Title: Comparison of Histamine Release from lung Mast Cells of Asthmatic and Non-Asthmatic Dogs.

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Introduction. Mediator release into the airway lumen is likely important in the pathogenesis of asthma. In attempts to understand the pathophysiology of asthma, interest has focused on the airway mast cell. The basenji-greyhound (BG) dog model of asthma is extremely well characterized with respect to atopy and airway hyperresponsiveness. This model has 5% to 9% mast cells in bronchoalveolar lavage (BAL). Although these cells appear morphologically similar to mast cells of control animals, their ability to release mediators may differ. We therefore determined whether mast cells obtained from BAL in a group of BG dogs functionally differed, with respect to histamine releasability, from cells obtained from allergic and nonallergic control dogs.

Methods. Studies were performed in 14 BG dogs, 5 purebred basenjis (B) (allergic controls) and 5 greyhounds (G) (nonallergic controls). The BG dogs and B, but not the G, displayed signs of atopy. The BG dogs were hyperresponsive to the aerosol methacholine compared to either the purebred B or the G. Dogs were anesthetized with thiopental (15 mg/kg). BAL was performed using 400 ml of sterile saline. Fluid recovered was centrifuged and the number of mast cells quantitated. Aliquots containing equal numbers of mast cells were incubated with A 23187 (10-6 to 4 X 10-5M) and C5a (10-9 to 10-7M) for 30 min and histamine release measured by an automated fluorometric method. All data were expressed as percent of total histamine released above spontaneous and were expressed as mean ± SEM. Unpaired t-tests with Bonferroni's correction were used to determine significant differences between groups with $P<0.02$ considered significant.

Results. Total histamine per mast cell was not different in the 3 groups. However, spontaneous histamine release was greater in both BG and B compared to G ($P<.001$) and averaged 6.6 ± 1.2% in BG, 6.6 ± 1.8% in B and 1.4 ± 0.2 in G. Both A 23187 and C5a produced dose related histamine release in the 3 groups (fig. 1 & 2). A 23187 (2 x 10-5M) released more histamine in both BG and B, compared to G with no difference between BG and B (fig. 1) ($P<.02$). C5a (10-8M) released more histamine in BG, compared to B and G (fig. 2) ($P<.02$).

Discussion. These studies demonstrate that mast cells obtained from BAL of BG dogs differ functionally from those of allergic (B) and nonallergic (G) control dogs and that mast cells obtained from BAL can be used to study mast cell function in the control and asthmatic state. Increased numbers of functionally unstable mediator-containing cells in the airway lumen of dogs with asthma is of great interest and potential importance in our understanding of mechanisms underlying airway hyperreactivity in these animals and perhaps in man.

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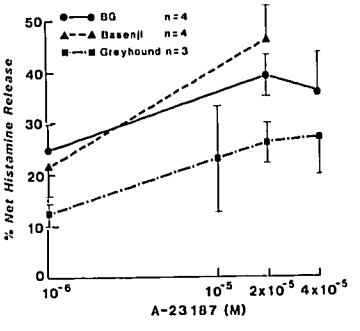

Figure 1. Increase in percent histamine release plotted against dose of calcium ionophore A 23187 in BG, B and G dogs.

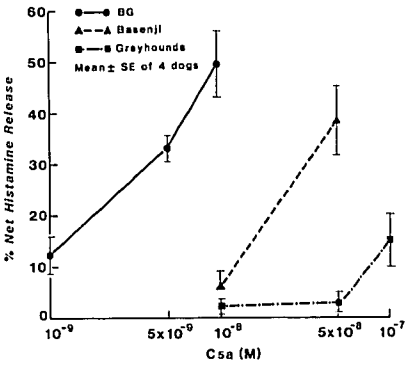

Figure 2. Increase in percent histamine release plotted against increasing concentration of C5a in BG, B and G dogs.