

The influence of Environment and Parasitism on the prevalence of Asthma in two Venezuelan regions

Doris Perdomo de Ponce, Lorena Benarroch, Oscar Aldrey, Dalila Rodríguez, Anselmo Rosales, Emilio Avila and Nicolas Bianco.

Hospital de Clínicas Caracas, Avda. Panteón con Alameda, San Bernardino and Clinical Immunology National Center and World Health Organization Collaborative Center for Clinical Immunology (WHO/PAHO-SAS UCV), Caracas, Venezuela.

Key Words: bronchial asthma, tropical environment, parasitism.

Abstract. The point prevalence of bronchial asthma and the influence of environmental conditions among 100 individuals chosen from two Venezuelan regions, i.e., rural and urban, were investigated by history, routine laboratory tests, determination of total and specific IgE antibody to common allergens and spirometric tests. The point prevalence of bronchial asthma was 3,0% in rural subjects who were also highly parasitized by helminths and 3,6% in subjects from the urban region. A significant difference in skin responses to *Dermatophagoides pteronysinus* was observed in urban asthmatics when compared with rural asthmatics. A similar response to selected allergens was found among both populations. The prevalence of infestation by *Ascaris* in rural asthmatics was high compared with that of rural controls. Total IgE levels were elevated for both populations, but significantly higher ($p < 0.05$) for rural individuals. Results suggest a significant point prevalence of bronchial asthma in both regions, despite the helminth infestation of rural subjects. The effects of environmental factors, their concentration and time of exposure are considered as main factors responsible for allergic reactivity observed in the Venezuelan regions studied.

Received: 24-04-91 • Accepted: 29-07-91

INTRODUCTION

The prevalence of allergic diseases varies extensively depending

upon the geographical area under study (1,9,24,45). It has been stated the allergic diseases are infrequent in tropical environments (21,48,50),

mainly due to the extensive distribution of intestinal helminthiasis (32). However, the lack of uniform evaluation criteria has hampered to mark the unveiling nature of such low prevalence in developing countries located in the equatorial zone.

Numerous studies have used inappropriate criteria for defining bronchial asthma, for they have established its prevalence through questionnaires and clinical signs, without the benefits of objective measurements of lung function, recording percentages ranging from 0 to 7.8% in countries possessing tropical and sub-tropical regions (11,21). Most recent findings have demonstrated that the prevalence of bronchial asthma is a worldwide phenomenon with high, middle and low figures in tropical regions and also warm zones of the world (15).

Moreover, important differences have been detected between the asthmatic prevalence in urban zones and that of individuals from rural zones (30,37,52). The low prevalence in the rural areas has been attributed to a postulated blocking effect of potential helminthic infestation in rural areas (48). On the other hand, the higher prevalence of *Ascaris* infestation in rural asthmatics compared with that in urbans, seems to be related with the higher reactivity shown by the former patients, to *Ascaris* antigen, or with the induction of bronchial asthma in the host, by the release of antigens from the parasite (33,34). Therefore, the socioeconomic levels of tropical populations can influence allergic reactivity and intestinal helminthic infestation (36).

A higher infestation with mites has also been demonstrated in humid areas than in dry zones (31). Previous studies have indicated that 100% of mites mortality occurs in any species in 4 to 11 days of 50% relative humidity and temperatures above 25°C (5).

In a previous work, a significant prevalence of respiratory allergic diseases in school children from Caracas was found in Venezuela through questionnaires and integral immunoclinical tests performed in a selected sub sample of the total surveyed population (44). A partial independence of helminthiasis in relation to the incidence of atopic diseases and an independent coexistence of helminthic infestation and allergic diseases, have both been shown (43,35).

In this work, an experimental protocol was designed to investigate the actual prevalence of allergic respiratory diseases and its possible relationship with helminthic infestation in two selected Venezuelan populations (rural and urban).

MATERIALS AND METHODS

Populations and subjects

Rural sample: El Morro de Puerto Santo, a 3.688 habitants town, with an average of 6.9 members per family and a total of 534 families, was selected as the rural region for the study. Following our previous protocol (41), the size of the representative sample was 100 subjects from a low socio-economic level population (type V) (37), comprising 14 families stratified randomly selected for the study and completed

the established protocol, with an age average of 18 years, ranging from one month to 52 years.

Urban sample: Caracas, with 4.2 million inhabitants was selected as the urban region. A group of 100 persons from a middle low socio-economic class population (type III), which represented part of the 48% of the population with health control, were used in this study. No cigarette smoking or alcohol habits were found in either sample population.

Asthma was characterized by symptoms of wheezing, chest tightness or cough in a person with hyperresponsiveness over a period of 12 months or more, and the response to bronchodilator therapy. Asthmatic subjects (with or without symptoms) and non asthmatics (controls) without allergic respiratory symptoms, negative skin tests, and normal pulmonary function tests from the rural region were strictly matched by age and sex with asthmatics and controls from the urban area of Caracas. However, a similar correlation concerning the socio-economic status was not possible, since the rural population belonged to a low class whereas urban habitants were middle-low class.

All individuals were subjected to an integral immunoclinical evaluation, through clinical history and physical examination, hematological tests, feces analysis (for ova and parasites concentration), total serum IgE levels (PRIST-Pharmacia) and specific IgE antibody determination (in vivo PRICK tests, Hollister-Stier) against selected allergenic extracts. Based

on available data on the surrounding flora and environment, the conditions fostering the presence of allergens with universal distribution, were also recorded. Extracts included preparations of Bermuda grass (*Cynodon dactylon*), Short ragweed (*Ambrosia elatior*), *Cladosporium*, *Alternaria*, *Aspergillus fumigatus*, *Cat dander*, *Dermatophagoides pteronysinus* and *Dermatophagoides farinae*. Because of financial considerations, the in vitro (RAST- Pharmacia) evaluation was only made to: Bermuda grass (*Cynodon dactylon*), *Alternaria*, *Cat dander* and *Dermatophagoides pteronysinus*. Pulmonary function tests (Vitalograf-Spirometer Ltd.) pre and post bronchodilator were performed in parallel, determining Vital Capacity (VC), Forced Expiratory Volume during the first second (FEV1) and Forced Mid-Expiratory Flow (FEV₂₅₋₇₅). The predicted normal values were derivated from nomogram by Kamburoff and Weitowitz (28). By using a Mini Peak Flow Meter, the Peak Expiratory Flow (PEF) was included in the group of three children of less than 8 years of age who were unable to perform full respiratory function tests. More than 15% improvement of FEV₁, following inhalation of the usual dose of a beta adrenergic was generally agreed to be diagnostic of asthma. (13)

Clinical History

A detailed clinical history was completed on each subject selected for the study. It included: a questionnaire that we have developed composed of approximately 300 words

TABLE I
GEOGRAPHICAL AND CLIMATOLOGICAL DATA OF THE REGIONS
STUDIED

	URBAN	RURAL
Geographical Location	Between 10°24'- 10°33'N and 66° 44'- 67° 00'W	10° 43' 06' LAT.N 63° 09' 16" LONG. W
Daily mean solar radiation(kcal/cm ² /day)	326	389 - 550
Mean annual relative humidity (%)	75 - 80	76 - 80 (74 - 86)
Mean annual rainfall (mm)	800 (60 - 1200)	500 (273 - 2144)
Mean annual temperature (°C)	22 - 23	25 - 35.8 (19 - 28)
Mean annual atms. pressure (mb)	919.2	1013 (995-1015)
Mean hourly wind speed (Km/hr)	7 - 8	10 (28 - 108)
Wind prevailing direction	51% ESE - SE - SSE	NE

Numbers in brackets represent the corresponding range, and without brackets lowest and highest values.

that the flora found in El Morro de Puerto Santo (rural region) consisted of abundant Huisaches (*Poponax sp.*) from xerophitic zones, and *Pareskia quamacho*, *Bulensia arborea*, *Tubeduita serratifolia* and *Bromelia humilis* from very dry forests, grasses and weeds. This is a fishing region close to the sea, with houses made of clay block with electricity but inadequate sanitary conditions. People slept in beds or hammocks covered by a sheet.

On the other hand, the flora of Caracas (urban region) included bushes, savannahs, tropical deciduous forests, gallery forests, transition forests, tropical cloudy forests and subparamo; exotic trees were generally prevalent (*pinus*, *casuarina*, *eucaliptus*, *cupressus*), ruderal herbs and cereals. More than 50% of inhabitants are distributed in an area of about 20 Km in length by 12 Km in width, which is occupied by residential zones (16). The selected sample lived in an area

with satisfactory sanitary conditions.

Immunologic and clinical characteristics

One hundred randomly selected subjects from the rural region completed the established protocol. The average age was 18 years, ranging from 1 month to 52 years. Equal numbers of females and males were represented in the sample studied. Twenty seven per cent of them were found to be asthmatics by clinical history and bronchodilator therapy response. From the remaining 70 with no allergic respiratory symptoms and negative skin tests, only 31 were used as controls by strictly matching their age and sex. Ninety three per cent of the rural asthmatic individuals and 83% of control subjects had helminthic infestation. Polyparasitosis was observed in both rural asthmatic and correspondent controls, with similar positive percentages due to the following hel-

and/or key phrases, and each one has been reproducible which allowed the specialist physician to adapt the questions according to the educational level of the individual under evaluation, physical examination, and results of complementary tests. The answers were tabulated in symbols (+, related; -, negative; 0, non exposed and ?, unknown). A final diagnosis was reached after discussing each particular case with the research staff, analyzing the clinical variables and the results obtained from laboratory immunodiagnosis. Criteria for different pathologies were included according to definitions currently used (6,17,38).

Total and Specific IgE levels

Ten ml of venous blood were collected from subjects of the rural region; sera were separated and transported by plane in dry ice in approximately 30 min. to our laboratories in Caracas. The specimens were kept at -20°C until their analysis was completed. Total and specific serum IgE levels for the selected allergens were evaluated by radioimmunoassay (Pharmacia Diagnostic, Uppsala, Sweden) (19).

PRICK tests (39) were performed in the forearm flexor region, 2.5 cm. apart between each test, using solvent and histamine at 1 mg/ml as control. Positive tests were rated by the following scale: ≈ 3 mm = (2+); >3 mm = (3+) and >3 mm with pseudopods = (4+); after measuring the bigger diameter of the wheal and obtained its mean at the perpendicular or smaller diameter. Erythema was of little value in this

study, since we worked in a population, whose dark skin prevented us from accurately measuring its borders in approximately 70% of the subjects. Skin tests were applied in those individuals who had negative dermographism and had not taken antihistaminic drugs, sedatives, xanthenes or hydroxyzine for a period of 96 hours before the study. The same 8 allergens were used in both population samples.

Intestinal Helminthiasis

A stool sample was taken for determination of parasites and helminth eggs according to the method described by Kato (29). When the foregoing results were negative, up to three samples were studied for each rural subject as confirmatory approach. Three samples were always taken for urban individuals.

Statistical analysis

The analysis of the data was performed by the application of the X² test, and Student t test for normal distribution. The geometric mean for the total serum IgE values was used by logarithmic transformation (base 10), and Mann-Whitney test to analyze the combined data from the rural and urban-areas.

RESULTS

Characteristics of the two selected regions

Table I summarizes the most relevant geographical and climatological characteristics of the two selected regions during the dry season (3,14,18). It is worth adding,

minths: *Trichuris trichuria*, 74% and 72%, and *Necator americanus* 4% and 3%, respectively. Furthermore, a high prevalence (85%) of *Ascaris lumbricoides* was detected in asthmatic subjects, as compared with controls (48%). No helminths were detected in the corresponding urban population, mainly due to permanent sanitary prophylaxis among middle-low classes.

In relation to precipitating allergens, house dust was the most important factor referred to by the 27 asthmatics of each region, followed by exercise in a 70.3% for urban subjects, and pets in 23% of rural subjects (Table II).

On the other hand, Table III shows the point prevalence of bronchial asthma. Among urban individuals, it was of 3.6% whereas for rurals was of 3.0% with no significant difference ($p < 0.05$) when evaluating the change in FEV1. The total serum IgE levels were analysed in the population sample by the Mann-Whitney test with a significant difference among urban individuals. In urbans, the IgE (IU/ml)

geometric means were: 867 in asthmatics and 54 in controls, whereas in rurals, they were 1529 in asthmatics and 322 in controls. Urban subjects showed two-fold increased levels when compared with rural subjects. The presence of specific IgE antibodies to the group of allergens selected by PRICK and RAST techniques was analysed, demonstrating a significant difference ($p < 0.05$) in favor of PRICK test when comparing both techniques, and for urbans when compared with rurals (Table III).

Moreover, it was found that among specific allergens giving a relevant percentage of response, dust components were the most important in urban individuals but not in the rural region, where other allergens gave lower reactivity (Table IV).

The distribution of skin reactivity percentage is shown in Fig. 1. A greater response towards *Dermatophagoides pteronnyssinus* was found in urbans and similar patterns for the remaining allergens were observed. When testing the

TABLE II
POSITIVE SYMPTOMATIC REACTION TO PRECIPITATING FACTORS IN
ASTHMATIC PATIENTS

FACTORS	URBAN		RURAL	
	N	%	N	%
House dust	22	81.48	8	29.62
Exercise	19	70.37	5	18.51
Respiratory tract infections	17	62.96	1	3.70
Musty places, molds	16	59.25	1	3.70
Animals	10	58.82	6	22.22
Cutting grass/pollen grains	4	14.81	4	14.81

A total of 27 individuals were evaluated per region

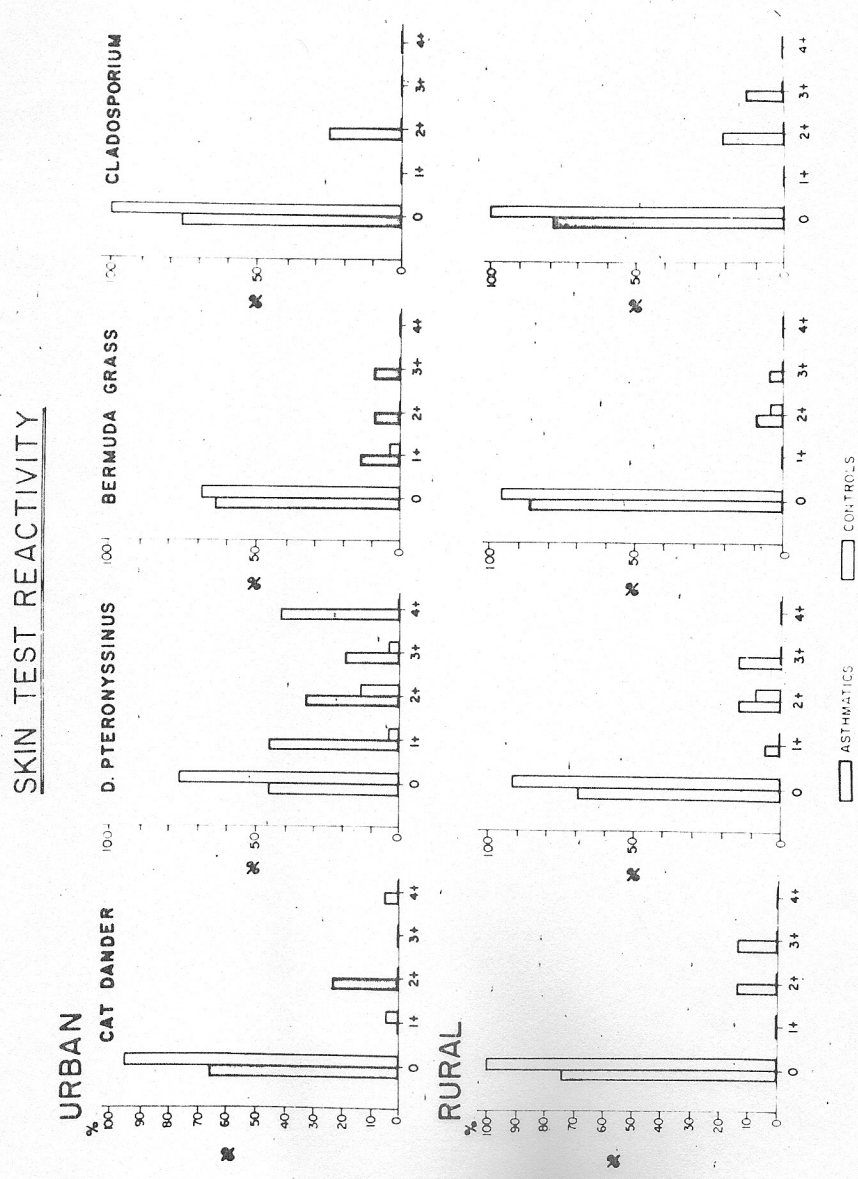


Fig. 1. The distribution of skin reactivity percentage.

TABLE III
IMMUNOLOGICAL AND CLINICAL CHARACTERISTICS OF THE TWO
SELECTED POPULATION

MEASUREMENTS	(% OF RESPONSE)			
	URBAN		RURAL	
	A	C	A	C
FEV1 (\geq 15% pos. response)	26 (+)	0	19	0
PRICK	96	16	64	12
RAST	50	23	33	0

A = asmatics (n=27); C = controls (n=31); (+) Only 23 were evaluated of 27

TABLE IV
PERCENTAGE OF SPECIFIC RESPONSE TO INDIVIDUAL ALLERGENS BY
SKIN TESTS REACTIONS

ALLERGENS	URBAN		RURAL	
	A	C	A	C
<i>D. pteronysinus</i>	91	16	28	8
<i>D. farinae</i>	78	7	24	8
<i>Cat dander</i>	40	0	24	0
Bermuda grass	19	0	12	4
Short radweed	26	0	-	-
<i>Alternaria</i>	19	0	12	0
<i>Cladosporium</i>	25	0	24	0

A = asmatics; C = controls.

reactivity percentage to the selected allergens by RAST, a similar result was detected in scale ($>2+$) (data not shown). Since the rural population were less often allergic to household allergens, one might expect that some times they can be more likely free of symptoms however, the contrary is shown in the previous figure. The patients were polysensitized specially to *Cat dander*, Bermuda grass, *Cladosporium*, as well as to the house dust mite *Dermatophagoides pteronysinus*.

DISCUSSION

Our figures for the point prevalence of bronchial asthma in rural and urban subjects, i.e., 3.0% and 3.6%, respectively, are found to be within the range of values reported for such diverse industrialized and developing countries as United Kingdom 1.2 to 9% (37), Australia 4.2 to 12% (51), New Zealand, 4.9 to 10% (49), The United States of America, 2.6 to 9% (8) and

the elevated prevalence of allergic diseases in children from Caracas, has been previously reported (4,7).

The existing controversy concerning the low prevalence of bronchial asthma found in tropical countries, is being modified as a result of numerous reports from rural populations, which tended to attribute to helminthic infestation, an inhibitory or blocking effect of IgE receptors in mast cells (20). On the other hand, the prevalence of asthma has also been viewed as a health problem, comparable to those in developed countries (30). Progressive studies carried out among urban and rural communities have contributed to clarify this question (2,23).

Today, the variations of climatic, ecological, cultural and genetic parameters are considered to be of major importance on the development of allergic pathologies (26). In our work, these parameters were taken into consideration, allowing the selection of allergens. Thus, other factors such as nutritional habits, and genetic factor seem to be involved and they will open a new research area in this wide point of view. The genetic factor, however, was not considered since the ethnic origin of our population has already been reported (41), as composed of mixed groups (Amerindians, Caucasics, Spaniards and Negroes).

The slight or moderate categories of bronchial asthma in both asthmatic groups prevailed. This could be explained through the adaptability of the autonomous and immune systems to the climatic conditions of the two regions studied

(10) and/or the concentration of environmental precipitant factors (27). The later was proved by the analysis of the percentage of reactivity to the selected set of allergens, where urban asthmatics were found to react highly to dust components (*Dermatophagoides pteronnyssinus* and *Dermatophagoides farinae*) and also presented a high and significant relation between the symptoms referred to dust than rural asthmatics. It is worth noting, that similar findings have been previously reported in other latitudes (22).

The rural region studied showed, in agreement with previous studies (31,5), more than 50% of relative humidity and temperature above 25° C, reaching the mentioned values during the dry season. Although the infestation levels with mite by species in both rural and urban regions could not be included in this work, we are aware of this as an interesting point to be considered in future investigations.

The significantly high level of total serum IgE found among rural asthmatics and their respective controls appears to suggest a stimulated synthesis of IgE, caused by helminthic infestation (25). A direct modulatory regulation in the expression of the response was not observed, but its independent coexistence was certainly demonstrated (42).

In addition, the relationship between asthma and allergic rhinitis among the two regions under study was found to be highly significant since 80% of patients with asthma had nasal symptoms; interestingly,

a similar tendency was reported in a Iowa community (46).

Finally, these observations led us to conclude that a high period prevalence of respiratory allergic diseases exist among the two Venezuelan regions studied in this work. Allergy to house dust mites appears to be a significant feature in the pathogenesis of the disease. The significant point prevalence of bronchial asthma, regardless of helminthic infestations, together with environmental factors, their concentration and time of exposure, appear to be the main feature responsible for the allergic reactivity demonstrated in this tropical climate.

ACKNOWLEDGEMENTS

The present investigation was funded by grants from CONICIT, (Fortalecimiento de Centro and S1 - 1373) and Ministerio de Sanidad y Asistencia Social.

The authors are grateful to Dr. Avilan Rovira and the editing service of CONICIT for reviewing the manuscript, to Tibisay for typing the manuscript and the people of El Morro de Puerto Santo for their cooperation.

RESUMEN

Influencia del medio ambiente e infestación parasitaria en la prevalencia de asma bronquial en dos regiones de Venezuela.
Ponce P.D. (Hospital de Clínicas Caracas, San Bernardino, Avenida Panteón con Alameda, consultorio 203, 2° piso, Caracas 1011,

Venezuela), Benarroch L., Aldrey O., Rodríguez D., Rosales A., Avila E., Bianco N. *Invest Clin* 32(2): 77 - 89, 199.

La prevalencia de asma bronquial e influencia de las condiciones ambientales entre 100 individuos escogidos de dos regiones venezolanas rural y urbana, fueron investigadas. A través de un protocolo pre-establecido se determinaron los siguientes parámetros: historia inmunoclínica, pruebas de laboratorio de rutina, determinación del anticuerpo IgE total y específico hacia alérgenos comunes y pruebas de funcionalismo pulmonar. Se obtiene una prevalencia puntual de asma bronquial de 3,0% en sujetos rurales altamente parasitados por helmintos y de 3,6% en sujetos de la región urbana no parasitados por helmintos. Se observó una diferencia significativa en la respuesta dérmica al *Dermatophagoides pteronnyssinus* de los asmáticos urbanos cuando se compara con los asmáticos de la región rural. Una respuesta paralela hacia los otros alérgenos seleccionados se encontró entre ambas poblaciones. La prevalencia de infestación por *Ascaris* en los asmáticos rurales fue elevada al ser comparada con la de los sujetos controles de la misma región. Niveles elevados de IgE total fueron detectados en ambas poblaciones, siendo más elevados ($p < 0.05$) en los individuos de la región rural. Los resultados sugieren una prevalencia puntual significativa de asma bronquial en ambas regiones, aún asociada a la infestación helmíntica de los sujetos rurales. Los efectos de los factores

ambientales tales como su concentración y tiempo de exposición de los individuos a riesgo, se consideran como posibles precipitantes de la reactividad alérgica observada en las regiones estudiadas.

REFERENCES

- 1- ABDERSON H.R.: The epidemiological and allergic features of asthma in the New Guinea Highlands. *Clin Allergy* 4: 171-175, 1974.
- 2- ALANKO K.: Prevalence of asthma in a Finnish population. A study of symptomatic subjects tested for bronchial hyperreactivity. *Scand J Respir Dis* 76(Supp):1, 1970.
- 3- ALVAREZ F.: Atlas climatológico de Venezuela. Imprenta Universitaria, pp. 19-132, 1983.
- 4- ANDERSON O., OROZCO A. PONCE P.D.: Incidencia de enfermedades atópicas en la población escolar venezolana. *Acta Cient Venez* 31: 145-148, 1980.
- 5- ARLIAN I.G.: Dehydration and survival of the European house dust mite. *Dermatophagoides pteronyssinus* *J Med Entomol* 12:437-441, 1975.
- 6- Asthma and other allergic diseases NIAID task Force report, NIH Publication N° 79-387, 117, 1979.
- 7- BENAÏM-PINTO C.: Resultados de pruebas cutáneas con polvos de casa de distinta procedencia. *Allergol et Innumopathol* 1: 133-136, 1971.
- 8- BRODER I., BARLOW P. and HORTON R.: The epidemiology of asthma and hay fever in a total community: Tecumseh, Michigan. *J Allergy* 33: 513-524, 1962.
- 9- BRODER I., HIGGINS M.W., MATHEWS K.P. and KELLER J.B.: III, Epidemiology of asthma and allergic rhinitis in a total community: Tecumseh, Michigan. *J Allergy and Clin Immunol* 53: 127-130, 1974.
- 10- BUCKLEY C. III, LARRICK J.: Population differences in methacholine responsiveness and circulating IgE concentration. *J Allergy and Clin Immunol* 76: 847-852, 1985.
- 11- CARSWELL F., MERRETT J., MERRETT T., MEAKINS R. and HARLAND P.: IgE, parasites and asthma in Tanzanian children. *Clin Allergy* 7:445-450, 1977.
- 12- CARSWELL F., MEAKINS R. and HARLAND P.: Parasites and asthma in Tanzanian children. *Lancet* 2: 706-708, 1976.
- 13- CIBA Guest Symposium report terminology, definition and classification of chronic pulmonary emphysema and related conditions. *Thorax* 44:286-290, 1959.
- 14- COPLANARCH.: Inventario Nacional de Tierras. Regiones Centro-Oriental y Oriental MAC-CENAIAP. Publicación N° 35.415-418, 1974.
- 15- DOWSE G., TURNER K., STEWART G., ALPERS M., WOOLCOCK A.: The association between *Dermatophagoides* mites and the increasing prevalence of asthma in village communities within Papua New Guinea Highlands. *J Allergy and Clin Immunol* 75: 75-79, 1985.
- 16- Estrategia de Desarrollo Urbano (OMPU). Plan General Urbano 1970-1990. Estructura económica de la región capital (MINDUR). Boletín Informativo.
- 17- FARR R.: One definition on asthma. *Chest* 87(1): 20-23, 1985.
- 18- FREILE A.: Regiones climáticas de Venezuela. Boletín de Geología 10(9): 3-8, 1968.
- 19- GLEICH G., JONES R.: Measurement of IgE antibodies by the radioallergosorbent test. *J Allergy and Clin Immunol* 55:334-338, 1975.
- 20- GODFREY R., GRADIDGE C.: Allergic sensitization of human lung fragments prevented by saturation of

- IgE binding sites. *Nature* 259: 484-488, 1976.
- 21- GODFREY R.C.: Asthma and IgE levels in rural and urban communities of the Gambia. *Clin Allergy* 5: 201-203, 1975.
 - 22- GREEN W., WOOLCOCKA., DOWSE G.: House dust mites in blankets and houses in the highland of Papua New Guinea. *Papua New Guinea Med J* 25: 219-223, 1982.
 - 23- GROVE D.: What is the relationship between asthma and worms? *Allergy* 37: 139-142, 1982.
 - 24- HAMMAN R.F., HALIL T., HOLLAND W.W.: Asthma in school children. *Br J Prev Soc Med* 29: 228-230, 1975.
 - 25- JOHANSSON S., MELLBIN T., VAHLQUIST B.: Immunoglobulin levels in Ethiopian pre-school children with special reference to high concentration of immunoglobulin E (IgND). *Lancet* i:1118-1121, 1968.
 - 26- JOUBERT J., VAN SCHLKWYK D., TURNER K.: *Ascaris lumbricoides* and the human immunogenic response. Enhanced IgE mediated reactivity to common inhaled allergens. *South African Med J* 57: 409-412, 1980.
 - 27- KABASAWA Y., ISHII A., MINATA H., TAKAOKA M.: Clinical significance of the house dust mites (*Dermatophagoides pteronnyssinus*) in asthmatic children in Japan. *Acta Allergol* 31: 442-444, 1976.
 - 28- KAMBUROFF P.L., WOITOWITZ H.J., WOITOWITZ R. H.: Prediction of spirometric indices. *Respiratory News Bull.* 17. 1- 4. Vitalograph Ltd., Buckingham, England. 1973.
 - 29- KATO K., MIURA M.: Comparative examination *Jap J Parasitology* 3:35-39, 1954.
 - 30- KNIGHT R., MERRETT.: Hookworm infection in rural Gambia. Seasonal changes, morbidity and total IgE levels. *Ann Trop Med and Parasitol* 75: 299-231, 1981.
 - 31- LANG J., MALLA M.: Seasonal dynamics of house dust mites. *Dermatophagoides* spp. in homes in southern California. *Environ Entomol* 7: 281-284, 1978.
 - 32- LARRICK J.W., MACHAMER C.E., SCHLAGEL G.D., YOST J.A., BUCKLEY C.E. III, BLESSING-MORE J., LEVY D.: Does hyperimmunoglobulinemia E protect tropical populations from allergic diseases? *J Allergy and Clin Immunol* 71(2): 184- 188, 1983.
 - 33- LYNCH N., ISTURIZ G., SANCHEZ Y., PEREZ M.: Bronchial provocation with *Ascaris* in asthma. *En Immunologia Clinica* 89.p 228-231. Machado I. y Bianco N. (Eds.) Fondo Edit. CONICIT. 1989.
 - 34- LYNCH N., LOPEZ R., ISTURIZ G., TENIAS-SALAZAR E.: Allergic reactivity and helminth infestation in Amerindians of the Amazon basin. *Int Arch Allergy appl Immunol* 72: 369-372, 1983.
 - 35- LYNCH N., MADOUZE L., DIPRISCO F.M., VERDE O., LOPEZ R., MALAVE C.: Incidence of atopic diseases in a tropical environment. Partial independence from intestinal helminthiasis. *J Allergy and Clin Immunol* 73: 229-233, 1984.
 - 36- LYNCH R.N., LOPEZ R.I., DIPRISCO-FUENMAYOR M.C., HAGEL I., MEDOUZE L., VIANA G., ORIEGA C., PRATO G.: Allergic reactivity and socio-economic level in a tropical environment. *Clin Allergy* 17: 199-203, 1987.
 - 37- MENDEZ C.H., MENDEZ M.C.: Estratificación social y biológica humana. *Arch Venez Puer y Ped* 49:93-102, 1986.
 - 38- MERRETT., MERRET J., COOKSON J.: Allergy and parasites: The measurement of total and specific IgE level in urban and rural communities in Rhodesia. *Clin Allergy* 6: 131- 134, 1976.
 - 39- MYGIND N., WEEKE B.: Allergic and nonallergic rhinitis. In *Allergy*.

- Principles and Practice", Vol. 2, Middleton, E. Jr., Reed C., Ellis E.F. (Eds), St. Louis, The C.V. Mosby Company, pp. 1101-1111, 1983.
- 40- NORMAN P.S.: Skin testing. In "Manual of Clinical Immunology", Rose, N., and Friedman, H. (Eds), ed. 2, Washington, D., American Society for Microbiology; Chap. 106, p. 789-794, 1989.
- 41- PEREZ-ROJAS G., MOYA P., BIANCO N., ABADI I.: Seronegative spondyloarthropathies and HLA antigens in a mestizo population. *Tissue Antigens* 23: 107-110, 1984.
- 42- PONCE P.D., ANDERSON O., ILJA A., BIANCO N.: Total serum IgE levels in Venezuelan schoolchildren. *Clin Allergy* 13: 521-524, 1983.
- 43- PONCE P.D., BENARROCH L.: Alergia y parásitos. Una asociación dissociable. En *Inmunología* 89, p 223-226, Bianco N y Machado I. Fondo Editorial CONICIT. Caracas, 1989.
- 44- PONCE P.D., BENARROCH L., ALDREY O., RODRIGUEZ D., ROSALES A., MARQUEZ P., RODRIGUEZ E., AVILA E., RODRIGUEZ P., PERDOMO M., BIANCO N.: Independent coexistence of allergic and parasitic infestation in the same population. *Annals of Allergy* 55(2) Abst. 429, 1985.
- 45- PONCE P.D., QUIJADA L., MUÑOZ J., FERNANDEZ R., OSSOT B., BIANCO N.: Prevalence of allergic diseases in Venezuela. *International Symposium on Prevention of Allergic Diseases (Italy)*, Abst. 101, 1984.
- 46- SMITH J.M.: Epidemiology and natural history of asthma, allergic rhinitis and atopic dermatitis (eczema). In "Allergy, Principles and Practice", Elliot Middleton Jr., pp 771- 803 Reed C.E. and Ellis E.F., (Eds). 2nd. Edit. Vol. II, 1983.
- 47- SMITH J.M., KHOWLER L.: Epidemiology of asthma and allergic rhinitis. I. In a rural area. II. In a university centered community. *Am Rev Respir Dis* 92: 16-19, 1965.
- 48- SMITH J.M.: Studies of the prevalence of asthma in childhood. *Allergol Immunopathol* 3: 127-129, 1975.
- 49- TURNER K.J.: The conflicting role of parasitic infection in modulating the prevalence of asthma. *Papua New Guinea Med J* 21: 86-89, 1978.
- 50- WAITE D., EYLES E., TONKIN S., O'DONNELL T.: Asthma prevalence in tokelavan children in two environments. *Clin Allergy* 10:71-75, 1980.
- 51- WARREL D.A., FAWCETT I.W., HARRISON B.D.W., AGAMAN A.J., IBU J.O., POPE H.M., MABERLY D.J.: Bronchial asthma in the Nigerian Savanna Region. *Quart J Med* XLIV: 325-326, 1975.
- 52- WOOLCOCK A., DOWSE G., TEMPLE K., STANLEY H., ALPERS M., TURNER K.: The prevalence of asthma in the South Fore People of Papua New Guinea. A method for fields studies of bronchial reactivity. *Eur J Respir Dis* 64: 571-575, 1983.