TOBACCO SMOKE EXPOSURE AND URINARY CADMIUM LEVELS IN US CHILDREN: DATA FROM NHANES III Mannino DM, Albalak R, Jones R,
Centers for Disease Control and Prevention, Atlanta, Georgia, United States.
RATIONALE: Environmental tobacco smoke (ETS) exposure is an important cause of morbidity in children. The metal cadmium, a constituent of ETS, is stored in the liver and kidneys and has a biologic half-life of 10 to 20 years. The goal of this analysis was to determine the effect of ETS exposure on urine cadmium levels in US children. METHODS: We analyzed data among children aged 6 through 16 years from the Third National Health and Nutrition Examination Survey, a nationally representative survey of the US population. We included never- smoking subjects from whom urinary cadmium levels had been obtained and used these covariates: reported smoke exposure, serum cotinine level, age, socioeconomic status, region of the country, race/ethnicity, sex, and dietary factors to predict the cadmium to creatinine ratio, using multiple linear regression. Our analytic sample included 4254 never smoking children who had data on all of the covariates available. RESULTS: The geometric mean level of urine cadmium was 0.09 μg/g creatinine. Geometric mean urine cadmium levels were increased in children with high ETS exposure as measured by serum cotinine (0.57 to 15 ng/mL), compared with children with low ETS exposure (< 0.106 ng/mL serum cotinine level, 0.10 μg/g creatinine vs. 0.07 μg/g creatinine, $p < 0.05$). After adjusting for other covariates, ETS exposure remained significantly associated with an increase in urine cadmium levels of approximately 20%. Other significant predictors of increased cadmium levels in the multivariate models included female sex and lower socioeconomic status. CONCLUSIONS: Urine cadmium levels are significantly increased in children with ETS exposure and cadmium has promise as a potential biomarker for long-term or historic tobacco smoke exposure because of its long half-life
This abstract is funded by: Centers for Disease Control and Prevention

RESPIRATORY EFFECTS OF ACUTE EXPOSURE TO ULTRAFINE IRON PARTICLES IN THE LUNGS OF ADULT HEALTHY RATS. YM Zhou, CY Zhong, IM Kennedy and KE Pinkerton. Center for Comparative Respiratory Biology and Medicine. University of California, Davis, CA 95616
The role of physicochemical characteristics of ambient particulate (PM) in eliciting adverse health effects is poorly understood. As critical constituents of PM, transition metals may play important role in health outcomes associated with PM exposure. The purpose of this study was to determine the effects and dose-response of ultrafine iron particles, the predominant transition metal found in PM, in the respiratory system of adult rats. 14 to 16 week old Sparague Dawley rats were exposed via inhalation to iron particles (57 $\mu g/m^3$ and 90 $\mu g/m^3$, respectively) or filtered air (FA) as controls with 6 hr /day for 3 days. The mass median aerodynamic diameter (MMAD) of iron particles was 72 nm. Following exposure, bronchoalveolar lavage (BAL) was performed to examine cell viability, cell differentiation, protein level and lactate dehydrogenase (LDH) activity. Lipid peroxidation, glutathione (GSH and GSSG), glutathione-S-transferases (GST) and total anti-oxidant power (FRAP assay) were measured in BAL and lung tissue. IL-1β and TNF-α levels were analyzed by ELISA. Ferritin expression was determined by Western blotting. NF-κB -DNA binding activity was assessed by electrophoretic mobility shift assay (EMSA). Exposure to ultrafine iron particles at 90 $\mu g/m^3$ caused significant increase in protein concentration compared with controls, NF-κB was1.3-fold of control. In addition, it also resulted the significant decrease in total antioxidant power, significant induction of GST activity, ferritin expression and IL-1β level compared with FA control and with iron particle exposure at 57 $\mu g/m^3$. In contrast, no significant changes was noted following exposure to iron particles at 57 $\mu g/m^3$ when compared with controls. We conclude that 1) exposure to ultrafine iron particles induces cytotoxicity, oxidative stress and inflammatory response in the lungs of adult rats, 2) activation of NF-κB may be involved in the regulation of biological response, and 3) dose-response is apparent for the effects observed. These data indicate the potential importance of transition metal iron in PM air pollution related health effects.
This abstract is funded by: Health Effects Institute, EPA 826246 and 827995

EFFECT OF CIGARETTE SMOKING ON CADMIUM AND METALLOTHIONEIN CONTENT OF ALVEOLAR MACROPHAGES.
R Grasseschi, D Levine, LJ Wesselius, Pulmonary Section, Carl T. Hayden VA Medical Center, Phoenix, Arizona, USA.
Introduction: Cadmium (Cd) inhalation can cause emphysema and lung cancer, and Cd is present in cigarette smoke as well as air pollution. Cells synthesize the protein metallothionein (MT) in response to Cd, and this protein binds Cd and limits its toxicity. It is uncertain whether cigarette smoking alters intrapulmonary concentrations of Cd or MT, or whether Cd toxicity contributes to lung disease in smokers. In this study we compared Cd and MT content of alveolar macrophages (AM) recovered from cigarette smokers (CS) and nonsmokers (NS)
Methods: Bronchoalveolar lavage was used to recover AM from 7 NS and 7 CS. Cd concentrations were determined by ICP mass spectrometry and MT was measured by a Cd/hemoglobin radioassay (Cd^{109}).
Results: AM content of Cd was increased in CS compared with NS (107 ± 35 vs 40 ± 8 ng/mg protein, $p < 0.01$). In contrast the MT content of AM was similar in both groups (1.4 ±0.3 vs 1.2 ±1.2 nmol/mg). There was a correlation between pack years and Cd content of AM in CS ($p < 0.05$).
Conclusions: Cigarette smoking is associated with an increased AM content of Cd, although not MT. Chronic accumulation of Cd from cigarette smoke may not induce a protective increase in MT concentrations in smoker's AM, thereby limiting the capacity of MT to inhibit Cd toxicity.

American Lung Association, Arizona Affiliate

This abstract is funded by:

ULTRAFINE INSOLUBLE IRIDIUM PARTICLES ARE NEGLIGIBLY TRANSLOCATED FROM LUNG EPITHELIUM TO EXTRAPULMONARY ORGANS WG Kreyling, M Semmler, S Takenaka, H Schulz, *G Oberdörster, A Ziesenis GSF-National Research Center, Institute for Inhalation Biology, Neuherberg / Munich, Germany and *University of Rochester, Medical Center, Rochester NY 14642, USA

Introduction Ultrafine particles may translocate from the lungs to systemic circulation eventually accumulating in critical organs such as liver and heart. The latter may play a role in the onset of cardiovascular diseases. Methods Ultrafine 15 + 80 nm iridium aerosols labelled with ^{192}Ir were generated with a spark generator. For inhalation, young adult, healthy, male WKY rats were ventilated for one hour via an endotracheal tube. At time points ranging from 6 h to 7 days, rats were sacrificed, and a complete balance of ^{192}Ir activity was determined either retained in various organs, tissues and the remaining carcass or excreted before. Results Auxiliary in vivo and in vitro studies indicated very low solubility of iridium particles (< 1% in 7 days). Both inhaled ultrafine iridium particles were almost exclusively retained in the lungs for one week after completion of fast clearance. About 1% of the particles were retained in bone and soft tissue; <0.5% in liver and even less in spleen, heart and brain. Conclusion This study indicates, only small fractions of ultrafine iridium particles have access to systemic circulation and extrapulmonary organs. However, particle properties like physical structure and chemical composition of the surface and the matrix of the particle may be other important determinants of systemic translocation.
This abstract is funded by: (GSF FE-75041 + EPA PM Center Grant R827354)

PULMONARY INFLAMMATORY RESPONSE OF RATS EXPOSED TO REPEATED NEBULIZATIONS OF CADMIUM.
G. Vincke[1], P. Danhaive[2], F. Stiernet[2], M. Peck[2], P. Gustin[1].
[1] Faculty of Veterinary Medicine, University of Liege, Belgium.
[2] UCB s.a., Pharma sector, R&D, Braine-l'Alleud, Belgium.
Rationale: The aim of the study was to investigate the pulmonary inflammatory reaction induced by long term repeated nebulizations of cadmium (Cd), a toxic known to be present in cigarette smoke and which could be associated with COPD. **Methods:** Groups of 6 Sprague-Dawley rats were nebulized three times a week during 1, 2, 3 or 5 weeks with saline (control groups) or 0.1% Cd chloride (treated groups). The degree of pulmonary obstruction was daily followed-up by whole body barometric plethysmography and calculation of the Penh. Broncho-alveolar lavages (BAL) were performed on the right pulmonary lobe for cells and mucopolysaccharides concentrations analysis. The left lobe was fixed with formaline to quantify peribronchiolar fibrosis. **Results:** Compared to controls, Cd-treated animals showed higher Penh values (on average ±1 vs ±0.4, n=6, $p<0.001$), and higher counts of macrophages, neutrophils and lymphocytes (on average, and respectively, ±0.9 vs ±0.15, ±0.8 vs ±0.001, and ±0.1 vs ±0.001, values in 10^6cells/ml, n=6, $p<0.01$), but not of mucopolysaccharides. The correlation coefficients (r^2) between Penh and cells counts measured simultaneously during the protocol were 0.64 ($p<0.001$), 0.59 ($p<0.001$) and 0.57 ($p<0.001$). After 3 and 5 weeks of treatment, no peribronchiolar fibrosis was detected neither in large nor in small bronchi. **Conclusion:** Cd repeated nebulizations induce a pulmonary obstructive syndrome probably due to the presence of an exsudate in the airways lumen but not to mucopolysaccharide hyper-secretion and peribronchiolar fibrosis. However, other mechanisms, like bronchospasm, could also occur, but remain to be investigated.
This abstract is funded by: F.R.I.A and ULg

PREDICTORS OF CHRONIC BERYLLIUM DISEASE AND SENSITIZATION. Rosenman KD, Rossman MD, Reilly MJ, Bush A, Hertzberg V, Regovich J, Aronchick J, Parker J, Rice C., Michigan State, East Lansing, MI, Univ. Of PA, Phila. PA, Emory Univ., Atlanta, GA, Univ West Va,Morgantown, WV, Univ. of Cinn. Cinn, OH.
A cohort of 1,464 current and former workers from two beryllium processing facilities in Eastern Pennsylvania were screened utilizing chest radiographs interpreted by a panel of three "B" readers, spirometry and blood beryllium lymphocyte proliferation testing (BLPT) to look at predictors of Chronic Beryllium Disease (CBD) and Beryllium Sensitization (BS). Individuals with radiographs which at least 2 of 3 "B" readers interpreted as showing changes consistent with pneumoconiosis and/or two positive BLPTs were referred for bronchoscopy with bronchial lavage and biopsy. Sixty (4.1%) individuals were diagnosed with definite or probable CBD, another 16 (1.1%) with possible CBD, 72 (4.9%) with BS and 10 (0.7%) with possible BS. Predictors examined included: facility A vs. facility B the OR = 1.5 (95% CI .9-2.7)for CBD and the OR = 1.3 (95% CI .8-2.2) for BS; female vs. male gender the OR = .9 (95% CI .4-2.8) for CBD and the OR = 2.3 (95% CI 1.1-4.9) for BS; never vs. ever smoked the OR = 1.3 (95% CI .8-2.4) for CBD and the OR = 1.5 (95% CI .9-2.5) for BS. No association was found between CBD and duration ($p = 0.3$). BS increased with shorter duration <1 year (7.1%), 1-4 years (5.3%), 5-14 years (5.2%), 15-24 years (2.9%) and 25+ years (2.3%) ($p = .01$). This study suggests that exposure and gender are associated with development of BS. Further work to better characterize parameters of exposure and individual genetic susceptibility are needed.

This abstract is funded by: NIOSH U60/CCU 512218, DOE-DE-FG03-98EH98027

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AMERICAN THORACIC SOCIETY

ABSTRACTS

2002 International Conference

May 17–22, 2002 • Atlanta, Georgia

This special supplement of the *American Journal of Respiratory and Critical Care Medicine* contains abstracts of the scientific papers to be presented at the 2002 International Conference. The abstracts appear in order of presentation, from Sunday, May 19 through Wednesday, May 22 and are identified by session code numbers. To assist in planning a personal schedule at the Conference, the time and place of each presentation is also provided.

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GMISP125        THE CDC GRANTS MANAGEMENT INFORMATION SYSTEM          06/17/03
GMISM035                      GRANT AWARD RECORD                      16:25
AH07AH00                      ( SCREEN NO.1 )

AWARD NO.....:  512218    PROGRAM CODE.....: U60   AWARD DATE.: 09/22/1995
CRS EIN..: 1-386005984-A1 AWARD TYPE.....: C   FED CAT NO.....: 93.283
CIO CODE.....: NIOSH      OBJ CLASS.....: 41.51  PHS LIST NO: CL-172-T00
PROJ PER FROM: 09/30/1995 PROJ PER TO: 09/29/2001 ANNOUNCEMENT NO.: 95059
PREV AWARD NO:            PROGRAM CATEGORY...: 15  FC CODE.....:
PROGRAM NAME:        AUTHORIZATION: 20A22E705HA29U5C669A671E7
 CHRONIC BERYLLIUM DISEASE AMONG BERYLLIUM-EXPOSED WORKERS
        GRANTEE NAME...: MICHIGAN STATE UNIVERSITY
        BUSINESS OFFICE: CONTRACT & GRANT ADMININSTRATION
        STREET.....: 302 ADMINISTRATION BUILDING
        CITY.....: EAST LANSING
        STATE: MI   ZIP CODE: 48824-         PHONE:( 517 ) 355-5040-

        PROJ DIRECTOR..: KENNETH ROSENMAN, MD
        DEPARTMENT.....: DEPT OF MEDICINE
        STREET.....: 117 WEST FEE HALL
        CITY.....: EAST LANSING
        STATE: MI   ZIP CODE: 48824-1316     PHONE:( 517 ) 353-1846-
     DISPLAY         PF10-RETURN GRANT AWARD MENU       PF16-MAIN MENU
```

```
GMISP125        THE CDC GRANTS MANAGEMENT INFORMATION SYSTEM          06/17/03
GMISM036                     GRANT AWARD RECORD                       16:25
AH07AH00                     ( SCREEN NO.2 )

AWARD NO.: 512218     SPECIALIST CODE:.......: SLH3    CONG DISTRICT:......
PMS PAY CODE:... P    INSTITUTION CODE:.... 5245901    ORG DESCRIPTORS: 19--10
ETHNIC CODE:.... 9    PM5 CLOSEOUT DATE:
CLOSEOUT FIRST LETTER DATE:              CONTAINS RE5EARCH ACTIVITY(S): Y

GRANTS MANAGEMENT OFFICER:.. MILDRED 5. GARNER
PROJECT OFFICER:............. PAUL HENNEBERGER, SC.D.
PROJECT OFFICER TITLE:......

 REMARKS:
 NO COST 12 MONTH EXTENSION



FOOTNOTES: 30
ATTACHED:
HUMAN EXEMPTION: N      IRB DATE: 07/27/2000      IRB DUE DATE: 07/27/2001

     DISPLAY          PF10-RETURN GRANT AWARD MENU       PF16-MAIN MENU
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GMISP125        THE CDC GRANTS MANAGEMENT INFORMATION SYSTEM          06/17/03
GMISM037                      GRANT AWARD RECORD                      16:25
AH07AH00                      ( SCREEN NO.3 )

 AWARD NO: 512218            YEAR.....: 5              FISCAL YEAR......: 1999
 ACTION TYPE...: 4           AMEND NO.: 2              ACTION DATE: 09/29/2000

 APPROVED BUDGET (1):        GRANT FUNDS ONLY (Y/N): Y
          SALARIES WAGES.....:        63,679
          FRINGE BENEFITS....:        16,574
          TOTAL PERSONNEL COSTS...:   80,253
          CONSULTANT COSTS...:
          EQUIPMENT..........:
          SUPPLIES...........:           300
          TRAVEL.............:         5,305
          OTHER..............:        91,114
          CONTRACTUAL COSTS..:       178,959
          TRAINEE EXPENSES...:
          TRAINEE STIPENDS...:
          TRAINEE TUITION & FEES....:
          TRAINEE TRAVEL.....:
          TOTAL DIRECT COSTS (FA):   355,931
     DISPLAY         PF10-RETURN GRANT AWARD MENU        PF16-MAIN MENU
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GMISP125        THE CDC GRANTS MANAGEMENT INFORMATION SYSTEM          06/17/03
GMISM125                      GRANT AWARD RECORD                      16:25
AH07AH00                      ( SCREEN NO.4 )

 AWARD NO: 512218            YEAR.....: 5              FISCAL YEAR......: 1999
 ACTION TYPE...: 4           AMEND NO.: 2              ACTION DATE: 09/29/2000

 APPROVED BUDGET (2):
          INDIRECT COST RATE.............: 47.5000
          INDIRECT COST RATE CODE........: G
          INDIRECT COSTS (FA)............:        84,062
          SBIR FEE.......................:

          TOTAL APPROVED BUDGET........:          439,993
          NON FEDERAL SHARE............:

 AWARD COMPUTATION FOR GRANT:
          FED SHARE/PHS ASSISTANCE.....:          439,993
          UNOB FINANCIAL ASSISTANCE....:          239,993
          CUM PRIOR AWARD THIS BUD (FA):          200,000
          AMOUNT THIS ACTION (FA).....:

     DISPLAY        PF10-RETURN GRANT AWARD MENU         PF16-MAIN MENU
```

GMISP125 THE CDC GRANTS MANAGEMENT INFORMATION SYSTEM 06/17/03
GMISM141 GRANT AWARD RECORD 16:25
AH07AH00 (FSR)

AWARD NO: 512218 YEAR: 5
UNOBLIGATED AMOUNT: 239,993

UNOB YEAR FROM	UNOB AMOUNT
4	150,000.00
4	89,993.00

PF10-RETURN GRANT AWARD MENU PF16-MAIN MENU

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GMISP125        THE CDC GRANTS MANAGEMENT INFORMATION SYSTEM          06/17/03
GMISM101                      GRANT AWARD RECORD                      16:25
AH07AH00                      ( SCREEN NO.5 )

   AWARD NO: 512218            YEAR: 5              FISCAL YEAR: 1999


   APPROVED DIRECT ASSISTANCE BUDGET:

          PERSONAL SERVICE.............:
          TRAVEL.......................:
          VACCINE......................:
          OTHER........................:
          OTHER DESCRIPTON:
          TOTAL DIRECT COSTS (DA)......:
          UNOB DIRECT ASSISTANCE.......:
          CUM PRIOR AWARD THIS BUD (DA):
          AMOUNT THIS ACTION (DA).....:

          COMPETITIVE ACTION (Y/N): N


    DISPLAY         PF10-RETURN GRANT AWARD MENU        PF16-MAIN MENU
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GMISP125        THE CDC GRANTS MANAGEMENT INFORMATION SYSTEM          06/17/03
GMISM110                     GRANT AWARD RECORD                       16:25
AH07AH00                     ( SCREEN NO.6 )

AWARD NO.:..... 512218      YEAR:.............. 5      FISCAL YEAR:...: 1999

CAN AWARD DATE  ALLOW CODE    FY-CAN       AMT FIN ASSIST     AMT DIR ASSIST
 09/29/1999      A3R0N      99-9277072            200,000
                              -
                              -
                              -
                              -
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                              -
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                              -
                              -
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                              -

     DISPLAY         PF10-RETURN GRANT AWARD MENU        PF16-MAIN MENU
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GMISP125        THE CDC GRANTS MANAGEMENT INFORMATION SYSTEM          06/17/03
GMISM038                     GRANT AWARD RECORD                       16:25
AH07AH00                     ( SCREEN NO.7 )

AWARD NO.:....... 512218     YEAR:............... 5     FISCAL YEAR:...: 1999
BUD PER FROM:. 09/30/1999    BUD PER TO:. 09/29/2001    PROGRAM INCOME:.... B
PROJ PER FROM: 09/30/1995    PROJ PER TO: 09/29/2001
RECOMMENDED FUTURE SUPPORT:
  YEAR  TOTAL DIRECT COST   YEAR  TOTAL DIRECT COST   YEAR  TOTAL DIRECT COST


  FREQ    REPORT      DUE DATE      REC DATE      LTR 1 DATE     LTR 2 DATE
          FSR         12/29/2001    12/31/2001
   S      PRO REP1    04/30/2000    05/05/2000
          PRO REP2    10/29/2001
          PRO REP3
          PRO REP4
          PRO REP5
          PRO REP6
          PRO REP7
          PRO REP8
       DISPLAY         PF10-RETURN GRANT AWARD MENU       PF16-MAIN MENU
```