ABSTRACT

Air pollution has been recognized as the major environmental stimuli which may cause health effect of lung function decrement and asthma exacerbation. The researches for prediction and assessment of the air pollution impact on the respiratory system are also growing in recent years. Therefore, the purpose of this dissertation were: (i) to conduct an aerosol experiment in a constructed exposure system to understand the characteristics of the respiratory deposition for inhaled aerosols, (ii) to develop an integrated probabilistic risk approach to assess the risk of airborne dust- and ozone (O_3)-induced lung function decrement, (iii) to quantify the time-varying dynamics of air pollutants to correlate the relationships between fluctuations in air pollution and asthma hospital admission, and (iv) to predict asthma hospitalization trends in Taiwan by statistical indicators-based regression model.

This dissertation conducted the aerosol exposure experiment to quantify the deposition characteristics of exposure aerosols in human respiratory tract. The experimental aerosols included reference oil droplet and road dust particulate sample. This study developed an aerosol dynamic model to simulate time-dependent particle concentration in exposure chamber and respiratory system. The parameters of particle lose in exposure chamber and deposition in respiratory system can be estimated by experimental measurements. Thus, the deposition risk can be calculated through particle size distribution and size-dependent deposition fraction. This study also linked an integrated probabilistic risk assessment framework with published experimental data from airborne dust and O_3 challenge in individuals. The toxicokinetic/toxicodynamic models were used to simulate the dose-response of lung function decrement as percentage forced expiratory volume in 1 second (%FEV_1) under exposure. The highest air pollution events for dust aerosol and O_3 exposure data

in Taiwan regions were also collected for exposure assessment. Then, this study employed the time-series data based detrended fluctuation analysis (DFA) exponent and statistical indicators of coefficient of variation, standard deviation, skewness, and kurtosis to correlate the relationships between fluctuations in air pollution and age-specific asthma hospitalizations. Five major pollutants such as PM with aerodynamic diameter less than 10 μm (PM_{10}), O_3, nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and carbon monoxide (CO) were included. This study further used the indicators-built regression model to validate and predict the impact of target air pollutants on asthma incidence.

The experimental result found that the generated aerosols were polydisperse and both followed lognormal distribution with geometric mean diameter of 0.52 μm and 0.26 μm for resuspended oil droplet and road dust, respectively. The predictable deposition rate ranged from 0.015 – 0.362 s^{-1} and 0.013 – 0.157 s^{-1} in particle size ranging from 0.3 – 3.0 μm and 0.3 – 4.0 μm for oil droplet and road dust, respectively. The experimental result also revealed that deposition risk in respiratory system for inhaled oil droplet was higher than road dust aerosol. The results of air pollution-induced lung function decrement indicated that there were 50% probabilities of %FEV_1 decrement exceeding 16.9% (95% confidence interval (CI): 12.4 – 21.5%), 18.9 % (14.3 – 23.4%), and 7.1 % (4.0 – 10.2%) in north, center, and south Taiwan during Asian dust storm period, respectively. In same study period, the 10% probabilities of %FEV_1 decrement were estimated to exceed 5.5% (4.4 – 6.8%), 4.4% (3.5 – 5.3%), and 12.7% (11.4 – 14.0%) for exposed to O_3 in north, central, and south Taiwan, respectively. The results from fluctuating air pollution-associated asthma exacerbation showed that standard deviation of PM_{10} time-series data was the most correlated indicators for asthma hospitalization for all age groups, particularly for

elderly. The skewness of O_3 time-series data gives the highest correlation to pediatric asthmatics. The results also indicated that the integrated DFA exponents were significantly correlated with pediatric asthma hospitalization rate. The variability and long-range correlation of air pollution can be implicated as the risk warning signals in asthma incidence prediction. The results for asthma prediction also showed that indicators-built regression model had a better predictability in annual asthma hospitalization trends among pediatrics.

This study provided an integrated framework to assess the risk for air pollution-associated lung function exacerbations. The study quantified the mechanisms of aerosol deposition and lung function decrement by a dynamic model and the risk assessment was also conducted. The experimental and collected data can assist in estimating parameter and help the model development. Additionally, the proposed fluctuation analysis approach can also provide the novel indicators to predict the potential probability in asthma incidence. The statistical indicators inferred from time-series information of major air pollutants can further implicate for atmospheric environment monitoring and chronic respiratory disease care.

Keywords: Air pollution; Asthma; Lung function; Particle deposition; Dynamic modeling; Fluctuation analysis; Statistical indicators; Exacerbations risk

中文摘要

空氣污染已被認定為一重要之環境刺激物，可造成肺功能下降及氣喘惡化之健康效應，相關於預測及評估空氣污染對呼吸系統影響之研究亦逐年增加。因此，本研究之目的為 (i)建構一暴露系統進行氣膠實驗，以了解吸入氣膠於呼吸道沉積之特性，(ii)發展一整合性機率風險之方法以評估環境中氣懸沙塵及臭氧造成肺功能下降之風險，(iii)藉由量化空氣污染物時變之動態建構空氣污染物擾動特性與氣喘住院之相關性，及(iv)藉由統計指標為基礎之迴歸模式以預測台灣氣喘住院之趨勢。

本研究進行一氣膠暴露實驗以量化暴露氣膠於人體呼吸道之沉積特性，其中暴露之氣膠包括參考油滴及街塵微粒樣本。本研究發展一氣膠動態模式以模擬人工暴露箱及呼吸系統內時變之微粒濃度。透過實驗結果之資料可推估微粒於暴露艙及呼吸道之減損及沉積之參數。因此，沉積風險可透過微粒粒徑分布及粒徑相關之沉積分率計算求得。本研究亦以一整合性機率風險評估架構應用於前人發表之氣懸沙塵及臭氧之人體暴露實驗數據中，並藉由毒理動力及毒理動態模式模擬暴露下肺功能第一秒強制呼氣量下降百分率改變之劑量反應關係，本研究亦收集高空氣污染事件下台灣地區性之沙塵氣膠及臭氧暴露濃度資料作為暴露評估。而後，本研究以去趨勢擾動分析指數及統計指標之標準差、變異係數、偏度及峰度建立擾動空氣污染物與不同年齡族群氣喘住院率之相關性，考慮之台灣五種主要空氣污染物則包括氣動直徑小於 10 微米之微粒物質(PM_{10})、臭氧、二氧化氮、二氧化硫及一氧化碳。本研究進一步以統計指標創建之迴歸模式驗證及預測標的空氣污染物對氣喘發生率之影響。

實驗結果發現產生氣膠皆為符合對數常態分佈之多分佈，其再懸浮油滴及街

塵之幾何平均數分別為 0.52 及 0.26 μm，油滴及街塵沉積率其在可預測粒徑範圍 0.3 – 3.0 μm 及 0.3 – 4.0 μm 分別為 0.015 – 0.362 s^{-1} 及 0.013 – 0.157 s^{-1}。實驗結果亦顯示呼吸系統吸入油滴之推估沉積風險高於街塵氣膠。空氣污染造成肺功能下降結果指出，在北、中、及南台灣亞洲沙塵期間內之沙塵微粒暴露有 50%機率其第一秒強制呼氣量下降百分率分別超過 16.9% (95%信賴區間：12.4 – 21.5%)、18.9 % (14.3 – 23.4%)、及 7.1 % (4.0 – 10.2%)。於同樣之研究期間內，於北、中、南台灣之臭氧暴露則僅有 10%機率會導致第一秒強制呼氣量下降百分率分別超過 5.5% (4.4 – 6.8%)、4.4% (3.5 – 5.3%)、及 12.7% (11.4 – 14.0%)。擾動空氣污染相關氣喘惡化結果顯示，對於各年齡之氣喘族群，PM_{10} 時間序列資料之標準差為最具相關性之指標，特別是針對老年氣喘族群。而臭氧時間序列資料之偏度則對孩童氣喘有最佳之相關性。結果亦發現整合之去趨勢擾動分析指標對孩童氣喘之住院率具有最顯著之相關性。因此，空氣汙染物之變異及長期相關性可作為預測氣喘發生率之風險警示指標。氣喘預測結果亦顯示以統計指標建構之迴歸模式對孩童氣喘住院率之逐年趨勢具有較佳之預測能力。

本研究提供一整合架構以評估空氣污染相關肺功能惡化風險。本研究以動態模式量化氣膠沉積及肺功能下降之機制並進行其風險評估。實驗及收集之數據則有助於重要參數之推估及模式發展。此外，本研究建構之擾動分析法亦可提供新穎之指標以預測氣喘發生之潛在可能性。由主要空氣污染物所計算之統計指標可進一步應用於大氣環境監測及慢性呼吸性疾病照護。

關鍵字：空氣污染；氣喘；肺功能；微粒沉積；動態模擬；擾動分析；統計指標；惡化風險