



<b>Title</b>	<b>Airway neutrophilic in bronchiectasis: the role of TNF- in vivo</b>
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#### S-RC-4

##### UP-REGULATION OF CIRCULATING ADHESION MOLECULES IN STABLE BRONCHIECTASIS

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Intense neutrophil influx into the airways occurs in bronchiectasis, which could be harmful when harmful neutrophil products, particularly elastase, are released in response to bacteria infection. Adhesion molecules expressed on the surface of endothelial cells and leukocytes mediate migration of leukocytes from the vascular compartment into inflamed tissue. To address the role of adhesion molecules in the pathogenesis of bronchiectasis, we have compared the levels of circulating E-selectin, ICAM-1 and VCAM-1 in bronchiectasis patients (n=37) with normal controls (n=17) by using capture ELISA, and examined the relationship between those circulating adhesion molecules with clinical markers of disease severity in bronchiectasis. Serum levels of E-selectin, ICAM-1 and VCAM-1 in patients with bronchiectasis were significantly higher than those in control subjects (p=0.02, <0.0001 and 0.0002 respectively). Among patients with bronchiectasis, serum levels of E-selectin correlated with serum ICAM-1 levels (r=0.58, p<0.001). Both E-selectin and ICAM-1 levels, but not VCAM-1 level, were inversely related to FEV<sub>1</sub> % predicted (r=-0.57, p<0.001; and r=-0.53, p=0.001 respectively) and FVC (r=-0.52, p=0.002; and r=-0.46, p=0.005 respectively). In addition, there was a correlation between serum ICAM-1 levels with 24 h sputum volume (r=0.34, p= 0.04), and correlation between serum E-selectin and ICAM-1, but not VCAM-1, with the number of lung lobes affected by bronchiectasis (r=0.35, p=0.04 and r=0.34, p=0.04 respectively). These observations strongly suggest that the adhesion molecules play a significant role in the pathogenesis of bronchiectasis. (Supported by a CRCG grant of the University of Hong Kong)

#### S-RC-5

##### AIRWAY NEUTROPHILIAN IN BRONCHIECTASIS: THE ROLE OF TNF- $\alpha$ *IN VIVO*

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Neutrophils (Neu.) are the most predominant cells found in the airway lumen of bronchiectasis. TNF- $\alpha$ , a mediator for Neu. infiltration, has been also found in abundance in sputum from the patients. But the most previous studies have primarily investigated the inflammations, cytokine profiles of bronchiectasis in sputum and blood, we, therefore, used endothbronchial biopsy (EBB) technique to evaluate Neu. infiltration, and the role of TNF- $\alpha$  in promoting Neu infiltration in brobchiectatic airways. EBB were taken from the affected airways in 15 bronchiectatic patients and from right low lobe in 14 controls. Neu elastase, macrophages (CD68) and TNF- $\alpha$  were stained with monoclonal antibodies by using immunohistochemical method on consecutive 3  $\mu$ m paraffin sections. The positive cells in the airway submucosa were counted by using a computer image analyzer at a final magnification of  $\times$  400, and expressed as positive cells/mm<sup>2</sup> of submucosa. Data are showed in the table (\*p<0.05 vs controls).

	Neu elastase	Macrophages	TNF- $\alpha$
Bronchiectasis	604 (101-1013)*	694 (145-1361)*	270 (61-654)*
Controls	127 (24-630)	298 (129-856)	75 (15-322)

A significant correlation of airway TNF- $\alpha$  with airway Neu. was found only in bronchiectasis (r=0.71, p=0.01), but a correlation between TNF- $\alpha$  and airway macrophages were seen in both bronchiectasis (r=0.82, p<0.001) and controls (r=0.66, p=0.02). Those findings provide further insight into the development of the chronic destructive inflammatory response occurring in the airway walls, that eventually destroys the airways in bronchiectasis. (Supported by CRCG grant of the University of Hong Kong)