

ORIGINAL ARTICLES

Airborne allergens and clinical response of asthmatics in Arad, a new town in a desert area in Israel

S. Zvi Kantor, M.D., Menachem Frank, M.D., Donna Hoch-Kantor, M.Sc., Rivka Barkai-Golan, Ph.D., Dina Marian, M.Sc.,** Elbio Schachnner, M.D., Arthur Kessler, M.D., and Andre de Vries, M.D., Tel Aviv and Arad, Israel.*

A clinical study of patients with intractable asthma coming to the new Judean desert town of Arad was carried out concurrently with an aerobiological survey. Pollen and mold concentrations in the air of Arad were about one third and one half, respectively, of those in the central coastal region of Israel. Excellent to moderate clinical responses to the stay in Arad were observed in 84 per cent of the asthmatic subjects. The moderate reduction of pollen and mold spore content in the air of Arad is not a satisfactory explanation for the beneficial results. The reason for improvement of asthmatics in desert climates in many instances still remains unsolved.

Intractable asthma in children and adults represents a worldwide sociomedical problem. Treatment in special sanatoria and in residential centers, mainly for

From the Allergy Research Unit, Rogoff-Wellcome Medical Research Institute, Department of Experimental Biology of the Tel Aviv University, Beilinson Hospital, Petah-Tiqua, the Central Allergy Clinic Zamenhof of the Labour Sick Fund, Tel Aviv, the Labour Sick Fund Clinic in Arad, the National and University Institute of Agriculture, Rehovot, and the Department of Botany of the Tel Aviv University, Israel.

Supported by the Arad Development Project, Ministry of Labour and Ministry of Housing and the Ministry of Health, Israel.

A part of this study was presented at the Fifth International Congress of Allergology in Madrid, October, 1964.

Received for publication January 25, 1965.

*Address: (S. Z. K.), Beilinson Hospital, Petah-Tiqua, Israel.

**The pollen survey in this study is a part of a Master of Science thesis submitted to the Department of Botany of the Tel Aviv University by Mrs. D. Marian.

asthmatic children, is known to have a favorable influence on patients with intractable asthma.¹⁻³ Yet failures are still recorded, and a considerable number of patients do not benefit from the stay in such institutions. Although the psychological effect of the change of environment has long since been appreciated,⁴ some of the failures of institutional treatment may be related to the fact that these sanatoria and homes are not free from offending allergens such as molds and pollen. Indeed, allergen-containing environments cannot be expected to help truly allergic patients, especially those allergic to various airborne inhalants.

The present study was prompted by the observation of marked clinical improvement in asthmatic subjects who were among the first settlers in a new town being established in the Judean desert at the historical location of the Biblical City of Arad. It was the aim of this study to investigate the aerobiological conditions of Arad which, because of its dry climate and scanty desert vegetation, might possibly become a future refuge for allergic asthmatics and to evaluate the clinical effects of this environment on such patients.

The present report includes a follow-up study, consisting of a comparison between aerobiological survey of pollen and mold spores in Arad and central coastal region of the country, and observations of asthmatic patients, adults as well as children, who were allergic to airborne inhalants and who spent a period of 4 to 6 weeks in Arad.

HISTORY AND LOCATION OF ARAD*

Arad is known from the Bible as the central town of the eastern Judean desert during the Canaanite and Israelite periods. The exact date of the conquest of Canaanite Arad is not known, but the king of this town is mentioned among the thirty-one kings who were conquered by Joshua and the sons of Israel (*Joshua XII*). One of the main Israelite fortresses was built in Arad by King Solomon.

The district of Arad (Fig. 1) covers an area of 750,000 dunams (1 dunam = 1,000 square meters) and lies northeast of Beersheba, bordering on the Hebron Mountains to the north and the Dead Sea to the east, about 12 Km. in straight airline from the Beersheba-Sodom Road in the south and the Beersheba-Hebron Road in the west. The position of Arad is about 600 meters above sea level and 1,000 meters above the Dead Sea. The district has meager rainfall and a dry desert climate. Because of the inadequate rainfall there is no intensive agricultural development, and the town is planned for a 50,000 population within 10 years, mainly for industrialization and as a holiday, tourist, and health resort. Meteorological data from Arad over the years 1961 to 1963, as compared to the central coastal region, are shown in Table I.

It may be seen from the table that, whereas there are no marked differences between the two regions in the temperatures, the humidity values in Arad are considerably lower than in the central coastal region. It has to be pointed out that in the summer months of August, September, 1963, when most of the patients were in Arad, the humidity values were relatively high, especially at night. During the year 1963-1964, the Negev district had an unusually rich rainfall and,

*Quoted from a pamphlet issued by the Arad Development Project of the Ministry of Labour, Government of Israel, 1963.

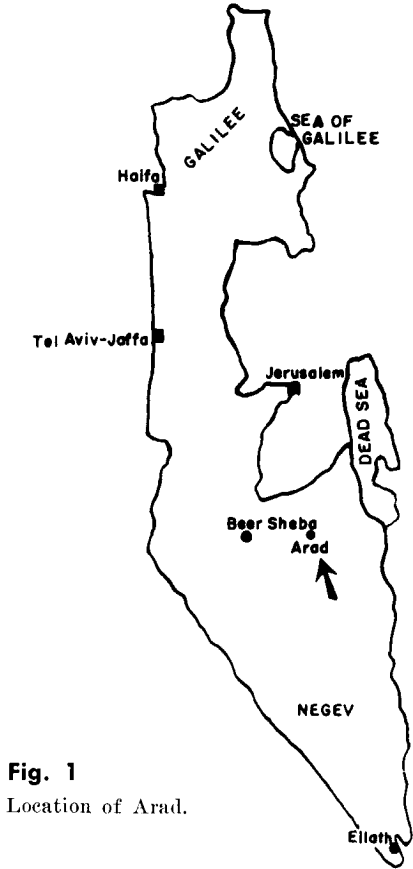


Fig. 1
Location of Arad.

Table I. Climatological means from Arad and the central coastal region (1961-1963)

Month	Arad					Central Coastal Region				
	Temperature (°C.)		Relative humidity (%)			Temperature (°C.)		Relative humidity (%)		
			8	2	8			8	2	8
	Maximum	Minimum	A.M.	P.M.	P.M.	Maximum	Minimum	A.M.	P.M.	P.M.
January	16.4	6.1	67	44	62	18.8	7.4	82.2	58.7	81.4
February	16.5	7.6	69	44	63	18.4	7.4	77.7	55.5	79.9
March	20.4	9.8	62	35	55	21.4	7.3	72.8	51.8	75.5
April	23.6	11.2	52	28	51	24.2	10.4	65.4	50.3	74.8
May	28.4	13.8	47	22	49	27.5	13.7	60.7	47.1	69.7
June	32.6	17.7	39	19	38	30.2	16.5	62.1	47.8	72.5
July	32.8	18.0	48	22	48	30.9	18.7	68.1	54.7	76.0
August	33.2	18.1	59	27	56	31.6	20.6	70.5	55.5	75.7
September	30.2	15.9	63	31	59	30.2	18.0	66.6	53.4	73.8
October	28.0	15.6	56	30	59	28.4	15.6	69.0	53.1	78.2
November	23.6	14.2	45	28	46	25.8	11.1	69.4	46.1	74.8
December	16.9	8.8	59	42	58	19.9	8.5	76.9	55.3	79.9

All figures were supplied by the Meteorological Service of the Ministry of Transport and Communications, Bet Dagon, Israel.

according to the native Bedouin nomads, such weather had not occurred for at least three decades.

MATERIAL AND METHODS

A. Aerobiological studies

Agar plates for molds and glycerin jelly slides for pollen were exposed simultaneously at Arad and at the Beilinson Hospital in Petah Tiqua, the latter located in the central coastal plain of the country, which has a humid climate (Table I) and is rich in vegetation.

1. *Collection and counting of atmospheric mold spores.* Petri dishes, 9 cm. in diameter, containing Sabouraud medium, were exposed horizontally for 15 minutes. Exposures were made every other day at 9 A.M. at fixed places exposed to all directions; two plates were exposed simultaneously. Since at the time of this study there were no high buildings in Arad, exposures were made about 4 M. above the ground at two locations, in the western and in the eastern parts of the locality, about 50 M. distance from each other. The meteorological data for air temperature and relative humidity were recorded. Exposures in the central coastal region at the Beilinson Hospital, the highest structure in the vicinity, were made on the roof at 18 M. altitude. The plates exposed in Arad were sent to the laboratory at the Beilinson Hospital where colonies were counted and identified after a one-week period of incubation at room temperature. The total number of colonies and the number of the most frequently found genera were calculated monthly.

2. *Pollen counts.* Pollen counts were performed by the gravity slide method according to Durham.⁵ Glass slides covered with a thin film of methyl green glycerin jelly were placed on a Durham exposure apparatus, simultaneously in Arad and on the roof of the Beilinson Hospital, as described above for exposure of mold plates. The slides were exposed for a period of 24 hours, and the pollens in a slide cover glass area (3.24 cm.²) were identified and tabulated after conversion to 1 cm.². Objective $\times 10$ with ocular $\times 12.5$ was used for counting. Averages of the numbers of different pollens were calculated monthly.

B. Clinical studies

Eighty-five subjects with asthma were followed clinically. Fifty-six of these patients had been referred to our allergy unit before going to Arad. After a detailed history of the allergy, these 56 patients were skin tested by the intradermal method for various inhalants such as house dust, molds, and pollen. Despite positive skin tests to various inhalants which generally correlated well with the patient's history of allergy, it was decided that upon their arrival in Arad they should not receive hyposensitization treatment, in order to make evaluation of climatic effects possible. The usual drugs for symptomatic relief were given if necessary. Corticosteroids were not given to the patients during their stay in Arad, except for the few who had previously been on them, and were gradually weaned from using them as they improved. A second group consisting of 15 patients, 8 adults and 7 children, came to Arad on their own, without previous work-up at our unit. This group of patients was also followed

clinically during their stay in Arad. All patients of both groups were asked to visit our unit at the Beilinson Hospital for follow-up observation after leaving Arad; however, only 22 of them responded.

A third group of 14 patients, 7 adults and 7 children, chose to settle permanently in Arad. They were included in this study as a separate group.

RESULTS

I. Mold counts

The monthly means of colony number per plate at each of the two sites in Arad were generally lower than those found at Beilinson Hospital (Fig. 2). The monthly means per plate at Beilinson Hospital were between 11.5 and 20 colonies, while at Arad means of 6.5 to 15.5 were obtained. A seasonal variation in the number of fungal spores in the air, which had been previously found in other parts of the country,^{6, 7} was noted in Arad, as well as in Beilinson. In both places a marked decrease in the number of colonies occurred typically during the winter months, January and February. In Arad, apart from this relative decrease during the winter months, comparatively low numbers appeared also in the still warm months of September and October. No studies were carried out at Beilinson during these latter months. The number of colonies obtained at the two sites in Arad were generally very similar.

The main components of the air spora both at Arad and in Beilinson, similar to what has been recorded for other parts of the country,^{6, 7} were of the following genera: *Hormodendrum* (*Cladosporium*), *Alternaria*, *Penicillium*, and *Aspergillus*.

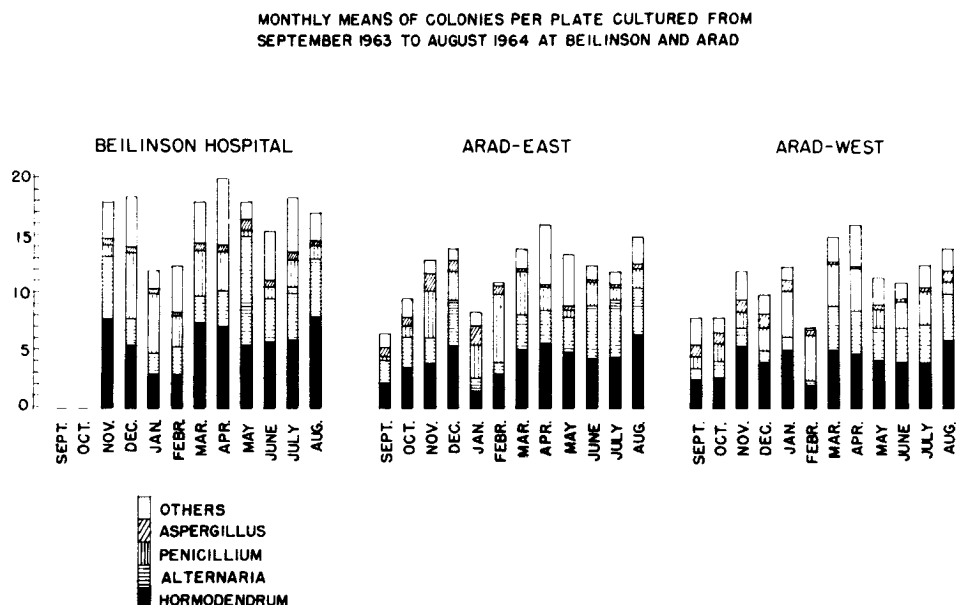


Fig. 2

Mold counts in Arad and at Beilinson Hospital.

lus. Other fungi which were rarely collected, as well as unidentified fungi with a sterile mycelium, were included as a miscellaneous group.

Hormodendrum was the most frequently found airborne mold at all sites of exposure. It constituted 35 per cent of the total population of molds collected at both sites in Arad and 33 per cent at Beilinson. Alternaria constituted 20 to 24 per cent of the fungal population at the three sites investigated. While no marked differences were seen in the distribution of the above two important airborne fungi, both Penicillium and Aspergillus attained a somewhat higher percentage at Arad than at Beilinson. Penicillium constituted 21 to 22 per cent at Arad and 19 per cent at Beilinson. Aspergillus attained almost 6 per cent at both sites in Arad as compared to only 2.5 per cent at Beilinson.

The miscellaneous group included many genera of which the commonest were: *Stemphylium epicoccum*, *Fusarium*, *Pullularia*, *Botrytis*, *Mucor*, *Rhizopus*, *Helminthosporium*, *Trichoderma*, *Cephalosporium*, *Phoma*, *Trichothecium* and *Paecilomyces*. These genera were collected both at Arad and at Beilinson. The more rarely found genera included: *Chaetomium*, *Nigrospora*, *Stachybotrys*, *Hormiscium*, *Geotrichum*, *Sporotrichum*, *Monilia*, *Papularia*, *Spondyloccladium*, *Curvularia*, *Memnoniella*, *Scopulariopsis*, *Gliocladium*, *Circinella*, and *Sclerotium*.

The group of Actinomycetes was represented by the genera *Streptomyces* and *Micromonospora* and constituted about 1 per cent of the total catches at all stations.

II. Pollen counts

Fig. 3 represents the monthly means of pollen counts per 1 cm.² slide area. The total amount of pollen was about 50 per cent lower in Arad than in the Beilinson region. In Arad a total of 962 pollen grains were counted, while in Beilinson 1,934 were counted. In Arad and Beilinson there were two pollination seasons, spring and fall, which occurred in the two areas in different months and with a difference in the kind of flowering. March showed the highest peak, a total pollen count of 1,222 per 1 cm.², in Beilinson, whereas a much lower count of 360 per 1 cm.² was found in April. It is noteworthy that, due to rich rainfall, pollination started very early and a large amount of pollen was already counted in Beilinson in February. February in Arad showed a very low count. During the months November, December, and January, the pollen count in Arad and Beilinson was very low but never reached zero. September-October showed the peak for autumn pollination, especially gramineae, artemisia and eucalyptus. In Arad, April reached a peak with a pollen count of 530, mostly gramineae and compositae. The amount of gramineae in this month was even higher than that counted at the Beilinson Hospital. March showed also a considerable high count of compositae and some gramineae. The autumn season, September-October, in Arad showed a much lower pollen count than at the Beilinson Hospital. Most of the pollen counted in these months were gramineae and Artemisia.

Fig. 3 shows also an entirely different kind of flowering in both places. We found, for example, large amounts of *Pinus*, *Cupressus*, and *urtica* (nettle) in Beilinson whereas no such pollens were found in Arad. We found also large

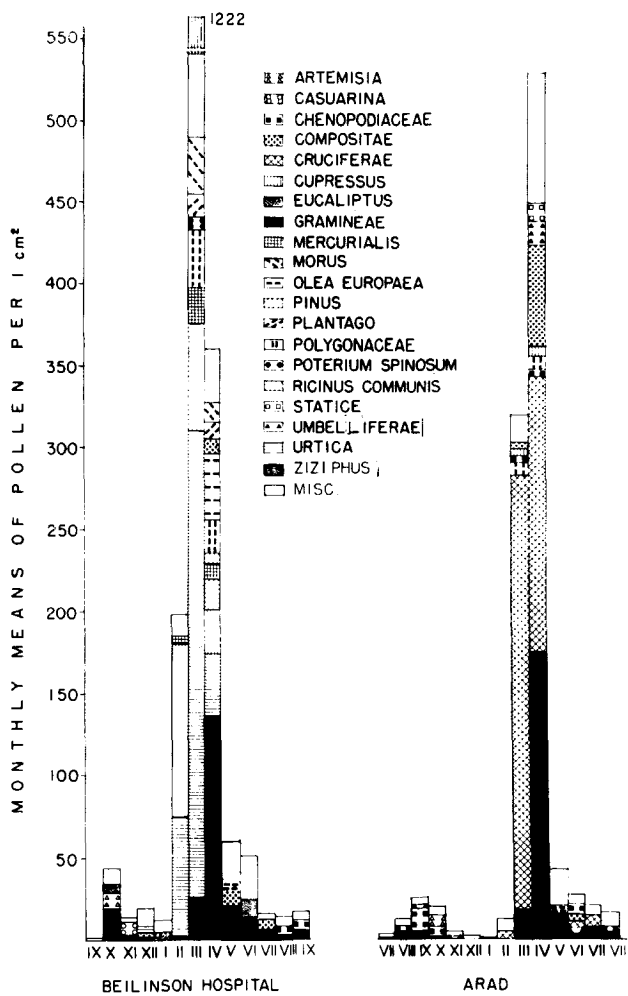


Fig. 3
Pollen counts in Arad and at Beilinson Hospital.

amounts of compositae and cruciferae in Arad, while only traces of these plants were found in the Beilinson Hospital area. Artemisia were found in the same amounts in both places.

III. Clinical results

Table II represents the clinical response of 56 patients staying in Arad at various periods during the year July, 1963 to June, 1964, most of them during July-August, 1963. Thirty-five had an excellent response. While the majority of these improved rapidly after arrival in Arad, some required at least one month to become free of asthma attacks. These subjects did not suffer from attacks for the rest of their stay in Arad and did not need any drug treatment. Their activities were normal without any restrictions. Children reacted more rapidly than adults.

Table II. *Clinical response to climatic conditions in Arad of 56 asthmatic patients with allergy work-up prior to admission*

Description of clinical observation	Excellent (35 patients)		Moderate (12 patients)		Failure (9 patients)	
	Adults	Children	Adults	Children	Adults	Children
a. Within 8 days in Arad	9	13				
b. Within 2 weeks in Arad	4	2				
c. Over one month in Arad	5	2				
a. On less medication and no asthma attacks			4	1		
b. Less medication but one asthma attack			5	2		
a. 3 weeks in Arad					4	
b. 3 months in Arad					1	
c. Hospitalized					2	2

Twelve subjects showed moderate improvement. They continued to require symptomatic medication but less than they used to take at their homes. In 5 patients some episodes of wheezing were recorded, but no real asthma attacks occurred. Seven patients had one asthmatic attack. As in the previous group these patients were not restricted in their activities.

Nine patients showed no improvement during their stay in Arad. Two adults and two children needed hospitalization, one because of intractable asthma and three others because of bronchopneumonia. Four adults with intractable asthma left Arad within three weeks without having improved and escaped follow-up. One adult with severe emphysema and recurrent respiratory infections showed some improvement at the beginning, but then relapsed. After spending three additional months in Arad he finally left without any improvement.

Of the group of 15 asthmatic subjects who came to Arad on their own, without having been previously examined at our allergy unit, the majority became free of attacks, but 20 per cent did not so improve.

Impressive results occurred in a group of 14 asthmatic subjects, 7 adults and 7 children, who settled in Arad and were followed for a period of 6 to 22 months. The over-all results were similar to those in the previous groups, but because of the prolonged follow-up period, the significance of the observation is much greater.

COMMENT

These observations constitute the initial part of a planned long-term study of the allergic history of the newly established desert community of Arad and of the influence of its climate on asthmatic subjects, either settling or temporarily visiting in this town. This study will comprise aerobiological, clinical and immunological aspects. To our knowledge no such allergic history of a desert town has been reported in the literature, except for the study by Wilkinson of Ahmadi in Kuwait.⁸

Although the clinical observations presented here cover only a short stay of asthmatic subjects in this new settlement, we were impressed by the over-all good results obtained. All patients studied have had severe asthma for several years with prolonged periods of status asthmaticus and failure of usual management, often including steroids. Only the subjects with intractable asthma, either by their own decision or that of the parents, agreed to a period of trial in this new settlement with its still primitive living conditions. Eighty-four per cent of the patients improved, either markedly (62 per cent) or moderately (22 per cent), whereas the remaining 16 per cent did not respond. It is noteworthy and of possible therapeutic significance that the nonresponding subjects had asthma with recurrent upper respiratory infections, and most of them had negative skin tests to airborne inhalants.

Whereas the good or fair response to Arad of those patients with positive skin tests to airborne inhalants might point to the favorable influence of an allergen-poor environment, it was surprising to find relatively high mold spore and pollen counts in Arad during the year of study. Although the counts, especially of pollen, were considerably lower than in the central coastal region, they were unexpectedly high for a desert area. The high pollen counts in this year may have been exceptional and due to the unusually rich rainfall, which according to the Bedouins had not been noted in the Negev desert for the past three decades. Still, it is possible that the good response of the truly allergic subjects occurred because the pollen and molds counts represented subthreshold values. This, however, must remain speculative. It is therefore gratifying that the Arad management has consented to consult with our team on the kinds of vegetation planned for Arad, with a view to keeping its environment as far as possible allergen-free.

We are not in the position to evaluate the psychosomatic factors which may have been active in the clinical improvement of the asthmatic subjects during their stay in Arad. It must be pointed out, however, that the improvement in most of the asthmatic children in Arad was attained while their parents and often siblings stayed with them for the period of observation.

Since in a still incomplete follow-up study it became evident that nearly all allergic patients with asthma relapsed within rather short intervals after returning home from Arad, and since permanent residents of Arad also experienced asthmatic attacks as soon as they visited the central coastal region, it seems worthwhile to institute prolonged hyposensitization treatment starting during the patient's stay in Arad. Such a therapeutic trial is being undertaken and will be evaluated in the future.

Our thanks are due to Center Laboratories, Inc., Port Washington, N. Y., and Hollister-Stier Labs, Los Angeles, Calif., for supplying of the allergy extracts, to Colonel J. Pundak, Director of the Arad Development Project, and Mr. Z. A. Aharoni, Arad, for their valuable assistance and close cooperation in this study.

REFERENCES

1. Bukantz, S. C., and Peshkin, M. M.: Institutional Treatment of Asthmatic Children, *Pediat. Clin. North America* 6: 755, 1959.

2. Bernstein I. L., et al.: A Community Approach to Juvenile Intractable Asthma, *Pediatrics* **26**: 586, 1960.
3. Steen, W. B.: Rehabilitation of Children With Intractable Asthma, *Ann. Allerg.* **17**: 864, 1959.
4. Peshkin, M. M.: Asthma in Children. IX. Role of Environment in Treatment of Selected Groups of Cases; Plea For a "Home" as a Restorative Measure, *Am. J. Dis. Child.* **39**: 774, 1930.
5. Durham, O. C.: The Volumetric Incidence of Atmospheric Allergens. IV. A Proposed Standard Method of Gravity Sampling, Counting and Volumetric Interpolation of Results, *J. ALLERGY* **17**: 79, 1946.
6. Barkai-Golan, R.: A Study of Airborne Fungi in Israel, *Bull. Res. Council of Israel, Sect. D., Botany* **1**: 247, 1958.
7. Barkai-Golan, R., and Glazer, J.: Airborne Fungi in Eilat and Tel-Hashomer, Israel, *J. ALLERGY* **33**: 342, 1962.
8. Wilkinson, W. M.: Development of Allergy in the Desert, *J. Trop. Med. & Hyg.* **67**: 16, 1964.