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RESEARCH ARTICLE

Neutrophilia induced by histamine challenge in guinea pig: The role of IL-5, IL-10 and IL-17A, but not CXCL8

Patricia Ramos-Ramírez,[a,e] María G. Campos,[b] Erasmo Martínez-Cordero,[c] Eduardo García-Zepeda,[d] Olivia Téllez-Jiménez,[a] Karen Larios-Martínez,[e] Blanca Bazán-Perkins[a,*]

[a] *Departamento de Hiperreactividad Bronquial, Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas, Mexico City, Mexico*
[b] *Unidad de Investigación Médica en Farmacología, Centro Médico Nacional Siglo XXI, Instituto Mexicano del Seguro Social, Mexico City, Mexico*
[c] *Departamento de Autoinmunidad, Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas, Mexico City, Mexico*
[d] *Departamento de Inmunología, Instituto de Investigaciones Biomédicas, Universidad Nacional Autónoma de México, Mexico City, Mexico*
[e] *Departamento de Ciencias Básicas, Instituto Tecnológico y de Estudios Superiores de Monterrey, Campus Ciudad de México, Mexico City, Mexico*

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Abstract

Background: Histamine is widely used as a pharmacological tool for the evaluation of airway responsiveness. Nevertheless, undesirable and contradictory effects have been described after histamine provocation tests. In previous evaluations of airway responsiveness in a guinea pig asthma model, the control groups consistently showed high neutrophil counts in bronchoalveolar lavage fluid (BALF) immediately after the histamine challenge. The changes in cytokine and chemokine levels in guinea pig lung associated with histamine induced-neutrophilia are described in this paper.

Methods: Immediately and 24 h after histamine challenge, airway wall and BALF eosinophil and neutrophil counts as well as lung cytokines (IL-5, IL-10, IL-17A, TNF-α and TGF-β) and chemokines (CCL11 and CXCL8) levels were evaluated.

Results: Histamine inhalation generated an all-or-none bronchial response, and the dose inducing airway obstruction was similar in all guinea pigs. Immediate increases in neutrophil counts in airway wall and BALF and in IL-5, IL-10 and IL-17A levels in the lung homogenate were observed after histamine challenge. Significant correlations were found between neutrophil counts from airway wall and IL-5, IL-10 and IL-17A levels in the lung homogenate.

*Corresponding author.
E-mail: perkins@unam.mx (B. Bazán-Perkins).

Conclusions: Histamine inhalation induced rapid neutrophil LBA and airway wall infiltration that was not associated with CXCL8 expression but with a Th2 and Th17 cytokines that probably are involved in the recruitment and activation of neutrophils.

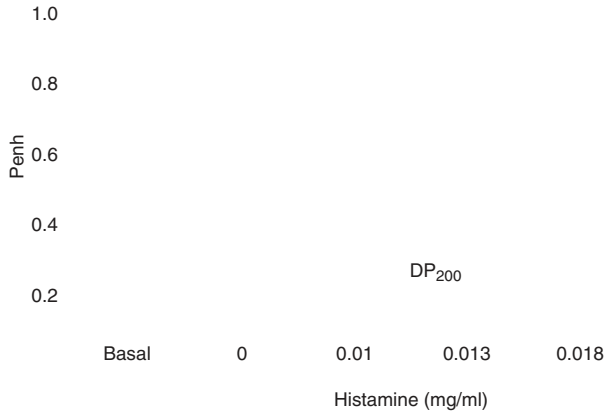


Figure 1 Dose-response curve to aerosolized histamine. After initial baseline acquisition, guinea pigs received noncumulative doses to histamine. The dashed arrow shows the provocative dose 200% (PD_{200}), i.e., the interpolated histamine dose that caused a three-fold increase of basal Penh.

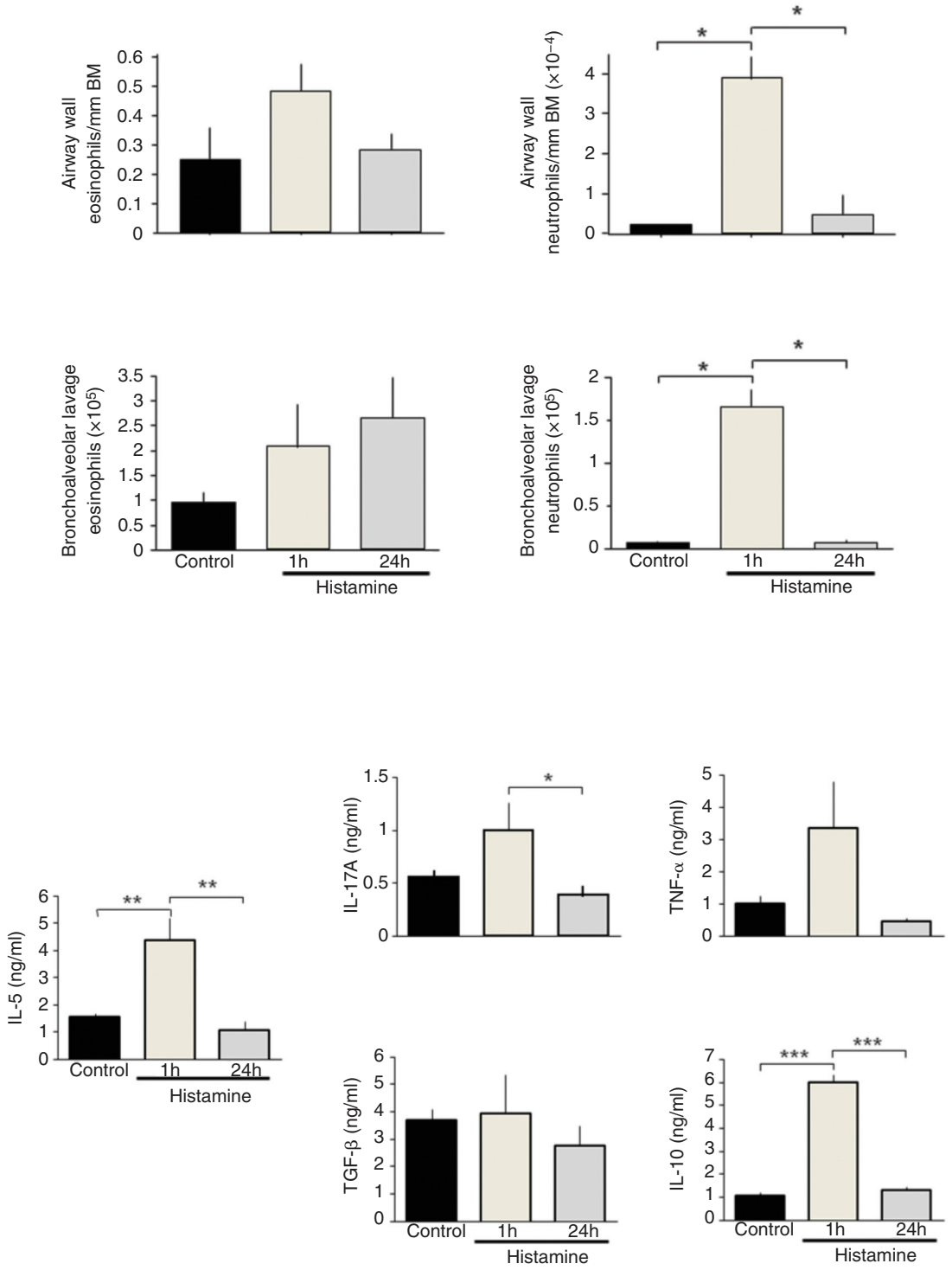
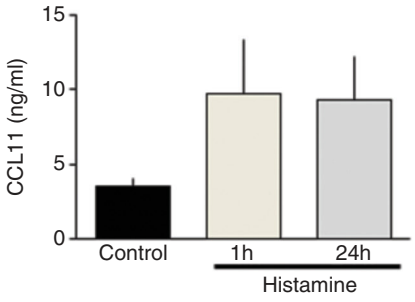
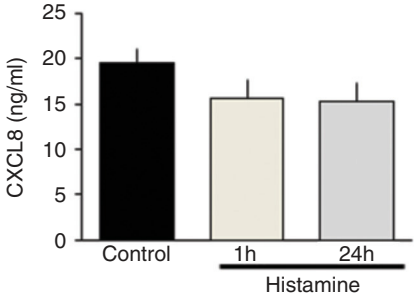


Figure 3 Cytokine expression in lung homogenates from histamine challenged guinea pigs. The bars represent the mean ± SE of $n = 5$ guinea pigs in each group. *p <0.05, **p <0.01, ***p < 0.001 (one-way ANOVA with Tukey's multiple comparisons test).


15
10
5
0
CCL11 (ng/ml)
Control
1h
24h
Histamine


25
20
15
10
5
0
CXCL8 (ng/ml)
Control
1h
24h
Histamine