lung cancer. Carcinogens common for smog and tobacco smoke include mainly polycyclic aromatic hydrocarbons. Nickel, non-metal oxides, and PM_{2.5} are also responsible for the development of primary lung cancers [34]. Nitrogen dioxide seems to be one of the key carcinogens; however, sulphates and dusts are to a higher extent also responsible for lung cancer mortality [6]. An increase in PM_{2.5} concentration of 10 $\mu\text{g}/\text{m}^3$ produces an increase in death rates of 14%. [34].

Gharibvand et al. examined the link between ambient PM_{2.5} exposure and incidence of adenocarcinoma of the lung in non-smokers. They found a 31% increase in lung adenocarcinoma occurrence in non-smokers that was associated with each 10 $\mu\text{g}/\text{m}^3$ increment in ambient PM_{2.5} concentration [35]. An earlier study by Puett et al. obtained similar findings of the NHS (33% increase) [36], as

well as the Netherlands Study of Hart et al. which showed 25% increase [37]. In comparison to studies mentioned above, the meta-analysis of data from 17 European cohorts (ESCAPE) has shown a much stronger (increase of 55%) influence of 5 $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} on lung cancer development [38].

A Canadian study also supports previous reports on the association between the increased risk of developing lung cancer and ambient PM_{2.5} air pollution. It also provides data showing strong associations between various subtypes of lung cancer and different compounds exposure: PM_{2.5} - adenocarcinoma and small cell lung cancer, NO₂ - adenocarcinoma, and ozone - squamous cell carcinoma [39].

Malignancies are also more often observed in individuals with other chronic respiratory disease that could be caused or modified by air pollution. The higher morbidity in patients with COPD is largely due to common ethological factors. Patients with a history of tuberculosis suffer from lung cancers twice as frequent, and this is usually a glandular type of lung cancer. Another risk factor is asthma in which the cancer risk in smokers increases up to 70% [34].

CONCLUSIONS

The negative impact of air pollution on the respiratory system is undeniable. The airways are the first-line target for different particles suspended in the inspiratory air. Having discussed the connection between ambient air pollution and selected diseases of the respiratory tract, the authors are strongly convinced of the importance to consider this matter in all its forms. Above all, it should be considered from the aspect of both primary and secondary prophylaxis of pulmonary diseases.

REFERENCES

- Koranteng S, Vargas AR, Buka I. Ambient air pollution and children's health: A systematic review of Canadian epidemiological studies. *Paediatr Child Health*. 2007; 12(3): 225–33.
- Krakiwiak A. Wpływ zanieczyszczenia środowiska na zdrowie. [The influence of environmental pollution on human health] In: Antczak A. editor. *Pulmonologia cz. II. Medical Tribune Polska, Warszawa; 2010. [polish]*
- Rozporządzenie Ministra Środowiska z dnia 13 września 2012 r. w sprawie dokonywania oceny poziomów substancji w powietrzu – załącznik nr 5. [Regulation of the Ministry of Environment of 13 September 2012 concerning evaluation of substances levels in the air – appendix nr 5]. [polish]
- Marek K. Choroby zawodowe układu oddechowego wywołane przez pył. [Occupational diseases of the respiratory system caused by dust]. In: Antczak A. editor. *Pulmonologia cz. II. Medical Tribune Polska, Warszawa; 2010. [polish]*
- Xu M, Li F, Wang M, Zhang H, Xu L, Adcock IM et al. Protective effects of VGX-1027 in PM_{2.5}-induced airway inflammation and bronchial hyperresponsiveness. *Eur J Pharmacol*. 2019; 5; 842: 373–383.
- Gładka A, Zatoński T. Wpływ zanieczyszczenia powietrza na choroby układu oddechowego. [The influence of air pollution on the respiratory system diseases]. *Kosmos*. 2016; 65; 4 (313): 573–582. [polish]
- European Environment Agency. Emissions of air pollutants from transport. Fig. 1. <https://www.eea.europa.eu/data-and-maps/indicators/transport-emissions-of-air-pollutants-8/transport-emissions-of-air-pollutants-6> (access: 2019.03.04).
- Pehnc G, Jakovljević I. Carcinogenic Potency of Airborne Polycyclic Aromatic Hydrocarbons in Relation to the Particle Fraction Size. *Int J Environ Res Public Health*. 2018; 7; 15(11).
- European Environment Agency. Persistent organic pollutant emissions. Fig. 6. <https://www.eea.europa.eu/data-and-maps/indicators/eea32-persistent-organic-pollutant-pop-emissions-1/assessment-9> (access: 2019.03.04).
- Organisation for Economic Co-Operation and Development (OECD. Stat). Emissions of air pollutants. https://stats.oecd.org/Index.aspx?DataSetCode=AIR_EMISSIONS (access: 2019.03.04).
- Rozporządzenie Ministra Środowiska z dnia 13 września 2012 r. w sprawie dokonywania oceny poziomów substancji w powietrzu – załącznik nr 4. [Regulation of the Ministry of Environment of 13 September 2012 concerning evaluation of substances levels in the air – appendix nr 4]. [polish]
- Rozporządzenie Ministra Środowiska z dnia 14 sierpnia 2012 r. w sprawie krajowego celu redukcji narażenia. [Regulation of the Ministry of Environment of 14 August 2012 concerning the national target of exposure reduction]. [polish]
- Rozporządzenie Ministra Gospodarki z dnia 4 stycznia 2007 r. w sprawie wymagań jakościowych dotyczących zawartości siarki dla olejów oraz rodzajów instalacji i warunków, w których będą stosowane ciężkie oleje opałowe. [Regulation of the Ministry of Economy of 4 January 2007 concerning quality requirements of the sulphur content for oils and the types of fittings in which a heavy fuel oils will be used]. [polish]
- Rozporządzenie Ministra Infrastruktury z dnia 22 kwietnia 2004 r. w sprawie wymagań, jakie powinny spełniać statki powietrzne ze względu na ochronę środowiska. [Regulation of the Ministry of Infrastructure of 22 April 2004 on requirements for the aircraft concerning environmental protection] [polish].
- Rozporządzenie Ministra Infrastruktury i Rozwoju z dnia 7 października 2015 r. w sprawie wymagań dotyczących zawartości siarki w paliwie żegludowym, w tym sposobu jej oznaczania. [Regulation of the Ministry of Infrastructure of 7 October 2015 on sulphur content limits requirements in the marine fuels, including the way of its measurements] [polish].
- Rozporządzenie Ministra Środowiska z dnia 11 września 2012 r. w sprawie programów ochrony powietrza oraz planów działań krótkoterminowych. [Regulation of the Minister of Environment of 11 September 2012. On air protection programs and short-term action plans] [polish].
- Directive 2008/50/EC of the European Parliament and of the Council of 21 May 2008 on ambient air quality and cleaner air for Europe.
- Directive 2009/28/EC of the European Parliament and of the Council of 23 April 2009 on the promotion of the use of energy from renewable sources and amending and subsequently repealing Directives 2001/77/EC and 2003/30/EC – app I, part A.
- Communication from the Commission to the Council and the European Parliament – Thematic Strategy on air pollution, Brussels, 21.09.2005 – chapter 2 „Assessment of the present situation”.
- Schraufnagel DE, Balmes JR, Cowl CT, De Matteis S, Jung SH, Mortimer KA. et al. Air Pollution and Noncommunicable Diseases: A Review by the Forum of International Respiratory Societies' Environmental Committee, Part 1: The Damaging Effects of Air Pollution. *Chest*. 2019; 155(2): 417–422.
- Air quality in Europe – 2015 report – EEA Report –Luxembourg: Publications Office of the European Union, 2018.
- Pope III CA, Burnett RT, Thun MJ, et al. Lung Cancer, Cardiopulmonary Mortality and Long-term Exposure to Fine Particulate Air Pollution. *JAMA*. 2002; 287(9): 1132–1141.
- Gutkowski P, Konturek SJ. Dyfuzja. [Diffusion] In: Konturek SJ editor. *Konturek Fizjologia człowieka. [Human physiology] 2nd ed. Elsevier Urban & Partner, 2007; 423–424. [polish]*
- Maitra A, Kumar V. Płuca i górne drogi oddechowe [Lungs nad upper Airways] In: Kumar V, Cotran RS, Robbins SL. *Robbins Patologia [Pathology]. Wydawnictwo Medyczne Urban & Partner, Wrocław; 2005: 519–580. [polish]*
- Sarkar S, Song Y, Sarkar S, Kipen HM, Laumbach RJ, Zhang J et al. Suppression of the NF- κ B pathway by diesel exhaust particles impairs human antimycobacterial immunity. *J Immunol*. 2012; 15; 1 88(6): 2778–93.
- Ghio AJ. Particle exposures and infections. *Infection*. 2014; 42(3): 459–67.
- Ko FWS, Tam W, Wong TW, Chan DP, Tung AH, Lai CK et al. Temporal relationship between air pollutants and hospital admissions for chronic obstructive pulmonary disease in Hong Kong. *Thorax* 2007; 62: 780–785.
- Pothirat C, Tosukhowong A, Chaiwong W, Liwsrisakun C, Inchai J. Effects of seasonal smog on asthma and COPD exacerbations requiring emergency visits in Chiang Mai, Thailand. *Asian Pac J Allergy Immunol*. 2016; 34(4): 284–289.

29. Pothirat C, Chaiwong W, Liwsrisakun C, Bumroongkit C, Deesomchok A, Theerakittikul T, et al. Influence of Particulate Matter during Seasonal Smog on Quality of Life and Lung Function in Patients with Chronic Obstructive Pulmonary Disease. *Int J Environ Res Public Health*. 2019; 16(1): 106.
30. Kowalska M, Zejda JE. Relationship between PM2.5 concentration in the ambient air and daily exacerbation of respiratory diseases in the population of Silesian voivodeship during winter smog. *Med Pr*. 2018; 30; 69(5): 523–530.
31. Hernández-Cadena L, Holguin F, Barraza-Villarreal A, Del Río-Navarro BE, Sienra-Monge JJ, Romieu I. Increased levels of outdoor air pollutants are associated with reduced bronchodilation in children with asthma. *Chest*. 2009; 136(6): 1529–1536.
32. Bharadwaj P, Zivin JG, Mullins JT, Neidell M. Early-Life Exposure to the Great Smog of 1952 and the Development of Asthma. *Am J Respir Crit Care Med*. 2016; 194(12): 1475–1482.
33. Vandini S, Corvaglia L, Alessandrini R, Aquilano G, Marsico C, Spinelli M, et al. Respiratory syncytial virus infection in infants and correlation with meteorological factors and air pollutants. *Ital J Pediatr*. 2013; 39: 1.
34. Potemski P. Rak płuca [Lung cancer] In: Antczak A. editor. *Wielka Interna – Pulmonologia cz. I* [Internal medicine – Pulmonology part 1] pod red. A. Antczaka. Medical Tribune Polska, 2010: 338–351.
35. Gharibvand L, Beeson WL, Shavlik D, Knutsen R, Ghamsary M, Soret S, et al. The association between ambient fine particulate matter and incident adenocarcinoma subtype of lung cancer. *Environ Health*. 2017; 24; 16(1): 71.
36. Puett RC, Hart JE, Yanosky JD, Spiegelman D, Wang M, Fisher JA, et al. Particulate matter air pollution exposure, distance to road, and incident lung cancer in the nurses' health study cohort. *Environ Health Perspect*. 2014; 122: 926–32.
37. Hart JE, Spiegelman D, Beelen R, Hoek G, Brunekreef B, Schouten LJ, et al. Long-term ambient residential traffic-related exposures and measurement error-adjusted risk of incident lung cancer in the Netherlands cohort study on diet and cancer. *Environmental health: a global access science source*. 2015; 2: 1–35.
38. Raaschou-Nielsen O, Andersen ZJ, Beelen R, Samoli E, Stafoggia M, Weinmayr G, et al. Air pollution and lung cancer incidence in 17 European cohorts: prospective analyses from the European study of cohorts for air pollution effects (ESCAPE). *The lancet oncology*. 2013; 14(9): 813–22.
39. Hystad P, Demers PA, Johnson KC, Carpiano RM, Brauer M. Long-term residential exposure to air pollution and lung cancer risk. *Epidemiology*, 2013; 24(5): 762–72.