

# INVESTIGATION OF THE PREVALENCE AND INHERITANCE OF BRONCHIAL ASTHMA IN SAN ANTONIO DE LOS BAÑOS, CUBA<sup>1,2</sup>

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*Cuban physicians consider bronchial asthma a common ailment in their country, but this opinion has not previously been supported by statistical analysis of data from medical service records or field studies. Pertinent data on the prevalence of asthma in other countries are also rather scarce. This article reports the results of a survey on the prevalence and inheritance patterns of bronchial asthma in a municipality of La Habana Province.*

## Introduction

Pertinent data on asthma prevalence, which have been obtained primarily through hospitals, vary widely from one country to another. A report from five pediatric hospitals in Moscow (1) cites a prevalence of 0.3 per cent. Richards (2) found a rate of 1.2 per cent at the Children's Hospital of Los Angeles, California, over the 30-year period 1935-1964. A survey of the entire population of Johnson County, Iowa (3) found 277 asthma cases among 7,330 persons, giving a rate of 3.8 per cent for this rural low-income region. Viswanathan (4) found a prevalence of 1.8 per cent among 363,700 inhabit-

ants of Patna, Bihar, India, in 1966. Wasunna (5) reported a rate of 2.8 per cent among 8,005 patients seen over a two-month period at the Kenyatta National Hospital in Nairobi, Kenya. And in Japan, Yoshida (6) reported finding a rate of 2.3 per cent in 1964, while Wada (7) found a rate of 18.9 per cent among women workers at cultured pearl beds in two areas. Figures from other studies (8) are shown in Table 1.

Not only are these world statistics sketchy, but in our own country there has until now

<sup>1</sup>Study carried out by the National Asthma Commission as part of the research program of the Ministry of Public Health of Cuba. Article based on a report previously presented at the VII Asthma Congress of the International Association of Asthmology held in July 1972 at Helsinki, Finland.

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TABLE 1—*Asthma prevalence rates found by studies in seven countries, 1961-1969.*

Country and area studied	Year of study	Asthma prevalence
Yugoslavia: Gasco Kopoanik, Sorplanine, and Zlatibor (mountain areas)	1968	0.2%
Canada: Chilliwack, B.C.	1963	0.7%
Sweden: Uppsala	1966	2.2%
Sweden: Uppsala	1968	2.4%
Sweden: Goteborg	1967	2.8%
United States: Houston, Texas	1966	2.8%
Finland: Harjavalta, Satakunta	1961	3.7%
England: Aberdeen	1962-1964	4.8%
New Zealand: Lower Hutt (schoolchildren)	1969	4.9% (girls) 9.2% (boys)

Source: World Health Organization, World Health Statistics Report 24 (7): 450-451, 1971.

been no statistical analysis of the asthma problem. The report that follows presents the findings from an investigation of bronchial asthma prevalence and inheritance patterns in San Antonio de los Baños, a municipality of La Habana Province, made as part of a nationwide survey.

### Materials and Methods

San Antonio de los Baños is in the west-central part of La Habana Province, about 14 miles from both the north and south coasts of Cuba and 18 miles south-west of the City of Havana. According to a fairly recent census (9), its population consisted of 29,892 persons living in 7,421 households. Of this total, 25,304 people and 6,274 households were classified as urban, the remainder (4,588 people in 1,147 households) being considered rural.

#### *Selection of the Sample*

Selection of our sample was based on a housing plan of San Antonio de los Baños provided by the National Planning Board of Cuba (JUCEPLAN). This detailed plan had been drawn up during a pilot census carried out in the municipality prior to the National Census of 1970.

For purposes of the present study, the whole municipality was divided into urban and rural

zones. The basic units selected for study were square city blocks in the urban zones and individual farms in the rural areas. The urban selection was made by sectoring the city into quadrants and taking random samples of urban units within each quadrant. The same procedure was followed for the rural units. Fortunately, the total number of blocks (212) and the total number of farms were both fairly equally distributed among the four quadrants.

#### *Size of the Sample*

It was assumed from the beginning, on the basis of available information, that the prevalence of asthma cases was at least 5 per cent, and it was felt that 100 cases (and preferably 150) would be needed in order to provide a sound basis for analysis. Therefore, the number of survey participants needed was on the order of 3,000 persons.

To assure a sufficiently large number of participants, an initial sample of 3,300 persons (10 per cent above the required minimum) was selected. In accord with the relative proportion of urban and rural dwellers, it was decided that 2,790 subjects should come from urban parts of San Antonio de los Baños and 510 from the farms. These figures were only slightly different from the actual numbers of people (2,744 urban residents and 551 farm residents) from

whom interviews were eventually obtained. In all, 825 households (698 urban and 127 rural) were included in the survey—these figures reflecting the average numbers of occupants per house in the urban and rural zones.

Because the number of inhabitants per block was fairly regular, we were able to select six blocks in each quadrant to obtain an urban sample of the desired size. However, this could not be done in the rural areas, because there was no precise data as to the number of houses per farm. Therefore, once the number of rural dwellers desired from each quadrant had been determined, the farms selected for the study were visited until this number of interviews had been obtained.

### Field Work

Raw data for the study were collected by fifth-year medical students who had received an intensive week-long seminar on the program's theoretical and practical aspects. Every student was also provided with precise written instructions for completing a basic questionnaire about each subject interviewed. The students then visited the homes selected, interviewed the residents, completed the questionnaire, and carried out a physical examination of each suspected or confirmed asthmatic.

The daily press and radio were used to tell the people of San Antonio de los Baños about the survey a few days before it began. Instructions were published and general cooperation

was requested. Local public health authorities and members of the National Asthma Commission also worked with the CDR (a popular mass organization) in order to further promote public collaboration. A general check on the whereabouts of the people to be interviewed showed the preliminary information used in planning the project to be correct for each of the four quadrants involved.

In some cases up to three visits were needed to obtain an interview, and in others even three visits were not enough. In the latter event, a note was left asking the people involved to visit the local headquarters of the National Asthma Commission between 7 a.m. and 11 p.m., so that they could be included in the study. Out of the 3,300 persons in the sample, all but five were eventually interviewed. That is, 3,295 persons (11 per cent of the population) were interviewed (see Table 2). In each case the opinion of the interviewer was reviewed by three of the authors and correlated with the subject's family history, clinical symptoms, age at onset, and physical examination. Most of the positive cases had been diagnosed previously at Cuban medical institutions. The diagnosis was also matched against a score-sheet of symptoms on which asthmatics were expected to accumulate 35 points or more (see Appendix). A previous test of this scoring system, using the clinical records of 279 known asthmatics at the Calixto García University Hospital, showed that these patients invariably accrued at least 35 points, whereas 212 non-asthmatics failed to do so.

TABLE 2—*Distribution of sample by sex and age, showing a comparison of the size of each age group in the sample and in the pre-1970 census.*

Age group (years)	Male	Female	Total	% of each age group in:	
				Sample	Pre-1970 census
<1 year	36	29	65	2.0	1.6
1-4 years	148	117	265	8.1	11.3
5-9 "	202	200	402	12.2	10.0
10-14 "	137	124	261	7.9	7.8
15-24 "	263	267	530	16.1	16.1
≥ 25 "	879	892	1,771	53.7	53.2
Not registered	1	0	--	--	--
Total	1,666	1,629	3,295*	100	100

\*This total represents 11.02 per cent of the population of San Antonio de los Baños.

## Results

Three hundred and twenty-one (9.7 per cent) of the persons interviewed were found to be asthmatics. Of these, 291 lived in urban parts of the municipality and 30 lived in rural areas. Therefore, the observed prevalences of bronchial asthma were 10.4 per cent among urban residents and 5.9 per cent among farm dwellers. Table 3 shows the distribution of the 321 asthmatics by sex and place of residence, and Table 4 provides a similar breakdown by sex and age.

TABLE 3—Survey participants classified as asthmatics, subdivided by sex and urban vs. rural areas of residence.

Area of residence	Male	Female	Total	
			No.	% of sample
Urban	140	151	291	10.43
Rural	13	17	30	5.88
Total	153	168	321	9.74

TABLE 4—Distribution of 321 asthmatics by age group and sex.

Age group (years)	Male	Female	Total
< 1 year	2	0	2
1-4 years	25	6	31
5-9 "	34	36	70
10-14 "	12	13	25
15-24 "	40	41	81
≥25 "	39	72	111
Not registered	1	0	1
Total	153	168	321

Efforts were also made to see if the observed asthma cases were linked to the eight presumably allergic manifestations listed in Table 5. As indicated, a majority of the asthmatics were found to suffer from a stuffed-up nose, coryza, and persistent sneezing, while relatively small percentages experienced urticaria and eczematous dermatitis. One hundred and forty of the 321 asthmatics said their asthma was seasonal, but only 29 associated it with their occupation (see Table 6). Treatments used by the 321 asthmatics are shown in Table 7.

To get a better idea of the relationship between asthma cases and a family history of allergy,<sup>8</sup> 321 persons were selected at random from the 2,674 non-asthmatics in our sample. It was found that 25.8 per cent of these subjects had a family history of allergy and 74.2 per cent did not. In marked contrast, 84.1 per cent of our 321 asthmatics had a family history of allergy (see Table 8).

We also tried to determine if a family history of allergy had a statistically significant effect on the age of asthma onset. However, since the age of onset could not be determined for 20 asthma cases, the number of cases considered in this analysis was reduced to 301. As Table 9 shows, the median age of onset for all cases with a positive family history of allergy was 3.23 years, while for those with a negative family history it was 4.47 years, and for the two groups combined it was 3.44 years. When asth-

<sup>8</sup>That is, a family history of asthma, coryza, or urticaria. Asthma was the disease cited in most cases.

TABLE 5—Percentages of 321 asthmatics experiencing other allergic disorders, by sex.

Disorder	Males		Females		Total	
	No.	%	No.	%	No.	%
Stuffy nose	101	66.0	105	62.5	206	64.2
Coryza	87	56.9	112	66.7	199	62.0
Persistent sneezing	86	56.2	97	57.7	183	57.0
Itching nose	69	45.1	87	51.8	156	48.6
Inflamed eyes	46	30.1	83	49.4	129	40.2
Itching eyes	56	36.6	71	42.3	127	39.6
Urticaria	27	17.6	30	17.9	57	17.8
Eczematous dermatitis	4	2.6	3	1.8	7	2.2
Total	153	100	168	100	321	100

TABLE 6—Share of 321 asthmatics associating their disease with seasonal variations or occupations.

	Males	Females	Total
<b>Seasons:</b>			
"Summer"-related	14	15	29
"Winter"-related	51	60	111
Present in both seasons	86	92	178
<b>Seasonal relationship</b>			
unknown	2	1	3
Total	153	168	321
<b>Occupations:</b>			
Occupation-related	15	14	29
Not occupation-related	120	134	254
<b>Occupational relationship unknown</b>			
18	20	38	
Total	153	168	321

matism with a positive history on one side of their families were compared to those with a positive history on both sides, the difference in the median age of onset (3.58 years vs. 3.06 years) was not found to be statistically significant ( $p < 0.35$ ). On the other hand, comparison of those with a positive family history against those without did show a statistically significant difference ( $p < 0.05$ ) in the respective ages of onset (3.23 years vs. 4.47 years).

## Discussion

No entirely satisfactory definition of asthma is yet available (9-12), but this does not create insurmountable obstacles for successful and accurate diagnosis. As previously noted, in our study the diagnosis was based on three things: a special form containing the subject's medical history and the results of a medical examination by the interviewer; the provisional diagnosis of the interviewer, reviewed by three of the authors; and the score attained by applying the forementioned 35-point scoring system to the completed form. The 321 cases diagnosed by these criteria represented 9.74 per cent of the total sample, a proportion considered indicative of the asthma prevalence in San Antonio de los Baños.

The study showed a much higher prevalence of asthma in urban parts of the municipality than in rural ones. Although many authors

(13-15) speak of environmental factors such as geographic location and man-created environments, we were unable to find any past reports comparing urban and rural prevalence of the disease (see Table 3).

No significant differences were found in the prevalences of asthma among the two sexes, a result in accord with the widely accepted view that asthma is not a sex-linked disease (16).

Seasonal variations in Cuba are not marked. For the purposes of this paper, "summer" means the period when slightly warmer temperatures prevail (from April through September), and "winter" refers to the October-March period when the climate tends to be slightly cooler. As shown in Table 6, most asthmatics in the survey (57 per cent) did not relate their disease to any particular season. Those who did cite a seasonal relationship most frequently cited the "winter" months.

No relation could be found between the asthmatics in our group and their occupations (see Table 6). Some reports cite "occupational asthma" as a special form of asthma (17-19), and some even consider it to be a non-immunological variety of the disease (20). Nevertheless, immunologic and genetic disorders can always be implicated to some degree, at the very least as silent factors that can be triggered by certain environmental conditions.

Most of the patients studied (88 per cent) became asthmatic before their fifteenth birth-

day. Only 37 (12 per cent) did so after that; only three (1 per cent) did so after their fortieth birthday, and no one became asthmatic after reaching 47. The oldest asthmatic in the group was 67 years of age and the youngest was approximately one month old (for additional details on age distribution see Tables 2 and 4).

Inheritance was found to strongly affect the prevalence of bronchial asthma. Roughly 84 per cent of the asthmatics in the sample had a family history of allergy (asthma, coryza, or urticaria), while less than 26 per cent of an equivalent group of non-asthmatics had such a family history. This difference has a very high degree of statistical significance ( $p < 0.0003$ ).

The inheritance of asthma was first discussed 300 years ago, when an unusually high incidence was noted in one family; but the matter did not receive widespread attention until Coca introduced the term "atopy" to describe an allergic state subject to hereditary influences, and until the role of these influences became recognized (21). Nevertheless, the nature of the genetic mechanism involved in asthma transmission has remained obscure.

On the other hand, a few basic conclusions have been reached. For one thing, lack of differences in the distribution of asthma by sex (a finding supported by the present study) implies an autosomal inheritance pattern. There has been some discussion about whether asthma could be passed on by one genetic character of a simple dominant or simple recessive type (22, 23). Though these terms are considered relative (24), if such a character were recessive, heterozygous parents could be expected to produce asthmatic children about one-quarter of the time. Likewise, if it were dominant, one non-asthmatic parent and one heterozygous asthmatic parent could expect to have asthmatic children about half the time. Lack of evidence, either from our research or from other studies, indicating inheritance patterns like these suggests more complex mechanisms are at work.

In a similar vein, dominant characteristics are often more pronounced in homozygotic people; but our work has shown no marked differences in the age of onset of seriousness of asthma cases in persons with a history of allergy on both sides of their families, as compared to

TABLE 7—Medical treatments received by the 321 asthmatics surveyed.

Medicaments	Males	Females	Total
	(No. of cases)	(No. of cases)	
Corticosteroids	121	124	245
Gargling solutions	102	112	214
Medicated aerosols	98	87	185
Aminophylline	86	79	165
Anti-asthmatic syrup	73	74	147
Anti-histamines	61	80	141
Anti-asthmatic pills	30	45	75
Vaccines	31	30	61
Epinephrine	16	25	41
Other treatments	28	42	70

TABLE 8—Family histories of allergy (asthma, coryza, or urticaria) found among 321 asthmatics and 321 non-asthmatics.

	Asthmatics		Non-asthmatics	
	No.	%	No.	%
Positive family history	270	84.1	83	25.8
Negative family history	51	15.9	238	74.2
Total	321	100	321	100

those with a history on only one side. Therefore, in our opinion the observed asthma inheritance patterns can probably best be explained by more complex phenomena involving multifactorial or polygenic transmission, influenced perhaps by linkages, pleiotropy, polymorphism, varying degrees of expression, or other factors.

Some authors (25, 26) have found that the age of onset tends to be earlier among patients with a history of allergy on both sides of their families than among those with such histories on only one side. These findings have not been statistically confirmed by our study.

In order to test various hypotheses about age of onset, three tests using data for the median age of onset were performed. The results are shown in Tables 9-12.

Table 9 shows the distribution of the 301 asthmatics studied, according to age of onset and type of family history. The median age of onset for each group is shown on the bottom line.

Table 10 compares the median age of onset for subjects with and without a family history of allergy. First, the number of cases above and below the overall median age (3.44 years) was determined. Then the average numbers that would be expected below the median age in each group were found by multiplying the total number of cases with a particular family history

(250 or 51) by the overall proportion of cases below the median age ( $\frac{151}{301}$ ); the average numbers that would be expected above the median age were found the same way (250 or 51 times  $\frac{150}{301}$ ). In each case the average number expected is shown beneath the actual number observed. Application of a  $X^2$  test to these results indicated a 90 per cent probability that the differences observed were significant.

A similar procedure was applied to the figures for asthmatics with a family history of allergy on both sides vs. no family history (Table 11). Again, statistically significant differences ( $p < 0.05$ ) were observed. However, a comparison of those with a family history on one side vs. a family history on both sides (Table 12) did not reveal a statistically significant difference ( $p < 0.35$ ). In the event of multifactorial inheritance, a difference of this kind could easily be explained merely by additive effects or varying degrees of expression.

Szentivanyi (27) has linked bronchial asthma to an enzyme defect involving adenyl-cyclase deficiency affecting normal stimulation of beta receptors. Kerr (28) has found unusual amounts of urocanic acid in the urine of asthmatic patients and has suggested that there may be delayed histamine breakdown with accumulation of histamine in the tissues.

TABLE 9—Classification of 301 asthma cases by the patient's age at onset and family history. The two types of family history considered in columns 2 and 3 are combined in column 4.

Age of onset of asthma	No family history of allergy		Family history of allergy (one side)		Family history of allergy (both sides)		All cases with a family history of allergy		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
<1 year	9	17.6	36	32.1	36	26.1	72	28.8	81	27.0
1-4 years	19	37.3	31	27.7	64	46.4	95	38.0	114	37.8
5-9 years	7	13.7	21	18.8	17	12.3	38	15.2	45	15.0
10-14 years	6	11.8	10	8.9	8	5.8	18	7.2	24	8.0
15-24 years	3	5.9	8	7.1	8	5.8	16	6.4	19	6.2
≥25 years	7	13.7	6	5.4	5	3.6	11	4.4	18	6.0
Total	51	100	112	100	138	100	250	100	301*	100
Median age of onset	4.47 years		3.58 years		3.06 years		3.23 years		3.44 years	

\*The patient's age at onset of the disease was not available for 20 of the 321 asthma cases observed.

TABLE 10—Possible effects of a family history of allergy on age of asthma onset: positive vs. negative family histories.

	Under median age of onset*	Over median age of onset*	Total
No. with positive family history .....	130	120	250
No. expected .....	(124.41)	(124.58)	
No. without positive family history .....	21	30	51
No. expected .....	(25.58)	(25.45)	
Total .....	151	150	301

\*Median age of onset: 3.44 years (see Table 8).

 $\chi^2 = 1.967$   $p < 0.10$  $\chi^2 = 1.64$ 

TABLE 11—Possible effects of a family history of allergy on age of asthma onset: positive histories (both sides) vs. negative family histories.

	Under median age of onset*	Over median age of onset*	Total
No. with positive family history (both sides) .....	74	64	138
No. expected .....	(68.63)	(69.37)	
No. without positive family history .....	20	31	51
No. expected .....	(25.37)	(25.63)	
Total .....	94	95	189

\*Median age of onset: 3.39 years.

 $\chi^2 = 2.71$   $p < 0.05$  $\chi^2 = 3.11$ 

TABLE 12—Possible effects of a family history of allergy on age of asthma onset: positive histories (one side) vs. positive histories (both sides).

	Under median age of onset*	Over median age of onset*	Total
No. with positive family history (one side) .....	59	53	112
No. expected .....	(57.34)	(54.66)	
No. with positive family history (both sides) .....	69	69	138
No. expected .....	(70.65)	(67.34)	
Total .....	128	122	250

\*Median age of onset: 3.23 years (see Table 8).

 $\chi^2 = 0.1779$   $p < 0.35$  $\chi^2 = 0.15$



Innate metabolic defects have been found for over sixty genetic diseases, and in all cases a gene (whether identified or not) is considered responsible for the defect. However, multifactorial genetic disorders are polygenic by definition, and if the inheritance of bronchial asthma belongs to this class, as we believe, a lone enzyme defect (and consequently a lone affected gene) cannot provide the full explanation. This idea does not directly contradict enzymatic theories of asthma etiology (which are probably correct); but it does suggest the need for a more comprehensive overview of immunologic and genetic asthma research.

### Conclusions

- Our survey indicated a bronchial asthma prevalence for San Antonio de los Baños of 9.74 per cent.
- Asthma prevalence in urban portions of the survey area was twice that in rural portions (10.43 vs. 5.88 per cent).
- Onset of a predominant share of the cases studied (87.75 per cent) occurred before the patient reached 15 years of age.

- Neither sex nor occupation appeared to have a significant effect on the prevalences observed.
- Other allergies were frequently found to be associated with asthma.
- Probably because of Cuba's mild climatic variations, the proportion of seasonal asthma cases was not high.
- A highly significant relationship between asthma and a family history of allergy (asthma, coryza, or urticaria) was observed when the family histories of asthmatics and a randomly selected group of non-asthmatics were compared ( $p < 0.0003$ ).
- Likewise, asthmatics with a positive family history tended to have an earlier age of asthma onset than those with negative family histories ( $p < 0.10$ ). However, our study showed no statistically significant difference between the age of asthma onset among patients with positive histories on one side of the family, as compared to those with positive histories on both sides ( $p < 0.35$ ).
- Our study tends to confirm that the inheritance of bronchial asthma is autosomal and does not conform to simple dominant or recessive inheritance patterns.

### SUMMARY

A survey of bronchial asthma prevalence and inheritance patterns was carried out in the municipality of San Antonio de los Baños, La Habana, Cuba, employing as a sample 3,295 of the area's inhabitants. These persons, selected by stratified, non-restricted sampling techniques, represented 11.02 per cent of the total population.

The asthma prevalence found in this sample, which was considered representative of the local population, was 9.74 per cent. No significant variations were noted in male and female prevalence rates.

The occurrence of bronchial asthma is strongly influenced by inheritance. Our survey

supported this view, and also showed that the age of asthma onset is influenced by whether or not the subject's family has a positive history of allergy or not. However, patients with a positive history on one side of their family had an age of onset that was not significantly different from patients with a positive history on both sides ( $p < 0.35$ ). Overall, the results tend to confirm that the inheritance of bronchial asthma is autosomal and does not conform to simple dominant or recessive inheritance patterns. Rather, asthma inheritance appears multifactorial, perhaps involving varying degrees of expression, indicating that more is involved than absence or deficiency of a single enzyme.

## ACKNOWLEDGMENTS

We are sincerely grateful to the Vice-Ministry of Medical Care and Medical Education of the Ministry of Public Health for the support given to this study. We also wish to thank the public health organizations at the provincial and regional levels in La Habana and San Anto-

nio, respectively, for their cooperation and for the facilities they made available for this work, as well as the Department of Technical Operations of the National Statistics Bureau of the Ministry of Public Health for computation and tabulation of the data obtained.

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## APPENDIX

## Diagnostic criteria (positive diagnosis based on accumulation of 35 points or more)

- |   |    |        |
|---|----|--------|
| 1) Subject's history of asthma symptoms:                                  |    |        |
| a) positive current symptoms .....  | 8  | points |
| b) positive past symptoms .....   | 4  | "      |
| 2) Known age of onset (only for adults $\leq 30$ years of age .....       | 8  | "      |
| 3) Presence of other concurrent allergic symptoms:                        |    |        |
| a) Coryza .....   | 3  | "      |
| b) Inflamed eyes .....  | 3  | "      |
| c) Sneezing .....   | 3  | "      |
| d) Rash .....   | 3  | "      |
| e) Itchy nose .....   | 3  | "      |
| f) Itchy eyes .....   | 3  | "      |
| g) Nasal obstruction .....  | 3  | "      |
| 4) Symptoms of respiratory distress:                                      |    |        |
| a) Seasonal symptoms .....  | 3  | "      |
| b) Respiratory wheezing .....   | 15 | "      |
| c) Sensation of weight on chest .....                                     | 2  | "      |
| 5) Family history of allergy .....  | 5  | "      |
| 6) Data from physical examination:  |    |        |
| a) Presence of emphysema (only for subjects $\leq 30$ years of age) ..... | 5  | "      |
| b) Presence of sibilants .....  | 3  | "      |
| c) Presence of rash .....   | 2  | "      |
| 7) Drugs used by subject:   |    |        |
| a) Aerosols .....   | 3  | "      |
| b) Aminophylline .....  | 3  | "      |
| c) Antihistamine tablets or syrup .....                                   | 1  | "      |
| d) Corticosteroids .....  | 2  | "      |
| e) Vaccines .....   | 5  | "      |
| f) Sympathomimetics .....   | 5  | "      |