and those of EU. We consider that presented data must be an alarm signal for organizers and workplaces managers in other to remedial the situation with negative impact upon health of employees, the presentation to the medical prophylactic examinations represents a way of finding incipient discover of illness for some entities sometimes irreversible.

343 Silicotics in Germany - mortality risk and exposure level

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Background: In order to prevent lung cancer among silica exposed workers a safe level needs to be established.
Method: In a prospective cohort study 630 silicotics (compensated between 1988 and 2000) from three different industries (stone & quarry, ceramics and tunnelling) have been enrolled.
Result: Within the follow-up over 212 of the workers died. The overall as well as the lung cancer mortality rate is about twice as high as in the general population. All workers have been exposed for at least for one year above the current MAK-value of 0.15 mg/m³. The cumulative exposure has been 2 mg/m³ year or greater. All workers have been exposed on average about 33 years.
Conclusion: This study shows the high mortality risk for compensated silicotics. As result of this study, the exposure has to be at a level of 0.15 mg/m³ at any time or lower. The latency period is too short to give additional information about a "safe" level, e.g. whether a value of 0.15 mg/m³ is sufficient in order to prevent silica induced lung cancer.

345 Mechanisms of crystalline silica and coal-induced emphysema development

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Background: The incidence of chronic obstructive pulmonary disease (COPD) has increased dramatically in the past few decades and now ranks as a major cause of morbidity and mortality on a worldwide basis. It is estimated that approximately 14 million people in the United States have COPD. The World Health Organization predicts that by 2020 COPD will become the 3rd most common cause of death. Cigarette smoking, environmental pollution, and occupational exposure are the most important risk factors associated with the development of COPD. Although COPD encompasses chronic obstructive bronchitis and emphysema the molecular mechanisms involved in their pathogenesis and expression of symptoms are dramatically different between these two diseases. Therefore, we will be focusing only on the potential mechanisms of silica or coal-induced emphysema development. In epidemiologic and pathologic studies occupational exposure to crystalline silica and coal are two important risk factors identified to be associated with the development of emphysema. Development of focal emphysema in coal miners who have never smoked is induced by the secretion of proteolytic enzymes from coal-activated macrophages and inactivation of α_1 antitrypsin. Similarly emphysema in silica-exposed workers is thought to be induced by the enhanced generation of reactive oxygen species secreted by activated macrophages and the resultant inactivation of α_1 antitrypsin. This hypothesis is supported by epidemiological studies documenting exposure-response for air flow obstruction in silica-exposed workers even in the absence of radiological signs of silicosis. In addition, *in vitro* and *in vivo* experimental studies corroborate the oxidative inactivation of antiproteinases and the subsequent breakdown of connective tissue in a dose-response fashion due to exposure to silica or coal. These experimental studies and other clinical observations suggest that silica-and coal dust-induced emphysema occur through similar mechanisms as that for smoking-induced emphysema.
Methods: In this report, we will review the epidemiologic and pathologic evidence and discuss the molecular mechanisms relevant to the development of emphysema in silica and coal-dust exposed workers within the context of recent findings.
Results and Conclusions: The evidence surveyed suggests that chronic exposure to silica or coal that may cause the development of chronic bronchitis, emphysema and/or small airways disease that can lead to airflow obstruction even in the absence of radiological disease.

346 Positron Emission Tomographic (PET) imaging of silicosis in a rabbit model using an ^{18}F-Fluorinated proline amino acid analog tracer

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The sensitivity of positron emission tomography using a proline amino acid analog was tested for detection of pulmonary response in early silicosis in an animal model subject to an acute instillation exposure to quartz dust. *Cis*-4-^{18}F fluoro-L-proline (FP) was synthesized as a positron-emitting ^{18}F-labeled analog of the amino acid proline. Proline and glycine are used extensively in procollagen synthesis by pulmonary fibroblasts in active silicosis. Proline is taken up by the fibroblasts to provide both the proline and hydroxyproline residues of procollagen, which is then secreted into the extracellular space for maturation into collagen scar tissue in fibrosis. ^{18}F is covalently bound in the FP proline analog. ^{18}F has an 110 minute half-life and decays by positron emission, finally resulting in emission of two 0.511 MeV gamma rays which provide a means to map the location of the tracer. Most clinical PET imaging uses an analog of sugar, fluorodeoxyglucose (FDG), to map areas of generally heightened metabolism, e.g., tumors. Instead, fluoroproline was tested here for above-background uptake associated with heightened metabolism specific to silicosis. Rabbits were instilled with respirable quartz dust in saline, or with saline alone for controls, and subsequently at 1, 2, 4, or 5 months animals were injected with 1mCi of FP and imaged in a clinical PET system. Animals were killed two days later and their lung tissue

subjected to histopathology examination for fibrosis distribution and severity. PET images were graded for features by consensus of three readers blinded to the identity of silica- or saline-challenged animals imaged in sets of three, with at least one control and one test animal in each set. Histopathology scores were statistically correlated with PET image scores. Innate PET resolution, the small animal size relative to the clinical imager, animal respiration, and the presence of an azygous lung lobe in some animals limited localization of the PET imaged features to about a centimeter. ^{3}H proline autoradiography studies are addressing the question of the specificity of location of heightened proline uptake, i.e., to pulmonary interstitial sites of fibroblast collagen synthesis activity or to pulmonary alveolar surface locations of neutrophil-associated inflammatory response. Resolution of questions of specificity of the uptake to collagen synthesis activity will clarify the feasibility of PET imaging for detection of active stages of fibrosis and for possible application for early disease detection and prevention or for evaluation of the active status of fibrosis for guiding medical management of advanced disease. Toxicological evaluations of FP will determine if FP is safe for use or if ^{11}C-proline is needed for possible further testing and development of the method.

347 Classroom chalk: a possible new source of exposure to crystalline silica

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In its 1997 publication, volume number 68, the International Agency for Research on Cancer raised its rating for silica to Group 1: sufficient evidence for carcinogenicity in humans. Its listings of possible sources of silica exposure, however, do not include classroom chalk. We were recently surprised, therefore, to hear of a teacher in Israel in whom bronchial carcinoma was diagnosed-surprised because this sentinel case, a 54-year-old female, was found to be devoid of all the risk factors commonly associated with her disease. She never smoked and, indeed, has had a lifelong aversion to environmental tobacco smoke. Nor is she aware of any exposure to the metallic or metal-like elements (including chromium, nickel, and arsenic). Preliminary radon activity concentrations in her home were found to be unremarkable, as were other exposures to ionizing radiation. Finally, with regard to asbestos, we were unable to elicit a possible link between either the patient or her husband and this carcinogenic mineral. In brief, only exposure to classroom chalk dust seemed to remain a viable possibility. Subsequently, with the help of Material Safety Data Sheets, we were able, to establish that numerous types of chalk currently in use contain crystalline silica. Furthermore, and closer to home, recent analyses by the Israel Ministry of Labor indicate that airborne concentrations of silica dust in a chalk factory exceeded the current NIOSH REL (0.05 mg/m^3) by as much as a factor of 10. The hypotheses generated by these findings, along with the assumed size (worldwide) of the potentially exposed population, suggest that even at this early stage a number of steps may reasonably be taken to begin to deal with the problem. First, current use of silica in chalk should be reduced or eliminated; even if exposures prove to be "low," the number of those potentially at risk is large. As in other, similar situations, we believe that the precautionary principle should be implemented. Second, screening and surveillance programs concerning silica should include questions relative to chalk – especially classroom chalk – exposure on their questionnaires. Third, should illness following exposure to chalk dust be recognized as work related, it is probably never too early for the public-health community to begin to consider the medico-legal aspects of the matter. Finally, to determine the risks from past exposures among teachers and others, appropriate epidemiologic studies should be carried out.

348 About one case of acute silicosis: a current risk in the rubber industry

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Introduction: Silicosis is considered a definitely declining occupational disease, as a result of a better control of the occupational risk. Current statistics from INAIL show that in the '90ths 4.161 cases were recognized compared to 45.194 cases from 1965 to 1974; those data refer mostly to chronic forms. No statistics are available about trends of the so-called acute or quickly-increasing silicosis; despite they seem to regard only outdated conditions of occupational risk, they are so far authoritative and recent works on occupational diseases.
Case report: A 41 years aged worker was admitted in hospital during 1996 november 1996 for a severe fibrogenic pneumopathy, suspecting a sarcoidosis or an autoimmune lung fibrosis. One out of the pneumatologists in charge posed, in addition, the diagnostic hypothesis of an occupational form and demanded a close examination by an industrial medicine specialist. The seriousness of the illness imposed a lung transplant; the whole removed lungs were granted for testings. The chemical analysis of lung samples showed a significant presence of nickel, molybdenum and tungsten, while vanadium and cobalt were under the analytical limit of 30 micrograms/kg. Under hystological examination a hard-metal pneumopathy was in any case excluded, at the same time with the evidence of a severe interstitial fibrosis, with both diffuse both hyaline nodular aspects, granulomatosis, capillaritis and sclero-calcific nodes. On polarized light, inside the parenchimal sclero-hyaline nodes were bi-refracting particles referable in greater part to silicates, in lesser share to crystalline silica. Out of the patient's jobs was, noteworthy appeared the one of attached to the open mixers inside a small firm producing siliconic rubber, where he worked for five years from 1988 to 1993. The Occupational Prevention and Safety Unit of the Local Health Administration for Brescia ascertained that, still during the first months of 1997, inside the firm siliconic blends were prepared using mineral fillers with quartz (Sicron) and cristobalite (Celite) respectively at concentrations of 90 and 60%. Those fillers, in the form of a fine powder with a mean consumption of about 5-6.000 kg/month, were manually taken from bags and put into the open mixer, having an extracting hood wrongly hanging above the respiratory zone of the attached worker, failing any respiratory personal protective device; the powder that, being not included

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