61 EFFECT OF ANTIGEN CHALLENGE ON CANINE TRACHEAL MUCUS. Malcolm King, Ph.D., Montreal, Canada.

Antigen challenge alters mucus clearance in both animals and man, but its particular effect on mucus rheology has not been examined. We studied the effects of inhalation of Ascaris suum extract on tracheal mucus in mongrel dogs exhibiting cutaneous sensitivity to the antigen. Each dog was prepared with a permanent tracheostomy through which mucus could be collected and aerosols delivered with the dog fully conscious. Increasing concentrations of Ascaris extract were delivered intra-tracheally by aerosol at half-hour intervals, and mucus samples, obtained by placing a cytology brush in contact with the tracheal mucosa, were taken in the 2-5, 8-12 and 20-25 min intervals following aerosolization. The viscoelastic properties of each sample were determined by the oscillating ball microrheometer technique (J Appl Physiol 1977:42,797). The weight of mucus collected per unit time was used as an index of mucus flux. In each dog, antigen challenge led to at least some degree of hypersecretion by the time a 1:100 dilution was reached. The alteration in viscoelastic properties was suggestive of that seen with methacholine inhalation (J Appl Physiol 1979:47,26), i.e. a fall in elasticity at low doses and a rise at high doses. The onset of tracheal mucus hypersecretion correlated roughly with cutaneous sensitivity in the 6 dogs studied, at least in rank order. Pre-treatment with aerosolized thiazinamium chloride, a quaternary salt of promethazine, blocked or greatly reduced the hypersecretion due to antigen challenge, and minimized the alterations in mucus viscoelasticity.

62 EFFECT OF FLAVONOIDS ON AGONIST-INDUCED AND ANAPHYLACTIC SMOOTH MUSCLE CONTRACTION. M. Fanning, P. McCander, J. Malolepszy, and E. Middleton, Jr. Buffalo, NY.

Certain flavonoids inhibit antigen-induced basophil histamine release (HR), lysosomal enzyme release from PMN, and the generation and effector function of cytotoxic lymphocytes, processes involving ligand-cell and cell-cell interactions. We examined the effect of flavonoids on another ligand-cell interaction, stimulation of smooth muscle (SM) by various agonists. Guinea pig ileum logitudinal SM was suspended in Tyrode's buffer, pH 7.4, gassed with 95% O_2:5% CO_2 and standard baseline contractions obtained with H, acetylcholine (ACh) or PGE_2. Then, quercetin, tangeretin, hesperetin, or naringin, were added at final conc. of 5-50uM. The flavonoids were dissolved in DMSO and diluted in Tyrode's giving final DMSO of 0.25% (no affect on smooth muscle responses). After 5 minutes incubation agonists were added and contraction (mm) compared to baseline. Conc.-response relationships were determined for each combination of agonist and flavonoid. Results indicated that quercetin, tangeretin, and hesperetin markedly inhibited SM contraction, affecting both phasic and tonic responses in a conc.-dependent manner. Naringin was not inhibitory except at the lowest conc. of agonists. In addition, quercetin, tangeretin, and hesperetin produced conc.-dependent inhibition of antigen-induced contraction of SM from sensitized animals. We conclude that certain flavonoids inhibit SM contraction caused by H, ACh, PGE_2, and anaphylactic mediators, another example of flavonoid effects on cell function.

63 INFLUENCE OF PULMONARY DYSFUNCTION ON PLASMA PROSTAGLANDINS AND THROMBOXANE. Nancy A. Sherman, Helen G. Morris and William S. Silvers, Denver, Colorado.

Prostaglandin concentrations were measured by radioimmunoassay in paired samples of arterial and venous blood from normal subjects and patients with pulmonary disease. The arterial samples were obtained from patients when arterial punctures were performed for diagnostic evaluation of blood gases. Most of the patients were receiving various medications. A second group of specimens, which were limited to venous samples, were obtained from a group of normal subjects and patients with mild asthma who had taken no medication of any kind for two weeks.

PGE_2 and Thromboxane B_2 (TXB_2) concentrations in both arterial and venous plasma were significantly higher in patients with asthma or COPD than in normal subjects ($p<.01$ to $p<.001$). The 3 groups of patients exhibited significant differences in the severity of pulmonary dysfunction as indicated by measurements of arterial pO_2 and the measurements of pulmonary function (FVC and FEV_1). Nevertheless, PGE_2 and TXB_2 concentrations did not differ in 1) symptomatic, 2) asymptomatic patients with asthma or 3) patients with COPD.

These observations indicate that pulmonary disease is associated with alteration in the release or disposal of cyclooxygenase metabolites of arachidonic acid; the alterations in arachidonic metabolism may not be limited to times when patients are symptomatic.

64 EFFECTS OF SALBUTAMOL (S), THEOPHYLLINE (T) AND FPL 55712 (FPL) ON LEUKOTRIENE-INDUCED CONTRACTION OF GUINEA PIG TRACHEA IN VITRO. C.L. Armour, B. Pharm., I.J. Nicholls B.Sc., R.R. Schellenberg M.D., Vancouver,B.C. Canada.

Airway smooth muscle contraction characteristic of bronchial asthma can be reversed by β-adrenergic agonists and theophylline. The slow reacting substance, leukotriene D(LTD), considered a major mediator of allergen-induced bronchoconstriction, contracts human bronchi and guinea pig trachea in vitro. We compared the inhibition of LTD responses by competitive (FPL) & functional (S & T) antagonists.

Guinea pig tracheal spirals were equilibrated under 2 g tension. The response to cumulative addition of LTD was compared in the presence & absence of S,T or FPL. Results were expressed as % of the maximum carbachol response. Comparative responses to the maximum concentration of LTD, $6x10^{-7}M$, were as follows: control, 56.6±2.7% ($\bar{x}$± s.e.m., n=5); S, $5X10^{-8}M$, 36.2±5.3% (n=5); S,$5x10^{-7}M$, 8.6±4.2%(n=5). T alone (up to $1x10^{-4}M$) did not modify LTD responses. T,$1x10^{-4}M$ plus S, $5x10^{-8}M$ reduced the LTD response to 23.2± 6.4%, n=7). FPL, $1x10^{-4}M$, reduced the LTD response from 63.2± 2.7% to 37.1±13% (n=3).

We conclude that S is a more effective inhibitor of the LTD-induced contraction than FPL. β-adrenergic agonists & theophylline in combination may be more effective therapy than either drug alone.