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Review Article on Pollutional Haze

The effect of pollutional haze on pulmonary function

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Abstract: Detrimental health effects of atmospheric exposure to ambient particulate matter (PM) have been investigated in numerous studies. Exposure to pollutional haze, the carrier of air pollutants such as PM and nitrogen dioxide (NO_2) has been linked to lung and cardiovascular disease, resulting increases in both hospital admissions and mortality. This review focuses on the constituents of pollutional haze and its effects on pulmonary function. The article presents the available information and seeks to correlate pollutional haze and pulmonary function.

Keywords: Air pollution; haze; pulmonary function; particulate matter (PM); adverse effect

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Introduction

Historically, several incidents of extreme air pollution, such as the incident in the Meuse Valley, Belgium, in December 1930 (1), the incident in Donora, Pennsylvania in 1948 (2), and the incidents in London, England (3,4) drove attention on the potential for adverse health effects of air pollution. Studies have suggested that pollutional haze is associated with jeopardized lung function, respiratory symptoms (5-7). Among these health problems, pulmonary function as an objective indicator of respiratory health is of special interest in evaluating effects of ambient particulate in most studies (8-11). China, the largest developing country, has experienced rapid economic development and urbanization over the past few decades. The fast urbanization and economic expansion are principally driven by the tremendous use of fossil fuels, bringing about a dramatic increase in emissions of both ambient air pollutants and greenhouse gases. Although the levels of indoor coal smoke pollution have decreased rapidly since the increasing use of gas or electric power, the quality of air has not been improved due to the rapid increasing use of motor vehicles. As a result, the type of urban air pollution has changed from the coal combustion type to mixed coal smoke and motor vehicle emission type since the mid of 1990s. Meanwhile, the rapidly growing use of new building materials, the increase of pet raising, and tobacco smoking have made the air quality even worse (12,13). Currently, China is suffering the worst air pollution in the world. Based on the reports of China Meteorological Administration, in 2013 China experienced the worst pollutional haze. Thirty provinces including about 100 large and medium-sized cities were invaded by severe pollutional haze. The yearly number of haze day on average was 43 days national wide, which had reached the record high since 1961. In the past, pollutional haze occurred mostly in cities of north China due to the massive use of coal for both industry and heating, especially in winter. For instance, several cities in the Liaoning province, including Shenyang, Anshan and Benxi, were historically among the most polluted cities in China. While the cities in south China rarely confronted the pollutional haze. However, since last year the cities in the middle east of China have been harassed by pollutional haze frequently and the haze weather has increased apparently. Statistic data showed that the number of pollutional haze day of Hangzhou city was more than 201 days in 2013. In

Figure 1 Haze weather of Changsha on Dec 22, 2013.

December 2013, there was only 5 days of good air quality in Changsha, the capital city of Hunan province, while the days of moderate and severe air pollution were as many as 19 days (*Figure 1*). Even the most southern city of China, Sanya city in Hainan province, once experienced a pollutional haze day in December 2013. Because of the remarkable increasing of pollutional haze days, the air quality is getting worse national wide. The levels of particulate matter (PM), SO_2, O_3, and NO_2 are reported to be higher than those of the national standard and criterion concentration of WHO in many cities (7,12-16). These particles and toxic compounds of high concentration can dramatically impair pulmonary function of human being, consequently resulting respiratory disorders or even death.

This review highlights the constituents of pollutional haze and its effects on pulmonary function. We summarize the available information and assess the correlation between pollutional haze and pulmonary function. Our intention is to provide general information of what the pollutional haze is and how pulmonary function and pollutional haze are related rather than to introduce a detailed, or complete review.

What is pollutional haze

Traditionally haze is an atmospheric phenomenon where dust, smoke and other dry PM composed of various components obscure the clarity of the sky. The coefficient of haze (COH) is used to measure the visibility interference in the atmosphere. To determine COH, 1,000 feet of air sample is taken from an air filter and obtain radiation intensity. Then, the coefficient is calculated based on following absorbance formula:

$$COH = -100 \log_{10}(\frac{I_1}{I_0})$$

where I_1 is the radiation (400 nm light) intensity transmitted through the sampled filter, and I_0 is the radiation intensity transmitted through a clean (control) filter (17).

Pollutional haze is quite different from fog or mist. Fog is an aerosol system and more than 90% of its component is water, which causes visibility less than one kilometer. Therefore the occurrence of fog mainly affects traffic condition but has no much harmful effect on health when air is not polluted. However, when air is polluted with dry particles like PM2.5 and PM10 and gases like ozone, nitric oxide, nitrogen dioxide and sulfur dioxide, pollutional haze may occur if the relative humidity is less than 80%. Because nitrogen dioxide and sulfur dioxide may react with tiny water drops in the air and form nitric acid and sulfuric acid respectively, in most cases the pollutional haze is of yellow or orange gray color since the particles of nitric acid and sulfuric acid primarily scatter visible light with relative long wavelength. So, pollutional haze particles are comprised of a complex range of chemically and physically diverse substances that exist in the atmosphere as discrete, suspended liquid or solid particles. The basic components of pollutional haze are gases (e.g., ozone, sulfur dioxide, nitric oxide, nitrogen dioxide, carbon monoxide, carbon dioxide), volatile organic compounds (e.g., Benzene), and PM (e.g., metals, nitrates, sulfates, organic carbon, microbial components, pollen) (18,19). These haze particulates are characterized by various physical and chemical properties due to their sources, size ranges, formation mechanisms, and chemical composition. The effects of the pollutional haze particle on health mainly depend on its size and chemical composition.

The size and sources of haze particles

Particulate of pollutional haze refers to an air suspended mixture of solid and liquid particles varying in size, composition, and origin. It is a mixture including numerous classes and subclasses of contaminants. The size of haze particles is one of the leading factors that determine their behavior in the respiratory system. The size of airborne PM has been basically divided into there principal groups according to their aerodynamic diameter: coarse particles,

fine particles, and ultrafine particles (UFPs).

Coarse particles (PM10)

Coarse particles are the particles that can penetrate the thoracic airways, but they are also called inhalable particles. Coarse particles often defined as those with an aerodynamic diameter in the range of 2.5–10 μm. These particles can suspend and float in the atmosphere over a long period of time, and are often naturally occurring and derived primarily from soil and other crustal materials.

Fine particles (PM2.5)

In 1997, the U.S. EPA promulgated a standard (20) for an even finer cut of particulate air pollution-particles PM2.5 with aerodynamic diameter less than 2.5 μm. Currently, fine particles are often defined as those with an aerodynamic diameter in the range of 0.1–2.5 μm. Fine particles are derived chiefly from primary pollution, which is caused directly by gases like nitrogen oxides, sulfur dioxide and carbon monoxide from combustion processes in transportation, manufacturing, power generation, etc. Secondary pollution, the products formed by reactions between primary pollutes and components in the atmosphere or the reactions between primary pollutes, also contributes to the formation of fine particles. For instance, sulfate and nitrate particles commonly generated by conversion from primary sulfur and nitrogen oxide emissions are common components of fine particles. Although fine particles PM2.5 are dominantly comprised of primary pollution-source particles and secondary pollution in most urban areas, soil dust, sea salts, pollen, spore, smoking, etc. are the sources of fine particles as well. The existence of PM2.5 dramatically affects air quality and visibility although it accounts for a quite small part of the atmosphere. Compared to coarse particle PM10, PM2.5 is characterized by smaller diameter, larger area, stronger activity, easier carrier of harmful substance like heavy metal and microbe, more time suspending in the atmosphere, and longer distance to be delivered, therefore, PM2.5 has more significant effect on human health and atmosphere quality.

Ultrafine particles (UFPs)

UFPs are often defined as particles with aerodynamic diameter less than 0.1 μm. UFPs are the particles of nanoscale size. There are two types of UFPs, carbon-based type or metallic type. So, UFPs can be further subdivided by their magnetic properties. Airborne UFPs can be measured using a condensation particle counter (21). UFPs can be either naturally occurring or derived from manufacturing processes. Ocean spray, hot volcanic lava, and smoke are common natural UFPs sources as well. Other UFPs sources are byproducts, like emissions from specific processes, combustion reactions, or equipment such as printer toner and automobile exhaust (22,23). In 2014, it was reported that harmful UFPs from the takeoffs and landings at Los Angeles International Airport were of much greater magnitude than previously thought (24). There are a number of indoor sources of UFPs like laser printers, fax machines, photocopiers, cooking, tobacco smoke, chimney cracks, vacuum cleaners, etc. Although UFPs have relatively short residence times in the atmosphere because they readily accumulate or coagulate to form larger fine particles, UFPs are the main constituent of airborne PM. Research shows that these ambient particles are far smaller than the PM10 and PM2.5 particles and are believed to have several more aggressive health implications than those classes of larger particulates (25).

All three types of haze particles have contributions from both primary sources (emitted directly into the atmosphere) and secondary processes (formed in the atmosphere from precursor emissions). Both primary emissions and secondary emissions can originate from either anthropogenic or natural sources.

The chemistry of pollutional haze

Generally haze particulates are produced from either primary pollution process or secondary pollution process. Not matter from which process does the PM of haze generate, the basic components of haze particles are chemical substances, including ozone, sulfur dioxide, nitric oxide, nitrogen dioxide, carbon monoxide, carbon dioxide, volatile organic compounds, metals, nitric acid, nitrates, sulfuric acid, sulfates, organic carbon, etc. Among these substances, sulfur dioxide, nitrogen dioxide, ozone, nitric acid, nitrates, sulfuric acid, and sulfates are the most common components of haze particles. These chemical substances have different effects on human health because they have different physical and chemical properties.

Sulfur dioxide (SO_2)

Sulfur dioxide is a colorless gaseous substance at normal temperature, which is a toxic gas with a pungent, irritating and rotten smell. Sulfur dioxide is found on earth and exists in very small concentrations in the atmosphere at approximately 1 ppbv (26,27). The oxidation number of

sulfur in Sulfur dioxide molecule is +4, it can function either as a reducing agent or as a oxidizing agent. For instance, Sulfur dioxide can be oxidized to form sulfur trioxide (SO_3), which is widely used in the production of sulfuric acid in industry. In the presence of water, sulfur dioxide is able to decolorize substances due to its oxidizing capability. The main source of sulfur dioxide in the atmosphere is the by-product of combustion of fossil fuels that contains sulfur, like coals, liquid fuels and natural gas. Sulfur dioxide is a noticeable component in the atmosphere, especially following volcanic eruptions. Because sulfur dioxide is a polar molecule and an acidic oxide, it can combine with water to form sulfurous acid, H_2SO_3. For the same reason, sulfur dioxide emissions are a precursor to acid rain, which is the common component of haze particulates. According to United States Environmental Protection Agency, Sulfur dioxide is a major air pollutant and has significant impacts upon human health. The concentration of sulfur dioxide in the atmosphere can influence the habitat suitability for plant communities as well as animal life (28). Exposure to SO_2, even at low level is linked to increased bronchoconstriction in people with asthma, and reduction in lung function has been observed at higher concentrations.

Nitrogen dioxide (NO_2)

Nitrogen dioxide is a gaseous substance with reddish-brown color at normal temperature. It is a toxic gas with a characteristic sharp, biting odor. NO_2 is an intermediate in the industrial synthesis of nitric acid, which is produced each year with millions of tons. Because the oxidation number of nitrogen in NO_2 molecule is +4, it can function either as a reducing agent or as an oxidizing agent. Nitrogen dioxide plays an important role in atmospheric chemistry, including the formation of tropospheric ozone. Nitrogen dioxide is generated from most combustion processes using air as the oxidant. At elevated temperature nitrogen combines with oxygen to form nitric oxide, NO. Nitric oxide can be oxidized in air to form nitrogen dioxide though at normal atmospheric concentrations this process is a very slow. The most prominent sources of NO_2 in the atmosphere are internal combustion engines, thermal power stations. Butane gas heaters and stoves are also its sources. Nitrogen dioxide is a polar molecule and an acidic oxide, it can combine with water to form nitric acid, HNO_3. So, Nitrogen is a large scale pollutant that can form acid rain due to the formation of HNO_3 when combining with airborne water. Nitric acid is also a common component of haze particulates. Compared to SO_2, NO_2 is more likely to reach the lower airways due to its lower water solubility. Exposure even at low levels of NO_2 induces inflammatory response.

Ozone

Ozone is a colorless or slightly bluish gas, which is slightly soluble in water and much more soluble in inert non-polar solvents such as carbon tetrachloride or fluorocarbons, where it forms a blue solution. Ozone is of a distinctively pungent, sharp, reminiscent of chlorine smell at standard conditions. It is an allotrope of oxygen but it is much less stable than O_2, easily breaking down in the lower atmosphere to normal dioxygen. Ozone is produced from oxygen either by the action of ultraviolet light or by atmospheric electrical discharges. Throughout the Earth's atmosphere ozone is present in low concentrations. Even in ozone layer the ozone concentrations are only 2–8 ppm. Ozone mostly exists in ozone layer, which is below stratosphere, the region 20–35 kilometers away from earth surface. In total, ozone makes up only 0.6 ppm of the atmosphere. Ozone is one of the most powerful oxidizing agents (far stronger than O_2) and has many industrial and consumer applications related to oxidation. Due to its high oxidizing ability, ozone may damage respiratory tissues in animals and tissues in plants if its atmosphere concentration is more than 100 ppb. In heavy concentrations, ozone is irritating to the eyes, nose and throat. This makes ozone a potent respiratory hazard and pollutant near ground level although the so-called ozone layer is beneficial since it is able to prevent damaging ultraviolet light from reaching the Earth's surface. Therefore, low level ozone (or tropospheric ozone) is reported to be an atmospheric pollutant (29). In the atmosphere ozone precursors are a group of pollutants, predominantly those emitted during the combustion of fossil fuels. Ground-level ozone pollution is created near the Earth's surface by the action of daylight UV rays on these precursors. There is evidence that Ozone can act either as a greenhouse gas, absorbing some of the infrared energy emitted by the earth or as a component to facilitate the formation of photochemical smog (30,31).

Nitric acid and nitrates

Nitric acid is one of the strongest mineral acids with high corrosiveness, which can be produced using different processes. The process to manufacture nitric acid in industry is called Ostwald process. In this process, anhydrous ammonia is oxidized to form nitric oxide, NO, at a high temperature and pressure in the presence of platinum

or rhodium gauze catalyst. Nitric oxide is then reacted with oxygen in air to form nitrogen dioxide. Nitrogen dioxide is subsequently absorbed in water to form nitric acid and nitric oxide. In this process nitric oxide is cycled back for reoxidation. In laboratory, nitric acid is generally produced from the reaction between sulfuric acid, H_2SO_4 and sodium nitrate, $NaNO_3$. The chief industrial use of nitric acid is for the production of fertilizers. Nitric acid is neutralized with ammonia to give ammonium nitrate, NH_4NO_3. The other main applications are for the productions of explosives, nylon precursors, and special organic compounds. As a strong acid, nitric acid is highly soluble in water, resulting a strong acidic solution. Highly acidic nitric acid is able to reacts with bases to form nitrates, for instance, nitric acid reacts with sodium hydroxide to form sodium nitrate, $NaNO_3$. Nitric acid is also a powerful oxidizing agent. It reacts violently with many organic materials and the reactions may be explosive. In the atmosphere, nitric acid may be generated from the reaction between pollutant NO_2 and airborne water, forming acidic haze particles. These haze particles are very harmful to environment because of the presence of nitric acid. Nathan S. Bryan composed a review targeted to the current state of the science on nitrate in human health and disease (32).

Sulfuric acid and sulfates

Sulfuric acid, H_2SO_4, is one of the strongest diprotic acid, which is highly corrosive. It is a pungent, colorless or slightly yellow viscous liquid at room temperature. Its corrosiveness on other materials, like metals, living tissues or even stones, can be mainly ascribed to its strong acidic nature. Concentrated sulfuric acid has strong dehydrating and oxidizing property, able to cause very serious damage upon contact. Because of its strong oxidizing property, damage posed by sulfuric acid is potentially more severe than that caused by other comparable strong acids, such as hydrochloric acid and nitric acid. It causes not only chemical burns via hydrolysis, but also secondary thermal burns via dehydration. It burns the cornea, leading to permanent blindness if splashed onto eyes. It readily decomposes proteins and lipids through amide hydrolysis and ester hydrolysis upon contact with living tissues. If ingested, sulfuric acid damages internal organs irreversibly and may even be fatal. Sulfuric acid is soluble in water at all concentrations, generating a highly acidic solution. It reacts with most bases to give the corresponding sulfate. The reaction between sulfuric acid and potassium nitrate can be used to produce nitric acid. Also, its strong oxidizing property makes it highly corrosive to many metals. Due to its chemical properties, sulfuric acid is a central substance in the chemical industry. It has a wide range of applications including domestic acidic drain cleaner, electrolyte in lead-acid batteries and various cleaning agents. Sulfuric acid is widely produced with different methods, such as contact process, wet sulfuric acid process and some other methods. Sulfuric acid is formed naturally by the oxidation of sulfide minerals, such as iron sulfide. Because sulfur dioxide is the main byproduct produced when sulfur-containing fuels such as coal or oil are burned, dilute sulfuric acid, which is formed by atmospheric oxidation of sulfur dioxide in the presence of water, is a constituent of acid rain. For the same reason, in some cases pollutant SO_2 is oxidized in the atmosphere to form sulfuric acid haze particles or sulfate aerosol in wet air.

The effects of pollutional haze on pulmonary function

It is widely reported that polluted air has negative effects on human health (7,33,34). Currently, pollutional haze is one of the main air pollution types which occur frequently worldwide, especially in China. More and more attention has been driven to the study of possible adverse effects of pollutional haze on health. What adverse effects the pollutional haze exert to health and how the adverse effect works are the major concerns among scientists. Studies show that these adverse effects include increased respiratory symptoms and diseases, aggravation of asthma, and a decrease in lung function, etc. (35,36). The effect of pollutional haze on lung function is closely related to its particle size and chemical composition.

The effects of particle size of haze on pulmonary function

Pollutional haze refers to an air suspended mixture of solid and liquid particles that vary in size, composition, and origin. The size distribution of total suspended particles (TSPs.) in the atmosphere is generally categorized into three types: coarse particles (PM10–PM2.5), fine particles (PM2.5–PM0.1), and UFPs (aerodynamic diameter less than 0.1 μm). In 1987 the U.S. Environmental Protection Agency (U.S. EPA) defined that all particles with aerodynamic diameter less than 10μm are the inhalable particles. The guideline value of WHO based upon TSPs is 90 $\mu g/m^3$. This level is commonly exceeded in many of the Asian megacities. All these inhalable particles have

negative effects on health (37), especially the fine and UFPs, although their health effects may differ by size and composition.

Coarse particles, derived dominantly from soil and other crustal materials, are easily stopped in mouth and nose and settle in upper airway. Most of them are discharged out of body as sputum or mucus. It is believed that the harmful effects of coarse particles on health are limited due to their larger size. A study projected by Chang *et al.* using a mass screening program investigated the association between air pollutants exposure and the lung function of junior high school students in a mass screening program in Taipei city, Taiwan. Forced vital capacity (FVC) and forced PM with diameter of 10 μm or less (PM10) were assessed by regression models controlling for the age, gender, height, weight, student living districts, rainfall and temperature. Results showed that FVC, had a significant negative association with short-term exposure to PM10 measured on the day of spirometry testing. FVC values also were reversely associated with means of PM10. Namely, the short-term exposure to PM10 was associated with reducing FVC and FEV_1 (38).

Compared to coarse particles, fine particles more readily penetrate indoors. They are transported over longer distances, and are somewhat uniform within communities, resulting in highly ubiquitous exposure. Fine particles may be comprised of sulfur dioxide, nitrogen dioxide, sulfates, nitrates, acids, metals, and carbon particles with various chemicals adsorbed onto their surfaces. Due to their smaller size, fine particles are deemed to be more biologically active than coarse PM and be breathed readily deep in the lungs, suggesting that exposure to fine particles is a more serious health concern. Study from Peters group demonstrated that PM2.5 was significantly associated with lower FVC, FEV_1, and maximal midexpiratory flow (MMEF). His group also reported that stepwise regression of adjusted pulmonary function values for girls in the 12 communities showed that PM2.5 was most strongly associated with FEV_1 ($r=-0.72$, $P<0.01$) (39). It is reported that, with prolonged outdoor exercise, low-level exposures to PM2.5 were associated with significant effects on pulmonary function among adults. Hikers with a history of asthma or wheeze had significantly greater air pollution-related changes in pulmonary function (40). Ebelt *et al.* reported that long-term exposure to ambient PM may lead to a marked reduction in life expectancy, and the reduction in life expectancy, this effect was primarily due to increased cardio-pulmonary and lung cancer mortality. Chronic exposure for PM2.5 was associated with increased mortality even at low level, and was associated with decreased lung function, decreased cystolic blood pressure and increased heart rate at high level of PM2.5 (41). A study aimed to evaluate the respiratory symptoms, lung function and oxidative stress markers in sugarcane workers and the residents of Mendonça, an agricultural town in Brazil, during the non-harvesting and harvesting periods and to assess the population and individual exposures to fine PM (PM2.5) was launched by Gustavo Faibischew Prado research group. They investigated the exposure of sugarcane workers and the inhabitants of a neighbouring town to high PM2.5 concentrations during the sugarcane harvest period. The higher incidence of respiratory symptoms, greater decrease in lung function and more notable elevation of oxidative stress markers among the sugarcane workers during the harvest confirmed the greater effect magnitude in this population and a dose-dependent relationship between PM2.5 pollution and the observed effects (42). Wu *et al.* investigated the short-term effects of various air pollutants and chemical components of ambient fine particles (PM2.5) on lung function in a panel of 40 healthy university students. Among the air pollutants, PM2.5 showed the most robust estimated effects on different lung function measures in a similar action pattern. Most air pollutants and PM2.5 chemical components were positively associated with lung function measures at a short-term averaging time (3-d moving average) and inversely associated with them at a longer averaging time (14-d moving average) (43). An investigation of effects of PM2.5 and temperature on human lung function simultaneously in a panel of 21 healthy university students from the Healthy Volunteer Natural Relocation study in the context of suburban/urban air pollution in Beijing, China was carried out by Shaowei Wu group. They detected that PM2.5 effects on evening peak expiratory flow (PEF) and morning/evening FEV_1 in the presence of high temperature were generally stronger than those in the presence of low temperature, suggesting that a PM2.5 and temperature may interact synergistically to alter lung function and cause adverse respiratory health effects (44). One important issue concerning the effects of PM2.5 on health is whether or not there is a threshold concentration of PM2.5, which no adverse effects on health occur. In the past decade several research groups have addressed this issue, none of which suggested a threshold for the effects of PM10 on cardio respiratory mortality, implicating that even at low levels of exposure, some adverse effect on health was expected to occur. For long-term

exposures, the issue of thresholds is more difficult to address, as there are no populations in which long-term exposure is absent. The ACS study suggested that for long-term exposures, adverse effects occur at very low levels of less than 10 μg/m^3 PM2.5 (45).

Relatively, UFPs, also named as nanoparticles, have short residence times in the atmosphere because they accumulate to form larger fine particles. However, these particles are a serious health concern as they are able to penetrate deep into alveoli, pass through the lining of the lung, and be distributed systemically in the body. Recently, much attention has been focused on the adverse effects of UFPs [PM<0.1 (M) on health]. In 2010, Int Panis *et al.* reported that, contrary to the behaviour of inhaled PM10 and PM2.5, almost 100% of UFPs in the atmosphere were capable of settleing in the lungs, where they had the ability to penetrate tissue and undergo interstitialization, or to be absorbed directly into the bloodstream. Therefore they were not easily removed from the body and may induce adverse effect (46,47). Exposure to UFPs, even if components are not very toxic, may cause oxidative stress (48), inflammatory mediator release, and could activate lung disease and other systemic effects (49-51). Potential human exposures to UFPs could be either occupational due to the direct manufacturing process or a byproduct from an industrial or office environment, or incidental from contaminated outdoor air and other byproduct emissions. In order to quantify exposure and risk, both *in vivo* and *in vitro* studies of various UFP species were undertaken using a variety of animal models including mouse, rat, and fish (52). These studies are aimed to establish toxicological profiles necessary for risk assessment, risk management, and potential regulation and legislation (53,54).

All air suspended particles in pollutional haze have harmful effects on health. As the main component of haze particle, PM2.5 is a pervasive component of current atmospheres, which has been linked to numerous adverse outcomes. Although a large amount of studies concerning PM2.5-related health problems have been reported, exact pathogenic mechanisms of PM2.5 are not known with certainty.

The effects of chemical composition of pollutional haze on pulmonary function

Pollutional haze is a mixture whose possible composition include gases (e.g., ozone, sulfur dioxide, nitric oxide, nitrogen dioxide, etc.), volatile organic compounds (e.g., Benzene, etc.), and PM (e.g., nitrates, sulfates, organic carbon, etc.). The health effect of the haze is largely depended on its chemical composition.

The effects of SO_2 and sulfates haze on pulmonary function

Sulfur dioxide is one of the major pollutants in pollutional haze, which is produced principally from diverse combustion sources like coal, fossil fuels and sulfur-containing ores. Sulfate particles are commonly generated by conversion from primary sulfur oxide emissions. Sulfate particles may be acidic because sulfuric acid is a very strong acid. In the atmosphere approximately 50% SO_2 is transformed into sulfuric acid or sulfates. When SO_2 is inhaled, it could be easily absorbed by mucosal surface to form sulfurous acid, H_2SO_3, and some of the sulfurous acid could be further oxidized to sulfuric acid, H_2SO_4. Therefore, the exposure to SO_2 will intensively irritate eyes and mucosa of respiratory passage. A large amount inhalation of SO_2 will result in pneumonedema and throat swelling, dramatically impairing lung function or even causing suffocation. When pollutional haze occurs, SO_2 may be carried by the floating aerosol particles and be delivered deep in lung. In this case, the toxicity of SO_2 will be significantly increased, causing fiber hyperplasia of alveolar wall. When fiber hyperplasia spread widely it will lead to the formation of lung fibrosis. As a result, lung fibres may break and emphysema occur. A number of studies regarding the adverse effects of SO_2 have been published. Early in 1975, Lawther group carried out an extensive series of experiments involving a total of 25 healthy normal subjects, reporting that when low concentrations (1–3 ppm) of SO_2 have been inhaled deeply and after higher concentrations (5–30 ppm) have been inhaled normally an increase in airway resistance was found. Also, they detected that deep breathing of SO_2 would bring a wide range of sensitivities to SO_2 among the subjects (55). A study from Koenig *et al.* (56) reported that statistically significant changes in total respiratory resistance, FEV_1, and maximum flow calculated at 50% and 75% vital capacity were observed after all ten adolescent subjects with extrinsic asthma exposures to SO_2 and H_2SO_4. The magnitude of change in FEV_1 and maximum flow calculated at 50% vital capacity was higher after oral compared to oronasal inhalation of SO_2, suggesting that oronasal inhalation of 0.5 ppm of SO_2 produces a significant increase in the nasal work of breathing and that the route of exposure reduces but does not eliminate the lower airway reactions observed on oral exposure.

Theodore J. Witek Jr studied the acute pulmonary effects of low-level exposure to sulfur dioxide (SO_2) (0–1.0 μL/L) and formaldehyde (FA) (0 and 2 μL/L) in a controlled environmental chamber. Both healthy and asthmatic subjects were tested at rest and with moderate activity. Lung function changes (partial and maximal flow-volume curves) were confined to SO_2 exposure with activity in asthmatics. Neither group demonstrated an untoward lung function response to FA. Respiratory symptoms were mild to moderate from both pollutants and did not persist when measured up to 24 h after exposure (57). The promoting effects of a combined exposure to two pollutants (NO_2, O_3 or H_2SO_4-aerosol) at near ambient levels on lung tumorigenesis induced by *N*-bis(2-hydroxypropyl) nitrosamine (BHPN) were investigated in male Wistar rats by Takamichi Ichinose group (58). The results exhibited that the combined exposure to O_3 or H_2SO_4 with NO_2 produces an additional increase in incidence of lung tumor. The incidence of slight-moderate to marked alveolar cell hyperplasia in the groups exposed to each air pollutant with BHPN treatment was higher than that in the groups exposed to clean air with BHPN. These results expressed that the exposure to O_3 + NO_2 or NO_2 + H_2SO_4 even at ambient levels of each pollutant may have a synergistic action as a tumor promoter. According to the report from Richard B and Schlesinger (59), it was strongly suggested that asthmatics are more sensitive to SO_2, responding with bronchoconstriction at much lower exposure levels than do normal individuals. Toxicologically, exposure to high levels of SO_2 are needed before obvious changes in pulmonary defenses occur, but exposure to lower levels of acidic sulfates will alter mucociliary transport, alveolar clearance of particles, and airway reactivity, even in normal individuals. The primary response to SO_2, such as bronchoconstriction, is because of contraction of airway smooth muscle via the parasympathetic reflex and/or following release of humoral mediators. This is probably due most directly to the bisulfite ion produced upon dissolution of SO_2 in airway fluids. In a study projected by Ferron (60), eight dogs were exposed to a sodium bisulphite aerosol during 290 days. Lung clearance was tested with moderately soluble and insoluble aerosol particles after a single inhalation. Three dogs showed significant changes in clearance rate of moderately soluble particles during the sulphite exposure compared to the clearance rate during clean air exposure. The results were confirmed by *in vitro* clearance measurements in alveolar macrophages. In 2000, Krewski *et al.* reported that Long-term exposure to SO_2 was associated with decreased pulmonary function and increased mortality (61). In the research launched by Tong *et al.* (62), six solutions contained PM2.5 aerosol particles, $FeSO_4$, $ZnSO_4$ and their mixtures were instilled intratracheally into mouse lungs for experiment in order to investigate $FeSO_4$, $ZnSO_4$ (the two of main metal compositions of Shanghai PM2.5) effects on acute lung injury. They found that the synchrotron X-ray microradiographs of live mouse lung showed different lung texture changes after instilled with different toxic solutions. Hemorrhage points in lung were observed more from those mice instilled by $FeSO_4$ contained toxin solutions groups. Bronchial epithelial hyperplasia can be observed in $ZnSO_4$ contained solution-instilled groups from histopathologic analysis. The results suggested that $FeSO_4$ mainly induced hemorrhage and $ZnSO_4$ mainly induced inflammation and bronchiolar epithelial hyperplasia in the early toxicological effects of PM2.5. Using geographical information systems (GIS) tools, Jonathan Dubnov group analyzed the association between children's lung function development and their long-term exposure to air pollution from a coal-fired power station. The study covered a cohort of 1492 schoolchildren living in the vicinity of a major coal-fired power station in the Hadera sub-district of Israel in 1996 and 1999. The children underwent subsequent pulmonary function tests (PFT), It demonstrated that a negative association was found between changes in the results of PFT and the estimated individual levels of air pollution. A sensitivity test revealed a FEV_1 decline from –4.3% for the average pollution level to –10.2% for the high air pollution level. The results of a sensitivity test for FVC were found to be similar (63). It is deduced that air pollution from a coal-fired power station, although not exceeding local pollution standards, had a negative effect on children's lung function development. The study projected by Chang *et al.* revealed that FVC values also were reversely associated with means of SO_2 exposed one day earlier and SO_2 exposure had a strong one day lag effect on FVC and FEV (38). In brief, as a common air pollutant emitted from both anthropogenic and natural sources, sulfur dioxide (SO_2) has long been known to cause adverse respiratory health effects such as decreasing lung function. SO_2 has been established as the chemical indicator for the National Ambient Air Quality Standards for gaseous sulfur oxides under the US Clean Air Act. Current SO_2 standards have been promulgated for 24-h and annual average concentrations. Although study showed that eye blink frequency, nasal airflow, and lung function were not affected by the acute SO_2 exposure investigated, and these physiological responses to moderate SO_2

exposures were not significantly affected by gender (64), there is a strong body of evidence demonstrating adverse respiratory effects at much shorter exposure durations. Studies of controlled human exposures have consistently observed increases in respiratory symptoms and decreases in lung function among exercising asthmatics following 5- to 10-min exposures to SO_2. These findings are supported by epidemiologic studies that have demonstrated associations between ambient SO_2 levels and both respiratory symptoms and emergency department visits and hospitalizations for respiratory causes (65).

The effects of NO_2 and nitrates haze on pulmonary function

Nitrogen dioxide is also one of the main pollutants in the pollutional haze, which is produced from most combustion processes using air as the oxidant. At high temperatures nitrogen combines with oxygen to form nitric oxide. Nitric oxide can be oxidized in air to form nitrogen dioxide. The most prominent sources of NO_2 in the atmosphere are internal combustion engines and thermal power stations. It is also generated naturally during electrical storms. Like the formation of sulfuric acid and sulfate particles in the atmosphere, nitric acid and nitrate particles are formed generally by the transformation from oxidation of primary nitrogen oxides emissions mainly comprised of vehicle exhaust. Nitrogen dioxide is toxic by inhalation and it mainly damage respiratory passage. Because nitrogen dioxide is acrid and easily detectable by smell at low concentrations, inhalation exposure can generally be avoided. However, low concentrations (4 ppm) will anesthetize the nose, it creates a potential for overexposure. Symptoms of poisoning such as lung edema tend to appear several hours after inhalation of a low but potentially fatal dose. There is some evidence that long-term exposure to NO_2 at concentrations above 40–100 μg/m^3 may decrease lung function and increase the risk of respiratory symptoms (66). Long term exposures to NO_2 induce neurasthenic syndrome, chronic airway inflammation, and pulmonary fibrosis. Nitrates are toxic and humans are subject to its toxicity. Infants are especially vulnerable to methemoglobinemia due to nitrate metabolizing triglycerides present at higher concentrations than at other stages. Some adults can be more susceptible to the effects of nitrates than others (67). In the study of Kerr *et al.* (68), twenty human subjects with asthma and chronic bronchitis and 10 normal, healthy adults were exposed to 0.5 ppm of nitrogen dioxide for 2 h in a confined environment. This study unveiled that exposure of subjects with asthma and chronic bronchitis to 0.5 ppm NO_2 for 2 h does not produce a significant decrement in their pulmonary function. In the investigation published by Drechsler-Parks *et al.* (69), the pulmonary function of eight men and eight women (51 to 76 years of age), all nonsmokers, was measured before and after 2-hr exposures to filtered air (FA) and 0.60 ppm nitrogen dioxide (NO_2). The results showed that there were no statistically significant (P>0.05) differences between the responses of men and women to FA or NO_2 exposure. There were no significant (P>0.05) changes in any variable consequent to FA or NO_2 exposure. Earlier reports from this group also indicated that older subjects had responses to NO_2 exposure similar to those of young adults, suggesting that, at least for healthy people, exposure to 0.60 ppm NO_2 has little effect. One study aimed to investigate whether or not well characterized groups of healthy adolescents and adolescents with asthma differed in their sensitivity to ozone and nitrogen dioxide at near ambient concentrations of these pollutants was projected by Koenig group (70). It is concluded that there were no differences in pulmonary function responses between asymptomatic, allergic asthmatic adolescents and healthy adolescents exposed to nitrogen dioxide under the conditions of these studies.

In 1989, Fischer *et al.* (71) investigated the health effects of indoor NO_2 pollution among two populations of adult women. One population was living in a rural area, one in an urban area. The results stated that significant associations were found between exposure to NO_2 and pulmonary function among the non-smoking women living in the rural area, but no significant associations among the smoking women in that area, or among the non-smoking and smoking women living in the urban area. However, Ackermann-Liebrich group (72) found that short-term exposure is associated with increased mortality and hospital admissions. The study carried by Chang *et al.* (38) using a mass screening program indicated that FVC values also were reversely associated with means of NO_2 exposed 1 d earlier. Study from Ponsonby *et al.* (73) also reported that no associations were found between NO_2 exposure or gas appliance use and asthma, wheeze or baseline lung function. The effect of low-level NO_2 exposure on these respiratory outcomes was not marked. This study suggested that the possible effect of low-level NO_2 exposure on non-specific bronchial reactivity required confirmation. The study from Ichinose *et al.* (58) revealed that exposure to O_3 + NO_2 or NO_2 + H_2SO_4 aerosol produced an additional increase in incidence of lung tumor. These results suggest that the

exposure to O_3 + NO_2 or NO_2 + H_2SO_4 even at ambient levels of each pollutant may have a synergistic action and that free radical generation and lipid peroxide production by exposure to those air pollutants may be related to lung tumor promotion. The report from Peters JM group in 1999 suggested that Stepwise regression of adjusted pulmonary function values for girls in the 12 communities showed that NO_2 was most strongly associated with lower FVC ($r=-0.74$, $P<0.01$) (39). One study focused on how exposure to a high ambient concentration nitrogen dioxide NO_2 prior to a bronchial allergen challenge modulated the inflammatory response in the bronchi was implemented by Barck *et al.* (74). The data conveyed that there was no NO_2 associated effect on symptoms or pulmonary function, suggesting that ambient NO_2 can enhance allergic inflammatory reaction in the airways without causing symptoms or pulmonary dysfunction. In 1979, Sackner *et al.* (75) undertook a study to determine whether brief exposure to submicronic aerosol of sodium nitrate in high concentrations adversely affects the cardiopulmonary system. They reported both normal and asthmatic adults who breathed submicronic aerosol of $NaNO_3$ (up to 1 mg/m^3) for 10 min showed no significant changes in lung volumes, distribution of ventilation, ear oximetry, dynamic mechanics of breathing, and oscillation mechanics of the chest-lung system. $NaNO_3$ aerosol (1,000 μg/m^3) for 10 min did not significantly change pulmonary capillary blood flow, diffusing capacity, oxygen consumption, and pulmonary tissue volume as measured by a rebreathing technique. Thus, it was concluded that brief exposure to high concentrations of submicronic aerosol of sodium nitrate does not produce immediate adverse effects on cardiopulmonary function of anesthetized dogs, conscious sheep, and normal and asthmatic adults. Kleinman *et al.* (76) published a report in 1980 which demonstrated that no substantial alterations in pulmonary function or overall reported symptoms attributable to the NH_4NO_3 exposure were found for two subject groups: volunteers, 20 normal and 19 asthmatic, were exposed to clean air (sham) and to ammonium nitrate (NH_4NO_3) aerosol (exposure) under conditions which simulated a "worst case" ambient pollution episode. Possibly meaningful pulmonary function changes or symptom increases were seen in a few individuals, but these showed no obvious pattern and may well have been chance occurrences. A study from Loscutoff group (77) discovered that rats exposed to NH_4NO_3 aerosols showed no consistent exposure-related changes. Compared with air-exposed animals, rats exposed to $(NH_4)_2SO_4$ aerosols had increased values of residual volume and functional residual capacity and decreased slope of single-breath N_2 washout curves. It was deduced that elastase treatment had no significant effect on lung function changes resulting from inhalation of $(NH_4)_2SO_4$ aerosols. Lung function was more affected by $(NH_4)_2SO_4$ exposure than by NH_4NO_3 exposure, and lung function changes were more pronounced in rats than in guinea pigs. Obviously, based on these studies there are still some disagreements.

The effects of ozone on pulmonary function

Ozone is a powerful oxidant and toxic air pollutant. As one of main gaseous pollutants in pollutional haze, ozone in the atmosphere is generally produced from secondary pollution. Ozone precursors are a group of pollutants, predominantly those emitted during the combustion of fossil fuels. Although very low natural background level of ozone is considered safe, it can be hazardous at even low concentrations. The Canadian Center for Occupation Safety and Health reports that: "Even very low concentrations of ozone can be harmful to the upper respiratory tract and the lungs. The severity of injury depends on both the concentration of ozone and the duration of exposure. Severe and permanent lung injury or death could result from even a very short-term exposure to relatively low concentrations (78)." Exposure to 0.5–1 ppm ozone in the atmosphere may bring some adverse reaction and exposure to 1–4 ppm ozone may induce cough. Long-term exposure to ozone has been shown to increase risk of death from respiratory illness. A study of 450,000 people living in United States cities showed a significant correlation between ozone levels and respiratory illness over the 18-year follow-up period. The study found that people living in cities with high ozone levels such as Houston or Los Angeles had an over 30% increased risk of dying from lung disease (79,80). Ozone is one of the most powerful oxidant, it is able to react with almost all biological tissues, causing various detrimental health effects like harming lung function, irritating therespiratory system, and impairing tissues. Exposure to ozone or the pollutants that produce ozone is linked to asthma, bronchitis, heart attack, and other cardiopulmonary problems (81,82). Those persons with asthma, bronchitis or emphysema are more susceptive to ozone. Bock *et al.* (83) designed a study to investigate the acute effects of exposure to ambient-air pollution choosing children who were 7 to 13 years old and healthy active in a summer recreational camp. They found that a general tendency for decreased lung function with increasing ozone

concentration; however only peak expiratory flow rate (PEFR) mean slopes for girls and for all subjects were statistically significantly different from zero. In the regression analysis, decrements in PEFR were significantly correlated with the ozone exposure. Overall, the decrements were small. In the investigation from Deborah group (84), the pulmonary function of 8 men and 8 women (51 to 76 years of age), all nonsmokers, was measured before and after 2-h exposures to FA and 0.45 ppm ozone (O_3). The study demonstrated that there were no statistically significant (P>0.05) differences between the responses of men and women to FA or O_3 exposure. Since men and women had similar decrements in pulmonary function when women inhaled less O_3, the data suggested that women may be somewhat more responsive to O_3 than men. The results also indicated that older individuals may be less responsive to O_3 than young individuals based on the results from the study projected by Koenig group (70). It is concluded that there were no differences in pulmonary function responses between asymptomatic, allergic asthmatic adolescents and healthy adolescents exposed to ozone under the conditions of these studies. However, an increase in total respiratory resistance was observed in both asthmatic and healthy adolescent subjects after their exercise exposure to 0.18 ppm ozone. A study focused on the dose-response relationship for the effects of ozone on pulmonary function in humans was launched by Kleinman *et al*. (85). The effects of ozone on pulmonary function in adults and children were evaluated using the model. On the basis of dose of ozone (micrograms O_3 per kg body mass), children, aged 8 to 15 years, and adults were equally sensitive. When dose is analyzed as a function of age, the data suggest that children, under the age of 6 years, receive greater doses to respiratory tract tissues than do older children or adults, under equivalent conditions of exposure. Ichinose group (58) investigated the promoting effects of a combined exposure to two pollutants (NO_2, O_3 or H_2SO_4-aerosol) at near ambient levels on lung tumorigenesis induced by *N*-bis (2-hydroxypropyl) nitrosamine (BHPN) in male Wistar rats. Their study showed that exposure to O_3 alone enhances tumor development and that the combined exposure to O_3 with NO_2 produces an additional increase in incidence of lung tumor. Exposure to each air pollutant had no effect on the development of bronchiolar mucosal hyperplasia in lungs of rats treated with BHPN. These results suggest that the exposure to O_3 + NO_2 even at ambient levels of each pollutant may have a synergistic action as a tumor promoter and that free radical generation and lipid peroxide production by exposure to those air pollutants may be related to lung tumor promotion. A report from Korrick group suggested that prolonged outdoor exercise, low-level exposures to O_3, PM2.5, and strong aerosol acidity were associated with significant effects on pulmonary function among adults. Stepwise regression of adjusted pulmonary function values for girls in the 12 communities showed that O_3 was most strongly associated with PEFR (r=–0.75, P<0.005). There was a statistically significant association between ozone exposure and decreased FVC and FEV_1 in girls with asthma. For boys, significant associations were seen between peak O_3 exposures and lower FVC and FEV_1, but only in those spending more time outdoors. These findings from Peters *et al.* (39) underlined the importance of follow-up of this cohort. In 2000, Mudway *et al.* (86) published that on reaching the lung surface, secondary oxidation products arising from ozone initiated a number of cellular responses, including cytokine generation, adhesion molecule expression and tight junction modification. These responses together led to the influx of inflammatory cells to the lung in the absence of a pathogenic challenge. Moreover, lung permeability was increased and oedema develops. The nature and extent of these responses were variable and often not related within an individual. Thus, although an improved appreciation of the general mechanism of action of ozone had been attained in recent years, the basis for individual susceptibility was still ambiguous. Hidemitsu Funabashi, et al examined the effect of repeated ozone exposure on the respiratory system in mice sensitized with ovalbumin (OA). OA-sensitized mice and saline-treated control mice were exposed to 1.0 ppm ozone or clean air for 6 h daily and five days weekly for five weeks. Subsequently, these mice were exposed to 1.0 ppm ozone for 1 h, and pulmonary function was evaluated by pneumotachography during ozone exposure and arterial blood gas analysis, and histopathological examination were performed. OA sensitization or repeated ozone exposure did not affect baseline pulmonary function. Histopathologically, alveolar epithelial hyperplasia occurred in repeatedly exposed mice. These results indicated that respiratory allergy might be a risk factor, which aggravates the effects of repeated ozone exposure (87). Applying multiple methods of estimating exposure for several air pollutants, a study from Son group (88) assessed associations between pollutants and lung function in linear regression models, controlling for age, sex, and body mass index. FVC was associated with all air pollutants under all methods of estimating exposure. Only ozone was associated with FEV_1. Chang *et al.* also report that FVC, had a

significant negative association with short-term exposure to O_3 measured on the day of spirometry testing. FVC values were reversely associated with means of O_3, exposed 1 d earlier. It was concluded that the short-term exposure to O_3 was associated with reducing FVC and FEV_1. An investigation conducted by Bates *et al.* (89) suggested that ozoneinhalation causes decreases in forced expiratory volume (FEV_1) and dead space (V_D) and increases the slope of the alveolar plateau (S_N) in non-smokers. There was no difference in total delivered dose. Dead space ventilation (V_D/V_T) was not initially different between the two groups, but increased in the non-smokers (16.4%±2.8%) during the exposure, suggesting that the inhaled dose may be distributed more peripherally in smokers. It is concluded that these cigarette smokers retain their airway responsiveness to O_3 and, uniquely, experience changes in V_D that lead to heterogeneity in airway morphometry and an increase in S_N. In short, although plenty of investigations are available, there is much to be desired to obtain widely accepted conclusions about the effect of O_3 in pollutional haze on health.

Summary and recommendations

In summary, the risk for undermining lung function due to pollutional haze could be related to several factors, such as dose, acquired predisposing diseases, age and genetic susceptibility, etc. Most investigations demonstrated that higher dose or long-term of exposure to pollutants including PM, sulfur dioxides, nitrogen dioxides, ozone, nitrates, and sulfates induce more observable symptoms. It accounts for why people living or working along highly trafficked roads, people with long commuting hours and an elevated level of outdoor activity, or people who are occupationally exposed, e.g., bus drivers, city sanitation worker, traffic police officers, power plant workers are more likely to be attacked by haze. Evidently, it is ascribed to the higher dose or longer-term of exposure to the polluted atmosphere. It is generally accepted that the persons with predisposing diseases like asthma, emphysema, bronchitis, especially the elder ones, are more readily to be affected compared to the healthy. Genetic susceptibility also plays an important role in lung-impairing process. For instance, in most cases women is more susceptible to the effect of short-term ambient air pollution. In some circumstance, age as another factor to weigh the adverse effects of pollutants on health may be of the most prominent, therefore, newborns and children are especially vulnerable to air pollution. This is largely due to the unique developmental status of their respiratory system. In addition, the types and seriousness of adverse effects of haze are diverse because the size and the chemical composition of the PM are different due to the atmospheric condition where it forms and the source from which it is derived. Based on the available information, PM2.5 is the most common particle able to initiate detrimental health effects compared to other inhalable particles. This is mostly attributed to its size, larger area, and stronger activity, making it an easier carrier of harmful substance. As to the chemical composition of the haze particles, Sulfur dioxides, nitrogen dioxides and ozone are the most harmful pollutants since they are stronger oxidizing agents and have higher reactivity than other haze components. Although a number of reports suggested that these air pollutants undermine lung function principally by way of changing FVC or FEV_1, there are still some exceptions, indicating that how these pollutants impair lung function and achieve their deleterious effect are difficult to disentangle. Both the complexity of the physical and chemical properties of the haze particles and the diversity of the factors impacting lung function impede the progress of the investigations concerned. There is still a long way to go for us to clearly understand the mechanism how haze undermines lung function.

With the development of economy, more and more air pollution related health problems occur worldwide, especially in Asia region. Studies show that the effects of air pollution, especially the pollutional haze, on health in Asia are more significant than those in North America or Europe. It is necessary for us to take immediate and effective steps to fight against the worsening situation. Firstly, although a great amount of studies concerning issues of air pollution have been published, disputes about individual susceptibility and specific mechanism still remain. To better understand individual susceptibility and specific mechanism, more investigations are needed. These findings may have implications for more targeted and effective pollution regulations aiming to improve the public health. Secondly, more strict and scientific regulations and standards regarding air pollution should be issued to prevent further pollution. For instance, restricting the number of vehicles of cities, utilizing clean energy instead of traditional ones, applying more stringent standards for vehicle exhausts, planning to minimize traffic congestions, and developing more public transportation will help in minimizing the air pollution in the megacities and significantly improve air quality and the quality of life. Finally, legislations should be promulgated to ensure

effective national education of environment protection, enhancing the awareness of environmental protection of citizens. Meanwhile, government, especially Chinese government, should spend more resources to insure the implementation of various regulations and policies.

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Footnote

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