

Total serum IgE and IgE antibodies specific to house dust mite found in two aged-matched cohorts of children with and without otitis media with effusion

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Objectives: To determine whether otitis media with effusion (OME) is associated with elevated serum immunoglobulin E (IgE) and IgE specific for house dust mite.

Design: Forty-seven children who had evidence of bilateral OME, both otoscopically and on tympanometry, on two separate occasions, 3 months apart were admitted for ventilation tubes. Forty-eight children admitted for minor eye surgery who had otoscopically normal ears and no history of middle ear problems were used as controls. Bloods samples were taken under anaesthesia. Total IgE and IgE radioallergosorbent test (RAST) to house dust mite was measured by the Pharmacia Unicap 100 system. The results from the two groups were compared.

Setting: Birmingham Children's Hospital.

Participants: Children between the ages of 3 and 10. Children with Down's syndrome, cleft lip and palate, ciliary abnormalities, known immunodeficiencies and cardiac abnormalities were excluded.

Main outcome measures: Total IgE and RAST to house dust mite. A RAST of >0.35 was taken to be positive.

Results: There was no statistical difference between the control and study groups for the total IgE. Six children from both study and control groups had a raised house dust mite RAST. There was no difference in the levels between either group.

Conclusions: Our findings indicate that there is no direct relationship between OME and biochemical evidence of allergy, specifically to house dust mite.

Persistent middle ear effusion peaks between 2 and 5 years of age and slowly tails away over the next 5 years.¹ The aetiology of otitis media with effusion (OME, syn, glue ear and serous otitis media) is multifactorial.^{2,3} Certain congenital diseases predispose to its development such as Down's syndrome⁴ and the presence of a cleft lip and palate.⁵ It has been suggested that OME is an inflammatory condition.³ The causes of the inflammation are varied and local allergy may play a part.^{3,6}

The middle ear is lined with respiratory mucosa in continuity with the nasal cavity and sinuses.² The middle ear mucosa functions normally in OME and all immunoglobulins have been demonstrated in the effusion.² Immunoglobulin (Ig)A, which has two subclasses, is the main immunoglobulin to confer mucosal protection. Levels of total IgA and IgA₁₊₂ are often low before the age of 2 and reach adult values around 10 years of age.

Once the mucosa has been breached, the IgG responses act.

The upper respiratory tract is frequently affected by acute coryza and this may be related to the development of allergy. Local allergic rhinitis is common, and along with asthma, is rising in the population. Its role in relation to OME is debated.^{2,7} Elevated levels of serum IgE are a hallmark of atopy, the levels are progressively higher with the three atopic conditions of asthma, hay fever and eczema. A positive radioallergosorbent (RAST) test against house dust mite allergen is found in individuals with IgE-mediated hypersensitivity to that allergen.

This study looked at two groups of children with and without OME. The aims were to determine if first, the levels of the serum IgE were different in the two groups and secondly whether there was a difference between these groups for IgE specific to house dust mite. House dust mite was used as it is a perennial allergen and therefore if allergy has a role in OME it is the most probable causative allergen.

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Materials and methods

Patients

Patients were selected from the routine admissions for insertion of ventilation tubes to improve hearing in children with chronic otitis media with effusion. The following patients were excluded: Down's syndrome, cleft lip and palate children, ciliary abnormalities, known immune deficiencies and any patient with cardiac disease. None of the children in the lead clinicians practice (Mr AB Drake-Lee (ADL)) received any medical treatment for their OME, i.e. nasal steroids, by general practitioner or ENT surgeon. The child had to have a bilateral effusion documented on two occasions, 3 months apart, prior to the admission by both otoscopy and tympanometry and had to have an effusion in one ear at the time of surgery. All children had to be between 3 and 10 years of age. The ages of the children were calculated to the nearest half-year of age at the time of venesection.

The control group of children were selected from those admitted for routine squint surgery. The presence or absence of allergy was not used by the ophthalmologist as a reason whether or not to operate. Those who had a history of OME were excluded. The controls all had normal otoscopy. They are called the controls in the tables.

Measurement of serum immunoglobulin levels

During general anaesthesia, venous blood samples were taken, and serum was separated and stored at -70°C until analysed. The samples of serum were loaded into the Pharmacia Unicap 100 system (Pharmacia Unicap, Uppsala, Sweden). Anti = IgE or the allergen of interest covalently coupled to the cellulose solid-phase ImmunoCap, reacts with IgE or specific IgE, respectively, in the patient's serum specimen. After washing, enzyme labelled antibodies against IgE are added to form a complex. The concentration of the IgE in the sample is measured by fluorescence.^{8–10}

The system was used to calculate both the total IgE and specific IgE (RAST) to house dust mite. The results were analysed using chi-squared test.

Ethics approval

Birmingham Children's Hospital Ethics Committee approved the study (3719).

Results

At the time of grommet insertion, nine patients had a unilateral effusion. There was no statistical difference

between this groups IgE and RAST tests compared to the patients with bilateral effusions.

The levels of total serum IgE were compared between the patients and controls. The results are shown in Table 1 and Fig. 1. The results were analysed with a chi-squared test, there was no statistical differences between the IgE levels for these two groups. There were five outliers in total, three OME and two controls. The two controls were much greater than the three OME patients. (The outlying controls were one child aged 9 with an IgE of 3956 kU/l and one child aged 6 with an IgE of 1213 kU/l, points not plotted on graph).

Six of the 48 control patients had a positive RAST to house dust mite extract and it was also positive in six of the patients with otitis media with effusion. The values were 0.99, 2.19, 4.8, 6.65, 11.7, 100 in the control group and 3.41, 21.8, 29.6, 42.7, 73.6, 81.8 in the patient group. These are shown with the total IgE in Table 2. The results were analysed with a chi-squared test, there was no statistical differences between the IgE levels for these two groups. Five of the patients had a strong positive RAST compared with one of the controls.

Discussion

The role of IgE-mediated hypersensitivity in the development of OME is hotly debated. Clinical studies have shown the incidence of allergy in OME varied from almost zero to more than 80%.^{10–14} The presumed mechanism by which OME is produced by allergy is controversial.¹¹ There have been three proposed mechanism:³

1 Middle ear as a target organ for allergens.

Table 1. Total serum IgE

	Number	Age range	Median	IgE (kU/L)
Controls	48	3–9	5	28 (0–955)
Patients	47	3–9	6	12 (0–411)
Ranges of normal				Total IgE (kU/L)
to 1 yr				30
to 2 yrs				35
to 3 yrs				40
to 7 yrs				50
to 10 yrs				65
Adult				90

The IgE values given are median (range). The children's ages are measured to the nearest half-year on admission. Reference range for 5 year olds median (15) + 1 SD (52).

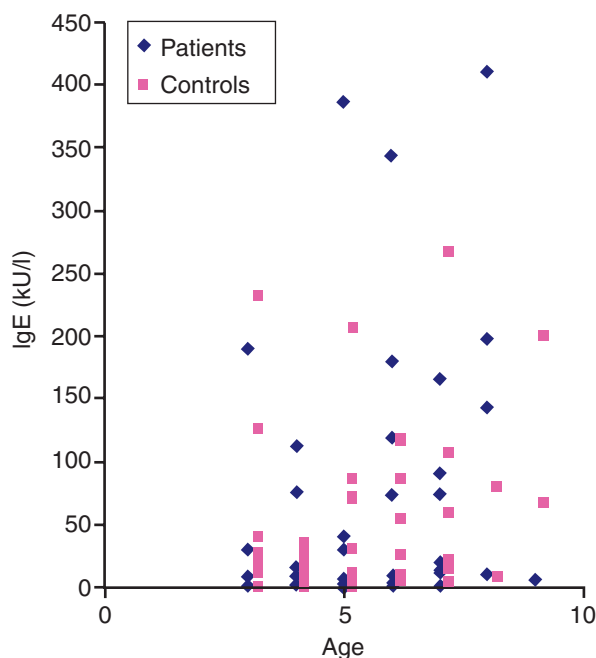


Fig. 1. Scatter diagram of age versus total IgE: patients and controls (two values are omitted, both in control group, one child aged 9 with IgE of 3955, one child aged 6 with IgE of 1213).

2 Inflammatory swelling of the eustachian tube with resulting obstruction.

3 Inflammatory obstruction of the nose and nasopharynx.

Middle ear as target organ for allergens

The site of the middle ear as a target for allergens has been investigated by numerous authors. Doyle *et al.*¹⁵ demonstrated with sensitized monkeys that the middle ear mucosa was capable of producing an allergic reaction. However, OME was not observed after the allergic reaction had taken place. Bernstein's study of 100 children with OME,¹² showed that 8% had a higher IgE level in

their middle ear fluid than in their serum. He concluded that the middle ear may act as a target organ in a proportion of patients with OME. Histamine and other inflammatory mediators have been demonstrated in middle ear effusions,¹⁶ but there is a lack of conclusive evidence that an allergic reaction takes place in the middle ear leading to OME. The level of IgE may be raised in respiratory mucosa above serum values. Patients with nasal polyps had IgE elevated in the nasal mucosa compared with serum values but there was no corresponding raised allergen-specific IgE.

Inflammatory swelling of the eustachian tube with resulting obstruction

Blocking an animals' eustachian tube by paralysing their tensor veli palatine muscle causes a middle ear effusion.¹⁷ It was therefore thought that any cause of persistent eustachian tube blockage would lead to OME. Intranasal allergen challenge causes nasal congestion and eustachian tube blockage in sensitized adults. It does not, however, result in a sustained middle ear effusion.^{18,19}

Inflammatory obstruction of the nose and nasopharynx

Complete nasal obstruction because of allergy was hypothesized to cause OME by the Toynbee phenomenon. When a patient with complete nasal obstruction swallows, an initial positive nasopharyngeal air pressure is followed by a negative pressure phase within a closed system. This leads to two effects, during the positive pressure phase, secretions, containing bacteria and allergens, might be insufflated into the middle ear. During the negative pressure phase, the eustachian tube will be prevented from opening and can become further obstructed.³ There are a number of problems with this theory. Bernstein⁶ demonstrated that in adults, total nasal obstruction caused by nasal packing led to no eustachian tube dysfunction, and Georgitis *et al.*²⁰ demonstrated that total nasal obstruction, as measured by anterior rhinomanometry, after histamine-induced or allergen induced rhinitis never occurred. Both these studies demonstrate that OME cannot be produced by the Toynbee phenomenon.

Our study showed that there was no difference in total IgE present in the blood of patients with OME compared with those without OME. When we looked at specific IgE to the perennial house dust mite allergen, we again demonstrated no difference in our patients with OME compared with our controls. We accept that five of the patients had a strongly positive RAST compared with one of the controls, however, the RAST test is primarily one of positive or negative with the absolute value being of

Table 2. IgE levels and radioallergosorbent (RASTs) in the six positive patients in each group

Controls	Patients
26.4 (0.99)	13 (3.41)
200 (2.19)	74.1 (21.8)
107 (4.8)	76.6 (29.6)
117 (6.65)	98.8 (42.7)
39.7 (11.7)	189 (73.6)
1213 (100)	387 (81.8)

IgE values (kU/l who 75/502) given and RAST levels in brackets. RASTs >0.35 are positive.

secondary importance. Whilst this association is noteworthy we have been unable to deduce anything further from it. We used RAST test to house dust mite as this has been shown to be the most common allergen causing perennial allergic symptoms in children (A.B. Drake-Lee, unpublished data). It is therefore the allergen most likely to cause OME if allergy plays a role. We accept that other allergens, e.g. food, may play a role, but this is likely to be small compared with house dust mite.

Conclusion

Our findings indicate that there is no direct relationship between OME and biochemical evidence of allergy, specifically to house dust mite.

Conflict of interest

None declared.

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