1708 IMMUNOTOXICOLOGY IN OCCUPATIONAL AND ENVIRONMENTAL CIRCUMSTANCES

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Aim of the session To discuss immunotoxicological alterations caused by occupational and envuironmental substances

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1708a SCORES PREDICTIVE FOR ASBESTOS EXPOSURE, MALIGNANT MESOTHELIOMA AND PLEURAL PLAQUE ON THE BASIS OF COMPREHENSIVE IMMUNOLOGICAL ANALYSIS

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Introduction Our findings about immunological profiles resulted from asbestos exposure and related with malignant mesothelioma (MM) allowed us to think a possibility to construct immunological scoring system to screen mesothelioma and asbestos exposure. Therefore, the present study comprehensively investigated immunological characteristics of plasma and peripheral blood mononuclear cells (PBMC) to obtain the formulae of the scores statistically.

Methods Blood specimens were obtained from 27 healthy volunteers (HV), 29 pleural plaque-positive people (PL) and 30 MM patients. Plasma and PBMC were assayed for cytokines and expression of cell surface molecules on $CD4^+$(Th), $CD8^+$(CTL), $CD56^+$(NK) lymphocytes and monocytes by luminex and flow cytometry. The part of PBMC was sorted into the four cell populations, which were assayed for mRNAs in fresh or after stimulation by realtime-PCR. The results were examined by multiple regression analysis to obtain the formulae of the scores.

Results Both of MM and PL showed decreases in CXCR3 and NKp46 on T and NK cells respectively and increase in granzyme B mRNA in stimulated CTL. IFN-λ and IL-17A in plasma were high in PL, whereas inflammatory cytokines including IL-6 and IP-10 were high in MM. Also, MM showed increase in CTLA-4 on Th cells. The 33 parameters with significant differences were examined by multiple regression analysis. The formulae of scores predictive for MM (M-score), both of MM and PL meaning asbestos exposure (A-score) and PL (P-score) were calculated and composed of the three parameters respectively. Every score showed a good ROC curve with sensitivity and specificity near 0.9.

Conclusion The findings of similarity between PL and MM might reflect alteration caused by inhaled asbestos. The high Treg marker with high inflammatory cytokines might be linked to MM development. Finally, we could obtain the three scores showing good ROC curves, which might be valuable to screen MM and asbestos exposure.

1708b THE IMMUNOTOXICITY AND NEUROTOXICITY OF ALUMINIUM

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Aluminium is omnipresent in the world, accounts 8.6% of the crust, and believed to be a neurotoxicant for a lot of years, and thought to be related with Alzheimer's disease and other neurodegenerative disease. In recent decades, aluminium, as metals, chemical compounds, powders, additives, adjuvants, and nanoparticles have being utilised widely in many fields including human's daily life and industries, and their potential adverse effect on health drew great concern. Aluminium, in the forms of ions, chemical compounds, fine particulate matters, can be ingested, inhaled, or even injected into human body, and translocated into blood stream and immune system to induce immutoxicity, and into central nervous system to induced neurotoxicity. Aluminium may induce neumocytes apoptosis by triggering oxidative stress, and inhibit or activate activity of cytokins, and the immuotoxicity and neurotoxicity induced by aluminium ions and fine aluminium particulate matters was higher than that of relatively large aluminium particles. Besides though blood compartment by which aluminium damage the blood brain barrier, it may enter into central nervous system though olfactory nerve. Aluminium impair behavioural performance of model organisms and rodents. The mechanisms of Al-induced immune and neurotoxicity may be:

- aluminium induces neural cell death by triggering oxidative stress, apoptosis, necroptosis and autophagy through complicate cell signal transmission pathways;
- promote Aβ deposit,
- promote tau hyperphosphorylation, and together induce neurodegeneration.
- promote cytokine release, trigger inflammation and immune reactions, and
- damage DNA and induce epigenetic changes.

1708c EXPOSURE TO SUB-10NM PARTICLES EMITTED FROM A BIODIESEL-FUELED DIESEL ENGINE: IN VITRO TOXICITY AND INFLAMMATORY POTENTIAL

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Introduction The inflammatory effects of organic sub-10nm particles generated and emitted from a diesel engine fueled with a biodiesel and a commercial diesel oil are analysed in this paper. Diesel combustion is the major sources of ultrafine

particles (UFP) in the environment, particularly in urbanised areas. In the last years, there is an increasing use of biomass-derived fuels because they are a renewable source of energy that may mitigate climate change through the reduction of net CO_2 with respect to conventional fossil fuels. Although there is a general agreement on biofuels ability to reduce conventional pollutants, new and potentially harmful pollutants can be formed during biofuel combustion. In particular, the emission of sub-10nm particles is strongly increased with respect to that of larger soot particles.

Methods Organic sub-10nm particles are separated from larger sizes particulate matter by collection in water suspension for toxicological and inflammatory tests. After exposure to sub-10nm particles, the effects on proliferation, apoptosis and secretion of cytokines, chemokines and growth factors networks production is analysed in immortalised non-tumorigenic human dermal keratinocyte cell line (HaCaT) and human alveolar epithelial-like cells (A549).

Results Nanoparticles exert different cytotoxic effects in the two cell lines, suggesting that the dermal way of exposure is more sensitive than the inhalant way. These differences are most evident in the secretion of pro-inflammatory, angiogenic and proliferative cytokines and chemokines whose expression is more finely modulated in HaCaT cells compared to A-549 cells.

Conclusion Considering the size of these particles, it is important to promote the culture of prevention also for the dermal way in particularly exposed workers.

1708d ALTERATION OF IMMUNE CELLS IN SILICOSIS: ROLES IN DEVELOPMENT OF AUTOIMMUNITY AND LUNG FIBROSIS

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In addition to lung fibrosis, silicosis (SIL) patients often suffer from complicated autoimmune disorders such as rheumatoid arthritis, systemic sclerosis and anti-neutrophil cytoplasmic antigen-related vasculitis/nephritis. Thus, chronic and recurrent exposure to silica particles located in the lung and lymph nodes can result in alterations in the function of immune cells, which can lead to the dysregulation of autoimmunity in addition to the development of lung fibrosis. Regarding B cells which produce various antibodies, in SIL many autoantibodies are often detected in autoimmune diseases, and specifically autoantibodies against apoptosis-related molecules. Responder T helper (rTh) cells which respond to foreign and auto-antigens have been reported to survive longer and have apoptosis inhibited. Additionally, regulatory T (Treg) cells seem to proceed to early apoptosis. This imbalance between rTh and Treg cells may make SIL patients prone to autoimmune disorders. Although the role of dendritic cells (DCs) including alveolar macrophages and T helper 17 (Th17) cells in the dysregulation of immune tolerance in SIL remains poorly understood, these cells play a role in pulmonary inflammation and the development of fibrosis via specific receptor and signalling molecules. Further studies are required to delineate the roles of DCs and Th17 cells in the disturbance of autoimmunity found in SIL, and investigation of the immunological alterations that lead to autoimmune dysregulation may assist in the recognition, prevention, and treatment of complicated autoimmune diseases found in SIL.

1707 ALLERGIES IN THE WORKPLACE

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Aim of the session To discuss occupational allergies in basic mechanisms, testing and newer clinical topics

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1707a TESTING FOR ALLERGY TO CHEMICAL PRESERVATIVES IN OCCUPATIONAL SETTINGS

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Introduction Methylchloroisothiazolinone/Methylisothiazolinone (MCI/MI) and methylisothiazolinone (MI) are chemical preservatives found in cosmetics, industrial and household products. There is a reported epidemic of allergic reactions to these substances in several countries (e.g. increases of 4.1% per annum over 16 years in England). Workers that come into contact with the agents may develop occupational contact dermatitis. Therefore, detecting these allergens is important to better manage workers' skin condition and exposure. The aim of this study was to determine the prevalence of contact dermatitis to MCI/MI and MI before and after changes in allergen testing was introduced.

Methods A retrospective assessment of workers referred to the NIOH Dermatology Clinic between 2006 and 2017 was conducted. Workers with work-related dermatitis were patch tested for sensitisation to MCI/MI and/or MI using the European baseline series (Chemotechnique). Frequencies of sensitisation to the allergens (MCI/MI and MI) were calculated using Microsoft Excel.

Results A total of 583 occupational referrals were seen and 413 were patch tested to determine a possible allergic aetiology for the dermatitis. Sixteen patients (3.9%) were positive to either one or both allergens (MCI/MI and MI) during the period January 2006 to June 2017. The testing concentration of the MCI/MI was doubled in 2014 and MI was introduced in 2015. More cases were identified (6/86; 7%) after changes were introduced post 2014 compared to previous allergen concentrations (10/327; 3.1%). The workers identified with sensitisation to the chemicals were from occupations such as