Food and Respiratory Allergy in Ghana
Insights from population studies among children

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Background: Allergies in Ghana

- Studies indicate that allergies are on the rise in Ghana
- Two surveys conducted 10 years apart in children (aged 9-16 years) in one area showed an increase in markers of allergy

Exercise-Induced Bronchospasm

Skin Prick Test Reactivity

Addo-Yobo et al, Plos Med 2007
Distinct urban-rural differences in allergy outcomes

Within urban area differences in allergy outcomes based on socioeconomic status

Addo-Yobo et al., Plos Med 2007
Factors associated with the rural to urban gradient in allergy

- Decrease in infection
- Increase in pollution
- Increase in allergy
- Dietary changes (rural diet to fast-food)

Adapted from van Ree and Yazdanbakhsh, 2007
Objectives

i. To determine urban-rural differences in the prevalence of aero-allergy in Southern Ghana

ii. To determine urban-rural differences in the prevalence of food allergy in Southern Ghana

iii. To examine associations between parasitic worm infections and allergy outcomes
Study area and population

Greater Accra Region

School-based cross-sectional study
- 13 Schools
  - 8 Rural
  - 5 Urban
- Target age-range: 5-16 years
- N=2,331 recruited
Study Methodology: Allergic sensitization based on serum-specific IgE levels

ImmunoCap® /RAST

Allergen-specific IgE
- Mite (Der p)
- Cockroach (Bla g)
- Peanut (Ara h)

Sensitization cut-off: \( \geq 0.35 \text{ kU/L} \)
Study Methodology: Allergic sensitization by skin prick testing

Skin prick test positivity cut-off
Average wheal size ≥ 3mm

Allergen panel

- Negative control
- Mite extract
- Cockroach extract
- Peanut extract
- 6 fresh fruits
- Positive control

Aero-allergens
Food Allergens
Study Methodology: Reported Symptoms

• Standardized questionnaire administered to parents or guardians of study subjects

• Symptoms of asthma & other allergic disorders:
  • Adapted from the International Study of Asthma and Allergies in Childhood
    • Weinmayr et al, Allergy 2010
    • Weinmayr et al, Eur Respir J 2008

• Symptoms of adverse reactions to food:
  • Adapted from EuroPrevall study
    • Kummeling et al, Allergy 2009
    • Wong et al, Allergy 2009
    • Mills et al, Allergy 2007

• Demographic and socioeconomic parameters
Study Methodology: Parasitological assessment

**Urine**
- Urine filtration
- *S. haematobium*

**Stool**
- Kato-Katz
- Intestinal helminths
Results: Aero-allergy outcomes stratified by area (N=1385)

- **Specific IgE > 0.35 kU/L**
  - **Mite**
  - **Cockroach**

- **Skin Prick Test (Wheal Size > 3mm)**
  - **Mite**
  - **Cockroach**

- **Respiratory Symptoms (Yes)**
  - **Wheeze (12 months)**
  - **Asthma**

* * p < 0.05  
**  p < 0.01  
*** p < 0.001
Worm infection and Skin Prick Test reactivity

Logistic regression models adjusted for age, gender and area

Wald’s Test: * P<0.05
Worm infection and respiratory allergy symptoms

Logistic regression models adjusted for age, gender and area
Wald's Test : * P<0.05
Reported adverse reactions to food (N=1407)

Food Items

- Beans
- Pineapple
- Peanuts
- Okro
- Cassava
- Mango
- Kontomire
- Sorghum
- Nutmeg
- Melon
- Pawpaw
- Avocado
- Wheat
- Sweet Potato
- Fish
- Cow Milk
- Soybean
- Palm Nut
- Corn
- Hen’s egg
- Coconut
- Apple
- Banana
- Carrot
- Millet
- Rice
- Cocoyam
- Water yam
- Potato
- Shrimp
- Orange
- Tomato
- Wheat Flour
- Plantain

% Reported Reactions

- All children
- Rural children
- Urban children
Reported symptoms of adverse reactions to food (N=1407)

1 ‘Tingling/swelling = swelling of the mouth, lips or throat’
2 ‘Rash/itch = itching of the skin including nettle sting-like rash’
**Ghana and peanuts (groundnuts)**

- High peanut consumption
- Relatively few reports of adverse reactions to peanut
- Lack of avoidance of peanuts during pregnancy
- Early introduction of peanut as part of weaning foods
Peanut allergy outcomes among urban and rural children in Ghana

Specific IgE > 0.35 kU/L
N = 1328

Skin Prick Test > 3mm
N = 1396

Reported Symptoms (Yes)
N = 1372

Peanut Allergy Outcomes

Prevalence (%)

Rural Urban Rural Urban Rural Urban

23.6 9.7 1.8 2.1 2.1 0.6

* p < 0.05
** p < 0.01
*** p < 0.001
Subjects reporting adverse reactions to peanut (N=21)

Reported Peanut Symptoms (N=21)

- Diarrhoea/Vomiting
- Itching/Tingling Mouth
- Headaches
- Stiffness in joints
- Runny/stuffy nose
- Red/sore/runny eyes
- Difficulty swallowing
- Breathlessness
- Fainting/Dizziness
- Rash/Itch

Reaction time following ingestion (N=21)

Reaction Time

- Minutes
- Hours
- Days

Percentage (%)
Peanut allergy outcomes (complete data, N=1004)

- Peanut Specific IgE
  - IgE ImmunoCap®
  - Cut-off: >0.35 Ku/L

- Peanut SPT Reactivity
  - Cut-off: ≥ 3mm

Reported Symptoms to Peanut Questionnaire

- 170
- 13
- 5
- 4
- 0
- 0
- 8
Worm infection and peanut-specific IgE sensitization

Logistic regression model adjusted for age, gender and area
Wald’s Test :  *** P<0.001
Additional sera measurements in a subset (N=43):

- Specific IgE responses to purified peanut allergens Ara h 1, 2, 3 (seed storage proteins)
- Recombinant non-glycosylated allergen produced in an *E. coli* strain

![Graph showing specific IgE responses to peanut allergens](image)
Peanut-specific IgE: Cross-reactive carbohydrate determinants

Additional sera measurements in a subset (N=43)

- Specific IgE responses to bromelain as a marker of cross-reactive carbohydrate determinants (CCDs) which are carbohydrate epitopes on glycoproteins
**N-glycan induced IgE cross-reactivity**

- Indications of the presence of IgE recognizing epitopes common to both peanut and bromelain.

- Possible cross-reactivity due to N-glycan epitopes commonly found in plants and helminths.

![Graph showing correlation between CCD-specific IgE and Peanut-specific IgE](image)

- Core $\beta(1,2)$-xylose
- Core $\alpha(1,3)$-fucose
Inhibition of IgE binding to peanut by bromelain & Schistosoma SEA

- More than 80% inhibition with both bromelain and Schistosoma soluble egg antigen
- High levels of peanut-specific IgE as a result of carbohydrate cross-reactivity
Peanut-specific IgE: responses to recombinant Ara h 9

Additional sera measurements in a subset (N=43)

• Specific IgE responses to purified peanut allergen Ara h 9 (lipid transfer protein)

• Recombinant non-glycosylated allergen produced in an *E. coli* strain
Stripped basophil histamine release assay

- Basophils from Dutch non-atopic donor
- Stripped basophils from Dutch non-atopic donor
- Basophils re-sensitized with IgE from Ghanaian donor and then stimulated with an allergen

lactic acid treatment: removal of IgE
incubation with serum: sensitization with IgE

Source: Ronald van Ree
### Basophil histamine release - Ara h 9 & whole peanut

#### Donor #1
- **ID**: AB051
- **Area**: RURAL
  - IgE to whole peanut: 40.2 kU/L
  - IgE to CCD: 1.8 kU/L
  - IgE to rAra h 9: 72.8 kU/L

#### Donor #2
- **ID**: GR211
- **Area**: URBAN
  - IgE to whole peanut: 21.0 kU/L
  - IgE to CCD: 4.9 kU/L
  - IgE to rAra h 9: 77.4 kU/L
**Basophil histamine release - Ara h 9 & whole peanut**

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**IgE to whole peanut:** 40.2 kU/L  
**IgE to CCD:** 1.8 kU/L  
**IgE to rAra h 9:** 72.8 kU/L  
**SPT to peanut:** -  
**Reported Symptoms:** Yes

**IgE to whole peanut:** 21.0 kU/L  
**IgE to CCD:** 4.9 kU/L  
**IgE to rAra h 9:** 77.4 kU/L  
**SPT to peanut:** +  
**Reported Symptoms:** No
Conclusions

• Significant urban-rural differences in allergy outcomes

• Schistosoma infection negatively associated with mite SPT reactivity
  • Indications of a protective effect

• High levels of allergen-specific IgE as a result of carbohydrate cross-reactivity
  • Possible helminth involvement in inducing cross-reactivity

• Little evidence of IgE-mediated peanut allergy

• Biologically active IgE to Ara h 9 observed
  • Factors associated with Ara h 9 sensitization in Ghana are currently unknown
Schistosome infection is negatively associated with mite atopy, but not wheeze and asthma in Ghanaian Schoolchildren
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Food Allergy in Ghanaian Schoolchildren: Data on Sensitization and Reported Food Allergy
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Peanut-specific IgE antibodies in asymptomatic Ghanaian children possibly caused by carbohydrate determinant cross-reactivity
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