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Inhalation of gaseous superoxide (GS) as adaptive oxidative training for asthma patientsN. Goldstein, G. Rehberg, T. Lewin, F.-R. Klefisch. *Department of medical investigations, Goldstein & Lewin technology GmbH, Stahnsdorf, Germany, Rudolf Vorchow hospital, Humboldt University, Berlin, Germany*

There is a direct correlation between the increased reactivity of the bronchial muscles and the endogenous oxidative stress (OS) suffered by the asthmatic. Two independent studies have been conducted into the influence of short-term intermittent GS inhalation on the reduction of OS and the improvement in the clinical picture of atopic asthmatics from different age groups. A total of 78 patients took part in the trials: 27 aged mean = 42 (Group A) and 51 aged mean = 12 (placebo-controlled double-blind trial in the case of Group B). In both groups there was a stable improvement in the spirometric parameters and clinical course in ca. 85% of cases. In Group A, a reduction of the initially high activity of superoxide dismutase and glutathione peroxidase ($p < 0.001$) was observed, as well as an increase in activity of glutathione reductase in the erythrocytes ($p < 0.001$) and an improvement in all major spirometric findings, including the results of the methacholine and salbutamol test. In Group B, a negative correlation between the initial values and the amount by which they changed was determined for PEF ($r = -0.72$; $p < 0.0001$), FEV1 ($r = -0.52$, $p = 0.006$), and FEF25% ($r = 0.72$; $p = 0.001$), as well as highly significant improvements in the scores with regard to subjective statements on frequency and severity of attacks, of coughing, and amount of sputum. The positive clinical findings arising out of this adjuvant therapy are being interpreted as the result of an adaptive course of training for asthma patients.

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Erdosteine and its metabolites as antioxidants in the FeCl₂-induced rats paw oedemaC. Mancini, M. Nicola, B. Lumachi. *Research Center, Edmond Pharma, Milano, Italy*

An *in vivo* test in rats based on the development of paw oedema due to the free radical inducer FeCl₂ was set up to evaluate erdosteine and three metabolites (Met I, II and III) activity. Passoni et al. (1992) suggested that the test is a valuable tool to assay compound with antioxidant activity, being glutathione (ED50 1100 mg/kg *i.p.*), sodium selenite (9.5 mg/kg *i.p.*) and GSH-ethyl ester (610 mg/kg *i.p.*) well active. Its specificity was also showed. The present study, set up like Passoni method in rats, proves that glutathione and sodium selenite give reproducible results (oedema inhibition 52.1% and 49.3%, respectively); moreover erdosteine at 600 mg/kg per os, and metabolites Met I, II, III (all at 600 mg/kg per os) significantly reduce the paw oedema development: 46.5% the former and between 19.7 and 50.7% the metabolites. These findings are related with those obtained by Pozzi *in vitro* assay (1990) to measure the inhibition of the NADPH-dependent lipid peroxidation in rat liver microsomes by the same metabolites and erdosteine. We conclude that erdosteine, inactive *in vitro*, shows in the *in vivo* oedema test anti-oxidant effects through its metabolites. The weight of these findings concerns the erdosteine therapeutical indications in respiratory diseases in which free radicals are involved.

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Effect of selective and non-selective phosphodiesterase inhibitors on allergen-induced contractions in passively sensitized human airwaysD. Schmidt, N. Watson, B.E. Morton, G. Dent, H. Magnussen, K.F. Rabe. *Krankenhaus Großhansdorf, Zentrum für Pneumologie und Thoraxchirurgie, D-22927 Großhansdorf, Germany*

The non-selective phosphodiesterase (PDE) inhibitors theophylline (Theo) and 3-isobutyl-1-methylxanthine (IBMX) block allergen-induced constriction of human airways *in vitro* by a dual mechanism involving a direct relaxant effect on smooth muscle and inhibition of cysteinyl leukotriene release from airways [Morton, B.E. *et al.* *Am J Respir Crit Care Med* 1995; 151: A388]. To further determine the involvement of PDE isoenzymes we investigated the effect of the methylxanthine adenosine receptor antagonist 8-phenyltheophylline (8-PT) and the selective PDE inhibitors motapizone (Mota; type 3), RP73401 (RP; type 4) and zardaverine (Zard; type 3/4) in addition to Theo and IBMX on allergen responses of human airways *in vitro*. Airways from 33 patients were sensitized overnight with IgE-rich sera (IgE levels > 600 U/ml) containing specific antibodies (FAST class ≥ 3) against allergen (*D. farinae*). Contractile responses were assessed in the organ bath by standard techniques. Compared to sensitized controls, pretreatment with Theo, IBMX and Zard inhibited concentration-dependently the contractile responses to allergen, whereas 8-PT, Mota and RP had no significant inhibitory effect. The response to a submaximal allergen concentration (3 U/ml) was almost completely suppressed by concentrations of 1 mM Theo ($94 \pm 2\%$ inhibition; $n = 8$), 100 μ M IBMX ($92 \pm 8\%$; $n = 5$) and 3 μ M Zard ($99 \pm 1\%$; $n = 4$); the concentration-effect curves were shifted to the right with a reduction of the maximal responses. We conclude that combined inhibition of PDE3 and PDE4 is effective in suppressing allergen-induced contractions of sensitized human airways and that adenosine antagonism plays no role in the action of methylxanthines in inhibiting this response.

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Surveys of selected occupational groups

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Health based selection for asthma, and not for chronic bronchitis, in pig farmers – A hypothesisP.F.J. Vogelzang¹, J.W.J. van der Gulden¹, C.P. van Schayck¹, H. Folgering².
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To study the mechanisms of respiratory disease in swine confinement farming, a questionnaire survey was performed among 239 pig farmers and 311 non-exposed controls. Pig farmers are exposed to a number of factors promoting the development of both chronic obstructive pulmonary disease and asthma. Still, in most prevalence studies, only an elevated prevalence of chronic bronchitis, and not one of asthma, is reported.

The prevalence of chronic bronchitis (phlegm on most days for 3 months during the last 2 years) was significantly higher in pig farmers than in controls (15.5 vs 3.9%, $p < .0001$), whereas self-reported asthma was not (5.9 vs 5.5%, $p = 0.84$). However, childhood atopy, defined by questions on hay fever, asthma, asthmatic bronchitis or eczema in childhood, was significantly less prevalent in pig farmers, than in controls (9.9 vs 17.2%, $p < 0.05$). As expected, childhood atopy was significantly associated with self-reported asthma (prevalence odds ratio 10.5, 95% confidence interval 4.8–22.9, adjusted for age and pack years of smoking). Therefore, a lower prevalence of asthma among pig farmers would be expected. It is probable that people suffering from signs of asthma at an early age avoid a career in confinement farming. This leaves a selected group of farmers, less susceptible to a development of asthma than the population at large. The factors in confinement farming promoting development of asthma subsequently lead to a prevalence of asthma just as high as in controls. This selection mechanism probably does not apply for the gradually developing symptoms of cough and phlegm in chronic bronchitis.

In conclusion we hypothesize a health based selection of profession for asthma, and not for chronic bronchitis, in pig farmers, obscuring associations between occupation and asthma.

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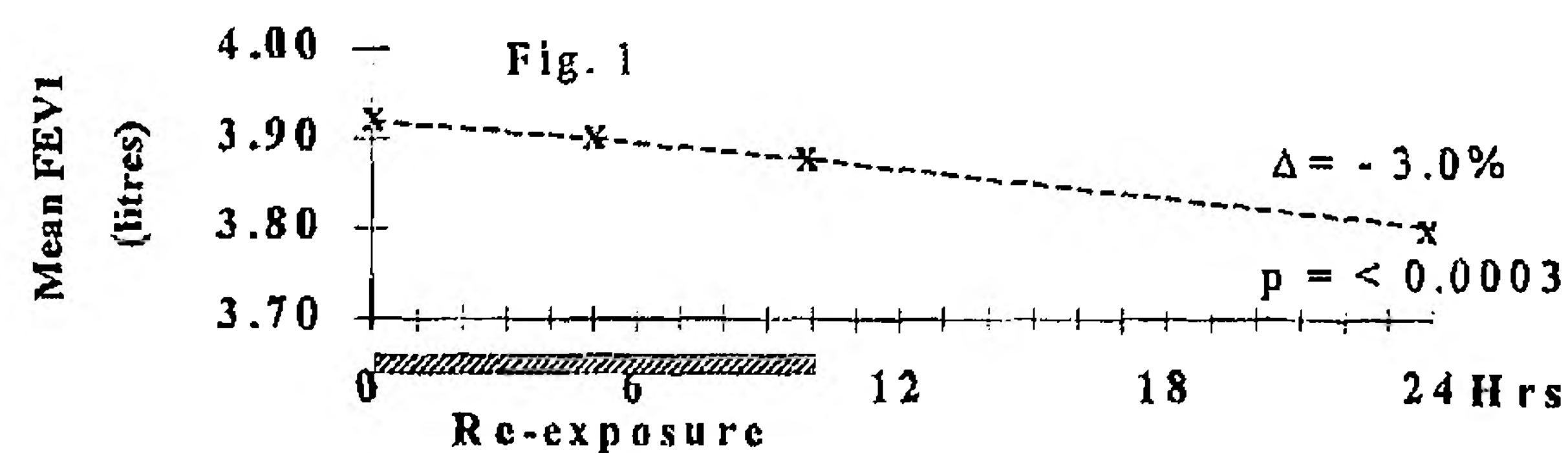
Respiratory symptom and lung function changes occurring within 24 hours of re-exposure in British pig farm workersJ.P. Hancock, H. Sandhar, J.R. Beach, I.A. Calvert, J.M. Harrington. *Institute of Occupational Health, Birmingham University, Birmingham, UK*

Background: Endotoxin exposure has been associated with delayed reduction in expiratory flow rates in workers manufacturing fibreglass (Milton DK et al, *Am J Ind Med* 1996;29:3–13).

Aims: To test the hypothesis that delayed reductions in expiratory flow rates would occur in pig farm workers (also exposed to endotoxins).

Methods: FEV1 and PEFR were recorded by spirometer in 28 pig farm workers after a weekend off work just before and at approximately 5, 10 and 24 hours after start of re-exposure (the Monday shift –07.00 to 17.00). Each worker retrospectively scored respiratory symptoms on a scale (0–10) for the 24 hour period before and after re-exposure.

Results: There was a progressive decline in both FEV1 (Fig. 1) and PEFR from start of re-exposure (mean decrements 0.020, 0.043, 0.119 litres and 1.26, 7.86 and 17.70 litres/min respectively). The only statistically significant difference from pre-exposure values occurred 24 hours later for FEV1 ($p = 0.0003$) and PEFR ($p = 0.02$) representing 3.0% and 3.5% reductions respectively (paired t-test).



No significant differences were seen between symptom scores before and after re-exposure for any respiratory symptom (Wilcoxon test).

Discussion: Overall these findings are not clinically significant. However the small reduction of 3.0–3.5% in expiratory flow rates at 24 hours was statistically significant and not due to diurnal variation. These changes may represent delayed airways inflammation from re-exposure to endotoxin and contribute to the pathogenesis of chronic airways limitation that has recently been shown in longitudinal studies of pig farm workers (Reynolds SJ et al, *Am J Ind Med* 1996; 29: 33–40).