

Analysis of clinical and diagnostic findings during exposures in Chemical Nanotechnology



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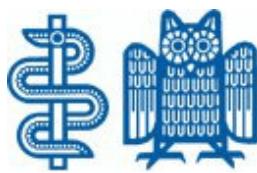
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INTRODUCTION

The rapid development of nanotechnology – the key technology of the 21th century - demands a consideration of risks and assessment of health effects during exposures to nanomaterials.

Due to their high surface to volume ratio, nanoscaled materials exhibit exceptional physical and chemical properties when compared to larger particles of the same composition. Therefore toxicological informations of the bulk material should be carefully applied to nano particles.

One of the most relevant uptake pathways is the inhalation of nanoscaled particles. Effects on the respiratory tract like inflammation, oxidative stress and pulmonary fibrosis, adverse effects on the cardiovascular and central nervous system are considered.

In addition, nanotubes with their structure similar to asbestos-fibres may have a carcinogenic potential.

Taking into consideration the various possible working mechanism of nanomaterials, an extensive diagnostic program was designed and offered to a collective of employees in chemical nanotechnology.

STUDY GROUP AND DIAGNOSTIC PROGRAM

The study group included 10 persons (3 woman, 7 men, mean age 42,7 years) involved in production, modification of surface and further processing of oxide nano particles with primary particle size < 10 to 100 nm for more than 11 years (*figures 1 - 4*). Medical examinations were carried out according to specified criteria set by us in 2009.

RESULTS

Half of the non smoking group showed a relevant obstructive ventilation disorder (with/without lung emphysema) in pulmonary function tests (*figures 5 & 6*). Correlating conjunctivitis, rhinitis and dyspnea – even at the workplace – were described in history.

X-rays of chest showed a lung emphysema in 5 out of 10 persons, in 3 cases signs of pulmonary emphysema were confirmed by CT scanning (*figures 7 & 8*).

Only 2 out of 5 persons with lung emphysema/obstruction presented a sensitization to IgE-mediated inhalative and immediate type allergens as a result of serologic tests and cutaneous allergy diagnostic according to an atopic diathesis.

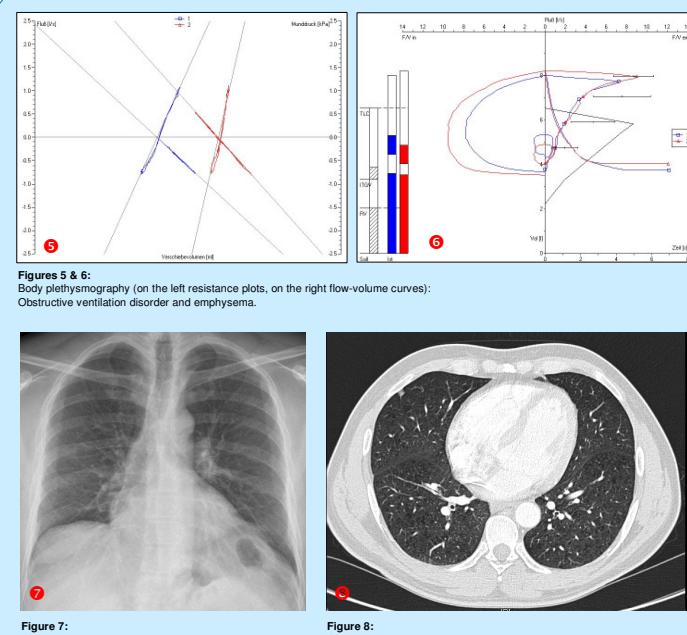
Additionally, half of the group showed a positive LTT reaction to Zirconium – without clinical correlation to a manifest (type IV-) allergy. As a nano particle ZrO_2 occupies the central position in the here shown exposition spectrum. One subject additionally showed a type I-sensitization to Zirconium. Here allergic rhinitis and chronic bronchitis are of clinical relevance.

CONCLUSION

These findings indicate that long-term exposure in nanotechnology may be related to potentially adverse health effects. Adequate health and safety measures as well as surveillance by an occupational physician should be encouraged.



Figures 1, 2, 3 & 4:
Handling of nanomaterials during processing.



Figures 5 & 6:
Body plethysmography (on the left resistance plots, on the right flow-volume curves):
Obstructive ventilation disorder and emphysema.

Figure 7:
Chest X-ray: Emphysema of the lung.

Figure 8:
CT scan of the lung:
Centrilobular emphysema accompanied by few small nodules.

LITERATURE

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Bartter T, Irwin RS, Abraham JL, Dascal A, Nash G, Himmelstein JS, Jederlinic PJ (1991): Zirconium compound-induced pulmonary fibrosis. Arch Intern Med 151: 1197-1201.

Borm PJA, Robbins D, Haubold S, Kuhlbusch T, Fissan H, Donaldson K, Schins R, Stohe V, Kreyling W, Lademann J, Krutmann J, Wahrheit D, Oberdörster D (2006)

DFG-Forschungsvorhaben „Arbeitsbedingte Erkrankungen nach direkter oder indirekter Arbeitsbelastung“: Diagnose und Risikoabschätzung von MAK-Werten: Zirkonium und seine Verbindungen. Senatskommission zur Prüfung gesundheitsschädlicher Arbeitsstoffe. 27. Lieferung. Verlag Chemie, Weinheim.

Kotter JM, Ziegler G (1992): Sarkoidale Granulomatose nach mehrjähriger Zirkoniumexposition, eine „Zirkoniumlung“. Pathologe 13: 104-9.

Lipko KK, Anttila SL, Taikura Aho, Ruokonen EL, Tolokon ST, Tuomi T (1993): Hyperensitivity pneumonitis and exposure to Zirconium Silicate in a young ceramic tile worker. Am Rev Respir Dis 148: 1089-1092.

Marcus RL, Turner S, Cherry NM (1998): A study of lung function and chest radiographs in men exposed to zirconium compounds. Occup Med Vol 46, No 2: 109-113.

Mittmann-Frank M, Berger H, Buchter A (2009): Arbeitsmedizinische und präventivmedizinische Untersuchungsprogramm bei Exposition mit Nanopartikeln und speziellen oder neuen Materialien. Zbl Arbeitsmed 59: 336-343.

Mittmann-Frank M, Berger H, Bücker C, Bücker A, Wilkens H, Arzt E, Schmitt KP, Wennemuth G, Hanig M, Buchter A (2010): Klinische und diagnostische Befunde bei Exposition gegenüber Nanopartikeln und neuen Materialien, Zbl Arbeitsmed 60: 328-349.

Müller M, Fritz M, Buchter A (2008): Nanotoxikologie. Zbl Arbeitsmed 58: 233 - 252.

Schneider J, Freitag F und Rödelberger K (1994): Durch Zirkonium-Einwirkung am Arbeitsplatz verursachte exogen-allergische Alveolitis (Nr. 4201 BeKV), Arbeitsmed Sozialmed Umweltmed 29: 382-385.

Xia T, Li N, Nel AE (2009): Potential health impact of nanoparticles. Annu Rev Public Health 30: 137 - 50.