## Inner City Pediatric Asthma: What are we doing about it?

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## Presentation Outline

- Overview of asthma
- Pharmacologic treatments
- Role of allergens in asthma
- Omalizumab (Anti-IgE) overview
- Inner City Asthma Consortium and ICATA study results
- Asthma management pearls

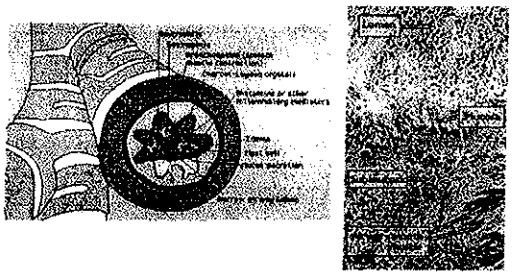
## Asthma in the U.S.

- Prevalence, morbidity, and mortality are increasing
- Prevalence, morbidity and mortality are highest among the urban poor

## Diagnosis of Asthma

- History or presence of episodic symptoms of airflow obstruction
- Airflow obstruction is at least partially reversible
- Alternative diagnoses are excluded

## Asthma Pathophysiology



## Pharmacologic Therapy
## The Medications

**Long-Term-Control Medications!!**

Quick-Relief Medications

**Patients requiring albuterol > 2 times/week require <u>daily preventive</u> therapy for asthma**

## Control of Factors Contributing to Asthma Severity

For at least those patients with persistent asthma on daily medications, the clinician should:

- identify allergen exposures and use the patient's history to assess sensitivity to seasonal allergens
- use skin testing or in vitro testing to assess sensitivity to perennial indoor allergens

## Seasonal Allergens

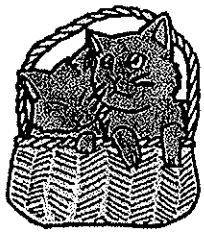
***Important causes of "hayfever"***

- Tree pollens - early spring
- Grass pollens - late spring
- Weed pollens - late summer to fall
- Outdoor molds - summer and fall

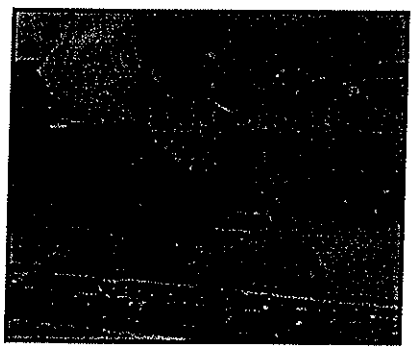
## Perrenial Allergens

***Important triggers of asthma***

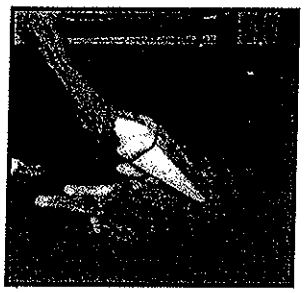
- Warm-blooded animals
- Cockroaches
- House dust mites
- Indoor molds



## How to Control asthma Triggers!!



## Questionably Effective Cat Allergen Control



## Terminating Dust Mites

- Encase bedding
- Wash bedding in hot cycle
- Carpet removal

## Cockroach Control Measures

- Caulk cracks and crevices
- Chemically treat cockroach runways
- Bait stations

## Cockroach Control Measures

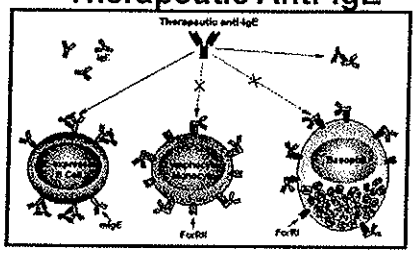
- Remove sources of food
- Store all food in sealed containers
- Reduce access to water (leaky pipes)

## New AsthmaTherapy: Omalizumab or "Anti-IgE"

## Omalizumab – Anti-IgE

- Recombinant humanized monoclonal anti-IgE antibody
- Binds IgE at the same site as FcεRI
- Decreases free serum IgE
- Is non-anaphylactogenic
- Does not fix complement

## The Binding Specificity of Therapeutic Anti-IgE




*Chang. Nature Biotech 2000, 18:157*

## Known Immunomodulatory Actions of Anti-IgE

- Decreases free IgE and FcεRI expression on basophils and dendritic cells
- Decreases basophil histamine release
- Decreases mast cell responsiveness

## Inner City Asthma Consortium

ICAC

- **Goals:**
  - Identify forms of immune-based therapy that are most likely to promote control and prevention of asthma
  - Design protocols that will evaluate immune-based therapies in the treatment of asthma in low income inner-city children
  - Determine both the mechanisms of immune-based therapies and the potential unique mechanisms associated with the pathogenesis of asthma in low income inner-city children via mechanistic studies

## Inner City Asthma Consortium (ICAC)

- Consists of 10 pediatric asthma centers across the country:
  - Baltimore
  - Boston
  - Chicago
  - Cleveland
  - Dallas
  - Denver
  - New York
  - Saint Louis
  - Tucson
  - Washington, DC
- Administrative center: Madison
- Data coordinating center: Rho; Chapel Hill,
- National Institute of Allergy and Infectious Diseases (NIAID)

## What we have learned from previous Inner City Asthma Studies...

- Cockroach allergy and exposure to high levels of this allergen may help explain the frequency of asthma-related problems in inner-city children (Rosenstreich et al, 1997 – National Cooperative Inner City Asthma Study - NCICAS)
- Home-based environmental remediation programs appear to offer an effective means of reducing asthma morbidity in this population (Morgan et al, 2004 – Inner City Asthma Study – ICAS)

## Inner City Anti-IgE Therapy for Asthma (ICATA) Rationale

- Children with asthma who live in the inner city have
  - Increased morbidity and mortality
  - High prevalence of sensitization to indoor allergens
  - Challenging environments with high levels of indoor allergens and irritants
  - Substantive barriers to adherence with complex medical regimens

## Inner City Anti-IgE Therapy for Asthma Rationale (cont.)

- Allergen-specific IgE is the fuel that drives allergic inflammation. The ICATA clinical study provided a unique opportunity to evaluate the spectrum of anti-inflammatory effects of omalizumab (anti-IgE) therapy of asthma
- A key question is the mechanism by which anti-IgE perturbs the allergic inflammatory response

## Background and Hypothesis

Because allergen sensitization and exposure is an important determinant of asthma severity and response to therapy, we hypothesized that the addition of omalizumab to guidelines-based treatment would improve disease control in allergic inner-city children with moderate-to-severe asthma and persistent symptoms.

## ICATA Clinical Study Overview

- Randomized, double-blind, placebo-controlled, parallel group efficacy and safety trial
- 500 inner-city children age 6-20 years old with moderate-to-severe allergic asthma (250/arm)
- Both arms received standardized specialist asthma care based upon NAEPP guidelines, including basic asthma education
- Treatment group received q2 or q4 week treatment with omalizumab
- Control group received placebo injection at similar intervals

## Enrollment characteristics

- 6 to 20 years of age with a diagnosis of persistent asthma
- Allergy to a perennial allergen
- Inner-city resident
- At recruitment, participants had uncontrolled asthma
- Weight and total serum IgE levels were suitable for omalizumab dosing

## Study Design

- Enrollment
  - Asthma control assessed
  - Using a Guidelines-based algorithm, treatment was begun or adjusted to achieve asthma control
- Randomization and treatment (60 weeks)
  - Following an adjustment of asthma medications during enrollment, participants were randomized to receive omalizumab or placebo every 2 to 4 weeks for 60 weeks

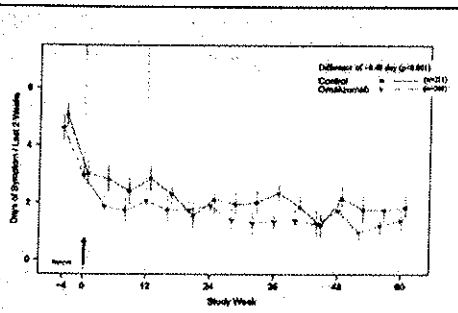
## Primary outcome – Days with asthma symptoms over last 2 weeks

- Wheezing, chest tightness or cough
- Sleep interruption
- Activity limitations

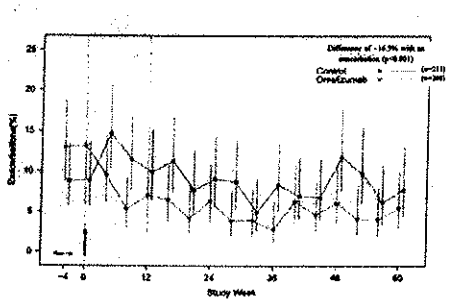
## Asthma control of participants at enrollment (n=419)

| | |
|---|---|
| • Days of asthma symptoms the previous 2 weeks | 4.9 ± 4.2 |
| • Childhood ACT® score in the last month (4 to 11 years) | 18.9 ± 4.1 |
| • ACT® score (12 years and over) | 18.8 ± 4.2 |
| • $FEV_1$ (% predicted value) | 92.1 ± 17.1 |
| • $FEV_1$/FVC | 77.1 ± 9.9 |
| • ≥ 1 Hospitalizations/past year | 25% |
| • ≥ 1 Unscheduled visits/ past year | 78% |

## The effect of omalizumab on the number of days with symptoms in last 2 weeks




## The effect of omalizumab on exacerbations



## Summary

- Omalizumab significantly improved asthma control in inner-city children with asthma who were receiving guideline-based treatment.
  - 25% reduction in days with asthma symptoms
  - 30% reduction in the percent of patients with an exacerbation
  - 15% reduction in ICS dose
  - Dramatically reduced the seasonal asthma exacerbation pattern
- No safety issues


## Asthma Management Pearls

- Have scheduled visits when well
- Perform routine PEFR or spirometry
- Err on side of overtreatment initially
- Don't be "steroidophobic"
- Don't forget about the nose

## Asthma Management Pearls

- Reinforce inhaler technique often
- Consider other diagnosis if poor response to treatment
- Intervene early in exacerbations
- Persistent asthma requires daily chronic therapy
- Simplify the treatment regimen

## PARTNERSHIP IN ASTHMA CARE

- Develop an Asthma Action Plan with the patient
- Fit the daily medication regimen into the patient's and family's routine
- Identify and address obstacles and concerns
- Ensure regular follow-up with the physician