

Trends in the Prevalence and Severity of Symptoms of Asthma, Allergic Rhinoconjunctivitis, and Atopic Eczema

Adegoke G. Falade, MBBS, MD, FMCPaed, FRCP(Edin); Olusoji M. Ige, MBBS, FWACP; Bidemi O. Yusuf, PhD; Modupe O. Onadeko, MBBS, MD, MPH, FWACP, FNMCPG(Nig); Babatunde O. Onadeko, MBChB, MD, FRCP(Edin), FRCP(Lond), FMCP(Nig), FWACP, FRCP(Edin), FAS

Funding/Support: The University of Ibadan, Ibadan, Nigeria, 2000 Senate Research Grant was awarded to Drs Falade, Yusuf, M. Onadeko, and Ige, as well as the grant from Glaxo Wellcome, New Zealand, through the ISAAC International Data Centre, New Zealand.

The increase in prevalence of asthma and other allergic diatheses has rarely been documented in the developing sub-Saharan countries. We assessed time trends in symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema among children in Ibadan, Nigeria, with cross-sectional data from 2 International Study of Asthma and Allergies in Childhood questionnaire-based surveys conducted 7 years apart in 1995 and in 2001-2002. The prevalence of current wheeze increased nonsignificantly in the 6- to 7-year age group (4.8%-5.5%) and significantly in the 13- to 14-year age group (10.7%-13.0%) ($p = .249$ and $p = .005$, respectively). The 12-month prevalence of allergic rhinoconjunctivitis decreased insignificantly in the 6- to 7-year age group ($p = .833$) but significantly in the 13- to 14-year age group ($p = .001$), while the diagnosis of atopic eczema decreased in both age groups. The current findings suggest that the symptoms of asthma have only increased significantly in the Nigerian adolescents.

Keywords: asthma-prevalence ■ rhinoconjunctivitis ■ atopic-eczema

J Natl Med Assoc. 2009;101:414-418

Author Affiliations: Departments of Pediatrics (Dr Falade), Medicine (Drs Ige and B. Onadeko), Epidemiology, Medical Statistics and Environmental Health (Dr Yusuf), and Community Medicine (Dr M. Onadeko), College of Medicine, University of Ibadan, Ibadan, Nigeria.

Corresponding Author: Professor A.G. Falade, Department of Paediatrics, University College Hospital, PMB 5116, Ibadan, Oyo State, Nigeria (afalade33@hotmail.com).

INTRODUCTION

In the last 4 decades, there has been an increase in the global prevalence of asthma and other allergic diseases.¹⁻⁶ Although there is no clear explanation

for the apparent surge, the trend may be ascribed to a general improvement in living standard and health care in industrialized communities. This plausible explanation is consistent with the well-known “hygiene hypothesis.”⁷ According to this hypothesis, the decrease in the incidence of childhood infections following improvement in hygiene and standard of living would stimulate the immune system in the direction that would enhance the development of asthma and other allergic states, rather than in “fighting” one infection or the other.^{8,9} Thus, with increasing westernization, less-developed communities such as ours may follow this trend. It has, however, been speculated that environmental influences associated with the modern life in some communities may have reached the maximum in inducing symptoms of asthma and other allergy-related conditions in genetically susceptible individuals.¹⁰⁻¹³

The results of the International Study of Asthma and Allergies in Childhood (ISAAC) phase 1 study (1994-1995) which involved 56 countries from the 6 continents of the world, have shown wide-ranging differences (up to 20-fold) in the 12-month prevalence of wheeze between communities (1.6%-36.8%).¹⁴ Specifically, the 12-month prevalence of wheeze in 6- to 7-year-olds in Ibadan (5.1%) is comparable to those found in other developing countries, but that of United Kingdom and other English-speaking developed countries (Australia, New Zealand, United States of America) is much higher at 18.4 and greater than 20%, respectively.¹⁵ The aim of the present study was to evaluate the changes in prevalence of symptoms of asthma and allergies by comparing the data from phase 1 and phase 3 of the ISAAC surveys conducted in Ibadan, Nigeria, 7 years apart.

SUBJECTS AND METHODS

This study was a comparison of cross-sectional data from ISAAC written questionnaire surveys carried out from January 1 to May 31, 1995 (phase 1), and May 2001 to July 2002 (phase 3). Detailed times of collection of data for phase 3 were May 11 to June 19, 2001, and Feb-

ruary 13 to June 18, 2002. The time frames for the 2 phases (1 and 3) were essentially within the months of January and June, and, hence, there was no significant difference in the months of data collection. Similarly, the study populations for the 2 phases were children, 6- to 7-year-olds in primary schools, and the 13- to 14-year-olds in secondary schools in Ibadan, Nigeria. With an estimated population of 4 million, Ibadan is reputed to be one of the most densely populated cities in Africa.¹⁶

SAMPLING METHOD

The sampling frames used were all the primary and secondary schools in Ibadan. The total number of schools for the 6- to 7-year-age group in the sampling frame was 272 with a total number of 40 800 children. As for the 13- to 14-year age group, the number of schools were 85 with a total number of 41 000 children. The random sampling methods used were as described earlier^{17,18} and were indeed identical for the 2 surveys. For phase 1, a total of 31 (10 public and 21 private) primary schools and 15 secondary schools were randomly selected from a total of the 272 primary schools and 85 secondary schools, respectively. In each of the schools, selection of children was by grade level. In Nigeria, children aged 6 to 7 years are usually in primary 1 and 2, whereas children aged 13 to 14 years are usually in the junior secondary school 3 (JSS 3) and senior secondary school 1 (SSS1). Hence, 2325 children aged 6 to 7 years were selected from grades 1 and 2, and 4 000 children aged 13 to 14 years from JSS 3 and SSS 1 for participation in phase 1 of the study. Concerning phase 3, the corresponding numbers were 25 primary schools and 23 secondary schools with children aged 6 to 7 years (2 778) and those aged 13 to 14 years (3 150). The ages of the children were ascertained from the class registers. Questionnaires were distributed to the primary school children, who took them home for their parents or guardians to complete and were subsequently returned to their teachers. For the 13- to 14-year-olds, the questionnaires were self-completed in the class rooms.

QUESTIONNAIRE

The ISAAC collaborators had earlier agreed that the cardinal symptoms of asthma would be variable narrowing of the airways and best described as “wheezing or whistling in the chest.” The questionnaire also incorporated sensitive (although not necessarily specific) questions for asthma and more specific questions related to the severity of asthma.¹⁹ A number of studies have compared responses to the ISAAC core wheezing questions with other indicators of asthma, including physician diagnosis, other questionnaires, and physiological measures, and indicate that the ISAAC questionnaire has a level of sensitivity and specificity that is acceptable for the purposes of international comparisons.¹⁹

It was considered appropriate to use the English ver-

sion of the ISAAC written questionnaires,¹⁹ since English is the official language in Nigeria, and the literacy rate among the parents or guardians in the study population of Ibadan in southwestern Nigeria is relatively high; 77% of females and 87% of males were reportedly literate in a recent local survey.¹⁶ The questionnaire has 4 sections comprising demographic data, 8 questions on wheezing and asthma, 6 questions on rhinitis, and 7 questions on eczema. The questionnaire concentrated on past and current wheezing episodes, wheezing frequency, sleep disturbances, and speech limitations during attacks, exercise-induced wheezing, nighttime cough unrelated to common cold, and a doctor's diagnosis of asthma. In addition, ISAAC core questions were included regarding the presence and severity of atopic eczema and allergic rhinoconjunctivitis—the latter being a more preferable local synonym for hay fever. The questionnaires were completed and returned within a period of 7 days by the parents/guardians for the 6- to 7-year age group and immediately by the students themselves in the 13- to 14-year age group. Where illiterate parents or guardians were involved, a literate relative was requested to complete the questionnaire.

PREVALENCE RATES

The prevalence of symptoms was calculated by dividing the number of positive responses to each question by the number of completed questionnaires. The proportions of children with symptoms of asthma, allergic rhinoconjunctivitis, or atopic eczema were determined. The overall 12-month prevalence of 1 or more symptoms of asthma, allergic rhinoconjunctivitis, or atopic eczema was calculated. Symptoms of rhinoconjunctivitis was defined as respondents who answered yes to the question about the corresponding nasal symptoms in the preceding year and those who answered yes to the question about these symptoms being accompanied by eye symptoms. Symptoms of atopic eczema were also defined as respondents who answered yes to the question about rash in the preceding year and also answered yes to the question about the rash affecting flexural areas.

ETHICAL CONSIDERATIONS

Informed consent to carry out the study was obtained from the head teachers and principals of the primary schools and secondary schools, respectively, the parents or guardians of the children, and the Oyo State Ministry of Education and Youth Development, Ibadan, Nigeria. The study received institutional approval from the Joint Ethical Committee of the University of Ibadan and the University College Hospital, Ibadan, Nigeria.

STATISTICAL ANALYSIS

The data were analyzed using the Epi-Info version 6 (Centers for Disease Control and Prevention, and World Health Organization, Geneva, Switzerland) software. Frequency tables were generated for the relevant vari-

ables. Descriptive statistics such as mean values, standard errors, and standard deviations were used to summarize quantitative variables, while categorical variables were summarized by percentages. The χ^2 test was used to compare proportions. The level of significance was specified at α/c , where α is 5% and c is the number of tests. A p value of .01 was considered to be statistically significant after correcting for multiple tests.

RESULTS

There were 1696 and 2396 responses in the surveys of 1995 and 2001-2002 for the 6- to 7-year-olds, giving response rates of 72.9% (1696 out of 2325) and 86.2% (2396 out of 2778) questionnaires served, respectively. For the 13- to 14-year-olds, responses were 3057 and 3142, giving response rates of 76.4% (3057 out of 4000) and 99.7% (3142 out of 3150), respectively.

The prevalence rates of symptoms of asthma and rhinoconjunctivitis taken together with atopic eczema for both studies and their comparison are presented in Table 1, respectively. An increase of 0.7% in 12-month prevalence of wheezing was seen in the 6- to 7-year age group. However, a decrease was observed in "wheezing during/after exercise" and "dry cough at night" in the preceding year, but neither of the changes in this age group reached statistical significance. In the 13- to 14-year age group, there was a significant increase in the prevalence of

wheezing from 10.7% to 13.0% over a 12-month period ($p = .005$). With regard to the prevalence of doctor-diagnosed asthma, there was a decrease in the rate amongst 6- to 7-year-olds and the 13- to 14-year-olds, while for rhinoconjunctivitis, there was a corresponding increase amongst the 2 age groups (p values $< .001$, in each case). A slight decrease was observed in the symptoms of rhinoconjunctivitis in the 6- to 7-year-olds (3.7-3.6, $p = 0.833$), while for the 13- to 14-year-olds, a decrease of about 23% was observed (39.7%-16.4%, $p < .001$).

With regard to atopic eczema, symptoms of eczema among respondents decreased in the 13- to 14-year-old age group, but the same symptoms increased in pupils aged 6 to 7 years, with the notable exception of rates recorded for the variable "ever diagnosed eczema."

Changes in the severity of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema are described in Table 2. There were significant increases in the number of episodes of wheezing among 6- to 7-year-olds ($p = .003$) and 13- to 14-year-olds ($p = .002$). Similarly, there was an increase in the severity of rhinitis symptoms interfering with daily activity in the 13- to 14-year-old category ($p = .010$).

DISCUSSION

The increase in the prevalence of asthma and other allergic diseases has been documented in Europe and

Table 1. Positive Response (%) for Symptoms With Percentage Change, in Different Age Groups for 1995 and 2001-2002

Asthma Symptoms								
	6- to 7-Year Age Group				13- to 14-Year Age Group			
	1995	2001-2002	Change	P Value	1995	2001-2002	Change	P Value
	n = 1696	n = 2396			n = 3057	n = 3142		
Asthma								
Ever wheezed	6.5 (0.6)	10.1 (0.6)	3.6 (0.9)	<.001	16.4 (0.7)	20.4 (0.7)	4.0 (1.0)	<.001
Wheeze in past year	4.8 (0.5)	5.5 (0.5)	0.7 (0.7)	.249	10.7 (0.6)	13.0 (0.6)	2.3 (0.8)	.005
Wheeze with exercise in past year	6.7 (0.6)	5.4 (0.5)	-1.3 (0.8)	.074	43.4 (0.9)	34.2 (0.9)	-9.2 (1.2)	<.001
Nocturnal cough in past year	9.3 (0.7)	8.0 (0.6)	-1.3 (0.9)	.142	31.7 (0.8)	27.7 (0.8)	-4.0 (1.2)	<.001
Ever diagnosed asthma	3.4 (0.4)	3.3 (0.4)	-0.1 (0.6)	.829	18.4 (0.7)	11.7 (0.6)	-6.7 (0.9)	<.001
Values in parentheses are standard errors.								
Nasal and Skin Symptoms								
	6- to 7-Year Age Group				13- to 14-Year Age Group			
	1995	2001-2002	Change	P Value	1995	2001-2002	Change	P Value
	n = 1696	n = 2396			n = 3057	n = 3142		
Rhinoconjunctivitis								
Ever had rhinitis	10.7 (0.8)	14.1 (0.7)	3.4 (1.0)	.001	55.2 (0.9)	43.8 (0.9)	-11.4 (1.3)	<.001
Rhinoconjunctivitis	3.7 (0.5)	3.6 (0.4)	-0.1 (0.6)	.833	39.7 (0.9)	16.4 (0.7)	-23.3 (1.1)	<.001
Ever diagnosed allergic rhinitis	10.7 (0.8)	14.4 (0.7)	3.7 (1.0)	<.001	16.1 (0.7)	19.2 (0.7)	3.1 (1.0)	<.001
Atopic Eczema								
Itchy rash ever	7.7 (0.7)	10.2 (0.6)	2.5 (0.9)	.007	26.1 (0.8)	18.0 (0.7)	-8.1 (1.0)	<.001
Itchy rash and atopic eczema in past year	4.5 (0.5)	5.0 (0.5)	0.5 (0.7)	.437	17.7 (0.7)	7.7 (0.5)	-10.0 (0.8)	<.001
Ever diagnosed eczema	9.4 (0.7)	6.8 (0.5)	-2.6 (0.9)	.003	38.4 (0.9)	19.4 (0.7)	-19.0 (1.1)	<.001
Values in parentheses are standard errors.								

North America in the last 4 decades,¹⁻⁶ but there is little information on these trends in Africa. The ISAAC phase 1 study represented the first-ever international study on the prevalence of asthma among the 6- to 7-year-olds¹⁷ and 13- to 14-year-olds in Nigeria.¹⁸ The only other comparable study was in a cohort of university students aged 15 to 35 years.²⁰

The main purpose of the present study was to ascertain if there was an increase in the prevalence of asthma symptoms, as determined through the use of questionnaires in ISAAC phase 3 study. The use of standardized written questionnaires was informed by the reported validity of this method for comparing prevalence data in large epidemiological studies.²¹ However, the use of objective measurement of variable airway narrowing might have improved the study outcome. It is noteworthy that the 2 surveys—ISAAC phase 1 and 3—were conducted using identical methods.

An increase of 0.8% in the prevalence of wheezing over a 12-month period, which fell short of the significant value, was seen in the 6- to 7-year age group. On the other hand, the 13- to 14-year age group recorded a corresponding significant increase of 2.3% for the same

symptom over a 12-month period. The findings in these 2 age groups are consistent with those of Latin American countries and China.² Increase in the asthma symptom prevalence during the past few decades, especially in western countries, has been ascribed to environmental risk factors. Data on family size, birth order, urban living, changes in gastrointestinal microorganisms and immunological evidence support the inherent concept of the “hygiene hypothesis.”²⁷ The rapid growth of population in Nigeria,¹⁶ which has not been matched with an increase in the delivery of potable water supply and improved sanitation facilities, would appear to negate the possibility of improved level of hygiene. In Nigeria, the efficiency of both water supply and sanitation systems remains poor. Other reasons which have been suggested for the increase in asthma symptoms prevalence are a combination of both improved diagnosis and management of asthma. Indirect markers for these are increase in doctor-diagnosed asthma and a decrease in 12-month asthma symptoms and severity. This was not the case in this study, as there was a decrease in doctor-diagnosed asthma and number of wheezing episodes, an increase in the 12-month asthma symptoms, and sever-

Table 2. Respondents (%) With Each of the Reported Symptoms in Different Age Groups for 1995 and 2001-2002 Surveys

Asthma Symptoms						
Responses for Asthma	6- to 7-Year Age Group			13- to 14-Year Age Group		
	1995	2001-2002	P Value	1995	2001-2002	P Value
	n = 1696	n = 2396		n = 3057	n = 3142	
No. of wheezing episodes						
1-3	71 (4.2)	211 (8.8)	.003	281 (9.2)	254 (8.1)	.002
≥4-12	46 (2.7)	68 (2.8)		99 (3.3)	146 (4.6)	
Woken by wheeze						
Never	538 (31.7)	697 (29.1)	.506	316 (10.3)	337 (10.7)	.874
<1 per week	48 (2.8)	72 (3.0)		154 (5.0)	162 (5.2)	
≥1 per week	35 (2.1)	56 (2.3)		112 (3.7)	128 (4.1)	
Wheezing attack limiting speech	66 (3.9)	116 (4.8)	.164	232 (7.6)	249 (7.9)	.654
Nasal and Skin Symptoms						
Responses for Rhinconjunctivitis	6- to 7-Year Age Group			13- to 14-Year Age Group		
	1995	2001-2002	P Value	1995	2001-2002	P Value
	n = 1696	n = 2396		n = 3057	n = 3142	
Interfering with daily activities						
Not at all	439 (25.9)	712 (29.7)		593 (19.4)	364 (11.6)	
Little	109 (6.4)	196 (8.2)		789 (25.8)	540 (17.2)	
Moderate	40 (2.4)	58 (2.4)	.558	269 (8.8)	176 (5.6)	.010
A lot	15 (0.9)	17 (0.7)		111 (3.6)	112 (3.6)	
Responses for Eczema						
Persistent rash without clearing	235 (13.9)	667 (27.8)	<.001	460 (15.0)	301 (9.6)	<.001
Kept awake by itchy rash						
Never	373 (22.0)	617 (25.8)		419 (13.7)	306 (9.7)	
<1 per week	59 (3.5)	105 (4.4)	.076	270 (8.8)	180 (5.7)	.035
≥1 per week	38 (2.2)	99 (4.1)		201 (6.6)	102 (3.2)	

ity. The symptom of nocturnal cough showed a decrease in the 6- to 7-year age group and in the 13- to 14-year age group. The decrease in nocturnal cough in the present study amongst the age groups studied is conceivably attributable to a decrease in the awareness of asthma symptoms among the parents.

Symptoms of eczema decreased in the 13- to 14-year age group. Increase in eczema prevalence usually parallels increases in other atopic diseases.^{9,22} This has also been recently substantiated in a German report that compared ISAAC phase 1 and 3 surveys,¹⁰ and by a cross-sectional epidemiology study in Singapore.²³ The observed digression in prevalence trends between asthma and eczema in our study may be explained by the suggestion that the genetic susceptibility to eczema may involve unique candidate genes, which are probably different from those for respiratory allergies.²⁴

In conclusion, the current findings from the 2 surveys in Ibadan, Nigeria, show that there is a rise in the prevalence of wheezing over the 7-year surveillance period in the young adolescents, which has also been documented in South Africa using the same methodology.²⁵ Although the possible contribution of an increase in parental awareness (regarding asthma and wheezing in childhood) to the present increase in asthma prevalence cannot be excluded, our data suggest that the increase can neither be individually ascribed to a temporal improvement in environmental sanitation or hygiene, nor entirely explained by an improvement in diagnosis and management of the disease.

ACKNOWLEDGMENTS

We are grateful to all the pupils and parents of the children who consented to take part in these studies.

REFERENCES

1. Shaw RA, Crane J, O'Donnell TV, Porteous LE, Coleman ED. Increasing asthma prevalence in a rural New Zealand adolescent population: 1975-89. *Arch Dis Child*. 1990;65:1319-1323.
2. Burr ML, Butland BK, Kings S, Vaughan-Williams E. Changes in asthma prevalence: two surveys 15 years apart. *Arch Dis Child*. 1989;64:1452-1456.
3. Peat JK, van den Berg RH, Green WF, Mellis CM, Leeder SR, Woolcock AJ. Changing prevalence of asthma in Australian children. *BMJ*. 1994;308:1591-1596.
4. Nystad W, Magnus P, Gulsvik A, Skarpass IJ, Carlsen KH. Changing prevalence of asthma in school children: evidence for diagnostic changes in asthma in two surveys 13 yrs apart. *Eur Respir J*. 1997;10:1046-1051.
5. Magnus P, Jaakkola JK. Secular trend in the occurrence of asthma among children and young adults: critical appraisal of repeated cross sectional surveys. *BMJ*. 1997;314:1795-1799.
6. Wieringa MH, Vermeire PA, Brunekreef B, Weyler JJ. Increased occurrence of asthma and allergy: critical appraisal of studies using allergic sensitization, bronchial hyperresponsiveness and lung function measurements. *Clin Exp Allergy*. 2001;31:1553-1563.
7. Strachan DP. Hay fever, hygiene, and household size. *BMJ*. 1989;299:1259-1260.
8. Holt PG. Parasites, atopy and the hygiene hypothesis: resolution of a paradox? *Lancet*. 2000;356:1699-1701.
9. Umetsu DT, McIntire JJ, Akbari O, Macaubas C, DeKruyff RN. Asthma: an epidemic of dysregulated immunity. *Nature Immunol*. 2002;3:715-720.
10. Maziak W, Behrens T, Brasky TM, et al. Are asthma and allergies in children and adolescents increasing? Results from ISAAC phase I and phase III surveys in Münster, Germany. *Allergy*. 2003;58:572-579.
11. Wang XS, Tan TN, Shek LPC, et al. The prevalence of asthma and allergies in Singapore: data from two ISAAC surveys seven years apart. *Arch Dis Child*. 2004;89:423-426.
12. Toelle BG, Ng K, Belusova E, Salome CM, Peat JK, Marks GB. Prevalence of asthma and allergy in school children in Belmont, Australia: three cross-sectional surveys over 20 years. *BMJ*. 2004;328:386-387.
13. Braun-Fahrländer C, Gassner M, Grize L, et al. No further increase in asthma, hay fever and atopic sensitisation in adolescents living in Switzerland. *Eur Respir J*. 2004;23:407-413.
14. Worldwide variations in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. The International Study of Asthma and Allergies in Childhood (ISAAC) steering committee. *Lancet*. 1998;351:1225-1232.
15. Asher MI, Anderson HR, Stewart AW, Crane J. 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.
16. National Population Commission (Nigeria) 2000: Nigeria Demographic and Health Survey 1999. Calverton, National Population Commission and ORC/Macro.
17. Falade AG, Olawuyi JF, Osinusi K, Onadeko BO. Prevalence and severity of symptoms of asthma, allergic rhino-conjunctivitis and atopic eczema in 6-7 year old Nigerian Primary school children: The International Study of Asthma and allergies in Childhood. *Med Princ Pract*. 2004;13:20-25.
18. Falade AG, Olawuyi JF, Osinusi K, Onadeko BO. Prevalence and severity of symptoms of asthma, allergic rhino-conjunctivitis and atopic eczema in secondary school children in Ibadan, Nigeria. *East Afr J Med*. 1998;75:695-698.
19. ISAAC Co-ordinating Committee: Manual for the International Study of Asthma and Allergies in Childhood (ISAAC). Bonchum and Auckland, ISAAC Co-ordinating Committee 1992.
20. Erhabor GE, Agbroko SO, Bamigboye P, Awopeju OF. Prevalence of asthma symptoms among university students 15 to 35 years of age in Obafemi Awolowo University, Ile-Ife, Osun state. *J Asthma*. 2006; 43:161-164.
21. Pekkanen J, Pearce N. Defining asthma in epidemiological studies. *Eur Respir J*. 1999;14:951-957.
22. Heinrich J, Hoelscher B, Frye C, Meyer I, Wjst M, Wichmann HE. Trends in prevalence of atopic diseases and allergic sensitization in children in Eastern Germany. *Eur Respir J*. 2002;19:1040-1046.
23. Tay YK, Kong KH, Khoo L, Goh CL, Giam YC. The prevalence and descriptive epidemiology of atopic dermatitis in Singapore school children. *Br J Dermatol*. 2002;146:101-106.
24. Shek LP, Tay AH, Chew FT, Goh DL, Lee BW. Genetic susceptibility to asthma and atopy among Chinese in Singapore - linkage to markers on chromosome 5q31-33. *Allergy*. 2001;56:749-753.
25. Zar HJ, Ehrlich RI, Workman L, Weinberg EG. The changing prevalence of asthma, allergic rhinitis and atopic eczema in African adolescents from 1995 to 2002. *Pediatr Allergy Immunol*. 2007;18: 560-565. ■

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.