Join the Allergy Run in Vienna!
EDITORIAL

ALWAYS TRYING TO BE BETTER!

In this first issue of 2006, we would like to introduce you to the new team behind the EAACI Newsletter. The coordination of the newsletter has been moved from the EAACI Brussels Office to the EAACI Executive Office in Stockholm, Sweden. Emma Jonsson from Congrex is the coordinator who manages the contact between everyone involved in the production. We have chosen to keep the design from 2005 since it is appreciated among our readers and reflects a fresh and modern view of our organisation and activities.

We have received a lot of interesting articles for this issue of the EAACI Newsletter and I hope you enjoy reading all of it. You will get to know the EAACI President better thanks to the interview made by Maria Staevska, and you are presented with four interesting State-of-the-art reports where the subjects range from the hygiene hypothesis to asthma mortality. These contributions have been made from researchers outstanding in their respective field for the members of EAACI, and further topics will come. Please do not forget that you can contribute to the next issue by sending us an article or other relevant information and comments!

2006 is an exciting year in the allergy and asthma field. The term “allergy” was first defined 100 years ago, and this field developed so enormously since then. This progress will be highlighted at the XXV Congress of EAACI in Vienna, Austria in June, with topics such as The Evolution of Allergy, Cells of the Allergic Immune Response - from dendritic cells to T regs, Different Target Organs of a Systemic Disease - the nose, lung, skin and gut, and New Horizons in Diagnosis and Treatment - recombinant allergens. More information about the programme can be found on www.congrex.com/eaaci2006.

I am sure you will not only enjoy the quality of the scientific presentations, but also the unique charm of Vienna and its surroundings. As we expect more than 7000 visitors, we recommend you to register for the conference and the social events as soon as possible. Deadline for late registration is 10 May 2006.

Claus Bachert, Editor
NEW YEAR, NEW POSSIBILITIES

2005 was a good year for EAACI. We were host to the largest ever World Allergy Congress, in Munich, which was a great success scientifically, socially and financially. On the back of this success, the executive committee was able to meet in Brussels in October and set a balanced budget that will allow us to carry out our main activities, and allows some scope for new developments. The new ExCom has already formed good working relationships and has generated a series of ideas that we will work on over the course of our two year mandate. In our first year, we are tidying up our legal status and our constitution. Recent changes in tax legislation and charity law mean that we need to make sure we have the correct status to pursue our goals, of supporting the specialty and its related science, as well as helping people with allergic diseases and their families, right across Europe. We are also using this opportunity to review our internal structures. The revision is in progress and we will be bringing forward concrete proposals to the general assembly in June.

A key objective of my presidency is to review the support we can give to our members in the less prosperous parts of Europe. Plans to offer reduced membership rates were discussed at the ExCom in October, but we have not yet finalised the package. I hope that we will be able to bring you some good news on this important topic by the middle of 2006.

Another area that requires our attention is the future of the specialty of allergology and clinical immunology. Although we have no doubts about the importance of the specialty, there is no doubt that we are relatively weak, compared to some other specialties, such as cardiology or neurology, where there is a clearly defined area of responsibility. Both at the national and European level, there is a desire to contain the costs of healthcare, and we are being challenged to show that our approach to clinical practice is both effective and cheaper than the available alternatives. As an organisation EAACI needs to respond to this challenge, without getting into internecine arguments with other specialties. We need to demonstrate that allergists bring added value to the care of people with allergic diseases, and we need to link that added value to possession of core competences in the specialty. One option that we are considering is to establish a supranational certificate of competence in allergology. A subgroup of the ExCom is currently looking into the practical and legal aspects of this, and they will report back later this year.

Abstracts have been pouring in, and our programme committee will be meeting at the end of February to assemble the free communication sessions and put the finishing touches to the programme. You can expect all the usual activities for clinicians, scientists and junior members, as well as some new features, including the first EAACI allergy run on the morning of Saturday 10th June. The congress website is continually updated, as these various additions are made to the programme. Do check it out at www.congresx.com/eaaci2006 and register for all the various courses and events! For those who have not been there before, Vienna is a wonderful city, with excellent cultural activities and public transport. Anyone who has visited before will know what I mean and will already have booked their place! I look forward to seeing you there.

Anthony Frew

The new ExCom has already formed good working relationships and has generated a series of ideas that we will work on over the course of our two year mandate.

And finally, of course, the major event of our calendar is our annual congress. Plans for the Vienna congress are going very well, and we expect another excellent meeting.
2006 AAAAI ANNUAL MEETING:
The Scientific Basis of Allergy Practice

With more than 400 educational sessions at the AAAAI Annual Meeting, March 3-7, in Miami Beach, FL, delegates will learn about the latest developments in the specialty and how that cutting-edge research applies to patient care.

From two keynote speakers, four new Bring Your Own Patient sessions and 13 Hands-on Workshops, to the Science & Surf: Featured Poster Session & Reception, Highlights of the Day Sessions and a special Presidential Plenary Session, the Annual Meeting Program Committee has designed a program that will appeal to a diverse audience of physicians, healthcare professionals and scientists.

Delegates will also have added opportunities to network with colleagues and may earn up to 50.5 CME/60.6 CE credits.

Approximately 500 session topic ideas were submitted for the 2006 Annual Meeting, and more than 80% were used in some form. AAAAI members played a critical role in developing the program, from submitting session topic ideas to their involvement in the Interest Sections that ultimately helped decide the Annual Meeting format.

Key sessions include:

Keynote sessions

Clinical Trials and the Public Trust Human Disease: A Sum Game of the Gene and the Environment

Four Plenary Sessions

The four Plenary Sessions are the premiere scientific sessions of the 2006 Annual Meeting and include the Presidential Plenary Session. The sessions reflect an innovative and diverse program that provides all Annual Meeting delegates with the opportunity to learn about important, new advances in the specialty.

- Seeing is believing: Host and Hostility (Presidential Plenary) - Anaphylaxis: Bridging the Gap from Basic Science to Clinical Practice
- The Science of Evidence-Based Medicine in Asthma
- Allergic/Inflammatory Diseases: Dissection and Modulation

Science & Surf: Featured Poster Session & Reception

Delegates will learn about science of high significance in the field and earn CME/CE when they visit the featured poster session. In addition, they will network with other Annual Meeting delegates and catch up with colleagues and friends while enjoying a pre-dinner reception. All Annual Meeting delegates and their registered guests are invited to attend this free event.

Anaphylaxis Day activities

From the Presidential Plenary Session and special seminars, to intubation simulations and new Anaphylaxis Education Tool Kits, Anaphylaxis Day will emphasize the importance of the role of the allergy/immunology specialist in anaphylaxis management and prevention.

Bring Your Own Patient Sessions

These new workshops offer delegates the opportunity to submit difficult patient cases from their practices for discussion by leading experts in the field.

Journal Club Seminars

Each Interest Section will host one of the new Journal Club Seminars, designed to be discussion-based forums for high-impact papers that affect each Interest Section.

Member Service Programs

Three new programs will address critical information for the successful practice of allergy/immunology.

Highlights of the Day/Meeting Sessions

Representatives from each Interest Section will summarize highlights from sessions they attended throughout the day. Interest Section representatives will provide a summary of the major issues advanced at the Annual Meeting.

Oral abstract sessions

With 1,272 abstracts already submitted, the 2006 oral abstract sessions will highlight new insights into the treatment of allergic disease in four daily sessions.

Oral abstract sessions feature top research submitted for the 2006 Annual Meeting. Each session will include a presentation from a senior investigator followed by oral presentations from selected abstracts related to the investigator's research. Researchers will discuss the details of their research during unopposed sessions.

New sessions from 2005, including the Pro/Con Debates, State-of-the-Art Sessions and Interest Section Forums, were well received and will be continued in 2006:

Pro/Con Debates

Topics are:
- Maintenance Medications for Mild, Persistent Asthma is Not Necessary
- In Vitro Testing for Specific IgE Obviates the Need for In Vivo Testing
- Best Indicators of Asthma Control
- Home Immunotherapy is Safe
- Is Chronic Rhinosinusitis an Inflammatory or Infectious Process?
- Food Allergy Plays a Major Role in Atopic Dermatitis
- Targeting a Single Molecule is Effective in Asthma Treatment
- Eosinophilic Esophagitis: an Epidemic or an Over-diagnosis?
- Mouse Asthma Models do not Really Assess Asthma
- All Patients with Specific Antibody Deficiency Should Receive Intravenous Immunoglobulins

Each Interest Section is designing a State-of-the-Art session and an Interest Section Forum.

For the most updated information about the 2006 Annual Meeting, visit the website, www.annualmeeting.aaaai.org.

Richard Lockey
WELCOME TO VIENNA IN JUNE!

XXV Congress of the European Academy of Allergology and Clinical Immunology
10 - 14 June 2006, Vienna, Austria

Basic Science in Allergology and Clinical Immunology, a Prerequisite for Improving Patient Care and 100 Years of ALLERGY as defined by Clemens von Pirquet.

The Social Programme includes many interesting tours and events. Whether you have been to Vienna before, or this is your first visit, you are guaranteed to discover new things. This year, the world celebrates Mozart’s 250th birthday, and now is the perfect time to visit Vienna since he spent part of his life here.

The 1st EAACI Allergy Run will take place in the morning of Saturday 10 June. Read more about this event on the Congress website www.congrex.com/eaaci2006 and register for the race, where local runners will also participate.

More than 1600 abstracts have been submitted to the Congress, which is a new record for an EAACI Congress!

The Scientific Programme reflects the fact that the term ALLERGY was defined 100 years ago by the Austrian paediatrician Clemens von Pirquet. The Local Organising Committee and EAACI will continue this tradition by generating a successful scientific programme of the highest standards comprising all aspects of Allergology and Clinical Immunology.

EAACI has developed to be the major meeting of Allergy and Asthma in Europe, and you will be able to attend numerous interesting sessions and join many discussions with colleagues from other countries.

Find out more about the EAACI Congress and register at www.congrex.com/eaaci2006
The summer school course “Allergy – From Basic Immunology to Clinical Care”, held in Prague in 2005, was jointly organised by EAACI and GA2LEN with the Czech Society of Allergology and Clinical Immunology. Professor Jan Löttvall headed the event.

The venue was the Top Hotel Prague, situated in the suburb of Chodov, which gave easy access to the centre of Prague by public transport and taxi. The hotel was sufficiently comfortable and well equipped for the event.

On Saturday 10th September, the participants met in the winter garden of the hotel for the welcome reception, which allowed for informal discussions with small groups of friends and colleagues and contributed to the event’s pleasant and relaxed atmosphere.

The scientific programme was introduced the following morning by Professor van Caemmerberge, who gave a speech of welcome. The first day’s sessions included “Epidemiology” (taken with the hygiene hypothesis and allergy prevention) and “Induction of allergy” (comprising allergens, infection, and allergy and diagnosis). After lunch, the programme continued with problem. This structured discussion was interesting and useful, and appreciated by participants and moderators. The scientific programme continued with the clinical topics “Immunotherapy” and “Atopic dermatitis” in the afternoon. On Tuesday evening, shuttle buses transferred the participants to a restaurant in the city, U Fleku, to enjoy a traditional Czech dinner. This event contributed to the participants getting to know each other better and was enjoyed by all.

On the final day, Wednesday 14th September, the morning programme commenced with a slightly decreased number of participants as some were obliged to leave before the official end of the event. The interesting topics included the first session on “Asthma” and the second on “Clinical allergy topics”, which covered topics from food allergy over drug and venom allergy to immune deficiencies. The course was then closed by Professor Marek Kowalski as a representative of GA2LEN and EAACI.

Feedback from the participants was positive and the event was considered a success, giving significantly improved knowledge about allergy and the immune mechanisms involved. It contributed to improving personal contacts and friendships between participants from many countries. In total, 108 participants from 22 countries and 23 speakers from 10 countries took part in this event. We would like to thank all the speakers for their excellent contributions, thanks to Professor Jan Löttvall for his great help in putting together such an excellent faculty, and last, but not least, thanks to GA2LEN and EAACI and local sponsors for the financial help which made it possible to organise this event.
News from junior members

The high response rate of JMAs to the 2005 JMA questionnaire has clearly shown that 80% of JMAs would like to have clinical educational courses at the EAACI annual congresses (Fig. 1).

Are JMAs interested in clinical educational courses?

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<th>Number [%]</th>
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The response to the questionnaire gives a more detailed view of the JMAs in our academy. The distribution of age is about 50% each for the 25-30 age group and the 31-35 group (Fig. 2). Interestingly, many female JMAs responded to the questionnaire! If you are interested in more details of the questionnaire, please check the JMA website, which presents all the responses, comments, and graphics.

The JMA activities for the EAACI congress in Vienna this year include a JMA poster session on the Saturday evening, where you can win a prize for an outstanding presentation, the JMA social event (no entrance fees for JMAs) which is going to be a terrific night out clubbing in a palace in traditional Viennese nightlife style, the JMA forum on “Neuro-immune findings in allergy” where some of the best junior scientists will give their presentations in that field, our JMA business meeting, and last but not least the JMA educational session on the skills required to successfully write your paper and get it through the jungle of reviewers...

By the way, if you take the time to answer our JMA questionnaire, presented soon on our website, you will have a possibility of winning a travel grant for the EAACI congress in Vienna in June 2006! As you can see (also on our JMA website) a lot is going on in and with the new JMA working group. Constant change is part of the personal development in the JMA working group, and Ioana Agache, Nina Blümchen, Gert-Jan Braunstahl, and Stephano del Giaco left our group in Munich in 2005 to become valuable new seniors of the academy. I would like to take this opportunity to thank them for their outstanding contribution to the success of our group in recent years. And with great pleasure, I would like to present my new team (which some of you might have already met at our JMA poster session and business meeting in Munich in 2005):

- Miguel Borrego, Portugal; Immunology section representative; miguel.borrego@sapo.pt
- Marcin Kurowski, Poland; Immunology section representative; marcin.kurowski@gmail.com
- Luis Miguel Borrego, Portugal; Pediatric section representative;
- David Gronenberg, Germany; Asthma section representative; david.gronenberg@charite.de
- Philippe Gevaert, Belgium; Previous chairperson; Philippe.Gevaert@UGent.be
- Peter Hellings, Belgium; ENT section representative; peter.hellings@med.kuleuven.ac.be
- Elena Borzova, Russia; Dermatology section representative; eborzova@online.ru
- Ulrike Raap, Germany; JMA chairperson (SPC, EX COM); mail@ulrike-raap.de
- Chrysanthis Kevak, Greece; JMA webmaster; ckevak@allergy.gr

Looking forward to seeing you in Vienna this year! With all best wishes for a happy and successful 2006.

On behalf of the JMA working group,

Ulrike Raap, JMA chairperson

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For the EAACI congress in Vienna 2006 we have conveyed the wish of many JMAs to have clinical educational workshops with new activities: We organised three workshops (which are open to all EAACI members) for the Saturday afternoon: (i) Diagnostics of rhinology, (ii) Diagnosis and management of contact eczema and (iii) Immunotherapy: Indications and management. These workshops will be very interactive: participants sitting in the front rows must be prepared for a high level of involvement!
Basic Immunology Research in Allergy and Clinical Immunology

EAACI-GA²LEN Davos Meeting in Grainau, Garmisch-Partenkirchen, Germany

The 4th EAACI-GA²LEN Davos Meeting, “Basic Immunology Research in Allergy and Clinical Immunology”, takes place 18-19th February 2006 in Grainau, Garmisch-Partenkirchen, Germany.

For the last five years, the EAACI Immunology Section has organised meetings for young doctoral and postdoctoral scientists with the goal to increase the impact of basic immunology research within the allergy and clinical immunology fields. The first three of these meetings took place in Davos and were a great success. Since then, the meetings are called “Davos Meetings”.

The 4th EAACI-GA²LEN Davos Meeting takes place in another alpine setting: Grainau in Garmisch-Partenkirchen, Germany. The meeting is organised by the Immunology Section and the ZAUM-Center for Allergy and Environment, Technical University Munich, with generous support from GA²LEN.

The meeting includes 5 symposia on 3 main topics: Inflammation, adaptive immunity and regulation and allergic inflammation. Each symposium will be opened by a keynote lecture followed by abstract presentations. The list of keynote speakers includes: Ulrich von Andrian, Boston, MA; Richard Flavell, New Haven, CT; Ron Germain, Potomac, MD; Philippa Marrack, Denver, CO; Dale Umetsu, Boston, MA; and Hermann Wagner, Munich, GER.

We have received a large number of outstanding abstracts which were reviewed by an international panel of experts. Based on the scientific quality of the submitted abstract, 70 participants were selected for the meeting. There will be 25 abstract presentations and two small poster sessions. At the poster sessions, the participants are given the opportunity to discuss their data with the keynote lecturers and organising scientists.

Between the morning and the evening sessions, there is time for winter sports or sightseeing.

The goal of the meeting is to create a warm scientific environment in which allergy and asthma related immunological concepts can be covered with ample time for discussions where young scientists can interact directly with well-known experts. The keynote speakers are asked to stay during the entire meeting in order to encourage these discussions – they can take place in the ski slopes, during lunch or dinner or in the evenings at the wine & cheese poster session.

The organisers are looking forward to a productive meeting and we hope that these kinds of meetings become a custom within EAACI and a way to promote young scientists active in basic allergy and clinical immunology research.

Thilo Jakob
Chairman of the EAACI Immunology Section

Dear friends and colleagues,

Registration has now commenced for the Training Course in Food Allergy, which will take place at Hindsgavl Castle in Middelfart, Denmark on 8–11th April, 2006.

The meeting is sponsored by EAACI and GA²LEN, with an educational grant from Pharmacia AB.

The boards of the Dermatology Section, the Paediatric Section, and the Interest Group for Food Allergy are responsible for the meeting.

Please visit the website for further information: www.eaaci.net/site/content.php?artid=948

We aim to create a congenial scientific environment that allows ample time both for discussion and also for practical training sessions.

The focus of the course is clinical, but it will also include sessions of a more theoretical nature.

A number of travel grants will be provided.

Looking forward to seeing you in Denmark!

On behalf of the Organising Committee,
Carsten Bindslev-Jensen

Training Course in Food Allergy

8–11th April, 2006

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EAACI CONSTITUTIONAL DEVELOPMENTS

People sometimes ask why we need a constitution and by-laws. The simple answer is that these set out what EAACI does, and how it is organised to achieve these objectives. Over the past few months, the new Executive Committee has reviewed our current structure, and has come up with some proposed changes which we will put forward to the General Assembly in June.

The main suggestion is that we plan to reorganize the ExCom into subgroups with clearly identified responsibilities. A core group (Board of Officers) will oversee the finances and set policy objectives. The subgroups would be responsible for defined areas of policy; each would be chaired by a vice-president, and report to the full ExCom.

The intention of the proposal is that one subgroup will manage our congresses and other larger meetings; another will address educational, training and speciality issues (postgraduate courses, summer schools etc); and the third will cover communications, including our website, journals, newsletter and dissemination of task force reports.

The precise details of the suggested changes will be sent to all members in March, and will be voted on at the General Assembly in June. We see considerable advantages from this reform, in that each ExCom member will have a defined responsibility. EAACI will also have a larger group of vice-presidents with clear leadership roles, and we believe this will lead to a stronger Academy. We will be pleased to answer any questions members may have concerning the proposed changes.

AJ Frew & J Lötvall

CRITICAL REMARKS ON THE HYGIENE HYPOTHESIS (HH)

Charles K. Naspitz, M.D.

The Hygiene Hypothesis (HH) introduced by David Strachan was based on the observation that early infections during the first years of life would skew the Th2 profile to a Th1 profile, diminishing the onset of allergic diseases some years later. A large number of children (siblings) in one family would be an ideal environment for the dissemination of these early infections.

However, several researchers showed that the association of asthma and total number of siblings was not significant. The correlation between atopic diseases and tuberculin reactions was also not observed in several papers. There is no agreement on the microorganisms and routes of infection that would be involved in the HH. The association with the hepatitis A virus is now conditioned to the presence of the TIM-1 gene in the individual.

In Brazil, infection with A. lumbricoides is an important risk factor for wheezing in pre-school children living in parasite-endemic areas. However, in the same geographical area, an inverse association between skin responses to Aero-allergens and Schistosoma mansoni infection was observed. The relationship between helminth infections and atopy is not completely elucidated: Low or high intensity of the infection, IL-10 production, regulatory T-cells etc., are involved in this process.

In developing countries in Latin America, with very poor hygiene, the prevalence of asthma and allergic rhinitis is as high as it is in developed countries. The prevalence of wheezing in the last 12 months (ISAAC study), a surrogate for asthma, is the same in Brazil, Peru, and the USA and second only to Australia and the UK (highest prevalence).

The present status of the HH was well defined by David Strachan in 2004: "The HH remains a credible but non-specific explanation for the observed variations over time, place, and persons at risk for developing allergic disorders. The clinical implications of these advances in our understanding of the aetiology of atopic allergic disorders are currently limited".

The HH has been critical in animating an important level of investigation and discussion worldwide, and therefore is of significant value in helping improve understanding of the development of allergic disorders. However, the HH is not likely to be the sole explanation for the ongoing asthma epidemic in industrialised and non-industrialised economies. Several recent reports show that the "allergic epidemic" may have reached a plateau.

It is believed that the remarkable progress made in the genetics and physiopathology of allergic diseases in recent years will further clarify areas under current investigation in the near future, and hopefully promote improved treatments for our allergic patients.
ASTHMA MORTALITY WORLDWIDE

Hugo E. Neffen, M.D.

Over the last four decades, two particular features of asthma mortality can be observed epidemics which occurred in a number of countries in the 1960s and particularly in New Zealand in the 1980s-90s: and gradual increases until the mid-1980s. Interest in asthma treatment has centered on its possible role in both these trends.

Several explanations have been offered to account for the rise in asthma mortality: on the one hand, the increasing severity and prevalence of asthma, and on the other the failure of management of asthma, and reactions to asthma medications. (1)

Fortunately, from the 1990s until now, the rate of asthma mortality, global and age-adjusted between 5-34 years of age, showed a gradual decreasing tendency in most countries. It has been hypothesised that better care, particularly concerning the use of inhaled steroids, may be partly responsible. This is consistent with recent studies showing that prescribed inhaled steroids are associated with a lower rate of hospital admissions for asthma. More recently, inhaled steroids were reported to be associated with a lower rate of asthma deaths. The association between inhaled steroids and a decreased risk of asthma death was found in a study published in 2018, showing that receiving at least six canisters of inhaled steroids per year. This group registered only one asthma death. (2)

However, there was a lack of data concerning asthma mortality in the Americas. A multi-centre study coordinated by the Latin-American Society of Allergy and Immunology, covering 12 countries during the 1980s: Argentina, Brazil, Chile, Colombia, Costa Rica, Cuba, Ecuador, Mexico, Paraguay, Peru, Uruguay, and Venezuela.

The highest death rates were found in Uruguay and Mexico (5.63) and the lowest in Paraguay (0.8) and Colombia (1.35). Age-adjusted (5-34) rates were higher in Costa Rica (1.88) and lower in Chile (0.28).

This analysis discusses the factors involved in the decrease in asthma mortality in Argentina in the 1990s.

We developed a five-year dissemination programme for the Global Initiative for Asthma in Argentina, which was launched in December 1995. In 1996-97, 600 specialists and more than 5,000 physicians, nurses, diabetics, general practitioners, and family doctors, were contacted nationwide. They participated in workshops and symposia, which increased their awareness of asthma management and the early implementation of anti-inflammatory therapeutic strategies, in accordance with the "Global Strategy for Management and Prevention" (WHO/NHLBI).

In 1999-2000, the dissemination of GINA through the implementation of a Distance Course: Asthma Update. This course was developed by Argentine asthma specialists working on the translation of the "Global Strategy for Management and Prevention". The entire course and its adaptation are local contributions with special considerations for children, and an evaluation questionnaire.

The changes in total anti-asthmatic drug sales in Argentina in 1999, compared with 1990, show an increase in anti-inflammatory drugs and inhaled route, the key concept disseminated during the activities based on GINA guidelines.

The most important differences between 1990 and 1999 were a 64% reduction in xanthines (p<0.02), an increase of 21% in inhaled beta 2 agonists (p<NS), a reduction of 36% in oral beta 2 agonists (p<0.02) and an increase of 441% in inhaled steroids (p<0.001). Although there was an increase in the prescription of inhaled steroids in this decade, the rate is strongly since the launch of GINA guidelines in 1996, having a statistical significance when comparing the increase in 1997-99 with 1990-96.

Simultaneously, asthma mortality decreased in the 1990s. Asthma mortality and age-adjusted rates (5-34) in Argentina in 1980-89 were 3.38 and 0.72, respectively. Mean values in 1990-99 were: 2.58 (p<0.05) and 0.38 (p<0.01), respectively. (3)

A relevant fall (48%) in asthma mortality age-adjusted rates (5-34) occurred during the 1990s, in comparison with the 1980s. This also occurred in children and adolescents, but the decrease is more evident in the age group 10-19, which was a high-risk group for asthma deaths.

If we correlate the decrease in global and age-adjusted asthma mortality rates with total anti-asthmatic drug sales changes, the greater use of inhaled corticosteroid (ICS) therapy, which increased fourfold in Argentina in this period, is the most evident change. The correlation between ICS sales and age-adjusted (5-34) asthma mortality rates was -0.84 (p=0.003), and the same occurred with global mortality rates: -0.81 (p=0.005).

In other Latin-American countries, including Colombia, Uruguay, and Venezuela, asthma mortality in the 1990s showed the same pattern as in Argentina: increased prescription of inhaled steroids and decreased asthma mortality rate.

Although asthma mortality in Latin America shows a decreasing trend, the undertreatment of asthma and the low rate of prescriptions of inhaled steroids is remarkable, because the recent publication of Asthma Insights and Reality in Latin America (AIRLA), covering 11 countries, shows that only 6% of asthmatics receive inhaled steroids and that 4% receive combination therapy with ICS plus LABA (4).

The current situation of asthma mortality can be summarised in the words of the Global Burden of Asthma. It is estimated that asthma accounts for about one in every 250 deaths worldwide. Many of the deaths are preventable, being due to suboptimal long-term medical care and delay in obtaining help during the final attack (5).

In conclusion, changes in asthma mortality should be especially sensitive to changes in quality of management. For this reason, we must continue working worldwide to implement guidelines and reduce morbidity and the cost of asthma treatment, and to consolidate the decreasing tendency in asthma mortality through varying postgraduate education programmes.

REFERENCES
Allergy Starts in the Blood

Judeh A. Denburg, M.D., FRCPC

The occurrence of allergic diseases, including allergic rhinitis and asthma, is believed to have an inflammatory basis for these conditions. Efforts to understand their development and immune basis are necessary. While persistence into early childhood of Th2 (allergic-type) immune responses is proposed as the biological basis for the development of atopic diseases, the reasons why some individuals do not undergo "immune deviation" to Th1 (non-allergic-type) responses, and do not develop atopy or asthma, remain unclear. Dysfunctional adaptive (T-cell) immunity is thus probably not the only abnormality underlying the genesis of atopy and asthma, abnormalities in innate immunity are also important.

Based on a previously demonstrated association of a reduction in hematopoietic progenitors (expressing CD34/45+) and either IL-5R or GM-CSFRα with increased risk for atopy (Upham et al, J Allergy Clin Immunol 1999;104:370), we examined whether or not alterations in CD34+ cord blood (CB) progenitors at birth might relate to the development of the allergic diathesis, i.e., does phenotypic switching of CB progenitors towards the Eo-B pathway predict atopy in early infancy? First, we showed an inverse correlation between maternal skin prick test responses to common allergens, and IL-5R or GM-CSFR expression on CB CD34+ cells at birth. Analyses of CB samples in a double-blind study of atopic, pregnant women, randomised to supplemental fish oil or olive oil from 20 weeks gestation until delivery (Denburg et al, Pediatr Res 2005;57:275) revealed that percentages of CB CD34+ cells were higher after PUFA than placebo (p<0.003), and that there were significantly more IL-5 responsive, but not IL-3 or GM-CSF responsive, CB Eo/B-CFU in the PUFA group compared to the control group (p<0.03). These alterations in progenitors correlated with clinical outcomes at one year of age: the number of IL-5 responsive Eo/B-CFU and the percent of CD34+ cells positively predicted atopic dermatitis at the age of 12 months, the number of IL-5 responsive Eo/B-CFU positively predicted wheeze at the same age.

By taking into consideration the large body of previous evidence which directly implicates inflammatory cell progenitors in the maintenance and propagation of allergic inflammation in the airways in rhinitis and asthma, we can now show these cells and hematopoietic processes are important in the initial development of the atopic diathesis and atopic disease. We have interpreted these findings as supportive of the bone marrow hypothesis of atopy and asthma.

Our next step will be to examine the roles that both cellular and molecular hematopoietic processes play in early infancy and childhood, hypothesising that cord blood eosinophil-basophil progenitor molecular and/or functional phenotypes at birth, independent of T-cell influences, contribute to or predict the development of allergic disease. Utilising access to two longitudinal birth cohorts in Canada in conjunction with ongoing collaborations with colleagues at the University of Western Australia and in the USA, cord blood progenitor cell phenotype and function will be studied in relation to atopic risk and symptoms, allergy skin test responses and development of allergic clinical outcomes, including asthma, into early childhood. This research will lead to greater understanding of molecular mechanisms in the genesis of atopy in early life, and the identification of novel phenotypes, biomarkers and therapeutic targets for early intervention in the atopic diathesis.

Downregulation of GM-CSF receptor expression on cord blood CD34 cells: hematopoietic immaturity in atopic at - risk infants?

Summary of Findings
- There is a negative association between atopic risk and cord blood IL-5R expression
- Maternal n-3 PUFA dietary supplementation alters IL-5 responsiveness of lineage - committed cord blood hematopoietic progenitors in newborns at risk of atopy
- In all infants (at-risk or not) there is positive association between IL-5 responsiveness of cord blood progenitors ex vivo/in vitro and clinical symptoms of atopy at 1 year
Does anti-IgE 
FULFIL THE UNMET NEED 
IN ASTHMA TREATMENT?

Roland Buhl, Mainz University Hospital, Mainz, Germany

This satellite symposium on the theme ‘Anti-IgE: addressing the unmet need in inadequately controlled severe allergic asthma’, was sponsored by Novartis in association with the main meeting. Professor Roland Buhl presented the latest findings from the omalizumab clinical trials programme.

Omalizumab, a humanised monoclonal anti-immunoglobulin E (IgE) antibody, is the first asthma medication that works by blocking IgE: an underlying cause of allergic asthma.

Professor Buhl introduced omalizumab, a humanised monoclonal anti-immunoglobulin E (IgE) antibody. Omalizumab is the first asthma medication that works by blocking IgE, an underlying cause of allergic asthma. Initial findings showed that omalizumab significantly reduced the level of exacerbations in asthma patients considered at high risk as a result of recent emergency room treatment, hospitalisation, or previous intubation. He said that this had suggested the potential for omalizumab to make an impact in fulfilling the unmet treatment needs of patients with severe allergic asthma who remain symptomatic, despite their current therapy. He described an analysis of pooled data from seven controlled trials of omalizumab treatment in severe asthma. “Omalizumab was designed to be an additional tool for patients with severe allergic asthma whose symptoms persist despite receiving the best available combination of therapies,” he said. “The pooled analysis of data studied five double blind studies in which omalizumab was added to current asthma therapy and compared with placebo, as well as two open label studies in which omalizumab was compared with current asthma therapy alone.”

The analysis parameters for pooled data were annualised rate ratios (omalizumab:control) for asthma exacerbations (events defined differently across the studies, but all involving a worsening of asthma symptoms resulting in the necessity of increased corticosteroid treatment, with or without physician intervention) and total emergency visits (a combination of hospital admissions, emergency room visits, and unscheduled doctor visits) due to asthma. Sub-group analyses were also performed to determine the effect of baseline factors on the efficacy of omalizumab, including older age and oral corticosteroid use. The pooled data were derived from a population of 4,308 patients with allergic asthma aged 12-79 years old, of whom 93% were categorised as having severe persistent asthma according to the Global Initiative for Asthma 2002 classification. “These patients were already receiving high-dose inhaled corticosteroids [average 1.462 μg per day beclomethasone dipropionate equivalent],” explained Professor Buhl. “More than half [57%] were being treated with long-acting β2-agonists before commencing treatment with omalizumab or placebo.”

The major finding of the pooled study was that omalizumab significantly reduced the annualised rate of asthma exacerbations by 38% versus control (0.91 and 1.47, respectively; p<0.0001) (figure 1) and the rate of total emergency visits showed a 47% reduction with omalizumab (0.332 versus 0.623 in the control group, respectively; p<0.0001).

“Compared with a control treatment group, patients treated with omalizumab demonstrated significantly reduced annualised rates of asthma exacerbation and total emergency visits — a composite of reductions in hospital admissions, emergency room visits, and unscheduled doctor visits.”

Roland Buhl

Professor Buhl said that omalizumab reduced hospital admissions by 51% (p=0.041), emergency room visits by 60% (p=0.013) and unscheduled doctor visits by 43% (p=0.0003). (figure 2) He showed that a sub-group analysis of the pooled data demonstrated that the efficacy of omalizumab in reducing asthma exacerbations was unaffected by baseline factors such as oral corticosteroid usage or patient gender. One exception was a trend for greater efficacy in patients having more severe asthma symptoms, defined as those patients having a lower value of percentage predicted forced expiratory volume in one second (FEV1) at baseline.
Further sub-group analysis has shown the similar efficacy of omalizumab in allergic asthma patients, irrespective of their being older or the extent of their use of oral corticosteroids. For patients taking oral corticosteroids as part of their asthma treatment regimen, for example, Professor Buhl pointed out that omalizumab significantly reduced the annualised rate of asthma exacerbations by 37% versus control patients (1.65 and 2.63, respectively; \( p = 0.001 \)); the corresponding reduction in patients not taking oral corticosteroids was 39% (0.82 and 1.34, respectively; \( p < 0.001 \)). Oral corticosteroid use also had no apparent effect on the efficacy of omalizumab in reducing emergency visits. (figure 3)

Overall, Professor Buhl's presentation introduced the potential for add-on therapy with omalizumab to fulfill an important unmet need in severe asthma treatment. Crucially, those difficult-to-treat patients with severe persistent allergic asthma who remain symptomatic, despite receiving high doses of inhaled corticosteroids and long-acting \( \beta_2 \)-agonists, would be the major beneficiaries, regardless of age or concomitant oral corticosteroid therapy usage.

The professor concluded that "omalizumab is poised to make a major clinical impact on the treatment of severe allergic asthma in Europe."

**Key slide 1**

Omalizumab significantly reduces asthma exacerbation rate: pooled data

**Key slide 2**

Omalizumab significantly reduces emergency visits for asthma: pooled data

<table>
<thead>
<tr>
<th>Rate per year</th>
<th>Omalizumab</th>
<th>Control</th>
<th>p-value for rate ratio</th>
<th>Treatment difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total emergency visits</td>
<td>0.332</td>
<td>0.623</td>
<td>&lt;0.0001</td>
<td>0.29</td>
</tr>
<tr>
<td>Hospital admissions</td>
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<td>0.062</td>
<td>0.041</td>
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<tr>
<td>Emergency room visits</td>
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<td>0.066</td>
<td>0.013</td>
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<tr>
<td>Unscheduled doctor visits</td>
<td>0.252</td>
<td>0.443</td>
<td>0.0003</td>
<td>0.19</td>
</tr>
</tbody>
</table>

*Note: J. et al. Allergy 2016*

**Key slide 3**

Omalizumab significantly reduces asthma exacerbation rate irrespective of baseline oral corticosteroid use: pooled data

1. **DCS**
   - Omalizumab: 3.23 (\( p = 0.001 \))
   - Control: 3.34

2. **Non-DCS**
   - Omalizumab: 1.66 (\( p = 0.001 \))
   - Control: 1.92

*Note: J. et al. Allergy 2016*
GA² LEN in action

Annual Conference

Berlin 2006
29 March - 1 April

SPECIAL EVENT - Friday 31 March, 11h00-13h30
Palais am Funkturm

More Info: www.ga2len.net

Allergy throughout life

Chairs: Paul van Cauwenberge - Jean Bousquet - Ana Nieto

Welcome
Paul van Cauwenberge

Pre-Natal influences
John Warner

Childhood environments
Erika von Mutius

Triggers for symptoms
Marianna van Hage

The future of the allergy epidemic and its consequences
Peter Burri

Improving care for allergic patients
Ingmar Koll

What patients want from a network of excellence
Moniavela Solapartas

EU future programmes in Allergy and Asthma
J.M. Silva Rodriguez, Director-General of the Research DG (tbc)

GA² LEN SYMPO - EAACI VIENNA
Tuesday 13 June 2006, 15h30-17h15

Does rhinitis lead to asthma?

Chairs: Rudolf Valenta, Vienna
Paul van Cauwenberge, Ghent

The epidemiology of airway allergic diseases: from rhinitis to asthma
Deborah Jarvis - WP Gender

Do viruses play a role in rhinitis and asthma exacerbations?
Nikos Papadopoulos - WP Viral Exacerbations

Inflammation in the nose – inflammation in the lung: where's the link?
Kees van Oosten - WP IgE sensitization and allergic diseases

Remodelling: similarities and differences between occurrence in the nose and in the lungs
Sven-Erik Dahlén - WP Airway remodelling

Revising guidelines for “Early Diagnosis, Early Treatment”, ARIA Update
Jean Bouquet - WP Dissemination to scientists and healthcare professionals

More Info: www.ga2len.net
The superantigen meeting in Ghent, initiated and chaired by Claus Bachert, brought together a group of outstanding researchers specialising in microbiology, immunology, paediatrics, dermatology, pneumology, epidemiology, and rheumatology. The purpose was to discuss the recent dramatic evidence that superantigens may have significant impact on inflammatory reactions in different organs, such as the skin and the airways. The time has come to discuss superantigens and their clinical implications in an open, highly interactive way between basic scientists and clinicians.

Superantigens (SAGs) are a class of immunostimulatory and disease-causing proteins with the ability to activate large proportions of the T-cell population. Unlike conventional antigens, SAGs bind to certain regions of major histocompatibility complex (MHC) class II molecules of antigen-presenting cells (APCs) outside the classical antigen-binding groove, and concomitantly bind in their native form to T-cells at specific motifs of the variable region of the beta chain (Vb) of the T-cell receptor (TCR). This cross-linking triggers the nonspecific activation and proliferation of T-cells and induces production of high levels of a variety of cytokines. The T-cell response to SAGs is polyclonal, Vb specific, involves both CD4+ and CD8+ cells and is MHC II dependent, but not MHC II restricted.

Bacterial superantigens, and here we focus on the classical and newly described egc-locus enterotoxins, have common characteristics: They are among the most potent pyrogens known, and they are capable of inducing a highly lethal toxic shock syndrome. The chronic disease is characterised by T-cell activation, with expansion of Vb-specific T-cells. Donald Leung showed very interesting and convincing data about superantigens enhancing allergic immune responses and skin inflammation because of their effect on T-cells. Superantigens contribute to persistent skin inflammation by subverting T regulatory cells and inducing corticosteroid resistance. Finally, superantigens (from gram+ bacteria) might counteract endotoxins (from gram- germs) and revert the hygiene hypothesis, contributing to the enhancement of atopy.

In early childhood, there is evidence for involvement of SAGs in eczema and wheezing in children. Adnan Custovic gave a lively presentation supporting the thesis that S. aureus enterotoxins (SAEs) may play a role in the pathophysiology of lower airway disease and eczema in early childhood. Children with eczema and wheeze have higher IgE levels to SAE than healthy children. The proportion of patients with IgE antibodies to SAE also increases with increasing severity of both wheeze and eczema. A likely disease-modifying role in children is thus allocated to SAEs.

SAEs are involved again when adult asthma patients are considered. Peter Howarth spoke about the potential effects of SAEs in asthma. As was shown before by Bachert’s group in nasal polyph disease, SAEs exert a conventional antigen effect producing anti-enterotoxin IgE antibodies in severe late-onset asthma also. Although non-allergic, SAE-IgE antibodies are significantly increased in this group of patients, associated with a specific V6 TCR expansion in both CD4+ and CD8+ T-cells. A similar finding has been reported in poorly controlled asthmatics, and mouse models actually do support the concept that intranasal Staph. aureus superantigens may result in upper and lower airway inflammation and hyperreactivity.

Aspirin hypersensitivity is often associated with asthma and nasal polyposis, and characterised by a massive eosinophilic inflammation of the airway mucosa. No direct impact of S. aureus can be established yet in the relationship between aspirin hypersensitivity and an immune response to SAEs, although there is a close link between both factors, namely the eosinophilic inflammation.

Finally, SAGs also seem to be involved in the induction of insensitivity to glucocorticoids. Staph. aureus enterotoxin B (SEB) induces steroid resistance in PBMCs by significantly increasing the percentage of corticosteroid receptor GRβ+ cells compared with PHA and unstimulated cells. A combination of antibiotics with corticosteroids seems to overcome insensitivity to glucocorticoids, and appropriate studies are ongoing.

Staph. aureus enterotoxins and other superantigens are thus perfect candidates to severely impact airway and skin disease from early childhood to adulthood, and clearly merit further attention. Nearly one third of the global population are lifelong carriers of these germs, and nearly all have the potential to produce these toxins! In the near future, superantigens might give us the answers to many questions, especially in severe airway and skin disease.
DENDRITIC CELLS

Favourite new characters in the allergic saga, or who makes the decision for initial Th2 polarisation

Maria Staevska

Atopic diseases are characterised by a predominance of Th2-biased immune responses to environmental allergens. Allergen-specific Th2 cells are the key orchestrators of allergic reactions, initiating and propagating inflammation through the release of a number of Th2 cytokines such as IL-4, which regulates isotype switching to allergen-specific IgE, and IL-5, which recruits and activates eosinophils. Whereas the biology of Th2 cells in allergy is well understood, little is known about the mechanisms that control the Th2 cell polarisation in response to exogenous allergens. In recent investigation into this issue, scientists focussed on dendritic cells (DCs). A growing body of evidence suggests that allergen-dependent mechanisms are determined at the DC level as a result of the Th2-type attributes of a specific protein. In addition, DCs play an important role not only in priming naïve T-cells but also in innate immune response, especially in the defence against virus infections.

The World Allergy Congress in Munich rewarded the recent interest in DCs by assigning a special workshop to the topic. One of the top young researchers in the field, Professor Natalia Novak, started the session by introducing the role of plasmacytoid dendritic cells in atopic and contact dermatitis.

Novak noted that two different types of dendritic cells can be detected in our immune system: Myeloid DCs (mDCs), characterised by the expression of CD11c; and plasmacytoid DCs (pDCs), which do not express CD11c but which express the blood dendritic cell antigen (BDCA2) and the α-chain of the interleukin (IL)-3 receptor (CD123) (Fig. 1).

However, it has been shown recently that pDCs are absent from normal skin but can be recruited into the dermis in cutaneous patch-test reactions from patients with contact dermatitis (1). Skin-homing molecules such as L-Selectin (CD62L), cutaneous lymphocyte antigen (CLA) and CXCR3 on pDCs seem to be critical in this process. Interestingly, pDCs can be found a few hours after hapten challenge in close proximity to CD56+ natural killer T-cells in the skin (1).

In contrast to other inflammatory skin diseases, such as allergic contact dermatitis and psoriasis vulgaris, only very low numbers of pDCs can be detected within the epidermal skin lesions of patients with atopic dermatitis (AD) (2). PDCs in the peripheral blood of patients with AD have been shown to bear high amounts of the high affinity receptor for IgE (FceRI) on their cell surface, which is occupied with IgE molecules (3). The surface expression of FceRI on pDCs directly correlates with IgE serum levels in AD patients. PDCs are able to take up allergens via IgE mounted to FceRI in vitro and induce immune responses of the Th2 type in naïve T-cells (3). Aggregation of FceRI on the surface of pDCs induces the release of interleukin-10 and IL-10 mediated apoptosis of the cells (3). Most importantly, pre-activation of pDCs via FceRI-mediated allergen challenges profoundly impairs the capacity of pDCs to produce interferon-alpha and interferon-beta, which are vital in any defence against virus infections. PDCs in the peripheral blood of patients with AD express lower levels of skin-homing molecules such as CD62L and cutaneous lymphocyte antigen (CLA), which are relevant for the recruitment of this cell type into the skin (3). Novak concluded by saying that in conjunction, the modified immune function of pDCs in patients with AD after FceRI-mediated allergen stimulation might contribute to the deficiency of pDCs in AD patients to produce Type I interferons in vivo, and thereby contribute to the high susceptibility of AD patients to contract viral skin infections such as Herpes simplex induced Eczema herpeticum (Fig. 2).
Pollen is one of the most common inducers of allergic symptoms. On contact with the mucosal surfaces in the upper respiratory tract, pollen grains rapidly release proteins/allergens into the aqueous phase. On the basis of a genetic susceptibility, atopic individuals develop allergen-specific Th2-biased immune responses that ultimately lead to clinical manifestations of IgE-mediated hypersensitivity. Allergists and immunologists immediately and often exclusively connect pollen with the release of allergens and the development of allergic diseases, said Professor Claudia Traud-Hoffmann, in introducing her presentation. This is most unfortunate, as first of all, pollen grains primarily bear a natural mission (4). Even in the context of allergy, however, little attention has been paid to the non-protein compounds of pollen. However, individuals are rarely exposed to pure allergens, but rather to particles releasing the allergen, such as pollen grains and pollen-derived granules, she said.

DCs are pivotal in the initiation of adaptive immune responses. It is generally accepted that DCs instruct the immune system to initiate an Ag-specific response by providing naïve Th cells with signal 1 (TCR triggering) and signal 2 (co-stimulation). In addition, it has recently been suggested that immature DCs in peripheral non-lymphoid tissue can adopt different Th1- or Th2-promoting effector functions, depending on the tissue- and/or pathogen-type context of their activation. This DC-dependent component of the initial polarisation of naïve T-cells (signal 3) was suggested to depend on pathogen derived or induced endogenous factors present in the local micro-environment at the time of antigen encounter. DCs produce IL-12 (one of the crucial Th1-polarising cytokines) upon activation by pathogen-associated molecular patterns such as LPS or by T-cell derived signals such as CD40 ligation.

However, the simultaneous presence of endogenous signals such as IL-10, TGFβ, corticosteroids, vitamin D₃, and PGE2 can convert DCs from Th1 to Th2 skewing antigen-presenting cells. Recent studies also demonstrate that exogenous factors such as lipids produced by parasites can modulate DC function for the purposes of evading host immunity. Notably, lipids are major components of pollen exine and exudate. Interestingly, part of these substances exhibits strong cross-reactivity with leukotriene B4 (LTB4) and prostaglandin E2 (PGE2). These pollen-associated lipid mediators (PALMs) were shown to stimulate and attract cells of the innate immune system, such as neutrophils and eosinophils granulocytes. The speaker demonstrated the results from her recent study: the effect of PALMs on the activation and functional maturation of human DCs. The activation of DCs with LPS depleted by Bet.-APE resulted in moderate DC activation as documented by selective up-regulation of HLA-DR surface expression. When DCs were stimulated simultaneously with LPS plus Bet.-APE, the presence of Bet.-APE resulted in an additional up-regulation of CD80, CD86, and HLA-DR surface expression. At a functional level, Bet.-APE–induced DC maturation resulted in enhanced allosstimulatory activity as demonstrated by enhanced proliferative responses of naïve allogeneic T-cells. In addition, Bet.-APE treatment induced a dose-dependent inhibition of the LPS or CD40L induced IL-12 p70 production of DCs, whereas IL-6, IL-10, and TNFα production was not impaired. Thus, water-soluble factors released from pollen grains are capable of selectively modulating various DC functions, including the inhibition of activation-induced IL-12 release from human DCs.

In her recent studies, the professor demonstrated for the first time that non-enzymatically formed phytoprostanes such as PPE1, PPF1, and PPB1 are present in aqueous pollen extracts in nanomolar concentrations. Interestingly, only PPE1, and not PPF1 or PPB1, inhibited the LPS or CD40L induced IL-12 production. The modulatory effect of PPE1 on DC IL-12 production and the ensuing T-cell response was dependent on the presence of a maturation signal such as LPS or CD40 ligation. Traud-Hoffmann concluded that these data provide compelling evidence for the role of xenogenous pollen-derived phytoprostanes in the decision-making process of DCs. She suggested that DCs that have been conditioned by PALMs, such as E1-phytoprostanes, provide one of the initial signals driving the development and perpetuation of Th2-dominated immune response in pollen allergy (Fig. 3). In fact, this represents the first study demonstrating that plant isoprostanes can affect the outcome of mammalian immune responses (5). We look forward to hearing the results of her ongoing group studies on the effects of in vivo exposure to PALMs.

References
5. Traud-Hoffmann C; Mariani V; Hochrehn H; Karg K; Wagner H; Ring J; Mueller MJ; Jakob T; Behrendt H. Pollen-associated phytoprostanes inhibit dendritic cell interleukin-12 production and augment T helper type 2 cell polarisation. J Exp. Med. 2005; 201:627-635.
Cells in Allergy and How They React

Jeroen Clement

The largest auditorium was filled to capacity for the morning session. Antony Frew, Alberto Mantovani, Peter Kramer, and Johan Deisenhofer gave details about the fundamentals in the topic, as well as the recent advances in allergy. Professor Frew captured everyone's attention with his introduction to the pathophysiology of allergy, noting that the key features of allergy are IgE antibodies and showing a stereotyped pattern of inflammation. He outlined how allergy basically remodels the airways, starting with an interaction between three key cells: the endothelium, the eosinophil, and the mast-cell and their mediators of inflammation. Frew showed how antigens trigger T-cells, B-cells, and mast-cells in a cascade of inflammation, resulting in recruitment, migration, activation, and epithelial damage. This overview gave instances of current medication interactions and possible future indications. Future pharmacotherapy may be the interaction in the effects of IL-5, which significantly raises the spurt eosinophil and makes the airway more responsive. Anti IL-5 lowers the BAL eosinophil count, but does not reduce that same airway responsiveness. The measurement of cytokine mRNA in BAL cells shows that eotaxin and chemokines are produced in the presence of IL-5. There must be an immune deviation, causing allergy and asthma. The subtle balance between Th1 and Th2 response is regulated by IFN-γ and IL-4, IL-5, and IL-13.

The Th1/Th2 balance causes autoimmunity, allergy, or symptoms to stay subclinical. While not much difference can be observed in genetic predisposition, a western lifestyle tips the scale to allergy and autoimmunity when the symptoms are required to stay subclinical. In conclusion, Professor Frew stated some important "take home" messages:

- Asthma is more than just inflammation
- Epithelium and smooth muscle cells are active contributors to inflammation and the remodelling process

- That which initiates airway inflammation may not be a valid target to switch it off
- Some counter-regulatory mechanisms may lock the asthmatic process

Massimo Locati talked about chemokines and allergy. He explained that chemokines are a large family of molecules defined by structure and function, which can be inflammatory, homeostatic, or both. There is a great overlap in their biological activity and they play a major role in various different parts of the body. The chemokines system is regulated by a balance in agonist production and processing on the one hand, and receptor expression and signalling on the other. The chemokines production is regulated in different ways, with again an overlap. Constitutive chemokines are present as a result of normal leukocyte traffic, while the production of inducible chemokines is triggered by inflammation and immunity. The processing of chemokines is an integrated system of homing and selection in the lymphatic system, inducible expression in T-lymphocytes, and post-transduction modification. Receptor expression is regulated by mediators and cellular interaction between T-helper cells, macrophages, eosinophils, and endothelial cells. Signalling of the receptor can be altered, depending on whether an agonist or an antagonist binds the receptor. Receptor coupling can produce conversion in functional decoy receptors.

In conclusion, chemokines play a role in immune responses by coordinating recruitment of functionally related leukocytes. They organise a highly complex system that is tightly regulated at several levels, such as chemokines induction at transcriptional level and processing at post-transcriptional level. There is also regulation at receptor level by expression and signalling.

Peter Krammer talked about T-cell apoptosis and auto-immunity. Lymphocyte development represents a strongly controlled immune process that normally prevents autoimmunity. It induces cellular selection through apoptosis to remove potentially autoreactive cells. If apoptosis is erroneous, auto-immune disease can occur. Mutations in cell death receptor Fas (CD95) and its ligand, Fasl(CD95L) have been identified. These errors lead to systemic production in excess, thus to apoptosis. Cell death can be induced via two different CD95 pathways. The principle stays the same; death receptors are bound, first-level Egl-1, CED-9, CED-4, and CED-3. The second level caspases induce apoptosis. Another pathway is the TCR mediated pathway. A patient becomes allergic or becomes auto-immune depending on the apoptosis rate of certain T-cells or the lack of the same. In vitro studies showed certain T-cells to be immune from apoptosis. Most of these mechanisms are still very hypothetical, but there may be a future for therapy in this area. This presentation was elaborate and occasionally demanding.

Johann Deisenhofer gave the final lecture, on the subtleties of signalling by peptide-MHC complexes. Major histocompatibility complex (MHC) is a conglomerate of genes that plays a role in recognition of self and nonself. These genes are highly homologous. A variety of biological or chemical modulators can alter MHC gene expression. The transcription of class I genes can be activated through several pathways, it has been seen that various biological molecules (IFN, GM-CSF, IL-2) and other chemicals up-regulate the MHC expression. High affinity and broad specificity is necessary to present a broad spectrum of peptide antigens to T-cell recognition. This is only possible through a unique structural three-dimensional atomic structure of the molecules, like a firm binding to the peptide main chain in addition to reiterative bonding with the peptide side chains. This results in a peptide-MHC complex with an antigenically unique surface to T-cell receptors.
INTERVIEW WITH THE EAACI PRESIDENT

Professor Anthony Frew

by Maria Staeveka

Many congratulations upon your election as the new EAACI President! Are you happy with your new role?

I’m delighted to be given the chance to serve the academy as its President. Of course it is very much a team effort, and I’m really pleased to have such a good team of officers and ExCom members to work with.

You were the EAACI Secretary General for seven years. Are you going to use your past experience in your new role?

Over the past seven years, I have learned a lot about EAACI, about how it works, and about how people manage to achieve a lot from the voluntary work that people do for it. There are also a few 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 general plan is to make our internal structures work efficiently, so that we can concentrate our time and energy on outside matters.

What are your impressions from the World Allergy Congress in Munich?

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 WAO for their constructive collaboration and to the local organisers, especially Johannes Ring, for making this a unique and very successful event.

For the last few years, EAACI has run a budget deficit. The ExCom planned to set a balanced budget for 2005. Now, after the successful Congress in Munich, do you think that your plans will become reality?

At the end of the day, the money is there for a purpose, and that is to support and undertake activity in support of our Academy’s goals. The finances for the past two years have been difficult to follow, as the financial model for the Munich Congress was completely different. This meant that we have had to budget for a large surplus in 2004 and a deficit in 2005. But the underlying budget has been stable for the past three years. It is true that we ran a budget deficit in previous years, but this was intentional, and allowed us to try out some new activities like different styles of summer schools, and to invest in the Brussels Office. This investment paid off handsomely with the award of the GA’LEN network, but we now expect to run a stable economy for a few years, to keep the finances under control.

Can EAACI afford to implement the planned policy for the members from lower income European countries: subsidized membership and congress registration fees?

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 of 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.

As a lecturer at the summer courses you meet a lot of young people. What are their impressions from these events? What are their expectations for the future?

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

What is the future of the EAACI Newsletter?

I certainly expect that the newsletter will continue. Feedback from members 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.

Considering your new responsibility, will you find enough time for yourself and your family? What do you usually do in your spare time?

In some ways I expect to have more time now. The position of president is very visible, and I will obviously have to represent EAACI at various meetings, but the job of secretary-general involves a lot of work behind the scenes, and I wish my successor Jan Lötvall every success in his important task. Outside work, I continue to sail my dinghy when I have the chance, and as a family we tend to walk either in the New Forest, or on the South Downs (the range of chalk hills between Southampton and Eastbourne).
EAACI 2006
Welcome to the XXV Congress of the European Academy of Allergology and Clinical Immunology
10-14 June 2006, Vienna, Austria

Basic Science in Allergology and Clinical Immunology, a Prerequisite for Improving Patient Care
and
100 Years of ALLERGY as defined by Clemens von Pirquet