

#### Change in Forced Vital Capacity during Occupational Challenge Test in Subjects with Occupational Asthma

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**Rationale:** In bronchial asthma, it has been demonstrated that during non specific bronchoprovocative testing the change in forced vital capacity (FVC) at a 20% fall of forced expiratory volume in 1 second (FEV1) follows a normal distribution curve. Also, the magnitude of FVC fall may be use as an index of asthma severity. For occupational asthma (OA), no data are available regarding the change in FVC at a 20% FEV1 fall during specific inhalation challenge (SIC). In the present study, we observe the FVC behavior during SIC in patients with OA. **Method:** We retrospectively reviewed 89 medical charts of patients diagnosed with OA. We recorded the patients' medication, the number of asthmatic exacerbations, the sensitizing agent and the change in FVC during SIC. **Statistics:** The change in FVC at a 20% FEV1 fall during SIC is expressed by a mean ( $\pm$ SD). We used linear regression analysis to evaluate the correlation between the FVC fall and the pulmonary function parameters (PC20, FEV1) and clinical characteristics. **Results and Conclusion:** The percentage of fall in FVC registered at a 20% FEV1 fall during SIC is  $13 \pm 5\%$  and follows a normal distribution curve, as it has been previously demonstrated in bronchial asthma. As opposed to bronchial asthma, the magnitude of fall in FVC does not correlate with the disease severity, evaluated by the medication or the number of asthmatic exacerbations.

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#### Longitudinal Respiratory Symptom Changes and Lung Function Decline in an Occupational Cohort

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**Introduction:** Epidemiologists often collect extensive data on respiratory symptoms in longitudinal studies but tend to report only changes in spirometry. However, changes in symptoms are what patients report to physicians. Our goal was to investigate the relationship between patterns of change in respiratory symptoms and FEV<sub>1</sub> decline in a longitudinal occupational cohort.

**Methods:** We used data from an occupational surveillance program among transportation workers. Each subject had a maximum of 4 visits from 1987 to 1999. Subjects with >1 visit (825 men, 101 women) were classified into 3 groups (never reported any symptom; reported the symptom at least once, but not at the last visit; persistent or new symptoms at the last visit) for each of chronic cough, phlegm, wheeze and dyspnea.

**Results:** 72% of women and 79% of men were consistently asymptomatic. Average annual FEV<sub>1</sub> decline was 25.0mL/yr (sd 51.0) for women and 48.9mL/yr (sd 58.6) for men. Male non-smokers reporting new or persistent wheeze, phlegm or dyspnea had accelerated annual loss of FEV<sub>1</sub> (about equal to FEV<sub>1</sub> decline in male current smokers with the same symptom). Cough did not appear to be related to FEV<sub>1</sub> decline in men. Among male smokers, neither symptom presence nor change was associated with FEV<sub>1</sub> decline. There was a trend towards greater FEV<sub>1</sub> decline among women reporting any of the 4 symptoms at any time during follow-up compared to asymptomatic women, regardless of smoking. Multivariable analyses including time-varying covariates are underway.

**Conclusion:** FEV<sub>1</sub> decline was associated with persistent or new wheeze, dyspnea or phlegm among men, only among non-smokers. Among women, new or persistent symptoms (of any type) appeared to be linked to FEV<sub>1</sub> decline irrespective of smoking. Further research is warranted into the predictive value (and potential sex differences) of longitudinal symptom changes.

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#### Validation of Medical Claims Data for Obstructive Lung Disease Diagnosis with Medical Records from an Occupational Clinic

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**Rationale:** Medical claims (MC) may be a valuable tool in occupational studies of obstructive lung disease (OLD); MC data can identify OLD and be linked to exposure and other datasets. Few occupational studies have validated MC usage. **Methods:** In a case control study, we compared the OLD MC diagnosis in aluminum workers with medical records from an onsite occupational clinic. Of 1293 workers with any MC between the 2 years 2001-2002, 64 had at least 1 OLD MC for asthma, chronic bronchitis, emphysema or chronic airflow obstruction. We reviewed records of 53 of 64 cases and 60 matched controls. We recorded chart OLD diagnosis, smoking status and spirometry. We used 2 MC diagnostic strategies: in the first, the presence of at least 1 OLD MC defined a case. In the second stricter strategy, we required at least 2 MC or any MC for a hospitalization. We calculated kappa statistics ( $\kappa$ ) for MC and chart agreement. **Results:** All workers were predominantly Caucasian male and had a mean age and employment duration of over 40 yo and 15 yrs. 46% of cases v 33% of controls ever smoked ( $p=0.17$ ). There were 181 claims for 81 service dates; 4 of 10 workers with MC for non-asthma OLD also had an asthma MC. 30 of 53 (56%) with 1+ OLD MC had a chart diagnosis compared to 16 of 19 (84%) with 2+ MC or any MC for a hospitalization. The  $\kappa$  when using the 1+ MC criteria was 0.47 (95% CI: 0.32-0.63) and 0.46 (95% CI: 0.29-0.64) when using the stricter criteria. Airflow obstruction (FEV<sub>1</sub>/FVC < 70%) was similar between cases and controls (18% vs. 20%,  $p=0.74$ ); 7 workers with obstruction had no OLD MC or chart record. **Conclusion:** Medical claims can identify OLD cases in occupational studies. Also, despite evidence of obstruction during spirometry surveillance, providers may not diagnose OLD.

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#### Prevalence of Asthma Symptoms and Exposure to Biomass Fuel Combustion among Young Population from High Altitude Cities

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**Objectives:** To determine the prevalence of asthma symptoms and biomass fuel exposure among high school students at Cuzco (3400 meters above sea level), and university students at Ayacucho (2700 masl), both in Peru.

**Material and methods:** We interviewed high school and university students asking them questions about respiratory symptoms (modified ISAAC questionnaire), smoking habits and biomass fuel combustion.

**Results:** We interviewed 599 students, 60% were males. The age mean was 18.2 (SD = 4.5). The lifetime wheezing prevalence was 29%. Wheezing during the last 2 years 12%, nocturnal cough 39%, wheezing after exertion 23%, wheezing during cold episodes 23%, asthma diagnosed by physician 7%. Propane gas was used by 79%, kerosene by 25%, wood by 18%, electricity 8%. Use of gas was associated with less wheezing after exertion (20% vs 33%,  $p<0.05$ ). Use of kerosene was associated with more wheezing after exertion (32% vs 20%,  $p<0.05$ ). Current use of wood was associated with more lifetime wheezing (36% vs 26%,  $p<0.05$ ), and wheezing during cold episodes (21% vs 31%,  $p<0.05$ ).

**Conclusions:** In young population from high altitude cities, use of gas was related to a protective effect on wheezing after exertion. On the other hand, kerosene and wood were associated with more respiratory symptoms.

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#### Drug/Xenobiotic-Metabolizing Enzyme (XME) Expression in the EpiAirway™ In Vitro Human Airway Model: Utility for Assessing Tracheal/Bronchial Biotransformation of Inhaled Pharmaceuticals and Occupational/Environmental Chemicals

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Human tracheal/bronchial epithelium contains xenobiotic metabolizing capabilities provided by a variety of phase I (oxidative) and phase II (conjugative) enzyme systems. These XMEs can play an important role in biotransformation of inhaled drugs, tobacco smoke and environmental/occupational chemicals. Biotransformation of inhaled chemicals may lead to altered drug activity or formation of toxic/mutagenic metabolites. The present work evaluated expression of XMEs in a highly differentiated in vitro model of human tracheal/bronchial epithelium that is cultured at the air-liquid interface to facilitate in vivo-like chemical exposures (EpiAirway, AIR-100). RT-PCR gene expression experiments were conducted to evaluate baseline and inducible expression of CYP isoforms in EpiAirway cultures derived from 4 individual donors. CYP1A1 (weak), CYP1B1, CYP2A6, CYP2B6 (weak), CYP2C8 (weak), CYP2C19, CYP2D6, CYP2E1 and CYP3A5 were expressed constitutively, while CYP3A4 and CYP3A7 were not detected. 3-Methylcholanthrene (3MC) strongly increased expression of CYP1A1 and slightly increased CYP2B6 and CYP2C8 expression. Thus CYP expression in EpiAirway showed a high concordance with CYP expression reported for in vivo human bronchial epithelium. Total glutathione S-transferase (GST) activity in EpiAirway was also evaluated by measuring conjugation of glutathione with 1-chloro-2,4-dinitrobenzene. High baseline GST activity was not further enhanced by 3MC treatment. The results demonstrate that the EpiAirway in vitro human tracheal/bronchial epithelial model possesses numerous in vivo-like XME activities and may thus be useful for evaluating airway metabolism of drugs, tobacco smoke and environmental/occupational chemicals.

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#### Interpreting Respiratory Symptom Questionnaires: Specific Symptom Outcomes and Their Relationship to Spirometry and Nonspecific Airway Responsiveness Test Results

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**Rationale:** Respiratory symptom questionnaires (RSQ) are useful in assessing the health of workers exposed to respiratory hazards. **Methods:** To facilitate interpretation of RSQ, we studied RSQ responses and results of objective tests among 199 underground coal miners and 212 non-miner blue collar workers. Spirometry, methacholine challenge, a self-administered standardized RSQ, and complete smoking, medical, and work histories were recorded initially and after 5 years of follow-up. For each symptom item, individuals who responded 'Yes' were compared to those who said 'No' at the same survey, assessing differences in percent predicted forced expired volume in one second (ppFEV<sub>1</sub>) and proportion of methacholine responders (%HR), using t-test and Chi-square statistics, respectively. **Results:** Significant associations included: 1) chronic cough, chronic phlegm, ever wheezing, or history of asthma with both lower ppFEV<sub>1</sub> and greater %HR; 2) dyspnea on level ground (SOB) with reduced ppFEV<sub>1</sub>; and 3) attacks of dyspnea with wheezing (SOBWZ), a history of asthma, or a history of hay fever with greater %HR. Multiple logistic regression analysis for repeated measurements of symptom prevalence was also done using generalized estimating equations, controlling for age, smoking, and coal mining status. Individuals with cough, phlegm, SOB, or ever wheeze had significantly lower ppFEV<sub>1</sub>; those with SOBWBZ, history of asthma, history of hay fever, or persistent wheeze had a greater %HR. Positive methacholine challenges were 3 and 5 times more likely in participants reporting SOBWBZ or ever asthma. **Conclusion:** Results of this study can facilitate the interpretation of individual responses to RSQ.

The findings and conclusions in this abstract have not been formally disseminated by NIOSH and should not be construed to represent any agency determination or policy.

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