ABSTRACTS

Vehicle exhaust outside the home and onset of asthma among adults.

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(Eur Respir J 2009; 33:1261-1267)

Few studies have investigated the relationship between vehicle exhaust and the new onset of asthma among adults. The aim of the present prospective cohort study was to investigate the relationship between the cumulative incidence of asthma and onset of asthma among adults and vehicle exhaust concentrations at home.

Participants from three Swedish cities included in the Respiratory Health in Northern Europe cohort constituted the study population. Exposure at each participant's home was calculated using dispersion models. We also used <50 m distance to nearest major road as a more simple indicator of exposure. The adjusted model included 3,609 participants, of which 107 were classified as onset cases and 55 as true incident cases of asthma.

There was a positive association between asthma onset (odds ratio (OR) per 10 $\mu g \Sigma m^{-3}$ 1.46, 95% confidence interval (CI) 1.07–1.99) and incident asthma (OR per 10 $\mu g \Sigma m^{-3}$ 1.54, 95% CI 1.00–2.36) and the levels of nitrogen dioxide (NO_2), which remained statistically significant after adjusting for potential confounders. The relationship between asthma and NO_2 was not significantly modified by sex, hay fever or wheeze. The risk of developing asthma was also significantly related to living close to a major road.

The current study suggests that elevated levels of vehicle exhaust outside the home increase the risk of onset and incident asthma among adults.

Increased incidence of respiratory symptoms among female woodworkers exposed to dry wood

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The aim of the present study was to investigate the occurrence of new respiratory symptoms in relation to wood dust exposure in a 6-yr follow-up study.

A total of 1,377 woodworkers (1,137 males; 240 females) and 297 reference workers (137 males; 160 females) participated. Data on respiratory symptoms, employment and smoking habits were collected. Wood dust exposure was assessed from baseline dust measurements, and cumulative wood dust exposure was assessed by study-specific job exposure matrices and exposure time.

The geometric mean (geometric SD) dust level decreased during the study period from 0.94 (2.1) to 0.60 (1.6) $mg \Sigma m^{-3}$. Adjusted analysis revealed positive associations for cumulative incidence proportion of chronic bronchitis and daily coughing for female woodworkers versus female reference workers. The cumulative incidence proportion of daily coughing and chronic bronchitis were found to be associated with baseline wood dust exposure in a dose-dependent manner. The odds ratio (95% confidence interval) for daily coughing (with reference to the lowest exposure quartile) was 1.6 (0.6–4.3), 3.2 (0.9–6.8) and 3.8 (1.5–9.7), respectively, in the second and third lowest and the highest quartile. The figures for chronic bronchitis were, accordingly, 2.3 (0.4–14.5), 3.0 (0.5–18.7) and 6.0 (1.2–28.8).

In conclusion, female woodworkers in this low exposure cohort showed an increased incidence of coughing and bronchitis, whereas no relations to wood dust exposure were seen for male woodworkers.

Effects of ciclesonide and fluticasone on cortisol secretion in patients with persistent asthma

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We compared the systemic and clinical effects of ciclesonide (CIC) and fluticasone propionate (FP) administered, in addition to CIC 160 $\mu g \Sigma day^{-1}$ and salmeterol 50 µg twice daily, in 32 patients with persistent asthma using a randomised double-blind, placebo-controlled, double-dummy, five-period crossover design.

All patients exhibited a provocative concentration leading to a 20% decrease in forced expiratory volume in 1 s (PC_{20}) methacholine <8 $mg \Sigma mL^{-1}$ and a PC_{20} adenosine <60 $mg \Sigma mL^{-1}$. Primary outcome was 24-h serum cortisol suppression after 7 days. Secondary outcomes were changes in PC_{20} methacholine and adenosine after 9 days.

FP 500 $\mu g \Sigma day^{-1}$ and 1,000 $\mu g \Sigma day^{-1}$ significantly suppressed cortisol secretion *versus* placebo by -46.2 (95% confidence interval (CI) -83.8– -8.5) $nmol \Sigma L^{-1}$ and by -76.1 (95% CI -112.9– -39.3) $nmol \Sigma L^{-1}$, respectively. Neither dose of CIC (320 nor 640 $\mu g \Sigma day^{-1}$) had a significant suppressive effect (-28.2 (95% CI -65.5–9.2) $nmol \Sigma L^{-1}$ and -37.3 (95% CI -74.7–0.0) $nmol \Sigma L^{-1}$, respectively). Differences between FP 1,000 $\mu g \Sigma day^{-1}$ and both CIC treatments were statistically significant (CIC 320 $\mu g \Sigma day^{-1}$: -48.0 (95% CI -84.8– -11.1) $nmol \Sigma L^{-1}$; CIC 640 $\mu g \Sigma day^{-1}$: -38.8 (95% CI -75.7– -1.9) $nmol \Sigma L^{-1}$). Compared with placebo, the increase in PC_{20} adenosine after the four treatments was small, but significant. Greater improvements in PC_{20} adenosine were seen with FP 500 $\mu g \Sigma day^{-1}$ (1.8 (95% CI 1.0–2.6) doubling concentrations) compared with CIC 320 $\mu g \Sigma day^{-1}$ (0.9 (95% CI 0.1–1.7) doubling concentrations). No significant difference was seen between CIC 640 $\mu g \Sigma day^{-1}$ and FP 1,000 $\mu g \Sigma day^{-1}$.

For a similar decrease in hyperresponsiveness, cortisol secretion was suppressed significantly with moderate-to-high doses of fluticasone propionate, but not with ciclesonide.

Exhaled nitric oxide as a marker of asthma control in smoking patients

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Exhaled nitric oxide fraction (F_{eNO}), which is a reliable marker of eosinophilic airway inflammation, is partially suppressed by tobacco smoking. Consequently, its potential as a biomarker in asthma management has never been evaluated in smoking patients. In the present study, the authors tested the validity of F_{eNO} to predict asthma control in this population.

F_{eNO} and the Asthma Control Questionnaire (ACQ) were recorded at least once in 411 nonsmoking (345 with at least two visits) and 59 smoking (51 with at least two visits) asthma patients.

Despite similar mean ACQ scores (1.5 versus 1.7), F_{eNO} was reduced in smoking asthmatics (18.1 ppb versus 33.7 ppb). A decrease in FeNO of <20% precludes asthma control improvement in nonsmoking (negative predictive value (NPV) 78%) and in smoking patients (NPV 72%). An increase in F_{eNO} <30% is unlikely to be associated with deterioration in asthma control in both groups of patients (NPV = 86% and 84% in nonsmoking and smoking patients, respectively).

It is concluded that, even in smokers, sequential changes in F_{eNO} have a relationship with asthma control. The present study is the first to indicate that cigarette smoking does not obviate the clinical value of measuring F_{eNO} in asthma among smokers.

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Single-dose desloratadine and montelukast and allergen-induced late airway responses

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Montelukast and desloratadine synergistically inhibit the allergen-induced early asthmatic response. Montelukast also suppresses the allergen-induced late asthmatic response, but there are no reports on the effect of desloratadine or the combination on the allergen-induced late asthmatic response.

Atopic asthmatics (n = 10) completed a multicentric randomised double-blind crossover study comparing single-dose placebo, 5 mg desloratadine, 10 mg montelukast and the combination administered 2 h prior to allergen inhalation challenge. Methacholine challenges were performed 24 h before and after allergen challenge. Exhaled nitric oxide measurements and sputum inflammatory cell counts were also carried out.

All active treatments significantly decreased the late asthmatic response area under the curve. Combination therapy provided the greatest inhibition compared to desloratadine and montelukast. Montelukast was nonsignificantly better than desloratadine but not as effective as the combination. There was a trend towards a decrease in airway responsiveness following montelukast and combination. Montelukast, but not desloratadine or the combination, decreased exhaled NO levels 24 h after allergen. The allergen-induced increase in sputum eosinophil numbers was significantly suppressed at 7 h with desloratadine and combination therapy, and at 24 h with montelukast and combination therapy.

Single-dose co-administration of desloratadine and montelukast 2 h prior to allergen inhalation clinically abolished the late asthmatic response and eosinophil recruitment.

Idiopathic Pulmonary Fibrosis and Emphysema: Decreased Survival Associated With Severe Pulmonary Arterial Hypertension

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(Chest 2009; 136:10–15)

Background: It has been suggested that the presence of emphysema modifies the outcome of patients with idiopathic pulmonary fibrosis (IPF). In this article we compare clinical features, smoking history, pulmonary function, estimated systolic pulmonary artery pressure (eSPAP), and mortality in IPF with emphysema vs IPF without emphysematous changes.

Methods: A cohort of 110 IPF patients was evaluated. Clinical data were collected from clinical charts. High-resolution CT (HRCT) scans were examined by an expert blinded to clinical data, and patients were classified into the following two groups: patients with IPF with emphysema; and patients with IPF without emphysema. The Kaplan-Meier method, log-rank test, and Cox regression model were used for statistical analyses.

Results: The prevalence of emphysema in the IPF cohort was 28% (31 of 110 patients). IPF with emphysema was significantly associated with male gender (odds ratio _OR_, 18; 95% confidence interval _CI_, 2.7 to 773.7; p _ 0.0003), and smoking (OR, 3.8; 95% CI, 1.36 to 11.6; p _ 0.004). Patients with IPF and emphysema had a higher mean (_ SD) decrease in oxygen saturation during rest and exercise (16.3 _ 6.7% vs 13.5 _ 4.6%, respectively; p _ 0.04), a higher mean fibrosis HRCT scan score (1.75 _ 0.36 vs 1.55 _ 0.38, respectively; p _ 0.015), a higher eSPAP (82 _ 20 vs 57 _ 15 mm Hg, respectively; p < 0.0001), and lower median survival time (25 vs 34 months, respectively; p _ 0.01) than patients with IPF without emphysema. The Cox regression model showed that the two most important variables associated with mortality were FVC < 50% predicted (hazard ratio _HR_, 2.6; 95% CI, 1.19 to 5.68; p _ 0.016) and eSPAP > 75 mm Hg (HR, 2.25; 95% CI, 1.12 to 4.54; p _ 0.022).

Conclusions: IPF patients with emphysema exhibited higher mortality compared with those with IPF without emphysema. This dire prognosis seems to be at least partially associated with the development of severe pulmonary arterial hypertension.

Physical Activity and Clinical and Functional Status in COPD

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(Chest 2009; 136:62–70)

Background: The mechanisms underlying the benefits of regular physical activity in the evolution of COPD have not been established. Our objective was to assess the relationship between regular physical activity and the clinical and functional characteristics of COPD.

Methods: Three hundred forty-one patients were hospitalized for the first time because of a COPD exacerbation in nine teaching hospitals in Spain. COPD diagnosis was confirmed by spirometry under stable conditions. Physical activity before the first COPD hospitalization was measured using the Yale questionnaire. The following outcome variables were studied under stable conditions: dyspnea, nutritional status, complete lung function tests, respiratory and peripheral muscle strength, bronchial colonization, and systemic inflammation.

Results: The mean age was 68 years (SD, 9 years), 93% were men, 43% were current smokers, and the mean postbronchodilator FEV1 was 52% predicted (SD, 16% predicted). Multivariate linear regression models were built separately for each outcome variable and adjusted for potential confounders (including remaining outcomes if appropriate). When patients with the lowest quartile of physical activity were compared to patients in the other quartiles, physical activity was associated with significantly higher diffusing capacity of the lung for carbon monoxide (DLCO) [change in the second, third, and fourth quartiles of physical activity, compared with first quartile (_ 6%, _ 6%, and _ 9% predicted, respectively; p _ 0.012 [for trend])], expiratory muscle strength (maximal expiratory pressure [PEmax]) [_ 7%, _ 5%, and _ 9% predicted, respectively; p _ 0.081], 6-min walking distance (6MWD) [_ 40, _ 41, and _ 45 m, respectively; p _ 0.006 (for trend)], and maximal oxygen uptake (V_ O2peak) [_ 55, _ 185, and _ 81 mL/min, respectively; p _ 0.110 (for trend)]. Similarly, physical activity reduced the risk of having high levels of circulating tumor necrosis factor _ (odds ratio, 0.78, 0.61, and 0.36, respectively; p _ 0.011) and C-reactive protein (0.70, 0.51, and 0.52, respectively; p _ 0.036) in multivariate logistic regression.

Conclusions: More physically active COPD patients show better functional status in terms of DLCO, PEmax, 6MWD, V_ O2peak, and systemic inflammation.