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**AIRWAY HYPERSENSITIVITY AND REMODELLING INDUCED BY
REPEATED EXPOSURE TO *ASCARIS SUUM* ANTIGEN:
AN OVINE MODEL OF HUMAN ASTHMA**

**A thesis presented in
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This study is dedicated with love to my mother.

ABSTRACT

This study was an attempt to develop a model of asthma which shows all the structural changes of airways that occur in human disease by repeatedly exposing sheep to an aerosol of *Ascaris suum* antigen.

Twenty two sheep were tested for cutaneous reactivity to a commercial preparation of the antigen. For each of three experiments three sheep were selected, two skin reactive and one non-reactive. One week prior to the experiment a tracheostomy was performed according to the method described by Dueck *et al.*, (1985). In each group, the respiratory response of the two reactive sheep to the *Ascaris* antigen was augmented using 2-3 fortnightly respiratory exposures to the antigen (82,000 protein nitrogen units /ml) for twenty minutes delivered via an endotracheal tube passed through the tracheostomy. One of the reactive sheep (experimental) was then further exposed to antigen for twenty minutes daily for two weeks. The other reactive sheep (sensitized control) and the non-reactive sheep (non-sensitized control) were exposed to the saline vehicle alone daily for two weeks. Airway resistance (Raw) and dynamic lung compliance (Cdyn) were measured before the antigen/saline exposures and at five minutes intervals during the exposure. On the last day the experiment was carried out under general anesthesia. In addition to respiratory measurements, cardiac output, pulmonary arterial pressure, pulmonary wedge pressure, systemic arterial pressure and central venous pressure were obtained to calculate cardiac power output. At the end of the last exposure sheep were killed, necropsied and samples of lung and airway fixed for morphological studies.

Sixty four percent of the sheep tested showed an immediate skin reaction to the antigen. The antigen exposure caused significant changes in respiratory parameters and increased the cardiac work load of the right side of the heart in the experimental sheep. Morphological studies revealed that antigen exposure caused an increase in number of

eosinophils and goblet cells in the airways and an increase in the thickness of the 'pseudo-basement membrane' at some levels of the respiratory tract. Antigen exposure also caused an increase in the percentage smooth muscle area in the airway wall cross-sectional area in the membranous bronchioles.

Based on these observations it can be concluded that repeated daily exposure of sheep airway to *Ascaris suum* antigen can be used to reproduced morphological changes observed in human asthmatic airways.

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LIST OF ABBREVIATIONS

Ae	external area
Ai	internal area
Asm	airway smooth muscle
ASM%	percentage smooth muscle in airway wall cross-sectional area
Aw	airway wall
BAL	broncho-alveolar lavage
Cdyn	dynamic lung compliance
CO	cardiac output
CVP	central venous pressure
F	respiratory flow
NAHR	non-specific airway hyperresponsiveness
LT	leukotrienes
PAF	platelet activating factor
Pap	pulmonary arterial pressure
PBS	phosphate buffered saline
PBM	pseudo basement membrane
Pe	external perimetre
Pi	internal perimetre
P _{IO}	intra oesophageal pressure
Pwp	pulmonary wedge pressure
Raw	airway resistance
SABP	systemic arterial blood pressure
V _T	tidal volume