Appendix

Study Questionnaire

GLOFAL
Questionnaire for Allergic Diseases
Multi-Centre Study

Date : __ __/ __ __/ __ __ __ __ Country: *GHANA*
Name of Interviewer : __
Name of Recorder : __

A. Child's details

1. Name / ID number :__ __ __ __ __ __ __ __ __ __ __ __ __ __/ __ __ __ __ __
2. Date of birth / Age : __ __/ __ __/ __ __ __ __ [ ] year(s)
3. Place of Birth (including Region): __ __ __ __ __ __ __ __ __ __ __ __ __ _____
   [Country IF NOT Ghana]: __ __ __ __ __ __ __ __ __ __ __ __ __ ___
4. Ethnicity: __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ _
   [Country of Origin IF NOT Ghana]: __ __ __ __ __ __ __ __ __ __ __ __ _
5. Sex : [ ] Male [ ] Female
6. What is the position of this child in sib-ship? : __ __ __ __ of __ __ __ children
7. School information
   Class : __ __ __ __ __ __ __ __
   Name of school : __
   __
8. House information
   House Number : __ __ __ __ __ __ __ __
   Suburb/ Area : __ __ __ __ __ __ __ __
   Telephone : __ __ __ __ __ __ __ __

   GPS Readings
   a. Latitude : __ __ __ __ __ __ __ __
   b. Longitude : __ __ __ __ __ __ __ __
   c. Altitude : __ __ __ __ __ __ __ __
9. How far is the school from home (GPS reading)? : __ __ __ __ __ __ __ Km

10. How does the child get to school most of the time?

[ ] Walk
[ ] Bicycle
[ ] Taxi
[ ] Bus / Trotro
[ ] Private Car
[ ] Other, please specify __ __ __ __ __ __ __ __ __ __

B. Socio-economic Status and Environmental Factors.

1. Has the child lived in this town/village since he/she was born? [ ] Yes [ ] No

2. If you answered "no" where has the child lived before and for how long?

Area A In. __ __ __ __ __ __ __ __ __ **for**__ __ __ **month(s)** __ __ __ **Year(s)**
Area B In. __ __ __ __ __ __ __ __ __ **for**__ __ __ **month(s)** __ __ __ **Year(s)**
Area C In. __ __ __ __ __ __ __ __ __ **for**__ __ __ **month(s)** __ __ __ **Year(s)**
Area D In. __ __ __ __ __ __ __ __ __ **for**__ __ __ **month(s)** __ __ __ **Year(s)**

3. Who provides financially for this child?

[ ] Father and Mother
[ ] Father
[ ] Mother
[ ] Other, please specify: __ __ __ __ __ __ __ __ __ __ __ __ __

4. Occupation of person in question number 3: __ __ __ __ __ __ __ __ __ __ __
   Occupation of the spouse of this person: __ __ __ __ __ __ __ __ __ __ __ __ __

5. The highest level of formal education completed by:

Person (question number 3)
[ ] Primary/Elementary [ ] Middle school [ ] JSS [ ] SSS
[ ] O'level [ ] A' level [ ] Vocational/ Commercial
[ ] Training College [ ] Polytechnic/University
[ ] Other, please specify __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __

Spouse of this person
[ ] Primary/Elementary [ ] Middle school [ ] JSS [ ] SSS [ ]
O' level [ ] A' level [ ] Vocational/ Commercial
[ ] Training College [ ] Polytechnic/University
[ ] Other, please specify __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __

6. Who does this child live with (if different from response in question "3" above)?
[ ] Father and Mother
[ ] Father

[ ] Mother

[ ] Other, please specify: __ __ __ __ __ __ __ __ __ __ __ __ __

7. Occupation of person in question number 6: __ __ __ __ __ __ __ __ __ __ __ __
   Occupation of the spouse of this person: __ __ __ __ __ __ __ __ __ __ __ __ __ __

8. The highest level of formal education completed by:
   Person (question number 6)

[ ] Primary/Elementary [ ] Middle school [ ] JSS [ ] SSS
[ ] O'level [ ] A' level [ ] Vocational/ Commercial
[ ] Training College [ ] Polytechnic/University
[ ] Other, please specify __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __

Spouse of this person

[ ] Primary/Elementary [ ] Middle school [ ] JSS [ ] SSS
[ ] O'level [ ] A' level [ ] Vocational/ Commercial
[ ] Training College [ ] Polytechnic/University
[ ] Other, please specify __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __

9. The house in which the child lives is made primarily of :

[ ] Cement [ ] Wood [ ] Mud [ ] Other, please specify __ __ __ __ __

10. What is the main source of water supply to the home?

[ ] Pipe-borne [ ] Tanker (treated) [ ] Tanker (untreated)
[ ] River/ Stream [ ] Well/ Borehole
[ ] Other, please specify __ __ __ __ __ __ __ __ __ __ __ __ __

11. What is the type of toilet in the home?

[ ] Indoor WC [ ] Compound latrine [ ] Public latrine
[ ] Other, please specify __ __ __ __ __ __ __

12. The fuel mostly used at home for cooking is*(tick one):*

[ ] LPG [ ] Electricity [ ] Charcoal [ ] Firewood
[ ] Kerosene [ ] Other__ __ __ __ __ __ __

13. What kind of accommodation does the child live in?

[ ] Detached house [ ] Semi-detached [ ] Flat
[ ] Compound house [ ] Other, please specify__ __ __ __ __ __ __ __

14. How much money did your family spend on electricity in the past month?

¢ __ __ __ __ __ __ __ __ __
[ ] Respondent unable to estimate

15. How much money did your family spend on food in the past month?

¢ __ __ __ __ __ __ __ __ __
[ ] Respondent unable to estimate

C. ISAAC Core Questionnaires

C1 Core Questionnaire for Wheezing and Asthma

All questions are about problems which occur when this child <u>DOES NOT</u> have a cold or the flu

1. Has this child ever had wheezing or whistling in the chest?

[ ] Yes **[ ] No**

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

2. Has this child had wheezing or whistling in the chest in the past 12 months?

[ ] Yes **[ ] No**

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

3. How many attacks of wheezing has this child had in the past 12 months?

[ ] None
[ ] 1-3
[ ] 4-12
[ ] > 12

4. In the past 12 months how often, on average, has this child's sleep been disturbed due to wheezing?

[ ] Never woken with wheezing
[ ] Less than one night per week
[ ] One or more nights per week

5. In the past 12 months, has wheezing ever been severe enough to limit this child's speech to only one or two words at a time between breaths?

[ ] Yes **[ ] No**

6. In the past 12 months, has this child's chest sounded wheezy during or after exercise?

[ ] Yes **[ ] No**

7. In the past 12 months, has this child had a dry cough ***at night***, apart from a cough associated with a cold or chest infection?

[ ] Yes **[ ] No**

8. Has a doctor ever diagnosed your child as having asthma?

[ ] Yes **[ ] No**

9. If yes to question number 8, what is the name of the medicine(s) the doctor gave to your child?

Medicine(s) __

[ ] Cannot recall name of medicine

10. Has any member of this child's family ever had asthma?

[ ] Yes [ ]No [ ] No idea

11. If you answered "yes" to question 10, indicate relationship to child (*tick all that apply*)

[ ] Father
[ ] Mother
[ ] Brother or Sister
[ ] Father's __ __ __ __ __ __ __ __ __ (family member eg. sister, father)
[ ] Mother's __ __ __ __ __ __ __ __ __ (family member eg. sister, father)

C2 Core Questionnaire for Rhinitis/Hayfever

All questions are about problems which occur when this child <u>DOES NOT</u> have a cold or the flu.

1. Has this child ever had a problem with sneezing or a runny or blocked nose (nose problem) without cold or the flu?

[ ] Yes [ ] No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

2. Has this child had this nose problem in the past 12 months?

[ ] Yes [ ] No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

3. In the past 12 months, has this child's nose problem been associated with itchy-watery eyes?

[ ] Yes [ ] No

4. In which of the past 12 months did this nose problem occur? (please tick any which apply)

[ ] January
[ ] February
[ ] March
[ ] April
[ ] May
[ ] June
[ ] July
[ ] August
[ ] September
[ ] October
[ ] November
[ ] December
[ ] Rainy season
[ ] Dry season
[ ] Anytime
[ ] No idea

5. In the past 12 months, how much did this nose problem interfere with this child's daily activities such as school or play?

[ ] Not at all
[ ] A little
[ ] A Moderate
[ ] A lot

6. Has a doctor ever diagnosed your child as having allergic rhinitis / hay fever?

[ ] Yes [ ] No

7. If "Yes" to question number 6, what is the name of medicine the doctor gave your child?

Medicine(s) __

[ ] Cannot recall name of medicine

8. Has any member of this child's family ever had allergic rhinitis / hay fever?

[ ] Yes [ ] No [ ] No idea

9. If you answered "yes" to question 8, indicate relationship to child (*tick all that apply*)

[ ] Father
[ ] Mother
[ ] Brother or Sister
[ ] Father's __ __ __ __ __ __ __ __ __ (family member eg. sister, father)
[ ] Mother's __ __ __ __ __ __ __ __ __ (family member eg. sister, father)

C3 Core Questionnaire for Atopic Dermatitis/Eczema

Show pictures from the* "Observer's protocol for recording signs of visible flexural dermatitis"** ***to the respondent

1. Has this child ever had one or more skin problem(s) like in the pictures accompanied by an itchy rash which was coming and going for at least 6 months?

[ ] Yes, Picture number__ __ __ __ [ ]No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

2. Has this child ever had this skin problem (itchy rash) in the last 12 months?

[ ] Yes [ ] No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

3. Has this skin problem (itchy rash) at any time affected any of the following places: The folds of this child's elbows, behind the knees, in front of ankles, under the buttocks or around the neck, ears or eyes?

[ ] Yes [ ] No

4. How often, on average, has this child been kept awake at night by this itchy rash?

[ ] Never in the past 12 months
[ ] Less than one night per week
[ ] One or more nights per week

5. Did this rash clear completely at any time during the past 12 months?

[ ] Yes [ ] No

6. Has a doctor ever diagnosed your child as having allergic eczema/ atopic dermatitis?

[ ] Yes **[ ] No**

7. If yes to question number 5, what is the name of the medicine(s) the doctor gave to your child?

Medicine(s) __

[ ] Cannot recall name of medicine

8. Has any member of this child's family ever had allergic eczema/ atopic dermatitis?

[ ]Yes **[ ]No** **[ ]No idea**

9. If you answered "yes" to question 8, indicate relationship to child (*tick all that apply*)

[ ] Father
[ ] Mother
[ ] Brother or Sister
[ ] Father's __ __ __ __ __ __ __ __ __ (family member eg. sister, father)
[ ] Mother's __ __ __ __ __ __ __ __ __ (family member eg. sister, father)

D. Health concerns

1. When was the last time this child had any medical treatment?

[ ] < 1 month ago **[ ] 1 to 3 months ago**
[ ] 3 to 6 months ago **[ ]> 6 months**

2. What was the name of the medicine in '1' and for which condition was it given?

Medicine1__ __ __ __ __ __ __ __ __ __ Condition1 __ __ __ __ __ __ __ __ __
Medicine2__ __ __ __ __ __ __ __ __ __ Condition2 __ __ __ __ __ __ __ __ __
Medicine3__ __ __ __ __ __ __ __ __ __ Condition3 __ __ __ __ __ __ __ __ __

3. When did this child last have treatment for worm infection?

[ ] < 1 month ago **[ ] 1 to 3 months ago**
[ ] 3 to 6 months ago **[ ]> 6 months**
[ ] No idea

4. What was the name of the medicine used when this child was last treated for worm infection? __ __ __ __ __ __ __ __ __ __ __ __ __

[ ] Cannot recall name of medicine

5. Is there any smoker in your house

[ ]Yes **[ ]No**

6. If you answered "yes" to question 5, does this person smoke when the child is present?

[ ]Yes **[ ]No**

7. Is this child exposed to tobacco smoke outside your home?

[ ] Yes [ ] No [ ] No idea

8. Do you use groundnut oil for any other purpose (example as skin ointment)?

[ ]Yes [ ]No

E. Diet

For this section, please ask the respondent how frequently **the child** consumes each food item and the cooking method used to prepare the food item.

FOOD ITEM	FREQUENCY OF CONSUMPTION					COOKING METHOD			
Staples	**Daily**	**1x weekly (at least)**	**1x monthly (at least)**	**Every half year (at least)**	**Never**	**Boiling/ Steaming**	**Frying**	**Smoking/ Grilling/ Roasting**	**Other**
Rice	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Cassava	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Plantain	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Yam	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Maize/ Corn	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Other	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Meat/Protein Source									
Cattle (Beef)	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Sheep (Mutton)	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Goat (Chevron)	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Pig (Pork)	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Chicken	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Fish	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Other__ __ __ __ __ __ __	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Shellfish (Crab, shrimp etc)	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Snail	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Mushroom	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Beans	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Eggs	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Other__ __ __ __ __ __ __	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _

FOOD ITEM	FREQUENCY OF CONSUMPTION					COOKING METHOD			
	Daily	1x weekly (at least)	1x monthly (at least)	Every half year (at least)	Never	Boiling/ Steaming	Frying	Smoking/ Grilling/ Roasting	Other
Industrially processed oils									
Cooking oil (e.g. Frytol, Palmin)	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Other__ __ __ __ __ __ __	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Home-made oils									
Palm oil	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Palm Kernel oil	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Coconut Oil	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Groundnut oil	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Shea Butter	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Other__ __ __ __ __ __ __	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Evaporated Milk (eg. Ideal)	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Powdered Milk (eg Nido)	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Margarine (e.g. Blue Band)	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Cheese/Butter (e.g. Even, Laughing Cow)	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Ice-cream/ Yoghurt (e.g. Fanice or FanYogo)	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Groundnuts/ Peanuts	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Pastries (e.g. Cakes, pies,)	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Fresh fruits (e.g., orange)	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _
Fresh vegetables (e.g. salads, fresh ground pepper sauce)	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	__ __ __ __ _

F. Food Allergy

The following questions are about the child's reactions to food OTHER than reactions caused by food poisoning, illness or a bacterial infection such as cholera etc.

1. Has your child ever had adverse events (reactions) after food intake?

[ ] Yes **[ ] No**

If yes which food? __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __
__ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __
(Show list in **Table F2** if needed)

2. Has the child had any problems eating any other food or foods that not listed in **Table F2**?

If yes please list:

__ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __

__ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __

IF YOU HAVE ANSWERED "NO" TO QUESTION 1 & 2 PLEASE SKIP TO QUESTION 13

3. How old was the child when s/he had the first problem eating this food?

__ __ __ __ **year(s)**

4. How old was the child when s/he had the most recent problem eating this food?

__ __ __ __ **year(s)**

5. Has the child had this illness or trouble after eating this food?

[ ] Only once
[ ] 2-4 times
[ ] More than 4 times

6. Has the child avoided eating that food since the illness or trouble?

[ ] Yes **[ ] No**

7. Did this illness or trouble include any of the following? (please mark if yes)

Table F1

	Yes	No
Itching, tingling or swelling in the mouth, lips or throat	[ ]	[ ]
A rash, nettle sting-like rash or itchy skin	[ ]	[ ]
Diarrhoea or vomiting (other than food poisoning)	[ ]	[ ]
Runny or stuffy nose	[ ]	[ ]
Red, sore or running eyes	[ ]	[ ]
Difficulty swallowing	[ ]	[ ]
Breathlessness	[ ]	[ ]
Stiffness in your joints	[ ]	[ ]
Fainting or dizziness	[ ]	[ ]
Headaches	[ ]	[ ]

8. Has the child had any other symptoms?

[ ]Yes [ ]No

If yes, please describe __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __

9. How long after eating the food did the child start having the first symptom?

[ ] Minutes [ ] Hours [ ] Days

10. How long did it last?

[ ] Minutes [ ] Hours [ ] Days

11. Did the child receive any treatment?

[ ]Yes [ ]No

12. If yes for question number 11, what was the name of medicine given?

__ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __

13. Have you ever been told by a doctor that the child has a food allergy?

[ ]Yes [ ]No

14. Say approximately how often the child eats the following foods, and whether or not s/he avoids them because they make him/her ill:

Table F2

Food	Any Reaction		How often does the child eat this food (in season) *Tick one column only*					Does the child avoid this food because it makes him/her ill?	
	Yes	No	Most Days	Most weeks	Most months	Rarely	Never	Yes	No
Cow's milk	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Hen's eggs	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Fish	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Shrimp	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Groundnuts	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Pineapple	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Banana	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Apple	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Cassava	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Soybean	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Mango	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Pawpaw	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Plantain	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Coconut	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Wheat	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Sweet potato	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Potato	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Sorghum	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Millet	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Carrot	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Avocado	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Beans	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Tomato	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Orange	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Palm Nut	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Corn	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Melon	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Rice	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Water Yam	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Cocoyam	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Kontomire	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Okro	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Flour	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Nutmeg	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Other	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]

G. Early Life factors

*For the following questions please ask to see the **child's weighing card**.*

Is the child's weighing card available? [ ] Yes [ ] No

1. Was your child born prematurely?
[ ] Yes [ ] No

2. If Yes, how many months premature?
_____ (in months)

3. What was your child's weight at birth?_____ kg
Date Recorded ___/___/___

4. After birth, when did your child START breastfeeding:
[ ] After Hours [ ] After Days [ ] After Weeks

5. For how long was your child breast-fed?
Duration_____ (in months)

6. For how long was your child fed with ONLY breast-milk?
Duration____(in months)

7. What was the first food OTHER than breast-milk given to your child?
Food_____ at what age? _____ (in months)

8. Was your child breast-fed by anyone OTHER than his or her mother at any point?
[ ] Yes [ ] No

9. What were the reasons that your child was stopped breastfeeding?
Please state these reasons:

_____
_____
_____

10. Did your child receive the following immunizations: (**Please Verify with Child's Immunization Record**)

	No	Yes	Not Sure
Oral Polio Vaccine (OPV)			
Bacillus Calmette Guérin (BCG)			
Diphtheria Pertussis Tetanus (DPT)			
Yellow Fever			
Measles			

Other Immunizations, please state: _____
_____

11. In your child's first 2 years of life, were you told by a health worker such as a doctor or nurse that your child suffered from any of the following? :

	No	Yes	Cannot Recall
Respiratory infection such as Pneumonia or Bronchiolitis			
Bacterial Meningitis			
Worm infection			
Measles			
German Measles (Rubella)			
Hepatitis A			

Other Diseases/Infections, please state:

_____

_____

_____

12. In your child's first 2 years of life, did he or she attend a crèche or nursery?

[ ] Yes **[ ] No**

Summary

Helminth Infections and Allergies in Ghana

Over the past few decades, there has been a dramatic rise in the prevalence of allergic disorders worldwide especially among children. This global increase has been linked to improved hygiene, better standards of living and fewer childhood infections. Infections in childhood are thought to be an essential part of the education of a developing immune system. In fact, immune function evolved in pathogen-rich environments to ensure a balance was maintained between strong effector mechanisms that counter pathogens and regulatory mechanisms that modulate these effector responses to prevent excessive inflammation. These regulatory mechanisms have been exploited by some micro-organisms and parasites to their own benefit. For example, chronic infections with parasitic worms known as helminths have been shown to induce such regulatory mechanisms which down-modulate the host's immune system and ensure the worm's own survival. Individuals with chronic helminth infections have also been shown to be less responsive to vaccines, to self-antigens and to harmless antigens that induce allergic reactions known as allergens. Consequently, through their ability to induce immune hypo-responsiveness, chronic helminth infections may protect against allergic disorders and autoimmunity.

The work highlighted in this thesis explores the complex relationship between helminth infections and allergies among children in Ghana, a rapidly urbanizing country where helminths are still prevalent. Recent studies indicate that allergies are on the rise in Ghana but there is little information on the relationship between helminth infections and allergies among Ghanaian schoolchildren. The study described in this thesis was a large cross-sectional investigation of children aged 5 to 16 years attending schools in urban and rural areas of the Greater Accra Region of southern Ghana.

Chapter 1 provided a general introduction to the research topic of the thesis and the overall objectives. A brief description of the study population and study area was also outlined in this chapter.

In Chapter 2, the relationship between current helminth infection and allergy outcomes was examined in detail. Allergy outcomes were specific immunoglobulin E (IgE) antibodies to house dust mite and cockroach allergens, skin prick test reactivity to these same allergens and information on reported wheeze and asthma. We observed that helminth infections were more prevalent among rural compared to urban children and that infection with the waterborne helminth *Schistosoma* was inversely associated with skin prick test reactivity to house dust mite. At the same time, increasing body mass index was positively associated with skin prick test reactivity to house dust mite. No associations were observed between helminth infections and reported symptoms of allergy (current wheeze and asthma). Findings outlined in this chapter suggest that schistosome infection may play a role in protection against mite skin prick test reactivity in our study population.

In Chapter 3, food allergy was examined among Ghanaian children for the first time. Adverse reactions to food determined by questionnaire were analyzed along

with skin prick test reactivity to peanut and six fruits available locally in Ghana. The most reported adverse reaction to food was to beans followed by pineapple and peanut. The most prevalent skin prick test responses were against pineapple and peanut. A case-control study was performed in a subset of those who were skin prick test positive to food allergens (cases) and in controls that were skin prick test negative. For all study participants in this matched case-control study, IgE antibodies to the food allergens that elicited the SPT responses in the cases were measured. Reported adverse reactions to food among cases and matched controls were also assessed. A good association was observed between elevated IgE antibodies against specific food allergens and corresponding SPT responses and this association was stronger among urban compared to rural children. Overall, the study demonstrated the importance of IgE-mediated adverse reactions to food in Ghanaian children and how notable urban-rural differences in the manifestations of food allergy outcomes existed.

The focus of Chapter 4 was on peanut allergy among children in Ghana. This particular allergy was of interest because peanut consumption in Ghana is known to be high but there are few reports of adverse reactions to peanut in this country. For this investigation, the outcomes used to assess peanut allergy were reported adverse reactions to peanut and peanut sensitization based on serum specific IgE levels as well as skin reactivity. Among study participants, elevated levels of IgE antibodies against whole peanut extract were observed but these levels did not translate into skin prick test reactivity or reported symptoms of peanut allergy. In addition, a strong association was seen between being infected with *Schistosoma haematobium* and IgE antibodies against whole peanut extract. Given this relationship, we went on to characterize the nature of peanut-specific IgE antibodies in a subset of study participants. This was done by examining whether antibodies directed against whole peanut extract would also recognize purified (recombinant) peanut allergen components that are associated with peanut allergy in developed countries. In addition, we also investigated whether peanut-specific IgE would recognize bromelain which is used as a marker of cross-reactive carbohydrate determinants (CCDs). CCDs are carbohydrate structures that are shared by allergenic extracts from different sources ranging from plants to insects and can also be found in helminths. We observed that IgE levels to the component peanut allergens were very low but IgE against bromelain was very high. In addition, IgE against whole peanut extract could be inhibited by bromelain as well as by soluble egg antigen from *S. haematobium* and showed low biological activity. The investigation outlined in Chapter 4 demonstrated that IgE against CCDs, which was possibly induced by past or current *S. haematobium* infection, may account for high levels of IgE to peanut seen among Ghanaian children. These IgE antibodies to peanut had poor biological activity which was supported by the fact that we found no evidence of IgE-mediated peanut allergy among our study population.

The association between immune response at the cellular level and allergy was addressed in Chapter 5. In this chapter, skin prick test reactivity to house dust mite was

used as a marker of allergy. Immune responsiveness described in Chapter 5 was based on cytokine responses determined by *in vitro* whole blood culture assays. The study was performed among a subset of children who were skin prick test positive for house dust mite and negative controls. Overall, we observed enhanced innate and adaptive cellular immune responsiveness associated with house dust mite skin prick test reactivity.

In the previous chapters, notable urban-rural differences were observed when it came to helminth infections and allergy outcomes. Therefore, in Chapter 6, we addressed whether there were significant differences in the gene expression profiles of children in our study population that resided in urban and rural areas. In a subset of participants attending a rural school, an urban low socioeconomic status (SES) school and an urban high SES school, whole blood samples were used to measure the expression of genes related to immune activation and regulation. We found significant urban-rural differences in the expression of genes including the one coding for the regulatory cytokine interleukin (IL)-10. Contrary to expectations, current helminth infection did not explain elevated IL-10 gene expression in the rural area. Moreover, we observed that underlying genetic differences did not fully account for urban-rural variations when it came to IL-10 gene expression. We concluded that past helminth infection or other infections may have played a role in elevated IL-10 expression in the rural area. There were also notable gene expression differences between children attending the two urban schools included in this study. Specifically, the expression of genes coding for receptors involved in the recognition of environmental microbes and pathogens was higher among children attending the urban high SES school compared to the urban low SES school. We speculated that specific lifestyle factors may have had a suppressive effect on the expression of genes involved in the recognition of environmental microbes and pathogens in our study population. This chapter highlighted how immune gene expression patterns are strongly influenced by environmental determinants which may explain the effects of urbanization on health outcomes.

Chapter 7 provided a review of the recent literature on helminth infections and allergies in childhood based on observations from population studies. The insights in this review covered topics ranging from associations in population studies, the effect of anthelmintic treatment on allergic responses, IgE cross-reactivity induced by helminths and an examination of immune mechanisms underlying the relationship between helminth infections and allergies.

The main findings of the thesis were summarized and discussed in Chapter 8 and placed within the context of other population studies. Overall, research into the relationship between helminths and allergies in Ghana has provided insights into immune responsiveness, IgE cross-reactivity as well as insights into variations in allergy phenotypes/outcomes in different geographical locations within one region of Ghana. Future studies are needed to build on these findings to generate tools to diagnose, treat and prevent allergic disorders in developing countries such as Ghana where these conditions are emerging as problems of public health importance.

Nederlandse Samenvatting

Worminfecties en allergieën in Ghana

Het aantal mensen met allergische aandoeningen is de laatste paar decennia wereldwijd dramatisch toegenomen, in het bijzonder bij kinderen. Deze wereldwijde toename wordt toegeschreven aan verbeteringen in hygiëne, levensomstandigheden en een afname van infecties in de kindertijd. Er wordt verondersteld dat infecties in de kindertijd essentieel zijn voor de ontwikkeling van het immuunsysteem. Het immuunsysteem is geëvolueerd in een omgeving rijk aan potentiele ziekteverwekkers, waardoor een balans kon ontstaan tussen sterke afweerreacties die ziekteverwekkers bestrijden en tolerantieprocessen die buitensporige reacties van het immuunsysteem tegen onschuldige stoffen moeten voorkomen. Deze tolerantieprocessen worden door sommige micro-organismen en parasieten uitgebuit. Chronische infecties door parasitaire wormen kunnen bijvoorbeeld tolerantieprocessen in werking stellen die het immuunsysteem van de gastheer onderdrukken en daarmee de overleving van de parasiet veiligstellen. Mensen met een chronische worminfectie reageren daardoor minder goed op vaccins, lichaamseigen stoffen (betrokken bij auto-immuunziekten) en allergenen (betrokken bij allergieën). Als gevolg van deze versterkte tolerantieprocessen kunnen chronische worminfecties mogelijk bescherming bieden tegen auto-immuniteit en allergische aandoeningen.

Dit proefschrift onderzoekt de complexe relatie tussen worminfecties en allergieën bij kinderen in Ghana. Ghana is een land dat snel verstedelijkt en waar parasitaire wormen nog veel voorkomen. Recente studies tonen aan dat het aantal allergische aandoeningen toeneemt in Ghana, maar er is weinig bekend over de relatie tussen worminfecties en allergieën bij Ghanese schoolkinderen. De resultaten die in dit proefschrift worden beschreven zijn gebaseerd op een omvangrijk cross-sectioneel onderzoek onder schoolkinderen in de leeftijd van 5 tot 16 jaar, woonachtig in stedelijke en plattelandsgebieden in Groot-Accra in het zuiden van Ghana.

Hoofdstuk 1 bevat een algemene inleiding tot het onderzoeksonderwerp en de algemene doelstellingen van het proefschrift. Daarnaast worden de studiepopulatie en het gebied van de studie beschreven.

In hoofdstuk 2 wordt de relatie tussen worminfecties en allergieën in detail onderzocht. Om te bepalen of er sprake is van allergie hebben we de volgende parameters onderzocht: specifieke immunoglobuline E (IgE) antilichamen tegen huisstofmijt- en kakkerlakallergenen, huidpriktestreactiviteit op dezelfde allergenen en zelf-gerapporteerde gegevens over piepende ademhaling en astma. De resultaten wezen er op dat worminfecties meer voorkomen bij plattelandskinderen dan bij stadskinderen. Ook bleken infecties met *Schistosoma* geassocieerd met lagere huidpriktestreactiviteit op huisstofmijtallergenen. Er werden geen associaties gevonden tussen worminfecties en gerapporteerde symptomen van allergie (piepende ademhaling en astma). De bevindingen van dit hoofdstuk suggereren dat schistosomiasis een beschermende werking kan hebben tegen een positieve huisstofmijt-huidpriktest in onze studiepopulatie.

Voor het eerst is voedselallergie bij Ghanese kinderen onderzocht, en dit is beschreven in hoofdstuk 3. Overgevoeligheidsreacties op voedsel zijn vastgesteld met een vragenlijst en met huidpriktestreactiviteit op pinda's en zes fruitsoorten aanwezig in Ghana. De meest gemelde voedselreacties waren reacties na het eten van bonen, gevolgd door reacties na het eten van ananas en pinda's. In een case-control onderzoek is een deel van de kinderen met positieve reacties op de huidpriktest vergeleken met een controle groep waar geen reacties waren waargenomen. Bij alle kinderen werden IgE antilichamen tegen de voedselallergenen gemeten. Ook werden gerapporteerde overgevoeligheidsreacties tegen voedsel vastgelegd. Er werd een duidelijke associatie gevonden tussen IgE antilichamen tegen specifieke voedselallergenen en de bijbehorende huidpriktestreacties. Deze associatie was sterker bij stadskinderen dan bij plattelandskinderen. Dit onderzoek heeft het belang aangetoond van IgE-gemedieerde overgevoeligheidsreacties op voedsel in Ghanese kinderen en dat er aanzienlijke verschillen bestaan tussen de stad en het platteland met betrekking tot voedselallergieën.

In hoofdstuk 4 ligt de nadruk op pinda-allergie bij Ghanese kinderen. Het interessante is dat pindaconsumptie in Ghana hoog is, terwijl er weinig nadelige gevolgen van pindaconsumptie gerapporteerd zijn. Als maat voor allergische reactiviteit is in dit onderzoek zowel gebruik gemaakt van zelf-gerapporteerde klachten na het eten van pinda's als serum specifiek IgE concentraties en huidreactiviteit als maat voor sensitisatie voor pinda. Onder de studiedeelnemers zijn verhoogde concentraties van IgE-antilichamen tegen pinda-extract gevonden, maar deze verhoging vertaalde zich niet in hogere huidpriktestreactiviteit of zelf- gerapporteerde klachten van pinda-allergie. Bovendien werd er een sterke associatie waargenomen tussen infectie met *Schistosoma haematobium* en IgE-antilichamen tegen pinda-extract. Vanwege deze associatie hebben we van een aantal kinderen de eigenschappen van de pinda-specifieke IgE-antilichamen gekarakteriseerd. We hebben onderzocht of de antilichamen tegen pinda-extract ook zuivere (recombinant) pinda-allergenen (die geassocieerd zijn met pinda-allergie in Westerse landen) konden herkennen. We hebben ook onderzocht of bromelaïne door pinda-specifiek IgE herkend werd. Bromelaïne wordt gebruikt als een marker voor CCD's ('cross-reactive carbohydate determinants'). CCD's zijn suikerstructuren die een gemeenschappelijk onderdeel zijn van allergeenextracten van verschillende bronnen, variërend van planten tot insecten en wormen. Wij vonden dat de IgE concentraties voor zuivere pinda-allergenen heel laag waren, maar IgE concentraties voor bromelaïne juist erg hoog. Bovendien kon de binding van deze IgE tegen pinda-extract door bromelaïne en ook door oplosbaar ei-antigeen van *S. haematobium* onderdrukt worden en vertoonde het weinig biologische activiteit. Het onderzoek in hoofdstuk 4 toont aan dat IgE's tegen CCD's, die mogelijk door eerdere of huidige *S. haematobium* infecties opgewekt zijn, de hoge niveaus van IgE tegen pinda's in Ghanese kinderen zouden kunnen verklaren. Deze IgE-antilichamen tegen pinda hadden een beperkte biologische activiteit, wat overeenkomt met het gebrek aan IgE-gemedieerde pinda-allergie in onze studiepopulatie.

De associatie tussen allergie en immuunreactiviteit op cellulair niveau wordt in hoofdstuk 5 onderzocht. In dit hoofdstuk werd allergie gemeten met huidpriktestreactiviteit op huisstofmijt. Immuunreactiviteit werd gemeten met cytokinereacties in *in vitro* volbloedkweken. Het onderzoek werd gedaan met kinderen die positieve huidpriktestreacties hadden tegen huisstofmijt en met een controle groep die geen reacties vertoonde. In kinderen met een positieve huidpriktestreactie vonden we een versterkte cellulaire immuunrespons.

In de voorgaande hoofdstukken zijn er opvallende verschillen tussen stads- en plattelandskinderen waargenomen met betrekking tot worminfecties en allergieën. In hoofdstuk 6 hebben we daarom onderzocht of er significante verschillen waren in genexpressie-profielen van stads- en plattelandskinderen in onze studiepopulatie. Bloedmonsters van kinderen van een plattelandsschool, en in een stedelijk gebied van een school met een lage sociaaleconomische status (SES) of juist een hoge SES werden gebruikt voor het meten van de expressie van genen gerelateerd aan immuunactivatie en immuunregulatie. We hebben significante verschillen tussen de stad en het platteland gevonden in genexpressie, onder andere voor het gen dat codeert voor de tolerantie-opwekkende signaalstof interleukine (IL)-10. Tegen onze verwachtingen in kon de verhoogde IL-10 genexpressie niet verklaard worden door huidige worminfecties in de plattelandsgebieden. Hieruit hebben we geconcludeerd dat eerdere worminfecties, of andere infecties, mogelijk een rol hebben gespeeld in de verhoogde IL-10 expressie in het plattelandsgebied.

In deze studie zijn ook opvallende verschillen gevonden in genexpressie tussen kinderen van de twee scholen uit het stedelijke gebied. De genexpressie van receptoren die te maken hebben met herkenning van microben en ziekteverwekkers was hoger bij kinderen van de school met hoge SES, vergeleken met kinderen van de school met lage SES. Wij speculeren dat specifieke levensstijlfactoren in onze studiegroep mogelijk een onderdrukkende werking hebben gehad op de expressie van genen die betrokken zijn bij herkenning van microben en ziekteverwekkers. Dit hoofdstuk benadrukt dat expressiepatronen van genen van het immuunsysteem sterk beïnvloed kunnen worden door omgevingsfactoren en dat dit de invloed van verstedelijking op gezondheid zou kunnen verklaren.

Hoofdstuk 7 geeft een overzicht van recente publicaties over worminfecties en allergieën tijdens de kindertijd, gebaseerd op bevindingen van populatiestudies. Dit overzichtsartikel behandelt de volgende onderwerpen: associaties in populatiestudies, het effect van anti-wormbehandeling op allergische reacties, IgE kruisreactiviteit veroorzaakt door wormen en immuun-mechanismen die ten grondslag liggen aan de relatie tussen wormen en allergieën.

De belangrijkste bevindingen van dit proefschrift worden in hoofdstuk 8 samengevat, bediscussieerd en in de context van populatiestudies geplaatst. Het onderzoek naar de relatie tussen worminfecties en allergieën in Ghana heeft inzichten opgeleverd over immuunreactiviteit, IgE kruisreactiviteit en variatie in de symptomen bij allergische

aandoeningen in verschillende geografische regio's in Ghana. Toekomstige studies zijn nodig om voort te bouwen op deze bevindingen, zodat methoden kunnen worden ontwikkeld om allergische aandoeningen te diagnosticeren, behandelen en voorkomen in ontwikkelingslanden zoals Ghana, waar zulke aandoeningen een steeds belangrijker maatschappelijk gezondheidsprobleem worden.

Curriculum Vitae

Abena Serwaa Amoah was born in Roma, Lesotho to Ghanaian parents on 8 February 1977. She completed her secondary school education in Swaziland at Waterford Kamhlaba, United World College of Southern Africa. In 2000, she graduated from Mount Holyoke College in the United States with a bachelor's degree in biological sciences and a minor in anthropology. Following her undergraduate training, Abena worked for two years as a clinical research assistant at Rockefeller University in New York City in the Laboratory of the Biology of Addictive Diseases where she was part of a research team determining neuroendocrine function in individuals with illicit drug addictions. At the end of 2002, Abena relocated to Ghana to gain experience in biomedical research in the tropics. She started with an internship in the Department of Parasitology at Noguchi Memorial Institute for Medical Research (NMIMR) in Accra where she was involved in a new project examining the association between parasitic infections and allergic diseases in Ghanaian children. In 2005, she attained a master's degree in Epidemiology from London School of Hygiene and Tropical Medicine that was funded by the Wellcome Trust. Abena then returned to Ghana and continued to work at NMIMR coordinating field studies for a number of multi-centre studies funded by the European Union that examined parasitic infections and immune responses in Ghana. Her PhD training was a result of ongoing collaborative projects between the Department of Parasitology, Leiden University Medical Center and the Department of Parasitology, NMIMR. Upon completion of her PhD studies, she hopes to continue with research focused on parasitic infections and non-communicable diseases in developing countries.

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1. Meurs L, Mbow M, Boon N, Vereecken K, **Amoah AS**, Labuda LA, Dieye TN, Mboup S, Yazdanbakhsh M, Polman K. Cytokine Responses to Schistosoma mansoni and Schistosoma haematobium in Relation to Infection in a Co-endemic Focus in Northern Senegal. *PLOS Neglected Tropical Diseases* (2014) Aug 7;8(8):e3080.
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