

Advances in Research on Atmospheric Particulate Matter Pollution and Carcinogenesis in China

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[Abstract] Outdoor air pollution and particulate matter in polluted air are a class of carcinogens, and in recent years, atmospheric particulate matter pollution in China has remained at a high level. By reviewing the current situation of atmospheric particulate matter pollution in China and the research on the mechanism of particulate carcinogenesis, analyze the evidence of carcinogenicity of particulate matter in experimental animals in China and the epidemiological clues of particulate carcinogenesis, to explain the relationship between atmospheric particulate matter and cancer, and to propose relevant research in China.

[Keywords] Air pollution; Particulate matter; Lung cancer

1. Introduction

In October 2013, the International Agency for Research on Cancer (IARC), a subsidiary of the World Health Organization (WHO), issued a report. The outdoor air pollution and particulate matter (PM) in the polluted air are classified into human carcinogens.^[1-3] The assessment fully considers the global evidence for human cancer epidemiology, animal carcinogenesis and carcinogenesis research, and believes that prolonged exposure to particulate matter and air pollution can increase the risk of lung cancer. The research evidence from China in this assessment report is extremely limited, and because China's particulate matter levels and chemical composition are quite different from existing studies, the age structure and genetic factors of the population are also quite different, and the risk of cancer associated with atmospheric particulate matter in China cannot be derived from this report. The following is a summary of existing research on atmospheric particulate matter pollution and cancer in China, from the perspectives of pollution levels, carcinogenic mechanisms and research evidence.

2. Current Status of Atmospheric Particulate Matter Pollution

Along with the rapid urbanization and industrialization process, China's atmospheric pollutants have shown a composite character in recent years. There is no fundamental change in the coal-based energy structure, and soot-type pollution has long existed as the main type of pollution. Although the pollution problem of absorbing particulate matter (aerodynamic diameter of 10 μm or less, PM_{10}) has been alleviated, it has not

been fully solved by effective control from the source of pollution. At the same time, with the increase in emissions from automobile exhausts and dices, The concentration of fine particulate matter (aerodynamic diameter less than or equal to $2.5\ \mu\text{m}$, $\text{PM}_{2.5}$) in some urban agglomerations is increasing, further exacerbating regional air pollution, and the scope of influence is expanding.

In 2012, before the Ministry of Environmental Protection formally adopted the monitoring scope of $\text{PM}_{2.5}$, the annual average concentration data of $\text{PM}_{2.5}$ in China's ambient air was very limited. In the domestic mortality risk study on $\text{PM}_{2.5}$ exposure,^[4-6] The average annual concentration of $\text{PM}_{2.5}$ during the study ranged from 54 to $177\ \mu\text{g}/\text{m}^3$. However, they are higher than the annual average concentration of $\text{PM}_{2.5}$ in China's current GB 3095-2012 Ambient Air Quality Standard. The annual average value of $\text{PM}_{2.5}$ is not more than $35\ \mu\text{g}/\text{m}^3$, which is much higher than the annual average concentration limit ($10\ \mu\text{g}/\text{m}^3$) proposed in the WHO Air Quality Guidelines.

Since 2013, a total of 74 cities in key areas such as Beijing-Tianjin-Hebei, Yangtze River Delta, and Pearl River Delta, as well as municipalities, provincial capitals, and cities with separate plans, have begun to monitor in accordance with the "GB3095-2012 Ambient Air Quality Standards". The annual average concentration of atmospheric particles is shown in Table 1.^[7-11] The results show that although the annual average concentrations of PM_{10} and $\text{PM}_{2.5}$ have decreased year by year, the annual average concentration of these 74 cities is still higher than the national standard. In 2016, all 338 cities above the prefecture level were monitored for new air quality standards.^[10] The monitoring results show that 84 cities have ambient air quality that meets the national secondary standard, accounting for 24.9%; 254 cities have exceeded the standard air quality, accounting for 75.1%. The average annual concentrations of PM_{10} and $\text{PM}_{2.5}$ were 82 (22~436) and 47 (12~158) $\mu\text{g}/\text{m}^3$, respectively, which exceeded the national secondary standards by 0.17 and 0.34 times, respectively.

Table 1. Annual Average Concentrations of Ambient Particulate Matters in 74 Chinese Cities (2013-2017)

Year	$\text{PM}_{10}/(\mu\text{g}\cdot\text{m}^{-3})$		$\text{PM}_{2.5}/(\mu\text{g}\cdot\text{m}^{-3})$	
	Average	Range	Average	Range
2013	118	47~305	72	26~160
2014	105	42~233	64	23~130
2015	93	40~174	55	22~107
2016	85	39~164	50	21~99
2017	80	37~154	47	20~86

Now, China's atmospheric particulate pollution has had a direct impact on people's daily lives. In 2015, there were 280 prefecture-level cities in 24 provinces (autonomous regions and municipalities) that prepared heavy pollution weather emergency plans. Only 5,000 times of heavy pollution warnings were issued in the Beijing-Tianjin-Hebei region (more than 60 times in 2014^[8]). It can be seen that atmospheric particulate pollution has increasingly become an important environmental factor that constrains China's economic and social sustainable development.

3. Discussion on Carcinogenic Mechanism of Atmospheric Particulate Matter

Air pollution has a complex chemical composition. Certain single components in atmospheric particulates, such as Benzo(a)pyrene (BAP), are themselves carcinogens in humans, making it difficult to explore the carcinogenic mechanisms of atmospheric particulate matter. At present, the carcinogenic mechanism of air pollution is still in the hypothesis stage, such as the genotoxic hypothesis, oxidative stress and inflammatory response hypothesis.

3.1 Genotoxicity

Genotoxicity caused by air pollution can be observed in population studies and in vitro cell studies conducted in China. In the population study, by comparing the frequency of chromosome aberrations in the chorionic villi of women in three cities with different levels of air pollution, in cities with severe and moderate pollution, the incidence of polyploid, triploid and chromosome structural abnormalities was significantly higher than in lightly polluted cities.^[12] In addition, the number of micronuclei in urban residents is higher than that in rural areas.^[13] Research on different occupational groups can also reveal evidence of genotoxicity of air pollution. For example, the incidence of DNA damage in blood lymphocytes of road traffic police is significantly higher than that of office police officers;^[14-15] the number of micronuclei and sister chromatid exchange (SCE) frequencies were higher than those of office police officers.^[16-17] Drivers or ticket sellers on buses in heavily polluted tunnels have higher micronucleus numbers and sister chromatid exchange frequencies than those with relatively clean environments^[18].

Experimental animals in China, as well as in vitro cultured animal and human cell studies, have also found that particulate extracts in the air can cause cytogenetic abnormalities and are dose-related increases.^[19-22] For example, particulate matter increases the chromosomal aberration rate of mouse and human lymphocytes cultured in vitro, and the organic extract of particulate matter increases the micronucleus rate in mouse bone marrow and human lymphocytes.

It is also worth noting that according to a database of 2,375 observations from 174 articles provided for the IARC assessment, airborne particulate matter extracts from an industrial area in Shanghai are highly mutagenic, and each cubic meter of airborne particulate matter can cause more than 2,500 revertants in *Salmonella typhimurium* strain TA98. One of the reasons for the high mutagenicity may be high concentrations of particulate matter (up to 1.3 mg/m^3) in the ambient air surrounding the gasworks^[23]. The results of these human genetic markers can directly prove that outdoor air pollution can cause damage to genetic material, which may increase the risk of cancer.

3.2 Oxidative Stress and Inflammatory Response

In the process of the health effects of particulate matter in air pollution, both oxidative stress and inflammatory reactions caused by particulate matter may be important pathways.

In a population research^[24-25] conducted during the Beijing Olympics, 125 healthy volunteers were selected and followed up before, during, and after the Olympics. A variety of biomarkers reflecting the levels of inflammation and oxidative stress in the body system were monitored to determine whether they were related to changes in air pollution levels. The results showed that compared with before the Olympic Games, the concentration of biomarkers during the Olympic Games decreased significantly (4.5%~72.5%); At the end of the Olympics, these indicators have increased significantly (48% to 360%), and the changes in pollutant concentrations are consistent with changes in biomarker levels, which indicates that exposure to atmospheric pollution can lead to an increase in lung and whole body inflammatory and oxidative stress levels in healthy individuals, indicating that oxidative stress and inflammatory responses are possible pathways in the process of air pollutants causing human health damage.

In experimental animal studies, exposure to PM_{2.5} resulted in pathological changes in the lungs of the interstitial and alveolar spaces, increased neutrophil counts, and slightly thickened alveolar septa in the experimental animals; the degree of sustained inflammatory damage in the body is increased with increasing dose and exposure time. The cytokine network disorder caused by PM_{2.5} can aggravate the damage of the immune system. The reason may be that after PM_{2.5} enters the target cell, it produces inflammatory factors into the blood, leading to oxidative stress, accelerating the development of lung diseases or causing damage to other organs; it is also possible to generate excess free radicals or reactive oxygen species, destroying mitochondria and cellular structures, and ultimately producing cell damage. In addition, due to the stimulation of particulate matter, alveolar macrophages can release cytokines and pro-inflammatory factors. Pro-inflammatory cytokines further stimulate fibroblasts and lung epithelial cells to promote their secretion of cytokines and adhesion factors, which in turn cause aggregation of various inflammatory cells.^[26,27]

4. Evidence of Atmospheric Particulate Matter on Carcinogenicity of Experimental Animals

Currently, only a few studies have exposed laboratory animals directly to outdoor air pollution and observed the incidence of cancer, but none of these studies were conducted in China.

Searching the literature reveals that China has conducted a two-stage skin carcinogenesis experiment with atmospheric particulate matter on experimental animals.^[27] During the research, the particles of different particle sizes in different regions were dissolved in acetone and then dropped into the back of the mouse for 2 days, and the control group was set at the same time. The tumor promoter was started after the second week, twice a week for 26 weeks. It was found that samples of different particle sizes from different regions (Beijing, Taiyuan, and Xuanwei) were carcinogenic, and the smaller the particle size, the stronger the carcinogenicity. However, the study was carried out earlier, and the details of the study were not sufficient.

5. Epidemiological Clues of Cancer Caused by Atmospheric Particulate Matter in China

In 2013, the IARC classified outdoor air pollution and particulate matter in polluted air into human carcinogens, analyzes more than 200 epidemiological studies in Europe, North America and Asia involving millions of subjects. Among them, a combined analysis of lung cancer occurrence in 10 European countries^[28] and a large US lung cancer cohort study had the greatest impact on the final assessment results.

In the IARC assessment, only one epidemiological study from China^[30] was able to be analyzed by the Chinese Hypertension Prospective Survey Team, which included 158,666 subjects in 1991-2000. The researchers selected 70,947 adults living in 31 urban areas from the cohort to investigate the relationship between outdoor air pollution and mortality. During the 10-year follow-up period, 624 lung cancer deaths occurred. The researchers further obtained annual average concentration data of total suspended particulate matter (TSP) from 1991 to 2000 through 103 national fixed environmental monitoring stations in 31 cities. The study found that after adjusting for the possible confounders (including smoking, education, occupation, etc.), the relative risk of lung cancer increased by 1.01 (95% confidence interval: 1.00~1.02) for every 10 μ g/m³ increase in TSP concentration. The study further used the conversion factor to convert the TSP concentration to the PM_{2.5} concentration, and roughly estimated the PM_{2.5}. For each 10 μ g/m³ increase in concentration, the relative risk of lung cancer was 1.03 (95% confidence interval: 1.00~1.07).

The relative risk of PM_{2.5} lung cancer obtained by this study is much lower than other studies cited in the IARC report. It is speculated that the exposure-response curve of Chinese urban residents tends to be flat under the exposure of high pollution levels. The sensitivity of changes in pollution concentrations decreases. The main shortcoming of this study is that the population PM_{2.5} exposure level is converted from the TSP concentration, which has considerable uncertainty, which may lead to an underestimation of the risk of lung cancer exposure in China. In addition, China has carried out a number of epidemiological studies on air pollution and lung cancer in the 20th century, but both lack strict queuing design, and the methods of environmental air quality monitoring and population exposure assessment are also extremely limited. Therefore, most studies can only provide a rough correlation and regression analysis of air pollutants and lung cancer morbidity/mortality, but it can also provide an epidemiological line of population of cancer caused by atmospheric particulate matter in China.

In the 1970s, Chinese scholars conducted surveys of urban air pollution and residents' deaths in about 25 million people in 26 cities including Beijing, Shanghai, Tianjin, Shenyang, and Guangzhou. Studying the relationship between the concentration of dust in the atmosphere and the mortality of major malignant tumors in the population, this survey has very limited public publications showing that, in urban areas where the degree of air pollution is relatively serious, the mortality rate of lung cancer in residents is higher than that in the control area. The degree of air pollution is positively correlated with the increase in lung cancer mortality among residents. However, the published research data is very limited and cannot be further evaluated.^[31]

A number of biologic studies and case-control studies on air pollution and lung cancer have been conducted in the Northeast.^[32, 33] The results showed that the incidence of lung cancer increased with the increase of pollution; after controlling for smoking, indoor pollution index and other factors, the risk of lung cancer among residents living in the smoking block is 30% higher than that in the clean area. The risk of lung cancer among residents within 200 m of the metallurgical and other Dingye mines increases with the extension of the residence period, and the risk of living for more than 20 years can be increased by 70%.

Studies in other regions have also found that the more severe the air pollution, the higher the mortality rate of lung cancer [34-37] the results of research conducted in Shanghai [34] found that, among the non-smokers, the ratio of standardized mortality of lung cancer in urban, suburban and remote suburbs showed no exposure effect; however, among the smokers, the ratio of standardized mortality of lung cancer was the highest in male urban areas (2.02). The suburbs were second (1.57) and the lowest in the outer suburbs (1.11); suggesting that there is a synergistic effect between air pollution and smoking in the process of lung cancer. Studies conducted in Chengdu [35], Qingdao [36], and Nanning [37] also showed similar results.

In addition, through the statistical analysis of ash measurement data (the ash is positively correlated with the concentration of PM_{2.5} to some extent), lung cancer incidence and mortality, smoking rate and meteorological data during the 52-year period from 1954 to 2006 in Guangzhou, it was found that the incidence of lung cancer increased with the increase of air pollution events; considering the 7-year lag period, the correlation coefficient between lung cancer mortality and aerosol concentration is as high as 0.97, which may also indicate that atmospheric particulate matter may be one of the major risk factors for lung cancer in Chinese population^[38].

6. Conclusion

Second language acquisition is the basis for improving the quality of second language learning. It is necessary to continuously explore the application potential of second language acquisition in cognitive linguistics and explore the essential meaning of application. At the same time, the category hierarchy can classify second-language vocabulary for easy memory. Dynamic mode can infer vocabulary according to contextual composition or contextual image, and strengthen the memory of vocabulary. Metaphors help students understand vocabulary awareness from different perspectives in order to better understand, master, and use second-language knowledge. In short, studying the new paradigm of second language acquisition from the perspective of cognitive linguistics theory and guiding the output of second language can help us understand the related issues of second language acquisition and promote us to study second language acquisition in greater depth. The IARC report believes that prolonged exposure to particulate matter and atmospheric pollution can increase the risk of lung cancer, and this conclusion applies to all regions of the world. However, the air pollution risk-causing studies that support this conclusion are mostly carried out in areas with an average PM_{2.5} concentration of 10 to 30 $\mu\text{g}/\text{m}^3$, and therefore represent only the cancer risk in areas with low global air pollution levels. Compared with developed countries, China's air particulate matter concentration level is relatively high, and the composition of particulate matter is quite different; in addition, the susceptibility of Chinese residents to air pollution is different from that of foreign residents due to factors such as age structure and genetic differences.

Therefore, foreign research results need to be further evaluated for the long-term exposure of Chinese residents to air pollution. Studies have shown that atmospheric particulate matter extracts from many cities in China have certain genotoxicity. Oxidative stress and inflammatory reactions caused by particulate matter may also be important pathways in the health effects of particulate matter. However, due to the complex chemical composition of particulate matter, the current carcinogenic mechanism of particulate matter is still in the hypothesis stage. In the future, the use of emerging toxicogenomics and epigenomics technologies, combined with molecular epidemiological studies, genetic marker studies, and traditional epidemiological studies, will help advance the carcinogenesis of particulate matter. According to the latest World Health Organization's "Global Air Pollution and Disease Burden

Assessment”^[39] in 2012, China was attributable to the deaths of air pollution as high as 1,032,833 cases. Epidemiological evidence in China also supports the direct correlation between air pollution and lung cancer mortality. However, the relationship between the same kind of pollutants and lung cancer is quite different in different studies, which may be related to the level and composition of air pollution, the accuracy of pollution and health data, and the consistency of research methods. Therefore, in order to better protect the health of residents, a large-scale high-quality prospective cohort study is needed to further confirm the relationship between air pollution and exposure to lung cancer. In short, in order to better protect human health, China urgently needs to conduct research to confirm the relationship between atmospheric particulate matter and cancer. However, at the same time as further research, we must first take a series of measures and actions to alleviate China’s air pollution and reduce health risks.

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