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THE ARTHUS REACTION TO CANDIDA ALBICANS IN ASTHMA PATIENTS

By

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Candida albicans, heretofore rarely considered of aetiological significance, has recently been reported as a not infrequent cause of bronchial asthma. In a previous paper an attempt was made to evaluate the incidence of *Candida albicans* sensitivity as detected by skin testing in respiratory allergic diseases (2). This is a further study to determine the frequency of the Arthus reaction in these candida sensitive asthmatic patients, to consider the effect of adding *Candida albicans* to the desensitizing extracts, and also to find out whether the presence of an Arthus reaction to candida had any relationship to the severity of the disease or effect on desensitization.

MATERIAL AND METHOD

The study included 190 asthmatic patients with a positive skin sensitivity test to *Candida albicans*. As well as skin testing with the common inhalants, they were tested with *Candida albicans*, using the prick method (9) with a 5 per cent extract solution (Beecham Research Laboratories). If this test proved negative, an intracutaneous test with a 1 per cent extract solution was used. Results were read by comparing the site of testing with a control. The reaction was considered a positive immediate one if there was redness and itching maximal at 15-30 minutes after testing. Patients were seen the next day for any evidence of a localised Arthus response, that is oedema, erythema, haemorrhage and in severe cases necrosis occurring a few hours after testing. Every patient's history included the duration and severity of the disease (14) and were graded into mild, moderate or severe (11). The frequency of corticosteroid therapy was also graded into those patients who had one to four short courses who were graded +, those receiving five to ten short courses were graded ++, while those cases receiving more than ten short courses or prolonged treatment for years

were graded +++ . The patients were hyposensitized for at least one year with aqueous extracts containing the appropriate allergens. They were divided into two groups:

Group I were given mixed allergens and *Candida albicans*.

Group II were given mixed allergens without *Candida albicans*.

The extracts used for hyposensitization were prepared by the author. The technique of preparing the extracts and the injection procedure have already been described (3), but the maximal dose of the candida extract never exceeded 10,000 Noon units. The patients received maintenance injections of the maximum tolerated dose at intervals of 2-3 weeks, over a period of 2-3 years. Results of desensitization were interpreted as excellent, good, poor and worse.

RESULTS

In the 190 asthmatic patients with a positive skin sensitivity test to *Candida albicans*, there were 99 males and 91 females. Table 1 shows the incidence and percentage of *Candida albicans* sensitivity detected by immediate skin test and/or an Arthus reaction in both sexes.

TABLE 1
The Incidence of Immediate Skin Sensitivity Tests and Arthus Reactions to Candida Albicans in 190 Asthmatic Patients.

	Number of patients	Immediate reaction	Arthus reaction
Males	99	94 (94.2 %)	26 (26.3 %)
Females	91	89 (98.8 %)	24 (25.3 %)
Total	190	183 (96.3 %)	50 (26.3 %)

When evaluating the Arthus reaction in relation to the age of the patients it was found that it was less frequent in the younger age group (Table 2).

Taking into consideration the duration of the asthma, the incidence of an Arthus reaction to *Candida albicans* was more frequent the longer the duration of the disease (Table 3).

Grading the bronchial asthma into mild, moderate and

severe (5), the Arthus reaction was found to be more prevalent in the severe types of the disease (Table 4).

As regards the frequency of receiving corticosteroid therapy, whether graded nil, +, ++, +++, the Arthus response was noted to be more marked in those asthmatics receiving frequent courses of the drug (Table 5).

TABLE 2

The Incidence of Arthus Reaction to Candida Albicans in the Different Age Groups of Asthmatic Patients.

Age group in years	Number of patients	Arthus reaction
0-10	33	6 (18.2 %)
11-20	41	8 (19.5 %)
21-30	48	16 (33.3 %)
31-40	38	8 (21.1 %)
41-50	20	9 (45.0 %)
<51	10	3 (30.0 %)
Total	190	50 (26.3 %)

TABLE 3

The Incidence of the Arthus Reaction to Candida Albicans in Relation to the Duration of Bronchial Asthma.

Duration of bronchial asthma in years	Number of patients	Arthus reaction
0-5	86	18
6-10	54	13
11-15	33	12
<15	17	7
Total	190	50

When analysing the results of hyposensitization with extracts containing *Candida albicans* as well as other antigens to which the patients proved to be sensitive, it was found that 76 per cent of children below the age of 10 years gave ex-

TABLE 4

The Incidence of the Arthus Reaction to Candida Albicans in Relation to the Severity of Bronchial Asthma.

Grade of bronchial asthma	Number of patients	Arthus reaction
Mild	93	4
Moderate	72	34
Severe	25	12
Total	190	50

TABLE 5

The Incidence of the Arthus Reaction to Candida Albicans in Relation to Frequency of Corticosteroid Treatment in Asthmatic Patients.

Frequency of treatment with corticosteroids	Number of patients	Arthus reaction
—	26	2
+	39	6
++	37	11
+++	88	31
Total	190	50

TABLE 6

The Result of Hyposensitization in the Different Age Groups with Extracts Containing Candida Albicans.

Age group in years	Number of patients	Excellent	Good	Bad	Worse
0-10	25	19	4	2	0
11-20	32	21	10	0	1
21-30	22	11	8	3	0
31-40	22	9	7	5	1
41-50	14	5	6	3	0
<51	6	2	2	1	1
Total	121	67	37	14	3

TABLE 7

The Result of hyposensitization in the Different Age Groups with Extracts not Containing Candida Albicans.

Age group in years	Number of patients	Excellent	Good	Bad	Worse
0-10	8	5	0	2	1
11-20	9	3	4	2	0
21-30	26	7	13	6	0
31-40	16	4	6	4	2
41-50	6	0	4	2	0
<51	4	0	0	4	0
Total	69	19	27	20	3

TABLE 8

The Results of Hyposensitization with and without Candida Extracts in Patients Showing an Arthus Reaction.

	Number of patients	Excellent	Good	Poor	Worse
Candida in vaccine	31	13	11	7	0
No candida in vaccine	19	2	7	6	4
Total	50	15	18	13	4

cellent results while the response became less in the older age groups (Table 6).

Table 7 shows the results in those asthmatics receiving hyposensitization with extracts not containing *Candida albicans*.

It was noted that results were much better in those showing an Arthus reaction who received candida in their treatment (Table 8).

Those patients who did not give an Arthus response to *Candida albicans*, gave better results when hyposensitized than those cases with an Arthus response (Table 9).

TABLE 9
*The Result of Hyposensitization in Asthmatics Sensitive to Candida Albicans
 with and without an Arthus Response.*

	Number of patients	Excellent	Good	Poor	Worse
With Arthus response	50	15	18	13	4
Without Arthus response	140	71	46	21	2
Total	190	86	64	34	6

DISCUSSION

Immediate (Type I) and delayed (Type III) (7) reactions to monilial antigens may be elicited in subjects suffering from allergic disorders but their clinical significance is obscure (1). *Candida albicans* may be one of the causative aetiological factors in bronchial asthma (5, 4, 2). An Arthus response (Type III) to *Candida albicans* was found in 26.31 per cent of asthmatic subjects. The reaction was more prevalent in the older age groups, and also depended upon the duration (41 percent) and severity (48 per cent) of the disease. This may be the reason why 35.21 per cent of patients gave an Arthus reaction to *Candida albicans* who had had frequent treatment with the corticosteroids.

Whether the Arthus type phenomenon ever forms the basis for clinical syndromes in man has not yet been fully investigated. It is known that it is a local interaction of antigen and antibody in the walls of small blood vessels and is mediated by circulating precipitating antibodies (8).

It is known that *Aspergillus fumigatus* in man can produce reaginic non-precipitating as well as precipitating antibodies (10). In the atopic patient the tissues of the lung are affected by Type I (reagin) reactions. In non-atopic subjects the tissue response is mediated by Type III (precipitating) reactions. The classical clinical condition when a farmer inhales mouldy hay, is a Type III alveolitis causing dyspnoea and is due to

inhalation of thermophilic actinomyces (12). However there is no doubt that when looked for, *A. fumigatus* can give rise to both Type I and Type III reactions (13). In the same way, it may be possible that such an antigen(s) as *Candida albicans* can produce different clinical conditions, depending upon the nature of the type of the allergic reaction. It would seem therefore that when using such an antigen as candida or aspergillus, not only should immediate (Type I) but also immediate delayed Arthus (Type III) reactions be looked for. In Type I atopic reactions the clinical condition is asthma, but in Type III Arthus response, the patient is dyspnoeic and has a fever with productive cough due to the alveolitis (6). It is suggested that the symptoms of some patients with so-called infective or intrinsic asthma, are due to such an immunological reaction occurring in the lung. Injections of an aqueous extract of *Candida albicans* produce in both normal and atopic patients precipitating antibodies (5). In the present state of our knowledge we do not know whether candida antigen antibody complexes are formed in the human and whether these might not be harmful. It was found in the group of patients under study that when hyposensitization was attempted, a poor response was obtained in those giving an Arthus response on skin testing with *Candida albicans*. Yet it was particularly this group that responded better when candida was included in the hyposensitization procedure, compared with the group that did not receive the candida. In general children showed a low incidence of an Arthus reaction to candida and did well whether candida was included or was omitted from the extract.

SUMMARY

One hundred and ninety asthmatic patients with skin sensitivity test to *Candida albicans* were subjected to further study. An Arthus response was present in 26.31 per cent of the cases. The Arthus response bore a definite relation to the age, duration and severity of the asthma as well as the fre-

quency of having corticosteroid medication. It also affected the results of desensitization.

ACKNOWLEDGEMENT

I am indebted to Dr. *A.W. Frankland* for much discussion during this work, and to Miss *R.A. Mace* for secretarial help.

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