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043P ACUTE CIGARETTE SMOKE-INDUCED LUNG INFLAMMATION IN THE RAT: EFFECTS OF DEXAMETHASONE

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Cigarette smoking is the predominant cause of Chronic Obstructive Pulmonary Disease. The aim of the present study was to begin to characterise the airway inflammation induced by acute (3 day) cigarette smoke (CS) exposure to rats.

Male Sprague-Dawley rats (n=4-9/group; 250-350g; Charles River UK) were exposed to either air (sham) or mainstream CS generated by 2-5 research cigarettes (2R4F; University of Kentucky Tobacco Research Centre). Rats were exposed once daily for three days and 24h after the final CS exposure were sacrificed (200mg sodium pentobarbitone, i.p.). Bronchoalveolar lavage (BAL) was performed for analysis of neutrophil numbers and mucin content. BAL fluid mucin levels were assessed using an enzyme linked lectin assay (Jackson *et al.,*2002). Lungs were removed and tissue leukocytes isolated by enzyme digestion (Holt *et al.,*1985). In subsequent studies, rats were dosed with either vehicle (PEG:H_2O) or dexamethasone (Dex; 3mgkg^{-1}, p.o.) 60min before each CS exposure (5 cigarettes). BAL fluid and tissue neutrophils are expressed as mean (±s.e.mean) cells mL^{-1} or cells mg^{-1} tissue respectively. BAL fluid mucin levels are expressed as mean (±s.e.mean) mucin units mL^{-1}. Groups were compared using a Student t-test with P<0.05 regarded as significant.

CS dose-dependently increased BAL fluid neutrophil numbers and BAL fluid mucin content (Table 1).

In subsequent studies Dex significantly attenuated the CS-induced increase in BAL fluid neutrophils (Table 2). In contrast, Dex significantly elevated neutrophil numbers in lung tissue. The CS-induced elevation in BAL mucin was not significantly affected by Dex treatment (P>0.05).

	Sham	2 CS	3 CS	4 CS	5 CS
Neut (x10^4 mL^{-1})	0.2 ±0.1	0.6 ±0.1	2.2 ±0.3*	5.5 ±0.6*	9.9 ±0.8*
Mucin (units mL^{-1})	0.5 ±0.1	1.4 ±0.4	1.9 ±0.6	2.5 ±0.8	3.5 ±0.9*

Table 1. Dose-dependent CS-induced changes in BAL fluid neutrophils (Neut) & mucin concentration. Data expressed as mean ± s.e.mean. *indicates significant difference from Sham (P<0.05).

	BAL Neut (x10^4 mL^{-1})	Tissue Neut (x10^4 mg^{-1})	Mucin
Sham	0.1±0.0	49.8±7.3	0.71±0.21
CS	4.3±0.5*	65.8±9.0	6.67±1.10*
Dex	2.6±0.9†	149±21.7†	12.43±3.39

Table 2. CS-induced changes in BAL & tissue neutrophils (Neut) & mucin (Muc, unitsmL^{-1}) & effects of Dex. Data expressed as mean ± s.e.mean. * indicates significant difference between sham & CS. † indicates significant difference between CS & Dex.

These studies indicate that acute exposure to CS induces dose-dependent changes in lung neutrophils and increases the mucin secreting capacity of the airways. It is of note that the BAL fluid neutrophilia was attenuated by Dex whilst tissue neutrophils were significantly elevated. The Dex-induced elevation of tissue neutrophils may be as a result of the anti-apoptotic effects of steroids on this cell-type or an inhibitory effect on transmigration (Liles *et al*., 1995), although further studies will be required to understand the complex mechanisms involved. This study also highlights a potential caveat of relying on BAL as the only marker of lung tissue leukocyte changes.

Holt P.G. *et al.* (1985) *Immunology* 54:139
Jackson A. *et al*. (2002) *Novartis Found Symp*. 248:94
Liles W.C. *et al* (1995) *Blood* 86:3181