368. Environmental exposure and disease mechanisms

P3312

LSC 2011 Abstract: Combined nasal exposure to sodium hypochlorite and ovalbumin induces airway hyperreactivity in mice through activation of the TRPA1 channel and mast cells

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Background: Some epidemiologic studies have indicated that attendance to chlorinated swimming pools is associated with bronchial hyperreactivity, allergies and asthma.
Aim: To investigate the effects of NaClO, the main pool disinfectant, on allergic sensitization and airway responses in mice.
Methods: Male BALB/c mice received 1 to 7 nasal instillations of ovalbumin (OVA, 1%) on alternate days 10 min after instillation of NaClO (3 ppm active

chlorine) or water. 48h after 1, 3, 5 and 7 instillations, we measured airway reactivity to methacholine (Flexivent), cellular inflammation in broncho-alveolar lavage (BAL), lung cytokines, and serum OVA-specific IgE. Later, methacholine reactivity 48 h after a single combined NaClO-OVA exposure was assessed in mice pretreated with the neurokinin1 receptor antagonist RP67580, in knock-out mice deficient in the transient receptor potential (TRP) channel A1 (TRPA1$^{-/-}$) or V1 (TRPV1$^{-/-}$) and in mast cell deficient mice (*Kit$^{W\text{-}sh}$/Kit$^{W\text{-}sh}$*).
Results: Combined nasal NaClO-OVA exposure induced airway hyperreactivity (AHR) to methacholine in the absence of airway inflammation and OVA specific IgEs. AHR was already induced after a single combined exposure to NaClO-OVA and it was not observed after either OVA or NaClO alone. The AHR response was reduced after pretreatment with RP67580. NaClO-OVA induced AHR in TRPV1$^{-/-}$ mice, but not in TRPA1$^{-/-}$ mice and mast cell deficient mice.
Conclusion: Combined nasal NaClO-OVA exposure induces AHR in the absence of allergic inflammation. This effect appears to involve TRPA1, mast cells and release of substance P, suggesting a neuro-immune interaction.

P3313
LSC 2011 Abstract: Changes in the proteome upon dermal sensitization in a mouse model of chemical-induced asthma
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In follow up of our studies on proteomic changes in a validated mouse model of immunologically mediated chemical-induced asthma, using toluene-2,4-diisocyanate (TDI) as a sensitizer [1 we evaluated the temporal changes at early time points following dermal sensitization. The identification of biomarkers of sensitization could help to move diagnosis to an earlier (pre-clinical) stage. We explored the proteome of the auricular lymph nodes and serum of mice dermally sensitized to TDI.
Mice were treated once (day 1) or twice (day 1 and 8) with TDI or with the vehicle (acetone-olive oil, 2:3, control) on both ears. Auricular lymph nodes and serum were collected three days later. Two-dimensional difference gel electrophoresis was used to analyze the differential proteins ($p<0.01$) of TDI-sensitized mice (n=12) vs. control mice (n=12).
Proteome analyses of the auricular lymph nodes resulted in 39 and 86 differential proteins and of serum in 7 and 16 differential proteins, after 1 and 2 sensitizations, respectively. Identification (MALDI-TOF MS) of these proteins mainly showed structural (e.g. vimentin), immune related (e.g. lymphocyte specific protein-1) and oxidative stress related proteins (e.g. peroxiredoxin 6) in both the lymph nodes and the serum.
Now, a software based pathway analysis of the differential proteins is performed (Ariadne Genomics). This will give more insight in the cellular and molecular events involved in early sensitization, leading to chemical-induced asthma. Possible biomarkers among the differential proteins will be validated.
Reference:
[1] Haenen S, Vanoirbeek JA, De Vooght V, Maes E, Schoofs L, Nemery B, Hoet PH, Clynen E. *J Proteome Res.* 2010;9(11):5868-76.

P3314
Inhalation of nano-scaled titianium dioxide particles aggravates airway inflammation in allergen-challenged mice
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Titanium dioxide (TiO_2) nanoparticles are manufactured worldwide and although TiO_2 is chemically inert, it may have adverse health effects especially in sensitive populations. The use of nanomaterials has increased over the past years and the detrimental effects on various airway diseases are poorly characterized. Thus we investigated if a single exposure of TiO_2 before or during ovalbumin (OVA)-challenge could promote airway inflammation in mice with allergic airway disease.
BALB/c mice were sensitized to OVA (10 μg i.p.) on day 0 and 14, then challenged with nebulized 1% OVA for 30 min on day 29,32 and 34. Lung exposure of aerosolized TiO_2 was performed before (day 28) and during OVA challenge (day 33). The approximated deposited dose of TiO_2 in the mouse lung was estimated to be 0.53 ml/m^3 (2h, nose-only exposure). The experiment ended on day 35 with assessment of bronchial reactivity to methacholine and inflammatory cell counts in bronchoalveolar lavage (BAL).Total inflammatory cell counts in BAL was increased both when TiO_2 was exposed on day 28 and day 33 (both $p<0.05$) compared to exposure to only OVA. When mice were exposed for TiO_2 before OVA challenge there was a larger decline in respiratory compliance ($p=0.03$) and a greater impact on peripheral airways (tissue resistance and tissue elastance (both $p<0.05$)) compared to TiO_2 administrated during the OVA-challenge and to animals exposed to only OVA. In conclusion, we aimed to study effects of combined exposure of nanoparticles and pro-allergic proteins in a mouse model of asthma, indicating that TiO_2 administration before and during allergen-challenge have proinflammatory effects in peripheral airways.

P3315
Endotoxin exposure protects against new onset of pollen sensitisation
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Background: Farmers are exposed to a wide range of organic and microbial components. We studied the relation between farm-related endotoxin exposure and changes in atopic sensitisation over time in young adults in The Danish Farming Cohort (SUS).
Method: The SUS cohort (n=1166) was examined twice with a 15 year follow-up period. Specific IgEs against cat, birch, grass, HDM and storage mite allergens were determined (ADVIA Centaur, ALK Abellò ®). Sensitisation was defined as sIgE≥0.35 kU/L, and atopy was defined as sensitisation to one or more of the 5 allergens tested for. Personal average yearly exposure to endotoxin during the follow-up period was estimated from more than 500 personal inhalable dust measurements and a farm-specific internal job exposure matrix.
Results: New onset atopy was negatively associated with endotoxin exposure in a dose dependent manner (Table 1). Endotoxin exposure was not seen to be related to new onset of mite sensitisation. In contrast, all levels of endotoxin exposure showed a significant and strong protective effect against new onset of pollen sensitisation.

Table 1. Logistic regression analysis on endotoxin and new onset sensitisation

Endotoxin	Atopy OR (95% CI)	Pollen OR (95% CI)	Mites OR (95% CI)
2. quantile	0.75 (0.37–1.54)	0.36 (0.18–0.73)*	2.28 (0.94– 5.53)
3. quantile	0.39 (0.17–0.91)*	0.14 (0.06–0.36)*	1.47 (0.57–3.83)
4. quantile	0.49 (0.22–1.09)	0.21 (0.09–0.47)*	1.14 (0.41–3.15)

*$p<0.05$. The model is adjusted for farm childhood, familial atopic disposition, pets and smoking status.

Conclusion: These analyses suggest endotoxin exposure to have a significant protective effect against new onset of pollen sensitisation.

P3316
Reduction of diesel exhaust-induced health effects by using a vehicle cabin air inlet filter
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Exposure to air pollution is associated with adverse health effects. During exposure in traffic, air pollution concentrations may reach levels that cause symptoms and affect diseases. One way to counteract such effects can be to use an air inlet filter in order to prevent particles and gases from entering the vehicle cabin. The aim of the present study was to evaluate the efficacy of two filters to reduce diesel exhaust (DE) related health effects.
Material and Methods: 30 allergic and non-allergic subjects were exposed in an exposure chamber on four occasions during 1 hour; to filtered air, unfiltered DE with PM_1 of 340 μg/m^3, DE filtered by an ultrafine particle (UFP) filter and a UFP filter with active charcoal (UFP+AC), in random blinded order.
Results: The UFP filter reduced PM_1 by 46%, while the UFP+AC filter not only reduced PM_1 by 74% but also NO_2 by 75% and hydrocarbons by 50%. Headache, dizziness, eye irritation, nasal irritation, unpleasant smell and throat irritation increased significantly after exposure to unfiltered diesel exhaust compared to filtered air. Symptoms were significantly reduced by the UFP+AC filter and were also associated with small but significant improvements in lung function (FEV_1, FEF_{75} and FEF_{25-75}). The UFP filter without charcoal was far less efficient.
Conclusions: The combination filter (UFP + active charcoal) significantly reduced ultrafine particle, NO_2 and HC concentrations from diesel exhaust, and significantly improved symptoms and lung function. The study indicates that vehicle cabin air inlet filters should not only contain an ultrafine filter component, as the addition active charcoal was necessary to improve symptoms and respiratory health.

P3317

Osteopontin and soluble mesothelin-related peptide levels in malignant and benign diseases due to environmental asbestos exposure and healthy people with environmental asbestos exposure

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Objective: To determine osteopontin and soluble mesothelin-related peptide (SMRP) levels in malignant mesothelioma (MM) patients, in subjects with pleural plaques (PP) due to environmental asbestos exposure and in healthy subjects with environmental asbestos exposure.
Methods: Blood samples were taken from 279 residents from villages close to ophiolitic units (OU) (serpentin asbest containing) with PP on chest X-ray, 123 healthy subjects from villages close to OU, 120 healthy subjects from villages >26 km distant to OU and 24 MM patients.
Results: Mean serum osteopontin levels for MM, PP, asbestos-exposed healthy subjects and healthy subjects not exposed to asbestos were 21.207, 8.956, 9.453 and 9.725 ng/L respectively. Mean serum SMRP levels for MM, PP, asbestos-exposed healthy subjects and healthy subjects not exposed to asbestos were 4.59, 1.10, 1.11 and 1.12 ng/L respectively. Mean levels of both biomarkers were significantly higher in MM patients. The comparisons of biomarkers levels between the other three groups revealed no significant difference. Area under ROC curve was 0.86, sensitivity 75%, specificity 86% for osteopontin (cutoff value:17.273 ng/L) detecting MM. Area under ROC curve was 0.75, sensitivity 58%, specificity 83% for SMRP (cutoff value:1.63 ng/L) detecting MM. No difference was found between the areas under ROC curves of the two biomarkers in the diagnosis of MM.
Conclusion: Osteopontin and SMRP levels are higher in MM patients than in subjects with PP and healthy subjects with environmental asbestos exposure. The two biomarkers have no superiority to each other.

P3318

Adipokine adipsin is associated with the degree of parenchymal fibrosis in asbestos-exposed patients

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Asbestos causes an inflammatory response in the lungs, that can lead to pulmonary fibrosis called asbestosis. Most of the asbestos-exposed subjects show either normal or borderline parenchymal changes in high resolution computed tomography (HRCT). The significance of these borderline changes and their relation to pulmonary inflammation are not known. Adipokines regulate inflammatory responses and they are secreted by adipocytes and macrophages, while alveolar macrophages are known to be involved in asbestos-related lung inflammation. We assessed if adipokines are associated with the degree of pulmonary fibrosis in asbestos-exposed patients.
We measured adipsin, adiponectin, leptin, resistin, IL-6 and IL-8 in blood, lung function, and thorax-HRCT in 85 men with a history of moderate or heavy occupational asbestos-exposure. The subjects were divided into three groups based on the HRCT-finding: normal, borderline or fibrosis.
There was an increasing linear trend in the plasma levels of adipisin ($p<0.0001$) and adiponectin ($p=0.0083$) between the three groups, i.e. the more parenchymal changes on HRCT the higher the levels of adipsin and adiponectin. Adipsin levels correlated positively with the serum levels of IL-6 and the extent of pleural plaques on HRCT. Adipsin levels correlated negatively with TLCO, i.e. the higher the adipsin, the poorer the pulmonary transfer factor. Leptin or resistin were not associated with the degree of parenchymal fibrosis.
In conclusion, adipokine adipsin was associated with the degree of parenchymal fibrosis and inflammatory activity in asbestos-exposed subjects, suggesting that adipsin may have a role in the pathogenesis of asbestos-induced lung injury.

P3319

Short-term exposure to concentrated ambient particles increases airway hyperresponsiveness in normal mice

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Epidemiological studies show an association between short periods of exposure to air pollution with increase of hospital admissions for respiratory diseases. This study investigated if short-term exposures (1-hour) to relatively low levels of concentrated ambient fine particles (CAP) induce bronchial hyperresponsiveness and lung inflammation in mice. 45 Balb/C mice divided at two groups: 22 exposed to filtered air (FA) and 23 exposed to CAP (200 $\mu g/m^3$ divided by 24 hours = ± 8 $\mu g/m^3$). The PM2.5 concentration inside the chamber was monitored in real time. The pulmonary responsiveness to methacholine (Mch) was obtained 30 minutes after exposure, and bronchoalveolar lavage (BALF) to verify lung inflammation, 24 hour after exposure. Lung mechanical showed significant differences between the groups on the parameters following: Penh, PEF ($p<0.05$), and PIF ($p<0.01$) was statistically different for the CAP compared to FA; in relation the dose, there was a increase of Penh at basal, PBS ($p<0.05$) and 50 mg/mL Mch ($p<0.01$) in CAP when compared to the FA; there was a decrease of PEF at basal, 6.25 and 12.5 mg/mL Mch ($p<0.05$) of CAP compared with FA; and was also observed a decrease of PIF at basal ($p<0.01$), PBS, 6.25 and 12.5 mg/mL Mch ($p<0.05$). BALF showed an increase in the total cells number ($p<0.001$), macrophages ($p<0.01$) and neutrophils ($p<0.05$) in the CAP when compared to FA. Our findings show that even though a daily mean concentration of PM2.5 below the average daily level recommended by the World Health Organization (25 $\mu g/m^3$), a single exposure to CAP was capable of triggering pulmonary responsiveness and the increase in the lung inflammatory infiltration.

P3320

Intratracheal fiber glass instillation in rats: Bronchoalveolar lavage interleukinl8 levels

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Fiberglass (FG) is the largest category of man –made mineral fibers (MMVFs). Many tipes of FG are manufactured for specific uses building insulation,air handling,filtration and sound absorbtion. Because of increasing use and potential for widespread human exposurea chronic toxicity instillation study was conducted in Wistar rats, which were found to be sensitive to the induction of mesotheliomas with another MMVF. Four groups of 8 female Wistar rats were included in the study. The animal were devided into three groups per 8 exposed to different doses of FG and one controll group. First group (1-8) was exposed to 6mg dose/0.2ml saline 5days/week 10 weeks; the second (9-16) group was exposed to 10mg/0.2 ml saline 5 days/week 10 weeks, the third group (17-24)was exposed to 12 mg FG/0.2 ml saline solution 5 days/week 10 weeks and the controll group (25-32) was exposed to the same volume of saline. The fibers had been size selected to be rat respirable: length $<20\mu m$ and diameter $\leq 1\mu m$. After exposure period of 10 weeks the rats were killed one week after the last exposure. Following preparation of the lungs, they were lavaged with 2x5 ml saline without massage. The lavage fluid was collected in calibrated tubes and harvested volume was recorded. Supernatant was obtained after centrifugation at 1500 r.p.m for 5 minutes and il8 levels were measured. IL 8 levels were ranged between 12.3-20.2pg/ml at the control group, 15.8-40.6 pg/ml first group, 33-86.6pg/ml second group and between 46.5-113.2 pg/ml. Theese findings indicate that il8 levels were dose related and also correlated with lavage citology and histopathological findings.

P3321

Enhanced inflammatory response to formaldehyde in human bronchial epithelial cells

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Formaldehyde (FA) is known as a major chemical substance that may induce sick building syndrome (SBS). The mechanism underlying development of SBS has not been fully elucidated. We hypothesized that low doses of FA may be harmless when airway is intact, but may enhance inflammation when airway is affected by other factors such as microorganisms.
A human bronchial epithelial cell line, BEAS2B cells were exposed to FA (1-10 μM) before and after poly(I:C) (10 $\mu g/ml$) stimulation. Expression levels of mRNA of IL-8, RANTES and TLR3 mRNA were measured by real-time RT-PCR and their protein concentrations were determined by using ELISA. Cell signaling pathways possibly involved in the response were further analyzed by Western blotting.
FA after poly(I:C) stimulation significantly enhanced IL-8 mRNA expression and increased IL-8 protein concentrations to lesser extent. Phosphorylation of extracellular signal-regulated kinase (ERK) and c-Jun N-terminal protein kinase (JNK) was enhanced in the cells exposed to FA after poly(I:C) stimulation, whereas p38 MAP kinase was unaffected. This in vitro model suggests that effect of FA is small in normal conditions, but may enhance inflammatory response in pathological conditions via selective activation of inflammatory cell signaling molecules. It may provide insights into pathogenesis of SBS.

P3322

Impact of traffic-related air pollution on pulmonary oxidative stress

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Exposure to traffic-related air pollutants is known to increase morbidity and mortality. The aim of the study was to evaluate the impact of air pollution on pulmonary oxidative stress of police officers.

An observational prospective study on traffic police officers and controls was performed since August 2009 to March 2010 in Monza, Italy. Active smokers and asthmatics were excluded from the study. 8-isoprostane (8-iso) values were evaluated on exhaled breath condensate during both summer and winter visits. 8-iso values and pulmonary function test (PFTs) were correlated to air pollutant values detected by fixed measurements stations during one-month period before the visits. "TOSCA project", supported by Cariplo Foundation.

A total of 17 officers (9 males; 41±1.4 yrs, mean±SE) and 12 controls (5 males; 34±2.4 yrs) were enrolled in the study. 8-iso values in officers were 5.30±0.83 and 12.43±0.98 pg/mL (mean±SE), respectively, in summer and winter period ($p<0.0001$). No difference in 8-iso mean values was found among officers and controls during winter-time (12.43±0.98 vs. 12.78±1.87 pg/mL, respectively, p=0.75). Among the entire study population, significant positive correlations were found between 8-iso values during both seasons and mean values of each air pollutant, see Table. No correlation was detected among air pollutants and PFTs results.

	PM10 prior 30 days	PM2.5 prior 30 days
8-iso vs.	r = 0.57	r = 0.6
	CO prior 30 days	NO2 prior 30 days
8-iso vs.	r = 0.66	r = 0.62

$p<0.0001$ for all correlations (Pearson test). PM: particulate matter; CO: carbon monoxide; NO2: nitrogen dioxide.

Air pollution, especially long-term exposure, seems to impact pulmonary oxidative stress regardless occupational risks.

P3323

Sputum neutrophilia and annual decline of FEV1 in dust exposed workers

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In a previous study in the smelting industry we found a significant relationship between dust exposure and accelerated annual decline in FEV1. The aim of the present study was to investigate the association between annual decline in lung function and different inflammatory markers in induced sputum from the production workers.

Methods: Employees (n=76 (27 current smokers)) who had been part of a longitudinal study (9-13 years) including spirometry (>6 measurements) and respiratory questionnaires, performed induced sputum and exhaled NO.

Results: All workers had neutrophil inflammation compared to unexposed controls. However neutrophil levels in sputum samples did not differ between workers with annual decline in FEV1 (>45ml - upper tertile) compared to workers with annual decline in FEV1<25ml-lower tertile), 59% [95%CI 52.6-66.2] and 58% [95%CI 51.6-64.8] respectively. There were no differences in the neutrophil levels between current smokers 59% [95%CI 52.4-66.0] and non-smokers 56% [95%CI 50.6-60.6]. Exhaled NO levels were decreased in smokers compared to non-smokers (11.8 ppb vs 20.5 ppb ($p<0.01$))

Conclusion: All production workers displayed airway inflammation characterized by neutrophilia. Surprisingly, there were no differences in the neutrophil level when comparing workers with rapid decline in lung function with those with slow decline in lung function. As expected smokers had low levels of exhaled NO, but there was no difference in neutrophil levels between smokers and non-smokers. Sputum neutrophilia was not a marker for increased decline in FEV1.

P3324

The percent black carbon content in PM as an effective metric for evaluating the impact of no-traffic Sundays on urban air quality. The results of the 2011 wintertime campaign in Milan, Italy

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Traffic restrictions are unpopular because costly, inconvenient to drivers and of scanty evidence of their positive impact on urban air quality.

Scope: To investigate the suitability of particle mass and black carbon monitoring for detecting air quality changes due to traffic restrictions.

Methods: Mass analyzer Aerocet 531, MetOne, for PM measurement, and Microaethalometer AE51, Magee, for black carbon (BC). The instruments were left operating 4 to 7 p.m. at sidewalk for 4 days Friday to Monday, including two car-free Sundays. Student's t-test was used for statistical comparisons.

Results: On normal traffic days mean (SD) concentrations of PM and BC were 67.0 (29) ug/m^3 and 8.3 (3) ug/m^3, while on Sundays 80.1 (28) and 5.1 (4.3), respectively. No significant differences were seen between car-free Sundays and normal traffic days. Even though PM concentrations on Sundays were higher than on normal traffic days, with 2nd Sunday ranking at the top of the whole recordings (PM10 = 120.6 ug/m^3), the percent BC/PM ratio showed a highly significant reduction on Sundays, with mean (SD) 5.8 (2.3)%, as compared to 12.04 (4.8)% on traffic days ($p < 0.01$).

Conclusions: Measuring BC as percent of PM, represents a "normalized" measure, able to detect the impact of traffic restrictions over a wide temporal range of measurements. These and other studies performed in traffic impacted areas also identify black carbon as a potentially valuable measure of local emissions. This metric is closely associated with diesel emissions in urban areas and as such may be an easily measured surrogate of this toxic pollutant.

P3325

Role of p53 in murine macrophages and alveolar epithelial cells response to nanoparticles

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Introduction: The mechanisms of toxicity of manufactured nanoparticles (NP) are poorly characterized, but may involve oxidative stress. p53 is a key protein implicated in cellular responses to oxidative stress.

Aim of the study: To examine the induction and the roles of p53 in murine macrophages and alveolar epithelial cells exposed to different NP.

Methods: Murine macrophages (RAW 264.7 cell line and peritoneal macrophages from C57Bl6 mice) and alveolar epithelial cells (MLE-12 cell line) were exposed to 2 carbon black (CB) NP (13 and 20 nm diameter), single-wall carbon nanotubes (SWCNT, diameter: 4-7 nm) and 2 titanium dioxide (TiO_2) NP (10 and 15 nm diameter). p53 protein activation, cellular viability, apoptosis, oxidative stress, and proinflammatory cytokines levels were quantified 6 to 48h after cells exposure to NP.

Results: The 5 NP activated p53 concomitantly with a decreased cellular viability (except CB), and an induction of apoptosis (except TiO_2), oxidative stress and inflammation in macrophages, whereas no effect in alveolar epithelial cells was found after exposure to all NP.

In macrophages, the antioxidant N-acetylcysteine prevented p53 activation only in response to SWCNT. Pifithrin-α, an inhibitor of the transcriptional effects of p53, did not significantly modify the effects of NP on macrophages viability, apoptosis and inflammation.

Conclusion: In macrophages p53 was activated by the 5 NP, but only SWCNT did it via oxidative stress. Since p53 was not involved in the loss of viability and inflammation induced by the different NP, the role of p53 in macrophages response to NP deserves further investigations. p53 is not involved in alveolar epithelial cells responses to NP.

P3326

Chronic exposure to microcystin-LR: Pulmonary and upper respiratory tract impairment

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Background: Microcystin-LR (MCYST-LR) is a toxin commonly released by cyanobacteria in water reservoirs. It can damage the lung if absorbed by oral, venous or respiratory routes.

Aim: To verify the putative lung mechanical and histological impairment and the upper airways of mice after chronic intra-nasal instillation of MCYST-LR.

Methods: Male Swiss mice (25-30 g) were daily intranasally instilled with 10 μL of distilled water (AD group, n=10) or 6.7 ng/kg of MCYST-LR diluted in 10 μL of distilled water (TOX, n=8) 7 days/week for 1 month. Lung mechanics was determined 24 h after the last instillation. Lungs and nasal cavity were prepared for histological analysis (hematoxylin-eosin and alcian blue, respectively).

Results: TOX showed higher static elastance and viscoelastic component of elastance (33.9±1.2 and 5.2±0.4 cmH_2O/mL, respectively), viscoelastic/inhomogenous pressure and total resistive pressure (1.0±0.1 and 2.0±0.2 cmH_2O, respectively) than AD (26.4±2.6 and 3.7±0.3 cmH_2O/mL, 0.7±0.1 and 1.5±0.1 cmH_2O, respectively). Alveolar collapse and polymorphonuclear cell content were significantly larger in TOX group (41.2%, and 8.1×10^{-3} cells/mm^2) than in AD (3.1% and 2.3×10^{-3} cells/mm^2). TOX displayed a significantly higher volume proportion of mucous substances in the nasal epithelium (61.5%) than AD (38.5%). T-test was used ($\alpha = 5\%$).

Conclusion: Prolonged exposure to low levels of microcystin-LR triggered pul-

monary tissue mechanical impairment, damage to lung histology and secretory changes in the nasal cavity of mice. Thus, frequent exposure to low levels of MCYST-LR can damage the respiratory system and should be avoided.
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Chronic exposure of diesel exhaust particles causes alveolar enlargement in mice
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In urban centres, diesel exhaust particles (DEP) are the most toxic pollutant released from automotive engines, affecting pulmonary health. The aim of this study was to investigate the effects of a chronic period of exposure to DEP (three months) in healthy mice (Yoshizaki et al., 2010) studying whether chronic, near-ambient levels of DEP exposure could induce changes in the lung parenchyma structure and in the profile of inflammatory cells. Male Balb/c mice were divided into two groups: 1) nasal instillation of 10 μL of saline (n=8) (control group) and 2) nasal instillation of 30 μg/10 μL of DEP (n=9) (DEP group). Nasal instillations were performed five days a week for three months. Lung parenchyma was evaluated by quantifying the mean airspace chord lengths (Lm) by morphometry (point counting). T lymphocytes total (CD3) and macrophages (Mac-2) densities were analyzed by immunohistochemistry. DEP exposure induced increase of CD3 T lymphocytes in DEP when compared to Control (p=0.028); no statistical difference was found in macrophages density. The Lm was larger in DEP animals than controls (p=0.018). These findings indicate that chronic, near-ambient levels of DEP exposure can cause alveolar enlargement and T- lymphocytes recruitment, providing a biological link between DEP exposure and the emphysema.

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Changes in exhaled breath condensate pH following specific inhalation challenge in patients with occupational asthma to persulfate salts
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Introduction: Exposure to persulfate salts in hairdressing professionals is one of the most common causes of occupational asthma (OA) in our setting. pH measurement in exhaled breath condensate (EBC) has proven to be a useful, noninvasive method for monitoring pulmonary inflammation. This study investigates possible changes in EBC pH in patients with OA to persulfate salts following specific inhalation challenge (SIC) testing.
Material and methods: The study population included 13 patients with OA caused by exposure to persulfate salts, diagnosed by a positive SIC (Group 1) and 25 patients exposed to persulfates, but with a negative SIC (Group 2). EBC samples were collected before and after SIC was performed. pH was determined in all samples following degasification with helium.
Result: The mean (SD) EBC pH values before and after SIC were 7.65 (0.63) and 7.32 (0.85), respectively, in Group 1, and 7.73 (0.68) and 7.88 (0.66) in Group 2. There were no significant differences in the pH values between the 2 groups. However, when a decrease in EBC pH greater than 0.4 units following SIC was established as significant, 6 patients in Group 1 (43%) and only 1 patient in Group 2 (4%) exceeded this value.
Conclusions: Persulfate salts can induce an inflammatory response in patients with OA. A larger percentage of SIC-positive patients showed a significant EBC pH decrease following the test. This fact could contribute to improving the diagnostic yield of SBC.
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Toxicity of wood smoke and diesel exhaust in a whole blood assay
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Combustion particles can cause detrimental effects on human health. Studies have focused on diesel exhaust but increased exposure to biomass combustion in affluent regions in addition to the widespread exposure in less affluent regions of the World stresses the need for more research on a wider range of pollutants.
A 3-hr controlled exposure of 6 human volunteers to wood smoke (WS) at 300 ug/m^3 from good combustion conditions was conducted. Venous blood sampled right after exposure and 48 hr earlier was used in a whole blood assay. In the assay, suspended combustion particles were added to the blood and selected inflammation-related proteins were measured after incubation. Combustion particles were from diesel engine exhaust (DE) and WS (good vs. poor combustion) collected on high volume filters and extracted with methanol. The aim was to find differences in toxicity among combustion particles and to study the impact of previous exposure to smoke. The positive control was endotoxin.
The IL-6 release to endotoxin was attenuated after previous smoke exposure: 2380±2748 vs. 6849±2733 pg/mL (p = 0.057). IL-6 release to particles was detectable in one subject and only with WS particles from good combustion. IL-1β release did not show statistically significant differences, but appeared to be highest 48 hr before the smoke exposure. In particular it was high to WS particles from good combustion. The IL-1β release tended to be higher to WS particles from good combustion conditions than to DE particles (10.8±26.1 vs. 3.4±10.0 pg/mL; p = 0.15).
This small study suggest a greater inflammatory potential of particles from good compared with poor wood combustion or from diesel exhaust. Responses may be related to previous exposure.