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Differences in species response to hyperactivity induced by lipopolysaccharide (LPS) from *Escherichia coli*

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Lipopolysaccharide (LPS) is part of the outer envelope of gram - negative bacteria. It is considered to be an important entity medically because it forms a major part of endotoxin, the causative agent of gram - negative sepsis (septic shock syndrome).

More recently, lipopolysaccharide has come to prominence in the field of air pollution and the effects of inhaled lipopolysaccharide are being extensively studied, especially in working environments where organic dusts are present Rylander (1993). Inhalation of dusts or aerosols containing LPS results in symptoms such as cough, wheeze, shortness of breath and fever Rylander (1997). In acute and chronic exposure situations, as a result of inflammation initiated by lipopolysaccharide and other components such as (1→3)-β-D glucan, clinically important diseases such as toxic pneumonitis and byssinosis may develop. Lipopolysaccharide can therefore be regarded as a ubiquitous and important air pollutant.

One of the key features of the LPS toxicological profile is the development of airway hyperresponsiveness. In order to further understand the nature of the hyperresponsiveness the following models have been studied.

The tracheae from male guinea pigs, rabbits and rats were cut into two 4cm spirals and mounted in organ baths for isometric muscle contraction recording. Dose - response (DR) profiles were then established for the preparations using the muscarinic bronchoconstrictor, carbachol. Following a return of the muscle to baseline tone, LPS (20μg ml^{-1}) was incubated with the preparations for one hour, the LPS was then washed out and an hour later (after a baseline had been restored) the DR profile for carbachol was redetermined. The DR profiles were analysed pre- and post - LPS exposure

Table 1. Table illustrating the change in responsiveness of rabbit trachea to the bronchoconstrictor carbachol after 1 hour exposure to LPS. (n=4,*p<0.05 Students' t-test)

Dose of carbachol (μg)	Pre - LPS response (Tension {g})	Post - LPS response (Tension {g})
0.01	0.00+/-0.00	0.095+/-0.08
1	0.54+/-0.10	0.90+/-0.19*
10	0.72+/-0.12	1.06+/-0.21*

Similarly (data not shown) hyperresponsiveness was demonstrated in the guinea pig trachea confirming earlier work Young & Nicholls (1996). For rat trachea, while dose - related responses to carbachol were elicited, LPS was unable to induce hyperresponsiveness.

Thus, species difference in response to inhaled LPS are important in demonstrating the potential toxicological effects of this agent. The rabbit trachea model appears to be an alternative to the guinea pig for such work.

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Rylander R. (1993). Ann. Occup. Hyg. 37(1): 57 - 63

Rylander R. (1997). Int. J. Occup. Environ. Health . 3: S1-S48

Young R.S. and Nicholls P.J. (1996). Pharm.Sci. 2: 77-81