ENT
Guiding good practice
In this issue, our newly elected President Antony Frew gives his vision for the European Academy for Allergy and Clinical Immunology. After serving seven years as Secretary-General, he is the right man to make a professional job of managing and guiding our Academy and for consolidating and preparing for our future development.

Consolidation is necessary both to defend allergy and clinical immunology as a specialty and, as new secretary general, Jan Lötvall explains, to increase the presence and visibility of the Academy. Do read on the next pages what the President and the Secretary General envisage for the future! The full list of members of the Executive Committee, including their functions, is provided thereafter.

It is my special pleasure that the focus in this issue is on the ENT Section of EAACI. The new ENT team, with Joaquim Mullol as chairman, will spread scientific and clinical knowledge on major respiratory diseases such as allergic rhinitis and acute and chronic rhinosinusitis. This will be achieved by setting standards for diagnosis and treatment and by organising many symposia to link the speciality of ENT with allergology.

The issue includes a presentation of a new position paper on rhinosinusitis. Fifteen per cent of Europeans suffer from rhinosinusitis. This makes it almost as frequent as allergic rhinitis; it is certainly no less disabilitating.

An exciting new hypothesis has recently been developed contributing especially to our understanding of severe chronic sinus disease. It relates to Staphylococcus aureus and the germs enterotoxines, which are known to act as superantigens. Mechanisms similar to those already described in relation to atopic dermatitis may apply to nasal polyposis (asthma of the sinuses) modifying the severity of inflammation and disease. Early evidence exists that superantigens may also modify lower airway disease, opening up new approaches for the treatment of chronic severe common airway disease.

The first symposium on the role of superantigens in airway disease will take place soon in Ghent. Supported by EAACI, Ga’len and a national fund (see announcement corner), it will bring together the latest knowledge in this area contributed from specialists ranging from microbiologists to immunologists and from dermatologists to pulmonologists. You will hear about our beloved IgE from a completely different point of view!
I am delighted to be given the chance to serve the Academy as President. Of course, this is very much a team effort and I’m really pleased to have such a good team of officers and Executive Committee members with whom to work.

Over the past seven years as Secretary-General, I have learned a lot about EAACI and how it works, and what I have noticed particularly is how so much is achieved from the voluntary work that people do for the EAACI.

Generally, things are going very well. The joint EAACI/WAO congress in Munich was wonderful. We had many more people than we expected, and the meeting itself was terrific, both scientifically and socially. We are grateful to World Allergy Organization for their constructive collaboration and to the local organisers, especially Johannes Ring (see Interview on page 6), for making this a unique and very successful event.

We were glad to be able to introduce preferential registration rates for those coming to the Munich Congress from poorer European countries. For next year, we have successfully negotiated a contract with our publishers, which will allow us to consider lower subscription rates for members from less prosperous countries. The final decision on the subscription rates will have to be made this autumn, but I definitely hope that we can offer an attractive rate to current and potential members from Eastern Europe.

There are a few internal things that I would like to improve and the new ExCom will be looking at these, among other things, when we meet in the autumn. The overall plan is to make our internal structures work efficiently so that we can concentrate our time and energy on outside matters.

The finances for the past two years have been difficult to follow. This is because the financial model for the Munich Congress was completely different. As a result, we had to budget for a large surplus in 2004 and a deficit in 2005. However, the underlying budget has been stable for the past three years.

At the end of the day, the money is there for a purpose, and that is to support and underwrite activity in support of our Academy’s goals. The budget deficit in previous years was intentional, and allowed us to try out some new activities, such as different styles of summer schools and investment in the Brussels Office. This latter investment paid off handsomely with the research grant award for the GALEN network. We now expect to run a stable economy for a few years, to keep the finances under control.

Generally speaking, the summer courses have been very popular with those who attend. We recognise that their educational needs vary and that we have to respond appropriately. This is one of the reasons that we collect feedback from participants, and carefully assess the information provided as we plan the next courses.

We also take note of the feedback from members on the EAACI Newsletter. It indicates that it is appreciated - and read! Providing members with information on our various activities adds to the sense of belonging to a vibrant organisation, and hopefully encourages people to consider becoming more active in our meetings and structures. I certainly expect that the newsletter will continue.

Becoming EAACI President is an exciting challenge but in some ways, I am tempted to think that I shall have more free time in my new role. The position of President is very visible, and I will obviously have to represent EAACI at various meetings. However, the job of Secretary-General involves a lot of work behind the scenes. I wish my successor, Jan Lötvall every success in his important task. In the extra free time that I hope to find for activities outside work, I shall continue to sail my dinghy and walking the hills and forests of Southern England with my family.

Anthony Frew
Promoting clinical knowledge: a key task

Professor Jan Lötvall, Göteborg University, Sweden introduces himself as the new EAACI Secretary-General. In this letter, he gives readers an update on immediate opportunities and longer term plans.

Tasks ahead

My general and primary vision as Secretary-General is to increase the Academy’s transparency and to bring the leadership and membership closer to each other. More specifically, I hope that EAACI can develop a long-term perspective on its finances. I have some suggestions how this possibly can be done. Monetary assets are clearly crucial to giving us the power to develop the Academy for future challenges.

Another key task is to strengthen the role of Clinical Allergy within the Academy. We need to create more clinical postgraduate courses to support the Continuous Medical Education (CME) of specialists all over Europe, as well as the fellows in training. We also need to spread knowledge of Clinical Allergy practice to other specialists, including General Practitioners. To be more visible in this field, we also have to find ways to increase the number of clinical posters and presentations at the Annual Congress. One of the main goals of the Academy should be to defend the specialty of Allergy and Clinical Immunology, where it exists, and to strongly promote it in countries where it does not exist. Ideally, we will work closely with national societies to develop strategies to achieve this goal in each country.

The Sections and Interest groups of the Academy run the core activities. Their role can be strengthened both in terms of their individual activities and the development of their programmes for the Annual Congress. These key groups will also need to be very intricately involved in developing new educational activities.

The EAACI web site is a very important and effective tool for communication between the leadership and the membership. It can also facilitate communication between members, giving them added value for their membership fee. At two years’ old, the web site is now under continuous and exciting development.

In the next few years, I believe there are many small steps that will need to be taken to develop the Academy for the more distant future. This job will involve many officers and members of the Academy, and I will do my best to assist in the process.

Jan Lötvall
Planning a congress: Tips for success

Professor Johannes Ring, Chairman of the Joint Steering of the XIXth World Allergy Organization Congress and XXIVth Congress of the European Academy of Allergology and Clinical Immunology, looks back on his achievement in Munich and offers advice to his successor.

Professor Ring, how do you feel after the success of Munich congress? Did it fulfill the expectation of being the biggest ever meeting on allergy?

Johannes Ring: I have a very good feeling at the end of this congress. Everyone involved, especially the steering, scientific and Host Organizing Committees, agreed that it completely fulfilled our expectations both in quantity - but even more in the quality of science and the friendly spirit. I do not know whether it was the “biggest ever meeting” in allergy. I think some congresses of the American Academy of Allergy, Asthma and Immunology may have had an even higher attendance. However, both for the EAACI and for the WAO it was - with 7000 people - the biggest congress so far.

The Munich congress was the first WAO Congress ever to take place in Germany. How important is this and what will be the impact on the development of your national society?

Johannes Ring: The German Society for Allergology and Clinical Immunology (Deutsche Gesellschaft für Allergologie und Klinische Immunologie - DGAKI) is very proud to have had the privilege of organising this congress. The relation between our society and the WAO goes back to the early 1980s when our honorary chairman, Professor Erich Fuchs served as a member of the Executive Committee. At that time, the organisation was known as “International Association of Allergology and Clinical Immunology”. Sometimes, I had the honour to replace him at committee meetings under the presidents Jack Pepys and Alain de Weck. Since 1988, I have served on the Board of Directors of the WAO.

As well as my thanks to WAO, I want to thank the president of the board of the German Society (DGAKI), and Professor Gerhard Schultze-Werninghaus for his continued support in this endeavour. This congress should have a major impact on the development of allergology in Germany and on our society.

Could you comment on the specificity to the organisation of joint EAACI/WAO congress?

Did you meet difficulties in balancing the interests of two big societies? Is it more complicated preparing the programme for such an event?

Johannes Ring: To organise a congress as a joint effort of several societies - particularly of such dimensions, when one partner represents already an association of a multitude of societies - is never easy. If you like a simple life, you should not do it. I see putting together the programme of a congress as being like producing a painting. Someone has to know how the final shape is going to look. If many people simply throw bits of colour on a screen, it may seem democratic but it will never look good! Somebody has to take the responsibility. If you want to have “a special event” that differs from the yearly routine experienced in many societies.

The motto of the Munich congress was “Allergy in a changing world”. Could you comment on that? Will we all be able to adapt to the new realities in the globalising world?

Johannes Ring: The motto “Allergy in a changing world” was very well reflected both in the programme and in the participation. The world is experiencing tremendous changes both in climate and geographical, political and cultural interchange. I think that all these changes have some impact on our specialty, and are therefore of direct relevance for allergic diseases. We should not only adapt to them but maybe also be able to shape the new realities of our globalising world.
EAACI offered special benefits to all young delegates from all over the world. Was this appreciated? Have you had any feedback on young representation in the congress?

Johannes Ring: The “junior member” policy is one of the best things EAACI ever did! That this gift was offered to all young delegates from all over the world was a very generous gesture and extremely well appreciated. There were 561 “juniors” at the congress.

For medical students with an interest in allergology, the MED-ALL-YOUNG programme (see page 9) was a big success. Close to 30 medical students from Munich, Regensburg, Innsbruck and Salzburg took part.

Tell us about the introduction of the new session format: “Sherlock Holmes in allergy”!

Johannes Ring: The new session “Sherlock Holmes in allergy” was very well received. It strongly emphasised the need for excellence in clinical care as the basis for all good science in allergy! You will never have patients for studies if you don’t treat your patients well.

To put “Debate of the day” in the middle of exhibition area was a brilliant idea: many people received useful information in a very entertaining way. How did you make this decision?

Johannes Ring: The “Debate of the day” in a “speakers’ corner”, which was originally called “agora”, was an experiment; it worked quite well and I am extremely thankful to the speakers and moderators who took on the challenge. They showed themselves willing to discuss in such an open and unprotected way - instead of hiding behind a laptop or a slide. The idea came to me after attending some very dull “controversy sessions” in which both speakers gave normal lectures and ended up in agreement.

Do you have some thoughts or possibly warnings to share with Rudolf Valenta, the President of the 2006 EAACI congress in Vienna?

Johannes Ring: The most important advice I want to give is: Do not worry too much about the money. This is a most prohibitive and time-wasting experience. The money will come if the congress is good, so just concentrate on a good congress!

Finally, what are your personal plans now? Will you manage to get some rest after these busy days in Munich?

Johannes Ring: I had already organised small symposia and a national and a European congress but this world congress was definitely a highlight in my professional life. Like the “Allergica Commedia” during the Bavarian evening, I am tempted to say that it was a “Sternstunde” - something one does not experience many times in life.

I am extremely thankful to our wonderful team and all the people involved in the preparation of this congress: the Presidents Carlos Baena-Cagnani (WAO) and Ulrich Wahn (EAACI), officers, committee chairpersons of all the societies involved, the people from Congrex, Interplan and the International Congress Centre in Munich (ICM). My thanks also go to the Free State of Bavaria and the City of Munich for giving permission for us to enjoy the museum open night, and especially to the members of our local arrangements committee, with Stephan Weidinger, Ulf Darsow, Thilo Jakob, Johanna Grosch, Heidrun Behrendt and all the enthusiastic hardworking people of our team! We all share the feeling: it was hard work, sometimes crazy, but it was absolutely worthwhile and it was such great fun!

Interview by Maria Staevska
Secondly, viral respiratory infections are the major causes of acute exacerbations of asthma, and are also implicated in fatal asthma. Patients with asthma are more susceptible to viral infections than non-asthmatic subjects, and have more severe and more long-lasting respiratory symptoms. Although still controversial, a synergistic effect between virus- and allergen-induced airway inflammation has been proposed.

Finally, certain infections, in particular food-borne and fecal-oral infections might also prevent the development of allergic diseases, including asthma. The influence of infection on asthma is most likely to depend on the nature of the pathogen involved, the route of infection and the genetically regulated innate and adaptive immune response.

Immune responses

Dr K Vermaelen (BE) spoke about immune responses in extreme environments such as space flight. Most space flight studies have addressed the effects on cardiovascular, musculoskeletal and neurovestibular physiology. The immune system is also affected although the mechanisms involved are less well understood. Factors such as psychological stress, alterations in microbial flora and radiation exposure all contribute to various levels of immune alterations in space. In addition, intriguing new evidence is accumulating that shows cells to be sensitive to changes in gravitational forces. Microgravity appears to affect signal transduction in several types of immune cells, which in turn affects the outcome of an immune response.
**Neuroimmune mechanisms**

U. Raap guided us through the impact of neuroimmune mechanisms in atopic dermatitis (AD). Patients with AD feature both skin inflammation and skin hyper reactivity to non-specific stimuli, which is partly neuronally controlled. The peripheral blood of patients with AD has been shown to contain increased levels of neuropeptides, such as substance P (SP), and neuropeptides, such as nerve growth factor (NGF). Brain-derived neurotrophic factor (BDNF) in Neurotrophins have been shown to be exceptional in supporting survival of neurons in the central and peripheral nervous system. In addition, neuropeptides and neurotrophins modulate the functional role of immune cells. Recently, it was shown by our group that BDNF modulates the functional role of peripheral blood eosinophils in AD but not in non-atopic controls. Moreover, it has also recently become evident that neuropeptides (SP) and neurotrophins (NGF, BDNF) are produced and released by inflammatory cells such as eosinophils. Solving the puzzle of interactions between the cutaneous nerve and immune system will not only improve our understanding of allergic disorders but it might also have major therapeutic implications for the future.

Philippe Gevaert

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**Working group**

The Munich Congress gave members of the Junior Membership Association (JMA) working group an opportunity to introduce themselves. They are:

- **JMA chair (Ex Com):**
  - Dr U Raap, Germany, mail@ulrike-raap.de
  - Philippe.Gevaert@UGent.be
  - Peter.Hellings@med.kuleuven.ac.be

- **JMA past chair (SPC):**
  - Dr P Helliings, Belgium

**Dermatology:**
- Dr E Bonzo, Russia, ebor-zou@online.ru

**Immunology:**
- Dr M Kurewski, Poland, marcin.kurewski@uj.edu.pl
- Dr D Gromberg, Germany, david.gromberg@charite.de

**Paediatrics:**
- Dr I Borrego, Portugal, miguel.borrego@raap.pt

**Webmaster:**
- Dr C Skevaki, Greece, cskevaki@allergy.gr

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**Winners named**

Ten poster prizes of 300 euros were awarded during the Munich Congress, sponsored by Pharmacia Diagnostics AB, as follows:

- **Asthma:**
  - P. Beqare (Belgium)

- **Rhinitis:**
  - H. Helling (Netherlands)

- **Dermatology:**
  - J. Schelle (Belgium)

- **Paediatrics:**
  - M. Schede (Germany)

- **Food allergy:**
  - Y. Laroze (Germany)

- **Asthma:**
  - P. Gromberg (Germany)

- **Immunotherapy:**
  - R. Weiss (Austria)

- **Clinical Immunology:**
  - M. Kurewski (Poland)

- **Immunology:**
  - V. Neurath (Germany)

- **Immunology:**
  - A. Taylor (Switzerland)

Over 180 junior members took part in the junior poster session on the opening evening of the congress. After presenting their work, they had an opportunity to discuss it with junior colleagues and senior members of the Academy. The poster session was followed by the junior social event in a former bathhouse. It provided junior members with an opportunity to get to know each other in a friendly and relaxed environment.

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**Educational session**

The educational session comprised two parts: the best possible ways of presenting a scientific project (Anthony Frew) and an introduction to understanding statistics in medical research (Thomas Keil).

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**Med-All-Young welcomes students**

One of the new features of the Munich congress was the “Med-All-Young project”. Here the young organisers, Claudia Traidl-Hoffmann, Stefanie Lubitz, Stefanie Förster and Kilian Eyerich describe its function and assess its success.

The Med-All-Young Project was founded by Prof. Ring and took place for the first time at the WAC 2005. Its aim is to give young local students interested in allergology and clinical immunology the chance to dive into the world of science and get an impression on how the scientific community works together.

Twenty-five students of medicine and health care gathered to enjoy the programme on Sunday, 26 June in the afternoon. It started with a welcome by Prof. Ring followed by an introduction to the basis of immunology given by Dr. Mempel, which ended in a lively and interesting discussion.

Afterwards the grant receivers joined the opening ceremony and the JMA poster session. The evening ended with the young students joining the EAACI junior members in a relaxed atmosphere at the social evening.

On the Monday, all participants joined a free communication, the plenary session and the debate of the day. During lunch, there was a brainstorming of impressions and critique.

“This project has offered us the chance to get a great insight into the scientific network and how research on the interesting field of immunology works. I just wish I could have taken part in this magnificent congress for a longer time” said Hannes Stefanowski. He seemed to speak for all grant receivers as everybody was really excited and stimulated by the Med-All-Young idea.

The programme resulted in eight students becoming a new junior members of the EAACI. The organisers are therefore happy to say that it has been a very successful initiative. It gave young students the opportunity to enter the world of immunology and brought new young members into the Academy. We hope, it will continue next year in Vienna!
Eosinophilic inflammation: a key

Eosinophilic inflammation in nasal polypsis and the role of the regulation of interleukin 5 and interleukin 5 receptor-isoforms.

In view of the prominence of eosinophilic inflammation associated with the vast majority of nasal polyps and the well recognised potential of eosinophils in eliciting tissue damage and subsequent re-modelling, it is likely that a better understanding of the mechanisms underlying the migration, activation and maintenance of eosinophils in nasal polyp tissue will be key to understanding the aetiology and pathogenesis of nasal polyps. Especially the regulation of interleukin-5 and the interleukin-5 receptor isoforms were studied with emphasis on future therapeutic strategies in NP.

Regulated alternative splicing of the IL-5Rα-subunit leads to the generation of either a signaling, membrane-anchored (TM) isoform, or a soluble (SOL) variant with antagonistic properties in vitro. It is suggested that eosinophils are able to control their responsiveness to IL-5 by regulated expression of these IL-5Rα isoforms (1). At the local tissue level, the TM IL-5Rα isoform is down regulated whereas the SOL IL-5Rα variant is up regulated in nasal polyp tissue, but eosinophils are still activated (2).

In vitro exposure of mature human blood eosinophils with rh IL-5 induces an extensive down-regulation of IL-5Rα TM and up-regulation SOL-IL-5Rα. It is suggested that the down-modulation of TM-IL-5Rα from the cell surface and the increased release of SOL-IL-5Rα into culture supernatant fluid dependent on MMP activity. Gregory and co-workers have demonstrated that exposure of blood eosinophils to IL-3, IL-5, or granulocyte-macrophage colony-stimulating factor in vitro leads to sustained down-regulation of surface IL-5R expression and reduced responsiveness to IL-5, but without sustained changes in CCR3 expression (3).

Taking all observations into account, we suggest that an IL-5 driven inflammation generates an eosinophil tissue phenotype that is characterised by a low TM but high SOL-IL-5Rα expression and that this process is partially the result of proteolytic receptor modulation and down-regulation of TM-IL-5Rα gene transcription. Furthermore, the expression of the IL-5Rα isoforms differs according to the eosinophil activation state, maturation and localisation in the body and may therefore be involved in the fine-tuning of the eosinophil homeostasis. Since IL-5R surface expression is down regulated in NP tissue, which probably causes IL-5 responsiveness, our findings indicate that strategies to antagonise IL-5 may have to face unexpected difficulties.

Philippe Gevaert


New look for patients’ website

The European Federation of Allergy and Airways Diseases Patients’ Association (EFA) has considerably improved its website as a resource for patient-focused information.

The “new look” website has an abundance of information on allergy, asthma and COPD and on the news and activities of the organisation itself. Highlights include:

- An opportunity to subscribe to EFA eZine, a monthly electronic newsletter. It aims to keep you informed on European policies, including those relating to environment and health.
- A news feed on allergy, asthma and COPD that keeps track of the hot topics in the Anglo-Saxon press.
- An EU policy section that provides links to European legislation and initiatives relating to allergy, asthma and COPD. From here, you can also access international guidelines on these diseases.
- Asthma and COPD sections (an allergy section is in development) features basic information on these diseases in lay-language.

In short, the EFA website aims to be a one-stop-shop for useful and timesaving information as well as a vital tool for keeping informed.

Without further ado, you are welcome to explore: www.efanet.org
Rhinosinusitis is a significant health problem. Its increasing frequency seems to mirror that of allergic rhinitis resulting in a major financial burden on society.

During the past decade, a number of guidelines, consensus documents and position papers on the epidemiology, diagnosis and treatment of rhinosinusitis and nasal polyposis have been developed. EAACI set up a task force to consider what is known and to develop evidence-based recommendations on diagnosis and treatment. The task force also suggested how progress in research could be made in this area. The resulting “EP3OS document” is approved by the European Rhinologic Society.

The EP3OS document is intended to provide state-of-the-art information for the specialist as well as for the general practitioner:

- To update their knowledge of rhinosinusitis and nasal polyposis
- To provide an evidence-based documented revision of the diagnostic methods
- To provide an evidence-based revision of the available treatments
- To propose a stepwise approach to the management of the disease
- To propose guidance for definitions and outcome measurements in research in different settings.

**Definition**

**Rhinosinusitis** (including nasal polyposis) is defined as inflammation of the nose and the paranasal sinuses resulting in:

1. Two or more of the following major symptoms:
   - Blockage/congestion
   - Smell
   - Discharge anterior/post nasal drip
   - Facial pain/pressure

   AND either

2. Endoscopic signs of:
   - Polyps
   - Mucopurulent discharge from middle meatus
   - Oedema/mucosal obstruction primarily in middle meatus

3. CT signs of:
   - Mucosal changes within ostiomeatal complex and/or sinuses.

**Severity of symptoms**

To evaluate the total severity, patients are asked to indicate where they consider themselves to be on a visual analogue scale (VAS) of 10 cm. The patient is asked the question: “How troublesome are your symptoms of rhinosinusitis?”

The disease can be divided into mild and moderate/severe based on total severity visual analogue scale (VAS) score (0-10 cm):

- Mild = vas 0-4 cm
- Moderate/severe = vas 5-10 cm

**Duration of the disease**

Furthermore the duration of the disease has to be indicated:

- **Acute/Intermittent**
  - <12 weeks
  - Complete resolution of symptoms.

- **Chronic/persistent**
  - >12 weeks symptoms
  - No complete resolution of symptoms.

Schemes for diagnosis and treatment by different professionals can be found in the EP3OS document. Below is an example the scheme for non-ENT specialist for chronic rhinosinusitis/nasal polyposis.

Evidence-based guidelines for non-ENT specialists for the diagnosis and management of adults with CRS/NP.

**Diagnosis**

Symptoms presenting for more than 12 weeks with nasal obstruction plus one or more additional symptom: discoloured discharge; frontal pain, headache; smell disturbance.

Additional diagnostic information includes anterior rhinoscopy, inspection with otoscope or ideally nasal endoscopy (if available); review of primary care physician’s diagnosis and treatment.

Completion of questionnaire and, if positive, allergy testing should be performed if it has not yet already been done.
X-ray is not recommended; nor is CT scan unless there are additional problems such as:
- Very severe disease
- Immuno-compromised patients
- Signs of complications.

Follow VAS to establish the severity of symptoms: mild /moderate /severe.

Treatment
- Topical steroids
- Nasal douches
- Antihistamines and allergen avoidance in allergic patients.

References:
The full document can be found on the EAACI website (www.eeaci.net) or in a supplement of:
An executive summary is published in Allergy (2005; 60: 583-601).

Wytske Fokkens

Scheme for non-ENT specialists:
Therapy for CRS/NP in adults

Nasal obstruction and one or more of the following symptoms:
- Discoloured discharge
- Frontal pain, Headache

Review after 4 weeks

mild

If better: Continue

Moderate/severe

If better: Continue

No progress: Recheck after 8 weeks

No progress: Recheck after 4 weeks

Is endoscopy available?

Yes

Medical treatment

No

follow the GP algorithm

Follow the ENT algorithm for CRS/NP
Refer to ENT specialist if operation is recommended

sinister signs:
requiring immediate referral
- unilateral symptoms
- bleeding
- crusting
- cacosmia
- orbital symptoms:
- swelling of eye or -lids
- eye redness
- displaced globe
- double vision
- reduced vision
- severe unilateral frontal headache
- frontal swelling
- signs of meningitis or focal neurological signs

Nasal polyp seen through an endoscope
New team sets its goals

Joaquim Mullol, Chairman of the ENT Section board 2005-2007 describes here plans and progress of the section he now leads.

The main objectives of the new ENT Section board were set out during a meeting held in Munich. They are:

1) Strengthening the SERIN/ENT Section Meetings by allocating an important part the section budget
2) Continuing distribution of EP3OS all over Europe, producing translations and creating and disseminating a new EP3OS pocket guide
3) Creating initiatives on new Task Forces
4) Continuing collaboration with ERS, AAAAI, national societies and GA\2LEN
5) Increasing membership especially in France, Italy, UK and in Eastern Europe
6) Improving the content of the website.

Although membership of the ENT section has grown enormously during the past four years, it is still the smallest of the EAACI sections. Our plans include a call to all the ENT doctors who are members of EAACI to join us and to bring in others from their respective countries. We also need to increase the interest of otolaryngologists.

Membership of the ENT Section now stands at 276, up 85% (from 199) since 2001. Junior members form 37% of the total. Members represent 47 countries. Seven countries have 15 or more members (Belgium, Turkey, Germany, Sweden, The Netherlands, and Spain).

Events planned include:
- Spanish Allergology Society (SEAIC) Annual Meeting 10-11 November, Seville where the ENT Section will collaborate in a Joint Symposium on “Rhinitis research: present and future”.
- Several speakers from the ENT Section will participate in a meeting on Superantigens in Airway Diseases organised by Claus Bachert, 25-26 November, Ghent.
- SERIN - ENT Section Meeting 9-11 February, Barcelona, where clinical and basic researchers from all over Europe will meet to report their work and discuss hot topics and new strategies for the diagnosis and treatment of nasal diseases.
- EAACI Congress 9-14 June 2006, Vienna, where the ENT section will participate in two symposia on the “Second Allergic March” and “European consensus on rhinosinusitis and nasal polyps”. There may also be a workshop on “Controversies in Rhinitis and Rhinosinusitis” and a Joint JMA-ENT Section pre-congress course on “Diagnostic tools in rhinitology”.

In addition, the ENT Section may collaborate in a plenary session on “Allergic Rhinitis” during the ERS-ISIAN Meeting in June in Tampere, Finland.

Achievements

Former chairperson of the ENT section, Wytske Fokkens, who was warmly thanked for her contribution to the ENT Section 2003-2005, reported on the achievements of the EAACI Taskforce on “Definition, diagnosis and therapy of chronic rhinosinusitis/nasal polyposis”.

A small group (Claus Bachert, Wytske Fokkens, Valerie Lund, and Joaquim Mullol) had met in Amsterdam in January 2003 to produce an outline for action reflecting the concepts of GINA and ARIA. Other section members prepared draft chapters of the final document and a second three-day meeting in Amsterdam in December 2003 finalised the manuscripts to produce “European Position Paper on Rhinosinusitis and Nasal Polyps (EP3OS)”. The full document was published in Rhinology (March 2005) and the Executive Summary in Allergy (May 2005).

The section has been involved in the organisation of major meetings. These include:
- European Rhinologic Society (ERS-ISIAN) Meeting June 2004, Istanbul with two scientific events: a Pre-Congress Course on “Everything you always wanted to know about allergic rhinitis - An interactive course”, and a Symposium on “Recent and future treatment of nasal allergy”.
- Intersama-EAACI Meeting November 2004, Bilbao with a Joint ENT and Asthma Section symposium on “Rhinitis, sinusitis, and asthma”.
- WAO-EAACI Congress 2005 June-July, Munich where the ENT section participated in the organisation of two symposia on “Rhinitis” and “Chronic rhinosinusitis. Answers to a hot topic”.

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Achievements

Former chairperson of the ENT section, Wytske Fokkens, who was warmly thanked for her contribution to the ENT Section 2003-2005, reported on the achievements of the EAACI Taskforce on “Definition, diagnosis and therapy of chronic rhinosinusitis/nasal polyposis”.

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The section has been involved in the organisation of major meetings. These include:
- European Rhinologic Society (ERS-ISIAN) Meeting June 2004, Istanbul with two scientific events: a Pre-Congress Course on “Everything you always wanted to know about allergic rhinitis - An interactive course”, and a Symposium on “Recent and future treatment of nasal allergy”.
- Intersama-EAACI Meeting November 2004, Bilbao with a Joint ENT and Asthma Section symposium on “Rhinitis, sinusitis, and asthma”.
- WAO-EAACI Congress 2005 June-July, Munich where the ENT section participated in the organisation of two symposia on “Rhinitis” and “Chronic rhinosinusitis. Answers to a hot topic”.

The main objectives of the new ENT Section board were set out during a meeting held in Munich. They are:

1) Strengthening the SERIN/ENT Section Meetings by allocating an important part the section budget
2) Continuing distribution of EP3OS all over Europe, producing translations and creating and disseminating a new EP3OS pocket guide
3) Creating initiatives on new Task Forces
4) Continuing collaboration with ERS, AAAAI, national societies and GA\2LEN
5) Increasing membership especially in France, Italy, UK and in Eastern Europe
6) Improving the content of the website.

Although membership of the ENT section has grown enormously during the past four years, it is still the smallest of the EAACI sections. Our plans include a call to all the ENT doctors who are members of EAACI to join us and to bring in others from their respective countries. We also need to increase the interest of otolaryngologists.

Membership of the ENT Section now stands at 276, up 85% (from 199) since 2001. Junior members form 37% of the total. Members represent 47 countries. Seven countries have 15 or more members (Belgium, Turkey, Germany, Sweden, The Netherlands, and Spain).

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Within the Early Diagnosis Campaign, EAACI Brussels Office disseminates today a new brochure “Is it allergy?” developed by the Pediatric Section, in collaboration with primary care physicians.

Eczema, rhinitis, wheeze… are often symptoms with underlying allergy.

The aim of the brochure is to help primary care physicians identify those patients who are allergic when they present with common, everyday symptoms.

Besides scientifically based recommendations for allergy testing, a real cooperation between primary care physicians and specialists in allergy is essential to ensure optimal diagnosis and treatment for the benefit of the children.

More info: eaaci.brussels@skynet.be
US focuses on anaphylaxis

The American Academy of Asthma, Allergy and Immunology (AAAAI) has launched an initiative to bridge the gap between basic science research in anaphylaxis and clinical practice. Important components include an Anaphylaxis Day during the Annual Meeting in 2006 and efforts to develop a universal definition of anaphylaxis, its diagnosis and treatment, and a comprehensive national public education outreach campaign.

“Advances in the diagnosis and treatment of anaphylaxis have lagged behind those of asthma, allergic rhinitis, urticaria, atopic dermatitis, and other allergy/immunology disorders,” says President F. Estelle R. Simons. “Under-recognition of anaphylaxis is a major concern. Many anaphylaxis deaths are probably preventable.”

Special day

Sunday, 5 March 5 2006, will be Anaphylaxis Day and the AAAAI Annual Meeting will begin with the presidential plenary session entitled “Anaphylaxis: Bridging the Gap from Basic Science to Clinical Practice”. Speakers will address animal models of anaphylaxis; improving diagnosis and treatment and prevention of anaphylaxis.

Other sessions during the 2006 Annual Meeting will high-impact publications for food allergy, dermatologic diseases and anaphylaxis, anaphylaxis in the allergy office; peri-operative anaphylaxis and a workshop on the treatment of a mock anaphylactic reaction.

Demonstrations

Anesthesiologists from the University of Miami will provide hands-on education using mannequins that can be intubated (Saturday, 4 March and Sunday, 5 March). Demonstrations of Epipen and Twinject trainers also will be provided. Michael A. Kaliner, MD, FAAAAI is responsible for the preparation of a display entitled “Anaphylaxis Research in the AAAAI: an Historical Perspective”, and a press conference will be held on Sunday, 5 March to highlight anaphylaxis-related abstracts presented at the 2006 Annual Meeting.

Definition and management

During the summer, 16 AAAAI members and Fellows took part in the Second Symposium on the definition and management of anaphylaxis, sponsored by the National Institutes of Health (NIH) and the Food Allergy and Anaphylaxis Network. Their participation helped to develop new collaboration and partnerships by bringing together representatives from 12 organisations involved in allergy/immunology, emergency medicine, pediatrics and anesthesiology as well as representatives of lay people and government.

The results of the first NIH Anaphylaxis Symposium were published in the March 2005 issue of the Journal of Allergy and Clinical Immunology. Attendees at the second symposium discussed further the diagnosis and definition of anaphylaxis, treatment and management, and the future anaphylaxis research agenda. The final recommendations from the second symposium will be submitted for publication to a peer-reviewed journal later this year.

Education campaigns

Numerous media relations efforts are focusing on educating the public about anaphylaxis as potentially deadly and with many potential triggers. In August 2005, AAAAI sent out a news release targeting parents and children as they prepared for heading back to school. More than 60 media outlets featured the story. In addition, Dr S. Alan Bock, FAAAAI, Chair of the AAAAI’s Anaphylaxis Committee, participated in an online chat with patients about anaphylaxis on WebMD, the healthcare information site.

EAACI members can learn more about the anaphylaxis initiative by attending the 2006 AAAAI Annual Meeting, 3-7 March in Miami Beach, Florida. Register at www.annualmeeting.aaaai.org.

Christy Pierce and Richard Lockey

Attend virtually…

Are you limited by lack of time or international travel costs? We can offer you an opportunity to attend the AAAAI 2006 Virtual Annual Meeting.

Log on to www.annualmeeting.aaaai.org, to see and hear the presenters, view their slides and access handouts for each session. Sessions may be viewed live during the actual session time, or anytime after the live session until 14 March 2006.

GA²LEN EXTENDS TO NEW COLLABORATING CENTRES

IF YOU ARE A EUROPEAN CENTRE AND WISH TO PARTICIPATE IN THE GA²LEN NETWORK, PLEASE LET US KNOW BY SENDING AN EMAIL TO THE GA²LEN MANAGEMENT OFFICE:

office@ga2len.net

YOU WILL RECEIVE ALL DETAILS ON THE PROCEDURE.

GA²LEN Annual Conference
Berlin, 29 March-1 April 2006

The date for the Annual Conference in 2006 has now been fixed.

It will take place from Wednesday, 29 March until Saturday, 1 April 2006 in Berlin at the main conference centre (Palais am Funkturm).

Date and location have been chosen to increase the visibility of GA²LEN, since there will be a public health fair (Berlin Vital) and a half marathon going on at the same time.

The exact agenda has not been arranged yet, but we would kindly ask you to block the dates already in your diaries and to inform your coworkers.

GA²LEN updates

Do you want to know what's happening in the EU-funded research programme known as the Global Allergy and Asthma European Network?

GA²LEN News is available at our site: www.ga2len.net, select “Professionals” section on the home page, and then click on “Newsletter” displayed in the left-hand column.
Anti-IgE therapy offers promise

Professor Ruby Pawankar, Nippon Medical School, Tokyo, Japan makes the case for an anti-IgE approach to targeting the IgE-FcεRI cascade in the treatment asthma or rhinitis.

She believes that the humanised monoclonal antibody, omalizumab, represents new therapeutic potential.

One of the characteristics of allergic diseases, such as asthma and rhinitis, is an elevated level of serum specific IgE in response to common environmental allergens. IgE plays a critical role in type I hypersensitivity reactions. It binds to high-affinity IgE receptors (FcεRI) on mast cells via the Ce3 domain on its Fc fragment. Mast cells and basophils, both express the FcεRI receptor, and the FcεRI expression in mast cells and basophils correlate with the levels of serum IgE.

In addition, a strong positive correlation has been demonstrated between the level of serum IgE and clinical symptoms in patients with allergic rhinoconjunctivitis. This may be explained at least in part by the observations that IgE as well as IL-4 can up-regulate the expression of FcεRI on human mast cells and basophils, which is associated with an increase in mediator release. Moreover, IL-4 and IgE in combination can further enhance the expression of the FcεRI on mast cells and mediator release. This may be explained by the fact that IL-4 occur locally in the target organ of AR patients enhances the potential role of the mast cells in forming important positive-feedback amplification loop by auto activating itself via the mast cell-IgE-FcεRI cascade.

Mast cells are an important source of IL-4 and IL-13. While IL-4 can enhance the production of SCF from epithelial cells, thus prolonging the survival of mast cells, IL-4 and IL-13 synergistically with TNF-α can enhance the production of Eotaxin and TARC in airway epithelial cells. These findings suggest that in an on-going allergic inflammation, as seen in persistent rhinitis, the mast cell activation (by IL-4 or IgE) in an autocrine manner can become increasingly damaging through the enhanced survival of mast cells and the more aggressive infiltration of eosinophils and Th2 cells.

GM-CSF has been strongly incriminated as a major determinant of the allergic reactivity to environmental allergens. Mast cell tryptase and histamine can enhance the production of GM-CSF from airway epithelial cells. Thus in on-going type I allergic reactions, mast cells can probably facilitate the sensitisation to novel environmental allergens via a mast cell/epithelial cell/dendritic cell sequential pathway. In this way, the mast cell-FcεRI-IgE cascade can be considered to play an important role in perpetuating on-going allergic inflammation.

The mast cells are not the only ones implicated. Dendritic cells and airway epithelial cells also express the FcεRI. Recently it has been shown that epithelial cells express HLA-DR and CD86 and can also function as antigen presenting cells. The expression of the FcεRI in these cells may be associated with greater allergen uptake and an increase in the resulting immune response.

Strategic treatment

Targeting IgE in the treatment of allergic diseases can possibly down regulate various aspects of allergic inflammation. Omalizumab is directed against the Ce3 domain on the Fc fragment of the high affinity IgE receptor. Strong support for the role of IgE in controlling the expression of FcεRI is provided by recent findings. A study showed that FcεRI expression on circulating basophils was significantly reduced (by 99% in the presence of low serum levels of IgE) by a 90-day treatment with the anti-IgE monoclonal antibody omalizumab of individuals allergic to ragweed. Furthermore, the responsiveness...
The mast cell-IgE-IgE receptor cascade in chronic on-going allergic inflammation.

(histamine releasability) of these cells upon ex vivo allergen stimulation has been shown to be significantly down regulated by approximately 90%.

Type II dendritic cells (DC2) are an important factor for Th2 cell responses. In a group of 24 subjects with ragweed-induced rhinitis, Prussin et al. demonstrated that omalizumab treatment was associated with a significant decrease in basophil FcεRI expression at all time-points during the study (day 7, 14, 21, 28, 35 and 42) compared with placebo (P< 0.001). The level of FcεRI expression on DC1 and DC2 cells was reduced in omalizumab-treated individuals, with a significant reduction observed as early as day 7. FcεRI expression on both DC1 and DC2 correlated with serum levels of IgE in patients receiving omalizumab. There was also a correlation between FcεRI expression on DC2 cells with that on DC1 cells and basophils. These results show that the anti-IgE effects of omalizumab also regulate FcεRI expression in these cell types. Overall, the maximum decrease in FcεRI expression was 73% on basophils, 52% on DC1 cells and 83% on DC2 cells.

The complexes of omalizumab and IgE formed as a result of treatment are small and not thought to be capable of triggering complementary activation or to give rise to immune complex mediated pathology. The ability to reduce circulating IgE with a humanised monoclonal antibody, such as omalizumab, thus represents a new therapeutic approach for the treatment of IgE-mediated allergic diseases.

Anti-IgE mAb (omalizumab) has demonstrated efficacy in attenuating both the early- and late-phase bronchial responses to inhaled aeroallergens. Therapy with omalizumab has shown both to reduce the frequency of asthma exacerbations and the need for inhaled corticosteroids (ICSs) and to improve asthma symptoms, lung function and quality of life. In patients with seasonal allergic rhinitis and perennial allergic rhinitis, nasal and ocular symptoms were significantly reduced and quality of life significantly improved. When administered together with specific immunotherapy (SIT) Omalizumab conferred a protective effect independent of the type of allergen suggesting its usefulness in the treatment of allergic rhinitis, particularly for polysensitized patients. Omalizumab is safe and well tolerated and can be re-administered in subsequent pollen seasons.

**Combined advantages**

Using the anti-IgE approach to target the IgE-FcεRI cascade in the treatment of asthma or rhinitis treatment has several potential advantages. These include the treatment of other concomitant atopic diseases, such as allergic conjunctivitis, atopic dermatitis, and food allergy. Another advantage is that it can also be used at the start of rush immunotherapy. Its favourable risk/benefit ratio, its positive effect on on-going allergic inflammation in both the upper and lower airway and its satisfactory pharmacological and clinical efficacy make anti-IgE a valuable potential therapy for allergic diseases by targeting a central component of the allergic inflammatory response.

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Pawankar R et al., Ann Allergy Asthma Immunol, 2001, 14, 109;
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Prussin C et al., J Allergy Clin Immunol, 2003, 112:1147-54;
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All references available on www.eaaci.net

Ruby Pawankar

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**Staphylococcus aureus: Just a germ?**

Joke Patou, Upper Airway Research Laboratory, ENT department, Ghent University, Belgium argues that *S. aureus* may play an important factor in respiratory disease.

Staphylococcus aureus (*S. aureus*), a Gram-positive bacterium, frequently colonizes the upper respiratory tract, the human skin and the gastro-intestinal tract. About 25% of the population are permanent nasal carriers of the *S. aureus*. In immunocompetent people this bacterium is a commensal pathogen. However, given appropriate conditions it may represent an etiological agent for several pathological conditions such as toxic shock syndrome, food poisoning, pneumonia, osteomyelitis, scaled skin syndrome, abscess formation, and so on.

The invasion of host tissue involves the production of extra cellular proteins such as α-toxin, leukocidin, coagulase and staphylokinase. Furthermore, these bacteria express a number of surface proteins that have the potential to interfere with host defence mechanisms such as a capsular polysaccharide and protein A. Moreover, *S. aureus* secretes two types of toxin with a super antigen activity namely the staphylococcus aureus-
derived enterotoxins (SAEs) and the toxic shock syndrome toxin (TSST-1).

**Mechanisms**

Super antigens have the ability to crosslink the class II major histocompatibility complex of antigen-presenting cells and the Vβ element of the T-cell receptor. This crosslinking takes place outside the conventional antigen-binding groove. This may lead to the stimulation of up to 20-25% of the T-cell population in a non-specific way, compared with stimulation of only about 0.1% via the conventional allergen-specific way. Once activated, T-cells may produce interleukins including IL-4, IL-5, IL-13, etoxin and many others, which may in turn lead to an eosinophilic inflammation and IgE-production. Moreover, there is growing evidence that staphylococcal enterotoxins have an influence on the activation of B cells and pro-inflammatory cells such as eosinophils, macrophages, mast cells and epithelial cells, which are known to play key roles in the pathogenesis of inflammatory airway disease.

**Upper airway disease**

Patients with nasal polyps have higher S. aureus colonization rates in the middle meatus compared to controls or patients with chronic rhinosinusitis without polyps. Colonization with S. aureus is present in 63.6% of subjects with polyps, with rates as high as 66.7% and 87.5% in the subgroups with asthma and aspirin sensitivity. The controls and patients with chronic rhinosinusitis have colonization rates of 33.3% and 27.3% respectively.

In polyp homogenates, specific IgE antibodies that have been identified as markers of a local immune reaction to the classical SAEs (enterotoxins A and/or B) have been found in about 50% of cases. This compares with 15% in controls and 6% in subjects with chronic rhinosinusitis. Nasal polyps with specific IgE antibodies to SAEs show a high total tissue IgE and a more pronounced eosinophilic inflammation with higher concentrations of eosinophil cationic protein (ECP), IL-5 and etoxin compared to SAE-IgE negative samples. The presence of those IgE antibodies is related to the severity of the local disease and co-morbidities. Aspirin sensitivity in asthmatic and polyp subjects is associated with increased concentrations of IgE antibodies to SAEs in polyp tissue.

When nasal polyps were analysed for T-, B-lymphocytes and IgE by immunohistochemistry, follicular structures were found in 25% of the samples. Diffuse lymphoid accumulations were seen in all nasal polyp samples. Follicle-like structures were composed of T- and B-lymphocytes, and stained positive for IgE and SAE binding sites. Plasma cells were prominent in the lymphoid accumulations, which also stained positive for IgE and SAE binding sites. These lymphocyte accumulations therefore may be considered to have developed from follicle-like structures, with B-cells maturing into IgE-producing plasma cells.

Total IgE and IgE-antibody concentrations to enterotoxins were higher in tissue than in serum in all cases. However, SAE-specific IgE-antibodies may be detected in the serum of polyp patients. The IgE/albumin ratios in polyp tissue and in serum were dissociated; this again indicated that tissue IgE is the result of a local IgE production rather than of extravasation.

**Lower airways disease**

In serum from patients with asthma, IgE antibodies to SAE mix (SAEs A, C and toxic shock syndrome toxin 1) are more often found in serum from asthmatic patients than in serum from controls. Within the group of asthmatic patients, they are more often found in those with severe asthma than in those with mild asthma. Furthermore, in patients with chronic obstructive pulmonary disease (COPD) the expression of total IgE and IgE-antibodies to SAEs is higher compared to levels in smokers without COPD and healthy controls. Furthermore, IgE to SAEs decreases significantly in exacerbated cases during hospitalisation accompanied by a significant increase in FEV1. This suggests a role for super antigens in exacerbated COPD similar to that in severe asthma.

**Conclusion**

It is not only in patients with nasal polyps but also those with asthma and COPD that specific IgE antibodies to SAE are higher compared to controls. Moreover in nasal polyps, the colonization rate of S. aureus is increased and the high total IgE is associated with a more pronounced eosinophilic inflammation. The presence of these IgE antibodies is related to the severity of local disease and co-morbidities. S. aureus and its super antigens may play a pivotal role in the pathomechanisms of upper and lower airway diseases.
SYMPOSIUM
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Immunology and clinics of superantigen-driven inflammation

Topics:
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- Superantigens and aspirin sensitivity
- A new therapeutic chance?

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