Mannose Binding Lectin (MBL) Gene Polymorphism and the Development of Progressive Massive Fibrosis (PMF) in Patients with Silicosis

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Silicosis is a fibrotic lung disease resulting from inhalation of silica particles. The severity of silicosis is mostly dependent on the total amount and the duration of dust exposure. Genetic factor is also supposed to play an important role in the development of silicosis, and to modify the individual variability under the same working environment. MBL deficiency is reported to be associated with increased susceptibility to infection and autoimmune disorders. Among 3 mutations (codon 52, 54, 57) identified, mutation at codon 54 (substitution from Gly to Asp; G54D) has been common in Japanese population and G54D results in the profound reduced levels of MBL. We made a hypothesis that MBL polymorphism might affect the pathophysiology of silicosis through its effect on infection. Mutant G54D was assessed in gender-, smoking history-, dust exposure- matched nodular lesion group (n=97), PMF group (n= 48), and non-exposed healthy control group (n=84). The association between the mutant allele frequency of G54D and the radiological type of silicosis was also assessed. G54D allele frequency in nodular lesion group, PMF group, and control are 12.9%, 19.8%, and 8.9%, respectively. PMF group has significant high frequency of mutant allele compared with that of control ($p<0.05$). This result suggests that MBL G54D polymorphism may enhance the development of PMF in silicosis.

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Role of Interleukin-4 in the Lung Response to Silica in Mice

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Inhalation of silica particles results in activation of alveolar macrophages (AM) with release of proinflammatory cytokines and neutrophils recruitment. IL-4 is known to activate mononuclear cells as well as fibroblasts, both important in the pathogenesis of pulmonary fibrosis. We have examined the role of IL-4 on evolution of silicosis in IL-4 knock-out mice (KO). Silica particles (SiO2) 20 mg/50 l or saline (50 l) were introduced by intratracheal instillation in IL-4 KO and BALB/c mice (WT). Animals were sacrificed after 10-30 d after silica instillation, and besides a histopathological study, respiratory mechanics evaluation (air flow, volume, and total, resistive, and viscoelastic/inhomogeneous pressures) and AM phagocytosis function were analyzed. Silica-treated KO animals showed a significant increase of elastance and Ptot, P1, and P2 pressures in 10 days-group in comparison to WT animals, which diminished in 30 d groups. These results could be correlated to the widespread increase in inflammatory cells in early stage but to the diminished inflammatory response and fibrotic lesion of these animals in late stages. Furthermore, silica nodules of KO animals contained a significant amount of free silica. AM from KO animals showed an impaired phagocytic function which was reverted with the addition of recombinant IL-4. The differential count in BAL showed an increase in neutrophils in KO silica group (10-30 d). The results suggest that IL-4 may have an important immunoregulatory role at least in the silica model.

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Exposure to Stainless Steel Welding Fume Suppresses Lung Defense Function after Infection in Rats

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Pulmonary infections are increased in severity, duration, and frequency among full-time welders. The objective was to examine the mechanisms by which a stainless steel welding fume may alter lung defense against infection. At day 0, male Sprague-Dawley rats were intratracheally instilled with a manual metal arc, stainless steel welding fume (MMA-SS) at a concentration of 1.0 mg/100 g body weight or saline (vehicle control). At day 3, the MMA-SS- and saline-treated rats were intratracheally inoculated with 5,000 *Listeria monocytogenes*. At days 6, 8 and 10, left lungs were removed, homogenized, cultured overnight, and colony-forming units counted to assess pulmonary bacterial clearance. Right lungs were lavaged to recover phagocytes and lavage fluid to measure the production of the anti-microbial agent, nitric oxide (NO) and immuno-modulatory cytokines, including IL-2 and IL-10. Exposure to the fume before infection significantly slowed the pulmonary clearance of the bacteria and severely damaged the lungs compared to control. Phagocytic cell NO production and lavage fluid IL-2 were significantly reduced in the MMA-SS + *L. monocytogenes* group early after infection compared to the saline + *L. monocytogenes* group. Pretreatment with MMA-SS before infection caused a significant increase in lavage fluid IL-10. In conclusion, the MMA-SS-induced suppression of lung defense against infection in rats involves a reduction in cellular production of NO and IL-2 as well as an increase in anti-inflammatory IL-10 production.

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Latex Textile Workers:Respiratory Symptoms,Sensitisation and Sp… Vitro Basophil Challenge

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Rationale: Natural rubber latex (NRL) is a known respiratory sensit… most of the literature desribes health care workers. Respiratory symptoms … textile workers led to a worksite investigation of symptoms, specific IgE … and response to in vitro basophil challenge with NRL. **Methods:**12 se… volunteers (attending as part of a larger study) from the NRL textile facto… recruited. Each undertook a physician led respiratory questionnaire, spirom… venesection. We performed RAST testing to both NRL and to common… allergens (NRL IgE and atopy IgE). We stimulated whole blood samples… 0.01,0.1,1 and 10μg/ml NRL. Cells were also stimulated with an irrelevant… as a negative control. Basophil activation was quantified using flow cy… analysis of $CD63^{bright}$ expression on basophils identified by side scat… $CD123w^{bright}$ backgating and $HLA\text{-}DR^{negative}$. **Results:** All 5 asymptomatic… uals were negative for NRL IgE and basophil activation. Of 5 subjects w… related (WR) upper respiratory problems, none were NRL IgE positive bu… had an increase in basophil activation. 2 subjects reported WR upper & lo… ratory symptoms and both were NRL IgE positive and demonstrated an in… basophil activation at 1μg/ml NRL. **Conclusions:** We have demonst… respiratory symptoms and sensitisation to NRL outside the health care se… basophil activation assay (as a specific in vitro challenge) may act as a mo… tive immunological endpoint than specific IgE and may better reflect the fu… consequences of allergen exposure.

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Serum Tumor Necrosis Factor Alpha and Interleukin 8 Levels in Coa… with Coal Workers' Pneumoconiosis

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Various cytokines and growth factors secreted from macrophages/mo… play the key role in the pathogenesis of pneumoconiosis. In vitro and in vivo … with coal dusts showed the up-regulation of important leukocyte recruiting … These can act as markers for the prediction of pneumoconiosis and progr… this study, we aimed to determine the relation of tumor necrosis factor-alp… alpha) and interleukin-8 (IL-8) serum levels with the degree of CWP and … history in active coal miners. We measured serum levels in 27 coal mi… CWP and 14 healthy controls. The mean underground working dura… 14.29+/-3.14 years. Miners were grouped as Category I (n=25) and II (… profusion I (n=15)and II (n=12) according to profusion category of CWP … roentgenogram (CXR) and HRCT respectively. Serum TNF-alpha in m… significantly higher ($p<0.001$) than controls. (23.30 +/-10.51 vs 1.43+/… ml), but IL-8 showed no difference. Underground working history was … pneumoconiotic stage but not to level of TNF-alpha or IL-8. This exclud… alpha and IL 8 as an exposure marker. Miners who showed abnormally hig… of TNF-alpha had an increased CWP category. TNF-alpha levels were sign… correlated ($p=0.003$) with CXR category rather than with HRCT p… ($p=0.52$), whereas IL-8 showed no correlation with both categories. We c… that there is a significant involvement of TNF-alpha in CWP and it may w… marker to estimate progression of pneumoconiotic disease, but the rou… serum TNF-alpha and IL-8 as a marker of exposure is not supported.

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The Evaluation of Pulmonary Epithelial Permeability in Early Stag… Worker's Pneumoconiosis

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The current study was designed to evaluate the role of pulmonary scint… an alternative test in the early diagnosis and staging of coal worker's pneum… (CWP). A total of 40 coal miners were studied using radioaerosol pulmona… raphy, HRCT(High Resolution Computerised Tomography) and pulmonary … tests. 20 healthy volunteers were studied as a control group. To assess diseas… patients were classified according to Hosoda-Shida 1993 HRCT clas… Dynamic scintigrams were obtained following inhalation of TC-99m-DTPA … a radioaerosol delivery system. Pulmonery half life (T1/2 min ± s.d.) val… measured as an indicator of pulmonary epithelial permeability. The measu… values were 50.3±11.1, 78.3±11.7 and 65.2±10.4, 99.8±5.1 min. for pneu… osis smoker-nonsmoker and control smoker-nonsmoker groups, respectivel… were statistically difference for pneumoconiosis smoker and nonsmoker ($p<$… pneumoconiosis smoker and control smoker ($p<0.01$), and also for pneu… nonsmoker and control nonsmoker ($p<0.05$). T1/2 values according to … findings were 50.2±11.9 (profusion1), 41.9.±7.5 (profusion2) min respe… there was a significant correlation between the stage of the disease and … epithelial permeability ($r=-0,37$, $p=0.03$). In conclusion, CWP increases the … nary epithelial permeability which is directly related to the degree of the dise… smoking shows negative effect on these patients' pulmonary epithelial per… It's suggested that pulmonary epithelial permeability can be used to dete… stage of the CWP in addition to the radiological findings.

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