

第二屆環境醫學國際研討會 2015 International Symposium of Environmental Medicine

OCT 24-25, 2015 Taipei, Taiwan
R201, NTU College of Public Health



主辦及贊助單位：臺灣大學醫學院附設醫院、臺灣大學醫學院、臺灣大學公共衛生學院、高雄醫學大學、
國家衛生研究院、衛生福利部國民健康署、科技部、財團法人安斯泰來醫學研究發展基金會、
中國鋼鐵股份有限公司

協辦單位：中華民國環境職業醫學會、社團法人台灣公共衛生學會、中華民國毒物學學會、台灣法醫學會

指導單位：教育部、衛生福利部

Organizers and Sponsors: National Taiwan University Hospital, National Taiwan University College of Medicine,
National Taiwan University College of Public Health, Kaohsiung Medical University,
National Health Research Institutes, Health Promotion Administration, Ministry of Health and Welfare,
Ministry of Science and Technology, Astellas Foundation, China Steel Corporation

Co-Organizers: Taiwan Environmental and Occupational Medicine, Taiwan Public Health Association,
The Toxicology Society in Taiwan, Taiwan Society of Forensic Medicine

Advisers: Ministry of Education, Ministry of Health and Welfare

大會手冊 Program Book



臺大醫院環境醫學中心
Environmental Medicine Collaboration Center,
National Taiwan University Hospital

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Welcome Message



Dr. Pau-Chung Chen 陳保中教授

Chair of the 2015 International Symposium of Environmental Medicine

Pau-Chung Chen

Director, Department of Environmental and Occupational Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine

Director and Professor, Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University College of Public Health

Chair, Scientific Committee on Reproductive Hazards in the Workplace (RHICOH), International Commission on Occupational Health (ICOH)

Welcome to the 2015 International Symposium of Environmental Medicine. On behalf of the symposium organizing committee, I am honored and delighted to welcome you in Taipei, Taiwan. This is the second year of Environmental Medicine Collaboration Center, National Taiwan University Hospital holding this symposium. Our center aims to enhance and exchange our knowledge of environmental medicine and improve our health eventually through enhancing exposure science, clinical service and risk communication.

As we know, environmental medicine is a multidisciplinary field involving medicine, environmental science, toxicology, chemistry and others. The scope of this field involves studying the interactions between human health and the environment including biological, chemical, and chemical exposures in air, water and food. The purpose of this symposium today is to learn each other and to pursue future cooperation in this field. We also have our distinguished guests from the United States, the United Kingdom, Germany, the Netherlands, China, Japan and Korea. I deeply appreciate your coming to share with us your unique experience.

Finally, I'd like to thank you for your support and your attendance. Wish you find the conference stimulating, fulfilling and enjoyable and most importantly live healthier and better.

僅代表第二屆環境醫學國際研討會歡迎各位的到來，這是臺大醫院環境醫學中心第二次舉辦環境醫學國際研討會。臺大醫院環境醫學中心旨在藉由環境醫學知識交流、增強暴露分析、臨床醫療服務和風險溝通以期增進大眾健康。

我們都知道環境醫學是一個包含環境科學、毒物學、化學和醫學的跨領域學門，其中涉及的研究範圍包括生物、化學、空氣、水和食物暴露等環境與人類健康的交互作用。本次研討會希望藉由知識與經驗的傳遞，以追求未來在此領域的合作交流。我們邀請了來自美國、英國、德國、荷蘭、中國、日本及韓國的各位貴賓，感謝您遠道而來與我們分享您寶貴的經驗！以及國內各位專家學者撥冗出席，才能促成此次各方的交流和學習。

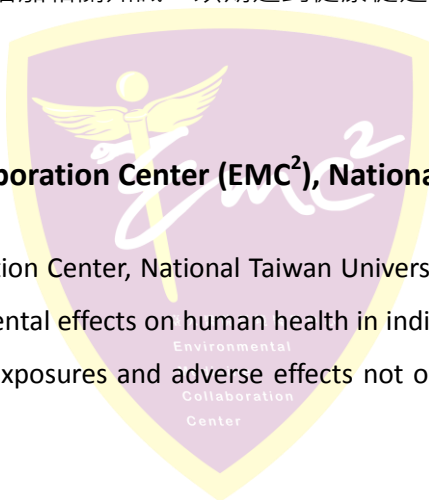
最後，對各位的參與和支持致上最深的謝意，希望研討會能給您激勵、充實和愉悅的兩天，更重要的是，可以生活的更好、更健康。

臺大醫院環境醫學中心

環境中充斥著各式各樣有害的汙染物，其中的暴露及累積對人體負面影響遠非我們所能想像，為了民眾的健康和提供更便利的醫療服務，臺大醫院於 2014 年成立環境醫學中心 (Environmental Medicine Collaboration Center, 簡稱 EMC²)，目的在於結合環境暴露檢測與臨床診斷以探討環境因子與疾病的關係，並提升國內環境醫學和預防醫學之研究能量。

環境醫學中心在環境及職業醫學部和小兒部成立環境醫學諮詢門診，提供包含重金屬和塑化劑檢測、不孕症、生育危害和兒童環境健康諮詢等項目。環境醫學中心與臺大醫院毒藥物鑑定暨檢驗中心和臺大公共衛生學院環境職業衛生研究團隊合作，建立量測人體內在或外來化學物質濃度與臨床醫療服務平台。

同時，醫學中心每年都會舉辦環境醫學國際研討會，邀請國內外的專家學者共同分享研究及實務經驗，希望讓國內外關心環境醫學議題的人員都可共襄盛舉。我們每年都會找出相關的事件為主題，希望喚醒大眾對環境醫學議題的關心並增加相關知識，以期達到健康促進和知識傳播的目的！



Environmental Medicine Collaboration Center (EMC²), National Taiwan University Hospital

Environmental Medicine Collaboration Center, National Taiwan University Hospital was established in 2014 to help people deal with environmental effects on human health in individual patients. We'd like to find out the links between environmental exposures and adverse effects not only for disease diagnosis, treatment but also health prevention as well.

Our clinic services include female infertility, reproductive hazards and children Health. We'd like to provide a comprehensive consultation of environmental toxins, endocrine disruptor, heavy metal and health impact. And our teams include Forensic and Clinical Toxicology Center, National Taiwan University Hospital and Environmental and Occupational Health Research Group, National Taiwan University College of Public Health which provide analytical testing services include metal, phthalate and toxic chemicals.

Meanwhile, Environmental Medicine Collaboration Center holds a conference every year. We'd like to establish a platform for the physicians, environmental medicine professionals to exchange opinions and share achievements of the work. Through the conference, we expect to share environmental and medical issues as well as innovative solutions with the audiences and wish every participant has fruitful results.

Day1: Oct 24, 2015 (Saturday)

0900-0920	Registration 報到
0920-0930	Welcome and Opening Remarks 開幕致詞
Session One: Environmental Toxins and Health 環境毒物與健康 Moderator: Dr. Chensheng Alex Lu (Associate Professor, Harvard University, United States) 哈佛大學呂陳生副教授	
0930-1020	Dr. Yi-Ping Lin (Associate Professor, Yang Ming University, Taiwan 陽明大學林宜平副教授) Arsenic, Radiation and Organic Solvents: A History of Environmental Toxins and Health in Taiwan
1020-1040	Coffee Break (休息)/ Poster Presentations & Discussion
1040-1130	Dr. Tony Fletcher (Senior Lecturer, London School of Hygiene & Tropical Medicine, United Kingdom 倫敦大學衛生與熱帶醫學院副教授) The Epidemiology of Perfluorinated Compounds – Studies in the General Population and Contaminated Communities
1130-1220	Dr. Ming-Tsang Wu (Professor, Kaohsiung Medical University, Taiwan 高雄醫學大學吳明蒼教授) Melamine and Kidney Diseases
1220-1320	Lunch 午餐/ Poster Presentations & Discussion
Session Two: Air Pollution and Health Impact 空氣汙染對健康影響 Moderator: Dr. Chun-Yuh Yang (Vice President, Kaohsiung Medical University, Taiwan) 高雄醫學大學楊俊毓副校長	
1320-1410	Dr. Chang-Chuan Chan (Professor, National Taiwan University, Taiwan 臺灣大學詹長權教授) Health Effects for Residents in the Vicinity of a Petrochemical Complex
1410-1500	Dr. Hai-Dong Kan (Professor, Fudan University, China 復旦大學闕海東教授) Ambient Air Pollution and Population Health in China
1500-1520	Coffee Break (休息)/ Poster Presentations & Discussion
1520-1610	Dr. Tsun-Jen Cheng (Professor, National Taiwan University, Taiwan 臺灣大學鄭尊仁教授) Inhalation Toxicity of Ambient Particles
1610-1700	Dr. Ta-Chen Su (Associate Professor, National Taiwan University, Taiwan 臺灣大學蘇大成副教授) Air pollution and Cardiovascular Health: Current and Future Perspectives
1800-2000	Symposium Banquet (Invited Only)

Day2: Oct 25, 2015 (Sunday)

0830-0850 Registration 報到

Session Three: Children's Environmental Health 兒童環境健康

Moderator: Dr. Mei-Hwan Wu (Superintendent, National Taiwan University Children's Hospital, Taiwan)
臺大兒童醫院吳美環院長

0850-0940 Dr. Peter van den Hazel (President, INCHEM and HEAL, Netherlands 國際兒童健康環境網絡和歐盟健康與環境聯盟主席)
The Importance of Children's Environmental Health to the World

0940-1030 Dr. David Bellinger (Professor, Harvard University, United States 哈佛大學教授)
Characterizing the Public Health Impact of Children's Exposures to Environmental Chemicals

1030-1050 Coffee Break (休息)/ Poster Presentations & Discussion

1050-1140 Dr. Joachim Heinrich (Senior Consultant, Ludwig Maximilian University, Germany 慕尼黑大學資深諮詢顧問)
Exposure to Greenness and Health Outcomes

1140-1230 Dr. Eun-Hee Ha (Professor, Ewha Womans University, Korea 梨花女子大學教授)
Indoor and Outdoor Air Pollution and Children's Health

1230-1330 Lunch 午餐/ Poster Presentations & Discussion

Session Four: Environmental Health Interventions 環境健康行為介入

Moderator: Dr. Hung-Yi Chiou (Vice President, Taipei Medical University, Taiwan)
臺北醫學大學邱弘毅副校長

1330-1420 Dr. Ching-Chang Lee (Professor, Cheng Kung University, Taiwan 成功大學李俊璋教授)
Developing an Intervention Strategy to Reduce Phthalate Exposure in Taiwanese Girls

1420-1510 Dr. Chisato Mori (Professor, Chiba University, Japan 千葉大學森千里教授)
Environmental Health Intervention & Preventive Medical Studies on Chemical Exposure Issues

1510-1520 Poster Awards

環境毒物與健康

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Dr. Chensheng (Alex) Lu (United States) 呂陳生副教授

Associate Professor, Department of Environmental Health, Harvard T.H. Chan School of Public Health

Visiting Associate Professor, National Taiwan University College of Public Health

E-mail: cslu@hsph.harvard.edu

Dr. Lu is interested in assessing human exposure to pesticides and its health effects. He is particularly interested in developing innovated biomarkers linking exposure to effects. His recent research effort extends to saving honeybees and other pollinators from the hazards of neonicotinoids, a group of most widely use insecticides in the world. Before joining Harvard, he was an Assistant Professor at Rollins School of Public Health, Emory University, from 2004-2008. He received the doctoral degree from the School of Public Health and Community Medicine at the University of Washington, Seattle WA, in 1996.

Professional Services

Domestic Services

2014	Member, <i>Post-Vietnam dioxin exposure in Agent Orange-contaminated C-123 aircraft</i> , Institute of Medicine (IOM) / The National Academies
2013-	Member, Scientific Advisory Board, The Organic Center
2013-2014	Member, <i>California Department of Pesticide Regulation's Risk Assessment Process for Pesticides</i> , National Research Council (NRC) / The National Academies
2006-	<i>Ad hoc</i> member, Science Review Board, Food Quality Protection Act (FQPA), US Environmental Protection Agency (US EPA)
2004-	<i>Ad hoc</i> member, Scientific Advisory Panel, Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), US Environmental Protection Agency (US EPA)

International Services

2015-	Visiting Associate Professor, College of Public Health, National Taiwan University, Taiwan
2012-	Academic lecturer, Frontier Lectures in Environmental Sciences, Peking University, China
2009-	Scientific Expert, European Food Safety Authority (EFSA), Italy
2008-	Adjunct Professor, Cyprus International Institute for Environmental and Public Health, Cyprus University of Technology, Cyprus

Honor and Awards

Innovative Faculty Development Award, Radcliffe Institute for Advanced Study, Harvard University (2014)
Joan Daisey Outstanding Young Scientist Award. International Society of Exposure Analysis (2005)

Editorial Board

2008-	Associate Editor, Environmental Health Perspectives (EHP)
2006-2012	Associate Editor, Journal of Exposure Science and Environmental Epidemiology (JESEE)



Dr. Yi-Ping Lin (Taiwan) 林宜平副教授

Associate Professor, Institute of Science, Technology and Society, Yang Ming University

E-mail: yplin3@ym.edu.tw

Dr. Lin received her bachelor and master degree in Psychology from National Taiwan University, a master degree in Bilingual Education from Boston University and later a PhD degree in Health Policy and Management. As an Associate Professor of Institute of Science, Technology and Society in Yang Ming University, her research combines her interdisciplinary knowledge of science and humanity. She is interested in environmental health and social epidemiology research especially by involving and publishing plenty of RCA lawsuit case study in Taiwan. Her vivid and elaborate expression could give us a different perspective of environmental history.

Research Interests

- Gender and Health
 - Occupational and Environmental Health
 - Risk Management and Communication
 - Public Health History
 - Social Epidemiology
 - Science, Technology and Society
 - Medical Anthropology
-

Education and Degrees

2004	PhD, Health Policy and Management, National Taiwan University
1986	MA, Department of Bilingual Education, Boston University, USA
1983	MSc, Department of Psychology, National Taiwan University, Taiwan
1981	BA, Department of Psychology, National Taiwan University, Taiwan

Professional Appointments

2011-	Associate Professor, Institute of Science, Technology and Society, Yang Ming University, Taiwan
2008-2011	Assistant Professor, Institute of Science, Technology and Society, Yang Ming University, Taiwan
2006-2008	Project Assistant Professor, Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University College of Public Health, Taiwan
2004-2006	Project Assistant Professor, Department of Public Health, National Taiwan University, Taiwan
2004	Post-Doctoral Fellow, Center of Health Risk Assessment and Policy, National Taiwan University

University College of Public Health, Taiwan

2001 Board of Directors, Taiwan Institute of Psychotherapy, Taiwan

Honors and Awards

- 2003 The Fifth Antonio T.C. Chong Award for Research in Occupational Health and Safety, American Bureau for Medical Advancement in China (ABMAC) (New York, USA)
- 2001 Best Oral Presentation by a Young Investigator, The Second Prize Winner, Pan-Pacific Conference of the International Society for Quality of Life Research (Tokyo, Japan)
-

Teaching Courses and Presentations

- Gender, Medicine and Technoscience
 - Environment, Society and Health
 - Social Worlds Theory and Research
 - Techno-science, Risk and Society
-

Selected Publications (2011-present)

1. **Lin YP**, Liu SY. Forgotten wars: Malaria eradication in Taiwan 1905-1965. In: Leung KC, Furth C. (eds), Health and Hygiene in Chinese East Asia: Policies and Publics in the Long Twentieth Century. Duke University Press, 2011:183-203.
2. **Yi-Ping Lin**. War against Mosquitoes-Science, Technology and Society Study of Post-War Malaria Eradication in Taiwan. Taiwan: A Radical Quarterly in Social Studies 2011;81: 187-235. (TSSCI)
3. **Yi-Ping Lin**. After the Death of Some Electronic Workers: The Health Risk Controversies of Organic Solvents. Taiwanese Journal for Studies of Science, Technology and Medicine 2011;12:61-112. (TSSCI)
4. Tseng MCM, **Lin YP**, Cheng TJ*. Prevalence and psychiatric co-morbidity of self-reported electromagnetic field sensitivity in Taiwan: A population-based study. Journal of the Formosan Medical Association 2011;110:634-41. (SCI)
5. Mei-Fang Chen, **Yi-Ping Lin**, Tsun-Jen Cheng. Public attitudes toward nanotechnology applications in Taiwan. Technovation 2013;33:88-96 (SCI).
6. Mei-Chih Meg Tseng, **Yi-Ping Lin**, Fu-Chang Hu, Tsun-Jen Cheng. Risks Perception of Electromagnetic Fields in Taiwan: The Influence of Psychopathology and the Degree of Sensitivity to Electromagnetic Fields. Risk Analysis 2013;33(11):2002-2012 (SCI).
7. Mei-Chih Meg Tseng, **Yi-Ping Lin**, Tsun-Jen Cheng. Effects of Psychopathology on the Characteristics of Individuals with Self-reported Electromagnetic Field Hypersensitivity. Taiwanese journal of psychiatry 2014;28(1):26-36 (TSSCI).

Arsenic, Radiation and Organic Solvents: A History of Environmental Toxins and Health in Taiwan

Dr. Yi-Ping Lin (Taiwan)

E-mail: yplin3@ym.edu.tw

Associate Professor, Institute of Science, Technology and Society, Yang Ming University

In this talk, I will use three Taiwanese case studies (arsenic, radiation and organic solvents) to elucidate how the victims, social movements, public health communities, and legal systems have reacted to the controversies of environmental toxins and health in Taiwan.

In the 1960s, an endemic disease in southern Taiwan known as “black foot disease” was proven to be correlated with exposure to arsenic via drinking water in deep wells. Further epidemiological studies indicate that drinking arsenic-rich water over a long period results in various health effects including skin problems, skin cancer, cancers of the bladder, kidney and lung, and increased the risk for diabetes, high blood pressure and reproductive disorders. Currently, the WHO's Guideline Value for arsenic in drinking water is 0.01 mg /liter.

In July, 1992, an extraordinary incident was uncovered by the Taiwanese media: recycled steel accidentally contaminated by discarded cobalt-60 sources was used in the construction of apartment buildings. The radiation contaminated more than 180 buildings (containing about 1,700 apartments), public and private schools, and small businesses in Taipei City and nearby counties. About ten thousand people occupied these buildings for periods ranging from nine to 22 years. Some residents, with the support of scientific evidence, brought the case to the court. In 1997, Taipei's district court announced the success of 57 residents in claiming national compensation for physical, property, and psychological losses resulting from the intentional negligence of government officers who concealed information about the radiation contamination for nearly a decade. Though many research papers published on the case confirmed the health hazards of long term low dose radiation exposure, there were some papers, supported by the Atomic Energy Council, which indicated that chronic exposure of the whole body to low-dose-rate radiation, even when accumulated to a high annual dose, may be “beneficial” to human health.

In 1994, a Radio Corporation of America (RCA) factory in Taiwan was accused of polluting the groundwater with trichloroethylene, tetrachloroethylene, and many other organic solvents. Subsequently, former RCA workers who had been diagnosed with cancer organized to voice their health concerns about exposure to these environmental and occupational hazards. In 1998, the government supported research on these organic solvents, including animal studies, environmental health-risk assessments, environmental epidemiology, and occupational epidemiology. Though these public health studies did not sufficiently verify a correlation between industrial pollution and human health, some of the former RCA workers brought the case to the court in 2004. Many Taiwanese public health researchers appealed to testify for the plaintiffs at court. On April 17, 2015, the Taipei District Court ordered RCA to pay NT\$560 million (US\$18.2 million) in damages to 445 former RCA employees. Nevertheless, the ruling was just a temporary victory for the former RCA workers and the many lawyers, activists, scholars, and students who worked together on the long-fought lawsuit. The controversies of environmental toxins and health in Taiwan continue.

砷、輻射和有機溶劑：臺灣的環境毒物與健康歷史

林宜平副教授 (臺灣)

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陽明大學科技與社會研究所副教授

本次的演講，我將用臺灣的案例研究(砷、輻射和有機溶劑)來闡明受害者、社會運動、公共衛生社區和法律體系如何反應臺灣的環境毒物與健康爭議。

1960 年代，臺灣南部的地方性流行疾病，也就是俗稱的「烏腳病」，被證實因飲用含砷的深井水而致病，更多的流行病學研究說明飲用富含砷的水會導致皮膚問題、皮膚癌、膀胱癌、腎臟癌和肺癌，並且增加糖尿病、高血壓和生育系統紊亂的風險等健康影響。目前，世界衛生組織的指南訂定飲用水的砷含量為 0.01 毫克/公升。

1992 年 7 月，一個特別的意外被臺灣媒體揭露：公寓建築使用的回收鋼材不慎被廢棄的鈷 60 污染。這些輻射污染了 180 棟建築物(包含 1,700 戶公寓)，台北市及鄰近城市的公立和私立學校、小型企業。上萬居民在這些建物裡居住 7 到 22 年不等。有些居民在科學證據的支持下，向法院提起訴訟。1997 年，台北地方法院宣布 57 名居民提起的國家賠償勝訴，因政府官員刻意隱瞞和忽略輻射污染消息數十年，導致身體、財產和精神等損害。雖然有些發表的研究論文證實長期低劑量的輻射污染對健康的危害，行政院原子能委員會(Atomic Energy Council)指出慢性暴露低劑量輻射，雖然長時間下來會累積可觀輻射量，但可能對身體健康是「有益的」影響。

1994 年，美國無線電公司(Radio Corporation of America, RCA)在臺灣的工廠被指控使用三氯乙烯(Trichloroethylene)和四氯乙烯(Tetrachloroethylene)等有機溶劑污染地下水。隨後，被診斷罹癌的 RCA 前員工組織起來為這個環境職業暴露危害發聲。1998 年，政府支持有機溶劑的動物實驗、環境健康風險評估、環境流行病學和職業流行病學研究。雖然這些公共衛生研究不夠清楚證明工業污染與人體健康的關聯，部分 RCA 前員工於 2004 年提起訴訟，許多臺灣的公共衛生學者為原告(RCA 的前員工)出席法院作證。2015 年 4 月 17 日，臺北地方法院宣布 RCA 必須支付新台幣 5 億 6 千萬元(約 1,820 萬美金)賠償 RCA 前員工的傷害。然而，裁決對共同參與漫長官司訴訟的 RCA 自救會成員、律師、社會運動參與者、學者和參與的學生來說只是短暫的勝利，環境毒物 and 健康的爭議在臺灣仍在持續中。

**Dr. Tony Fletcher (United Kingdom)**

Consultant Epidemiologist, Department of Environmental Change, Centre for Radiation, Chemical and Environmental Hazards, Public Health England

Senior Lecturer, Department of Social and Environmental Health Research, London School of Hygiene & Tropical Medicine

E-mail: Tony.Fletcher@lshtm.ac.uk

Dr. Fletcher works as an Environmental Epidemiologist, part time in London University at London School of Hygiene and Tropical Medicine (LSHTM) and part time for UK Government in the Centre for Radiation Chemical and Environmental Hazards of Public Health England (PHE). He holds an honorary post, Adjunct Research Professor in Environmental Health at Boston University. He was Scientist at IARC, Lyon, and President of the International Society for Environmental Epidemiology (ISEE) 2004 to 2005. During 2006 to 2013, he was part of the C8 Science Panel established to assess the links between Perfluorooctanoic acid (PFOA) contamination and disease. He has over 30 years work in occupational and environmental epidemiology and risk assessment, with experience of studies of risk factors for cancer, respiratory disease, endocrine disruptors and other adverse effects along with genetic and other mechanisms.

Education and Degrees

1987	PhD, Epidemiology, Aston University
1977	MSc, Occupational Health and Safety, Aston University
1976	BA & MA, Natural Sciences, Cambridge University

Professional Appointments

2007-	Adjunct Research Professor in Environmental Health in the School of Public Health, Boston University, Massachusetts, USA
2003-2004	Recipient of Senior Visiting Scientist Award at IARC, Lyon, France, in the Unit of Environmental Cancer Epidemiology
1995-1998	Head of Environmental Epidemiology Unit, London School of Hygiene and Tropical Medicine
1988-1989	Research Fellow (epidemiologist) in Institute of Occupational Health, University of Birmingham
1987	Research Fellow (epidemiologist) in the Medical Research Council Environmental Epidemiology Unit, Southampton
1984-1986	Scientist (epidemiologist) in the Unit of Analytical Epidemiology, IARC, Lyon
1983-1984	Research Officer at the Department of Occupational and Environmental Health, Aston University

Editorial and Society Activities

Reviewer of articles for journals including Environmental Health Perspectives, Environmental Research, International Journal of Epidemiology, Lancet, Occupational and Environmental Epidemiology, Epidemiology.

2013-2016 Member of Scientific Council of ANSES - French Agency for Food, Environmental and

Occupational Health & Safety

- 2006-2013 Member of "C8 Science Panel"
- 2004-2005 ISEE: President of International Council of International Society for Environmental Epidemiology.
- 1999 WHO/EURO: Member of WHO working group preparing documents on transport and health for Ministerial Conference on Environment and Health London
- 1996 WHO/UNECE Convention on Long-range Trans-boundary Air pollution: Expert Working Group on Health effects of ozone and nitrogen oxides in an integrated assessment of air pollution
-

Selected Publications (2014 -present)

1. Juliette Legler, **TONY FLETCHER**, Eva Govarts, Miquel Porta, Bruce Blumberg, Jerrold J. Heindel, Leonardo Trasande. Obesity, Diabetes and Associated Costs of Exposure to Endocrine Disrupting Chemicals in the European Union Journal of Clinical Endocrinology & Metabolism; Online March 2015.
2. Tamara S. Galloway, **TONY FLETCHER**, Oliver J. Thomas, Ben P. Lee, Luke C. Pilling, Lorna W. Harries. PFOA and PFOS are associated with reduced expression of the parathyroid hormone 2 receptor (PTH2R) gene in women. Chemosphere, Volume 120, February 2015, Pages 555-562.
3. Engström KS, Vahter M, **FLETCHER T**, Leonardi G, Goessler W, Gurzau E, Koppova K, Rudnai P, Kumar R, Broberg K. Genetic variation in arsenic (+3 oxidation state) methyltransferase (AS3MT), arsenic metabolism and risk of basal cell carcinoma in a European population. Environmental and Molecular Mutagenesis. 2015 Jan;56(1):60-9.
4. Simona Surdu, Edward F. Fitzgerald, Michael S. Bloom, Francis P. Boscoe, David O. Carpenter, Richard F. Haase, Eugen Gurzau, Peter Rudnai, Kvetoslava Koppova, Marie Vahter, Giovanni Leonardi, Walter Goessler, Rajiv Kumar, **TONY FLETCHER**. Polymorphisms in DNA repair genes XRCC1 and XRCC3, occupational exposure to arsenic and sunlight, and the risk of non-melanoma skin cancer in a European case-control study. Environmental Research, Volume 134, October 2014, Pages 382-389.
5. Helsingør statement on poly- and perfluorinated alkyl substances (PFASs). Scheringer M, Trier X, Cousins IT, de Voogt P, **FLETCHER T**, Wang Z, Webster TF. Chemosphere. 2014 Nov;114:337-9. doi: 10.1016/j.chemosphere.2014.05.044. Epub 2014 Jun 14.
6. Steenland, K, Savitz, DA, **FLETCHER, T**. Commentary: Class Action Lawsuits: Can They Advance Epidemiologic Research? Epidemiology. 25(2):167-169, March 2014.
7. Looker, C, Luster, M.I., Calafat, A.M., Johnson, V.J, Burleson, G.R., Burleson, F.G. and **FLETCHER, T**. Influenza vaccine response in adults exposed to perfluorooctanoate (PFOA) and perfluorooctanesulfonate (PFOS). Toxicol. Sci. 2014 Mar;138(1):76-88.
8. Deborah J. Watkins, Gregory A. Wellenius, Rondi A. Butler, Scott M. Bartell, **TONY FLETCHER**, Karl T. Kelsey. Associations between Serum Perfluoroalkyl Acids and Line-1 DNA Methylation. Environment International, Volume 63, February 2014, Pages 71-76.
9. Debapriya Mondal, Rosana Hernandez Weldon, Maria-Jose Lopez-Espinosa, Ben Armstrong, Lorna Gibson, Maria-Jose Lopez-Espinosa, Hyeong-Moo Shin, **TONY FLETCHER**. Breastfeeding, a potential excretion route for mothers and implication for infant exposure to PFOA and PFOS. Environmental Health Perspectives. 2014 Feb;122(2):187-92.

The Epidemiology of Perfluorinated Compounds – Studies in the General Population and Contaminated Communities

Dr. Tony Fletcher (United Kingdom)

Consultant Epidemiologist in the Department of Environmental Change of Centre for Radiation, Chemical and Environmental Hazards at Public Health England; Senior Lecturer in the Department of Social and Environmental Health Research at London School of Hygiene & Tropical Medicine

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Most epidemiology research on perfluorinated substances (PFAS) has focussed on PFOA and then PFOS. Endocrine disrupting effects with outcomes such as thyroid function, birthweight and obesity, and carcinogenic risks have been of particular interest, with recent reviews focusing on some of these outcomes. On cancers, the International Agency for Research on Cancer (IARC) in a recent monograph classified PFOA as possibly carcinogenic to humans (Category Group 2B). This presentation will summarise evidence on adverse effects of PFOA and how different epidemiology designs can affect results and contribute to the assessment of causality.

Studies in the general population have generally relied on measured serum levels of PFAS to distinguish high and low exposure. Furthermore, these studies have in the main been cross-sectional studies where exposure is measured at the same time as health effects, rather than longitudinal studies where exposure demonstrably precedes effect. Longitudinal studies provide more convincing evidence of causality. Studies of contaminated communities allow populations to be contrasted by external degree of exposure with more confidence. An example of this is the C8 study, a large study of a population in the Mid-Ohio Valley contaminated with PFOA, data were collected on biomarkers of PFAS and health among 69000 volunteers. The C8 Science Panel studies on this large population with substantial and well-characterised PFOA exposure, have provided both important evidence on a range of health effects related to PFOA, and insights into some methodological issues in studying these compounds.

Stable biomarkers of exposure with long half lives are attractive exposure indicators, and key components of the “internal exposome”. Perfluoroalkyl substances (PFAS), principally PFOA and PFOS, have a long half-life in humans, thus serum PFAS is a stable biomarker and is often the exposure measure of choice. The long half-life of PFAS reflects relatively low net excretion, mediated by passage into, then active reabsorption, via kidneys and gut. Individual variation in these reabsorption pathways will thus affect measured serum PFAS levels and this talk will consider the vulnerability to confounding of the use of biomarker levels as markers of exposure.

一般大眾和被污染社區的全氟碳化合物流行病學研究

Dr. Tony Fletcher (英國)

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流行病學研究的全氟碳化合物(Perfluorinated substances, PFAS)大多著重於全氟辛酸(PFOA)·其次是全氟辛磺酸(PFOS)。研究 PFAS 暴露和內分泌干擾表現在甲狀腺功能、出生體重、肥胖和癌症風險的探討備受關注。以癌症來說·國際癌症研究所(International Agency for Research on Cancer, IARC)最近將 PFOA 列為有可能令人類致癌的物質(Possibly carcinogenic to humans, 2B)。本次演講將總結 PFOA 的不良影響證據·以及不同的流行病學研究方法設計如何影響結果和因果關係的評估證據。

研究大多量測血清中的 PFAS 濃度以區分一般族群暴露濃度的高低。此外·這些研究大多在同一時間測量這些暴露濃度來判斷健康影響·而非用明確知道暴露前後影響的縱向研究。縱向研究可提供較具說服力的因果關係·研究受污染族群可對比一般族群外在暴露的影響。其中一個例子便是 C8 研究：在俄亥俄中部山谷大規模 PFOA 污染的研究·收集 PFAS 生物標記以及 69,000 名自願者的健康情況。C8 科學小組利用遭受污染的大樣本且有良好表徵的居民研究·提供 PFOA 對健康影響的重要證據·以及研究這些化合物的方法見解。

半衰期較長的穩定暴露生物標記是有吸引力的暴露指標·也是內在暴露體學的關鍵組成。全氟碳化合物主要是 PFOA 和 PFOS·在人體內都有相當長的半衰期·血清中的 PFAS 濃度是相當穩定的生物標記·可作為暴露量測的選擇。PFAS 半衰期較長·藉由腎臟和腸道的傳送與主動再吸收·反映相對較低的淨排出。個體的再吸收途徑差異於是影響測量血清 PFAS 高低·本次演講內容也將提及生物體的易感特性·以及僅用暴露濃度做為生物標記可能造成的干擾。



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Prof. Wu is Occupational Medicine Physician and Family Physician who received his PhD from Harvard School of Public Health. He is Professor, Director of Center of Environmental and Occupational Medicine at Kaohsiung Medical University. He is also Director of Occupational Medicine Center at Kaohsiung Municipal Hsiao-Kang Hospital. His interest is to examine the interactive effects of environmental and occupational exposures, genetic susceptibility, biomarkers on the health outcomes and newly-emerging environmental toxins such as melamine.

Research Interests

Community Medicine; Preventive Medicine; Molecular Epidemiology; Environmental Health & Occupational Medicine

Education and Degrees

1997	ScD, Occupational Health, Harvard University
1992	MOH., Occupational Health, Harvard University
1987	MD, Chung Shan Medical & Dental College

Professional Appointments

2007-2010	Director, Center for International Affairs, Kaohsiung Medical University
2006-2007	Director physician, Department of Occupational Medicine, China Medical University & Hospital Attending physician, Department of Family Medicine, China Medical University & Hospital
2004-2006	Director, Center for Labor Safety & Health, Kaohsiung Medical University
2003-2004	Director, Center for International Academic Exchange, Kaohsiung Medical University
2000-2006	Adjunct attending physician, Department of Occupational Medicine, Kaohsiung Medical University Hospital
1996-1997	Adjunct attending physician, Occupational Medicine, Chinese Steel Corporation, Kaohsiung

Awards

Taiwan Harvard Alumni Scholarship (1993); Harvard Alumni Scholarship at Harvard School of Public Health (1994); Orville Redenbacher Scholarship (1994); Chinese Steel Corporation Award (1995); American Bureau for Medical Advancement in China (ABMAC) Award (2000); John M. White Award (2003); Distinguished Research Award, Kaohsiung Medical University (2005, 2008, 2009, 2010)

Selected Publications (recent 5 years)

1. Chien CY, Wu CF, Liu CC, Chen BH, Huang SP, Chou YH, Chang AW, Lee HH, Pan CH, Wu WJ, Shen JT, Chang MY, Huang CH, Shiea J, Hsieh TJ, **Wu MT***: High Melamine Migration in Daily-use Melamine-made Tableware. *J Hazard Mater* 188: 350-356, 2011.
2. Liu CC (equal contribution), Wu CF (equal contribution), Chen BH, Huang SP, Goggins W, Lee HH, Chou YH, Wu WJ, Huang CH, Shiea J, Lee CH, Wu KY, **Wu MT***: Low exposure to melamine increases the risk of urolithiasis in adults. *Kidney Int.* 2011 Oct;80(7):746-52.
3. Liu CC, Wu CF, **Wu MT***: Reappraisal of melamine exposure and adult calcium urolithiasis. *Kidney Int [Letter]* 82(3):361-2, 2012.
4. **Wu MT***, Wu CF, Wu JR, Chen BH, Chen EK, Chao MC, Liu CK, Ho CK*: The public health threat of phthalate-tainted foodstuffs in Taiwan: the policies the government implemented and the lessons we learned. *Environ Int* 44: 75-79, 2012.
5. Liu CC (equal contribution), Wu CF (equal contribution), Shiea J, Cho YT, Hsieh TJ, Chou YH, Chen BH, Huang SP, Wu WJ, Shen JT, Chang MY, Huang CH, Chang AW, **Wu MT***: Detection of melamine in a human renal uric acid stone by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS). *Clin Chim Acta* 413(19-20): 1689-1695, 2012.
6. Hsieh TJ, Hsieh PC, Tsai YH, Wu CF, Liu CC, Lin MY, **Wu MT***: Melamine induces human renal proximal tubular cell injury via transforming growth factor-beta and oxidative stress. *Toxicol Sci* 2012 Nov;130(1):17-32.
7. Wu CF, Hsieh TJ, Chen BH, Liu CC, **Wu MT***: A crossover study of noodle soup consumption in melamine bowls and total melamine excretion in urine. *JAMA Intern Med.* 2013 Feb 25;173(4):317-9.
8. Lin YT (equal contribution), Tsai MT (equal contribution), Chen YL, Cheng CM, Huang CC, Wu CF, Liu CC, Hsieh TJ, Shiea J, Chen BH, **Wu MT***: Can melamine levels in one-spot overnight urine specimen predict the total previous 24-hours melamine excretion in school children? *Clin Chim Acta* 420: 128–133, 2013.
9. **Wu MT***, Wu CF, Chen BH, Chen EK, Chen YL, Shiea J, Lee WT, Chao MC, Wu **JR***: Intake of phthalate-tainted foods alters thyroid functions in Taiwanese children. *PLoS One* 2013;8(1):e55212.
10. Wu CF, Chen BH, Shiea J, Chen EK, Liu CK, Chao MC, Ho CK, Wu **JR**, **Wu MT***: Temporal changes of urinary oxidative metabolites of di(2-ethylhexyl)phthalate after the 2011 phthalate incident in Taiwanese children-Findings of a 6-month follow-up. *Environ Sci Technol.* 47(23):13754-62, 2013.
11. Wu CF, Liu CC, Chou YH, Shiea J, Shen JT, Wang HS, **Wu MT***: Increased detection rate of melamine-containing calcium urolithiasis by using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry technique in clinical practice. *Clin Chim Acta* 431: 294-298, 2014.
12. Wu CF, Chang-Chien GP, Su SW, Chen BH, **Wu MT***: Findings of 2,731 suspected phthalate-tainted foodstuffs during the 2011 phthalate incident in Taiwan. *J Formos Med Assoc* 113: 600-605, 2014.
13. Liu CC, Hsieh HM, Wu CF, Hsieh TJ, Huang SP, Chou YH, Huang CN, Wu WJ, **Wu MT***: Long-term prescription of α -blockers decrease the risk of recurrent urolithiasis needed for surgical intervention-a nationwide population-based study. *PLoS One* 2015 Apr 13;10(4):e0122494.

Melamine and Kidney Diseases

Prof. Ming-Tsang Wu (Taiwan)

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Professor in Department of Public Health at Kaohsiung Medical University; Attending Physician in Department of Family Medicine at Kaohsiung Medical University Hospital; Director of Center of Environmental & Occupational Medicine at Kaohsiung Municipal Hsiao-Kang Hospital

The melamine chemical is still ubiquitously present in our environment, even after the 2008 melamine incident in China that caused kidney-related diseases and kidney failure in children due to a large amount of melamine intake. Although our previous study has found the associated between urinary melamine levels and the risk of renal stones in adults, the relationship of environmental melamine exposure with the risk of renal damage in adults has not been explored. In this talk, I will state our recent findings about that link by using one unique occupational population: melamine tableware manufacturing workers. In the meantime, how to prevent against environmental melamine exposure from melamine tableware will be touched, also.

三聚氰胺與腎臟疾病

吳明蒼教授 (臺灣)

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高雄醫學大學公共衛生學系教授、高雄醫學大學附設中和醫院家庭醫學科主治醫師、高雄醫學大學環境醫學頂尖研究中心主任

三聚氰胺仍普遍存在於我們的生活環境中，即使在 2008 年中國(乳製品)三聚氰胺(汙染)事件，因大量三聚氰胺暴露，造成(當地)幼童腎病變與腎衰竭的(案件)發生。過去我們的研究團隊已報導尿中三聚氰胺濃度與成人腎結石風險的關聯性，然而環境中三聚氰胺暴露與腎功能損害的風險尚未被探究。這次演講內容，將透過特定職業暴露對象-美耐皿餐具製造工人的研究，說明近期研究成果。同時，演講內容也會提及如何預防美耐皿餐具中三聚氰胺的暴露。

空氣汙染對健康影響

Session Two: Air Pollution and Health Impact

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Prof. Chun-Yuh Yang (Taiwan) 楊俊毓副校長

Distinguished Professor and Vice President, Kaohsiung Medical University

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Dr. Chun-Yuh Yang obtained his PhD degree at Yale University. He is the Vice President of Kaohsiung Medical University. He is an expert in the Environmental epidemiology, particularly in Air pollution epidemiology. Also, he served as an associate editor of Journal of Toxicology and Environmental Health since 2006.

Education and Degrees

1993	PhD, Department of Epidemiology and Public Health, School of Medicine, Yale University
1984	MPH, Graduate Institute of Public Health, School of Medicine, National Taiwan University
1982	BSc, Department of Public Health, School of Medicine, National Taiwan University

Professional Appointments

2012-	Vice president, Office of Vice President, Kaohsiung Medical University.
2012-	Distinguished Professor, Institute of Public Health, Kaohsiung Medical University
2006-2012	Dean, Office of Information Technology, Kaohsiung Medical University
2003-	Joint appointed investigator, Division of Environmental Health and Occupational Health, National Health Research Institute (NHRI)
2001-2006	Dean, College of Health Sciences, Kaohsiung Medical University
2000-2006	Chairman, Institute of Public Health, College of Health Sciences, Kaohsiung Medical University
2000-2001	Acting Dean, College of Health Sciences, Kaohsiung Medical University
1999-2012	Professor, Institute of Public Health, Kaohsiung Medical University
1999-2001	Director of Graduate Studies, Kaohsiung Medical University
1994-1999	Associate professor, Institute of Public Health, Kaohsiung Medical College

Awards

2008	Ho Chin-Tui Outstanding Honorable Award, Ho Chin-Tui Foundation, Taiwan.
2001	Biography included in the 18th edition of Who's Who in the world
2001	Outstanding award for research, Kaohsiung Medical University Alumni Foundation
1997	Cheng Kung-Pei Memorial Award, Taiwan Public Health Association, Taiwan

Editorial Activities

Editorial Board Member, Global Health Perspectives (2013-); Editorial Board Member, Advances in Environmental Research (2012-); Editorial Board Member, Inhalation Toxicology(2008-); Issue Editor, Encyclopedia of Environmental Health (2008-); Associate Editor, Journal of Toxicology and Environmental Health (2006-); Editorial Board Member, Magnesium Research (2003-); Guest Editor, Journal of Toxicology and Environmental Health (2002&2005); Editorial Board Member, Kaohsiung Journal of Medical Sciences (2002-); Editorial Board Member, Taiwan Journal of Public Health (2000-)



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Prof. Chan is Professor, Associate Dean and Director of Global Health Center at National Taiwan University College of Public Health. He serves as a Councilor for International Society for Environmental Epidemiology (ISEE), Chair for International Society for Environmental Epidemiology–Asia Chapter (ISEE-AC) since 2015 and President of the Society for Risk Analysis in Taiwan (TSRA). He is currently involved in cross-country epidemiological studies with an international partner of ESCAPE. His research pertains to major issues of public health concern and environmental pollution.

Education and Degrees

1990	ScD, Air Pollution Control, Harvard School of Public Health
1987	MSc, Industrial Hygiene and Air Pollution Control, Harvard School of Public Health
1982	BA, Chemistry and Biology of Public Health, National Taiwan University, College of Medicine

Professional Appointments

2007-2011	Director of International Health Center in Taiwan, College of Public Health, National Taiwan University
1999-2005	Director of Institute of Occupational Medicine and Industrial Hygiene, College of Public Health, National Taiwan University
1997-1998	Takemi Fellow in International Health, Harvard University Fulbright Visiting Scholar
1996-	Professor, Institute of Occupational Medicine and Industrial Hygiene, College of Public Health, National Taiwan University

Society Activities

2015-2017	Councilor, International Society for Environmental Epidemiology (ISEE)
2015-	Chair Elect, International Society for Environmental Epidemiology – Asia Chapter (ISEE-AC)
2014-2016	Steering Committee Member, Association of Pacific Rim Universities (APRU) Global Health Program
2009-	Chairman, Taiwan Chapter of Society for Risk Analysis
2008-2011	Councilor of International Society of Exposure Analysis (ISEA)
2008-	President of Society for Risk Analysis in Taiwan
2003-	Member of Disaster Response and Relief Committee, Taipei County Member of the National Health Information Committee, Ministry of Health, Taiwan

2002-	Member of the Comprehensive Preventive Health Care Committee, Ministry of Health, Taiwan
2000-	Member of the National Sustainable Development Committee, Executive Yuan, Taiwan
	Member of the National Environmental Quality Committee and Environmental Impact Assessment Committee, Taiwan Environmental Protection Agency
1996-2000	Member of Environmental Impact Assessment Committee, Taipei City
1994-1997	Member of Technical Committee of Air Pollution Fee, Taiwan Environmental Protection Agency

Selected Publications (2014-present)

1. Lee JH, Wu CF, Hoek G, de Hoogh K, Beelen R, Brunekreef B, **Chan CC***. Land use regression models for estimating individual NO_x and NO₂ exposures in a metropolis with a high density of traffic roads and population. *Science of the Total Environment* 2014;472:1163-1171.
2. Chio CP, Yuan TH, Shie RH, **Chan CC***. Assessing vanadium and arsenic exposures for residents near a petrochemical complex by two-stage dispersion models. *Journal of Hazardous Materials* 2014;271:98-107.
3. Chen SY, **Chan CC***, Lin YL, Hwang JS, Su TC*. Fine particulate matter results in hemodynamic changes in subjects with blunted nocturnal blood pressure dipping. *Environmental Research* 2014;131:1-5.
4. Chen YM, Lin WY, **Chan CC***, The impact of petrochemical industrialisation on life expectancy and per capita income in Taiwan: an 11-year longitudinal study. *BMC Public Health* 2014;14:247.
5. Wu CF, Lin HI, Ho CC, Yang TH, Chen CC, **Chan CC**. Modeling horizontal and vertical variation in intraurban exposure to PM_{2.5} concentrations and compositions. *Environmental Research* 2014;133:96-102.
6. Lin RT, Chien LC, Chen YM, **Chan CC***. Governance matters: an ecological association between governance and child mortality. *International Health* 2014;6:249-257.
7. Chen CH, Chao HJ, **Chan CC**, Chen BY, Guo YL. Current asthma in schoolchildren is related to fungal spores in classrooms. *Chest* 2014;146:123-134.
8. Chen CH, **Chan CC**, Chen BY, Cheng TJ, Guo YL. Effects of particulate air pollution and ozone on lung function in non-asthmatic children. *Environmental Research* 2015;137:40-48.
9. Yuan TH, Shie RH, Chin YY, **Chan CC***. Assessment of the levels of urinary 1-hydroxypyrene and air polycyclic aromatic hydrocarbon in PM_{2.5} for adult exposure to the petrochemical complex emissions. *Environmental Research* 2015;136:219-26
10. Yuan TH, Chio CP, Shie RH, Pien WH, **Chan CC***. The distance-to-source trend in vanadium and arsenic exposures for residents living near a petrochemical complex. *Journal of Exposure Science and Environmental Epidemiology* 2015 (Accepted).
11. Chen SY, Lin YL, Chang, WT, Lee CT, **Chan CC***. Increasing emergency room visits for stroke by elevated levels of fine particulate constituents. *Science of The Total Environment* 2014;473-474:446-450
12. Chen YT, Huang YK, Luvsan ME, Gombojav E, Ochir C, Bulgan J, **Chan CC***. The influence of season and living environment on children's urinary 1-hydroxypyrene levels in Ulaanbaatar, Mongolia. *Environmental Research* 2015;137:170-175

Health Effects for Residents in the Vicinity of a Petrochemical Complex

Prof. Chang-Chuan Chan (Taiwan)

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Professor and Associate Dean of National Taiwan University College of Public Health; Director of Global Health Center of National Taiwan University College of Public Health

Situated on the west coast of central Taiwan, the No. 6 Naphtha Cracking Complex is the largest petrochemical complex in Taiwan. With a total area of 2,603 ha, this facility houses 64 plants within a single complex, including oil refineries, naphtha cracking plants, cogeneration plants, coal-fired power plants, heavy machinery plants, boiler plants, and downstream petrochemical-related plants in Mailiao Township, Yunlin County, Taiwan.

Firstly, we compared life expectancies and personal income between the industrial county (Yunlin County) to one reference county (Yilan County), which had no significant industrial activity that might emit pollutants, in Taiwan. And, we found that residents of the industrialized county had lesser increases in life expectancy over time than did residents in the reference county, with difference means ranging from 0.89 years ($p < 0.05$) to 1.62 years ($p < 0.001$) at different stages, but there were no significant differences in individual income between the two counties.

Secondly, we established a sustainable environmental epidemiological cohort study with a total of 3,230 residents to clarify the comprehensive environmental exposure and health status of residents in Yunlin County. The main findings of health examinations are that the abnormal rates of lung functions, BMI, platelet, BUN, GOT (AST), GPT (ALT), hepatitis C, cholesterol, and LDL-C for residents who lived within 10 km radius from a petrochemical complex were significantly higher than those lived farther from the complex.

Thirdly, we analyzed all cancer incidence rate (ICD-9:140-165, 170-176, 179-208) of the cohort after the operation of the complex (1999-2010), and we found that the all cancer incidence rate of older than 35-year-old female residents lived within 10 km radius from the complex during 2008-2010 was 1.60 times higher than those lived farther from 20 km from the complex (95% CI 1.07-2.39), 1.55 times (95% CI 1.00-2.38) for older than 60-year-old residents, 2.17 times (95% CI 1.16-4.08) for older than 60-year-old female residents after adjusting confounding factors.

Fourthly, we found that emissions from the petrochemical complex can elevate particle-phase PAH concentrations in surrounding areas and increase the urinary 1-OHP levels of adults living nearby, and a distance-to-source gradient in V and As exposures exists for residents living near the petrochemical complex and the two-stage dispersion model can predict such a trend for V when inhalation is the major exposure route. In addition, amino acid and carbohydrate metabolite profiles of residents nearby were linked to exposure to heavy metals and organics emitted from the petrochemical complex and affected human health through PPAR and insulin signaling pathways, with altered physiological stress responses.

石化綜合工業區附近居民的健康影響

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臺灣大學公共衛生學院副院長及教授、全球衛生中心主任

位於臺灣西海岸，六輕工業區是臺灣最大的石化綜合廠，位於雲林縣麥寮鄉，坐擁 2,603 公頃土地，包含煉油廠、石油煉解廠、汽電共生廠、火力發電廠、重型機械廠、鍋爐廠和石油下游廠等 64 個工廠。

首先，我們比較工業縣 (雲林縣)以及另一個沒有明顯工業污染源的參考縣(宜蘭縣)居民的平均餘命和平均收入，我們發現隨著時間推移，工業縣的居民平均餘命較參考縣增加的幅度較低，工業縣與參考縣的平均餘命差距更從 0.89 年($p < 0.05$)隨著時間上升到 1.62 年($p < 0.001$)。但這兩個縣的居民平均收入並無明顯差異。

此外，我們建立了一個持續的環境流行病學研究世代，其中包含 3,230 名居民，以釐清雲林縣居民全面的環境暴露與健康狀態。健康檢查發現距離六輕 10 公里內的居民肺部功能、BMI、尿素氮(BUN)、肝指數 GOT(AST)、GPT (ALT)、C 型肝炎(Hepatitis C)、膽固醇(Cholesterol)和低密度膽固醇(LDL-C)異常狀況明顯高於距離六輕較遠的居民。

再者，我們分析了六輕營運後(1999-2010)的世代族群的癌症發生率(ICD-9:140-165, 170-176, 179-208)，發現在 2008 年至 2010 年間，經過干擾因子調整後，居住在六輕半徑 10 公里內 35 歲以上女性居民的癌症發生率是居住在半徑 20 公里以上的 1.6 倍(95% CI 1.07-2.39)，60 歲以上居民為 1.55 倍(95% CI 1.00-2.38)，而 60 歲以上的女性居民則為 2.17 倍(95% CI 1.16-4.08)。

最後，我們發現六輕的排放物會增加週遭環境中的粒狀多環芳香烴(PAH)的濃度而造成附近成年人尿液中的 1-羥基焦腦油(1-OHP)濃度上升。也發現六輕附近居民的尿中鈾(V)和砷(As)濃度與其距離六輕的遠近有著明顯的梯度關係，而當空氣吸入為主要之暴露途徑時，兩階段擴散模式(Two-stage dispersion model)可有效預測鈾(V)的趨勢。再者，六輕附近居民的胺基酸和碳水化合物代謝情形與其暴露到六輕所排放出的重金屬及有機物相關聯，並藉此來改變 PRAR 與胰島素信號等途徑而影響身體健康，且會伴隨著一些生理壓力反應的變化。

**Prof. Hai-dong Kan (China) 闕海東教授**

CMB Distinguished Professor and Director, Department of Environmental Health,
School of Public Health, Fudan University
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Prof. Kan is Professor and Director of Department of Environmental at Fudan University in Shanghai, China. He received a MD in Preventive Medicine from Shanghai Medical University and a PhD in Environmental Epidemiology from Fudan University. Also, he was Post-Doctoral Fellow of NIEHS in the US. His research focuses in air pollution and health impact and environmental epidemiology. And he is Regional Editor of Environment Health Perspectives journal, Reviewer for journals such as Lancet, JAMA and American Journal of Epidemiology. He was awarded by American Thoracic Society for David Bates Award in 2007 and China Medical Board for Distinguished Professor Award in 2011.

Education and Degrees

2003	PhD, Environmental Epidemiology , Fudan University, Shanghai, China
2000	MSc, Environmental Health Sciences, Fudan University, Shanghai, China
1997	MD, Preventive Medicine, Shanghai Medical University, Shanghai, China

Professional Appointments

2008	Associate Professor, Deputy Director, Department of Environmental Health, School of Public Health, Fudan University
2005-2007	Post-doctoral fellow , Epidemiology Branch , National Institute of Environmental Health Sciences, National Institutes of Health, U.S.A
2001	Visiting fellow at P. Catholic University of Chile
1996	Intern in Medicine, 5th Hospital, Shanghai, China

Awards

China Medical Board (CMB) Distinguished Professorship Award (2011), Shanghai Municipality, Science & Technology Progress Award (2009), Chinese Preventive Medicine Association, Science & Technology Progress Award (2009), Shanghai Medical Association, Science & Technology Progress Award (2009), Meiji Life Science Award (2008), American Thoracic Society, David Bates Award (2007), Shanghai Municipality, Science & Technology Progress Award (2005), Shanghai Medical Association, Science & Technology Progress Award (2005) , Science & Technology Commission of Shanghai Municipality, Rising Star Award for Young Investigators (2004)

Editorial and Society Activities

Regional Editor: Environment Health Perspectives; Editorial Board member: Epidemiology

Editorial Advisory Board member: Atmospheric Environment

Member: China National Consultative Committee of Environment and Health, International Society of Environmental Epidemiology, Chinese Medical Association, Chinese Preventive Medicine Association, Chinese Society of Particulate

Reviewer for journals: Lancet, JAMA, American Journal of Epidemiology, Environmental Health Perspective, Epidemiology, Environmental Science and Technology, Atmospheric Environment, Stroke, Environmental Research, Journal of Environmental Management, BMC Public Health, International Journal of Health Geographics, Journal of Applied Microbiology, Advance in Atmospheric Science, Inhalation Toxicology

Selected Publications (2014 -present)

1. Chen R, Zhao Z, Sun Q, Lin Z, Zhao A, Wang C, Xia Y, Xu X, **Kan H*** (2015). Size-fractionated particulate air pollution and circulating biomarkers of inflammation, coagulation and vasoconstriction in a panel of young adults. *Epidemiology*, 26(3):328-36.
2. Zhao A, Chen R, Wang C, Zhao Z, Yang C, Lu J, Chen X, **Kan H*** (2015). Associations between size-fractionated particulate air pollution and blood pressure in a panel of type II diabetes mellitus patients. *Environ Int*, 80: 19-25.
3. Cai J, Chen R, Wang W, Xu X, Ha S, **Kan H*** (2015). Does ambient CO have protective effect for COPD patient? *Environ Res*, 136: 21–26.
4. Wang C, Chen R, Zhao Z, Cai J, Lu J, Ha S, Xu X, Chen X, **Kan H*** (2015). Particulate air pollution and circulating biomarkers among type 2 diabetic mellitus patients: the roles of particle size and time windows of exposure. *Environ Res*, 140: 112–118.
5. Dai J, Chen R, Meng X, Yang C, Zhao Z, **Kan H*** (2015). Ambient air pollution, temperature and out-of-hospital coronary deaths in Shanghai, China. *Environ Pollut*, 203: 116–21.
6. GBD 2013 Mortality and Causes of Death Collaborators (2015). Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 385(9963):117-71.
7. **Kan H*** (2014). Globalisation and environmental health in China. *Lancet*, 384(9945): 721-723.
8. Chen R, Cai J, Meng X, Kim H, Honda Y, Guo L, Samoli E, Yang X, **Kan H*** (2014). Ozone and daily mortality in 21 cities of East Asia: how does season modify the association? *Am J Epidemiol*, 180(7):729-36.
9. Chen R, Li T, Cai J, Yan M, Zhao Z, **Kan H*** (2014). Extreme temperatures and out-of-hospital coronary deaths in 6 large Chinese cities. *J Epidemiol Community Health*, 68:1119-1124.
10. Yang C, Chen A, Chen R, Qi Y, Ye J, Li S, Li W, Liang Z, Liang Q, Guo D, **Kan H***, Chen X* (2014). Acute effect of ambient air pollution on heart failure in Guangzhou, China. *Int J Cardiol*, 177: 436–441.
11. Ma W, Chen R, **Kan H*** (2014). Temperature-related mortality in 17 large Chinese cities: how heat and cold affect mortality in China. *Environ Res*, 134: 127-133.
12. Gordon SB, Bruce NG, Grigg J, Hibberd PL, Kurmi OP, Lam KH, Mortimer K, Asante KP, Balakrishnan K, Balmes J, Bar-Zeev N, Bates MN, Breyse PN, Buist S, Chen Z, Havens D, Jack D, Jindal S, **Kan H**, Mehta S, Moschovis P, Naeher L, Patel A, Perez-Padilla R, Pope D, Rylance J, Semple S, Martin WJ (2014). Respiratory risks from household air pollution in low and middle income countries. *Lancet Respir Med*, 2(10):823-60.
13. Tang D *, Wang C, Nie J, Chen R, Niu Q, **Kan H***, Chen C, Perera F (2014). Health Benefits of Improving Air Quality in Taiyuan, China. *Environ Int*, 73: 235–242.
14. Cai J, Zhao A, Zhao J, Chen R, Wang W, Ha S, Xu X, **Kan H*** (2014). Acute Effects of Air Pollution on Asthma Hospitalization in Shanghai, China. *Environ Pollu*, 191C:139-144.
15. Wang C, Chen R, Kuang X, Duan X*, **Kan H*** (2014). Temperature and daily mortality in Suzhou, China: a time series analysis. *Sci Total Environ*, 466-467C: 985-990.

Ambient Air Pollution and Population Health in China

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As the largest developing country, China has been changing rapidly over the last three decades and its economic expansion is largely driven by the use of fossil fuels, which leads to a dramatic increase in emissions of ambient air pollutants. China is now facing the worst air pollution problem in the world. A number of epidemiological studies on air pollution and population health have been conducted in China, using time-series, case-crossover, cross-sectional, cohort, panel or intervention designs. The increased health risks observed among Chinese population are somewhat lower in magnitude, per amount of pollution, than the risks found in developed countries. However, the importance of these increased health risks is greater than that in developed countries, because the levels of air pollution in China are very high in general and Chinese population accounts for more than one fourth of the world's totals. Future research will need to clarify the lifetime course of air pollution effects with full control of potential confounders (e.g., prospective cohort studies), examine the relevance of cumulative exposures, disentangle effects of multiple pollutants, investigate gene–environment interactions and other factors that may modify air pollution health effects, and identify pathophysiologic links between air pollution and health hazards for the Chinese population.

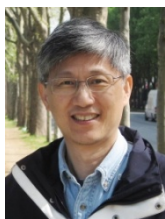
中國的環境空氣污染與人群健康

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作為最大的發展中國家，中國在過去三十年裡一直迅速變化，它的經濟擴張來自化石燃料的使用，這導致大氣污染排放量的顯著增加。中國正面臨世界上最嚴重的空氣污染問題，一些對空氣污染與人群健康的流行病學研究已在中國進行，利用時間序列(Time-Series)、病例交叉(Case-Crossover)、橫斷式(Cross-Sectional)、世代(Cohort)、追蹤(Panel)或介入(Intervention)的研究設計。觀察到的中國人民健康風險增加程度比其他已開發國家少，單位污染量較低。然而，健康風險增加的重要性卻較這些已開發國家要大上許多，因為中國的空氣污染普遍非常嚴重，而中國佔了全世界四分之一以上的人口。未來的研究需要控制潛在混雜因素(例如：前瞻性世代研究)釐清空氣污染全面影響程度，檢視累積暴露、理清多種污染的影響、研究基因與環境的交互作用、或是其他可能的空污健康影響因子，並且確認中國人口在空氣污染與健康危害之間的病理生理關聯。



Prof. Tsun-Jen Cheng (Taiwan) 鄭尊仁教授

Professor, Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University College of Public Health
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Prof. Cheng received his MSc in Public Health and PhD in Cancer Biology from Harvard University. He was Occupational Medicine Resident at Harvard School of Public Health and Internal Medicine Resident at Brown University Memorial Hospital in the US. He has served as Director for the Department of Occupational Safety and Hygiene at National Taiwan University Hospital in 1996-1997 and Director for the Institute of Occupational Medicine and Industrial Hygiene at National Taiwan University in 2005-2011. His research interests include environmental and occupational Medicine, molecular epidemiology and inhalation toxicology.

Research Interests

Occupational and environmental medicine; Inhalation toxicology; Air pollution and health; Nanotechnology and health; PVC workers and liver cancer

Education and Degrees

1995	ScD, Cancer Biology, Harvard School of Public Health, USA
1984	MPH, Harvard School of Public Health, USA
1980	MD, Taipei Medical College, Taiwan

Professional Appointments

2006-	Visiting Staff, Environmental and Occupational Medicine, National Taiwan University Hospital
2005-2011	Director, Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University College of Public Health
2004-	Professor, Division of Environmental and Occupational Medicine, National Taiwan University College of Medicine
2002-	Professor, Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University College of Public Health
2000-2005	Director, Occupational Hygiene Section, Environmental Protection and Occupational Safety and Hygiene Center, National Taiwan University
1996-2002	Associate Professor, Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University College of Public Health
1996-1997	Director, Department of Occupational Safety and Hygiene, National Taiwan University Hospital
1995-2006	Visiting Staff, Internal Medicine, National Taiwan University Hospital
1991-1992	Occupational Medicine Resident, Harvard School of Public Health, USA
1988-1991	Internal Medicine Resident, Brown University Memorial Hospital of Rhode Island, USA

Society Activities

2008-2011	Associate Editor, Environmental Health Perspectives
2004-2007	Editorial board, Inhalation Toxicology
2003-2008	Editorial review board, Environmental Health Perspectives
2001-	Editorial board, Institute of Occupational Safety and Health Journal
2001-2013	Editorial board, Taiwan Journal of Public Health

Selected Publications (2014-present)

1. Chen TT, Chuang KJ, Chiang LL, Chen CC, Yeh CT, Wang LS, Clive G., Tim J., Kelly B., Lee CN, Chuang HC *, **Cheng TJ ***. Characterization of the interactions between protein and carbon black. Journal of Hazardous Materials. 2014;264:127-135.
2. Juang YM, Lai BH, Chien HJ, Ho M, **Cheng TJ**, Lai CC. Changes in protein expression in rat bronchoalveolar lavage fluid after exposure to zinc oxide nanoparticles: an iTRAQ proteomic approach. Rapid Commun Mass Spectrom 2014;28:974-80.
3. Liu WT, Bien MY, Chuang K J, Chang TY, Jones T, BeruBe K, Lalev G, Tsai DH, Chuang HC *, **Cheng TJ** and Taiwan CardioPulmonary Research Group. Physicochemical and biological characterization of single-walled and double-walled carbon nanotubes in biological media. J Hazard Mater 2014;280C:216-225.
4. Jung CC, Tsai YS, Chang CC, **Cheng TJ**, Chang CW, Liu PY, Chiu YJ, Su HJ. Allergen exposure induces adipose tissue inflammation and insulin resistance. Int Immunopharmacol 2014;23:104-112.
5. Chuang HC, Juan HT, Chang CN, Yan YH, Yuan TH, Wang JS, Chen HC, Hwang YH, Lee CH, **Cheng TJ ***. Cardiopulmonary toxicity of pulmonary exposure to occupationally relevant zinc oxide nanoparticles. Nanotoxicology. 2014; 8:593-604.
6. Chen WL, Lin CY, Yan YH, Cheng KT, **Cheng TJ ***. Alterations in rat pulmonary phosphatidylcholines after chronic exposure to ambient fine particulate matter. Mol Biosyst 2014;10:3163-9.
7. Yan YH, C CKC, Wang JS, Tung CL, Li YR, Lo K, **Cheng TJ ***. Subchronic effects of inhaled ambient particulate matter on glucose homeostasis and target organ damage in a type 1 diabetic rat model. Toxicol Appl Pharmacol 2014;281:211-220.
8. Chen CH, Chan CC, Chen BY, **Cheng TJ**, Leon Guo Y. Effects of particulate air pollution and ozone on lung function in non-asthmatic children. Environ Res 2014;137C:40-48.
9. Meg Tseng MC, Lin YP, **Cheng TJ***. Effects of Psychopathology on the Characteristics of Individuals with Self-reported Electromagnetic Field Hypersensitivity. Taiwanese Journal of Psychiatry 2014;28:27-37.
10. Shih TJ, Lin YP, **Cheng TJ**. Public perception of nanotechnology and its policy in Taiwan. Chinese Journal of Communication Research, 2015. (Accepted, in Chinese)
11. Chuang HC, Chen LC, Lei YC, Wu KY, Feng PH, **Cheng TJ***. Surface area as a dose metric for carbon black nanoparticles: A study of oxidative stress, DNA single-strand breakage and inflammation in rats. Atmospheric Environment 2015; 106: 329-334.
12. Huang KL, Lee YH, Chen HI, Liao HS, Chiang BL, **Cheng TJ***. Zinc oxide nanoparticles induce eosinophilic airway inflammation in mice. Journal of Hazardous Materials 2015; 297: 304-312.

Inhalation Toxicities of Ambient Particles

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Ambient particles have been reported in epidemiological studies to be associated with the mortality and morbidity from respiratory and cardiovascular diseases. However, the causal relationship and underlying mechanisms were unclear.

We have conducted a serial inhalation studies to answer the questions. To expose the animals with real-world ambient particles, the state of the art particle concentrator was used to generate particles. We first investigated if ambient particles caused acute hemodynamic changes. Blood pressure and electrocardiogram were recorded continuously before, during and after the exposure. We found that acute exposure to ambient particles caused the alterations of blood pressure, heart rate and heart rate variability. This system was also used to investigate the toxicity of particles during Asian dust event. Again, we found an increase of systemic and lung inflammation, heart rate, and blood pressure during the dust event. These studies have demonstrated that acute exposure to ambient particles may affect the autonomic function of the cardiovascular system.

In addition to acute toxicity, we are interested in the health effects from chronic exposure to ambient particles. The association of PM with the development of diabetes and subsequent cardiovascular diseases has been reported. We constructed a non-concentrated ambient particle exposure system, Taipei Air Pollution Exposure System (TAPES). The system is easy to operate and maintain for chronic exposure as compared to the particle concentrator. Hyperglycemic rats were induced and exposed to ambient particles for three months. The average concentration of ambient particles during the three months of exposure period was around $13 \mu\text{g}/\text{m}^3$. We found emphysematous changes of lung, increased wall thickness of aorta, myocardial inflammation, and advanced glomerulosclerosis and proximal tubule changes. There were biochemical changes including increased HbA1c, fibrinogen and systemic inflammation. In the healthy rats, we also observed increased wall thickness, focal myocarditis, systemic inflammation and increased insulin resistance. Thus, PM exposure may induce the macro-and micro-vascular complications in the diabetics through chronic hyperglycemia and systemic inflammation.

Furthermore, findings in healthy animals support the hypothesis that diabetes may be caused by PM through insulin resistance. Our results not only provided evidence of causal relationship to support the epidemiological studies, but also provided directions for future epidemiological studies. It is also noted that the average concentration of PM_{2.5} during exposure was lower than the current national standard and close to WHO guideline. Therefore, our results have important policy implication in air pollution control.

大氣微粒的吸入性毒性

鄭尊仁教授 (臺灣)

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臺灣大學公共衛生學院職業醫學與工業衛生研究所教授

流行病學研究已揭露大氣微粒對呼吸系統及心血管疾病的發病率與死亡率的關係，然而，因果關係和潛在的機制並不清楚，對此我們進行了連續性的研究設計來回答這個問題。

為了讓動物暴露在真實世界環境中的空氣微粒，我們使用微粒濃縮器(Art particle concentrator)製造大氣微粒。首先，我們先調查是否大氣微粒引起急性血液動力的改變。連續記錄下血壓和心電圖在暴露前、暴露中及暴露後的狀態，我們發現急性暴露於大氣微粒會導致血壓、心跳和心律變動的變化，這個系統也可用在調查亞洲塵暴期間的毒性研究。再者，我們發現塵暴期間全身和肺部的發炎情況增加，心跳、血壓變高，這些研究說明，急性暴露於環境中的微粒可能導致心血管系統的自主功能。

除了急性毒性外，我們感興趣的還有慢性暴露於環境微粒對健康的影響。PM 與糖尿病和心血管疾病發展的關係已經被報導，我們建造了一個非微粒濃縮暴露系統(Non-concentrated ambient particle exposure system) — 臺北空氣污染暴露系統(Taipei Air Pollution Exposure System, TAPES)。對於慢性暴露研究，這個系統比起微粒濃縮器的操作和維護容易。高血糖大鼠被誘導暴露於環境微粒中三個月，這段時間周圍的環境微粒平均濃度約為 13 微克/立方米，我們發現肺氣腫、主動脈壁增厚、心肌炎、腎絲球硬化和近端小管改變，生化的變化包含糖化血色素(HbA1c)、纖維蛋白原(Fibrinogen)和全身發炎反應；而健康的大鼠，我們也觀察到血管壁增厚、局部性心肌炎、系統性發炎和胰島素阻抗增加等情況。因此，對糖尿病患者 PM 暴露可能藉由慢性高血糖和全身性發炎誘發宏觀及微觀的心血管併發症。再者，在健康大鼠身上發現支持 PM 可能導致胰島素阻抗而造成糖尿病的假說。我們的結果不僅提供因果關係的證據來支持流行病學研究，還提供今後的流行病學研究的方向。同時還注意到，本研究的 PM_{2.5} 暴露平均濃度小於目前國家標準，而接近世界衛生組織(WHO)的準則。因此，我們的研究結果在空氣污染控制上有重要的政策含意。



Dr. Ta-Chen Su (Taiwan) 蘇大成醫師

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Associate Professor, National Taiwan University College of Medicine
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Dr. Su is Clinical Associate Professor at National Taiwan University College of Medicine and Attending Cardiologist of Department of Internal Medicine at National Taiwan University Hospital. He has 23 years of experience in academic research and teaching in the fields of cardiovascular disease, vascular biology, dyslipidemia, and occupational and environmental health. His recent research has focused on environmental and cardiovascular health, particularly the health effects of air pollution and endocrine disrupting chemicals in various susceptible populations. He also served as a committee member in Taiwan Society of Cardiology and Taiwan Society of Hypertension and scientific committee member of Asia-Pacific Society of Atherosclerosis and Vascular Disease (APSAVD).

Education and Degrees

1998-2005	PhD, Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University College of Public Health
1985-1990	MD, National Cheng Kung University
1979-1983	BA, National Taiwan University College of Public Health

Professional Appointments

2012-	Clinical Associate Professor, Department of Internal Medicine, National Taiwan University College of Medicine
2004-2005	Visiting physician, Center for Occupational and Environmental Health, UC Irvine, USA
1995-1996	Physician, Aeronautical medical center, Civil Aeronautics Administration, Ministry of Transportation and Communication
1990-1993	Internal Medicine Resident, National Cheng Kung University Hospital

Society Activities

Committee: Preventive cardiology in Taiwan Society of Cardiology, Taiwan Society of Hypertension, Asia-Pacific Society of Atherosclerosis and Vascular Disease (APSAVD , 2012-)

Selected Publications (2014-present)

1. Wang J, Ning X, Yang L, Lu H, Tu J, Jin W, Zhang W, **Su TC***. Trends of hypertension prevalence, awareness, treatment and control in rural areas of northern China during 1991-2011. J Hum Hypertens. 2014;28:25-31.
2. Cheng Y, Du CL, Hwang JJ, Chen IS, Chen MF, **Su TC***. Working hours, sleep duration and the risk of acute coronary heart disease: a case-control study of middle-aged men in Taiwan. Int J Cardiol. 2014;

171:419-22.

3. Chen SY, Chan CC, Lin YL, Hwang JS, **Su TC***. Fine particulate matter results in hemodynamic changes in subjects with blunted nocturnal blood pressure dipping. *Environ Res.* 2014 May; 131:1-5.
4. Lin LY, Wen LL, **Su TC**, Chen PC, Lin CY. Negative association between serum perfluorooctane sulfate concentration and bone mineral density in U.S. premenopausal women: NHANES, 2005 to 2008. *J Clin Endocrinol Metab.* 2014 June; 99:2173-80.
5. Wang J, Ning X*, Yang L, Tu J, Gu H, Zhan C, Zhang W, **Su TC***. Sex differences in trends of incidence and mortality of first-ever stroke in rural Tianjin, China, from 1992 to 2012. *Stroke* 2014 June; 45:1626-1631
6. Tsao TM, Tsai MJ*, Wang YN, Lin HL, Wu CH, Hwang JS, Hsu SHJ, Chao H, Chuang KJ, Chou CCK, **Su TC***. The health effects of a forest environment on subclinical cardiovascular disease and health-related quality of life. *PLoS One* 2014 Jul 28;9(7):e103231.
7. Hsiao SM, **Su TC**, Chen CH, Chang TC, Lin HH. Autonomic dysfunction and arterial stiffness in female overactive bladder patients and antimuscarinics related effects. *Maturitas.* 2014 Sep;79(1):65-9.
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14. Wang J, An Z, Li B, Yang L, Tu J, Gu H, Zhan C, Liu B, **Su TC**, Ning X. Increasing stroke incidence and prevalence of risk factors in a low-income Chinese population. *Neurology.* 2015 Jan 27;84(4):374-81.
15. **Su TC**, Hwang JJ, Chen YC, Chan CC. Carotid intima-media thickness and long-term exposure to traffic-related air pollution in middle-aged residents of Taiwan: A cross-sectional study. *Environ Health Perspect* 2015; March 20 Epub.
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Air Pollution and Cardiovascular Health: Current and Future Perspectives

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More and more evidences indicated environmental pollutions are important risk factors affecting cardiovascular diseases (CVDs). Among these, urban air pollution shared the greatest contribution on human health, which is not only confined to illness but also involves a higher impact on CVDs morbidity and mortality.

The mechanisms linking air pollution and cardiovascular diseases are proposed in the scientific statement from the American Heart Association by Brook et al., and our previous studies may add support for these mechanisms. We have provided evidence that exposure to air pollution may decrease pulse pressure in the general population. Short-term exposure to PM_{2.5} contributes to pulse pressure narrowing along with cardiac and vasomotor dysfunctions in office workers with non-dipper of blood pressure at night. Moreover, in middle-aged adults, the carotid intima-media thickness (CIMT) and inflammation indices in terms of blood leukocyte and monocyte are associated with the individual's exposure to air pollution of PM_{2.5} absorbent, PM₁₀, NO₂, and NO_x as derived from long-term air pollution exposure estimated by land-use regression models of the European Study of Cohorts for Air Pollution Effects. These studies provide supporting evidence of an increased risk of subclinical cardiovascular health following long-term air pollution exposure in Asia.

In searching for which kind of natural environments may benefit our health, we have demonstrated the potential favorable health effects on subclinical CVD in terms of CIMT and subjective HRQOL in workers living in forest environment compared to those of living in urban city. In addition, we also found a significant effect on activation of natural killer cell after a 3-day's short-term stay in forest (XiTou).

Air quality in Asia has deteriorated significantly in recent decades because of rapid industrialization, urbanization, and motorization. How to cope with these issues and critical conditions, searching for possible solutions are anticipated.

空氣污染與心血管健康：現況與未來展望

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越來越多的證據顯示環境污染是影響心血管疾病的重要因素。其中，都市空氣污染對人體健康的影響最大，不僅是一般疾病，還會導致較高的心血管疾病發病率和死亡率。

美國心臟學會布魯克(Brook)等人提出的科學聲明顯示空氣污染與心血管疾病的連結機制，我們之前的研究結果也支持此項作用機制。我們的研究顯示一般大眾在空氣污染暴露下可能導致脈搏壓(收縮壓與舒張壓的差距)降低，短期暴露在 $PM_{2.5}$ 下的上班族會造成脈搏壓變小、心臟和血管收縮功能障礙、晚間非杓型(non-dipper)^{註一}血壓等影響。再者，利用歐洲空氣污染世代追蹤研究(European Study of Cohorts for Air Pollution Effects, ESCAPE)所發展的土地利用迴歸模式(Land-use Regression Model)研究顯示，中年成人的頸動脈內膜-中層厚度(CIMT)^{註二}、炎症指標(Inflammation Indices)、白血球細胞、單核細胞和長期暴露空氣污染物如 $PM_{2.5}$ (粒徑小於 $2.5\ \mu m$ 的細懸浮微粒)、 PM_{10} 、 NO_2 與 NO_x 有相關性！

尋找哪種自然環境對健康可能有幫助，我們比對住在森林中和一般城市的工作者，證明了潛在有利的健康效果如亞臨床心血管疾病、頸動脈內膜-中層厚度和主觀健康相關生活品質(Health-Related Quality of Life, HRQOL)。此外，我們的研究發現在溪頭森林區短暫停留三天對於自然殺手細胞(Natural Killer Cell)的激活有顯著效果！

亞洲的空氣品質近年來因為快速的工業化、都市化和機動化而顯著惡化，預期尋求可能的解決之道來處理這個議題和嚴峻的條件！

註一：一般人的血壓到了夜間會下降，血壓波動呈現杓型，非杓型(non-dipper)即無明顯夜間血壓降低的情況。

註二：頸動脈內膜-中層厚度(CIMT)指的是頸動脈管壁的內膜加上中層的厚度，以高解析的超音波測量，經常被應用於流行病學與臨床研究。可代表早期動脈粥狀硬化的程度，與心血管或腦血管疾病有很高的相關性。

兒童環境健康

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Dr. Mei-Hwan Wu is Superintendent of National Taiwan University Children's Hospital. She obtained her MD and PhD at the National Taiwan University in Taiwan and also completed her EMBA from National Taiwan University. She is an expert in the cardiac electrophysiology, from cellular to cardiac catheterization theater. She is a pioneer in pediatric transcatheter arrhythmia therapy. Besides, her research foci cover widely the spectrum of congenital heart disease and acquired heart disease in children.

Research Interests

- Clinical aspects of arrhythmias, including the mechanism (particularly the unique mechanism in complex CHD, such as AV node-to-AV node tachycardia), the ablation technique, and the outcome assessment
 - Cellular electrophysiology, including the maturation the cardiac ionic channels, the age-related difference of pharmacological reaction such as cisapride, quinidine, lidocaine, etc
 - Genetic alteration underlying the QT syndrome
 - Clinical scenario from congenital heart disease and long QT gene polymorphism
 - Population study for the congenital heart disease
 - Cardiologic aspects of Kawasaki disease, particularly assessment and intervention for CV risk
 - Cardiologic aspects of Marfan syndrome, the intervention and the pharmacological risk reduction trial
 - System dynamic modeling for medical economic analysis
-

Education and Degrees

1986-1992 PhD, National Taiwan University

1973-1980 MD, National Taiwan University

Professional Appointments

2012-2014 President, Asian Pacific Pediatric Cardiac Society

2011-2014 President, Taiwan Pediatric Association

2000-2003 Chief Editor of the Pediatrics and Neonatology

Publications

More than 300 papers in peer reviewed journals.



Dr. Peter van den Hazel (Netherlands)

President, Health and Environment Alliance (HEAL) & International Network for Children's Health, Environment and Safety (INCHES)

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Dr. Hazel received his MD from University of Amsterdam. He is Co-Founder of International Coordinator of International Network for Children's Health, Environment and Safety (INCHES). He is also President of Health and Environment Alliance (HEAL) since 2012. He has received advanced training in management of non-profit organizations, epidemiology, medical statistics, radiation safety, corporate environmental care, and project management. He has coordinated several EU-funded projects, such as PINCHE, CHEST and Climate TRAP.

Education and Degrees

2010-	Public Health Advisor HazMat
1986-1989	MPH: degree in Environmental Medicine, Dutch Institute of Preventive Medicine (TNO- PG)
1985	General Practitioner (House Physician); degree University of Amsterdam
1982	Medical Doctor, University of Amsterdam
1972	Gymnasium (Cartesius Lyceum, Amsterdam) Diploma

Professional Appointments

2010-2012	Vice-president, Health and Environment Alliance (HEAL)
2009-2012	Project coordinator for Climate TRAP-EU funded project on Climate change and public health
2008-2010	Contract at Radboud University for PHEEDUNET project as Scientific coordinator
2007-2010	Project coordinator for PRONET – EU funded project
2005-	President EUPHA section Environment Related Diseases
2004-	Co-chair Healthy Environments for Children Alliance, (secretariat at WHO)
2003-2006	Project leader for CHEST (Children's Health, Environment and Safety training)
2001-2003	President International Society of Doctors for the Environment
1998-	Chair of the Board of International Network on Children's Health, Environment and Safety (INCHES)
1988-1998	President, Dutch Association of Environmental Medicine
1986-	Environmental Health Specialist, working for Combined Municipal Health Services in Gelderland, the Netherlands
1982-1984	District medical officer, Commonwealth of Dominica

International Service

2000-2001	INCHES coordinator for UN Special Session on children (Prep Com meetings)
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1998-2001	NGO representative at European Roundtable on Children's Environmental Health
1998	Founder, International Network on Children's Health, Environment and Safety (INCHES)
1997	Member, WHO Working Group on Epidemiological Approaches to Assessment of Health Consequences of Accidents and Disasters
1992	Committee member Dutch Platform Brasil UNCED
1989-1991	Committee member FOZ (Financiële Overzicht Zorg (Financial Health Care Committee)) of KNMG (Royal Dutch Medical Society)

Selected publications

1. Athos, photos and poems, Uitg. Luyten, 1981 (poetry)
2. **van den Hazel P**, van Loenhout J, Slottje P, Jongeneel R. The PRONET project: pollution reduction options network to enhance implementation of successful transport and indoor environment practices in Europe. Int. J. Environment and Health, Vol. 2, Nos. 3/4, 2008. 293-303.
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4. **van den Hazel, P.** Liu, Hai-Ying, Bartonova, A. Information materials for external users and dissemination plan. HENVINET OR 37/2010. Norwegian Institute for Air Research. 2010
5. Zuurbier M, Hoek G, Oldenwening M, Lenters V, Meliefste K, **Van den Hazel P**, Brunekreef B. Commuters' exposure to particulate matter air pollution is affected by mode of transport, fuel type, and route. Environ Health Perspect. 2010; 118: 783-789.
6. Zuurbier M, Hoek G, Oldenwening M, Meliefste K, **Van den Hazel P**, Brunekreef B. Respiratory effects of commuters' exposure to air pollution in traffic. Epidemiology. 2011; 22(2): 219-227
7. Zuurbier M, Hoek G, Oldenwening M, Meliefste K, Krop E, **Van den Hazel P**, Brunekreef B. In-traffic air pollution exposure and CC16, blood coagulation, and inflammation markers in healthy adults. Environ Health Perspect. 2011 Oct;119(10):1384-9. Epub 2011 Jun 10.
8. **Hazel, P van den**, Stauffer A. Children and Environmental Health. Chapter in IMPROVING THE QUALITY OF CHILDHOOD IN EUROPE 2012, VOLUME 3
9. Keune H, Ludlow D, **van den Hazel P**, Randall S, Bartonova A. A healthy turn in urban climate change policies; European city workshop proposes health indicators as policy integrators. Environ Health. 2012 Jun 28;11 Suppl 1:S14.
10. Bartonova A, Koppe JG, Fucic A, Gutleb AC, **van den Hazel P**, Keune H. The Health and Environment Network and its achievements. Environ Health. 2012 Jun 28;11 Suppl 1:S1.
11. Grossberndt S, **van den Hazel P**, Bartonova A. Application of social media in the environment and health professional community. Environ Health. 2012 Jun 28;11 Suppl 1:S16.
12. **van den Hazel P**, Keune H, Randall S, Yang A, Ludlow D, Bartonova A. The challenge of social networking in the field of environment and health. Environ Health. 2012 Jun 28;11 Suppl 1:S15.
13. Böse-O'Reilly S, Lob-Corzius T, **van den Hazel P**. Klimawandel und Gesundheitssysteme in Europa. Pädiatrische Allergologie in Klinik und Praxis. 15. Jg./Nr. 3. 2012. 31-34.
14. Mark J Nieuwenhuijsen, et al. Positive health effects of the natural outdoor environment in typical populations in different regions in Europe (PHENOTYPE): a study programme protocol. BMJ Open2014;4:e004951

The Importance of Children's Environmental Health to the World

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Children are the litmus test for the future. Will the future turn acid or not? One cannot have a healthy population of children on a sick planet. The exposures of children are increasing every year. Air pollution in Asia, food related issues in Latin America, noise and more chemical compounds in Europe, heavy metals in different hot spots, endocrine disruptors everywhere. More scientific knowledge emerges that environmental stressors may lead to adverse epigenetic changes, resulting in multigenerational and transgenerational effects. Currently we are burdening generations to be born after the year 2050.

Exposure to environmental stressors and occupational risks have life-long implication on developmental processes in children. Dietary deficiency or oversupply and psychological stress are covariates in studies on developmental stressor exposure. Exposome studies aim at integrating assessment of the totality of hazards. Further, epigenomics are an important study area as mechanism for effects on health by environmental stressors.

Relevant exposure levels and new technology testing have to be identified to pinpoint outcome assessments. Focus on vulnerable windows of exposure, e.g. in the preconceptional period, and mechanisms leading to genome effects, resulting in transgenerational effects are needed for a new characterization of risk factors and their interactions on humans. In the preconception period a variety of possible mechanisms are leading to effects. Validity of animal models, tissue specificity and biomarker development are needed in research to make scientific progress.

Children are the vulnerable group that are incapable to change their changing exposure. They depend on adults for protecting their health. The policy makers, the producers, society at large have to make protective decisions. They have to become responsible for future generations. Information-sharing between academic research and decision-making world is essential to provide a public health and scientific perspective. Children's environmental health is a global problem with regional differences: epidemic obesity versus malnourishment, mega-cities with air pollution versus rural exposure to persistent pesticides. Complex environmental exposures need to be interpreted by experts, to prevent misunderstandings, to support appropriate discussion on possible societal implications, to overcome challenges and to steer towards appropriate interventions to promote children's health.

兒童環境健康對世界的重要性

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歐盟健康與環境聯盟(Health and Environment Alliance, HEAL)以及國際兒童健康環境網絡(International Network for Children's Health, Environment and Safety, INCHEs)主席

兒童是未來世界的酸鹼試劑，知道未來的世界是否變成酸性？**一個生病的星球無法孕育出健康的孩童**。亞洲的空氣污染、拉丁美洲的食物問題、歐洲的噪音和化合物暴露、重金屬和內分泌干擾物的污染隨處可見。越來越多的科學知識證實了環境壓力可能導致不良的表觀遺傳(Epigenetic)變化，導致多代及跨代的影響，目前，我們正背負著 2050 年後出生孩童們的健康！

環境壓力及職業風險暴露對兒童發展過程影響是終生的。飲食不足、過剩或是心理壓力都是兒童發展暴露研究的共同影響因子。暴露體研究(Exposome study)係量測個體自受孕開始到生命最終所接觸的總暴露，用以描繪環境因子與疾病的關係，另外，表徵基因體學(Epigenomics)是環境壓力對健康影響的重要機制研究領域。

相關的暴露基準及新技術測試需要確定之後方能做出結果評估。專注於脆弱的暴露窗口，例如孕前、基因影響和跨世代作用機制等研究來了解這些風險因子對人體健康的作用。目前我們已了解懷孕前許多機制會有健康的影響，促進科學研究發展需要有效的動物模型、組織特異性、生物標誌性。

兒童是脆弱的族群，他們無法改變生活的暴露環境，所以依賴大人們守護他們的健康。決策者、生產者以及整個社會必須制定保護的政策，替未來的世代負責。學術與政策制訂機構間以科學或是公共衛生角度的資訊交流是不可或缺的。兒童環境健康是全球的問題然而有存在著區域間的差異性：肥胖以及營養不良、巨型都市的空氣污染以及農村長效性農藥暴露。複雜的環境暴露需仰賴專家來解釋，以防誤解，並支持合適的社會影響討論，克服挑戰，施行合適的介入措施以促進兒童的健康！

**Prof. David Bellinger (United States)**

Professor, Neurology and Psychology Harvard Medical School and Department of Environmental Health, Harvard School of Public Health

Senior Research Associate in Neurology and Senior Associate in Psychology, Children's Hospital Boston

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Prof. Bellinger is Professor of Neurology at Harvard Medical School and Professor of Environmental Health at Harvard School of Public Health. He is also a Senior Research Associate in Neurology and a Senior Associate in Psychiatry at the Children's Hospital Boston. He edited a textbook entitled Human Development Neurotoxicology. And he is currently President of the International Society for Children's Health and the Environment. He has served as a member of several committees of EPA, CDC, and ATSDR, as well as served as an advisor to the WHO's Joint Expert Committee on Food Safety and chairperson to WHO's Guidelines on the Prevention and Management of Lead Poisoning.

Education and Degrees

1987	MSc, Epidemiology, Harvard School of Public Health
1977	PhD , Psychology, Cornell University
1971	BA , Williams College

Professional Appointments

2010-	President, International Society for Child Health and the Environment
1994-2003	Associate Professor of Neurology (Psychology), Harvard Medical School
1991-2000	Director of Research, Behavioral Pediatrics Fellowship Program, Children's Hospital Boston
1978-1979	Public Health Service Postdoctoral Fellow, Department of Psychology, Boston University

Awards and Honors

2013	Environmental Health Perspectives, Reviewer of the Year
2013	Bernstein Lecturer, Department of Psychiatry, Boston Children's Hospital
2011	M.I.N.D. Institute Distinguished Lecturer, University of California-Davis
1985-1990	National Institute of Environmental Health Sciences Research Career Development Award

Committee and Editorial Service

Committee: Member, Biology and Medicine Panel, Research Grants Council, University Grants Committee, Hong Kong (2014-), Member, WHO Expert Advisory Panel on Food Safety, World Health Organization (2011-), WHO Guidelines on the Prevention and Management of Lead Poisoning, World Health Organization (Chairperson) (2011-), Consultant, European Food Safety Authority, Use of the Benchmark Dose Approach in Risk Assessment (2009), Committee on Clinical Investigation (Institutional Review Board), Children's Hospital Boston (2007-2011), WHO/International Programme on Chemical Safety (1997)

Editorial Positions: Medicine (2014), Editor-in-Chief, Toxics (2012-), Environmental Health Perspectives

(2011-), Environmental Health (2010-), Nutrition and Dietary Supplements (2009-), Clinical Epidemiology and Risk Assessment (2008-), Open Environmental Sciences (2008-), Neurotoxicology (2007-), Neurotoxicology and Teratology (2005-), Neurotoxicology and Teratology (2001-2004), Neurotoxicology and Teratology (1995-2001)

Selected Publications (2014-present)

1. Stein CR, Savitz DA, **Bellinger DC**. Perfluorooctanoate exposure in a highly exposed community and parent and teacher reports of behavior in 6-12 year old children. *Paediatric and Perinatal Epidemiology* 2014; 28:146-156.
2. Maserejian NN, Shrader P, Trachtenberg FL, Hauser R, **Bellinger DC**, Tavares M. Dental sealants and flowable composite restorations and psychosocial, neuropsychological, and physical development in children. *Pediatric Dentistry* 2014; 36:68-75.
3. **Bellinger DC**, Rivkin MJ, DeMaso D, Robertson RL, Stopp C, Dunbar-Masterson, Wypij D, Newburger JW. Adolescents with tetralogy of Fallot: Neuropsychological assessment and structural brain imaging. *Cardiology in the Young* 2014;11:1-10.
4. Manji KP, McDonald CM, Kupka R, Bosch RJ, Kisenge R, Aboud S, **Bellinger DC**, Fawzi WW, Duggan CP. Effect of multivitamin supplementation on the neurodevelopment of HIV-exposed Tanzanian infants: A randomized, double-blind, placebo-controlled clinical trial. *Journal of Tropical Pediatrics* 2014;60:279-286.
5. Fortenberry GZ, Meeker JD, Sanchez BN, **Bellinger D**, Peterson K, Schnaas L, Solano-Gonzalez M, Ettinger AS, Hernandez-Avila M, Hu H, Tellez-Royo M. Paraoxonase polymorphisms and attention/hyperactivity in school-age children from Mexico City. *Environmental Research* 2014; 132: 342-349.
6. Cheng HH, Wypij D, Laussen PC, **Bellinger DC**, Stopp CD, Soul JS, Newburger JW, Kussman BD. Cerebral blood flow velocity and neurodevelopmental outcome in infants undergoing surgery for congenital heart disease. *Annals of Thoracic Surgery* 2014; 98: 125-132.
7. Oulhote Y, Mergler D, Barbeau B, **Bellinger DC**, Bouffard T, Brodeur ME, Saint-Amour D, Legrand M, Sauvé S, Bouchard MF. Neurobehavioral function in school-age children exposed to manganese in drinking water. *Environmental Health Perspectives* 2014; 122:1343-1350.
8. Karwowski MP, Just AC, **Bellinger DC**, Jim R, Hatley EL, Ettinger AS, Hu H, Wright RO. Maternal iron metabolism gene variants modify umbilical cord blood lead levels by gene-environment interaction: a birth cohort study. *Environmental Health* 2014;13(1):77
9. Cassidy AR, White MT, DeMaso DR, Newburger JW, **Bellinger DC**. Executive function in children and adolescents with severe congenital heart disease. *Journal of the International Neuropsychological Society* 2014; 9:1-16.
10. Choi AL, Zhang Y, Sun G, **Bellinger D**, Wang K, Yang XJ, Li JS, Zheng Q, Fu Y, Grandjean P. Association of cognitive deficits with prenatal exposure to fluoride in Chinese children: A pilot study. *Neurotoxicology and Teratology* 2015; 47: 96-101.
11. Panigrahy A, Schmithorst VJ, Wisnowski JL, Watson CG, **Bellinger DC**, Newburger JW, Rivkin MJ. Relationship of white matter network topology and cognitive outcome in adolescents with d-transposition of the great arteries. *Neuroimage Clinical* 2015; 7: 438-48.

Characterizing the Public Health Impact of Children's Exposures to Environmental Chemicals

Prof. David Bellinger (United States)

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Professor of Neurology and Psychology at Harvard Medical School and Department of Environmental Health at Harvard School of Public Health; Senior Research Associate in Neurology and Senior Associate in Psychology at Children's Hospital Boston

Efforts to estimate the societal burden of children's exposures to neurotoxic environmental chemicals tend to focus on the monetary or health costs associated with specific outcomes, e.g., diseases such as Attention Deficit Hyperactivity Disorder and Intellectual Disability (i.e., an intelligence score that is reduced to <70). In this presentation, I argue that such approaches substantially underestimate the public health impact of early-life exposures to these chemicals. Two major limitations are discussed.

The first is the need to consider "subclinical" toxicity as well as clinical toxicity. Because of the high prevalence of some exposures, even a small effect size associated with it can result in a surprisingly large impact on the population level. This is illustrated by comparing the total population IQ losses associated with chemical exposures (lead, methylmercury, organophosphate pesticides), to those associated with major pediatric health conditions and events. The second limitation is the failure to design, analyze, and interpret studies of neurotoxicity in terms of an explicitly developmental perspective. The major elements of such a perspective are discussed and illustrated. These include the concept of "developmental cascades," whereby early-life neurotoxicant exposure sets in motion a process that unfolds over time, including epigenetic expressions that are initially silent, and alters the normal aging process; the concept that co-exposures and contextual characteristics influence the expression of neurotoxicity; and the concept that early-life neurotoxicant exposure acts as an effect modifier, limiting the way in which a child can respond to future neurodevelopmental challenges.

兒童暴露環境化學物的公共衛生影響描繪

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評估兒童暴露於環境神經毒性化學物質的社會負擔，往往把重點放在如醫療費用等具體結果，如疾病，注意力不足過動症(ADHD)和智力障礙（即智商低於 70）。我認為這樣的做法持續低估了早期暴露於這些化學品的公共衛生影響，在這次演講中，將討論兩個主要限制。

首先，除了臨床毒性外，需要考慮「亞臨床」毒性。因為某些暴露的高盛行率，即便只有很少的劑量，也會對人體產生出乎意料的顯著影響，兒童主要健康狀況和事件可藉由暴露化學物質(鉛、甲基汞、有機磷殺蟲劑等等)降低智力影響等關係得知。第二個限制則是在明確的前瞻性研究下，設計、分析和解釋神經毒性研究的失敗。主要的前瞻性元素將進行討論與說明。這些主要元素包含發展串聯(Developmental Cascades)，意思是起初表觀遺傳(Epigenetic)靜默，但由於早期神經毒性暴露，隨著時間推移而改變正常老化過程；共同暴露和脈絡特徵的概念會影響神經毒理的表現；並且早期的神經毒物暴露扮演修飾因子(Effect modifier)，限制兒童未來的神經發育！

**Dr. Joachim Heinrich (Germany)**

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Dr. Heinrich is the Unit Head of population studies and Senior Consultant at Ludwig-Maximilians-University since 2015. He is also an Epidemiologist and Director of the Institute of Epidemiology at Helmholtz Zentrum München (German Research Center for Environmental Health). He has authored more than 700 publications and has been involved in numerous national and international epidemiological research projects examining common chronic diseases especially the relationship between air pollution and respiratory health. He has coordinated several international projects such as ENRIECO, ESCAPE and INTARESE.

Research Interests

Long-term and short-term effects of ambient air pollution on several health parameters; Measurement and monitoring of ambient air pollution and assessment of exposure to ambient air pollution; Determinants of asthma and allergies (including indoor biocontaminants, dietary factors, life-style related factors) ; Longitudinal data analysis

Education and Degrees

1982-1986 Postgraduate Training in Biomathematics and statistics in medicine, Berlin, Germany
1982 PhD in Epidemiology, Medical School Erfurt
1970-1974 Study of Mathematics, Friedrich-Schiller University of Jena, Jena

Professional Appointments

2011-2015 Director of Institute of Epidemiology I, Helmholtz Zentrum München, Neuherberg/Munich
1992-2011 Group leader, Helmholtz Zentrum München, Institute of Epidemiology, Neuherberg/Munich
1990-1992 Scientist, University of Wuppertal
1983-1989 Group leader, Department of Preventive Cardiology, Medical School Erfurt
1974-1983 Scientist, Medical School Erfurt

Membership and Editorial Activities

Member of several Review Panels for German Ministries such as the BMBF, the German Research Foundation, the EU, the Wellcome trust, several national research funding institutions, WHO and other funding agencies; Associate editor and member of editorial boards of several scientific journals; Reviewer for numerous scientific journals such as New England Journal of Medicine, The Lancet, Environmental Health Perspectives, European Respiratory Journal, JACI, Allergy, etc; Member of steering committee of several national and international scientific research projects and consortia; International ranking of worldwide leading researchers on asthma on rank 16; top 10 ranking in air pollution epidemiology authors (Zell et al J Occup Med Toxicol. 2010; 5: 5.)

Selected Publications (2014 -present)

1. Tiesler CM, **Heinrich J**. Prenatal nicotine exposure and child behavioural problems. *Eur Child Adolesc Psychiatry*. 2014 Oct;23(10):913-29.
2. Cai Y, et al. Cross-sectional associations between air pollution and chronic bronchitis: an ESCAPE meta-analysis across five cohorts. *Thorax*. 2014 Aug 11. pii: thoraxjnl-2013-204352.
3. Wacker ME, Hunger M, Karrasch S, **Heinrich J**, Peters A, Schulz H, Holle R. Health-related quality of life and chronic obstructive pulmonary disease in early stages - longitudinal results from the population-based KORA cohort in a working age population. *BMC Pulm Med*. 2014 Aug 9;14:134.
4. Eeftens M, Hoek G, Gruzieva O, Mölter A, Agius R, Beelen R, Brunekreef B, Custovic A, Cyrys J, Fuertes E, **Heinrich J**, Hoffmann B, de Hoogh K, Jedynska A, Keuken M, Klümper C, Kooter I, Krämer U, Korek M, Koppelman GH, Kuhlbusch TA, Simpson A, Smit HA, Tsai MY, Wang M, Wolf K, Pershagen G, Gehring U. Elemental composition of particulate matter and the association with lung function. *Epidemiology*. 2014 Sep;25(5):648-57.
5. Vimalaswaran KS, et al. Association of vitamin D status with arterial blood pressure and hypertension risk: a mendelian randomisation study. *Lancet Diabetes Endocrinol*. 2014 Sep;2(9):719-29.
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7. Loth DW, et al. Genome-wide association analysis identifies six new loci associated with forced vital capacity. *Nat Genet*. 2014 Jul;46(7):669-77.
8. Markevych I, Thiering E, Fuertes E, Sugiri D, Berdel D, Koletzko S, von Berg A, Bauer CP, **Heinrich J**. A cross-sectional analysis of the effects of residential greenness on blood pressure in 10-year old children: results from the GINIplus and LISAplus studies. *BMC Public Health*. 2014 May 20;14:477.
9. Fuertes E, Markevych I, von Berg A, Bauer CP, Berdel D, Koletzko S, Sugiri D, **Heinrich J**. Greenness and allergies: evidence of differential associations in two areas in Germany. *J Epidemiol Community Health*. 2014 Aug;68(8):787-90.
10. **Heinrich J**, Koletzko B, Koletzko S. Timing and diversity of complementary food introduction for prevention of allergic diseases. How early and how much? *Expert Rev Clin Immunol*. 2014 Jun;10(6):701-4.
11. Wang M, et al. Performance of multi-city land use regression models for nitrogen dioxide and fine particles. *Environ Health Perspect*. 2014 Aug;122(8):843-9.
12. Cousminer DL, et al. Genome-wide association study of sexual maturation in males and females highlights a role for body mass and menarche loci in male puberty. *Hum Mol Genet*. 2014 Aug 15;23(16):4452-64.
13. Park SL, et al. Pleiotropic associations of risk variants identified for other cancers with lung cancer risk: the PAGE and TRICL consortia. *J Natl Cancer Inst*. 2014 Apr;106(4):dju061.
14. Bousquet J, et al. Birth cohorts in asthma and allergic diseases: report of a NIAID/NHLBI/MeDALL joint workshop. *J Allergy Clin Immunol*. 2014 Jun;133(6):1535-46.
15. Pinart M, et al. Comorbidity of eczema, rhinitis, and asthma in IgE-sensitised and non-IgE-sensitised children in MeDALL: a population-based cohort study. *Lancet Respir Med*. 2014 Feb;2(2):131-40.
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Exposure to Greenness and Health Outcomes

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Exposure to nature and in particular to green vegetation is intuitively suggested to have beneficial effects on human health since centuries. New technologies such as data from geographical information systems (GIS) and satellite images substantially improved the assessment of exposure to greenness and allowed to describe the association between these exposures and health outcomes. This review will summarize the current knowledge on empirical associations between exposure to greenness and a broad spectrum of health indicators and will explore potential underlying mechanisms.

A small number of epidemiological studies consistently showed a lower total mortality and in particular due to cardio-vascular causes with increasing exposure to greenness in the residential area. Also cardio-vascular morbidity is lower in subjects highly exposed to greenness. The most consistent finding is related to higher birth weights in the exposed populations. Even sensitivity analyses showed consistently that those babies born to underprivileged families have a stronger benefit in terms of higher birth weights compared to babies from families with a higher socio-economic background. Less consistent are the effects of higher exposure to greenness for being small for gestational age or preterm birth. Several studies reported that more neighborhood greenness or easy access to green space was associated with less psychiatric morbidity in adults. The epidemiological studies are different in design (most cross-sectional, a few cohort studies, some register based ecological studies), in methods to assess exposure to greenness (objective measures, questionnaire based data, access to green space, vegetation intensity by NDVI, canopy cover, etc.), the intensity of adjustments for potential confounders, and the climatic conditions. Despite these strong methodological differences, the consistency of some findings is even more surprising.

The mechanisms for these empirical associations are not clear so far. Several speculations and hypothesis are in discussion. The oldest attempt to explain these associations is based on Ulrich's psychoevolutionary theory, which suggests that exposure to nature decreases stress. Other explanations are related to a committing reduced exposure to noise, ambient air pollution, and heat waves. There is some data supporting this speculation, but the evidence is not strong. Physical activity (and consequently normal body weight) might be increased if green parks are close to the residential addresses. Apart of these explanations, the potential of residual confounding, even if the associations were adjusted for educational level and income, is substantial. Finally publication bias cannot be ruled out. It is always a problem if a recent emerging risk was described. However the value of these recent study findings is enormous, because of the quantification of the health benefits and the motivation to city planners to increase green space areas in particular in metropolitan areas.

接觸綠地的健康成效

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德國慕尼黑大學資深顧問、赫慕尼黑姆霍茨中心(德國環境健康研究中心)流行病學所所長

幾個世紀以來，直觀的認為接觸自然特別是綠色植物對人體健康有助益，新科技如地理資訊系統(Geographical Information Systems, GIS)、衛星影像改善接觸綠色植物的量測和研究健康效益之間的關係。這次的研究回顧會歸納目前的知識經驗連結廣泛的健康指標，探討潛在的底層機制。

少部分的流行病學研究一致顯示接觸住家附近的綠色植物越多，死亡率越低，特別是心血管方面的因素；而腦心血管的發病率也因接觸較多的綠色植物而降低。較一致的研究發現，多接觸綠色植物的族群，嬰兒出生體重較重；即便敏感性分析(Sensitivity Analyses)也是一致的，比起家庭較富裕的小孩，來自貧困家庭的小孩在出生體重上受益較多；較不一致的研究顯示多接觸綠色植物會有早產的現象。許多研究報告顯示較容易接近綠色植物或是社區有綠地會降低成人的精神疾病。這些流行病學研究在設計方法上不盡相同，大多是橫斷面研究(Cross-Sectional)，有些是世代研究(Cohort Studies)，有些則是採用生態研究(Ecological Studies)。而接觸綠色植物多寡的量測方法包含問卷資料、客觀度量，並用常態化差異植生指標(NDVI)、林冠被覆度(Canopy Cover)等等方式了解接觸綠地和植被的強度，並調整潛在干擾因子以及氣候因素。即便這些方法學上的差異，呈現結果的一致性依舊令人驚訝。

這些機制的實證關聯尚不明確，許多猜測和假設仍在討論中，最早試圖解釋的是 Ulrich 的心理演化理論(Psychoevolutionary theory)，這說明接觸自然能降低壓力。其他的解釋則與減低噪音、空氣污染和心跳有關。有些數據支持這猜測，但是證據不夠強烈。若公園綠地在住家附近，則體能活動(體重)會增加。除了這些解釋，調整潛在干擾因子如教育水準和收入，影響依舊不可小覷。這些論文研究的偏差無法被排除，最近的新興風險闡述這個事實，然而，最近的這些研究價值無比珍貴，來自對健康效益量化和城市規畫者增加綠地的動機增加，特別是在大都會區！

**Prof. Eun-Hee Ha (Korea)**

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Prof. Ha received a MD from Ewha Womans University, a MSc in Public Health from Seoul National University and a PhD in Occupational and Environmental Medicine from Catholic University. She is Professor of Preventive Medicine at Ewha Womans University and Director of Center for Mothers and Children's Environmental Health (MOCEH). She was Visiting Scholar at Harvard School of Public Health in 1999-2000. She has also served for WHO's Children's Health and the Environment (CEH) and International Collaboration on Air Pollution and Pregnancy Outcomes (ICAPPO) as an advisor.

Education and Degrees

1997	PhD, Graduate School of Catholic University
1992	MSc, Graduate School of Seoul National University
1987	MD, College of Medicine, Ewha Womans University

Professional Appointments

1999-2000	Visiting Scholar, Environmental Epidemiology, Harvard School of Public Health, USA
1994-	Professor, Department of Preventive Medicine, Ewha Womans University School of Medicine
1993-1994	Assistant Professor, Department of Preventive Medicine, Dongguk University School of Medicine
1991-1993	Director Dept. of Health Management, Korean Industrial Health Association
1988-1991	Residency, Preventive Medicine, Ewha Womans University Medical Center
1987-1988	Internship, Severance Hospital, Yonsei University College of Medicine

Awards

2009	Presidential awards, Korea Ministry of Environment
2004	Prizes for distinguished scientific and technological papers, Korean Federation of Science and Technology Societies

Selected Publications (2014-present)

1. Kwon JH, Kim E, Chang MH, Park EA, Hong YC, Ha M, Park H, Kim Y, Park C, Ha EH. Indoor total volatile organic compounds exposure at 6 months and atopic dermatitis prevalence at 3 years in children. *Pediatr Allergy Immunol.* 2015 Apr 13.
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10. Ha EH, Cho YK. The Mediating Effects of Self-Esteem and Optimism on the Relationship between Quality of Life and Depressive Symptoms of Breast Cancer Patients. *Psychiatry Investig.* 2014 Oct;11(4):437-45.
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12. Kim BM, Choi AL, Ha EH, Pedersen L, Nielsen F, Weihe P, Hong YC, Budtz-Jørgensen E, Grandjean P. Effect of hemoglobin adjustment on the precision of mercury concentrations in maternal and cord blood. *Environ Res.* 2014 Jul;132:407-12.
13. Lee WK, Lee HA, Hwang SS, Kim H, Lim YH, Hong YC, Ha EH, Park H. A time series study on the effects of cold temperature on road traffic injuries in Seoul, Korea. *Environ Res.* 2014 Jul;132:290-6.
14. Eum JH, Cheong HK, Ha EH, Ha M, Kim Y, Hong YC, Park H, Chang N. Maternal blood manganese level and birth weight: a MOCEH birth cohort study. *Environ Health.* 2014 Apr 29;13(1):31.
15. Kim E, Park H, Hong YC, Ha M, Kim Y, Kim BN, Kim Y, Roh YM, Lee BE, Ryu JM, Kim BM, Ha EH. Prenatal exposure to PM₁₀ and NO₂ and children's neurodevelopment from birth to 24 months of age: mothers and Children's Environmental Health (MOCEH) study. *Sci Total Environ.* 2014 May 15;481:439-45.
16. Park B, Shin A, Jung-Choi K, Ha E, Cheong HK, Kim HJ, Park KH, Jang S, Moon BI, Ha M. Correlation of breast cancer incidence with the number of motorvehicles and consumption of gasoline in Korea. *Asian Pac J Cancer Prev.* 2014; 15(7):2959-64
17. Lee BE, Park H, Hong YC, Ha M, Kim Y, Chang N, Kim BN, Kim YJ, Yu SD, Ha EH. Prenatal bisphenol A and birth outcomes: MOCEH (Mothers and Children's Environmental Health) study. *Int J Hyg Environ Health.* 2014 Mar;217(2-3):328-34.

Indoor and Outdoor Air Pollution and Children's Health: Evidences from a Birth Cohort Study (MOCEH) in South Korea

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There have been some evidences that exposure to air pollution might be negatively associated with children's health. In this study, we investigated the association between Indoor and outdoor air pollution and children's health. This study is a part of MOCEH (Mothers and Children's Environmental Health) study which is an on-going, prospective birth cohort study in South Korea.

In Methods, to estimate exposure to outdoor air pollution, average PM₁₀ of 1,129 mother-child pairs during entire pregnancy and early childhood were estimated using inverse distance weighting (IDW) method. TVOC, HCHO, and formaldehyde of 360 mothers during mid-pregnancy and late pregnancy and 257 newborns at 6 months were measured by personal air samplers to investigate their exposure level of indoor air pollution. Child weights were measured at birth and each visits of children at 6, 12, 24, 36, and 60 months of age to obtain the information of their growth development and the measured weights were transformed to weight for age z-scores. Neurodevelopmental assessments were conducted using the Korean Bayley Scale of Infant Development II (K-BSID-II) at ages of 6, 12 and 24 months. Korean version of the International Study on Allergies and Asthma in Childhood (ISAAC) was used to investigate the development of allergic diseases in children at 6, 12, 24, and 36 months of age.

Main results of the study are (1) The children who had lived in constantly higher level of PM₁₀ (>50 $\mu\text{g}/\text{m}^3$) from pregnancy to 24 months of age were 0.438 lower in weight z-scores (1,114 g lower in weight) at 60 months than children who had lived in lower level of PM₁₀ ($\leq 50 \mu\text{g}/\text{m}^3$) during the same period. Among the children whose birth weight was lower than 3.3kg, higher postnatal exposure to PM₁₀ (>50 $\mu\text{g}/\text{m}^3$) significantly lowered their weight. (2) There were negative associations between maternal exposure to PM₁₀ and MDI ($\beta=-2.83$; $p=0.003$) and PDI ($\beta=-3.00$; $p=0.002$) throughout the first 24 months of life as determined by the generalized estimating equation (GEE) model. In a multiple linear regression model, there were significant effects of prenatal air pollution exposure on MDI ($\beta=-4.60$; $p=0.001$) and PDI ($\beta=-7.24$; $p=0.001$) at 6 months, but no significant association was found at 12 and 24 months of age. (3) Newborn's birth weight was adversely associated with prenatal TVOC exposure ($\beta=-45.89$, $p=0.04$). In the high TVOC exposure group ($\geq 75^{\text{th}}$), the adjusted mean birth weight was approximately 300g lower than that in the low exposure group ($<75^{\text{th}}$). (4) The average exposure concentration of TVOCs at 6 months was $174.7 \pm 115.1 \mu\text{g}/\text{m}^3$. An increased risk of atopic dermatitis was observed in the high TVOCs exposure group at 6 months, (OR = 3.116, 95% CI 1.041-9.323). Risk of atopic dermatitis was increased when the family bought new furniture within 1 year. (5) The average exposure concentration of formaldehyde at 6 months was $116.5 \pm 77.2 \mu\text{g}/\text{m}^3$. The risk of upper respiratory illness at 6 months and chronic cough at 36 months was higher in high formaldehyde expos group ($\geq 75^{\text{th}}$) than the others ($<75^{\text{th}}$).

In conclusion, these results suggest that both indoor and outdoor air pollution are associated with adverse effects on children's development and health. Furthermore, the exposure may have an impact on their health from fetal period as well as early childhood. Further follow-up in the study will be needed to investigate whether the effect will be shown continuously or disappear at certain age.

* This study was supported by MOCEH (Mothers and Children's Environmental Health) project of the National Institute of Environmental Research, Republic of Korea.

室內及室外空氣污染及兒童健康：南韓 MOCEH 出生世代研究證據

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有一些證據顯示，暴露於空氣污染中對兒童健康有不良影響。在研究中，我們將針對室內和室外空氣污染以及兒童健康的關係做調查。MOCEH(Mothers and Children's Environmental Health)是南韓一個正在進行的前瞻性世代研究，本研究設計源自部分的 MOCEH 研究。

室外空氣污染的部分，是利用反距離權重法(Inverse distance weighting, IDW)測量 1129 位配對母子在孕程和兒童早期暴露的平均 PM₁₀ 濃度；室內空氣污染則是利用個人空氣採樣器，量測 360 位懷孕中晚期母親和 257 位六個月大的新生兒，他們生活中室內空氣樣本的總揮發性有機物(Total Volatile Organic Compounds, TVOC)和甲醛濃度。並且在小孩出生時、六個月、一歲、二歲、三歲和五歲大時量測體重生長的資訊，再依據年齡轉換為 Z 分數(Z-scores)；在小孩六個月大、一歲和二歲大時利用韓國貝氏嬰兒發展量表 II (Korean Bayley Scale of Infant Development II, K-BSID-II) 評估神經發育；同時在小孩六個月大、一歲、二歲和三歲大時，以韓國版的國際孩童過敏氣喘研究組織(ISAAC)的問卷了解過敏性疾病的情況。

研究主要的結果有五點：(1)從懷孕期間開始到小孩兩歲，若持續生活在高劑量 PM₁₀(>50 $\mu\text{g}/\text{m}^3$)環境下，五歲時這些孩童的體重 Z 分數比生活在低劑量 PM₁₀($\leq 50 \mu\text{g}/\text{m}^3$)孩童低 0.438(體重少了 1,114g)。若孩童出生時體重小於 3.3 公斤，出生後高劑量 PM₁₀(>50 $\mu\text{g}/\text{m}^3$)的環境暴露，會顯著降低其體重生長。(2)利用廣義估計方程式 (Generalized estimating equation, GEE)，得到母親暴露於 PM₁₀ 與兒童兩歲內的心智發展指數(Mental Development Index, MDI) ($\beta=-2.83$; $p=0.003$)、動作發展指數(Psychomotor Development Index, PDI) ($\beta=-3.00$; $p=0.002$)呈現負相關。利用多變項線性迴歸模式(Multiple linear regression model)發現，產前空氣污染暴露對六個月大嬰兒的 MDI ($\beta=-4.60$; $p=0.001$)和 PDI ($\beta=-7.24$; $p=0.001$)有影響，但與一歲及兩歲大的孩童的發展則沒有明顯關聯。(3)新生兒的出生重量與懷孕期間暴露的總揮發性有機物 (TVOC) ($\beta=-45.89$, $p=0.04$)有負向的影響。暴露的總揮發性有機物濃度較高族群($\geq 75^{\text{th}}$)，調整後的出生重量比起暴露量較低的族群，少了將近 300 公克。(4) 六個月大孩童暴露的總揮發性有機物(TVOC)的平均濃度是 $174.7 \pm 115.1 \mu\text{g}/\text{m}^3$ ，另外，觀察到這個年紀的孩童，總揮發性有機物(TVOC)暴露較高的族群出現異位性皮膚炎(Atopic dermatitis)的危險性增加(OR = 3.116, 95% CI 1.041-9.323)。若是家庭一年內購買新家具，異位性皮膚炎的風險也會增加。(5)六個月大的孩童平均暴露的甲醛濃度為 $116.5 \pm 77.2 \mu\text{g}/\text{m}^3$ 。而暴露甲醛濃度高($\geq 75^{\text{th}}$)的族群，比起其他族群，在六個月大時罹患上呼吸道疾病和三歲時罹患慢性咳嗽的危險性增高。

總結來說，這些結果顯示不論是室內或是室外的空氣污染均會對兒童健康和發展產生不利影響。此外，這些暴露對健康的影響，可能從胎兒時期直至兒童早期！後續的研究將需要了解這些影響是否會持續或是在某個年紀後便會消失。

* 這篇研究由南韓國家環境研究所 MOCEH 計畫贊助(Mothers and Children's Environmental Health)

環境健康行為介入

Session Four: Environmental Health Interventions

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Prof. Hung-Yi Chiou is Vice President of Taipei Medical University. He received his PhD in the department of Epidemiology at National Taiwan University. He has gained considerable administrative experience. Except of his contribution for college and societies, he also won a lot of research awards. His research interests include Public Health, Preventive Medicine, Cancer Epidemiology, Vascular Diseases Epidemiology and Biostatistics.

Research Interests

Public Health, Preventive Medicine, Cancer Epidemiology, Vascular Diseases Epidemiology ,Biostatistics

Education and Degrees

1991-1996 PhD, Graduate Institute of Epidemiology, National Taiwan University, Taiwan

1987-1989 MSc, Institute of Public Health, National Taiwan University, Taiwan

1981-1985 BA, National Taiwan University College of Public Health, Taiwan

Honor and Awards

Research Grant Award, Taipei Medical University, 2009, 2011, 2012, 2013

Excellent Research Award, Taipei Medical University, 2006, 2011, 2013

Research Achievement Award, Taipei Medical University, 2011

Best Paper Award, Taipei Medical University, 2011

Teaching Excellence Award, Taipei Medical University, 2010

NSC Outstanding Undergraduate Project Research Innovation Award, 2000, 2006, 2007, 2010

Research Award, National Science Council, 1995, 1997, 1998, 2001 – present

Excellent thesis Award, Taiwan Public Health Association, 1996

Professional Appointments

2012- Vice President, Taipei Medical University

2011- President, Taiwan International Classification of Functioning, Disability and Health (ICF) Association

2010-2013 President, Taiwan Public Health Association

2010- Honorary Treasurer, Asia-Pacific Academic Consortium for Public Health

2002-2008 President, Taiwan Epidemiology Association

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Research Interests

Air pollution control; Risk assessment and management of toxic substances; Endocrine disruptor exposure and health outcomes; Sampling and analysis of environmental and occupational trace pollutants; Environmental and Occupational Health

Education and Degrees

1987-1992	PhD, Graduate Institute of Environmental Engineering, National Taiwan University
1980-1982	MSc, Environmental Engineering, National Taiwan University
1976-1980	BA, Department of Public Health, National Taiwan University

Professional Appointments

1999-	Director, Research Center of Environmental Trace Toxic Substances
1996-1999	Director, Department of Environmental and Occupational Health
1991-1993	Lecturer, Department of Environmental and Occupational Health
1987-1988	Section Chief, Environmental Protection Administration, Taiwan
1986-1987	Section Chief, Environmental Protection Bureau, Department of Health, Taiwan

Society/Committee Activities

2010-	Member, Sustainability Group, National Policy Foundation
2011-	Environmental Impact Assessment Committee, Tainan City Government
2009-	Member, Environmental Impact Assessment Review Committee, Environmental Protection Administration, Taiwan
2004-	Advisor, Taipei City Government
2012-	President, Taiwan Society of Indoor Environmental Quality

Honors

2010	Excellent Award in Industry-Academy Cooperation, National Cheng Kung University
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2009	Excellent Faculty of Industry-Academy Cooperation Award, National Cheng Kung University
2000	Best Risk Assessment Experimental Science Presentation

Selected Publications (2013-present)

1. Jer-Pei Fong, Fang-Jin Lee, I-Syuan Lu, Shi-Nian Uang, **Ching-Chang Lee***, Relationship between urinary concentrations of di(2-ethylhexyl) phthalate (DEHP) metabolites and reproductive hormones in polyvinyl chloride production workers, *Occup Environ Med*, vol 72, Pages 346–353, 2015
2. Chung-Yu Chen, Yen-Yin Chou, Shio-Jean Lin, **Ching-Chang Lee ***, Developing an intervention strategy to reduce phthalate exposure in Taiwanese girls, *Science of the Total Environment*, Vol 517, Pages 125–131, 2015
3. **Ching-Chang Lee**, Ling-Ying Jiang, Yi-Ling Kuo, Chung-Yu Chen, Chia-Yi Hsieh, Chung-Feng Hung, Colin S. Chen, Chien-Jung Tien, Characteristics of nonylphenol and bisphenol A accumulation by fish and implications for ecological and human health, *Science of the Total Environment*, Vol 502, Pages 417–425, January 2015
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5. Huang, Huang-Wen, Chang, Bea-Ven, **Lee, Ching-Chang**, Reductive debromination of decabromodiphenyl ether by anaerobic microbes from river sediment, *INTERNATIONAL BIODETERIORATION & BIODEGRADATION*, 87:60-65, Feb 2014
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7. Li-Ping Huang, **Ching-Chang Lee (equally contribution with Li-Ping Huang)**, Jer-Pei Fan, Po-Hsiu Kuo, Tung-Sheng Shih, Ping-Chi Hsu, Urinary metabolites of di(2-ethylhexyl) phthalate relation to sperm motility, reactive oxygen species generation, and apoptosis in polyvinyl chloride workers, *Int Arch Occup Environ Health*, Aug 2013
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9. **Ching-Chang Lee**, Ling-Ying Jiang, Yi-Ling Kuo, Chia-Yi Hsieh, Colin S. Chen, Chien-Jung Tien, The potential role of water quality parameters on occurrence of nonylphenol and bisphenol A and identification of their discharge sources in the river ecosystems, *Chemosphere*, 91(7):904-911, May 2013.
10. Jung-Wei Chang, Horng-Yih Ou, Hsiu-Ling Chen, Huey-Jen Su, **Ching-Chang Lee***, Hyperuricemia After Exposure to Polychlorinated Dibenzo-*p*-dioxins and Dibenzofurans Near a Highly Contaminated Area, *Epidemiology*, 24(4):582-589, July, 2013
11. Chung-Yu Chen, Chien-Jung Tien, Yih-Min Sun, Chia-Yi Hsieh, **Ching-Chang Lee (corresponding author)**, Influence of water quality parameters on occurrence of polybrominated diphenyl ether in sediment and sediment to biota accumulation, *Chemosphere*, 90(9):2420-2427, Mar 2013

Developing an Intervention Strategy to Reduce Phthalate Exposure in Taiwanese

Girls

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Children in Taiwan seem to be exposed to higher concentrations of phthalates than do children in Western countries. The present study developed intervention strategies to effectively reduce the body burden of phthalates in prepubescent girls.

We hypothesized that the intervention strategies we designed would effectively reduce the concentration of urinary phthalate metabolites and that modified behaviors would be correlated with decreases in the concentrations of specific urinary phthalate metabolites. We invited 30 girls 4–13 years old (median:9.7 years) who had higher total scores in the previous study to participate the present study. To reduce their phthalate-exposure sources, we developed seven intervention strategies: handwashing, not using plastic containers, not eating food with a plastic bag/plastic-wrap cover, not microwaving food, not taking nutrition supplements, and reducing use of cosmetics/personal care products.

Pre- and post-intervention urine samples were collected during a one-week study. HPLC-MS/MS was used to analyze urinary phthalate metabolites. The dominant urinary phthalate metabolite was mono-n-butyl phthalate (MBP), followed by mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), and mono-(2-ethyl-5-carboxypentyl) phthalate (MECPP).

Post intervention concentrations of eight urinary phthalate metabolites were significantly lower. Girls in the high frequency handwashing group had significantly lower urinary MBP ($p = 0.009$) and mono-methyl phthalate (MMP) ($p = 0.07$) than did girls in the low-frequency handwashing group. Girls who drank fewer beverages from plastic cups had significantly lower urinary MBP ($p = 0.016$), MEHHP ($p = 0.038$), and MECPP ($p = 0.012$). Girls who used less shampoo and shower gel also had marginally significantly lower urinary MBP ($p = 0.06$) and mono-ethyl phthalate (MEP) ($p = 0.06$). The intervention strategies that we set up in this study were effective for reducing exposure to phthalates in children. Handwashing and drinking fewer beverages from plastic cups were the most effective strategies for reducing phthalate metabolites in urine, especially MBP and di(2-ethylhexyl) phthalate (DEHP) metabolites. Education and voluntary self-restraint were useful for reducing the body burden of phthalates.

發展行為介入策略以減少臺灣女童塑化劑暴露

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成大環境醫學研究所特聘教授、環境保護暨安全衛生中心主任、環境微量毒物研究中心主任

臺灣孩童的塑化劑暴露濃度似乎比西方國家來得高，目前的研究在於發展行為介入策略以有效減少青春期前的女童體內的塑化劑濃度。

研究假設行為介入策略可以有效減少尿液中塑化劑代謝物的濃度，並且改變的行為可以減低特定塑化劑的尿液代謝物濃度。參與研究對象挑選自前期研究中塑化劑暴露分數較高的30位4-13歲(中位數：9.7歲)的女童，為了減少她們的塑化劑暴露來源，我們發展七種行為介入策略：洗手、不使用塑膠容器、不吃塑膠袋裝/覆蓋保鮮膜的食物、不吃微波食物、不吃營養補充品、減少化妝品(保養品)/個人護理用品(沐浴乳、洗髮精)使用。

在為期一週的研究期間內，採集行為介入前後的尿液樣本。我們利用液相層析/串聯式質譜儀(HPLC-MS/MS)來定量分析尿液中塑化劑代謝物。尿液中主要的塑化劑代謝物是鄰苯二甲酸單丁酯(Mono-n-butyl phthalate, MBP)、其次是MBP的二階代謝物Mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP) 和Mono-(2-ethyl-5-carboxypentyl) phthalate (MECPP)。

在行為介入後，八種尿液中塑化劑的代謝物明顯降低。在勤洗手的族群中，尿液中的MBP濃度($p = 0.009$)和mono-methyl phthalate (MMP) ($p = 0.07$)濃度明顯較不常洗手的族群低；較少喝塑膠杯裝飲料的族群尿液中的MBP ($p = 0.016$)、MEHHP ($p = 0.038$)和 MECPP ($p = 0.012$)也較低；使用較少洗髮乳和沐浴乳的族群也比常使用族群的MBP ($p = 0.06$)和單乙基酯(Mono-ethyl phthalate, MEP) ($p = 0.06$)略低。本實驗的行為介入策略能有效減低兒童的塑化劑暴露，其中以洗手和少喝塑膠杯裝飲品減少尿液中塑化劑代謝物最有效，特別是MBP和鄰苯二甲酸二(2-乙基己基)酯(DEHP)，而教育和自我約束對於減少塑化劑暴露很有幫助。



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Prof. Mori received a MD from Asahikawa Medical College and a PhD from Kyoto University. He spent one year as a Visiting Instructor at University of Manitoba in Canada and two years as a Visiting Associate in Laboratories of Reproductive and Developmental Toxicology of NIEHS in the US. He is Professor at Chiba University, Director for Center for Preventive Medical Sciences since 2008, Adjunct Professor at University of Minnesota in the US and Inje University in Korea. His research interests include environmental medicine and the health impact of exposure in children. He has published several books in the field of environmental medicine.

Education and Degrees

1989	PhD, Kyoto University
1984	MD, Asahikawa Medical College

Professional Appointments

2009-	Adjunct Professor, College of Medicine, Inje University, Korea
2006-	Adjunct Professor, Division of Environmental Health Sciences, University of Minnesota, School of Public Health, USA
2000-2001	Professor, Department of Anatomy and Cell Biology, School of Medicine, Chiba University, Japan
1992-2000	Associate Professor, Department of Anatomy and Developmental Biology, Faculty of Medicine, Kyoto University, Kyoto, Japan
1990-1992	Visiting Associate, Gamete Biology Section, Laboratories of Reproductive and Developmental Toxicology, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, North Carolina, U.S.A.
1989	Visiting Instructor, Department of Physiology, Faculty of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada

Awards

Young Investigator Award of the Japanese Association of Anatomists (1995)

Selected Publications (2013-present)

1. Sugiura S, Aoki Y, Toyooka T, Shiga T, Otsuki K, Aikawa E, Oyama T, Kitoh K, Sakaida C, Tanaka Y, Ishizaki T, Omori Y, Kiguchi Y, Tanaka A, Kote A, Nakanishi K, Matsushita Y, Suzuki T, **Mori C**, Takahashi K and Nishikawa S: Characteristics of low back pain in adolescent patients with early-stage spondylolysis evaluated using a detailed visual analogue scale. Spine, 40: E29-E34, 2015

2. **Mori C**, Kakuta K, Matsuno Y, Todaka E, Watanabe M, Hanazato M, Kawashiro Y and Fukata H: Polychlorinated biphenyls levels in the blood of Japanese individuals ranging from infants to over 80 years of age. *Environmental Science and Pollution Research*, 21: 6434-6439, 2014
3. **Mori C**, Nakamura N, Todaka E, Fujisaki T, Matsuno Y, Nakaoka H and Hanazato M: Correlation between human maternal-fetal placental transfer and molecular weight of PCB and dioxin congeners/isomers. *Chemosphere*, 114: 262-267, 2014
4. Miyaso H, Naito M, Hirai S, Matsuno Y, Komiyama M, Itoh M and **Mori C**: Neonatal exposure to diethylstilbestrol causes granulomatous orchitis via epididymal inflammation. *Anatomical Science International*, 89: 215-223, 2014
5. Senuma M, **Mori C**, Ogawa T and Kuwagata M: Prenatal sodium arsenite affects early development of serotonergic neurons in the fetal rat brain. *International Journal of Developmental Neuroscience*, 38: 204-212, 2014
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7. Mochida Y, Sakurai K, Matsuno Y, Ochiai S, Watanabe M and **Mori C**: Relationship between dioxin compounds and hepatic disorder with obesity in Japanese adult males. *Jpn. J. Clin. Ecol.*, 23: 49-59, 2014
8. Nakamoto M, Miyaso H, Komiyama M, Matsuno Y and **Mori C**: Changes in expression levels of oxidative stress-related genes in mouse epididymides by neonatal exposure to low-dose decabromodiphenyl ether. *Reproductive Medicine and Biology*, 13.3: 127-134, 2014
9. Ochiai S, Shimojo N, Yuka I, Watanabe M, Matsuno Y, Suzuki S, Kohno Y and **Mori C**: A pilot study for foetal exposure to multiple persistent organic pollutants and the development of infant atopic dermatitis in modern Japanese society. *Chemosphere*, 94: 48-52, 2014
10. Ogawa Y, Itoh M, Hirai S, Suna S, Naito M, Qu N, Terayama H, Ikeda A, Miyaso H, Matsuno Y, Komiyama M and **Mori C**: Cadmium exposure increases susceptibility to testicular autoimmunity in mice. *J Appl Toxicol*, 33: 652-60, 2013
11. Kitaoka M, Hirai S, Terayama H, Naito M, Qu N, Hatayama N, Miyaso H, Matsuno Y, Komiyama M, Itoh M and **Mori C**: Effects on the local immunity in the testis by exposure to di-(2-ethylhexyl) phthalate (DEHP) in mice. *J Reprod Dev*, 59: 485-90, 2013
12. Nakaoka H, Todaka E, Seto H, Saito I, Hanazato M, Watanabe M, and **Mori C**: Correlating the symptoms of sick-building syndrome to indoor VOCs concentration levels and odour. *Indoor and Built Environment*, 23(6): 804-813, 2013
13. Ochiai S, Shimojo N, Morita Y, Tomiita M, Arima T, Inoue Y, Nakaya M, Uehara N, Sato Y, **Mori C**, Suzuki Y and Kohno Y: Cytokine biomarker candidates in breast milk associated with the development of atopic dermatitis in 6-month-old infants. *International Archives of Allergy and Immunology*, 160: 401-408, 2013
14. Nakaoka H, Todaka E, Hanazato M, Saito I, Seto H, Chemiless Town Project Consortium and **Mori C**: Total odor threshold ratio can be a new method to evaluate indoor air quality. *Jpn. J. Clin. Ecol.*, 20: 115-122, 2013

Environmental Health Intervention and Preventive Medical Studies on Chemical Exposure Issues

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It has been concerned the adverse health effect (e.g. allergic disease, congenital anomaly and neurological developmental disorders) by uncountable chemicals in the environment including indoor air and foods to susceptible children. Here, our studies about environmental health intervention and preventive medical trails on chemical exposure issues will be presented. There are two topics on reducing chemical exposure to prevent children's health; (1) health examination approach on reducing internal exposure of persistent organic pollutants (POPs) such as PCBs/dioxins by food chain and (2) town planning trial to prevent sick building syndrome by indoor chemical exposure.

(1) Health examination approach on reducing internal exposure of POPs:

Our previous studies revealed that human fetuses and their mothers were exposed to several POPs including polychlorinated biphenyls (PCBs) (Mori, 2004; Fukata et al, 2005). As blood PCB level is associated with other major organochlorines in blood, we reported that PCBs can represent POPs contamination in humans (Mori et al, 2009). Moreover, we proposed to establish the health examination system using PCBs data to know the POPs contamination level in future mothers in order to prevent possible adverse effects on the next generation (Mori and Todaka, 2009). In Japan, it has been reported that food is the major source of exposure to POPs. Our previous studies revealed that colestimide (fiber; a medication prescribed for hyperlipidemia) and dietary fiber intake were effective to reduce PCBs/dioxins levels in human body. It is important to know how PCB contamination levels are affected by eating habits to reduce the contamination level effectively. Our recent studies will be also presented to find a preventive intervention method to reduce human exposure to PCBs/dioxins by analyzing data on the correlation between the results from questionnaire and the PCB contamination level in the blood samples in our Chiba birth cohort.

(2) Town planning trial to prevent sick building syndrome by indoor chemical exposure "Chemiless Town project":

There has been a concern about the adverse health effects of various indoor air chemicals from building materials on humans. To prevent the adverse health effects of indoor air pollution, a model town with fewer chemicals called "Chemiless Town" was constructed in the campus of Chiba University in 2007, and the "Chemiless Town Project" was started based on the concept of environmental preventive medicine (EPM). EPM is an advanced concept of public health that attempts to prevent adverse health effects caused by environmental pollution through improvements to the environment.

We carried out the following in cooperation with about 20 house building related companies:

1. Developed a prototype of a house that prevents adverse health effects such as the sick building syndrome (SBS) by periodically measuring volatile organic compounds (VOCs) in indoor air and conducting human sensory tests with healthy volunteers at laboratory sites in Chemiless Town.
2. Developed an online questionnaire to check one's sensitivity to chemicals.
3. Proposed guidelines for indoor air quality to the public.

We successfully resulted in house and classroom prototypes that reduced VOCs in indoor air for the prevention of SBS. We also proposed Σ VOCs (Sum of VOCs) as an evaluation index for indoor air quality and a "Chemiless standard for assessment" to ensure air in which people can stay comfortably, in which "S" represents the standard value for sensitive people (250 $\mu\text{g}/\text{m}^3$ of Σ VOCs) and "A" the standard for non-sensitive people (400 $\mu\text{g}/\text{m}^3$ of Σ VOCs). Σ VOC is important to evaluate indoor air quality because there are countless VOCs in indoor air and it is very difficult to determine cause-and-effect relationships between these substances and human health.

化學物質的環境健康行為介入與預防醫學研究

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易感兒童因為環境中無數的化學物質包含室內空氣和食物，而可能導致不良的健康影響，如過敏性疾病、先天性異常和神經發育障礙。在這裡，我們將呈現化學品暴露在環境健康介入和預防醫學的研究。以下有兩個主軸以減少化學品暴露增進兒童健康：(1) 健康檢查探討以減少持久性有機污染物(POPs)如多氯聯苯(PCBs)和戴奧辛經由食物鏈而暴露和(2)藉由減少室內化學品暴露的城市設計以防止病態大樓症候群(Sick Building Syndrome)。

(1) 健康檢查探討以減少持久性有機污染物暴露：

我們之前的研究顯示人類胎兒和母親暴露在好幾種持久性有機污染物，其中包含多氯聯苯(Mori, 2004; Fukata et al, 2005)。血液中的多氯聯苯濃度與主要的有機污染物相關，因此建議以多氯聯苯數據來代表體內有機污染物濃度(Mori et al, 2009)。再者，我們提出健康檢查系統的建立，利用多氯聯苯資料來了解持久性有機污染物對未來世代是否會有不良的健康影響(Mori and Todaka, 2009)。在日本，研究顯示食物是主要的持久性有機污染物來源。我們之前的研究揭露 colestimide (一種纖維；降血脂藥物)和多攝取膳食纖維可以有效降低人體多氯聯苯/戴奧辛濃度。了解飲食習慣如何有效減少多氯聯苯污染濃度相當重要，我們最近的研究利用千葉出生世代血液樣本的多氯聯苯污染濃度和問卷資料結果，呈現預防性的介入方法以減少人體暴露多氯聯苯/戴奧辛。

(2) 藉由減少室內化學品暴露的城市設計以防止病態大樓症候群的「無化學城鎮計劃」(Chemiless Town Project)：各種室內建材中的化學品對健康的不良影響已被大家關注，為了預防室內空氣污染對健康的負面影響，一個示範的無化學城鎮(Chemiless Town)於 2007 年在千葉大學校區建造，而無化學城鎮計劃的概念始於環境預防醫學(EPM)。環境預防醫學是公共衛生中利用改善環境以預防環境污染導致健康負面影響的先進概念。我們與 20 家建築相關公司進行合作：

1. 發展可以預防不良健康影響(如病態大樓症候群，SBS)的房子原型，利用定期測量室內有機揮發物(VOCs)，以及找來健康的志願者到無化學城鎮中進行人體感測實驗。
2. 發展線上問卷測試人對化學品的敏感性。
3. 擬議大眾室內空氣品質標準。

我們成功地建立良好的房屋及教室原型，減少室內有機揮發物防止病態大樓症候群。我們同時提出利用有機揮發物的總量(Σ VOCs)來做為室內空氣品質和無化學標準評估的評量指標，以確保人可以舒適地生活。其中 S 代表易感族群的 VOCs 濃度($250 \mu\text{g}/\text{m}^3$ of Σ VOCs)；A 代表非易感族群的 VOCs 濃度($400 \mu\text{g}/\text{m}^3$ of Σ VOCs)。有機揮發物的總量是評量室內空氣品質的重要指標，因為室內的有機揮發物相當多，而判定這些物質對人體健康之間的關係非常困難。

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(A1) Liver Injury Induced by Paraquat Is Associated with the Elevation of Oxidative Stress and Transition Metal Concentration

巴拉刈引發之肝損傷與氧化性壓力和過渡金屬濃度上升有關

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Background Non-selective herbicide of paraquat has been commonly used in public and agriculture area worldwide. Paraquat intoxication in human has been indeed postulated in resulting liver damage. Proper transition metal levels such as iron and copper are necessary for a variety of physiological functions to the human health. In this present study, we attempted to explore the influence of paraquat exposure on the transition metal level of iron and copper. Meanwhile, intensity of oxidative stress in the liver of rats after paraquat administration will be investigated.

Methods The transition metal level in the liver of rats after paraquat exposure was analyzed by means of the instrument of atomic absorption spectrometer. On the other hand, the intensity of oxidative stress, as represented by the level of malondialdehyde, was assayed by spectrophotometer at the wavelength of 532 nm in this experiment.

Results Experimental results showed that paraquat administration not only may significantly increase the level of iron and copper but also may enhance the oxidative stress statistically as represented by an increased malondialdehyde level in the liver.

Conclusion Taken all experimental results together, it seems reasonable to state the possibility here that hepatotoxicity induced by paraquat exposure is highly associated with enhanced oxidative stress in the liver of rats. Moreover, it seems possible to note here that hepatotoxicity conducted by paraquat administration is closely responsible for the elevated oxidative stress and the increased transition metal concentration.

(A2) The Disturbance Effect of Phthalate Derivative X on Camptothecin-Treated Human Breast Cancer Cells *in Vivo* and *in Vitro*

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Eing-Mei-Tsai

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Breast cancer is a leading cause of death in women worldwide, and chemotherapy is one of the primary strategies for breast cancer treatment. However, the chemoresistance often causes the poor prognosis of breast cancer patients. Phthalate derivatives have been shown to affect the expression of genes, and could take effects on genotoxic sensitivity and the ability of DNA repair in cells. Recent evidence suggested phthalate exposure may be closely correlated with the chemoresistance of breast cancer cells. However, the underlying mechanism of phthalate rendering the acquisition of chemoresistance to breast cancer is largely unclear. In the study, we investigated whether phthalates affect the chemoresistance depends on reinforcing the ability of DNA repair. Our preliminary results showed that phthalate DEHP attenuates the camptothecin (CPT)-induced DNA damage in breast cancer cells MCF-7. Moreover, phthalate DEHP pre-treatment significantly inhibits the two hallmarks of double-strand breaks (DSB) of DNA, including γ H2AX and the phosphorylation of ATM, were significantly reduced in CPT-treated MCF-7 cells. Consistently, the results of zebrafish xenograft assay confirmed the disturbance effect of DEHP on CPT-induced anti-breast cancer. Accordingly, our present work suggests that phthalate DEHP may disturb the anti-breast cancer effect of CPT through attenuating the induction of DNA damage.

(A3) Associations among Phthalate Exposure, Steroid Hormone and Prostatic Disease in Adult Man

鄰苯二甲酸酯暴露、生殖荷爾蒙調控及攝護腺疾病之相關性研究

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Background

In the past decades, researchers reported the prevalence and incidence rate of benign prostatic hyperplasia (BPH) and prostate cancer (PCa) were increased in elderly population worldwide and had raised concern by publics. Multiple risk factors including age, genetic, lifestyle and environmental toxicants might cause prostatic disorders. For environmental contamination, endocrine disruptor is the most important among the risk factors. Evidences indicated that exposure of PAEs may causes several detrimental reproductive and developmental defects through acting anti-androgenic activity. It was spread around environment and human beings via multiple exposure routes. However, little is known to explore the active mechanism and impact of PAEs on prostatic disorders.

Aim

The objectives of present study are to assess the relationships between steroid hormones and prostatic disease, then to explore the association and active mechanism among phthalate exposure, steroid hormone and prostatic disease in adult man.

Methods

BPH and PCa subjects were recruited respectively from urology clinic, NCKU hospital. The participants provided a spot urine sample, had a blood sample drawn and a completed questionnaire. The standardized EDCs exposure questionnaire were completed to assess the major exposure sources and routes of PAEs. Urinary PAEs metabolite concentrations were analyzed by HPLC-MS/MS. The peripheral blood samples were collected to analyze the reproductive hormones levels for all subjects. In addition, the clinical information including PSA, voided volume, maximum flow, mean flow, TRUS and IPSS were collected. The data analysis was performed using SPSS 17.0.

Results

85 men with prostate disease were recruited through urology clinics, and all were categorized based on the urologist' diagnoses. All subjects were divided to 3 groups (group 1: prostate volume $\leq$ 33.3% (27.13 mL), group 2: prostate volume 33.3% - 66.7% and group 3: prostate volume $\geq$ 66.7% (41.00 mL)). The group 3 subjects had a significant higher PSA levels and intravesical protruding ratio ($P < 0.001$). E_2 /TT ratio showed significant difference among three groups ($P = 0.039$). MECPP had the highest urinary concentrations of all PAEs. Urinary MMP, MnBP, MEHP, MBzP, Σ DBP showed significant difference among three groups ($P < 0.05$). After adjusting age, BMI and time of blood drawing, urinary MnBP, MBzP were significantly negatively associated with LH. MEP was significantly negatively associated with E_2 . MINP, MIDP were significantly negatively associated with DHEA-S. MiBP, Σ DBP were significantly positively associated with PSA. MMP, MEHP were significantly positively associated with prostate volume. MMP, MnBP were significantly negatively associated with voided volume. The subjects with larger prostate volume had higher estrogen receptor binding effect and androgen receptor antagonistic effect than the other two groups.

Conclusion

In conclusion, phthalates exposure were significantly associated with increased prostate volume. Due to the size of subjects is small, further study is needed to collect more subject to explore the active mechanism between phthalates exposure and prostatic disease.

(A4) Improving the Incubation and Exposure Procedures to Increased the Sensitivity with Ad-DR Bioassay for Screening Dioxin Samples

改良細胞培養與暴露步驟以增加 Ad-DR bioassay 篩選戴奧辛樣本之靈敏度

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Introduction

The present study aimed to increase the sensitivity of the Ad-DR bioassay of dioxin by increasing DRE copy numbers, lowering incubation temperature, and adding PMA to the culture medium during the exposure period. The addition of a fast-cleanup system to the Ad-DR bioassay resulted in a fast-screening tool for measurement of dioxin in dioxin-contaminated soils.

Materials and Methods

Each 10 g dry soil sample (n=114) was homogenously mixed for extraction with an automated Soxhlet system (Extraction System B-811 LSV, BÜCHI, Switzerland). Extracted samples were evaporated to near dryness, and then transferred to a CAPE column (i.e., an acid silica column connected to an activated carbon mini-column) for cleanup, and dissolved in 100 µl of DMSO for bioassay, or toluene for chemical assay. The Ad-DR bioassay of dioxin-like compounds and the analytical protocol of the Ad-DR bioassay has been described previously (Lin et al. 2013).

Results and Discussion

Dioxins contamination in soils from northern, middle, southern, and eastern Taiwan was investigated by the Ad-DR bioassay. Reduction of the incubation temperature from 37 to 33°C obviously enhanced TCDD-induced luciferase activation in the Ad-DR bioassay ($p < 0.001$). The mean soil dioxin-BEQ level was 107 (SD=85.3) ng BEQ/kg d.w. in Taiwanese soils (n=114) (Table 1). There were no significant differences in dioxin-BEQs among soils from northern, middle, southern, and eastern Taiwan as evaluated by the nonparametric Kruskal-Wallis H test ($p = 0.381$). The soils (n=800) collected for the first soil dioxins survey were used in the present study.

Conclusions

A new Ad-DR bioassay incubated at 33°C was successfully applied to the survey of dioxins in areas with background levels or slightly higher than background levels, but improvement and modification of the Ad-DR bioassay for better resolution and sensitivity is still needed in future work.

(A5) Investigation of Estrogen-Like Endocrine Disrupting Chemicals Levels from Drinking Water Treatment Plants in Taiwan

調查台灣飲用水處理廠中類雌激素內分泌干擾物之濃度

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Introduction

In recent years, estrogen-like endocrine disrupting chemicals (EEDCs) represented by bisphenol A (BPA), nonylphenol (NP), and phthalic acid esters (PAEs) were found ubiquitous in the aquatic environment (Bergé et al. 2014; Karalius et al. 2014; Nie et al. 2014). Some studies showed that drinking water is a potential source of human exposure to EEDC contaminants (Colin et al. 2013; Fan et al. 2013; Sui et al. 2014). In the present study, we used chemical analyses, E-Screen and T47D-KBluc assay to determine BPA, NP, and PAEs concentration and total EEQs of samples collected from 10 different DWTPs in Taiwan, before and after treatment.

Materials and Methods

Fifty-six samples were collected from seven DWTPs located in Northern-, Central- and Southern Taiwan from 2011 to 2012 and subjected to chemical analyses and two bioassay methods for total estrogenic activity (E-Screen and T47D-KBluc assay). A second batch of samples collected from other five DWTPs in April and September 2013 were analyzed with T47D-KBluc assay alone.

Results and Discussion

Among of the considered EEDCs, only dibutyl phthalate (DBP) and di (2-ethylhexyl) phthalate (DEHP) were detected in both drinking and raw water samples. DBP levels in drinking water ranged from <MDL to 0.840 µg/L and from <MDL to 0.760 µg/L in raw water. Our results observed that only DEHP, DBP and THMs were detected in this study. DEHP was detected in all locations both on raw and drinking water and the range of <MDL-2.36 µg/L was detected in location A for raw water. The highest daily drinking water intake of DEHP calculated for male and female were 0.0823 and 0.115 µg/kg per day. The two selected bioassays were conducted for the first batch of 56 samples and a detection rate of 23% for estradiol equivalent (EEQ) lower than the LOQ to 1.3 and 15% for EEQ lower than LOQ to 0.757 for the second 53 samples.

Conclusions

Our results suggested that DEHP and DBP persisted in the drink water sample at low concentrations and EEQ levels. Based on the highest concentration of DEHP in drinking water, the daily water intake calculated for male and female were 0.0823 and 0.115 µg/kg per day. Both are still within the established tolerated value for daily intake; therefore, the water quality of drinking water is still acceptable and safe in Taiwan.

(A6) Assessment of Exposure to Insecticides in Home Environments -A Pilot Study

家戶環境殺蟲劑暴露評估前導研究

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Background

As the usage of pesticides increases in recent years, exposure to pesticides/insecticides in home environments becomes important, in addition to dietary ingestion exposure. The distributions and species of pesticide residues in home environments are not well known.

Objectives

There are three objectives in this study: 1) To establish the analytical method for pesticides/insecticides in dust; 2) To assess the association between demographic characteristics variables and pesticide/insecticide concentrations in the home environments; 3) To assess non-dietary insecticide exposure for residential children.

Methods

We recruited subjects from participants of an ongoing study, which was to assess the health effects on new born babies' behavioral development. A total of 41 pregnant women were enrolled in this study. We utilized vacuum and surface wipe methods to collect dust in their homes. Dust samples were extracted with solvents and analyzed using GC/MS. Nine commonly seen pesticides were analyzed, including Chlopyrifos, Terbufos, Permethrin, Cypermethrin, Carbofuran, Prallethrin, Tetramethrin, Cyphenothrin and Deltamethrin.

Results

The analytic results from house dust samples shows that pyrethroids are the dominant compounds. The highest frequency of detects is permethrin (24% and 95th concentration is 2.3 µg/g) from dust in vacuum samples. The highest frequency of detects is cypermethrin (15% and 95th concentration is 19.13 µg/m²) from dust in wipe samples.

Conclusion

In general, the levels of permethrin and cypermethrin in the study are similar to an American survey in vacuum samples. The levels of permethrin and cypermethrin are higher than another American survey in wipe samples.

Keywords: Insecticides, dust, vacuum, wipe

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(A7) The Metabolite of DEHP, MEHP Cause Genotoxicity in Mammalian Chinese Hamster Ovary Cells

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DEHP, Di-(2-ethylhexyl) phthalate, the most common phthalate plasticizer used in the production of polyvinyl chloride (PVC). Several in vivo studies have shown that DEHP absorbed in the body is metabolized to produce MEHP, mono-ethylhexyl phthalate and other metabolite. The metabolite can be absorbed through the villi and travel in the circulation system then causes series damages in endocrine and reproductive system. In addition, investigations also demonstrated an association with elevated induction of rat hepatic cancer, testicular cancer, and developmental toxicity in reproductive system under MEHP exposure. However, the mechanism regarding to carcinogenicity induced by DEHP or its metabolite MEHP remains unclear up to date.

We therefore are investigating the cell viability and mutagenicity of DEHP and MEHP in Chinese hamster ovary (CHO) cells. Cytotoxicity and mutagenicity induced by these chemicals in AS52 cell which inserted gpt gene. Results show that the parental chemical, DEHP, as well as MEHP derivatives caused dose-dependent decreases in cell survival, but with very different potencies: MEHP has the high potency; and DEHP lower. Exposure to these compounds induced dose-dependent production of ROS, as determined by Cm-H₂DCF-DA fluorescence. It was noted however that simultaneous treatment of ROS scavenger N-acetylcysteine (NAC) shows the protection against DEHP and MEHP induced DNA damages. In 6-TG selection assay, data indicate that exposure MEHP cause dose-dependent mutant frequency as compare to the control.

In summary, DEHP and MEHP are cytotoxic to the cells and require induction of ROS to exert their genotoxicity effects.

(A8) Plant Growth Retardant, Paclobutrazol, Exposure and Disruption of Pancreas Function

植物成長抑制劑(巴克素)與胰臟的傷害

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Background

Paclobutrazol (PBZ), a well-known growth retardant of the triazole family, is mostly used for controlling growth and plant size of crops, vegetables, flowers and turf in the world. Wide and long-term usage of PBZ in agriculture and natural environments has resulted in residual PBZ in our food, the soil and water; this may lead to high health impairment risk of organisms. Our previous study indicates PBZ impairs digestive system (including liver, gut and pancreas) development during zebrafish embryogenesis.

Methods

In this study, zebrafish embryos or adult are acute or chronic exposed in PBZ. Detection of pancreas developmental pattern in embryos and function in adult zebrafish was evaluated by marker gene expression, immunohistochemistry staining and blood glucose detection.

Aim

Pancreas, a glandular organ in endocrine and exocrine system, is one of important organ in the maintenance of glucose homeostasis and food digestion of vertebrates. In this research, we investigate the toxic risk of PBZ on embryonic pancreas development after acute exposure and the function in adult after chronic exposure.

Results

During embryogenesis, zebrafish embryos acute exposure to PBZ results in the abnormalities in dosage dependent. In adult zebrafish, the blood glucose level was increased after PBZ chronic exposure. Immunohistochemistry results indicate the number beta-cell cluster was reduced in PBZ exposed zebrafish. Quantitative PCR results indicate the expression of insulin was reduced which results in the disruption of blood glucose homeostasis. Our data also reveals that expression of trypsin in PBZ treated zebrafish, it suggests PBZ may affect the food digestion.

Conclusion

Our study indicates that PBZ has obvious toxic on pancreas development via AhR2-mediated pathway during zebrafish embryogenesis. Number of pancreatic beta-cell cluster and insulin secretion were reduced in PBZ treated adult zebrafish, which result in the dysfunction of pancreas on blood glucose balance. The molecular basis mechanism of PBZ toxic effects on adult pancreas is still not clear and need to be further investigated.

(A9) Small Molecule Inhibitors of the Phthalates Antagonize the Tumorigenesis in Human Breast Cancer Cell

塑化劑小分子抑制劑拮抗乳癌腫瘤之生成

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Background

Previous investigations have reported that environmental hormone factors, such as phthalates, stimulate breast cancer through activation of the Wnt/ β -catenin signaling pathway that contributes to tumorigenesis and epithelial-mesenchymal transition. However Wnt signaling is a central regulator of cancer and a potential target for developing anti-tumor growth agents. Mechanistic studies suggest that β -catenin/TCF4/LEF-1 is a major complex in Wnt signaling.

Aim

Thus, we attempted to design the fusion peptide, which blocks the interaction binding of β -catenin and LEF-1 to inhibit tumor growth of breast cancer.

Results

Therefore, we synthesized TAT-NLS-peptide to analyze the biological function in breast cancer cell. We found that TAT-NLS-peptide inhibited breast cancer cells invasion, migration and proliferation through specific binding to β -catenin in the nuclei; it also represented no signs of toxicity for body weight and suppressed breast tumor growth in nude mice and zebrafish xenotransplantation models. Furthermore, the human global gene expression profiles and Ingenuity Pathway Analysis (IPA) software showed that 21 overlapped candidate genes between MCF-7, MDA-MB-231 down regulated of TAT-NLS-peptide and Wnt downstream was consistently identified and association with IL-9 and HER-2 signaling in breast cancer.

Conclusion

Our study suggests that TAT-NLS-peptide is a drug candidate with phthalates for the development of specific effective therapeutic for Wnt signaling inhibition in the future.

(A10) Phthalate-Induced Metastasis and the Proportion of CSCs-Like in Hepatocellular Carcinoma Were Suppressed by Curcumin

薑黃素抑制塑化劑引起肝癌之轉移及癌幹細胞增生

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Background

Phthalates have been widely used as plasticizers to increase the flexibility of plastics in cosmetics, personal care products, food packaging and medical products. Exposure to phthalates has been reported to be associated with a number of adverse health outcomes, including cancers recently.

Methods

The hepatocellular carcinoma (HCC) cell line Huh7 cells was treated either with bis(2-ethylhexyl) phthalate (DEHP) or curcumin. Cell viability was conducted by WST1 assay. The images were stained using immunofluorescence (IF) and pictured by the fluorescence microscopy. Side population analysis and purification were performed by flow cytometry. The mRNA levels were measured by q-PCR and protein levels were measured using western blot. Cell migration and invasion assays were evaluated by wound healing and transwell assays. Nude mice were used to investigate tumor growth and metastasis *in vivo*, and IHC to identify specific marker for HCC cancer stem cells.

Aim

The aim of this study is to investigate whether phthalate exposure induces HCC metastasis and CSCs maintenance, evaluated the signaling pathways during these processes and to find a possible antidote for phthalate-induced tumor progression.

Results

Curcumin has the ability to reverse the phthalate-induced cell migration, invasion, and epithelial-mesenchymal transition and decreased the proportion of CSC-like cells in HCC cell lines *in vitro*, and tumor growth and metastasis *in vivo*. The mechanisms were evaluated that through the inhibition of the aryl hydrocarbon receptor (AhR)/ERK/SK1/S1P3 signaling pathway

Conclusion

The results provide a novel finding that that curcumin inhibits DEHP-induced metastasis and CSCs-like maintenance via AhR/ERK/SK1/S1PR3 signaling and may thus be a potential antidote for phthalate and therapeutics for HCC.

(A11) Phthalate Attenuates the Differentiation Ability of Endometrial Mesenchymal Stem Cells through PITX2 Regulated by Mir-137

塑化劑經由 Mir-137 調控 PITX2 降低人類子宮內膜間質幹細胞之分化能力

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Background

It is believed that environment hormone affects differentiation of stem cells and progenitor cells. However, the impact of environment hormone on stem cell mechanism is unknown.

Methods

We investigate the effect of BBP on differentiation ability and find the novel signaling pathway in endometrial mesenchymal stem cells (EN-MSCs).

Results

First, we found that BBP decreased the differentiation ability of osteogenesis and myogenesis in EN-MSCs. We used the cDNA microarray assay to screen BBP regulation of gene expression and analyzed the biological function network with Ingenuity Pathways Analysis (IPA) software in EN-MSCs. We demonstrated that the candidate genes, PITX2, regulate concomitantly the Skeletal and Muscular Disorders, the Cell Morphology, Tissue Development from the Top Bio Functions group. Further, we used a web-based miRNA target prediction program (miRanda) to search for potential targets. We confirmed the significant targets with RT-PCR by overexpression of miRNA. Thus we explored the novel signaling pathway that miR-137 can target PITX2 when BBP treatment in EN-MSCs. Then we validated the *in vivo* results by immunohistochemistry stain in the tissue specimen obtained from the animal model. Finally, we confirmed that BBP reduced the differentiation ability of myogenesis of EN-MSCs in muscle regeneration animal model.

Conclusion

In conclusion, BBP decreases the differentiation ability of EN-MSCs through activation of miR-137 expression. Subsequently, miR-137 targets PITX2 to affect myogenesis. These findings contribute to our understanding of the differentiation ability of EN-MSCs in human, and the hazard potential of environmental hormone.

(A12) The abstract is not available here, but you can find it on Poster Presentation in the conference venue.

(A13) The abstract is not available here, but you can find it on Poster Presentation in the conference venue.

(A14) Societal and Financial Impacts of Asbestos-Related Malignant Mesothelioma in Taiwan

量化石綿指標癌症惡性間皮細胞瘤對台灣人民的社會及財務影響

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Background Asbestos is a human carcinogen that causes malignant mesothelioma (MM). It is still in use in many Asian countries. MM is an indicator cancer closely related to previous asbestos exposure but is difficult to be diagnosed in developing countries. There is a lack of studies that comprehensively estimate societal and economic costs incurred by asbestos.

Objectives To quantify the impact of MM using expected years of life lost (EYLL), working years of life lost (WYLL), productivity loss, and lifetime healthcare expenditures in Taiwan

Methods We estimated numbers of pleural MM based on the previous asbestos consumption in Taiwan and extrapolated the estimates of Taiwan studies to assess the disease burden of asbestos-related MM. Based on consumption of asbestos in Taiwan during 1960-2010, we assumed that every 170 tons cause one pleural MM. We estimated numbers of pleural MM based on the previous asbestos consumption per capita for Taiwanese population aged over 15 years by applying the regression formula proposed by Tossavainen (2004). The prediction model of Park et al. (2011) was also utilized for 1960-2010 asbestos use to estimate future pleural MM during 2035-2059 (25 years). Taiwanese patients diagnosed with pleural MM (ICD-O 163) with pathological evidence (M codes 9050/3, 9051/3, 9052/3, 9053/3) were retrieved from the Taiwan Cancer Registry (TCR) through linkages with (1) the National Mortality Registry up for survival estimation and (2) the National Health Insurance (NHI) reimbursement database to estimate the lifetime direct medical costs. Assuming a constant excess hazard, we extrapolated lifetime survival function by a semi-parametric method. For each cancer patient, we simulated an age- and gender-matched referents based on the vital statistics of Taiwan to estimate the EYLL. The lifetime healthcare expenditures (LTHE) were calculated by using the mean monthly direct medical costs multiplied by the corresponding monthly survival probability. We estimated productivity loss by human capital method using National Income per capita as the proxy of opportunity cost.

Results Total asbestos consumption in Taiwan was 650,800 tons during 1960-2010 with a peak of 2.5 kg/person/year in 1985-1987. The estimated peak annual number of pleural MM would be 220 for 2020-2030. There would be 2040 pleural MM during 2035-2059 based on Park's model, or 4,700 MM during 2000-2060 according to Tossavainen's approach. Based on a total of 300 pleural MM identified in the TCR during 1998-2009, pleural MM would cause on average EYLL of 18.2 (95% confidence interval [CI]: 17.9-18.4) years, and average WYLL of 4 years, respectively. The LTHE per case of pleural MM with a 3% annual discount were predicted to be US\$ 29,375 (95% CI: 24,174-32,968), and average productivity loss US\$ 66,600. The total EYLL were 85,540 life years, and WYLL were 18,800 from 4,700 victims of asbestos-related pleural MM. The total financial costs caused by pleural MM were US \$326.5 million, which would be a lower bound compared to the willingness-to-pay method.

Conclusions The impacts of asbestos related pleural MM on Taiwanese people are substantial. Such estimates can provide useful evidence for environmental and occupational health policy-making. A total ban of asbestos as early as possible would reduce such a huge burden.

(A15)The Risk Management of Laboratory Pollutants -Evaluation of Brand New Device for Fecal Examination 實驗室危害物風險管理-新式糞便檢驗容器之效用評估

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Background

The contamination of reagents, solvents, and chemical material used in laboratory is the main cause of indoor air pollution in the clinical laboratory. The most common chemical material used in laboratory is formaldehyde, colorless, irritant, volatile organic compound lead to chronic hazards, has been classified as the Group I carcinogen by the International Agency for Research on Cancer (IARC). The standard method of stool parasite analysis for foreign laborer health examination is merthiolate-iodine-formaldehyde (MIF, containing 5% formaldehyde) concentration method carried out on different stool containers may impact on human health.

Aim

The aim of this research is to compare the potential occupational hazard risk of formaldehyde between two stool containers in clinical medical laboratory.

Methods

The subjects were obtained from foreign laborers participating in health examination at Taipei City Hospital. Stool specimens of 250 foreign laborers were examined for intestinal parasites. Stool specimens were microscopically examined after staining by MIF method. All stool samples were collected by two devices, the brand new device Siloam Feces Collection Device (SFCD) and Chang's Feces Examination Apparatus (CFEA), to compare the test efficacy and formaldehyde emission-concentration characteristics.

Results

The prevalence of intestinal parasitic infections was 11.6%. *Blastocystis hominis* (93.3%) had the highest prevalence among the species of parasites detected. There was no difference of the detection rate between these two devices. The average formaldehyde emission concentration of CFEA and SFCD were 0.092 ppm/tube/24hr and 0.0074 ppm/tube/24hr, respectively. The average waste amount of CFEA and SFCD were 34.38 gram and 15.13 gram, respectively.

Conclusion

To prevent the potential occupational hazards, we must carefully choose the suitable sample collection container and safety chemical hood.

(A16) Asbestos in Lung and Lymph Nodes of a Female Case of Lung Adenocarcinoma and Malignant Mesothelioma

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Background

Asbestos is a human carcinogen that increases risk of lung cancer (LC) and malignant mesothelioma (MM). MPM is difficult to be diagnosed. Asbestos-related lung cancer (ARLC) is hard to be distinguished from other etiologies. Identification of asbestos in human tissues is a crucial yet challenging task for causal relationship determination and compensation for asbestos-related diseases from occupational or environmental origin.

Purpose

To illustrate methodology to identify asbestos fibers in tissues of a cancer patient diagnosed with ARLC and MM using polarized light microscopy and confirmation of type of asbestos with Scanning Electron Microscopy (SEM) coupled with Energy Dispersive X-ray Spectrometry (EDS) and synchrotron X-ray diffraction.

Case presentation

We presented a female case of double cancer (lung adenocarcinoma and malignant mesothelioma) and asbestos analysis with advanced technology. This 70-year-old lady suffered from cough with bloody sputum and chest X-ray revealed a lung nodule in her right upper lung. The chest computerized tomography revealed a ground-glass nodule without pleural effusion or thickening. She received right lung lobectomy, and well-differentiated adenocarcinoma was diagnosed; furthermore, the pathologist observed many asbestos bodies in the lung parenchyma, and atypical mesothelial malignant cells in mediastinal lymph nodes and in lung cancer tissues section near the pleura. MM, the primary site at mediastinum with metastasis to lung, was pathologically diagnosed. She then received chemotherapy with pemetrexed, but metastasis to peritoneum and liver were found one year later. She died 2.5 years after the operation. Occupational history disclosed that she had been heavily exposed to dusts from asbestos spray in a construction worksite for 1-2 month at age of 38. She also had paraoccupational exposure to dusts in washing clothes of her husband working in the shipyard for 5 years. SEM (in high vacuum setting) with EDS was used to identify the core of asbestos body to be amphibole, and polarized fibers in the lymph nodes to be chrysotile.

(A17) Phthalates and Asthma: A Literature Review

塑化劑以及氣喘：文獻回顧

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Background

Phthalates are widely used in our lives. They are used as plasticizers in plastics, cosmetic products, and medications. Phthalates are absorbed through ingestion, dermal absorption, inhalation, or intravenous routes, and they are metabolized into monomers and excreted from urine. Phthalates are regarded as endocrine disrupting compounds (EDCs) due to their reproductive effects; however, some reports also indicated they are associated with some allergic diseases such as asthma.

Method and Aim

In this report, we reviewed the current epidemiology researches in five years and the laboratory studies about the association between phthalate exposure and asthma.

Results

Previous database studies showed that the phthalates metabolites in urine are associated with allergic symptoms. Another cohort study indicated that the elevation of the MEP and MBzP concentration in urine was related to the increase of FeNO, a biomarker of pulmonary inflammation. Further, studies also indicated that the elevation of phthalates level in environmental dust increased the risk of developing allergy, asthma and related symptoms. On the other hand, animal studies also revealed the similar outcome. Phthalate exposure may affect the immune system, through the mechanism of up-regulating cytokines, or inhibiting neutrophils apoptosis. Besides, the expression of eosinophil cationic protein, G-CSF, IL-5, and IL-6 were also reported to be altered by phthalates. Recent studies suggested that phthalates may enhance the development of allergic disease through their potential estrogen effects.

Conclusion

Previous evidence indicated that phthalates may contribute to allergic asthma. This brief literature review summarize the current studies about their association, while and further studies are required to elaborate the mechanism.

(A18) The Association of Endometriosis and Phthalate Exposure: A Meta-Analysis of Observational Studies

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Purpose

The potential association between endometriosis and elevated phthalate metabolites level has been analyzed in several epidemiological studies. In order to establish whether phthalate exposure influences the risk of endometriosis, we summarize the evidence from published studies on this issue.

Method

We performed a meta-analysis of epidemiological studies published up to April 2014 using PubMed/MEDLINE and EMBASE. We computed summary odds ratio (OR) of endometriosis associated with different phthalate metabolite levels.

Data extraction

Data were extracted from eligible studies and cross-checked by at least two reviewers, following the reporting format of Meta-analysis of Observational Studies in Epidemiology (MOOSE).

Result

We identified five eligible studies, including a total of 468 women with endometriosis and 1720 controls. The odds of endometriosis for the high urinary MEHP concentration group was 1.029 (0.562–1.877) folds higher than the low concentration group.

Conclusion

The present meta-analysis provided no evidence for an association between urinary MEHP concentration and the risk of endometriosis.

(A19) Association between Serum Metabolome and Perfluoroalkyl Substances in Children by ¹H NMR Spectroscopy

以核磁共振光譜儀為基礎的代謝體學探討孩童血清中全氟碳化物之不良影響

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Background

Perfluoroalkyl substances (PFASs), commonly existed in consumer products, have long half-lives in humans. Although numerous epidemiologic studies have been focused on some adverse health effects of PFASs, thorough molecular effects of PFASs and possible mechanisms of PFASs in leading to health effects in humans are limited.

Methods

Two hundred and ninety children (8-9 years) exposed to background levels of PFASs were included in this study. Thirteen PFASs in serum were determined by high performance liquid chromatography/tandem mass spectrometry. Proton nuclear magnetic resonance spectrometry combined with pattern recognition methods were applied to examine metabolic patterns in children exposed to different levels of PFASs. Moreover, questionnaire data were collected to associate with levels of PFASs or changes of metabolome.

Aim

The purpose of this study is to use metabolomic approach to understand possible mechanisms of PFASs in causing adverse health effects in children, who can provide a trajectory for significant effects in adulthood.

Results

In our results, perfluoro-n-octanoic acid (PFOA), perfluoro-n-octyl sulfonate (PFOS) and perfluoro-n-decanoic acid (PFDA) were detected in more than 2/3 of serum samples. Different metabolic patterns were also associated with different levels of PFAS exposure. Conclusion Metabolomics is a powerful approach to identify metabolic perturbation caused by PFASs exposure and to suggest possible modes of action of PFASs and their possible adverse health effects.

(A20) Direct Analysis Method of Phthalate Monoester Metabolites in Urine Using Ultrahigh-Performance Liquid Chromatography-Tandem Mass Spectrometry

以液相層析質譜法分析尿液中塑化劑代謝物

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Phthalates, are a group of industrial chemicals widely used in consumer products and as solvents, additives, and plasticizers. Studies from Asia, Europe, and the United States suggest that childhood exposure to the phthalates may cause reproductive and developmental toxicities and increase the risk of allergic diseases. In humans phthalates are rapidly metabolized to their respective monoesters. Since those monoester metabolites are non-persistent chemicals with short half-lives, they are used as biomarkers of human exposure to phthalates. In the study, a sensitive and selective namely dilute and shoot method combined with ultrahigh-performance liquid chromatography-tandem mass spectrometry (UHPLC–MS/MS) has been developed to determine the monoester metabolites of phthalates in urine including mono-methyl phthalate, mono-ethyl phthalate, mono-n-butyl phthalate, mono-(3-carboxypropyl) phthalate, mono-isobutyl phthalate, mono-(2-ethylhexyl) phthalate, mono-(2-ethyl-5-hydroxyhexyl) phthalate, mono-(2-ethyl-5-oxohexyl) phthalate, monobenzyl phthalate, mono-cyclohexyl phthalate, mono-n-octyl phthalate, mono-isononyl phthalate. The recovery of the phthalate monoester metabolites ranged between 80% and 120%. The interday and intraday precision for the replicate analysis (n = 15) were all lower than 15%. The limit of quantification (LOQ) was set equal to 0.05-0.1 ng mL⁻¹ for the majority of the compounds.

(B1) Is Nonylphenol Exposure Associated with Oxidative and Nitritative Stress in Pregnant Women?

孕婦暴露壬基酚是否和氧化和硝化壓力有關？

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Background

As the predominant environmental biodegradation product of nonylphenol (NP) ethoxylates, NP is formed during alkylation process of phenols. NP has proven estrogenic effects. Animal studies have shown that exposure to NP increases oxidative stress, but whether it also does so in humans is unknown. This study examines maternal and prenatal exposure to NP and its effects on oxidative damage, lipid peroxidation, and the activities of antioxidants.

Methods

A total of 146 urine and blood specimens were collected from women during the third trimester of pregnancy and upon delivery of their baby at the hospital. Prenatal urinary NP exposure was analyzed by high-performance liquid chromatography (HPLC) coupled with fluorescence detection. Urinary biomarkers of oxidative and nitritative DNA damage and lipid peroxidation, which includes 8-hydroxy-2'-deoxyguanosine (8-OHdG), 8-nitroguanine (8-NO₂Gua), 8-iso-prostaglandin F_{2α} (8-isoPF_{2α}), and 4-hydroxy-2-nonenal-mercapturic acid (HNE-MA) were simultaneously analyzed using isotope-dilution liquid-chromatography-electron spray ionization tandem mass spectrometry (LC-ESI-MS/MS). The activities of maternal plasma superoxide dismutase (SOD) and glutathione peroxidase (GPx) were analyzed by ELISA assays. The socio-demographics, lifestyle, dietary, and work history of the women were collected using a questionnaire.

Results and discussion

The GM (GSD) levels of urinary NP, 8-OHdG, 8-NO₂Gua, 8-isoPF_{2α}, and HNE-MA were 4.06 (1.77), 5.00 (2.35), 39.74 (2.77), 13.57 (2.04), and 108.57 (3.05) μg/g creatinine, respectively. Multivariate regression analysis reveals that urinary NP level is significantly associated with 8-OHdG and 8-NO₂Gua levels in late pregnancy, after adjustment for potential covariates. These results suggest that NP as an enhancing factor of oxidative and nitritative DNA damage. Logistic regression analysis shows that the association between NP and 8-OHdG is stronger than that with 8-NO₂Gua, as evidenced by the fact that the adjusted OR of 8-OHdG level above and below the 50th percentile revealed a significantly dose-response relationship by stratifying NP level into quartiles. 8-OHdG appears to be a more sensitive biologically effective biomarker of NP exposure than 8-NO₂Gua. Further studies with larger study groups may be needed to shed light on the mechanism by which NP affects oxidative stress and its effects on the health of a vulnerable population.

(B2) Airborne Endotoxin and Asthma and Allergy in Elementary-School-Age Children: A Case-Control Study

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Background

Few studies evaluated airborne endotoxin, and the presence of asthma and allergy sensitization in children.

Aim

The objective of this study is to evaluate the association between the presence of asthma and allergy sensitization, and airborne endotoxin in homes of school-age children in Kaohsiung City, Taiwan.

Methods

We conducted this study using a case-control study design from a general population of children by matching age and class exposure. Data collection of home visits included an interviewer-administered questionnaire, air sampling of participants' homes for endotoxin, bacteria and fungi, as well as temperature and relative humidity measurements. Airborne endotoxin was collected on filters with a sampling time of 24 hours. The houses of each case-control pair were visited within one week to ensure the similarity of the ambient environment. Questionnaires were administered to record housing characteristics. SAS statistical package (version 9.3) was used for data analyses.

Results

Endotoxin was detected in all air samples with a mean value of $1.45 \pm 1.67 \text{ EU/m}^3$. In both the univariate and multivariate analyses, incense burning was consistently associated with increased concentrations of airborne endotoxin in the bedroom, while air fresheners and dehumidifiers were associated with decreased concentrations of airborne endotoxin. We observed that higher airborne endotoxin concentrations increased the risk of asthma/allergy. In addition, interquartile range increases of airborne endotoxin were significantly associated with asthma/allergy status (OR= 3.83).

Conclusion

Airborne endotoxin was significantly associated with asthma/allergy status. Reduced incense burning, and using air fresheners and dehumidifiers, may decrease airborne endotoxin in homes.

(B3) Effect of Paclobutrazol on Eyes Development in Zebrafish

探討巴克素對胚胎眼睛發育的影響

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Background

Paclobutrazol (PBZ), a triazole-containing pesticide, is widely used to regulate plant growth, flower blooming and fruit setting by inhibiting plant hormone, gibberellin biosynthesis and increasing cytokine. Up today, PBZ has been globally used on crops, fruits, vegetables, and turf (yard and golf) for more than 30 years. Long-term and widely use of PBZ results in residual PBZ in our food and environmental contaminations. Our previous study reveals the eye size of PBZ treated embryos was significantly smaller than control. Eyes are an important organ for vision which is due to the absorption of light by photoreceptor cell on the retina of the eye. There are 2 types of photoreceptors in the retina: rods and cones. During embryogenesis, vitamin A and B2 play an important role to regulate the development of rod cells (light sensitive) and cone cells, respectively. Here, we show the retinal cells, rod and cone cells, development were affected after PBZ exposure, and how vitamin (A or B2) works on PBZ injured eyes.

Methods

Zebrafish embryos were exposed to PBZ and the eye development was analyzed by in situ hybridization staining with marker genes which are specifically expressed in cone or rod photoreceptor cells.

Aim

Our previous study revealed that the average size of eye in PBZ treated embryos was smaller than in control. In this study, we examined what the PBZ toxic effects on cone and rod photoreceptors cells. Also, we further study part of the molecular mechanism of PBZ toxic on eye.

Results

In our study, we demonstrated that PBZ specially impairs embryonic eye development, especially on retinal photoreceptor cells. Decreased expression of aldehyde dehydrogenase (ALDH) in PBZ treated embryos suggests that PBZ may influence vitamin A signaling in the embryos. Ectopic addition of retinoic acid or riboflavin (vitamin B2) specifically rescues rod or cone cells development in PBZ treated embryos. This data indicates PBZ disrupts vitamin signaling, which result in the toxic retinal injury.

(B4) Maternal Exposure to Di-(2-ethylhexyl) Phthalate Disrupts Placental Formation and Development in Rat

探討懷孕母鼠暴露於鄰苯二甲酸二酯對胎盤的形成及發育之影響

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DEHP is the most abundant phthalate plasticizer in polyvinyl chloride (PVC) formulations, including vinyl flooring, wall covering, food containers, gloves, and infant toys. It can be leached into a liquid that comes in contact with plastics, suggesting concerns about the health risk of human exposure. Previous animal studies have suggested that maternal exposure to phthalates during fetal and/or neonatal periods may cause reproductive and developmental toxicities in offspring according to their actions as endocrine disrupting chemicals (EDCs). However, there is no detailed mechanism regarding the effect on placentation during pregnancy. We hypothesize that DEHP have direct impact on the alternations of formation of placenta. We gave DEHP (125 mg/kg) to pregnant Sprague-Dawley rats by daily with oral gavage from second day of gestation (GD 2) to GD18, and sacrifice at GD 19. The placentas were fixed by formaldehyde, embedded in OCT, and soaked in liquid nitrogen. Frozen sections are prepared at 8 μ m thickness and stained with hematoxylin and eosin. The thickness and the area of the placentas were measured. The results suggested no difference in the placental shape and weight between control and the DEHP-treated samples, however, decrease of the thickness in labyrinth was observed. Oppositely, the thickness of spongiotrophoblast area increases. The results showed as well that increase of widths in labyrinthine vessels lead to labyrinthine morphology change irregularly and vasculature disorganization in DEHP-treated group. In addition, DEHP might induce ROS generation, which is able to disrupt the placental organization and its development. Thus, our findings showed that maternal exposure to DEHP influence placental formation and development in rat.

Keyword: DEHP, Placenta, Labyrinth morphology

(B5) Reproductive and Developmental Hazards in the Aviation Service – A Proposal for Maternal Protection for Airline Industry in Taiwan

台灣航空業之母性保護

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Background and Aim

Nowadays women make up a great proportion of the aviation workforce globally, but yet there is still no practical maternal protection guideline designed for this special group of workers in Taiwan; therefore, we have drafted a health management proposal that aims at improving the maternal protection of female employees working in the airline industry.

Methods and results

Pubmed and google were searched for articles and other country's guidance on reproductive health managements for female aviation workers. The main occupational hazards may include cosmic ionizing radiation (galactic cosmic radiation and solar particle events), circadian rhythm disruption or shift work, and physical demands such as lifting or pushing heavy objects, bending from the waist repetitively, standing or walking for long periods of time. Others might also concern about exposures to noise, infectious disease, and hazardous chemicals used in aircraft maintenance, etc. Therefore, estimates of cosmic radiation doses need to be calculated and monitored, working overnight should be avoided, ergonomic risks and chemical and biological hazards need to be evaluated and assessed in each individual case.

Conclusion

Even though the causal relationship has not been clearly established between the occupational risk factors and adverse pregnancy outcomes in the airline industry, a hazard evaluation and exposure assessment should still be performed in order to reduce potential reproductive risks and uncertainties in the airline industry.

Keywords: maternal protection, airline or aviation industry

(C1) Urban Particulate Matter Impair of Skin Barrier Function by Down-Regulation of Filaggrin via COX2/PGE2 Expression: Role of AhR-Dependent NADPH Oxidase 2 Activation
城市懸浮粒子物質藉由環氧化酶/前列腺素的表現及甲角蛋白的向下調節作用造成皮膚障礙的損壞：芳香烴受體依賴性 NADPH 氧化酶活化扮演的角色

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Background: Cyclooxygenase-2 (COX2) are known as critical mediator of skin inflammation process. Increasing reports have indicated that ambient particulate matters (PMs) exert severe inflammatory responses on human skin. In this study, we explore and characterize COX2 expression and PGE2 production induced by urban PMs in the human keratinocytes (HaCaT cells), and investigate the signaling pathways involved.

Methods: The various doses (25 and 50 $\mu\text{g}/\text{cm}^2$) of PMs primarily containing polycyclic aromatic hydrocarbons (PAHs, 1649b)-induced COX2 protein levels, mRNA expression, promoter activity and PGE2 production were analyzed by western blotting, qPCR, luciferase reporter assay and ELISA assay, respectively. The generation of ROS was measured by a fluorescent dye, DCF-DA and confocal microscope. The role of transcription factors activity was investigated by gel-shift assay. Finally, the molecular pathways activated were further examined using specific inhibitors or siRNAs.

Results: PMs-induced COX2 protein levels, mRNA expression, promoter activity and PGE2 production were attenuated by transfection with siRNAs of AhR, gp91^{phox} and p47^{phox}, by pretreatment with the antioxidants (APO, DPI, and NAC), as well as inhibitors, including AhRI (AhR antagonist), U0126 (ERK1/2), SB202190 (p38), SP600125 (JNK1/2), Bay117082 (NF- κ B) and Tanshinone IIA (AP-1). In addition, PMs-stimulated activation of p47^{phox}, generation of ROS production and NADPH oxidase 2 (Nox2) activities were attenuated by pretreatment with AhRI or antioxidants. Moreover, Nox-dependent ROS generation led to phosphorylation three MAPKs, including ERK1/2, p38, and JNK and then activated the downstream molecules NF- κ B and AP-1, respectively. In vivo studies have shown that in keratinocytes of PMs treated mice, the AhRI and APO exerted anti-inflammation effects by decreasing COX2 protein levels.

Conclusion: Our results reveal the first mechanism that PMs-induced ROS generation was mediated through the AhR/NADPH oxidase / p47^{phox} pathway, in turn initiates the activation both of ERK1/2, p38/NF- κ B and JNK/AP-1, and ultimately induces COX2 expression in HaCaT cells. Development of specific agents suppressed the activation of AhR/Nox2 pathway may protect human skin against PMs-induced damage.

(C2) The Influence of Children Jumping on the Bed on Airborne Endotoxin and PM₁₀/ PM_{2.5}/ PM₁ Concentration Profile

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Background

Making the bed and jumping on the bed are common activities in children, and these behavior stirs up (re-suspend) house dust and aggravates the symptoms of asthma. Additionally, resuspended house dust is also the important indoor source of particulate matter (PM) containing toxin, allergens, and carcinogens. However, no study investigates the PM and airborne endotoxin concentrations through the behavior of jumping on the bed so far.

Aim

The purpose of the present study is to detect the concentrations of airborne endotoxin, PM₁, PM_{2.5}, and PM₁₀ through the behavior of jumping on the bed and making the bed as well as the background period to understand the influences of those behaviors.

Methods

60 schoolchildren's houses in Kaohsiung city in Taiwan were evaluated. Firstly, PM₁₀/ PM_{2.5}/ PM₁ concentration was simultaneously monitored over the first five minutes to obtain background concentration profiles. Then, a common cane was used to tap the bed for about one minute, followed by keeping motionless in 7 to 10 minutes to let PM settle down. Then, we made children's bed by raising bed sheets for about one minute, followed by keeping motionless in 7 to 10 minutes. This evaluation was conducted by the same person for consistency of the beating strength, beating frequency, and beating location. We collect airborne endotoxin on 1µm pore size and 37mm diameter of Teflon filters in the plastic cassettes by using a sampling pump operating at 20 L/m for 25minutes when we performed the action of jumping on the bed and making the bed.

Results

This is the first study to detect the concentrations of airborne endotoxin, PM₁, PM_{2.5}, and PM₁₀ through the behavior of jumping on the bed and making the bed. When jumping on the bed and making the bed, the airborne endotoxin concentrations is higher more than eighteen times of background, and the PM concentrations of jumping on the bed is higher more than ten times of background concentrations, and making the bed is higher nearly double than background. And also indicated that the largest ratio of PM in background was PM₁ (PM₁, PM_{1-2.5} and PM_{2.5-10} accounted for 0.916, 0.009 and 0.075, respectively). When jumping on the bed and making the bed, the ratio of PM₁ and PM_{1-2.5} were decreased, specifically, the ratio of PM₁ were decreased more than PM_{1-2.5} (the ratio of PM₁ when jumping on the bed was 0.905, and when making the bed was 0.895). However, the ratio of PM_{2.5-10} were increased when jumping on the bed and making the bed (the ratio of PM_{2.5-10} was 0.090 and 0.097, respectively).

Conclusion

In conclusion, jumping on the bed and making bed significantly increased airborne endotoxin and PM concentration. These actions may increase the risk of respiratory symptoms, especially for asthma children.

(C3) The Effect of Early Life Exposure to Air Pollution on Lung Function in Non-Asthmatic Taiwan School Children Born in 1996-2004

幼兒時期空氣汙染對台灣1996至2004年間出生之非氣喘學童肺功能之影響

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Background

Although air pollutants have been associated with lung function changes in children, only few studies investigated life-long exposure to ambient air pollution on the schoolchildren's lung function. This study examined effects of air pollutants on schoolchildren's lung function in different time period.

Methods

In 2011, spirograms were obtained from a random sample of non-asthmatic children from 22 middle schools in 22 administrative districts in Taiwan after a questionnaire survey for atopic diseases. Based on air pollutant data obtained from Taiwan Environmental Protection Agency monitoring stations, concentrations of pollutants in each township was estimated using the Arc9 Geographic Information System's Kriging method. Yearly exposure of the participants to CO, NO₂, O₃, PM₁₀, and SO₂ was estimated according to their living townships. Hierarchical linear regression and was used to calculate lung function percent and simple linear regression was used analyze the relationship between lung function parameters and exposures in the first year after birth, and in 2-6 years of life.

Results

A total of 535 girls and 481 boys without asthma history were enrolled in the study. After adjustment with 2-month average exposure, forced expiratory volume in forced expiratory flow at 25% of FVC (FEF_{25%}) was negatively associated with O₃ in 2-6 years of life. Each 4 ppb O₃ increment 2-6 years of life was related to 4.38% decrement of FEF_{25%} with 95% confidence interval [-8.61%, -0.14%]. Exposure to CO, NO₂, PM₁₀, or SO₂ in the first year of life and 2-6 years had no significant association with forced vital capacity, forced expiratory volume in 1 second, forced expiratory flow at 25% of FVC, and maximal-mid expiratory flow (MMEF) in complete study group or in other subgroup analysis.

Conclusion

In addition to the negative effect of past two-months level of PM_{2.5} and ozone, early life exposure to ozone has significant negative influence on lung function in schoolchildren with allergic rhinitis. This effect is not observed in children without allergic rhinitis. This observation indicates that allergic rhinitis may be the susceptible marker of ozone's effect on lung function.

(C4) The Effect of PM_{2.5} Incense Exhaust Particles on Human Endothelial Culture Vitro

利用體外培養模型評估香灰懸浮粒子對內皮細胞的影響

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Background

Incense is used for a variety of purposes, including the ceremonies of the main religions in most Asian countries. However, incense releases various toxic materials, including carbon monoxide, nitrogen oxides, sulfur oxides, volatile organic compounds, aromatic pollutants, and particulate matter when burned. Although several epidemiological studies have linked exposure to incense exhaust particles (IEP) with adverse cardiovascular events and DNA damages, the mechanisms for how IEP gain access to the vasculature lumen and how they cause deleterious effects on the lung vasculature are unclear.

Methods

To elucidate possible mechanisms, we have used human umbilical vein endothelial cells (HUVEC) plated on plastic as in vitro culture model. IEP was collected and sonicated to size of PM_{2.5} in 0.05% TWEEN/PBS for 1 min. IEP at concentrations of 1 to 1000 µg/mL were applied. After 24 h exposure, MTS cytotoxicity assay was used to examine cell viability, H2DCFDA was used to detect the generation level of ROS, TUNEL assays were used to determine the extent of apoptosis, and Comet assay was used to evaluate the single strand DNA break in the treated HUVEC cultures.

Results

At 100 µg/mL IEP, over 80% of the cells die within 24 h. Cells treated with 1 µg/mL IEP doubled every 24 h, as do untreated cells. However, 10 µg/mL IEP delayed doubling. TUNEL assays indicated that some cell death was occurring at this concentration. In addition, Comet assay revealed that IEP cause DNA damages in HUVEC. This endothelial DNA were slightly affected at 1 µg/mL, more affected at 10 µg/mL, and were almost totally destroyed at 100 µg/mL or higher.

Conclusion

Our results suggest that IEP might change vascular permeability by altering the endothelial cell junctions and cause subsequently cardiovascular mortality.

Key words: Incense, PM_{2.5}, cardiovascular, HUVEC, junction

(C5) Indoor Air Chemicals Found after Reports of Office Odor and SBS Symptoms

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Background

“Sick Building Syndrome (SBS)”, in which people show several symptoms (e.g., headache, eye irritation, throat ache) has been a problem in some buildings in Japan. The major cause of SBS is suspected to be volatile organic compounds (VOCs) in indoor air, however, the chemicals that cause the symptoms varies depending on the patient.

In April 2015, the Center for Preventive Medical Sciences of Chiba University rented an office and renovated it for a new project. On a date immediately after the use of the office began, five out of eight workers reported a bad odor and SBS symptoms such as headache and sensory irritation.

Aims

The aim of this study was to identify the relationship between the co-occurrence of odor, SBS symptoms, and exposure to indoor air chemicals.

Materials and Methods

The indoor air of the office was collected three times on Apr 3, Apr 16, and Aug 1; at which time 86 volatile organic compounds (VOCs) were analyzed. Air samples were collected using the active sampling method for 60 min, using Tenax TA for VOCs and LpDNPH for aldehydes.

Workers, whose age ranged from 20s to 60s, were asked to complete a questionnaire about their symptoms at the beginning of April and August.

Results

The concentration of Σ VOCs was $1945 \mu\text{m}^3$ for the first measurement on Apr 3, and was much lower ($242 \mu\text{m}^3$) on Aug 1. However, the SBS symptoms of three of the workers did not disappear even though Σ VOCs value was low in August. The major compounds detected on Aug 1 were formaldehyde (FA), $29 \mu\text{m}^3$ and 2-ethyl-1-hexanol (2E1H), $18 \mu\text{m}^3$. The concentrations of these two chemicals did not decrease with time (FA - Apr 3: $12 \mu\text{m}^3$, Apr 16: $7 \mu\text{m}^3$, Aug 1: $29 \mu\text{m}^3$ and 2E1H - Apr 3: $20 \mu\text{m}^3$, Apr 16: $8 \mu\text{m}^3$, Aug 1: $18 \mu\text{m}^3$) and they seemed to increase according to humidity and temperature (humidity - Apr 3: 56 %, Apr 16: 59 %, Aug 1: 65% and temperature - Apr 3: 19°C , Apr 16: 23°C , Aug 1: 31°C .)

Discussion and Conclusion

There are many reports about adverse health effects from FA, which is regulated by the Japanese government as a chemical known to cause SBS. However, few reports identify other chemical substances that may also cause SBS symptoms, or verify their causal relationship with the symptoms. This means that substances without existing guidelines are being overlooked. The results of this study indicate that workers may react to FA or 2E1H. There is also a possibility that they may react to low-dose exposure to multiple chemicals that cannot be detected by the current method of analysis. Although 2E1H is currently an unregulated substance, there are some reports that indicate an association between 2E1H in indoor air and SBS symptoms.

In conclusion, it is necessary to pay attention to currently unregulated chemicals, as well as the regulated ones, if SBS symptoms are to be prevented.

(C6) Impacts of Frontal Pollution Cases on the Concentrations of Viable Bacteria in the Indoor and Outdoor Air of Southern Taiwan

長程傳輸高污染事件對台灣南部室內、外空氣中活性細菌濃度之影響

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Background: Taiwan lies off the southeast coast of China across the Taiwan Strait. During northeast monsoon season, the Siberian high may move southeastward and transport dusts from arid/semi-arid regions and/or air pollutants from industrial areas to Taiwan. Frontal pollution cases (FP), one kind of long-range transport (LRT) associated with Siberian high, have been reported to increase the levels of air pollution. However, it's a lack of research about the impacts of FP on bioaerosols, especially indoor air.

Aim: To investigate the influences of FP on the levels of viable bacterial concentrations in the indoor and outdoor air in southern Taiwan.

Method: During November 2014 to March 2015, FP cases were forecasted and confirmed according to the information obtained from Taiwan EPA and CWB and HYSPLIT model. Before (1-2 days), during, and after FP (1-2 days), Indoor and outdoor air samples were collected daily in Tainan city with closed-face cassettes containing 0.2- μm Teflon-polytetrafluoroethylene at flow rate of 15.5~30.6 L/min. Outdoor samplers were set on the 6th floor roof of a building located in the campus of National Cheng Kung University, and the sampling of each day was continued for 24 hours. For indoor air, sampling was performed in the living room of a 5th floor household from 8:00 to 18:00. During sampling, all windows of the household were open. After sampling, samples were analyzed by real-time quantitative PCR coupled with the pre-treatment of propidium monoazide (0.05 M) to quantify viable bacterial concentrations. The concentrations of bacteria in the air before, during, and after FP were compared to assess the impacts of FP.

Result: This study found that FP cases would increase the bacterial levels in the atmosphere. The median concentrations during FP days increase from 530 copies/ m^3 to 2572 copies/ m^3 , whereas a decline was detected after FP days 596 copies/ m^3 . Such increases caused by FP cases were also observed in the indoor environment. The bacterial levels in the indoor air were 566, 717, 289 copies/ m^3 before, during, and after FP days, respectively. Moreover, during FP days, northeast or north wind dominates Tainan city according to the information of Taiwan CWB. These results suggest that the viable bacteria may be carried to Taiwan by FP cases, and then further be transported from Northern to Southern Taiwan.

Conclusion: The FP cases may transport viable bacteria to Taiwan and thereby increases the levels of viable bacteria in both indoor and outdoor air, which indicates the importance of considering the risk exposure to viable bacteria during FP days.

(C7) Levels of Urinary Thiodiglycolic Acid Exposure in School-Aged Children Nearby a Petrochemical Complex in Central Taiwan

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Background

Children living nearby vinyl chloride (VCM)/polyvinyl chloride (PVC) factories may have an increased risk of exposure to hazardous air pollutants.

Methods

We recruited 343 students from 5 elementary schools based on distance to the VCM/PVC factory. First-morning urine and blood samples were obtained from our subjects from October 2013 to September 2014. Urine samples were analyzed for urinary creatinine and TDGA using LC/MS-MS. Hepatitis virus infection were assessed using blood samples. We determined their vitamin consumption, resident location, parent's employment, and other demographic or lifestyle characteristics using a questionnaire.

Aim

We aimed to evaluate the urinary thiodiglycolic acid (TDGA), the suggested biomarker of VCM by ATSDR, level for students at elementary schools nearby a petrochemical complex in central Taiwan.

Results

Median urinary TDGA levels for 316 students at 5 elementary schools from the closest (<0.9 km) to the farthest (~8.6km) with respect to the petrochemical complex were 147.6, 95.5, 115.5, 86.8, and 17.3 µg/g creatinine, respectively. After adjusting for age, gender, hepatitis virus infection, vitamin B consumption, passive smoking, and home to source distance, we found that urinary TDGA levels for the closest students was significantly higher than those at other schools. Further, median urinary TDGA levels for students during school time were 4.1-fold higher than those during summer vacation.

Conclusions

After adjusting for confounders, we found that urinary TDGA levels for the school-aged children decreased with increasing distances between the elementary schools and the petrochemical complex.

(C8) Volatile Organic Compounds in Indoor Air: A Review of Concentrations Measured in New Houses

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Background

In recent years, there has been a growing awareness regarding health and the environment issues. Sick building syndrome (SBS) remains a social concern globally, and is known to be caused primarily by the emission of substances from volatile organic compounds (VOCs) in the construction materials such as wall materials, ceiling materials, floor materials, and adhesive agents.

Aim

The objectives of this study were to Measurement formaldehyde, VOCs and ventilation rates in 42 newly houses which were tried to build with fewer chemicals and to examine their trial by comparing to the guidelines set by Japanese government.

Methods

The substances, on which the measurements were carried out, include formaldehyde and VOCs; samples were collected from three spots in each house (outside, living room, and bedroom).

Air sampling was carried out with an active sampling method for 60 min, using Tenax TA for VOCs and LpDNPH for aldehydes. Before air sampling was conducted, windows and doors were kept open for 30 min for ventilation, and then, all windows and doors were closed for 5 h. After that, air sampling begun. The collected samples of VOCs were analyzed by gas chromatography-mass spectrometry (GC/MS), and for the aldehyde analysis, high-performance liquid chromatography (HPLC) were used.

Results

The highest concentration value of Σ VOCs (using the response factor of toluene) was $2700 \mu\text{g}/\text{m}^3$. The lowest concentration of Σ VOCs was $130 \mu\text{g}/\text{m}^3$. The average value of Σ VOCs was $801 \mu\text{g}/\text{m}^3$. The average value of the high concentration of a substance were undecane ($155.3 \mu\text{g}/\text{m}^3$), butyl acetate ($35.2 \mu\text{g}/\text{m}^3$), ethyl acetate ($30.7 \mu\text{g}/\text{m}^3$). The average value of the ventilation rate was 1.01 r/h and all of them were equal to or more than 0.5 r/h in all the houses.

Conclusion

In conclusion, the observed values were below the guidelines limits set by the Ministry of Health, Labour and Welfare of Japan. However, in a few cases, Σ VOCs concentrations exceeded the $400 \mu\text{g}/\text{m}^3$ interim target value of the Japanese governmental guidelines. It is necessary to decrease the concentration levels of Σ VOCs in indoor air to prevent SBS.

(C9) Time-Dependent Change in the Indoor Chemical Concentrations: A Review of Concentrations Measured in New Houses

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Background

Indoor air quality has a great impact on human health. In recent years, there has been growing awareness regarding health issues. To prevent sick building syndrome (SBS), the residential environment must have reduced volatile organic compounds (VOCs).

Aim

The aims of this study were to show Time-dependent Change in the Indoor Chemical Concentrations data of formaldehyde, acetaldehyde, toluene, xylene, ethylbenzene, and styrene in 15 new houses which were considered of the indoor air quality and to verify their trial by comparing to the guideline set by Japanese government.

Methods

The measured substances include six chemicals; samples were collected from three specific spots in each house (outside, living room, bedroom). The measurement carried out immediately after the construction was performed using an active sampling method. Another measurement carried out three months after the construction was conducted using a passive sampling method. VOCs was analyzed by gas chromatography-mass spectrometry (GC/MS), and for the aldehyde analysis, high-performance liquid chromatography (HPLC) were used.

Results

The average concentrations values of the substances at completion were formaldehyde (18.98 $\mu\text{g}/\text{m}^3$), acetaldehyde (24.19 $\mu\text{g}/\text{m}^3$), toluene (16.54 $\mu\text{g}/\text{m}^3$), xylene (8.88 $\mu\text{g}/\text{m}^3$), ethylbenzene (9.56 $\mu\text{g}/\text{m}^3$), styrene (6.61 $\mu\text{g}/\text{m}^3$). Three months after completion, the values were formaldehyde (10.25 $\mu\text{g}/\text{m}^3$), acetaldehyde (9.05 $\mu\text{g}/\text{m}^3$), toluene (8.71 $\mu\text{g}/\text{m}^3$), xylene (2.07 $\mu\text{g}/\text{m}^3$), ethylbenzene (2.35 $\mu\text{g}/\text{m}^3$), styrene (0.40 $\mu\text{g}/\text{m}^3$). The measured concentrations of chemical substances were below the guideline values by the Japanese Ministry of Health, Labour and Welfare. Chemical concentration has tended to decrease with time.

Conclusion

All measurements were below the government guidelines values. However, in a few cases, chemical concentrations became higher three months after it was first detected. To prevent SBS, it is necessary to reduce the indoor chemicals concentrations. Furthermore, it should be noted that the chemical concentration changes are highly time-dependent.

(C10) Outdoor Air Pollution and Current Regulations in Taiwan

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Introduction and Overview

Air pollution has gained increasing attention since the dramatic episode in Meuse Valley, Belgium in 1930. This poster aimed at discussing hazards of outdoor air pollution and current regulations in Taiwan. We conducted discussion of air pollutants according to NAAQS criteria by literature review, and the current regulations were searched from governmental database of Taiwan (R.O.C).

Health Concerns about Air pollutants

Outdoor air pollution from human activity can be stationary or mobile. Stationary sources were mainly from power plants and manufacturing plants with sulfur dioxide, nitrogen oxides and particulate matter, and mobile sources were from automotive tailpipes with NO_x and VOCs. Gas and aerosols lead to inhalation injury. The site of gas deposition is determined largely by water solubility, with highly water soluble gas deposited by upper respiratory tract, whereas aerosol deposition can be affected by size (Primary factor), chemical characteristics, anatomy of respiratory tract and breathing pattern of the exposed person. Discussion of health effects was categorized according to the six criteria pollutants enlisted in National Ambient Air Quality Standard (NAAQS).

Current Regulations in Taiwan (R.O.C)

The regulations and standards of air pollution stemmed from air pollution control act, which has been revised for seven times since 1975. The central competent authority upgraded from ministry of the interior in 1971 to environment protection administration of executive Yuan. The general control strategies include: 1) Enlisting PM_{2.5} standards, 2) Air quality zoning management, 3) Improving economic incentive, 4) Air emission data inventory. Currently, there were improvements of air pollutant concentration, but the concentration of particulate matter (Especially PM_{2.5}) was still above the standard of developed countries.

(C11) Pulmonary Exposure of Diesel Exhaust Particle Associates with Sleep Electroencephalography and Serum Serotonin in Rats

於大鼠肺部暴露柴油引擎微粒對睡眠腦波及血清素的相關性

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Exposure to air pollution is associated with cardiovascular disease and pulmonary disease; however, effects of particulate matter (PM) on sleep remain unclear. In this study, we monitored cerebral electrical message from 7-week-old healthy male Sprague Dawley (SD) rats by electroencephalography (EEG) in sleep. Rats were exposed to diesel exhaust particle (DEP) and phosphate buffered saline (PBS) by intratracheal instillation. Serum serotonin was determined after exposure. Associations between alteration in EEG and serotonin with DEP exposure in rats were observed. We concluded that exposure to diesel exhaust particle may alter cerebral electrical message such as EEG and serum serotonin in rats when they are sleeping, although the underlying mechanisms are unclear. Effects of air pollution on sleep disorder should be concerned in public health and clinical medicine.

(C12) Effects of Fine Particulate Matter on Serum Glucose Levels during Pregnancy

細懸浮微粒對孕婦血糖值之效應研究

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Background

Exposure to fine particulate matter (PM_{2.5}) has been linked to gestational diabetes mellitus (GDM), but the association with hyperglycemia during pregnancy is unclear.

Methods

A total of 3,589 non-diabetic pregnant women who were received a 3-hour, 100-g oral glucose tolerance test (OGTT) were enrolled from a tertiary teaching hospital in Taiwan between 2006 and 2014. Fasting, 1-hour, 2-hour, and 3-hour serum glucose (SG) levels of an OGTT were used. Concentrations of PM_{2.5} and gaseous air pollutants were obtained from nearby fixed-site monitoring stations. We used mixed models to estimate the effects of PM_{2.5}, which were adjusted for individual-specific effects (nulliparous status, age, body mass index, season, and year) and the moving averages of temperature and relative humidity in the corresponding study period.

Aim

We investigated the short- and long-term effects of PM_{2.5} on SG levels of 3-hour, 100-g OGTTs during pregnancy.

Results

The moving averages of PM_{2.5} were 42.7 to 44.4 µg/m³ before the OGTTs from 1 month to 12 months. There were significant relationships between PM_{2.5} and SG levels, including fasting, 1-hour, 2-hour, and 3-hour SG levels of OGTTs in the single-pollutant covariate-adjusted model. The pre-OGTT 1 month to 1 years moving averages of interquartile range (IQR) increases in PM_{2.5} were significantly associated with elevated fasting SG level (1.32-7.34 mg/dL). There was no short-term (<1 month) effect of PM_{2.5} on the SG levels of OGTTs. The two-pollutant covariate-adjusted models had the similar results.

Conclusion

Long-term exposure to PM_{2.5} was associated with significantly increased levels of SG during pregnancy. Air pollution may contribute to hyperglycemia and subsequent development of GDM in pregnancy.

(C13) Lung Response to Ambient Particulate Matter in Sprague-Dawley Rats: Genome-Wide Analysis of Gene Promoter DNA Methylation

大氣懸浮微粒對 SD 大鼠肺組織 DNA 甲基化之效應研究

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Background

Fine particulate matter (PM with diameter $\leq 2.5 \mu\text{m}$; PM_{2.5}) may have effects on epigenetics. Previous studies have shown that PM_{2.5} may have effects on methylation levels of certain CpG sites. However, toxicological evidence is limited.

Methods

We constructed a PM_{2.5} exposure system for continuous, non-concentrated PM_{2.5} exposure studies. Sprague-Dawley (SD) rats were exposed to PM_{2.5} or HEPA-filtered air (FA) in Taipei, Taiwan, for 24 hours/day, 7 days/week for a total of 4 months. To explore methylation changes in response to PM exposure, we used a methylated-CpG island recovery assay (MIRA)-assisted microarray method. An Agilent 105k CpG microarray, Gene Pix 4000A Scanner, GenePix Pro 4.0 and DNA Analytics v.4.0 software were used to identify methylated target genes of lung tissue. Gene network and pathway analyses were performed using Ingenuity Pathway Analysis (IPA) software.

Aim

To investigate the effect of subchronic, non-concentrated ambient PM_{2.5} on DNA methylation in lung of healthy SD rats.

Results

The average concentration of PM_{2.5} in the exposure chambers of the system was 13.30 $\mu\text{g}/\text{m}^3$. Altered CpG methylation was found in 970 genes (1112 probes) among 56,455 CpG islands (105,000 probes) using criteria of fold change: 2.5. IPA analysis demonstrated that STAT3 was the key pathway.

Conclusion

Genome-wide analysis of gene promoter DNA methylation showed PM_{2.5} has effect on methylation levels of certain promoter CpG sites in lung of SD rats. Role of PM on epigenetics, and the influence of STAT3 pathway need further investigation.

(D1) Statins and the Risk of Cancer in Hypertensive Elderly Patients

探討高血壓老年族群使用斯達汀類藥物與癌症風險關係

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Background

Hypertension is recognized as one of the worldwide chronic diseases, a risk factor of many common diseases such as: cardiovascular disease and stroke. The risk of hypertension increases greatly with age, and rates are higher in adult males. Statins are currently widely used by hypertensive patients as lipid-lowering drugs. So far, many studies have examined the correlation between cancers in a few particular populations, but we haven't found any research for determining the effects of statins in reducing the risk of cancer in hypertensive elderly patients.

Aim

The purpose of this study is to investigate whether using statin drugs can reduce the risk of cancer in hypertensive elderly population.

Methods

The study design was a retrospective cohort study and the medical records of subjects including cancer events and statins use were collected by Longitudinal Health Insurance Database since January 1, 2000, and observed through December 31, 2011. Cox proportional hazards regression models were used to estimate the relationship between statins use and cancer occurring in hypertensive elderly patients. The statins dosage of exposure, estimated as the sum of the dispensed defined daily doses (DDDS) of any statins is used to correlate statin use to cancer risk.

Results

The result shows that statins use may reduce the risk of cancer incidence. It also shows the dose response effect in hypertensive elderly patients.

Conclusion

Statins may reduce the risk of cancer in hypertensive elderly patients in a dose-dependent manner. It is a worth issue to be further studied to assess this relationship among different population. Further research is needed to clarify the mechanism responsible for this effect.

Key words : Statins, Cancer, Hypertensive elderly patients

(D2) The Risk Assessment of Pesticide Residues in Vegetables and Fruits in Taiwan: Carbofuran, Chlorothalonil, Dimethoate, Methamidophos, Terbufos **台灣攝食蔬果農藥殘留風險評估：加保扶、四氯異苯腈、大滅松、達馬松、托福松**

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Background

Carbofuran, Chlorothalonil, Dimethoate, Methamidophos, Terbufos which have been used widely in agriculture are classified as toxicity class I - highly toxic by WHO. Due to their highly toxic nature, these chemicals are usually evaluated with acute toxicity and without chronic risk assessments. The mechanism of carbofuran, dimethoate, methamidophos, terbufos was the inhibition of cholinesterase and neuropathic target esterase, while chlorothalonil is carcinogenic to kidney or stomach.

Methods

LADD was based on a model of Bayes' theorem in Markov Chain Monte Carlo simulation (MCMC) and TMDI was according to the newest MRLs rules in Taiwan. Meanwhile, ADIs were calculated by benchmark dose with existing animal studies.

Aim

we proceeded to assess the risk of pesticide residues by monitoring different food, and re-evaluate the appropriateness of the existing MRLs in Taiwan with reference to the Codex system. We assessed the five pesticides individually in order to understand which pesticide affects the Taiwanese population most and which existing MRL should be revised.

Results

LADD of carbofuran, chlorothalonil, dimethoate, methamidophos, terbufos was 3.26, 3.48×10^{-5} , 3.20×10^{-5} mg/kg/day, respectively. The percent of LADD to ADI of the five pesticides was 15.8, 2.33, 0.31, 0.90, 0.029, respectively. Only Chlorothalonil was on-carcinogen, its cancer slope factor was 7.13×10^{-3} below 0.015(RfD, WHO).

Conclusion

Although all LADDs were below ADIs, MRLs of the five pesticides should undergo revision. Admittedly, in fact, people are exposed to multiple pesticides in food, so if we considered all kinds of pesticides using in vegetables and fruits, the hazard index of pesticides may be greater than 1 and it means that the aggregation of residual pesticides are harmful to humans. Therefore, this study informs the government to further review each MRL in agriculture and decrease pesticide abuses.

(D3) Assessing the Health Risks of Gossypol in the Taiwanese Population

棉酚對台灣人之健康風險評估

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Background

In 2013, a food safety incidence occurred in some manufactures had illegally mixed cottonseed oil into other forms of cooking and edible oil. To date, no health-based guidance value has been established for gossypol. Moreover, quantitative risk assessments are lacking in the scientific literature. This study aims to quantify concentrations of gossypol consumed by the general Taiwanese population through benchmark dose calculation, then assess the risk of gossypol to human health to general population.

Methods

We estimated the reference dose (RfD) by using the data which from a large clinical trial in China involved 8,806 men who were administered gossypol 15 mg/day and 20 mg/day for various periods. Risks were characterized using the Hazards Index (HI) method. The Life-time Average Daily Dose divided by the estimated ADI, whereby estimated HI was compared to an HI of 1. There is insufficient data on gossypol content in edible oil in Taiwan. Therefore, the Life-time Average Daily Dose was estimated by the data of edible oil consumption from National Food Consumption Database of Taiwan and the detection limit of the current method of analysis for free form gossypol (0.05 ppm).

Results and Conclusion

The results of two BMDL₁₀ divided by uncertainty factors of human (10). The ADI were 0.020 mg/kg/day and 0.0177 mg/kg/day, respectively. The Hazards Index for general population was less than 1; indicating that the concentration of gossypol in edible oil is under the detection limit of current analysis method and pose no adverse health effects. Considering that cottonseed meal can be used as a livestock feed. The risk of gossypol residues in edible tissues should be assessed by using the Markov Chain Monte Carlo simulation (MCMC) in further work.

(D4) Cosmetic Talc Use and Ovarian Cancer

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Introduction

The goal of this poster is to review the association between cosmetic talc use and ovarian cancer, and to point out specific considerations of discussing this issue in Taiwan.

Literature Reviews

Talc has been used in many cosmetic products, such as feminine hygiene body powders, baby powders, deodorants, blushers and eye shadows, which contain variable proportions of mineral talc ranging from 35% to 100%.

The studies investigating ovarian cancer risk mainly focused on perineal use of talc. Talc-based powder can be applied perineally, on napkins or on underwear. Prevalences of ever use of talc for female hygiene were higher in studies from Canada, USA and the United Kingdom (up to 59%), whereas the lowest prevalences were reported in studies conducted in other countries, including China and Greece (2.2–3.6%).

The association between ever perineal talc use and ovarian cancer was investigated in 20 case-control studies and 1 cohort study. Among the 20 case-control studies, 10 of them showed significant excess risk with odds ratios ranging from 1.27 to 1.61. The cohort study found no overall association between perineal talc use and epithelial ovarian cancer but did report such an association with invasive serous ovarian cancer (RR = 1.40; 95% CI = 1.02–1.91). In 2010, IARC Working Group concluded that perineal use of talc-based body powder is possibly carcinogenic to humans (Group 2B).

Discussion

Although cosmetic talc containing asbestos was a less concern in the USA after 1976, it still remains an issue in Taiwan. Since there has not been regulation on restraining asbestos use in cosmetic talc-based products in Taiwan until 2009, the exposure time of asbestos through cosmetic talc for users in Taiwan might be much longer.

Perineal use of talc-based powder seems to have been a common practice in countries in North America and Europe. However, the prevalences of perineal talc use are unknown in Taiwan. Therefore, it is difficult to evaluate the health risks caused by exposure of cosmetic talc.

It is worth addressing more attention to further studies and evaluation to the health effect of cosmetic talc use and the potential presence of asbestos in cosmetic talc products in Taiwan.

(D5) Fast Food and Rising Urinary Phthalate Metabolites among U.S. Adults

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Background

Phthalates represent a major public health threat due to their widespread use in plastics, despite numerous adverse health effects that are associated with current exposure levels. Phthalates are endocrine disruptors, and have been linked to conditions such as insulin resistance, impaired male genital development, and early menopause in human studies. Although certain types of foods (e.g. pork, poultry) have been identified as being high in phthalates, the relationship between food sources and phthalate exposure is underexplored. In the U.S. population, four urinary phthalate metabolites have been steadily increasing since 2001: monocarboxyoctyl (MCOP), mono (3-carboxypropyl) (MCPP), monocarboxynonyl (MCNP), and monoisobutyl phthalate (MiBP). Common sources of these phthalates include food, food packaging, and PVC applications.

Objective

The objectives of our study were a) to describe factors associated with concentrations of the four urinary phthalate metabolites in a nationally representative sample of U.S. adults, and b) to evaluate fast food restaurants as potential food sources of urinary phthalate metabolites.

Methods

The study population was comprised of a subsample from the National Health and Nutrition Examination Survey (NHANES) 2007-2012 cycles, which included individuals who had urinary phthalate metabolites measured within 24 hours of completing a 24-hour dietary recall survey. Exclusion criteria included pregnancy, < 20 years old, and dialysis within 12 months of examination. Multivariable linear regression was performed to assess if self-reported fast food consumption (including pizza) is independently associated with the creatinine-adjusted, log₁₀ transformed phthalate metabolites, after adjusting for *a priori* selected confounders (i.e. age, sex, race, socioeconomic status, and education level). We evaluated obesity status (BMI ≥ 30 kg/m²) as an effect modifier of the association between fast food and urinary phthalates.

Results

Our final sample included 4,553 individuals (51.1% women, median age 45.4 years) who represented 186,350,327 U.S. adults. The highest median metabolite concentrations were seen in MCOP (10.3 ng/mL), and the lowest in MCNP (2.5 ng/mL). Fast food exposure (33%) was significantly associated with increased levels in three of the four phthalates, including MCOP, MCNP, and MCPP. The difference in log₁₀ concentration (95% CI) between exposed and non-exposed were: 0.20 (0.14, 0.25), 0.06 (0.03, 0.10), and 0.11 (0.07, 0.14), respectively, independent of the selected confounders. Among obese individuals who had fast food, the urinary MCNP was 1.2 times higher than that among the non-obese who had fast food (interaction p=0.049), but not statistically higher for the remaining phthalates. The association did not significantly differ between men and women.

Conclusion

To our knowledge, our study is the first in the U.S. to demonstrate that fast food may play an important role in adult phthalate exposure. Further studies are needed to provide policy guidance aimed at decreasing phthalate exposure from this source of phthalates.

(D6) Cumulative Risk Assessment of Methyl Yellow Residues in Food

食物中二甲基黃累積風險評估

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Background

In 2014 it was found that dried tofu products have been adulterated with an industrial dye, para-Dimethylaminoazobenzene, intermittently for the past 20 years. The scandal was initially uncovered by authorities in Hong Kong regarding the many flavored types of dried preserved tofu, that were recalled after the contamination broke.

Methods

A number of dose-response models can be used to fit dichotomous response data. The models, which can be fit in the US EPA bench-mark dose software. The benchmark dose method involves fitting a mathematical model to all the dose-response data within a study, and thus more biological information is incorporated in the resulting estimates of guidance values. The human dietary intake of methyl yellow via foods was estimated based on National Food Consumption Database consumption data of different food groups.

Aim

This study aims to estimate human exposure to methyl yellow from food and provide a quantitative risk assessment. Further to estimate the concentration of food which could be permissible.

Results

The permissible concentration of food was estimated by the usual limits for cancer risks set 1 in 1000000. The BMDL was estimated at 0.710741 mg/kg bw/day, and the permissible concentration of food was estimated at less than 4.24ppb.

Conclusion

We strongly recommend the food content of methyl yellow is less than 4.24ppb.

(D7) Statin Use and the Risk of Cirrhosis Development in Patients with Hepatitis B Virus Infection

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Purpose

Previous studies has indicated that statins can prevent the development of hepatic fibrosis in patients with hepatitis C virus infection but data for patients with hepatitis B virus (HBV) infection is lacking. This study investigated the association between the use of statin and the risk of cirrhosis development in patients with HBV infection.

Study Population and Methods

We conducted a population-based cohort study by using the Taiwan National Health Insurance Research Database. A total of 891,136 patients with HBV infection were included as the study cohort. Each patient was followed from 1997 to 2010 to identify incident cases of cirrhosis. A Cox proportional hazard regression was performed to evaluate the association between statin use and cirrhosis risk.

Results

A total of 59,646 cases of cirrhosis were identified in the cohort with 891,136 HBV infection patients during the follow-up period. There were 3,254 cirrhosis cases (3.1%) of cirrhosis among 104,012 statin users (defined as those who used more than 28 cumulative defined daily doses (cDDD)), and 56,392 cirrhosis cases (6.3%) among 787,124 statin nonusers. A dose-response relationship between statin use and cirrhosis risk was observed. The adjusted hazard ratios were 0.31 (95% CI, 0.29 to 0.32), 0.23 (95% CI, 0.21 to 0.24), and 0.11 (95% CI, 0.10 to 0.12) for statin use of 28 to 83, 84 to 365, and more than 365 cDDD, respectively, relative to no statin use (< 28 cDDD).

Conclusion

Among the patients with HBV infection, statin use was associated with a reduced risk of cirrhosis development in a dose-dependent manner. Further clinical research is required.

Keywords: statin, hepatitis C virus, cirrhosis

(E1) Antibiotic-Resistance Patterns of Microorganisms in Taichung Han River Conti Section after Conti Remediation

臺中旱溪康堤整治後的微生物抗藥性之研究

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Purpose

Han River originates in Fengyuan mountains and flows through four eastern districts of Taichung City, which is a basin, namely Fengyuan, Tanzi, South, and Dali. It finally joins into Dali creek. Taking advantage of the broader river course, the “Conti Plan” was performed in 2013-2015 by the government to reform the section near National Chung Hsing University (called Conti riverbank) into a hydrophilic environment with functions of recreation, flood control, and ecological protection. After completion of the Plan, activities of fishing, paddling, and swimming are popular near the Conti riverbank, especially in holidays. The purpose of this study was to compare the amounts of drug-resistant bacteria in the Conti water before and after the Plan to evaluate the biological safety of this area.

Methods

Water samples were collected from the river before and after the Plan. After serial dilutions, the collected water samples were plated on MAC (MacConkey agar) and LA (Luria-Bertani agar) plates with or without antibiotic kanamycin, ampicillin, or tetracycline. Results: Water samples collected before the Plan (November, 2013) had a neutral pH, about 6.9, 4,560 CFU/ml of bacteria, 8 types of colony morphology, and 7 types of antibiotic-resistance pattern, Ap^r,Km^r,Tc^r, Ap^r,Km^r,Tc^s, Ap^r,Km^s,Tc^s, Ap^r,Km^s,Tc^r, Ap^s,Km^r,Tc^s, Ap^s,Km^s,Tc^r and Ap^s,Km^s,Tc^s (r, resistant; s, sensitive). Water samples collected after the Plan (April, 2015) had a near neutral pH, about 7.7, 6,300 CFU/ml of bacteria, 2 types of colony morphology, and 5 types of antibiotic-resistance pattern, Ap^r,Km^r,Tc^r, Ap^r,Km^r,Tc^s, Ap^r,Km^s,Tc^s, Ap^r,Km^s,Tc^r, and Ap^s,Km^s,Tc^s. Percentage of Ap- and Km- resistant bacteria changed from 8.8% to 13.3% and 1.6% to 1.7%, respectively, indicating that antibiotic-resistant bacteria are still prevalent in the water body. The Ap^r, Km^r, Tc^r strains included *Proteus mirabilis* and *E. coli*.

Conclusion

When *E. coli* exists, it is possible that other morbid bacteria exist as well. Activities around the Conti have increased significantly, but the water pollution situation remains the same. Therefore, biological safety of Han river is still an environmental protection concern.

(E2) The Characteristics and Prevention of Dust Explosions

粉塵爆炸特性及預防

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Background

On 06/27/2015, 12 people were killed and more than 500 were injured in explosion at Taiwan Formosa Water Park outside Taiwan's capital Taipei. It is believed that the corn dust sprayed in the air during the "Color Play Asia" party caught ignited and resulted in the massive explosion. Combustible dust explosion has also been a potential hazard in the manufacturing and food industries for more than 200 years. We all should get a deeper understanding of the characteristics and prevention of dust explosions.

Method

Systematically review the literatures, mainly from the Occupational Safety and Health Administration (OSHA) and National Fire Prevention Association (NFPA), about different aspects of combustible dust explosion, including a brief history, the dust explosion pentagon, explosion characteristics, common ignition sources and hazard mitigation.

Aim

Employees should be able to recognize and prevent hazards associated with combustible dust in the industry. Supervisors should be aware of and support the plant dust and ignition control programs.

(E3) The Risk between Statins and Gastric Cancer in Diabetes Mellitus

探討糖尿病族群使用斯達汀類藥物與癌症風險關係

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Background

Diabetes mellitus (DM) is a common and major chronic disease around the world. The domestic and worldwide studies investigate that diabetes is a risk factor in many diseases, for example: hypertension stroke nephrology and cancers. Currently, statins have been widely used as cholesterol lowering drugs. In addition to cholesterol reduction, statins have anti-proliferative, proapoptotic, anti-angiogenic effects to potentially reduce the risk of cancers incidence. Previous researches have assessing the general relationship between statins and cancers, but few studies focusing on statins use in diabetes group associated with gastric cancer.

Aim

The study investigates statins use whether reduces the incidence of gastric cancer.

Methods

The study design is a retrospective cohort study using database from the Taiwan National Health Insurance program to track the cases eligible for the study conditions, excluding the cases suffering from gastric cancer before 1999. The follow up period is from January 1, 1997 to December 31, 2010. The levels of diabetes using statins are classified by the Cumulative Defined Daily Dose. Cox Proportional Hazards Model is used to investigate the relationship of different statin use levels and the risk of gastric cancer with times in the diabetes group.

Results

Statin use is associated with reduction in risk of gastric cancer. Dose-response curve is further observed.

Conclusion

Statins may reduce the risk of gastric cancer in diabetes group in a dose-dependent manner. The study potentially provides more effective prevention/intervention strategies to reduce the incidence of gastric cancer in diabetes group. Further research is promised to clarify the mechanism responsible for this effect.

Key words : Statins 、 Gastric cancer 、 Diabetes mellitus

(E4) Determination of Volatile Organic Compounds in Water Using Headspace Knotted Hollow Fiber Microextraction

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An efficient and effective headspace microextraction technique named static headspace knotted hollow fiber microextraction (HS-K-HFME) has been developed for the determination of volatile organic compounds (VOCs) in water samples. The knot-shaped hollow fiber is filled with 25 μL of the extraction solvent. The excess solvent forms a large droplet (13 μL) and is held in the center of the knot. Even after 20 min of extraction time at high temperature (95 °C) without cooling, there was still enough volume of extraction solvent for gas chromatography–mass spectrometry (GC–MS) analysis, which extends the choice of solvents for headspace LPME. Moreover, the knot-shaped fiber has a larger extraction contact interface, which increases the rate of mass transfer between the headspace and extraction solvent film attached to the fiber, thus improving the extraction efficiency. The effects of extraction solvent, temperature, stirring rate, salt concentration and extraction time on extraction performance were optimized. The calibration curves exhibited coefficients of determination (R^2) ranging from 0.9957 to 0.9999 and the limit of detection (LOD) ranged from 0.2 to 10 $\mu\text{g L}^{-1}$. Relative standard deviations (RSDs) ranged from 4.5% to 11.6% for intraday measurements ($n = 5$). Interday ($n = 15$) values were between 2.2% and 12.9%. The relative recoveries (RRs) ranged from 90.3% to 106.0% for river water and 95.9% to 103.6% for wastewater.

Keywords: Headspace; Hollow fiber microextraction; Volatile organic compounds; Gas chromatography–mass spectrometry; River water; Wastewater

(E5) Workplace Tobacco Exposue and Policies in Taiwan

台灣職場菸害暴露與政策

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Background and Aim

Smoking or exposure to second hand smoke may increase health risk, and there had been one report in Taiwan that smoking related productivity losses (US\$1032 million) accounted for 0.36% of total GDP in 2000. Concerning the health risk and the financial loss, the need for smoke-free workplace is important and emergent. There have been many strategies applied for tobacco exposure workplace in recent years. However, the workplace tobacco exposue is still existent in Taiwan. The policies for workplace tobacco prevention and further strategies would be reviewed and discussed in this article.

Methods

The reports from the government of Taiwan for environmental tobacco smoke with the current smoking policies were collected. The latest 2015 NIOSH publication "Current Intelligence Bulletin 67: Promoting Health and Preventing Disease and Injury Through Workplace Tobacco Policies" was also taken into discussion for Taiwan policies.

Results

The *Tobacco Hazards Prevention Act* in 2009 had strong effect to prevent smoking in workplace. The percentage of smokers in workplace was significantly decreasing. However, the exposure to second-hand smoke in workplace sustained. The expansion of non-smoking areas in 2009 significantly decreased exposure to second-hand smoke in public places but didn't prevent the second-hand smoke in workplace.

Conclusion

The tobacco cessation program and the *Tobacco Hazards Prevention Act* were effective and needed to be continued. The further prevention for second-hand smoke should be taken into consideration and totally smoke-free workplace is needed to protect the non-smoker's health in workplace.

(E6) Occupational Health Risk Assessment of Gallium Arsenide

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Gallium arsenide (GaAs) is a synthetic carcinogenic compound that is insensitive to heat, resistant to radiation degradation, and offers great flexibility when used as an alloy; such properties ensures its extensively application in the semiconductor industry. Thus, employees working in this industry are likely to be at risk, particularly through inhalation and dermal absorption. Conducting health risk assessment in occupational settings becomes increasingly important as employees' exposures are constant and consistent. Since Taiwan has yet to establish guidelines such as biological exposure index (BEI) or permissible exposure limit (PEL) for occupational exposure to GaAs, this study evaluated the health risks associated with GaAs by calculating reference concentration (RfC) using the Benchmark Dose Software. Based on a chronic toxicity study on fifty F344 rats, in which the animals underwent inhalation exposure of GaAs at the following doses: 0, 0.01, 0.1 and 1.0 mg/m³, hyperplasia Results demonstrated that alveolar epithelial hyperplasia was observed in the lungs of female rats; while that of male rats showed evidence of inflammation. The benchmark dose, based on existing animal data, is calculated at 2.27×10^{-4} mg/m³ and the human equivalent RfC to be 2.27×10^{-2} mg/m³. Based on the aforementioned calculations, we quantified the employees' cancer risk at 1.46×10^{-1} . Our results demonstrate that employees exposed to GaAs are subject to its profound carcinogenic adverse health effects. An attempt to ascertain accurate exposure concentration can be done by applying Bayesian probability combined with Markov Chain Monte Carlo (MCMC) simulation, which would help determine the PEL. Further Investigation focusing on the risks of other compounds is warranted; a review of risk management protocol for GaAs should be considered.

(E7) Asbestos-Related Malignant Pleural Mesothelioma and Ovarian Cancer: A Female Case of Environmental Origin in Taiwan

環境石棉暴露相關惡性肋膜間皮瘤及卵巢癌：一台灣女性病例報告

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Background Malignant mesothelioma (MM) is the primary malignancy of the mesothelium, of mesenchymal origin. Epidemiologic evidences disclose it is closely associated with previous asbestos exposure. Increasing incidences of MM was observed in both genders in Taiwan. High-grade serous carcinoma of the ovary is the most common type of the ovarian cancer and accounts for 70 to 80 percent of all ovarian malignancy.

Objective We present a case of malignant pleural mesothelioma and high-grade serous carcinoma of the ovaries.

Case report This 63-year-old lady had been a grocery clerk at a coal mine in Northern Taiwan for 2 years in her early twenties. At the age of 61, she developed right subcostal pain for days. The chest computerized tomography revealed a right pleural effusion and pleural thickening. Cell block study revealed atypical mesothelial cells. Video-assisted thoracic surgery disclosed MM of the right pleura, involving right lower lung with metastasis to lymph nodes pathologically. After she received pleuropneumectomy and chemotherapy with pemetrexed, bilateral ovarian tumors and ascites were found one year later. Cell block study of ascites showed metastatic adenocarcinoma. Debulking surgery was done in July 2011 when pathology revealed high-grade serous carcinoma of both ovaries and then she died 9 months after the debulking surgery. Her occupational history disclosed that she might have bystander exposure to dusts at workplace in her early twenties, working as an accounting clerk in a coal mining industry for 2 years. Then she had been a teacher in an elementary school for 25 years later. In addition, her family claimed that she had lived in the asbestos cement roofing house for more than 10 years in her childhood, of which chrysotile was the major component. Trace amount of polarized fibers length about 2 μm in the non-tumor ovarian tissue were found by the polarized light microscopy.

Discussion This case may be the first index case of environmentally asbestos-related double cancers in Taiwan. The association between risk of both MM and ovarian cancer, and asbestos exposure was addressed by the International Agency for the Research on Cancer (IARC). We demonstrated a practical approach to screen possible asbestos fibers in the ovarian tissue sections, which may be casually linked to double cancers in this index case.