Complement components and IgE in patients with asthma and aspirin idiosyncrasy

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Delaney, J. C. and Kay, A. B. (1976). *Thorax*, 31, 425–427. Complement components and IgE in patients with asthma and aspirin idiosyncrasy. Levels of circulating IgE, total haemolytic complement, and components C4 and C3 were measured in 16 asthmatics with aspirin idiosyncrasy and in control subjects. IgE levels were mostly within normal limits. No differences were found between the complement profiles—in particular the C4 levels—in the two groups. As low levels of C4 have been found in patients with intrinsic asthma, these results would suggest a fundamental difference between asthmatics with aspirin idiosyncrasy and others with intrinsic asthma.

The development of increased airways obstruction soon after aspirin ingestion is a well recognized clinical entity (Samter and Beers, 1967). It is seen more commonly in females and typically it is associated with the presence of vasomotor rhinitis and nasal polyposis. The same effect may be produced by other simple analgesics, eg, paracetamol (Smith, 1971). The underlying pathogenetic mechanism is unknown. The sharp increase in airways obstruction soon after ingestion suggests an allergic reaction. Extensive studies, however, have failed to find an immunological mechanism (Giraldo, Blumenthal, and Spinks, 1969; Girard, Hildenbrandt, and Favre, 1969), and IgE levels have been within normal limits (Henderson, Swedlund *et al.*, 1971). Asthmatics with aspirin idiosyncrasy are considered to form a subgroup of intrinsic asthma.

It has been suggested that the complement system may be activated directly by aspirin in sensitive subjects (Yurchak, Wicher, and Arbesman, 1970) and that this may lead to the elaboration of anaphylatoxins which in turn release histamine and other mediators of the allergic response by a mechanism independent of IgE.

Measurements of complement components in asthma have recently revealed high levels of C4 in the serum of allergic asthmatics and low levels in the serum of non-allergic asthmatics (Kay *et al.*, 1974).

In the present study, serum IgE measurements were undertaken to confirm that, in general,

normal levels occur in asthmatics with aspirin idiosyncrasy. Measurements of serum complement components were undertaken to determine if there was any alteration in the complement profile, especially C4, in this condition. Absence of an altered profile would distinguish this subgroup of asthma from others in the intrinsic group.

PATIENTS AND METHODS

PATIENTS Sixteen patients with asthma and aspirin idiosyncrasy were investigated. The diagnosis of aspirin idiosyncrasy had been suggested by the history and was confirmed by oral challenge with paracetamol and small doses of soluble aspirin. The clinical features of those patients are outlined in the Table. Nasal speculum examination revealed the presence of polyps in all the patients. Skin testing by the prick-method revealed four patients with positive reactions to one or more common allergens.

Age- and sex-matched adults attending the general medical clinic were used as controls. None of these patients had allergic disease, asthma or other respiratory disorders. The age-range in asthmatics was 21 to 67 years (mean 46.6 years) and in the controls it was 25 to 67 years (mean 47.5 years). Sera were collected at outpatient clinics, randomly numbered, and stored at -70°C . Measurements of IgE and complement components were made by one of us (ABK) without knowledge of the origin of the samples.

T A B L E
CLINICAL FEATURES OF PATIENTS WITH ASTHMA AND ASPIRIN IDIOSYNCRASY

Patient	Age	Sex	Skin Tests	Nasal Polypectomy (No.)	Asthma (years)	Steroid Therapy (daily dose)
MB	63	F	Positive DP A	4	9	Nil
SM	39	F	Positive DP A	3	16	Pred 5 mg
BP	40	M	Positive DP	7	34	Nil
PR	51	F	Positive DP	0	3	Pred 7.5 mg
PC	32	F	Negative	4	14	Becotide
LT	63	F	Negative	8	30	Pred 5 mg
DJ	54	F	Negative	6	29	Pred 5 mg
JS	50	F	Negative	5	16	Nil
JD	64	M	Negative	1	2	Pred 10 mg
LT	61	F	Negative	3	20	Pred 5 mg
SA	35	F	Negative	0	4	Pred 5 mg + Bextasol
HC	50	F	Negative	3	4	Pred 5 mg
JA	36	M	Negative	13	22	Nil
SR	44	F	Negative	3	10	Pred 2.5 mg
SK	21	M	Negative	3	4	Pred 5 mg
LK	43	F	Negative	1	12	Pred 5 mg

DP = *Dermatophagoides pterynissinus* (house-dust mite).

A = aspergillus.

G = grass-pollen.

Pred = prednisolone

METHODS The total haemolytic complement (CH_{50}) was measured by the method of Mayer (1961). Sheep cells were optimally sensitized by antisera prepared in the rabbit. Increasing dilutions of serum were added to constant volumes of sheep cells and the degree of haemolysis (Y) was measured by spectrometry at OD 414. The total haemolytic complement giving 50% haemolysis (CH_{50}) was calculated as $1-1/Y$.

Levels of C3 and C4 were measured by radial immunodiffusion using monospecific antisera raised in the rabbit (Lachmann, Hobart, and Aston, 1973).

Levels of IgE were measured by solid phase radioimmunoassay using the Phadebas Kit (Pharmacia) in which the anti IgE was raised in the rabbit. The IgE of the standard sera in the kit was checked against WHO standard 68/341 and both had virtually identical values.

RESULTS

The complement profiles and IgE values for the groups with aspirin idiosyncrasy and for the control groups are outlined in the Figure.

The mean complement components for the two groups were as follows:

Asthmatics: CH_{50} =132, C4=119, C3=136

Controls: CH_{50} =148, C4=125, C3=129

(The values are expressed as a percentage of the normal pooled serum.)

There was no significant difference in the complement profiles between the two groups.

The IgE levels were mostly in the lower range in both groups. The mean IgE in the asthmatic groups was 281 IU per ml and in the controls it was 150 IU per ml. The two asthmatic patients with raised IgE levels had positive skin tests.

DISCUSSION

Asthmatic patients with aspirin idiosyncrasy form a subgroup of chronic (intrinsic) asthma. Recently, chronic asthmatics have been shown to have lower levels of circulating C4 than episodic (extrinsic) patients. In the present study, however, there was no significant difference in the levels of complement components between asthmatic patients with aspirin idiosyncrasy and controls. Apart from the two atopic patients the finding of normal IgE values is in agreement with previous reports. Measurements of complement components have not previously been recorded in this condition. The normal profile does not exclude direct activation of the complement system by aspirin and, in this respect, measurements of complement levels during acute episodes provoked by aspirin would be helpful.

The absence of an altered complement profile in asthmatics with aspirin idiosyncrasy would support the belief that patients with this syndrome form a subgroup quite separate from others in the intrinsic asthma group.

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FIGURE Complement and IgE levels in patients with asthma and aspirin idiosyncrasy (●) and age- and sex-matched controls (○). The bars represent the mean values. There was no statistical difference between patients and controls as assessed by the Student *t* test. NHP=normal human pool (serum).

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