II. Anatomy and Physiology

B. Pathology of Primary Atopic Disorders

1. Rhinitis and rhinosinusitis

a. Allergic

LANDMARK PAPER:
Meltzer EO, Hamilos DL, Hadley JA, et al
Rhinosinusitis: Establishing definitions for clinical research and patient care
J Allergy Clin Immunol 2004;114:155-212)

BACKGROUND: There is a need for more research on all forms of rhinosinusitis. Progress in this area has been hampered by a lack of consensus definitions and the limited number of published clinical trials. OBJECTIVES: To develop consensus definitions for rhinosinusitis and outline strategies useful in clinical trials. METHODS: Five national societies, The American Academy of Allergy, Asthma and Immunology; The American Academy of Otolaryngic Allergy; The American Academy of Otolaryngology Head and Neck Surgery; The American College of Allergy, Asthma and Immunology; and the American Rhinologic Society formed an expert panel from multiple disciplines. Over two days, the panel developed definitions for rhinosinusitis and outlined strategies for design of clinical trials. RESULTS: Committee members agreed to adopt the term “rhinosinusitis” and reached consensus on definitions and strategies for clinical research on acute presumed bacterial rhinosinusitis, chronic rhinosinusitis without polyposis, chronic rhinosinusitis with polyposis, and classic allergic fungal rhinosinusitis. Symptom and objective criteria, measures for monitoring research progress, and use of symptom scoring tools, quality-of-life instruments, radiologic studies, and rhinoscopic assessment were outlined for each condition. Conclusion -The recommendations from this conference should improve accuracy of clinical diagnosis and serve as a starting point for design of rhinosinusitis clinical trials

2. Early and late responses to allergen challenge:

a. Nasal Challenge:

LANDMARK PUBLICATION:
Raphael GD, Igarashi Y, White MV, Kaliner MA.
The pathophysiology of rhinitis. Sources of protein in allergen-induced nasal secretions.
J Allergy Clin Immunol. 1991;88:33-42.

Allergic rhinitis is characterized by a profuse rhinorrhea in addition to paroxysms of sneezing, nasal congestion, and pruritus. To define better the sources of nasal secretion produced during rhinitis, nasal allergen challenges were performed on nine atopic subjects with seasonal rhinitis. A single dose of allergen was sprayed into one side of the nose, and nasal lavages were collected bilaterally for 7 hours. Nasal lavages were assayed for protein (total protein, albumin, lactoferrin, and lysozyme) and mediator (histamine and prostaglandin D2) content. Protein concentrations increased and remained elevated above baseline levels in both ipsilateral and contralateral secretions for up to 3 hours after allergen challenge. The proportion of albumin relative to total protein (the albumin percent) increased on the ipsilateral side, whereas the relative proportions of lactoferrin and lysozyme (the lactoferrin percent and lysozyme percent) increased on the contralateral side. Prostaglandin D2, but not histamine, increased selectively on the ipsilateral side. These data suggest that the ipsilateral protein secretory response is due to allergen-induced mast cell mediator release causing increased vascular permeability, whereas the contralateral protein secretory response is primarily a reflex-induced glandular secretion.

b. Bronchial Challenge:

LANDMARK PUBLICATION:
Cockcroft DW, Murdock KY, Kirby J, Hargreave F.

Prediction of airway responsiveness to allergen from skin sensitivity to allergen and airway responsiveness to histamine.
Am Rev Respir Dis. 1987;135:264-7

Previous data have indicated that airway responsiveness to allergen, expressed as the provocation concentration causing a 20% FEV1 fall (PC20), was dependent on nonallergic airway responsiveness (histamine PC20) and sensitivity to allergen (skin sensitivity or end-point titration). From retrospective data in 24 subjects, we developed a formula to predict allergen PC20 and examined its accuracy prospectively in 26 new subjects undergoing allergen inhalation test with doubling allergen concentrations. Allergen PC20 (APC20) was predicted from histamine PC20 (HPC20) and skin sensitivity (SS) by the formula: Log10 (APC20) = 0.69 Log10 (HPC20 X SS) + 0.11 (r = 0.85). Allergen PC20 was accurately predicted in 6, and overestimated or underestimated by 1 doubling concentration in 11, by 2 concentrations in 6, by 3 concentrations in 3, and by greater than 3 concentrations in none. From the total of 50 subjects, a new relationship was developed: Log10 (APC10) = 0.68 log10 (HPC20 X SS) (r = 0.82) from which 46 of 50 (92%) of allergen PC20 values fall within 2 doubling concentrations of the regression line (and all within 3). Early airway responsiveness to a given allergen can be predicted within a +/- 8-fold range, which is better than some investigator's test reproducibility of +/- 1 log (10-fold). Allergen inhalation tests to determine early asthmatic responsiveness to different IgE-mediated allergens can probably be replaced by the simpler and safer determinations of allergen sensitivity (SS, RAST) and histamine or methacholine airway responsiveness.

LANDMARK PUBLICATION:
Killian D, Cockcroft DW, Hargreave FE, Dolovich J.
Factors in allergen induced asthma: Relevance of the intensity of the airways allergic reactionand non-specific bronchial reactivity.
Clin Allergy 1976; 6:219–225.

Early asthmatic responses (EAR) of similar severity were produced by allergen inhalation challenges in nine asthmatic subjects. The severity of the airways allergic reaction was estimated by measuring the skin test weal size produced by the same dilution of allergen which caused the EAR. The non-specific bronchial reactivity was assessed by inhalation of incresing concentrations of histamine acid phosphate. Possible relationships between the severtiy of the airways allergic reaction, the level of non-specific bronchial hyper-reactivity and the pattern of asthmatic response were examined. There was a marked inverse correlation between the required severity of the airways allergic reaction and the non-specific bronchial reactivity (log10) of the individual (r = -0-96, P less than 0-001). The EAR was followed by a late asthmatic response (LAR) in five subjects. There was no evident correlation between the magnitude of the EAR and that of the LAR. In addition, no correlation was obtained between the pattern of response interms of EAR or LAR and the severity of the allergic reaction, or the level of non-specific bronchial reactivity. These results indicate that the allergic reaction and the non-specific bronchial reactivity are interrelated in the production of allergen-induced asthma. Thus a mild allergic reaction will induce and EAR in patients with markedly increased non-specific bronchial reactivity, whereas a severe allergic reaction is required to produce an EAR in those with only slightly increased non-specific reactivity. The lack of correlation between the occurrence of the LAR and the intensity of the airways allergic reaction, the non-specific bronchial reactivity and the intensity of the EAR indicates that other factors are involved in the development of LAR.