Rhinology, 30, 265-275, 1992

Allergic rhinoconjunctivitis: Diagnostic and clinical assessment

F.A. Salzano[1], L. d'Angelo[1], S. Motta[1], A. del Prete[2], M. Gentile[1] and G. Motta jr.[1]

[1] Dept. of Otorhinolaryngology, University of Naples, Italy
[2] Dept. of Ophthalmology, University of Naples, Italy

SUMMARY

In allergic rhinoconjunctivitis not only the nasal mucosa but also the conjunctiva and, in severe cases, the cornea are affected by reactive phenomena. This pathological process is often encountered in clinical practice, its incidence ranging from 10% to 30% of the whole population, as reported by many authors. Up to now, the pathogenetic mechanisms of allergic reactivity are not completely understood. In our opinion this is due to insufficient standardization of the diagnostic procedures; even the clinical picture of such a pathological process seems to be insufficient, especially with regard to the analogies between the nasal and conjunctival pathologies. To a great extent this depends on the different clinical pictures both in otorhinolaryngology and ophthalmology.

Our study has been carried out on 98 patients suffering from rhinoconjunctivitis, and presents an accurate documentation with regard to the existence of analogies in reactivity at the immunoallergic level, in both the nose and conjunctiva. These are evident when we refer not only to specific routine allergological tests but, mainly, to local examinations. The evaluation of the selected data enables us to formulate a single classification of allergic rhinoconjunctivitis, taking into account the common reactive phenomena.

INTRODUCTION

In allergic rhinoconjunctivitis not only the nasal mucosa but also the conjunctiva and (in severe cases) the cornea are affected by reactive phenomena. The clinical picture shows repeated sneezing, abundant hydrorhinorroea, almost constant nasal obstruction, conjunctival itching, lacrimation, photophobia, and the feeling of the presence of a foreign body. Actually, in rhinoscopy, a common finding is oedema of the nasal mucosa, and (in severe cases) hypertrophy and even polypoid degeneration. The colour and type of secretion are extremely variable, and are not always related to the allergic condition. In fact, other factors (e.g. the

use of topical drugs, infections) can change the rhinoscopic aspect of the nasal allergic mucosa. The conjunctiva can show different degrees of hyperaemia with as extreme forms chemosis with palpebral ptosis or granulomatous nodules; sometimes, the cornea becomes involved, and this can lead to the development of ulcers.

This pathological process is frequently encountered in clinical practice, mainly in subjects between five and thirty years of age. Several studies show a frequency ranging between 10% and 30% of the whole population (D'Ermo et al., 1985; Dhermy et al., 1985; Perfumo et al., 1987; Bousquet et al., 1988).

The existence of analogies in reactivity at the immunoallergic level in the nose and conjunctiva must be carefully evaluated, especially in cases of Type-I hypersensitivity, mainly in pollinosis. In predisposed subjects, organs in direct contact with the external environment can become sensitized as a result of prolonged contact with allergenic substances. Although the pathogenetic mechanisms underlying this process have been studied in great detail, some aspects remain unclear and, as a consequence, diagnostic procedures have not been sufficiently standardized. In this context, many authours have suggested that IgE can be produced in the target organ without modifications in systemic reactivity, as can be detected with prick test and serum RAST (Donovan, 1970; Ishizaka et al., 1970; Hodday, 1971; Liotet et al., 1982; Liotet et al., 1983, Okuda et al., 1983; Aalders-Deenstra et al., 1985; Del Prete et al., 1986; Del Prete et al., 1989). Indeed, Bachert (1987) has suggested that with routine procedures alone there is a risk that 50% of patients will not be given adequate de-sensitizing therapy.

Therefore, in allergic rhinoconjunctivitis specific tests providing more accurate data, not only regarding the type of local allergic sensitization but also its degree, are demanded for, in addition to those commonly used. For this purpose, nasal and/or ocular provocation tests as well as the RAST test, for the evaluation of specific IgE in nasal and lacrimal secretions, have been shown to be very reliable (Ballow et al., 1980; Del Prete et al., 1982; Wihl, 1983; Del Prete et al., 1985; De Dionigi et al., 1985; Moller et al., 1986; Motta et al., 1988; Bachert et al., 1988; Clarke, 1988; D'Ermo et al., 1989; Motta et al., 1989). Moreover, a microbiological examination should be carried out on nasal and conjunctival secretions in order to identify possible bacterial, mycotic or *Chlamydia* infections, which may produce local reactive phenomena and make the commonly used anti-allergic treatments ineffective.

Taking account of these recent findings, a re-examination of the clinical picture of rhinoconjunctivitis is mandatory: In the past, such a disorder was treated differently by otorhinolaryngologists and ophthalmologists. As for rhinitis, in particular, the aspects of the nasal mucosa at the clinical examination enabled us to classify: (1) simple forms; (2) hypertrophic forms; (3) atrophic forms; and (4) specific chronic forms (Bruzzi, 1948; Rossi, 1971).

Mygind (1981) has suggested the following (etiopathogenetic) classification: (1) allergic form, characterized by an atopic etiology; (2) pseudoallergic form, where the same symptomatology of the allergic form occurs, but no allergen responsible for the disorder can be detected; and (3) neurovegetative form, featured by aspecific nasal hyperreactivity, which is presumably linked to an unbalanced control of the vasomotor activity; the absence of eosinophils as well as the unresponsiveness to steroid treatment mark the difference between this and the pseudoallergic form.

For allergic conjunctivitis, an organic picture has been suggested by Duke-Elder (1965), who pointed out a simple form (including atopic conjunctivitis or hay-fever, and contact dermoconjunctivitis) and an interstitial form (including phlyctaenar keratoconjunctivitis and spring catharral keratoconjunctivitis). A further discrimination was made according to the etiopathogenetic aspect: (1) hay-fever conjunctivitis caused by an immediate IgE-specific immunologic reactivity; (2) atopic spring conjunctivitis, in which we can find a mixed immunologic mechanism: immediate (Type I) and delayed (Type IV).

Recently, four pathological forms have been described depending on their different clinical manifestations:

(1) hay fever, with symptoms such as hyperaemia, chemosis, palpebral oedema, lacrimation, itching and irritation, occurring immediately after the contact with the sensitizing allergen;
(3) spring keratoconjunctivitis, caused by a self-limiting, recurrent and bilateral interstitial inflammation of the conjunctiva, with a typically seasonal frequency;
(4) atopic keratoconjunctivitis, with a non-seasonal frequency and often linked to atopic dermatitis;
(5) giant papillae, commonly found in subjects wearing contact lenses.

The aim of our study was to provide an accurate documentation concerning the existence of analogies in reactivity at the immunoallergic level, in both the nose and conjunctiva, and to suggest an organic picture of this pathology.

MATERIAL AND METHODS

We examined 98 subjects with ages ranging from 6 to 53 years (mean 20 years) who suffered from symptoms of rhinoconjunctival hyperreactivity. A detailed record of their medical history was made and the patients underwent systemic allergological tests (prick test and specific IgE testing). For the prick test was used a score ranging from 0 to 4, with respect to the size of the weal and of the erythematous area after stimulation.

Specific IgE was evaluated using the RAST method, and the concentration was scored as follows:

- Class 0: no IgE antibodies (0.00–0.35 PRU/ml),
- Class 1: low level of specific IgE (0.35–0.70 PRU/ml),

- Class 2: moderate level of specific IgE (0.70–3.50 PRU/ml),
- Class 3: high level of specific IgE (3.50–17.50 PRU/ml),
- Class 4: very high level of specific IgE (>17.50 PRU/ml).

Patients then underwent the following examinations to determine the presence of local allergic reactivity and possible infections: Nasal tests included: (1) cytological investigation with scraping of the inferior turbinate; (2) tests for specific IgE in the nasal secretion, using the RAST; (3) rhinomanometry before and after specific allergenic stimulation; and (4) microbiological investigations for the detection of bacteria, mycetes and *Chlamydia*. Ocular tests included: (1) cytological investigation with scraping of the conjunctival mucosa; (2) tests for detection of specific IgE in lacrimal secretion using the RAST; (3) histamine determination in lacrimal secretions before and after specific allergenic stimulation; (4) microbiological investigations for the detection of bacteria, mycetes and *Chlamydia*.

Cytological investigation was performed on the scrapings of both conjunctival and nasal mucosa. The material was collected with Ayre's special spatula, fixed on a slide and stained with the May-Grünwald-Giemsa method. The presence of eosinophils in the smear was evaluated, and an eosinophil concentration higher than 10% was considered positive. Specific IgE concentrations were determined with the RAST method on nasal secretions, which were collected by squeezing cotton pads introduced in the middle meautus of each nasal cavity for 20 min, and ocular secretions collected by aspiration with a siphon system.

Rhinomanometry (RNM) was performed with the anterior active dynamic method, using an NR3D computerized rhinomanometer. Two recordings were taken, i.e with the patient in a sitting position (static RNM) and in a supine position (dynamic RNM) (Motta et al., 1988). This examination was performed before and after nasal stimulation with a specific allergen dissolved in an aqueous solution, at concentrations of respectively 5, 10, 20, 50, 100, 200, and 500 AUR/ml. Three drops of each dilution of the allergen solution were instilled with an insuline syringe on the inferior turbinate of the nasal cavity (the one that was the most open at rhinoscopy). The degree of positivity after stimulation was evaluated on the basis of changes that occurred in nasal resistance. The challenge test was considered positive when an increase in nasal resistance more than 100%, with respect to the basal values, was recorded. The opposite nasal cavity was stimulated only with three drops of the solvent (albumin).

Using high-performance liquid chromatography, the levels of histamine were measured in lacrimal secretions collected before and after specific stimulation. The dilution methods and quantities were the same as those adopted for nasal stimulation. The solvent was instilled in the opposite eye to test for aspecific reactions. Also in this case, the response to stimulation was considered positive if the histamine concentration in lacrimal secretions was at least 100% higher than the basal levels.

Microbiological investigations involved bacterial and mycotic culture on pads in nasal and ocular secretions, as well as the *Chlamydia* test with immunofluorescence examination of the scrapings of both nasal and ocular mucosa. Bacteria over 3 CFU's (Colony Forming Units) were considered indicative; 10 bodies per slide were considered indicative for *Chlamydia*.

RESULTS

Systemic allergological investigations (Table 1)

Twenty-five patients (25.5%) had a negative prick test, and 73 (74.5%) were positive to one or more allergens. With respect to specific IgE in serum, 39 patients (39.8%) were assigned to class 0; 59 (60.2%) showed specific IgE to one or more allergens, of variable degree (classes 1–4).

Table 1. Systemic allergological investigations

number of cases: 98	positive	negative
prick	73 (74.5%)	25 (25.5%)
RAST	59 (60.2%)	39 (39.8%)

Local allergological investigations: Nasal tests (Table 2)

Forty-nine patients (50%) showed a significant concentration of eosinophils. Seventy-seven patients (78.6%) showed a variable level of specific IgE (classes 1–3) for one or more allergens, as determined with RAST of nasal secretions.

Table 2. Local allergological investigation: Nasal tests

number of cases: 98	positive	negative
eosinophils	49 (50%)	49 (50%)
RAST	77 (78.6%)	21 (21.4%)
provocation with 1 allergen	62 (63.3%)	10 (10.2%)
provocation with 2 allergens	26 (27.5%)	

Static rhinomanometry, before stimulation, showed resistance values between 0.30 and 0.71 Pa.s/ml (mean 0.51), and dynamic rhinomanometry (performed after the patient had been in a supine position for 30 min) showed values between 0.30 and 1.00 Pa.s/ml (mean 0.60). This means that before testing, the nasal cavities presented a moderate resistance to the passage of air and the dynamic evaluation showed a slightly reduced patency (Figure 1).

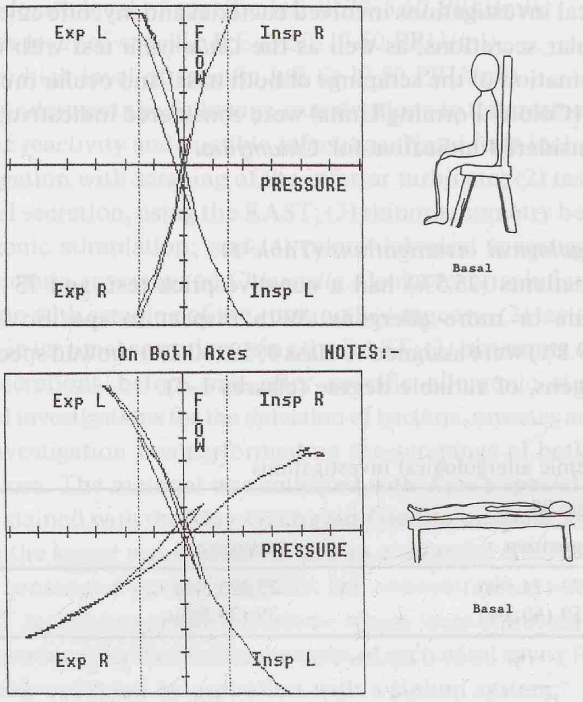
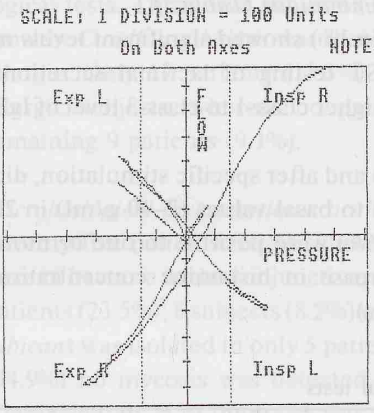


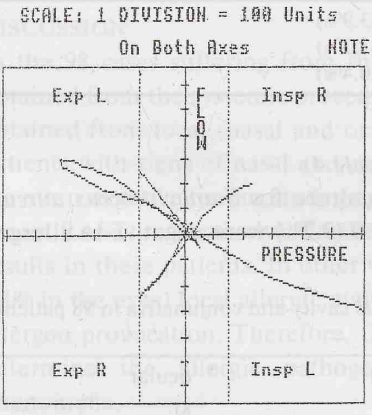
Figure 1. Anterior active dynamic rhinomanometry of a patient suffering from allergic rhinoconjunctivitis. The upper diagram represents static rhinomanometry (sitting position); the lower represents dynamic rhinomanometry (supine position). A moderate resistance to the passage of air is observed in the nasal cavities, with a slight increase in the supine position.

After stimulation with specific allergen, static rhinomanometry did not show modifications of the trace in 10 cases (10.2%), as compared with basal conditions; dynamic rhinomanometry confirmed the findings recorded before stimulation. Of the remaining 88 patients (89.8%), 62 patients (70.5%) showed markedly altered resistance values on the stimulated side for only one allergen, using both static rhinomanometry and dynamic rhinomanometry (Figure 2); whereas 26 patients (29.5%) presented only significant modifications of resistance values after provocation with two allergens (Figures 3a and b). From the differences in the resistance values and the morphological variations of the traces after stimulation with the individual allergens an accurate evaluation of the sensitization threshold of these subjects to the given allergen can be made. Provocation with the solvent alone did not induce any significant changes, with both the static and dynamic traces.



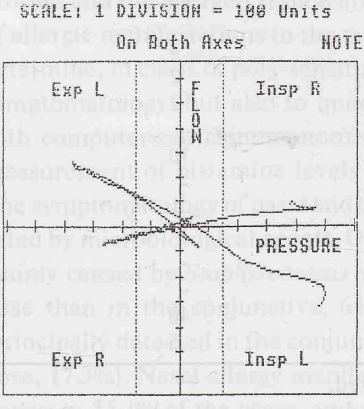
Dermatophagoides
Pteronyssinus
100 AUR sx

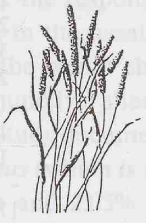
Figure 2. Anterior active dynamic rhinomanometry after nasal provocation test. In a patient, suffering from allergic rhinoconjunctivitis, specific stimulation of the left nasal cavity was done with *Dermatophagoides pteronyssinus* at a concentration of 100 AUR/ml. In the right one albumin was instilled. The stimulated side with specific allergen shows markedly increased resistance values.



Pellitory of the wall
5 AUR sx

Figures 3a and b. Anterior active dynamic rhinomanometry after nasal provocation test. Patient suffering from allergic rhinoconjunctivitis had the left nasal cavity specifically stimulated with *Parietaria judaica* (wall pellitory) at a concentration of 5 AUR/ml (3a), otherwise the right nasal cavity was instilled with *Graminacea* at a concentration of 10 AUR/ml (3b). Both sides presented a significant increase in resistance values.





Graminacea
10 AUR dx

Local allergological investigations: Ocular examinations (Table 3)
Upon cytological investigation, 55 patients (56.1%) showed significant levels of eosinophils in conjunctival secretions. RAST testing of lacrimal secretions demonstrated that 81 subjects (82.7%) had a higher class-1 to class-3 level of IgE antibodies for one or more allergens.
Histamine levels in lacrimal secretion, before and after specific stimulation, did not show a significant increase, as compared to basal values (2–10 g/ml) in 20 subjects (20.4%). Seventy-eight patients (79.6%) were positive to one or more allergens. They presented a significant increase in histamine concentration (more than 100% with respect to basal values).

Table 3. Local allergological investigation: Ocular tests

number of cases: 98

	positive	negative
eosinophils	55 (56.1%)	43 (43.9%)
RAST	81 (82.7%)	17 (17.3%)
provocation	78 (79.6%)	20 (20.4%)

Microbiological investigations: Nasal tests (Table 4)
Sixty-three patients (64.3%) had a positive culture for *Staphylococcus aureus*. Fifty-four (55.1%) were allergic subjects, and 9 (9.2%) were negative to allergo-

Tabel 4. Microbiological investigation of the nasal cavity and conjunctiva in 98 patients with rhinoconjunctivitis

	nasal	ocular
	N:	N:
Staphylococcus epidermidis	30	40
*Staphylococcus aureus**	62	23
Corynebacterium spp.	–	–
Streptococcus viridans	–	4
Neisseria spp.	–	2
Proteus	2	2
Streptococcus pneumoniae	2	–
Streptococcus A/B haemolyticus	3	10
Escherichia coli	2	–
Acinetobacter spp.	–	–
Enterobacter	1	–
Haemophilus influenzae	1	–
Enterococci	–	–
*Chlamydia***	17	40
Candida	4	5

* Only bacteria over 3 CFU's have been considered.
** 10 bodies per slide have been regarded.

logical tests. Thirty-five subjects (35.7%) did not show any significant bacterial growth. *Candida albicans* was identified in only 4 patients (4.1%), who were all allergic. Only 17 patients (17.3%) were positive for *Chlamydia*; 8 (8.2%) were allergic subjects, whereas no presence of allergy could be detected in the remaining 9 patients (9.1%).

Microbiological investigations: ocular examinations (Table 4)
Seventy-five patients (76.5%) showed no significant bacterial growth. The presence of bacteria in the conjunctiva, mainly *Staphylococcus aureus*, was found in 23 patients (23.5%); 8 subjects (8.2%) were allergic, and 15 (15.3%) were not. *Candida albicans* was isolated in only 5 patients (5.1%), whereas in the remaining 93 cases (94.9%) no mycosis was detected. Only 40 patients (40.8%) were positive for *Chlamydia*; in 25 of them (25.5%), the presence of allergic manifestations could be documented.

DISCUSSION

In the 98 cases suffering from rhinoconjunctivitis, a comparison of the data obtained from the systemic procedures (prick test and serum RAST) with those obtained from local (nasal and ocular) diagnostic procedures revealed that in patients with signs of nasal and ocular hyperreactivity, systemic investigations are often negative (in our study population, 25% and 40% with the prick test and serum RAST, respectively). Furthermore, local tests usually give more reliable results in these patients. In other words, in some cases (15.3% in the nose and 5.1% in the eyes) local allergic manifestations can be revealed only with topical allergen provocation. Therefore, these diagnostic procedures can be useful to determine the allergic pathogenesis of rhinoconjunctival hyperreactive phenomena.

In fact, these tests allow to ascertain the causal relationship between the disease process and the allergen responsible for the disorder, documenting the presence of allergic manifestations in the target organ. Moreover, they permit not only to determine, in cases of poly-sensitization, the main substance responsible for the symptomatology, but also to quantify the response to the stimulus (evaluated with computerized rhinomanometry, in the nasal challenge test, and with the measurement of histamine levels in the ocular challenge test).

The symptomatology of nasal and conjunctival allergy can persist or can be aggravated by microbiological agents. Our study documents the presence of infections mainly caused by *Staphylococcus aureus* (which is more frequently found in the nose than in the conjunctiva, 64.3% and 23.5% respectively) and *Chlamydia* (principally detected in the conjunctiva, 40.8%, but also frequently present in the nose, 17.3%). Nasal allergy manifestations can be aggravated by *Staphylococcus aureus* in 55.1% of the cases, and ocular manifestations in 8.2% of the patients;

this microbiological agent may be the sole responsible for the clinical manifestations in the nose in 9.2% of the cases, and in the conjunctiva in 15.3% of the patient. Nasal allergy can be complicated by *Chlamydia* in 8.2% of the cases, and ocular allergy in 25.5%. This micro-organism may be the sole responsible for the clinical manifestations in the nose in 9.1% of the patients, and in the conjunctiva in 15.3%. (These findings are original and up to now have never been reported in literature.)

The evaluation of the data in the literature together with the results of our study let us to formulate a single classification of allergic rhinoconjunctivitis due to inhalant pathogens, and taking into consideration the common reactive phenomena:

(1) *specific form,* in which it is possible to detect with systemic and/or local tests a specific antigenic agent responsible for the disease (it can be seasonal, if caused by pollen, or perennial, when due to acarids);

(2) *aspecific form,* in which the responsible agent can not be detected: in relation to the presence of eosinophils it can be subdivided into an eosinophilic form, and an non-eosinophilic form, due to an unbalanced neuro-vegetative control system or caused by aspecific irritants;

(3) *mixed form,* in which allergic hyperreactivity manifestations are aggravated by endogenous (e.g. hormones, psychogenic stimuli) or exogenous factors (e.g. infections, chemical and physical agents, foreign bodies).

REFERENCES

1. Aalders-Deenstra V, Kok PTM, Bruynzeel PLB. Measurement of total IgE antibody levels in lacrimal fluid of patients suffering from atopic and non-atopic eye disorders. Evidence for local IgE production in atopic eye disorders. Br J Ophthalmol 1985; 69: 380-384.
2. Bachert C. Untersuchungen zur Reproduzierbarkeit des intranasalen Provokationstestes. Laryngol Rhinol Otol 1987; 66: 157-160.
3. Bachert C, Keilmann A. Zur Sensitivität und Spezifität der intranasalen Provokation. Laryngol Rhinol Otol 1982; 67: 57-60.
4. Ballow M, Mendelson L. Specific immunoglobulin and antibodies in tear secretions of patients with vernal conjunctivitis. Allergy Clin Immunol 1980; 2: 112-118.
5. Bousquet J, Guerrier B. Rhinites allergiques. Revue du Practicien 1982; 38: 745-753.
6. Bruzzi S. Otorinolaringoiatria. Idelson Ed., Naples, 1948.
7. Clarke PS. Improved diagnosis and treatment of allergic rhinitis by the use of nasal provocation test. Ann Allergy 1988; 60: 57-60.
8. De Dionigi L, Chiaravalli E, Calzolari M, Falagiani P, Centanni S. Il test di stimolazione nasale specifico con allegene titolato in unità Rast: Validità e sensiblità. Folia Allergol Immunol Clin 1985; 31: 111-120.
9. Del Prete A, Cuomo F, Magli A. Correlazione tra sensibilizzazione a livello cutaneo ed a livello congiuntivale nelle cheratocongiuntiviti allergiche. Atti del XVI Convegno della Società Oftalmologica Meridionale Simposio su "Occhio e cute". Viterbo, 1982, pp. 145-158.
10. Del Prete A, Cuomo F, Mensitieri I, Carlini G. La diagnosi delle cheratocongiuntiviti allergiche. Utilita dei metodi enzimatici e dei tests di provocazione oculare. Atti del LXV Congresso della Societa Oftalmolocica Italiana, Siena, 1985, pp. 301-305.

11. Del Prete A, Cuomo F, Masucci A, Gravina A. Etiologic diagnosis of allergic keratoconjunctivitis by RAST and FAST. Proc XXVth International Congress of Ophthalmology. Amsterdam, Kugler and Ghedini Publications, 1987, pp. 2809-2812.
12. Del Prete A, Magli A, Cuomo F, Giardino I, Giordano R. Le cheratocongiuntiviti allergiche diagnosi e trattamento. Bollettino di Oculistica 1989; Supplement 3.
13. D'Ermo F, Bonini S. Congiuntiviti allergiche: Valutazione dei dati clinici e di laboratorio a scopo diagnostico. Bollettino di Oculistica 1985; 64: 9-10.
14. D'Ermo F, Bonini S, Todini V, Bonini S. Inflammatory cells in conjunctival scraping of patients with vernal conjunctivitis. In: Secchi AG, Fregona IA, Ed. Modern Trends in Immunology and Immunopathology of the Eye. 1989, pp. 395-398.
15. Dhermy P, Pouliquen Y, Foels MO, Savoldelli M. La plaque vernale, complication de la conjonctivite dite "Printaniere". J Francais Ophtalmol 1985; 8: 711-719.
16. Donovan R. Immunoglobulins in nasal polyp fluid. Archs Applied Immunol 1970; 37: 154-166.
17. Duke-Elder S. System of Ophthalmology. Volume 3, part 1, Ed Kimpton, 1965.
18. Hodday JD. A comparison of immunoglobulins IgA, IgG and IgE in nasal secretions from normal and asthmatic children. Clin Immunol 1971; 9: 577-583.
19. Ishizaka K, Newcomb RW. Presence of IgE in nasal washings and sputum from asthmatic patients. J Allergy 1970; 46: 197-204.
20. Liotet S, Warnet VN, Sainte-Laudy S, Arrata M, Hartmann C. Production locale dans les armes d'immunoglobines et au cours de manifestations conjonctivales allergiques. J Franc Ophtalmol 1922; 5: 401-407.
21. Liotet S, Warnet VN, Arrata M. Lacrimal immunoglobulines and allergic conjunctivitis. Ophthalmologica (Basel) 1983; 186: 31-34.
22. Möller C, Dreborg S, Lanner A, Bjorksten B. Oral immunotherapy of children with rhinoconjunctivitis due to birch pollen allergy. Allergy 1986; 41: 271-279.
23. Motta G, Pucci V, Villari G, Motta G jr, Salzano FA, O'Avenia E. La criochirurgia nel trattamento della rinite cronica ipertrofica. In: Passali D, Ed. "Around the nose", Atti della Prima Giornata Internazionale di Rinologia, Florence, 1988, pp. 189-203.
24. Motta G, Salzano FA, Salerno G, Del Prete A. Diagnostic evaluation of allergic rhinoconjunctivitis. Proc XIV Congress of Otorhinolaryngology/Head and Neck Surgery, Madrid, 1989, pp. 10-15.
25. Motta G jr, D'Angelo L, Pucci V, D'Avenia F, Salzano FA. Valutazione rinomanometrica del test di provocazione nasals specifico in età pediatrica. Atti del X Congresso Nazionale Società Italiana di Otorinolaringologia Pediatrica, Rome, 1988, pp. 259-265.
26. Mygind N. Allergie Nasali. Liviana Ed., Padua, 1981.
27. Okuda M, Ohtsuka B, Sakaguchi K, Watase T. Nasal histamine sensitivity in allergic rhinitis. Ann Allergy 1983; 51: 51-55.
28. Perfumo G, Pastorini A. La terapia chirurgica in "La rinopatia vasomotoria". Atti dell' XI Convegno Internazionale di Aggioroamento AOOI: Sanit Vincent, 1987, pp. 339-351.
29. Rossi G. Otorinolaringoiatria. Minerva Medica Ed, Torino, 1971.
30. Wihl JA. Methods for assessing nasal reactivity. Eur J Resp Dis 1983; 64: 175-179.

Dr. F.A. Salzano
Via Chiatamone 60/B
I-80121 Naples
Italy