

PARASITES AND ASTHMA—PREDICTIVE OR PROTECTIVE?

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Helminthic infections and atopic asthma are associated with similar immune phenomena: eosinophilia and increased serum immunoglobulin E (IgE) antibody (1, 2). This association has led to two conflicting hypotheses, that parasitic infection protects against subsequent asthma and that parasitic infection predisposes to asthma.

In support of the theory that parasitic disease protects against asthma, there is some evidence that the IgE induced by helminthic infections may block allergic responses. Mast cell degranulation occurs only after IgE bound to mast cell receptors combines with its specific antigen and cross-links with other IgE antigen complexes. It has been shown that most of the IgE produced by parasitic invasion is not specific for reaction with parasitic antigens (3, 4). IgE for which no antigen is available could saturate mast cell receptors and block subsequent binding of IgE directed at extrinsic allergens. This would inhibit degranulation and immediate hypersensitivity responses to these allergens (5–8). Such a protective role of parasite-induced IgE has been demonstrated with inhibition of skin reactions in animal models as well as in humans. Interestingly, the protective effect seems to be most pronounced in very young subjects when parasitic infection precedes exposure to the allergen (9).

On the other hand, this theory has been

criticized as being too simplistic. Data suggest that parasite-induced IgE does not protect against allergic reaction because there is high turnover of IgE on mast cells, and the relative proportion of nonspecific IgE to total IgE produced by parasitic infection is too small to block all mast cell IgE receptors (10). Furthermore, binding experiments have shown that the number of mast cell IgE receptors depends on total serum IgE concentration, so that when serum IgE is elevated, there are more mast cell binding sites available to accommodate the additional antibody (11). Finally, studies of patients with *Sarcoptes scabiei* suggest that IgE produced in response to this parasite antigen cross-reacts with house dust mite antigen, a common precipitant of asthma. In this case, the antiparasite IgE might actually cause asthma (12).

Other mechanisms for a protective role of parasitic infection in the development of asthma have been proposed. For example, patients with chronic filariasis have serum IgG which blocks histamine release from sensitized basophils that are exposed to the parasite antigen (13). Furthermore, a small molecular weight substance extracted from *Schistosoma mansoni* has been shown to directly inhibit mast cell degranulation in vitro and in vivo (14). Thus, host-derived antibodies other than IgE may be protective.

The proposed association, causative or preventive, between asthma and parasites has been noted in the popular press (15). Reports in the scientific literature typically cite only the epidemiologic evidence in support of their particular theory. No single review has examined the occurrence of asthma in parasitized versus nonparasitized populations. We have reviewed the

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available epidemiologic data in an effort to clarify this controversial issue.

Literature pertaining to asthma and parasites is divided into three types: anecdotal, prevalence surveys, and case-control studies. Anecdotal evidence is not quantitative and is therefore presented in narrative form. Information obtained on the prevalence of asthma versus the prevalence of parasites as determined by survey or case-control study is presented in tabular form. This review does not address the well known association of acute asthma with parasite pulmonary migration in sensitized subjects, although it was not possible to exclude the effect of such cases on the observed prevalence rates.

ANECDOTAL EVIDENCE

Letters published in the scientific literature support the theory that parasites either cause asthma or at least do not prevent its development. In the Gaza Strip, asthma "is more common in areas where parasitic infections are rampant, and where ascariasis may reach a prevalence of 90–100%" (16). In India, "bronchial asthma is almost invariably due to either hookworm or roundworm infestations" (17). In Malaysia, where 50 per cent of children are said to have parasites, childhood asthma is said to be "common" (18).

Support for this association came from a Canadian study published in 1970, in which *Ascaris* eggs were said to be present in the stool of 198 of 201 asthmatics, while no parasites were found in the stool of 20 controls (19). These results were challenged on the grounds that *Ascaris* eggs had been confused with microscopic artifacts, pseudoparasites, and/or vegetable particles (20). Subsequently, investigators at the Mayo Clinic reported that none of 123 asthmatic patients had fecal parasites (21).

Proponents of the "parasites prevent asthma" viewpoint are equally vigorous in defense of their position, stating that asthma is virtually nonexistent in areas in which worm infection is endemic. Assum-

ing that helminthic infections were much more common in rural versus urban areas, physicians in Gambia, Rhodesia, and South Africa noted the rarity of asthma in the country, compared with a higher frequency in the city (22–24). A physician in England cited historical evidence that atopic rhinitis dates from the time when hygienic disposal of sewage began. He also reported that several naval officers who had suffered from hay fever and then developed ascariasis were subsequently free of hay fever symptoms for up to three years (25).

PREVALENCE SURVEYS

Statistics on the prevalence of asthma and of parasitic infection are listed by country in table 1 and shown graphically in figure 1. The criteria for a diagnosis of asthma vary among countries as well as in different surveys conducted within a particular country; in general, more rigorous criteria including pulmonary function testing was used in those countries with a higher prevalence of reported asthma. The criteria for parasitic infection also vary, but most survey results are based on only a single stool examination. Possible seasonal variation in asthma prevalence or parasitism is generally ignored.

These within-country comparisons usually reflect investigations of different populations, often conducted several years apart. Every effort was made to find comparison groups of similar age and local environment, but the sample sizes were often small, usually well under 5 per cent of the total population, and the diversity of the populations in these countries was not addressed. Although most of the countries with high parasite rates had low asthma frequency, there are several notable exceptions, as shown in figure 1. Nevertheless, the overall association of parasites with asthma based on these data was negative, as shown in figure 2.

CASE-CONTROL STUDIES

Case-control studies of the asthma-parasite connection are shown in table 2. Most

of these investigations involved selecting a group of asthmatic patients, matching them with nonasthmatic controls of similar age and sex, and examining the stool of both groups for ova and parasites. In only one of the seven studies was the frequency of intestinal parasites in asthmatics significantly different from that in controls. The South African study found significantly *more* asthma only in subjects who had both parasites in stool and a positive skin test to *Ascaris* extract (50).

In three of these studies, serum IgE was also measured with conflicting results. In Tanzania, Carswell et al. (27) found a high but similar mean serum IgE (3,144 units/ml) in asthmatics and controls. In Nigeria, Macfarlane et al. (51) found higher serum IgE in rural asthmatics than in rural controls or urban asthmatics, but Warrell et al. (52) found serum IgE to be significantly lower in 97 asthmatics than in 71 controls.

Contending that the stimulus for massive IgE production could be a function of the worm burden, investigators in Gambia quantitated the parasite load by fecal egg count in a population in which hookworm infection was universal and other intestinal helminthic infections were not seen (35). In this study of 50 nonasthmatic atopic villagers (positive skin test to one of a variety of ubiquitous allergens), 24 asthmatic inpatients, and 139 controls (non-atopic villagers), significantly lower geometric mean hookworm egg counts were seen in asthmatics (600 eggs/g of feces) and in nonasthmatic atopics (1,250 eggs/g of feces) compared with controls (2,900 eggs/g of feces) ($p < 0.001$).

Investigators in New Guinea conducted similar studies on hospital inpatients and also found that patients with asthma had significantly lower egg counts than other patients (54). Twelve (67 per cent) of 18 asthmatics had egg counts of less than 500 eggs/g of feces, while only 164 (34 per cent) of 481 other patients had so few eggs/g of feces ($p < 0.05$).

DISCUSSION

The strikingly contradictory anecdotal data can be used only to document the controversy surrounding the relationship of parasites to asthma. The general impression from the prevalence survey data is that asthma is less common where intestinal parasites are endemic. Exceptions to this finding, the limitations of prevalence survey data based on nonconcurrent comparison groups, and the failure to consider ethnic diversity and local environmental conditions, however, confound interpretation of the data. Furthermore, the prevalence of asthma detected by survey *for a particular country* varies from study to study, probably reflecting differences in diagnostic criteria which range from any history of wheezing to 15 per cent or greater reduction in postexercise FEV₁ (forced expiratory volume in one second) at the time of the survey. In general, where asthma was rare, surveys used very broad definitions, while survey criteria were stricter where it was more prevalent. Prevalence of parasitic infection was also dependent upon how diligently fecal parasites were sought.

Despite the different survey methods and definitions of asthma, there seems little doubt that the prevalence of asthma differs by geographic location. As reviewed by Turner (55), asthma prevalence rates vary from high (>2.5 per cent) to low (<1 per cent); the United States, United Kingdom, Australia, New Zealand, Tristan da Cunha, and Tanzania fall into the former group, while Finland, Denmark, Japan, Nigeria, Gambia, South Africa, Papua New Guinea, and India fall into the latter group. Most surveys suggest that asthma is less common in low-income populations living in tropical areas. These, of course, are the same areas in which intestinal parasites are more apt to be prevalent. Whether geographic differences in asthma prevalence reflect early exposure to parasitic antigens prior to exposure/sensitization to environmental antigens or reflect inadequacies of diagnosis,

TABLE 1
Parasite/asthma prevalence survey data

Country and study (reference no.)	Predominant parasite	% infected	% asthma	Population
South Africa	<i>Ascaris</i> or <i>Trichuris</i>			
Burger (1968) (26)		97.5		325 black school- children in West Cape (rural)
van Niekerk et al. (1979) (24)			0.14	671 rural blacks 6- 9 years of age
			3.17	694 urban blacks 6-9 years of age
Taiwan	Any helminth			
Chang et al. (1973) (56)		93.1		710 rural residents in Hsinchu County
Liu et al. (1972) (57)			0.89	36,000 rural resi- dents in Taipei County
Nigeria	<i>Ascaris</i> , <i>Trichuris</i> , or hookworm			
Oduntan (1974) (43)		86.7		Urban schoolchil- dren
		95.7		Rural schoolchil- dren
Ejezie (1981) (44)		92.3		5,595 primary schoolchildren in Logos State
Sotowora (1970) (45)			2.4	
Gambia	Hookworm			
Knight and Merrett (1981) (31)		90		
Godfrey (1975) (22)			0	1,200 rural resi- dents
New Guinea	Hookworm			
Grove and Forbes (1975) (35)		100		Rural highlands; 213 stools exam- ined
Ewers (1972) (36)		80		656 subjects from five villages
Vines (1970) (37)		80	0	2,000 subjects
Anderson (1974) (38)			0.25	2,000 subjects
Puerto Rico	<i>Trichuris</i>			
Knight et al. (1973) (47)		78		Combined rural and urban resi- dents (children)
Greenberg and Ferguson (1971) (48)		78		
Sifontes and Mayol (1976) (49)			5.4	

TABLE 1—continued

Country and study (reference no.)	Predominant parasite	% infected	% asthma	Population
Maldives	<i>Trichuris</i>			
Wolstenholme (1979) (29)		70	12.2	14,000 subjects from Addu Atoll (total population survey)
India	<i>Hookworm</i>			
Banik (1978) (39)		50		
Kulkarni et al. (1978) (40)		50		
May (1958) (32)		60		
Chowdhury and Schiller (1968) (41)		78		Rural residents, near Calcutta
Viswanathan et al. (1966) (42)			1.76	16,000 urban sub- jects surveyed
Rhodesia (Zimbabwe)	<i>Hookworm</i>			
May (1958) (32)		55		
Buckley (1946) (33)		52		
Merrett et al. (1976) (23)			0	1,200 rural villagers
			0.5	Salisbury urban population
Cookson (1977) (34)			1.6	Township adults
			1.2	Township children
Tanzania	<i>Any fecal para- site</i>			
Carswell et al. (1977) (27)		60	7.8	242 rural school- children
Nhonoli et al. (1974) (28)		30		1,000 subjects, 15% of population of three villages
Ecuador	<i>Any fecal hel- minth</i>			
Kaplan et al. (1980) (30)		43	1.3	293 Waoroni In- dians (highest se- rum IgE levels recorded)
Tokelau Island (Polynesia)	<i>Filaria</i>			
Stanhope and Prior (1976) (46)		10.8	12.4	Males
		0.4	11.3	Females
United States	<i>Any pathogenic intestinal parasite</i>			
Center for Disease Control (1978) (58)		8.1		% positive of 332,312 stools examined by all public health labs
US National Health Sur- vey (1973) (59)			6	
Muschenheim and Cran- ston (1972) (60)			1.8	
National Heart and Lung Institute (1972) (61)			5.5	
Davis (1972) (62)			5.5	

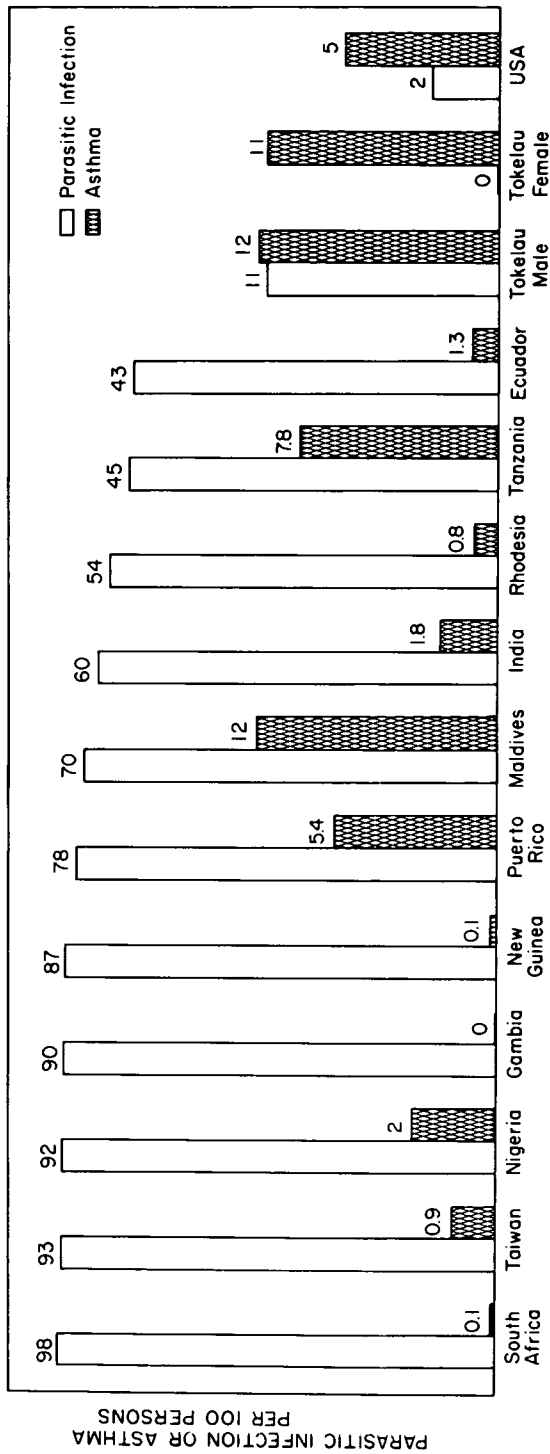


FIGURE 1. Prevalence of asthma and of intestinal parasites, by country. See table 1 for details of population studied.

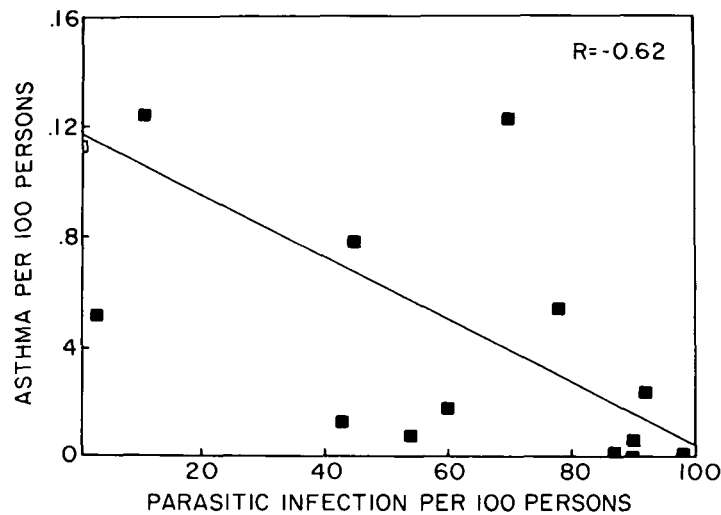


FIGURE 2. Pearson's product-moment correlation of asthma versus parasite prevalence in different populations, based on data shown in table 1.

genetic differences, nutritional variables, or allergen exposure cannot be determined.

In general, the case-control studies do not support the suggestion that parasites and asthma are inversely related. In these studies, the definition of asthma was based on clinical diagnosis, usually patients being treated for asthma, with verifying pulmonary function or allergy testing in none or at best a subset of cases. Parasites were usually determined by examination of a single unconcentrated stool specimen. The case-control studies were not controlled for other factors such as genetic predisposition, nutritional status, psychosocial variables, and allergen exposure, and are flawed by small samples and too frequent basic differences in controls versus asthmatics, such as inpatient versus outpatient. Also, those studies do not detail the probable age of parasitic infection; presumably, parasite exposure must occur early or at least prior to onset of asthma to confer protection (10).

Although each of the case-control studies is flawed, their consistency in finding no significant paucity of parasites in asthmatics, compared with controls, suggests that the putative protective effect is an ecologic fallacy. One cannot exclude the possibility, however, that earlier parasitism, possibly

now lost as a consequence of acquired immunity, provided a protective antigenic stimulus that cannot be determined in cross-sectional studies.

SUMMARY AND CONCLUSIONS

Most prevalence surveys (figures 1 and 2) suggest that asthma is less common in heavily parasitized countries, but case-control studies either show no association or an increase in parasitism in asthmatics. Studies which included egg counts suggest that asthmatics have a lower parasite burden than normals, compatible with the notion that asthma protects against parasitic infection, or vice versa. The completely contradictory findings of serum IgE in three studies do not help to elucidate any association or its mechanism.

The available epidemiologic data neither refute nor support the theory that parasitic disease protects against or causes asthma. A more definitive answer might come from a comparison of asthma prevalence in heavily parasitized and parasite-free subjects, or from a prospective study of asthma incidence in two or more comparable communities where one population is naturally or therapeutically free of intestinal parasites. If an effective antihelminthic vaccine is developed, it would also be interesting to

TABLE 2
Case-control studies

Country and study (reference no.)	Parasite prevalence		p value	Population
	In asthmatics	In controls		
South Africa (West Cape)	(n = 124)	(n = 70)		
Joubert and deKlerk (1979) (50)	45% +Stool* 41% +Sk.Rx.† 23% +Both 35% -Both	32% +Stool* 18% +Sk.Rx.† 6% +Both 54% -Both	NS¶¶ NS <0.01 NS	Asthmatics were from outpatient clinic; controls were from hospital wards.
Tanzania	(n = 14)	(n = 175)		
Carswell et al. (1977) (27)	57% +Stool‡	64% +Stool‡	NS	Survey of 242 rural schoolchildren
	(n = 8)	(n = 137)		
	25% +Urine§	37% +Urine§	NS	
Maldives	(n = 85)	(n = 817)		
Wolstenholme (1979) (29)	74% +Trichuris 33% +Ascaris¶	69% +Trichuris 36% +Ascaris¶	NS NS	Whole population survey of the islands
Nigeria	(n = 32)	(n = 30)		
Macfarlane et al. (1979) (51)	34% +Stool**	40% +Stool**	NS	Asthmatics were from outpatient clinic; controls were from the community.
Nigeria	(n = 36)	(n = 415)		
Warrell et al. (1975) (52)	22% +Stool††	37% +Stool††	NS	Asthmatics were from outpatient clinic; controls were other patients from clinics.
Scotland	(n = 24)	(n = 21)		
Jarrett and Kerr (1973) (53)	42% +Stool‡‡	28% +Stool‡‡	NS	Asthmatics were hospital admissions; controls were from the general surgical ward.
Singapore	(n = 108)	(n = 300)		
Cheah and Kan (1972) (63)	23% +Stool§§	18% +Stool§§	NS	Asthmatics and controls were patients of Department of Medicine, University of Singapore.

* +Stool, ova of *Ascaris* or *Trichuris* in stool.

† +Sk.Rx., skin reaction to *Ascaris* extract.

‡ Stool, any fecal parasite (mostly *Ascaris*).

§ +Urine, *Schistosoma haematobium* in urine.

|| +*Trichuris*, ova of *Trichuris* in stool.

¶ +*Ascaris*, ova of *Ascaris* in stool.

** +Stool, fecal parasite (not specified) present.

†† +Stool, ova of *Necator*, *Taenia*, or larvae of *Strongyloides* in stool.

‡‡ +Stool, ova of *Enterobius vermicularis* (threadworm) in stool.

§§ +Stool, ova of *Ascaris*, *Necator*, and/or larvae of *Strongyloides* in stool.

¶¶ NS, not significant.

watch vaccinees for development of, or changes in, asthma symptoms, and to determine whether these findings correlate with vaccine-induced changes in IgE.

REFERENCES

- Geller M, Flaherty DK, Capanema de Souza AP. Serum IgE levels in toxoplasmosis. *Ann Allergy* 1980;45:251-2.
- Bennich H, Johansson SGO. Structure and function of human immunoglobulin E. *Adv Immunol* 1971;13:1-55.
- Turner KJ, Feddema L, Quinn EH. Non-specific potentiation of IgE by parasitic infections in man. *Int Arch Allergy Appl Immunol* 1979;58:232-6.
- Dessaint JP, Capron M, Bout D, et al. Quantitative determination of specific IgE antibodies to schistosoma antigens and serum IgE levels in patients with schistosomiasis (*S. mansoni* or *S. haematobium*). *Clin Exp Immunol* 1975;20:427-36.
- Stanworth DR, Humphrey JH, Bennich H, et al. Specific inhibition of the Prausnitz-Kustner reaction by an atypical human myeloma protein. *Lancet* 1967;2:330-2.
- Stanworth DR. The experimental inhibition of reagin-mediated reactions. *Clin Allergy* 1971;1:25-35.
- Jarrett EEE, Orr TSC, Riley P. Inhibition of allergic reactions due to competition for mast cell sensitization sites by two reagins. *Clin Exp Immunol* 1971;9:585-94.
- Bazaraal M, Orgel HA, Hamburger RN. The influence of serum IgE levels of selected recipients, including patients with allergy, helminthiasis and tuberculosis, on the apparent P-K titre of a reaginic serum. *Clin Exp Immunol* 1973;14:117-25.
- Turner KJ, Fisher EH, Mayrhofer G. Age-dependent modulation of serum IgE and mast cell sensitization by *Nippostrongylus brasiliensis* infestation in rats. *Aust J Exp Biol Med Sci* 1981;59:491-502.
- Jarrett E, Mackenzie S, Bennich H. Parasite-induced "non-specific" IgE does not protect against allergic reactions. *Nature* 1980;283:302-4.
- Weltman JK, Senft AW. An analysis of allergy, immunoglobulin E, and diagnostic skin tests in schistosomiasis. *Parasite Immunol* 1981;3:157-63.
- Falk ES, Bolle R. IgE antibodies to house dust mite in patients with scabies. *Br J Dermatol* 1980;103:283-8.
- Ottesen EA, Kumaraswani V, Paranjape R, et al. Naturally occurring blocking antibodies modulate immediate hypersensitivity responses in human filariasis. *J Immunol* 1981;127:2014-20.
- Mazinqe C, Camus D, Dessaint JP, et al. *In vitro* and *in vivo* inhibition of mast cell degranulation factor from *Schistosoma mansoni*. *Int Arch Allergy Appl Immunol* 1980;63:178-89.
- Clark M, Shapiro D, Lindsay JJ. Allergy: new insights. *Newsweek*, August 23, 1982, 40-5.
- Lasch EE. IgE, parasites, and allergy. (Letter). *Lancet* 1976;2:255.
- Chacko DD. Intestinal parasites and asthma. (Letter). *N Engl J Med* 1970;283:101.
- Kok A, Robinson MJ. IgE, parasites, and allergy. (Letter). *Lancet* 1976;2:633.
- Tullis DCH. Bronchial asthma associated with intestinal parasites. *N Engl J Med* 1970;282:370-4.
- Farzan S. Intestinal parasites and asthma. (Letter). *N Engl J Med* 1970;282:1273.
- van Dellen RG, Thompson JH. Absence of intestinal parasites in asthma. *N Engl J Med* 1971;285:146-8.
- Godfrey RC. Asthma and IgE levels in rural and urban communities of the Gambia. *Clin Allergy* 1975;5:201-7.
- Merrett TG, Merrett J, Cookson JB. Allergy and parasites: the measurement of total and specific IgE levels in urban and rural communities in Rhodesia. *Clin Allergy* 1976;6:131-4.
- van Niekerk CH, Weinberg EG, Shore SC, et al. Prevalence of asthma: a comparative study of urban and rural Xhosa children. *Clin Allergy* 1979;9:319-24.
- Preston PJ. The biology of the atopic response. *R Naval Med Service J* 1970;56:229-35.
- Burger PJ. Die voorkome van intestinale parasiete by skoolkinders in die Tygerberagse omgewing. *S Afr Med J* 1968;42:811-12.
- Carswell F, Merrett J, Merrett TG, et al. IgE, parasites and asthma in Tanzanian children. *Clin Allergy* 1977;7:445-53.
- Nhonoli AM, Kihama FE, Ramji BD. Infection rates of Tanzanian rural communities by the common parasites and some of their haematological effects. *East Afr Med J* 1974;51:829-36.
- Wolstenholme RJ. Bronchial asthma in the southern Maldives. *Clin Allergy* 1979;9:325-32.
- Kaplan JE, Larrick JW, Yost JA. Hyperimmunoglobulinemia E in the Waorani, an isolated Amerindian population. *Am J Trop Med Hyg* 1980;29:1012-17.
- Knight R, Merrett TG. Hookworm infection in rural Gambia: seasonal changes, morbidity and total IgE levels. *Ann Trop Med Parasitol* 1981;75:299-314.
- May JM. The ecology of human disease. New York: MD Publications, Inc, 1958:231-48.
- Buckley JJC. A helminthological survey in northern Rhodesia. *J Helminthol* 1946;21:111-74.
- Cookson JB. "A handful of dust." Asthma and bronchitis in Rhodesia. *Cent Afr J Med* 1977;23:96-101.
- Grove DI, Forbes IJ. Increased resistance to helminth infestation in an atopic population. *Med J Aust* 1975;1:336-8.
- Ewers WH. Parasites of man in Papua-New Guinea. *Southeast Asian J Trop Med Public Health* 1972;3:79-86.
- Vines AP. An epidemiological sample survey of the highlands, mainland, and island regions of the territory of Papua and New Guinea. Port Moresby, New Guinea: VP Bloink, Government Printer, 1970:205, 210-12, 317.
- Anderson HR. The epidemiological and allergic features of asthma in the New Guinea highlands. *Clin Allergy* 1974;4:171-83.

39. Banik NDD. Epidemiology of gastroenteritis of pre-school children in slum areas in Delhi with reference to helminthic and parasitic infection. *Indian J Pediatr* 1978;45:303-9.
40. Kulkarni SW, Panicker PVRC, Gadkari AS, et al. Prevalence and patterns of parasitic infections in rural areas around Nagpur. *Indian J Med Res* 1978;68:583-91.
41. Chowdhury AB, Schiller EL. A survey of parasitic infections in a rural community near Calcutta. *Am J Epidemiol* 1968;87:299-312.
42. Viswanathan R, Prasad M, Thakur AK, et al. Epidemiology of asthma in an urban population: a random morbidity survey. *J Indian Med Assoc* 1966;46:480-3.
43. Oduntan SO. The health of Nigerian children of school age (6-15 years). II. Parasitic and infectious conditions, the special senses, physical abnormalities. *Ann Trop Med Parasitol* 1974;68:145-56.
44. Ejezie GC. The parasitic diseases of school children in Lagos State, Nigeria. *Acta Trop (Basel)* 1981;38:79-84.
45. Sotowora EO. Bronchial asthma in the tropics: a study of 250 Nigerian patients. *East Afr Med J* 1970;47:434-9.
46. Stanhope JM, Prior IAM. The Tokalau Island migrant study: prevalence of various conditions before migration. *Int J Epidemiol* 1976;5:259-66.
47. Knight WB, Lee D, Cline BL. Prevalence of intestinal parasites in a Puerto Rican community. *Bol Asoc Med PR* 1973;65:205-7.
48. Greenberg ER, Ferguson FA. Prevalence of intestinal helminth infections in 6-year old children in 18 municipalities of Puerto Rico. *Bol Asoc Med PR* 1971;63:208-11.
49. Sifontes JE, Mayol PM. Bronchial asthma in Puerto Rican children. *Bol Asoc Med PR* 1976;68:336-9.
50. Joubert JR, DeKlerk HC. *Ascaris lumbricoides* and allergic asthma. *S Afr Med J* 1979;56:599-602.
51. Macfarlane JT, Bachelor M, Ridyard JB, et al. Asthma, IgE and environment in northern Nigeria. *Clin Allergy* 1979;9:333-7.
52. Warrell DA, Fawcett IW, Harrison BDW, et al. Bronchial asthma in the Nigerian savanna region. *Q J Med* 1975;44:325-47.
53. Jarrett EEE, Kerr JW. Threadworms and IgE in allergic asthma. *Clin Allergy* 1973;3:203-7.
54. Shield JM, Scrimgeour EM, Vaterlaws AL. Intestinal helminths in an adult hospital population in the eastern highlands of Papua New Guinea: relationship with anaemia, eosinophilia and asthma. *Papua New Guinea Med J* 1980;23:157-64.
55. Turner KJ. The conflicting role of parasitic infections in modulating the prevalence of asthma. *Papua New Guinea Med J* 1978;21:86-104.
56. Chang KC, Sun YL, Chiu JK. A survey on parasitic infections among aborigines in remote mountain area of Chien-Shih District, Hainchu County, Taiwan. *J Formosan Med Assoc* 1973;72:297-303.
57. Liu HM, Ko RT, Lin TM, et al. A retrospective study on bronchial asthma in Shulin township, Taipei County, Taiwan. *J Formosan Med Assoc* 1972;71:493-8.
58. Center for Disease Control. Intestinal parasite surveillance annual summary, 1978. US DHEW, 1979.
59. US DHEW, PHS, HRA. US vital and health statistics data from the National Health Survey, series 11, no. 129, p. 14, November 1973.
60. Muschenheim C, Cranston WH, eds. *Bronchopulmonary diseases and related disorders*. Vol 2. New York: Harper and Row, 1972:667.
61. National Heart and Lung Institute. *Respiratory diseases—Task Force Report*. DHEW publication no. (NIH) 73-432, 1972:64.
62. Davis DJ. NIAID initiatives in allergy research. *J Allergy Clin Immunol* 1972;49:323-8.
63. Cheah JS, Kan SP. Lack of association between helminthic infestations and bronchial asthma in Singapore. *Aust NZ J Med* 1972;2:383-5.