Co-morbidities of allergic disease

Carmen Vidal

Athens, September 11, 2014
1. The major player in driving the immune response is the T lymphocyte and the T helper subpopulations –Th1 and Th2- as well as the T regulatory cells.

2. T lymphocytes are responsible for tolerance or reactivity to allergens.
Genetic regulation of IgE responses: Achilles and the tortoise

Donata Vercelli, Tucson, Ariz.

Rostrum

GENETICS AND SUSCEPTIBILITY TO ALLERGY, OR, WHY IT IS TIME FOR FUNCTIONAL GENOMICS

J Allergy Clin Immunol 2005;116:60-4
comorbidity (ˌkəʊməˈbɪdɪtɪ)
Definitions
noun
1. the occurrence of more than one disease at the same time

In theory, theory and practice are the same. In practice, they are not.

Albert Einstein
The prevalence of allergic diseases has shown an increase in the last few years. Allergic diseases develop in persons with a genetic background, this genetic trait being known as atopy. The main pathophysiological characteristic of allergy is inflammation. This inflammatory process explains the diversity of symptoms and signs. The early sensitization increases the risk of developing different symptomatic forms of allergy, and one person may present different symptoms and signs of this disease.
But some people can become allergic without atopy trait in conditions of a higher and longer exposure to allergens (e.g. occupational allergy, drug allergy and so on). In the last years new allergens have induced symptoms, sometimes with a life-threatening evolution. The load of allergen in public areas is also increasing. In this context, ALLERGY must be understood as a unique SYSTEMIC DISEASE with various forms of presentation.
COMORBIDITIES RELATED TO IMMUNE MECHANISMS:

1. Due to the same or related agent (allergen):
   1.1. Rhinitis or rhinoconjunctivitis and asthma
   1.2. Nasal polyps or chronic sinusitis
   1.3. Food allergy: OAS

2. Due to a different agent (allergen-antigen):
   2.1. Food allergy
   2.2. Drug allergy
   2.3. Anaphylaxis (latex, hymenoptera, etc)

3. With or without allergen:
   3.1. Atopic dermatitis
   3.2. Eosinophilic esophagitis or enteritis
COMORBIDITIES DUE TO DIFFERENT MECHANISMS:

1. Common diseases:
   1.1. Gastroesophageal reflux disease (GERD)
   1.2. Adenoid hypertrophy
   1.3. Otitis media and tubal dysfunction
   1.4. Obesity

2. Common treatments:
   2.1. Beta-blockers
   2.2. ACE inhibitors
   2.3. Estrogens

3. Alcohol
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FACTS:

1. 20-40% of patients with AR have concomitant asthma and 78-93% of asthmatics have AR.
2. Rhinitis usually precedes asthma. Patients with AR were found to be three-times more likely to develop asthma than negative controls.

The link between allergic rhinitis and allergic asthma: A prospective population-based study. The Copenhagen Allergy Study

Linneberg et al. Allergy 2002;57:1048-52
MORE FACTS:

3. AR and asthma share the same inflammatory mechanism (allergens, infections).
However, the role of systemic inflammation in asthmatic patients is still unclear and, consequently, debated. Airway inflammation in asthma is heterogeneous in nature and may involve an allergen-specific acquired immune response with IL-5-mediated eosinophilic inflammation or a dysregulation of innate immune responses involving IL-8-induced neutrophilic airway inflammation [12]. Apparently, systemic inflammation is increased in asthmatic patients with neutrophilic airway inflammation [13*].

FINALLY:

4. AR treatment influences asthma control or development?

Fluticasone Propionate Nasal Spray Is Superior to Montelukast for Allergic Rhinitis While Neither Affects Overall Asthma Control*

Robert A. Nathan, MD; Steven W. Yancey, MS; Kelli Waitkus-Edwards, PhD; Barbara A. Prillaman, MS; John L. Stauffer, MD; Edward Philpot, MD; Paul M. Dorinsky, MD; and Harold S. Nelson, MD

Chest 2005;128:1910-20
4. AR treatment influences asthma control or development?

Effect of Treating Allergic Rhinitis With Corticosteroids in Patients With Mild-to-Moderate Persistent Asthma*

Rafael Stelmach, MD; Maria do Patrocínio T. Nunes, MD; Marcos Ribeiro, MD, FCCP; and Alberto Cukier, MD, FCCP

Chest 2005;128:3140-7
FINALLY:

4. AR treatment influences asthma control or development?

What about the effect of allergen immunotherapy on preventing asthma to develop from rhinitis?
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ACCURATE CLINICAL SUSPICION:
   Persistent obstruction
   Anosmia
   Sinus pain

ACCURATE DIAGNOSIS:
   Physical exam
   Image scan
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Due to cross-reactivity between a prior aeroallergen sensitization and labile plant or animal derived proteins.

Class 2 food allergy (different from traditional class 1 food allergy secondary to sensitization through gastrointestinal tract)
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• Food allergy in young children may be considered a marker of atopy.
• Milk or egg white allergy is associated with a 70% risk of respiratory allergic disease (asthma or allergic rhinitis) at age of 5 years.
• Subjects with past and current food allergy should be considered at high risk for asthma and environmental allergy.
Systematic review of prevalence of aspirin induced asthma and its implications for clinical practice

Christine Jenkins, John Costello, Linda Hodge

DRUG ALLERGY

✓ 0.6-2.5% general population
✓ 4.4-12% asthma patients

>50% of asthma patients react against 80 mg Aspirin or an equivalent dose of:

IBUPROFEN \( \leq 400 \text{ mg} \)
NAPROXEN \( \leq 100 \text{ mg} \)
DICLOFENAC \( \leq 40 \text{ mg} \)
Association of thromboxane A1 synthase (TBXAS1) gene polymorphism with acute urticaria induced by nonsteroidal anti-inflammatory drugs


The prevalence of atopy (skin prick test [SPT] response positivity) was significantly higher in the MR group than in the SR group (66.2% vs 37.8%, respectively; \( P < .0001 \)).
**ANAPHYLAXIS**

### IMMUNOLOGIC MECHANISMS (IgE dependent)
- Foods:
  - Peanut
  - Tree nuts
  - Shellfish
  - Fish
  - Milk
  - Egg
  - Soybean
  - Peach
  - Sesame
- Venoms:
  - Stinging insects
  - Beta-lactam antibiotics
- Medications:
  - NSAIDs
  - Biologic agents

### IMMUNOLOGIC MECHANISMS (IgE independent)
- Contrast media
- NSAIDs
- Dextran
- Biologic agents

### NONIMMUNOLOGIC MECHANISMS (Direct mast cell activation)
- Physical factors: Exercise, cold, heat, sunlight
- Ethanol
- Medications: Opioids

### IDIOPATHIC ANAPHYLAXIS (No apparent trigger)
- Previously unrecognized allergen?
- Mastocytosis/clonal mast cell disorder?

*Trigger anaphylaxis by more than one mechanism
**NSAIDs, non-steroidal anti-inflammatory drugs
***HMW, high molecular weight
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ATOPIC DERMATITIS

Inflammatory condition of the skin

The Allergic March

Birth
3 months
1 year
2 years
3 years
7 years
15 years

Typical Age of Onset

Eczema
Food Allergy
Rhinitis
Asthma

ATOPIC DERMATITIS

Inflammatory condition of the skin
EOSINOPHILIC ESOPHAGITIS OR ENTERITIS

Eosinophilic Esophagitis: Asthma of the Esophagus?

J. Christian Virchow

Dig Dis 2014;32:54–60
DOI: 10.1159/000357010

Both share same:

Epidemiology
Atopy
Eosinophilic inflammation
Treatment
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Prevalence of GERD in general population is 10-20% in western countries.

Cough related to GERD is described as “something” in the larynx or pharynx rather than the chest (depends on patient perception).

MUTUAL INTERACTION ?
Cochrane review of all controlled trials of GERD therapy in adults and children with asthma found a lack of benefit in achieving asthma control, although there is a suggestion of reduced albuterol use and clinical benefit.
Asthma or asthma therapy may aggravate or appear to aggravate GERD.

Because bronchodilators may reduce esophageal sphincter tone, systemic corticosteroids may increase gastric acid production, and inhaled corticosteroids may cause hoarseness similar to the hoarseness caused by GERD.
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   1.4. Obesity
Exploring the obesity–asthma link: do all types of adiposity increase the risk of asthma?

R. V. Fenger¹, A. Gonzalez-Quintela², C. Vidal², F. Gude², L. L. Husemoen¹, M. Aadahl¹, N. D. Berg¹ and A. Linneberg¹
¹Research Centre for Prevention and Health, Glostrup University Hospital, Copenhagen, Denmark and ²Department of Medicine, Complejo Hospitalario Universitario, Santiago de Compostella, Spain


☑ All adiposity measures were associated with a higher risk of asthma
☑ Associations were stronger among non-atopics
☑ FVC and FEV1 decreased with increased obesity
☑ Adiposity was not associated with FeNO
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Adverse Respiratory Effect of Acute \(\beta\)-Blocker Exposure in Asthma

A Systematic Review and Meta-analysis of Randomized Controlled Trials

Morales DR et al. CHEST 2014;145:779-86
A significant mean decrease in FEV1 is observed after beta-blockers.

Response to beta-agonists is blunted by beta-blockers.

The effect is more evident with non-selective beta-blockers.
COMORBIDITIES DUE TO DIFFERENT MECHANISMS:

2. Common treatments:
   2.1. Beta-blockers
   2.2. ACE inhibitors
   2.3. Estrogens
Chronic Cough 2
Management of chronic cough
Ian D Pavord, Kian Fan Chung
Lancet 2008;371:1375-84

ACE Inhibitor–Induced Bronchial Reactivity in Patients with Respiratory Dysfunction
Kathleen A Packard, Richard L Wurdeman, and Amy J Arouni
Ann Pharmacother 2002;36:1058-67

The risk is not higher than in general population
COMORBIDITIES DUE TO DIFFERENT MECHANISMS:

2. Common treatments:
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   2.2. ACE inhibitors
   2.3. Estrogens
Asthma and the menopause: A systematic review and meta-analysis

E. Zemp\textsuperscript{a, b,*}, T. Schikowski\textsuperscript{a, b}, J. Dratva\textsuperscript{a, b}, C. Schindler\textsuperscript{a, b}, N. Probst-Hensch\textsuperscript{a, b}

Menopause does not increase the risk of asthma

Maturitas 2012;73:212-7
Menopause patients divided into 2 groups depending on the use of hormone therapy:

NO THERAPY

NO THERAPY

RISK OF ASTHMA

THERAPY

THERAPY
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3. Alcohol
Sensitization to cross-reactive carbohydrate determinants in relation to alcohol consumption

A. Gonzalez-Quintela*, M. Garrido†, F. Gude‡, J. Campos*, A. Linneberg§, S. Lojo† and C. Vidal†

Clin Exp Allergy 2007;38:152-60

Alcohol intake can induce false positive results in serum specific IgE due to CCD-interaction.

Prevalence of self-reported hypersensitivity symptoms following intake of alcoholic drinks

A. Linneberg*, N. D. Berg†, A. Gonzalez-Quintela‡, C. Vidal† and J. Elberling†

Clin Exp Allergy 2007;38:145-51

Self-reported hypersensitivity symptoms following alcohol ingestion are common.
comorbidity

Definition

noun

1. the occurrence of more than one disease at the same time