

PREVALENCE AND MORTALITY

High Asthma Prevalence and Associated Factors in Urban Malagasy Schoolchildren

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Introduction. Studies about bronchial asthma in Africa are impeded by the dearth of reliable data for the vast majority of countries on the continent. This study was conducted to establish the first epidemiological data concerning bronchial asthma in urban Malagasy schoolchildren. **Methods.** From three public and five private schools 1236 students aged 7–14 years were recruited and examined using a modified International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. In a subgroup of 111 schoolchildren from two schools, lung function tests were conducted together with bronchodilator response (BDR) to establish reversible obstruction (change in FEV1 $\geq$ 12%). **Results.** The overall prevalence of wheezing in schoolchildren was 25.2%, with strikingly more wheezing in children attending private schools than public schools ($p = .0012$). The risk was diminished in students with older siblings ($p < .03$), but was not affected by other variables like smoking habits at home, body mass index, or cooking fuel. In the schools where BDR was performed, we found a point prevalence for reversible bronchial obstruction of 9% through lung function tests. **Conclusion.** Bronchial asthma is of great relevance for schoolchildren living in urban Madagascar. Socioeconomic factors and air pollution seem to have a major impact in addition to the number of older siblings.

Keywords Africa, lung function, pollution, poverty, socioeconomic

INTRODUCTION

Bronchial asthma is a chronic inflammatory disorder of the lower airways affecting over 300 million people worldwide (1). As such, it is one of today's most significant diseases causing disability-adjusted life years (DALY) for people affected (2). While awareness of bronchial asthma has grown in industrial countries over the past decades, research investigating its prevalence in African children in particular is scarce and the condition remains greatly underrecognized (3–5).

Although limited, data on asthma and allergy prevalence rates for some African countries have been reported since the early 1990s and were established by the International Study of Asthma and Allergies in Childhood (ISAAC) (4–6). In its third iteration, ISAAC found asthma prevalences in African children to range between 2.6% in Ethiopia and 21.5% in Reunion Island (6, 7). While these levels are substantially lower in comparison to most industrialized countries, it is notable that prevalence on the African continent increased by 0.16% annually during the 10 years following the first ISAAC assessment in 1994.

Recent research moreover suggests that reported prevalence rates may be less accurate than assumed because children suffering from bronchial asthma are often misdiagnosed as suffering from pneumonia or not diagnosed at all—in developing as well as in industrialized countries (8–14).

Both clinical conditions often present with similar and overlapping symptoms, making a correct diagnosis difficult, especially in children and under tenuous health conditions.

Specifically, due to the high mortality rate associated with pneumonia, research focuses mainly on triggers such as bacteria, while bronchial asthma has received inadequate attention as a potential risk factor or contributor to the former (2, 15–21).

This study concentrates on Madagascar. It presents a particularly interesting country for investigating the possible significance of bronchial asthma because the effects of the human immunodeficiency virus (HIV) in exacerbating mortality rates associated with pneumonia are negligible (16, 22, 23). Despite the low prevalence of HIV, however, pneumonia as one complication of bronchial asthma remains the leading cause of death for Malagasy children (24).

Even though some relevant data are available (25), the impact of bronchial asthma on the health of African children is still not known to the full extent. Furthermore, it is unclear whether this disease affects children not only by causing breathing abnormalities but also by facilitating the onset of pneumonia and thereby increasing morbidity substantially.

In order to investigate whether bronchial asthma is a possible contributor to the high mortality rate in children, it is crucial to establish its prevalence in African children (18). This study focuses on Malagasy children who grew up in an urban environment and, Madagascar being one of the least developed countries in the world, have a relatively low socioeconomic status (SES). The urban environment,

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low SES, and associated challenges such as air pollution and diet are identified as risk factors increasing the likelihood of developing asthma or other respiratory conditions (25, 26).

Therefore, this study also focuses on risk factors and their correlation with asthma prevalence in urban Malagasy children by comparing children with wheezing to those without wheezing ever. Since these children are exposed to many risk factors, it is expected that they exhibit a greater prevalence than their African counterparts.

METHODS

Participants

Eight schools from central Antananarivo with high exposure to traffic air pollution were included in this study. From three public and five private schools in Antananarivo, 1236 children, aged 7–14 years, participated in this study. They were on average 10.31 years old (SD 1.55), 134.9 cm tall (SD 11.9), and weighed 29.4 kg (SD 9.7) with 51% being female. From the study group, 59% attended public and 41% private schools. This ratio was chosen to reflect the relative share of children attending public and private schools in Madagascar. Around 30% of the Malagasy population is living in the capital Antananarivo (22). The vast majority belong to the Merina tribe, which is predominant in the central region of Madagascar and of mainly Polynesian heritage, and settled in Madagascar long before people from the African continent came to this island (27). The city of Antananarivo is about 1300 m above sea level.

All participating children had no known underlying medical illness as determined by one of three physicians. Of these children, a total of 1093 had a valid lung function. In two of the eight schools participating, we did bronchodilator response (BDR) in all of the children ($n = 111$).

Written parental consent and ethical approval from the Ethical Committee of the Ministry for Public Health were obtained prior to starting this study. The cross-sectional study was conducted in the period from April to November 2009.

Anthropometric Data

Standing height was measured without shoes, with the child standing with the back to a wall in the classroom. It was recorded to the nearest millimeter. Weight was taken with light clothes and without shoes (Seca™ 254, Hamburg, Germany).

Lung Function

Spirometry was performed with KokoLegend Spirometer (Koko™ Legend, nSpire Health Inc., Longmont, CO, USA) according to the ATS/ERS criteria with the children in an upright position (28).

BDR was performed in every child presenting a pathologic spirometry with salbutamol (two puffs of 100 µg salbutamol) in two of the schools (school 1: *Baby*

Bercail, Cité Perrier; school 2: *Mme. de Seigne*, Ambohitatovo), both situated in Metro-Antananarivo with 111 students in total. A positive BDR was defined as a change in FEV1 $\geq 12\%$.

Questionnaire

The ISAAC questionnaire was completed in French using only the questions related to respiratory symptoms and environmental questions. In addition we asked further questions relating the regional environmental factors important for children in Madagascar with respiratory diseases. The interview was conducted by one study nurse. Most children and parents required translation of the questionnaire into Malagasy, the predominant language spoken in the highland of Madagascar, as many of them are not fluent in French.

Statistical Analysis

All statistical analyses were performed in a descriptive manner after extensive data plausibility checks. Due to the study design, individual data queries were not possible. Thus, all individual patient data records with grossly implausible data, especially obviously invalid lung function measurements, were treated as missing for the purposes of this analysis.

Continuous variables were analyzed by means of the usual statistical characteristics mean, standard deviation, median, minimum, and maximum, whereas categorical variables were analyzed in terms of absolute values and proportions.

A multivariate regression analysis was performed to assess the influence of respective demographic and social variables on the existence of bronchial asthma for taking into account possible confounding.

Separate simple linear regression functions were fitted to obtain equations for normal lung function values (FEV1 and FVC). Regression coefficients for each lung function parameter were estimated in two separate simple linear regression models, one for each sex, after log-transformation (natural logarithm) of body height and the respective lung function parameter. These coefficients were subsequently transformed back to their original scale for a more straightforward interpretation and use of the resulting normal equations. The simple linear log-transformed regression functions were chosen in order to allow for a straightforward comparison with published models and the concerned populations (29).

Statistical calculations were performed using SAS®, version 9.1 (SAS Institute Inc., Cary, NC, USA), and figures were created using Microsoft Office Excel® 2007.

RESULTS

As expected in light of growing poverty in Madagascar we found body mass indices (BMIs) to be generally low, with a mean of 15.9 kg/m² (SD 2.95). None of the children ever had an inhalation therapy.

TABLE 1.—Demographic characteristics.

Patients		
Total	1236	100%
Female	639	51.6%
Male	597	48.4%
School		
Public	735	59.4%
Private	501	40.6%
Wheezing		
Ever	311	25.2%
Last 12 months	112	9.1%
Cooking fuels ^a		
Charcoal	1051	85.0%
Gas	345	27.9%
Electricity	93	7.5%
Smokers at home	691	55.9%

^aMore than one answer possible.

Questionnaires from all 1236 children could be obtained for the study. Of these 1236 children, 311 (25.2%) children reported ever wheezing and 112 (9.1%) respondents recalled a wheezing episode in the last 12 months (Table 1).

Of 1093 healthy children from all eight schools presenting an analyzable lung function, only 58 (5.3%) lived in a single-child family, whereas, on average, they had 2.4 siblings (1.3 older and 1.1 younger siblings) with a maximum of 12 siblings. We compared those children who reported ever wheezing in the questionnaire ($n = 311$) with others without an indication of bronchial asthma ($n = 782$) in a multivariate analysis (Table 2). A high position in sibship was associated with a lower risk for bronchial asthma (OR 0.70, 95% CI 0.51–0.98; $p = .038$). All other variables included in this analysis showed no statistically significant influence on asthma. In particular, no positive connections could be confirmed between the suspicion of asthma (“wheezing”) and smoking in the family, attending a private versus a public school, or using charcoal in an open fire as the means of cooking (90% of the households) versus gas and electricity (5%). Even a higher BMI was not correlated to asthma prevalence.

In the two schools, where all children ($n = 111$) were tested with spirometry and BDR in case of a conspicuous lung function or questionnaire information, 10 children showed a positive BDR on the day of examination (9% point prevalence). None of these were aware of their bronchial obstruction, nor had they ever experienced any lung function testing.

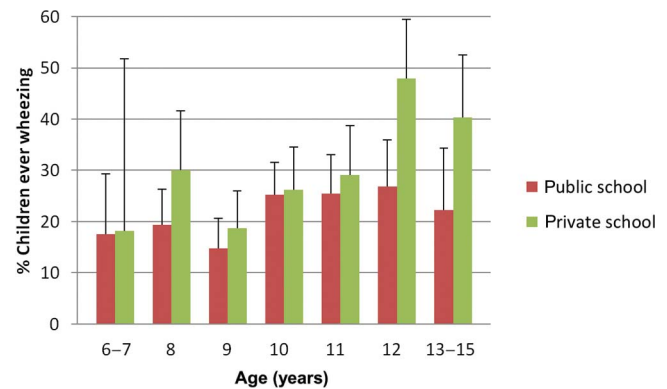


FIGURE 1.—Percentage of wheezing ever.

Percentage of children in public (red columns) and private (green columns) schools reporting “ever wheezing” according to the ISAAC questionnaire (in black: 95% CI), p -value = .0012 (Chi-Quadrat-Test).

Comparing the results from private and public schools, we established highly significant differences for the BMI being (with age taken into account) much lower in public than in private schools ($p < .001$). The same difference could be shown for the two school types concerning the frequency of “wheezing ever” ($p = .0012$) with great variances for different age groups (Figure 1).

DISCUSSION

The purpose of this study was to gain more insight into the prevalence of bronchial asthma in Malagasy children and detect possible factors contributing to this condition. Prevalence rates were found to be higher than initially expected based on the existing literature on African children.

Since the standardized ISAAC questionnaire was used in the study, the prevalence of wheezing in Malagasy children is comparable to rates established in ISAAC Phase III (7). Malagasy children showed a higher rate of wheezing (25.2%) in relation to other African countries, directly followed by La Reunion with 21.5% (with a study population aged 13–14 years (6)). It is interesting that both islands in the Indian Ocean have comparable prevalence rates even though lifestyles and living conditions differ greatly and perhaps even more so than between any other two countries in Africa.

TABLE 2.—Likelihood and odds ratios for bronchial asthma in relation to environmental factors ($n = 1093$).

Parameter	OR	Low 95% conf. limit	High 95% conf. limit	P-value
BMI	0.990	0.893	1.098	.849
School type: private versus public	1.602	0.857	2.994	.140
Fuel: electricity versus charcoal/gas	0.417	0.056	3.136	.396
Number of siblings	1.149	0.882	1.497	.304
Number of older siblings	0.704	0.505	0.980	.038 ^a
Smokers	0.926	0.670	1.279	.641

^aSignificant.

A similarly high rate of bronchial asthma was also demonstrated with lung function tests and BDR in two private schools. Asthma point prevalence was more than twice as high as found in European children (30, 31), which suggests that bronchial asthma is significantly impairing children's health.

This apparently high number of children exhibiting symptoms of asthma raises the question of causation. The only environmental factor diminishing the risk for asthma in urban Malagasy children was a higher number of older siblings, supporting the "hygiene hypothesis" (32). By contrast, a small study with Ghanaian children found a reduced risk for asthma with lower sibship position (5). Most European studies concerning bronchial asthma, however, did not find a correlation between the two.

Other risk factors such as the type of school children attended likewise did not reveal any correlation. This was to be expected, since public schools as well as private schools are unaffordable for a quarter of Malagasy children, who live in extreme poverty and were therefore not reached by this study (1, 33). It is probably for this reason that we were unable to establish a correlation between poverty and prevalence of bronchial asthma.

Similarly, BMI as well as household cooking fuels did not prove to be a significant risk factor likely because the study group as a whole was quite homogeneous, with the vast majority of children having an equally low BMI and almost all households using solid fuels. In addition, cigarette smoking is too expensive for most, which is probably why at a smoker's rate of 17.6% the long-term exposure is low (34).

Even though most of the risk factors investigated have not been proven to be significant, asthma prevalence in Malagasy children is high. Prevalence levels are also high compared to major African cities like Cape Town in South Africa and Ibadan in Nigeria (7). This discrepancy may be explained by differences in lifestyle.

First, all children tested in our study belong to the Merina, a tribe of Polynesian heritage, which came to Madagascar approximately 1200 years ago (27). Black Africans from the continent settled centuries later with only a moderate influence in the Malagasy highlands. Therefore, the high prevalence of asthma is not strongly related to the African heritage as it is with African Americans. It is possible that the Asian heritage, which also exists on the neighboring Island of La Reunion, contributes to the higher asthma prevalence. Compared to Madagascar, La Reunion remained unsettled until the seventeenth century, when slaves from Madagascar and East Africa were imported by the French settlers. Now they exhibit a similar high rate of wheezing as Malagasy children, notably the highest rate demonstrated in ISAAC Phase III for Africa (7).

Second, it seems that the location of the city of Antananarivo at a high altitude of 1300 m presents a unique geographic factor which amplifies the grade of pollution through a photochemical smog phenomenon (35, 36). Traffic-related air pollution is a phenomenon particularly pronounced on weekdays with levels for PM

2.5–10 exceeding the WHO guideline by almost six times (37, 38). Also, at the time of investigation, political turmoil in Madagascar's capital was at its peak. Air pollution in urban Antananarivo was increased for more than 3 months due to the use of teargas by the authorities.

Third, as shown in Table 1, the vast majority of households used carbon as their energy fuel, thus increasing the toxic burden of their children, especially as cooking is mostly done indoors. The monthly mean lower temperatures in Antananarivo never rise over 16°C during the entire year, so cooking is typically used to raise the indoor temperature. As biomass fuels are in use in nearly every household, the effect of other energy sources is not demonstrable.

Fourth, malnutrition was presumably worse in Madagascar than in most other African countries during the time of investigation because of the growing poverty accompanying the political crisis starting in 2009 (39). As indicated by the BMI, there were highly significant differences between public and private schools. In our study, wheezing was much more prevalent in children attending private schools than public schools (Figure 1). The reason for this remains unclear, but a relatively better lifestyle could cause more asthma as it is the case in Western countries. Data reflecting SES like parent income, social violence, or general burden of chronic diseases in families have not been established so far (40).

CONCLUSIONS

With this study, we established the first epidemiological data in schoolchildren living in an urban environment at a high altitude in Madagascar revealing a substantially high prevalence of bronchial asthma. The question why the two islands off the coast of Africa, La Reunion and Madagascar, are showing such high wheezing prevalences remains unanswered. It could be speculated that, as was the case in Germany, a sharp change in urban lifestyle over the past years, prompting significantly higher air pollution without substantial changes in living conditions, is a causal factor (41). We are planning a follow-up study to further investigate the causes for asthma in Malagasy children under these conditions.

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DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

REFERENCES

1. Masoli M, Fabian D, Holt S, Beasley R. Global Initiative for Asthma (GINA) Program: the global burden of asthma: executive summary of the GINA. Dissemination Committee Report. *Allergy* 2004; 59:469–478.
2. World Health Organization. Global Surveillance, Prevention and Control of Chronic Respiratory Diseases: A Comprehensive Approach. 1st ed. Geneva: World Health Organization, 2007:15–20.
3. Lötval J, Pawankar R, Wallace DV, Akdis CA, Rosenwasser LJ, Weber RW, Burks AW, Casale TB, Lockey RF, Papadopoulos NG, Fineman SM, Ledford DK; American Academy of Allergy, Asthma & Immunology (AAAAI), the American College of Allergy, Asthma & Immunology (ACAAI), the European Academy of Allergy and Clinical Immunology (EAACI), and the World Allergy Organization (WAO). We call for iCAALL: International Collaboration in Asthma, Allergy and Immunology. *J Allergy Clin Immunol* 2012; 129(4):904–905.
4. Pearce N, Ait-Khaled N, Beasley R, Mallol J, Keil U, Mitchell E, Robertson C and the ISAAC Phase Three Study Group. Worldwide trends in the prevalence of asthma symptoms: Phase III of the International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax* 2007; 62:758–766.
5. Ait-Khaled N, Odhiambo J, Pearce N, Adjoh KS, Maesano IA, Benhabyles B, Bouhayad Z, Bahati E, Camara L, Cateau C, El Sony A, Esamai FO, Hypolite IE, Melaku K, Musa OA, Ng'ang'a L, Onadeko BO, Saad O, Jerry M, Kayembe JM, Koffi NB, Khaldi F, Kuaban C, Voyi K, M'Boussa J, Sow O, Tidjani O, Zar HJ. Prevalence of symptoms of asthma, rhinitis and eczema in 13- to 14-year-old children in Africa: the International Study of Asthma and Allergies in Childhood Phase III. *Allergy* 2007; 62:247–258.
6. ISAAC Steering Committee. Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC). *Eur Respir J* 1998; 12:315–335.
7. Weinmayr G, Weiland SK, Björkstén B, Brunekreef B, Büchele G, Cookson WO, Garcia-Marcos L, Gotua M, Gratzou C, van Hage M, von Mutius E, Riiikjær MA, Rzehak P, Stein RT, Strachan DP, Tsanakas J, Wickens K, Wong GW. ISAAC Phase Two Study Group: atopic sensitization and the international variation of asthma symptom prevalence in children. *Am J Respir Crit Care Med* 2007; 176(6):565–574.
8. Addo-Yobo EO, Custovic A, Taggart SC, Craven M, Bonnie B, Woodcock A. Risk factors for asthma in urban Ghana. *J Allergy Clin Immunol* 2001; 108(3):363–368.
9. Okoromah CN, Oviawe O. Is childhood asthma underdiagnosed and undertreated? *Niger Postgrad Med J* 2002; 9(4):221–225.
10. Joseph CL, Foxman B, Leickly FE, Peterson E, Ownby D. Prevalence of possible undiagnosed asthma and associated morbidity among urban schoolchildren. *J Pediatr* 1996; 129(5):735–742.
11. Moustaki M, Nicolaidou P, Stefos E, Vlachou V, Patsouri P, Fretzayas A. Is there an association between wheezing and pneumonia? *Allergol Immunopathol* 2010; 38(1):4–7.
12. Mallol J. Childhood asthma in developing countries. Low income aspects and related matters. *Allergol Immunopathol* 2000; 28:283–286.
13. Cuijpers CE, Wesseling GJ, Swaen GM, Sturmans F, Wouters EF. Asthma-related symptoms and lung function in primary school children. *J Asthma* 1994; 31(4):301–312.
14. Momas I, Dartiguenave C, Fauroux B, Bourdais M, Poinard R, Grimfeld A, Just J. Prevalence of asthma or respiratory symptoms among children attending primary schools in Paris. *Pediatr Pulmonol* 1998; 26(2):106–112.
15. Emeryk A, Chojna E, Bartkowiak-Emeryk M, Postepski J. Prevalence of asthma and some respiratory symptoms in the years 1995 and 2001 in schoolchildren from rural regions of Poland. *Ann Agric Environ Med* 2004; 11(1):63–66.
16. Jaffar S, Lazarus JV, Onyebujoh P, Chakaya J, Garrib A, Mwaba P, Mboup S, Bellis K, Egwaga S, Corrah T, Coutinho A. Health services strengthening in Africa—research is a key component. *Trop Med Int Health* 2010; 15(11):1270–1273.
17. Zar HJ, Mahdi SA. Childhood pneumonia—progress and challenges. *S Afr Med J* 2006; 96:890–900.
18. Paynter S, Ware RS, Weinstein P, Williams G, Sly PD. Childhood pneumonia: a neglected, climate-sensitive disease? *Lancet* 2010; 376(9755):1804–1805.
19. Teepe J, Grigoryan L, Verheij TJ. Determinants of community-acquired pneumonia in children and young adults in primary care. *Eur Respir J* 2010; 35(5):1113–1117.
20. Glew RH, Kassam H, Vander Voort J, Agaba PA, Harkins M, VanderJagt DJ. Comparison of pulmonary function between children living in rural and urban areas in northern Nigeria. *J Trop Pediatr* 2004; 50(4):209–216.
21. Lodha R, Puranik M, Chandra U, Natchu M, Kabra SK. Persistent pneumonia in children. *Indian Pediatr* 2003; 40(10):967–970.
22. World Health Organization. Madagascar health profile. 2010. Available at: <http://www.who.int/gho/countries/mdg.pdf>. Accessed April 24, 2012.
23. UNICEF. Children and AIDS: Fourth Stocktaking Report. 1st ed. Geneva: United Nations Publication, 2009:44.
24. UNICEF/WHO. Pneumonia: The Forgotten Killer of Children. New York: UNICEF/WHO, 2006. Available at: http://whqlibdoc.who.int/publications/2006/9280640489_eng.pdf. Accessed April 24, 2012.
25. Georgy V, Fahim HI, El-Gaafary M, Walters S. Prevalence and socio-economic associations of asthma and allergic rhinitis in northern [corrected] Africa. *Eur Respir J* 2006; 28(4):756–762.
26. Laumbach RJ, Kipen HM. Respiratory health effects of air pollution: update on biomass smoke and traffic pollution. *J Allergy Clin Immunol* 2012; 129(1):3–11.
27. Cox MP, Nelson MG, Tumonggor MK, Ricaut FX, Sudoyo H. A small cohort of Island Southeast Asian women founded Madagascar. *Proc Biol Sci*. 2012 Mar 21. [Epub ahead of print] 06-12-2012.
28. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, Crapo R, Enright P, van der Grinten CP, Gustafsson P, Jensen R, Johnson DC, MacIntyre N, McKay R, Navajas D, Pedersen OF, Pellegrino R, Viegi G, Wanger J. ATS/ERS Task Force: standardisation of spirometry. *Eur Respir J* 2005; 26(2):319–338.
29. Trabelsi Y, Ben Saad H, Zabka Z, Gharbi N, Bouchez Buvry A, Richalet JP, Guenard H. Spirometric reference values in Tunisian children. *Respiration* 2004; 71:511–518.
30. Zilmer M, Steen NP, Zachariassen G, Duus T, Kristiansen B, Halken S. Prevalence of asthma and bronchial hyperreactivity in Danish schoolchildren: no change over 10 years. *Acta Paediatr* 2011; 100(3):385–389.
31. Lang A, Carlsen KH, Haaland G, Devulapalli CS, Munthe-Kaas M, Mowinkel P, Carlsen K. Severe asthma in childhood: assessed in 10 year olds in a birth cohort study. *Allergy* 2008; 63(8):1054–1060.
32. Strachan DP. Family size, infection and atopy: the first decade of the 'hygiene hypothesis'. *Thorax* 2000; 55(Suppl. 1):S2–S10.
33. UNICEF. Statistics Madagascar. 2010. Available at: http://www.unicef.org/infobycountry/madagascar_statistics.html. Accessed April 24, 2012.
34. World Health Organization. WHO Report on the Global Tobacco Epidemic. 2011. Available at: http://www.who.int/tobacco/surveillance/policy/country_profile/mdg.pdf. Accessed April 24, 2012.
35. US EPA. Altitude as a Factor in Air Pollution. Washington, DC: US Environmental Protection Agency, EPA/600/9-78/015 (NTIS PB285645), 1978.
36. Escamilla-Núñez MC, Barraza-Villarreal A, Hernandez-Cadena L, Moreno-Macias H, Ramirez-Aguilar M, Sienra-Monge JJ, Cortez-Lugo M, Texcalac JL, del Rio-Navarro B, Romieu I. Traffic-related air pollution and respiratory symptoms among asthmatic children, resident in Mexico City: the EVA cohort study. *Respir Res* 2008; 9:74.
37. Andriambololona R, Rakotondramanana HT, Rasoazanany EO, Randriananivo LV, Rasolofonirina M, Andrianarivo RR. Air quality in terms of particulate matter (PM10) and element components in Antananarivo City. 2001. Available at: http://webh01.ua.ac.be/mitac1/pages/pers_rasoazan.html. Accessed April 24, 2012.
38. Randriananivo LV, Andriambololona R, Rasoazanany EO, Andriamahenina NN, Ravoson H, Ramaherison H. Air pollution in

- term of PM_{2.5} and PM_{2.5-10} in Andravohangy area. 2009. Available at: <http://www.slac.stanford.edu/econf/C0908211/pdf/023.pdf>. Accessed April 24, 2012.
39. Stewart AW, Mitchell EA, Perace N, Strachan DP, Weiland SK. The relationship of per capita gross national product to the prevalence of symptoms of asthma and other atopic diseases in children (ISSAC). *Int J Epidemiol* 2001; 30(1):173–179.
40. Berntsen S, Lødrup Carlsen KC, Hageberg R, Aandstad A, Mowinckel P, Anderssen SA, Carlsen K-H. Asthma symptoms in rural living Tanzanian children; prevalence and relation to aerobic fitness and body fat. *Allergy* 2009; 64:1166–1171.
41. von Mutius E, Weiland SK, Fritzsch C, Duhme H, Keil U. Increasing prevalence of hay fever and atopy among children in Leipzig, East Germany. *Lancet* 1998; 351(9106):862–866.

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