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# RINOLOGIA

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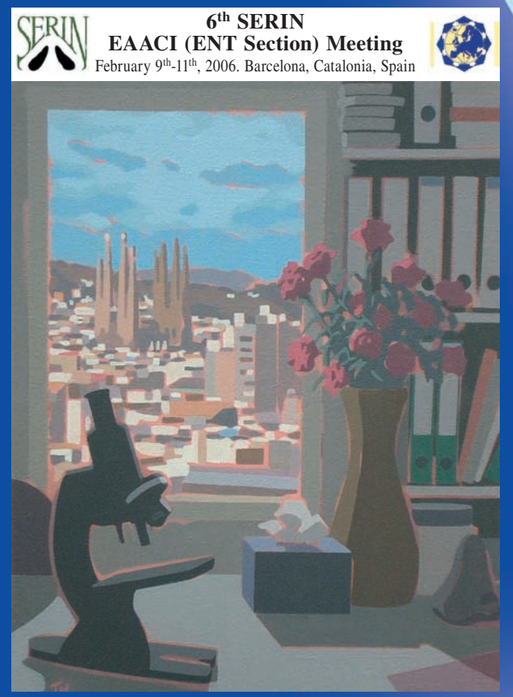


PUBLICACIONES PERMANYER

**DENOMINACIÓN DEL MEDICAMENTO:** Rupafin 10 mg Comprimidos. **COMPOSICIÓN CUALITATIVA Y CUANTITATIVA:** Cada comprimido contiene: 10 mg de rupatadina (como fumarato). **FORMA FARMACÉUTICA:** Comprimido. Comprimidos redondos de color salmón claro. **INDICACIONES TERAPÉUTICAS:** Tratamiento de los síntomas asociados a la rinitis alérgica estacional y perenne. **POSOLOGÍA Y FORMA DE ADMINISTRACIÓN:** Adultos y adolescentes (mayores de 12 años). La dosis recomendada es de 10 mg (un comprimido) una vez al día, con o sin alimento. Ancianos Rupafin debe utilizarse con precaución en pacientes ancianos. Niños no se ha establecido la seguridad ni la eficacia de rupatadina en pacientes menores de 12 años. Pacientes con insuficiencia renal o hepática dado que no hay experiencia clínica en pacientes con insuficiencia renal o hepática, actualmente no se recomienda el uso de Rupafin 10 mg Comprimidos en estos pacientes. **CONTRAINDICACIONES:** Hipersensibilidad a rupatadina o a cualquiera de los excipientes. **ADVERTENCIAS Y PRECAUCIONES ESPECIALES DE EMPLEO:** No se recomienda el uso de Rupafin 10 mg Comprimidos en combinación con ketoconazol, eritromicina o cualquier otro inhibidor potencial del isoenzima CYP3A4 del citocromo P450, ya que estos principios activos aumentan las concentraciones plasmáticas de rupatadina. Rupafin 10 mg Comprimidos debe utilizarse con precaución en pacientes ancianos (más de 65 años). Aunque en los ensayos clínicos realizados no se observaron diferencias en la eficacia o seguridad, debido al bajo numero de pacientes incluidos, no puede excluirse una mayor sensibilidad en algunos individuos. **INTERACCIÓN CON OTROS MEDICAMENTOS Y OTRAS FORMAS DE INTERACCIÓN:** La administración concomitante de rupatadina y ketoconazol o eritromicina aumenta 10 veces y 2-3 veces respectivamente la exposición sistémica a rupatadina. Por tanto no se recomienda el uso de rupatadina con estos fármacos y, en general, otros inhibidores del isoenzima CYP3A4. Estas modificaciones no se acompañaron de efectos en el intervalo QT ni se asociaron con un aumento de los efectos adversos en comparación con los fármacos administrados por separado. No se han realizado estudios "in vivo" con otros substratos distintos a ketoconazol o eritromicina. Interacción con alcohol: La administración concomitante de alcohol y 10 mg de rupatadina produjo efectos marginales en algunos ensayos sobre la función psicomotora que no fueron significativamente distintos a los efectos producidos por una ingesta única de alcohol. Con una dosis de 20 mg de rupatadina se observó un incremento de los efectos producidos por el alcohol. Interacciones con otros depresores del Sistema Nervioso Central: Como ocurre con otros antihistamínicos no puede excluirse la interacción con fármacos depresores del Sistema Nervioso Central. **EMBARAZO Y LACTANCIA:** No hay datos clínicos sobre la exposición a rupatadina durante el embarazo. Los estudios llevados a cabo en animales no mostraron efectos perjudiciales directos o indirectos respecto al embarazo, el desarrollo embrionario o fetal, el parto o el desarrollo. Las mujeres embarazadas no deberían utilizar rupatadina a menos que los potenciales efectos beneficiosos para la madre justifiquen el riesgo potencial para el feto. No hay estudios clínicos controlados que den información sobre si rupatadina se excreta en la leche humana, por lo que no debe utilizarse durante el periodo de lactancia a menos que los potenciales efectos beneficiosos para la madre justifiquen el riesgo potencial para el lactante. **EFECTOS SOBRE LA CAPACIDAD PARA CONDUCIR Y UTILIZAR MÁQUINAS:** La administración de 10 mg al día de rupatadina no ha mostrado efectos significativos sobre la función del sistema nervioso central en estudios específicos sobre la función psicomotora, no obstante, el paciente deberá tener precaución al conducir o manejar maquinaria, hasta que no se establezca cómo le puede afectar la toma de rupatadina de forma individual. **REACCIONES ADVERSAS:** En los estudios clínicos llevados a cabo las reacciones adversas atribuibles a Rupafin 10 mg Comprimidos se comunicaron en un 8% de pacientes más que en los tratados con placebo. Los acontecimientos adversos y sus frecuencias, una vez restadas las incidencias en el grupo placebo, fueron, en orden decreciente: Frecuentes (> 1/100, 1/10): somnolencia, astenia, fatiga. Infrecuentes (> 1/1000, 1/100): sequedad de boca, faringitis, dispepsia, aumento de apetito, rinitis. **SOBREDOSIS:** No se han comunicado casos de sobredosis. Una ingestión accidental de dosis muy elevadas debería ser tratada sintomáticamente junto a las medidas de soporte necesarias. **INCOMPATIBILIDADES:** No procede. **PERÍODO DE VALIDEZ:** 3 años. **PRECAUCIONES ESPECIALES DE CONSERVACIÓN:** Mantener el envase en el embalaje exterior. **NATURALEZA Y CONTENIDO DEL RECIPIENTE:** Blíster de PVC/PVDC/aluminio. Envases de 20 comprimidos. **INSTRUCCIONES DE USO Y MANIPULACIÓN:** Ninguna especial. **PRESENTACIÓN Y PVP IVA 4:** Rupafin 10 mg 20 comprimidos: 11,63 € **ESTIMACION DEL COSTE TRATAMIENTO: 0,58 €/día CONDICIONES DE PRESCRIPCIÓN Y DISPENSACIÓN:** Con receta médica. Financiable por la Seguridad Social. GRUPO URIACH. J. Uriach & Cía., S.A. Av. Camí Reial 51-57 08184 Palau-solità i Plegamans (Barcelona-España) **FECHA DE REVISION DE TEXTO:** Octubre 2002.

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Mallorca, 310 - 08037 Barcelona
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# 6th SERIN
# EAACI (ENT Section) Meeting
# February 9th – 11th, 2006
# Barcelona
# Catalonia, Spain

**President: Joaquim Mullol (Barcelona, Spain)**

## Commitees

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| Kees Van Drunen | (The Netherlands ) |

# Welcome Letter

On behalf of the Local Organizing Committe, the Scientific Advisory Committee, the ENT Section Board (EAACI), and GA 2 LEN, I have great pleasure to welcome you to the 6th Symposium on Experimental Rhinology and Immunology of the Nose (SERIN) that takes place in Barcelona (Catalonia, Spain), from 9th to 11th of February, 2006. For the first time, the SERIN Meeting will be hold together with the Meeting of the ENT Section (EAACI).

The objective of the meeting is gather together people working in the rhinology field, from young researchers to experienced leaders, and to let them discuss the new findings and future scopes of the field in a free and open atmosphere.

Experts in rhinology from all over Europe, and some from overseas, will present subjects from basic research to diagnosis and treatment. Each session will focus on dynamic exchanges between the experts and the participants, this being a strong characteristic that marks all sessions. In the poster sessions, all the poster authors will have the chance to briefly present their work.

The Meeting takes place in the Hotel Feria, located at the Monjuic mountain area, very well comunicated with other parts of the city by public transportation (subway, bus, taxi). Barcelona will also offer you, to both delegates and accompanying persons, many interesting places (Sagrada Família, Parc Güell, Casa Batlló, La Pedrera, the Gothic Quarter, Palau de la Música) and museums (Tàpies, Picasso, Thyssen-Bornemisz, MNAC, Miró, FC Barcelona) to visit, as well as many restaurants to enjoy the Catalan, Spanish, and International cuisine.

Welcome and enjoy the Meeting and Barcelona!

**Joaquim Mullol**
President
6th SERIN - ENT Section (EAACI) Meeting

# Scientific programme

## Thursday, February 9th, 2006

**8:00–9:00** **Registration and Opening**

**9.00–10.30** **Oral Session 1 – *Verdi Room***
Upper Airway Inflammation
***Chairpersons:*** *Ignacio Ansotegui (E) / James N Baraniuk (USA)*

09:00–09:30 **INTRODUCTORY LECTURE 1: Neurogenic inflammation**
James N Baraniuk (USA)

09:30–09:45 **The prostanoids and tryptase in different types of rhinitis**
Swierczynska-Krepa M, Nizankowska-Mogilnicka E, Grzywacz M, Szczeklik A
*Jagiellonian University, Cracow, Poland*

09:45–10:00 **Evaluating the relation of chronic sinusitis and nitric oxide metabolites levels in nasal lavage**
Naraghi M, Farajzadeh Deroee A, Shadman M, Ebrahimkhani MR, Dehpour AR
*Amir Alam Hospital, Departments of Otorhinolaryngology and Pharmacology, School of Medicine, Tehran University of Medical Sciences (TUMS). Tehran, Iran*

10:00–10:15 **Nasally administered capsaicin does not influence the expression of vanilloid receptor 1 in nasal tissue of idiopathic rhinitis patients**
In 't Veen JPM, De Groot EJJ, Van Drunen CM, Fokkens WJ
*Department of Otorhinolaryngology, Academic Medical Center, Amsterdam, The Netherlands*

10:15–10:30 **Evaluation of nasal obstruction and inflamation in patients affected of nasal polyposis.**
Bartra J[1], Valero A[1], I Alobid[2], Serrano C[1], Mullol J[2], Picado C[1]
*[1]Unitat d'Al·lèrgia, Servei de Pneumologia i Al·lèrgia Respiratòria, ICT; and [2]Unitat de Rinologia, Servei de ORL, ICEMEQ, Hospital Clínic. Barcelonia, Catalonia, Spain*

**10:30–11:00** **COFFEE BREAK**

**11.00–12.30** **Oral Session 2 – *Verdi Room***
Rhinitis
***Chairpersons:*** *Gianni Passalaqua (I) / Stephen R Durham (UK)*

11:00–11:30 **INTRODUCTORY LECTURE 2: Allergen Immunotherapy**
Stephen R. Durham (UK)

11:30–11:45 **Expression profiling of the response of airway epithelial cells to house dust mite extract**
Vroling AB, van Drunen CM, Fokkens WJ
*AMC, Amsterdam, The Netherlands*

11:45–12:00 **Leukocyte-lymphocyte phenotyping of persistent allergic and idiopathic non-allergic rhinitis by nasal flow cytometry**
Rondón C, Romero JJ, López S, Rodríguez R, Fuentes S, Antúnez C, Blanca M
*Allergy Service and Research Laboratory, Carlos Haya Hospital. Málaga, Spain*

12:00–12:15 **Ex-vivo nasal challenge model to investigate mast cell activation**
Patou J, Holtappels G, Gevaert P, Van Cauwenberge P, Bachert C
*Upper Airway Research Laboratory, Department of Otorhinolaryngology, Ghent University, Ghent, Belgium*

12:15–12:30 **Clinical response to grass pollen allergen challenge is less in subjects with concurrent house dust mite allergy**
Reinartz SM, Jansen A, van Drunen CM, Fokkens WJ
*Department of Otorhinolaryngology, Academic Medical Center, Amsterdam, The Netherlands*

**12:30–13:45** **LUNCH**

**13:45–14:30** **Special Lecture 1 – *Verdi Room***
***Chairperson:*** *Joaquim Mullol (E)*
The Sense of Smell
*Nancy Rawson (USA)*

**14:30–16:00** **Oral Session 3 – *Verdi Room***
Treatment of Nasal Diseases
***Chairpersons:*** *Kees van Drunen (NL) / Glenis Scadding (UK)*

14:30–15:00 **INTRODUCTORY LECTURE 3: New targets for the treatment of nasal diseases?**
Glenis Scadding (UK)

15:00–15:15 **Effectivennes of endosinusal treatment and prognostic factors of sinus lavage in patients with chronic maxillary sinusitis**
Drvis P, Baudoin T, Grgic M, Zurak K, Ajduk J, Kalogjera L
*Department of ENT – Head and Neck Surgery, University Hospital Sestre Milosrdnice Vinogradska. Zagreb, Croatia*

15:15–15:30 **Presence of local specific IgE antibodies in nasal lavage of patients with persistent idiopathic rhinitis**
Rondón C, Romero JJ, Lopez S, Doña I, Robles S, Rodriguez JL, Blanca M
*Allergy Service and Research Laboratory, Carlos Haya Hospital. Málaga, Spain*

15:30–15:45 **Amphotericin B nasal lavages: no solution for chronic rhinosinusitis**

Ebbens FA[1], Scadding G[2], Bachert C[3], Mullol J[4], Van Zele T[3], Badia L[2], Hellings PW[5], Lund VJ[2], Fokkens WJ[1]
*[1]Dept. of Otorhinolaryngology, Academic Medical Center, Amsterdam, the Netherlands; [2]Dept. of Rhinology, Royal National Hospital, London, United Kingdom; [3]Dept. of Otorhinolaryngology, University Hospital Ghent, Ghent, Belgium; [4]Rhinology Unit, ENT Dept., Hospital Clinic, Barcelona, Spain; [5]Dept. of Otorhinolaryngology, University Hospital, St. Rafael, Leuven, Belgium*

15:45–16:00 **Rupatadine inhibits cytokine production and NF-κB activity by a histamine H1 receptor-dependent mechanism**
Barrón S, Roman J, Michelena P, Ramis I, Merlos M
*J. Uriach y Compañia S.A. Barcelona, Spain*

**16:00–17:00** **SYMPOSIUM 1 – *Verdi Room***
Global Alliance against Chronic Respiratory Disease (GARD)
***Chairperson:*** *Jean Bousquet (F)*

16:00–16:20 **Why GARD?**
Ronald Dahl (DK)

16:20–16:40 **World Health Organization and GARD**
Nikolai Khaltaev (RU)

16:40–17:00 **GARD mission**
Jean Bousquet (F)

**16:00–17:00** **SYMPOSIUM 2 – *Rossini Room***
European Consensus on Rhinosinusitis and Nasal Polyposis (EP3OS)
***Chairpersons:*** *Wytske Fokkens (NL) / Valerie Lund (UK)*

16:00–16:20 **Definitions and classification**
Valerie Lund (UK)

16:20–16:40 **Acute RS. Diagnosis and EBM treatment**
Pontus Stierna (SE)

16:40–17:00 **Chronic RS and nasal polyps. Diagnosis and EBM treatment**
Wytske Fokkens (NL)

**17:00** **WELCOME RECEPTION**

## Friday, February 10th, 2006

**9:00–10:30** **Oral Session 4 – *Verdi Room***
Glucocorticoids
***Chairpersons:*** *Jean-Baptiste Watelet (BE) / Laura Pujols (E)*

09:00–09:30 **INTRODUCTORY LECTURE 4: Regulation of glucocorticoid receptors**
Laura Pujols (E)

09:30–09:45 **Effects of glucocorticoids on mucin expression in human nasal polyps**
Martínez-Antón A, de Bolós C, Garrido M, Roca-Ferrer J, Oliveras G, Barranco C, Alobid I, Xaubet A, Picado C, Mullol J
*Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Serveis d'Otorinolaringologia and Pneumologia. Hospital Clínic. Barcelona, Catalonia, Spain*

09:45–10:00 **Topical capsaicin or furosemide vs. oral steroid in the management of nasal polyposis**
Kalogjera L, Kroflic B, Baudoin T, Coer A, Ferencic Z
*ORL Dept, University Hospital «Sestre milosrdnice» and Pathology Dept. «Pliva Research Institute, Zagreb, Croatia. ORL Dept., General Hospital, Celje, Slovenia, Institute of Histology, Med. Univ. Ljubljana, Slovenia*

10:00–10:15 **Techniques of internasal drug use**
Rapiejko P, Wojdas A, Ratajczak J, Szczygielski K, Jurkiewicz D
*Military Institute of the Health Services. Warsaw, Poland*

10:15–10:30 **In vivo regulation of glucocorticoid receptor isoforms in human nasal polyps by systemic and intranasal glucocorticoids**
Pujols L, Mullol J, Benítez P, Alobid I, Fuentes M, Martínez A, Roca-Ferrer J, Ramírez J, Picado C
*Serveis d'Otorinolaringologia and Pneumologia, IDIBAPS. Hospital Clínic. Barcelona, Catalonia, Spain*

**10:30–11:00** **COFFEE BREAK AND POSTER DISCUSSION**

**11:00–12:30** **Oral Session 5 – *Verdi Room***
United Airways: nose and bronchi
***Chairpersons:*** *Wytske Fokkens (NL) / Manel Jordana (CA)*

11:00–11:30 **INTRODUCTORY LECTURE 5: Upper and lower airway interactions**
Manel Jordana (CA)

11:30–11:45 **Pulmonary upregulation of IL-4 and IL-13 mRNA following selective nasal allergen provocation in a mouse model of airway allergy**
Hens G, Meyts I, Verbinnen B, Cadot P, Dilissen E, Bullens D, Jorissen M, Ceuppens J, Hellings P
*ENT Department, University Hospitals Leuven; and Lab of Experimental Immunology, Catholic University. Leuven, Belgium*

11:45–12:00 **Nasal pathology in bronchiectasis**
Guilemany JM, Centellas S, Alobid I, García-Piñero A, Angrill J, Bernal-Sprekelsen M, Picado C, Mullol J
*Rhinology Unit, Department of ENT and Pneumology, Hospital Clínic, University of Barcelona, IDIBAPS, Barcelona, Spain*

12:00–12:15 **Influence of air pollution on symptoms of seasonal allergic rhinitis and bronchial asthma**
Jadczak M, Rapiejko P, Lipiec A, Dzaman K, Jurkiewicz D
*Military Institute of the Health Services. Warsaw, Poland*

12:15–12:30 ***Staphylococcus aureus* enterotoxin b aggravates allergic rhinitis and asthma in a mouse model**
Hellings PW[1,2], Hens G[1,2], Meyts I[1], Bullens D[1], Van Oirbeek J[1], Gevaert P[4], Jorissen M[2], Ceuppens JL[1], Bachert C[4]
*[1]Laboratory of Experimental Immunology; [2]Department of Otorhinolaryngology-Head and Neck Surgery; [3]Department of Internal Medicine, University Hospitals Leuven; [4]Department of Otorhinolaryngology, University Hospital Ghent, Belgium*

**12:30–13:45 LUNCH**

**13:45–14:30 Special Lecture: 2 – *Verdi Room***
***Chairperson:*** *César Picado (E)*
Leukotrienes in Upper Airways
*Leif Bjermer (SE)*

**14:30–16:00 Oral Session 6 – *Verdi Room***
Inflammatory mediators
***Chairpersons:*** *Peter Hellings (BE) / Philippe Gevaert (BE)*
*Joint Session with the JMA Section*

14:30–15:00 **INTRODUCTORY LECTURE 6: Eosinophils and IL-5 in upper airways. Dead or alive?**
Philippe Gevaert (BE)

15:00–15.15 **Eicosanoid metabolism and eosinophilic inflammation in nasal polyp patients with immune response to Staphylococcus aureus enterotoxins**
Perez-Novo CA, Claeys C, Van Zele T, Van Cauwenberge P, Bachert C
*Ghent University Hospital, Ghent, Belgium*

15:15–15.30 **Leukocyte populations and eosinophilic cationic protein level in nasal lavage from patients with persistent allergic rhinitis: correlation with symptom severity**
Rondon C, Romero JJ, Rodríguez R, López S, Antunez C, Torres MJ, Blanca M
*Allergy Service and Research Laboratory, Carlos Haya Hospital. Málaga, Spain*

15:30–15:45 **Surgical therapy of nasal polyposis has no influence on the postoperative production of cytokines**
Wagenmann M, Mansour N, Chaker A
*HNO-Klinik, Universität Düsseldorf, Germany*

15:45–16.00 **The expression of endothelial L-selectin ligands in nasal mucosa and nasal polyps in patients with nasal polyps**
Toppila-Salmi S, Ebbens FA, Renkonen J, Renkonen R, Mullol J, van Drunen CM, Fokkens WJ
*Dept. of Otorhinolaryngology, Tampere University Hospital, Finland; Dept. of Otorhinolaryngology, Academic Medical Center, Amsterdam, the Netherlands; Dept. of Bacteriology and Immunology, University of Helsinki, Finland; Rhinology Unit, Dept. of Otorhinolaryngology. Barcelona, Spain*

**16:00–16:30 COFFEE BREAK AND POSTER DISCUSSION**

**16:30–17:30 SYMPOSIUM 3 – *Verdi Room***
The sense of smell in upper airway diseases
***Chairpersons:*** *Nancy Rawson (USA) / Joaquim Mullol (E)*

16:30–16:50 **Epidemiologic study of olfaction in the Catalan population. Olfacat Study**
Isam Alobid (E)

16:50–17:10 **Psychophysical and behavioral perspective**
Thomas Hummel (G)

17:10–17:30 **Basic research perspective: Cell biology of olfactory loss in Rhinosinusitis**
Nancy Rawson (USA)

**16:30–17:30 SYMPOSIUM 4 – *Rossini Room***
The role of infection in Rhinosinusitis: fungi or enterotoxins?
***Chairpersons:*** *Glenis Scadding (UK) / Herbert Riechelmann (G)*

16:30–16:50 **The fungal hypothesis**
Jens Ponikau (USA)

16:50–17:10 **The enterotoxin hypothesis**
Claus Bachert (BE)

17:10–17:30 **Treatment of infections in rhinosinusitis. The future**
Pontus Stierna (SE)

**17:40–19:00 SYMPOSIUM IN SPANISH – *Verdi Room***
Through an Educational Grant from Uriach SA
Investigación en Rinitis y Rinosinusitis en España / Rhinitis and Rhinosinusitis research in Spain
*Simposio Conjunto de los Comités de Rinitis de la SEAIC y de Rinología y Alergia de la SEORL / Joint Symposium of the Rhinitis (SEAIC) & Rhinology (SEORL) Committees*
*(Simultaneous Translation)*

***Chairpersons / Moderadores:***
*Ignacio Antépara, SEAIC / Joan Ramon Montserrat, SEORL*

17:40–18:00 **Clasificación ARIA de la rinitis según su gravedad/ARIA classification of rhinitis depending on its severity**
Joaquín Sastre (E)

18:00–18:20 **Rinitis y esfuerzo / Rhinitis and exercise**
Antonio Valero (E)

18:20–18:40 **Patología ciliar en la mucosa nasosinusal / Mucociliary pathology in the nose and paranasal sinuses**
Miguel Armengot (E)

18:40–19:00 **Regulación de la secreción mucosa nasal / Regulation of mucus nasal secretion**
Jordi Roca-Ferrer (E)

**21:00 GALA DINNER**

## Saturday, February 11th, 2006

**9:00–10:30 Oral Session 7 – *Verdi Room***
Chronic Rhinosinusitis and Nasal Polyps
***Chairpersons:*** *Claus Bachert (BE) / Herbert Riechelmann (G)*

09:00–09:30 **INTRODUCTORY LECTURE 7**
**Chronic rhinosinusitis and nasal polyps. One or two diseases?**
Herbert Riechelmann (G)

09:30–09:45 **Systemic and local immunoglobuline production in chronic rhinosinusitis with and without nasal polyps**
Van Zele T, Gevaert P, Holtappels G, Van Cauwenberge P, Bachert C
*University Hospital Ghent. Ghent, Belgium*

09:45–10:00 **Local and systemic impact of bacteria on granulocyte activation in asthmatics with chronic rhinosinusitis**
Kalogjera L, Vagic D, Bukovec Z, Baudoin T, Grbac I
*Dept. of ORL Head & Neck Surgery, Endocrinology Lab, Dept. of Pulmonology, University Hospital «Sestre Milosrdnice». Zagreb, Croatia.*

10:00–10:15 **Epidemiology of Nasal Polyps – The Skövde Population-Based Study**
Johansson L, Brämersson A, Holmber K, Melén I, Bende M
*Dept. of Oto-Rhino-Laryngology, Central Hospital. Skövde, Sweden*

10:15–10:30 **Nitric oxide: a new concept in chronic rhinosinusitis pathogenesis**
Naraghi M, Farajzadeh Deroee A, Ebrahimkhani MR, Kiani S, Dehpour AR
*Otorhinolaryngology & Pharmacology Departments, Tehran University of Medical Sciences. Tehran, Iran*

**10:30–11:00 COFFEE BREAK**

**11:00–12:00 SYMPOSIUM 5 – *Verdi Room***
Functional Genomics and Proteomics in Rhinology Research
***Chairpersons:*** *Mikael Benson (SE) / Marek Kowalski (PL)*
*Joint Symposium with the Interest Group on Genomics and Proteomics*

11:00–11:20 **Microarray research in rhinology**
Mikael Benson (SE)

11:20–11:40 **Disease phenotyping**
Martin Brutsche (CH)

11:40–12:00 **Challenges in proteomics**
Rainer Bischoff (NL)

**12:00–13:30 SYMPOSIUM 6 – *Verdi Room***
Eicosanoids in rhinitis and rhinosinusitis: prostaglandins or leukotrienes?
***Chairpersons:*** *César Picado (E) / Leiff Bjermer (SE)*

12:00–12:20 **The lypoxygenase pathway**
Marek Kowalski (PL)

12:20–12:40 **The cyclooxygenase patway**
César Picado (E)

12:40–13:00 **Aspirin desensitization**
Glenis Scadding (UK)

13:00–13:20 **Antileukotriene drugs**
Leif Bjermer (SE)

**13:30–13:45 CLOSING OF THE CONGRESS**

# ——Thursday, February 9th, 2006——

## 9:00-10:30 Oral Session 1
## Verdi Room Upper Airway Inflammation
## Chairpersons Ignacio Ansotegui (E) and James N Baraniuk (USA)

**Introductory Lecture 1. Neurogenic inflammation**

**Author:** Baraniuk JN
**nstitution, city and country:** Georgetown University, Washington DC, USA.

Stimulation of the nasal sensory nerves leads to sensations of pain and stuffiness. Type C nociceptive nerve releases neuropeptides including substance P (SP) and calcitonin gene related peptides (CGRP) that increase plasma extravasation and glandular secretion. This axonal response acts as an immediate protective mucosal defense mechanism. Recruited parasympathetic reflexes cause submucosal gland secretion via acetylcholine and muscarinic $M_3$ receptors. Itching, sneezing, `and other avoidance behaviors rapidly clear the offending agents from the upper airways and protect the lower airways. Dysfunction of these nerves may contribute to allergic rhinitis, infectious rhinitis, nasal hyperresponsiveness, and possibly sinusitis. Sympathetic arterial vasoconstriction reduces mucosal blood flow, sinusoidal filling, and mucosal thickness, and so restores nasal patency. Loss of sympathetic tone may contribute to some chronic, nonallergic rhinopathies. Human axon responses differ from these in animal – an important distinction that limits extrapolation from other species.

We have used hypertonic nasal provocations to investigate nociceptive nerve responses in humans. Pathophysiological differences were compared between acute sinusitis (n=25), chronic fatigue syndrome subjects with nonallergic rhinitis (n=14), active allergic rhinitis (n=17) and normal (n=20) subjects [JN Baraniuk, et al. Am J Respir Crit Care Med 2005;171:5-11]. Increasing strengths of hypertonic saline were sprayed into their nostrils at 5 min intervals. Sensations of nasal pain, blockage and drip increased with concentration and were significantly elevated above normal. These parallels suggested activation of similar subsets of afferent neurons. Urea and lysozyme secretion were dose dependent in all groups suggesting that serous cell exocytosis was one source of urea after neural stimulation. Only allergic rhinitis and normal groups had mucin dose responses and correla tions between symptoms and lysozyme secretion ($R^2$=0.12-0.23). The lysozyme dose responses may represent axon responses in these groups. The neurogenic stimulus did not alter albumin (vascular) exudation in any group. Albumin and mucin concentrations were correlated in sinusitis suggesting that non-neurogenic factors predominated in sinusitis mucous hypersecretion. Chronic fatigue syndrome had neural hypersensitivity (pain) but reduced serous cell secretion. Hypertonic saline nasal provocations identified significant, unique patterns of neural and mucosal dysregulation in each rhinosinusitis syndrome. The chronic fatigue syndrome group was of further interest, since they appear to release a unique pattern of neuropeptides compared to control subjects.

Further refinements of nasal provocation methods may be useful for studying separate subsets of nociceptive neurons that can be defined by the patterns of transient receptor potential (TRP) and other sensors that they use to observe the mucosal environment and the conditions of inhaled air.

**Title:** The prostanoids and tryptase in different types of rhinitis
**Author:** Swierczynska-Krepa M, Nizankowska-Mogilnicka E, Grzywacz M, Szczeklik A
**Institution, city and country:** Jagiellonian University, Cracow, Poland

*Background*. Tryptase and $PGD_2$ are crucial mediators of inflammation of upper respiratory tract in allergy and aspirin hypersensitivity, whereas their role in the non-allergic rhinitis with eosinophilia syndrome (NARES) is not fully elucidated.
*Objectives*. To compare the baseline levels of serum tryptase and plasma stable $PGD_2$ metabolite, 9alpha,11beta-$PGF_2$, in patients with aspirin-induced rhinitis and asthma (AIAR, n = 30), allergic rhinitis (AR, n = 24) and NARES (n = 29).
*Methods*. Plasma levels of 9alpha,11beta-$PGF_2$ were assessed by gas chromatography / mass spectrometry, whereas serum tryptase levels - by the immunofluorescence method.
*Results*. The baseline levels of 9alpha, 11beta-$PGF_2$ were higher in the AIAR patients, as compared to the AR ones and comparable to NARES group (6.27 ± 5.2, 3.68 ± 1.5 and 6.07 ± 4.48 pg/ml respectively; AIAR *vs*. AR - $p < 0.03$, AR *vs*. NARES - $p < 0.02$). The same held true for tryptase levels (in AIAR - 9.06 ± 6.91, in AR - 5.38 ± 2.12 and in NARES - 8.97 ± 10.24 ng/ml, respectively; AIAR *vs*. AR - $p = 0.015$). The incidence of bronchial asthma or nasal polyposis in NARES did not significantly influence levels of these mediators.
*Conclusions*. The basal levels of $PGD_2$ and tryptase in NARES were significantly higher than in allergic rhinitis and similar to the ones observed in aspirin hypersensitivity, known for particularly severe course of rhinosinusitis. Therefore we suggest that those mediators, possibly released by mast cells, might account for pathogenesis of NARES.

**Title:** Evaluating the relation of chronic sinusitis and nitric oxide metabolites levels in nasal lavage
**Authors:** Naraghi M, Farajzadeh Deroee A, Shadman M, Ebrahimkhani MR, Dehpour AR
**Institution, city and country:** Amir Alam Hospital, Dept.s. of Otorhinolaryngology and Pharmacology, School of Medicine, Tehran University of Medical Sciences (TUMS). Tehran, Iran

*Background*. Nitric Oxide (NO) in produced mainly in the paranasal sinuses and the nasal mocusa. Nasal NO has been suggested to be a marker of nasal inflammation and a mucociliary transport stimulant. Decreased exhaled NO is found in chronic sinusitis. NO metabolites have been measured in sinus lavages with a rabit model of chronic sinusitis and were shown that NO metabolites were significantly higher in infected sinuses.
*Objectives*. Considering the possible relation of NO and chronic sinusitis made us design this study to compare the exhaled NO etabolites levels in chronic sinusitis patients and normal ubjects.
*Methods*. We performed nasal lavage in patients (N = 20) with documented diagnosis of chronic sinusitis (confirmed by CT or endoscopy) who were candidates for surgical interventions and control group (N = 20). The NO metabolites (nitrate and nitrite) in the lavage fluid were measured using the Griess Method.
*Results*. NO metabolites levels (mean ± SEM) were 27.31 ± 2.51 mmol/l in the control group and 14.34 mmol/l in the patient group. The NO metabolites level in nasal lavage on the control group was significantly higher ($P < 0.001$).
*Conclusions*. According to our study results, NO metabolites were significantly higher in the nasal lavage fluid of the control group. Our group's other studies show an increased NO content in the affected sinuses. We suggest that the decreased amount of nasal lavage fluid NO in chronic sinusitis may be due to impaired transport of NO from sinuses because of the partial obstruction of the ostiums (a possible trapping mechanism) or the decrease in production of nasal NO as a consequence of damaged nasal mucociliary lining. This result was consistent with previous study results that showed decreased exhaled gaseous NO in chronic sinusitis. This study also showed measuring NO metabolites in nasal lavage fluid can be an indirect estimate of gaseous nasal NO.

**Title:** Nasally administered capsaicin does not influence the expression of vanilloid receptor 1 in nasal tissue of idiopathic rhinitis patients

**Authors:** In 't Veen JPM, De Groot EJJ, Van Drunen CM, Fokkens WJ

**Institution, city and country:** Dept. of Otorhinolaryngology, Academic Medical Center, Amsterdam, The Netherlands

*Background.* Repeated nasal applications of capsaicin have a therapeutic effect in idiopathic rhinitis (IR) patients through a largely unknown mechanism. Given the presence of the capsaicin receptor (VR1 also TRPV1) on nerve fibres, speculations have centered on depletion of sensory C-fibres by repeated capsaicin applications. However, data from our group could not substantiate this idea. Interestingly, it was shown that VR1 is likely to be also present on mast cells, skin epithelial cells and dendritic cells. Hardly any data is available for human nasal mucosa.

*Objective.* We set out to investigate the expression pattern of VR1 in the nasal mucosa of IR patients and whether treatment with capsaicin leads to changes in the level or activity of the receptor.

*Methods.* Nasal biopsies from thirty IR patients were taken at baseline, 15 minutes and 1 hour after single capsaicin provocation or placebo and 14-30 days after repeated capsaicin applications. The biopsies were stained with a polyclonal antibody against human vanilloid receptor type 1 (VR1).

*Results.* VR1 is expressed not only on nerve fibres, but also on epithelium and several, still unidentified cells in the lamina propria. A large variability in VR1 expression was seen between patients. No significant difference was found in the expression of VR1 in nasal tissue of IR patients before and after single capsaicin provocation or after repeated capsaicin applications.

*Conclusion.* Multiple cells express VR1, but nasally administered capsaicin does not have any influence on the expression of VR1 in nasal tissue. In future experiments we will investigate differences in VR1 expression between IR and healthy controls, and potential differences in downstream signalling events after receptor triggering.

**Title:** Evaluation of nasal obstruction and inflamation in patients affected of nasal polyposis

**Authors:** Bartra J[1], Valero A[1], Alobid I[2], Serrano C[1], Mullol J[2], Picado C[1]

**Institution, city and country:** [1]Unitat d'Al·lèrgia, Servei de Pneumologia i Al·lèrgia Respiratòria, ICT and [2]Unitat de Rinologia, Servei de ORL, ICEMEQ, Hospital Clínic, Barcelona, Catalonia, Spain

*Background.* Chronic rhinosinusitis with nasal polyps (NP) is an inflammatory process involving the mucosa of the nose and one or more sinuses. NP affects 2-4% of general population and 15-20% of all asthma patients.

*Objectives.* Acoustic rhinometry (AR) and peak nasal inspiratory flow (PNIF) are objective methods to evaluate nasal obstruction. Nasal nitric oxide (nNO) can be a good inflammation marker to nasal mucosa. The aim of this study was to evaluate nNO and AR in patients affected of NP.

*Material and methods.* 47 subjects (30 women and 17 men, mean age 50 ± 2 yr) with NP were enrolled in this study. The minimal cross-sectional area (MCSA) and right and left nasal volumes for 0 to 6 cm ($Vol_{0-6}$) and 0 to 12 cm ($Vol_{0-12}$) into the nostrils were measured with AR. PNIF and nNO were also measured in all patients.

*Results.* Mean nNO value was 248 ± 29 ppb. Media volume values for $Vol_{0-12}$ (right: 24.3 ± 2 $cm^3$; left: 30.2 ± 3 $cm^3$) and $Vol_{0-6}$ (right: 6.2 ± 0.4 $cm^3$; left: 7.2 ± 0,5 $cm^3$) were measured. Media MCSA values were: right: 0.42 ± 0.003 $cm^2$, and left: 0.43 ± 0.03 $cm^2$. Mean PNIF was 88.9 l/min (it could not be performed in 12 patients). A significant negative correlation ($p < 0.05$) was found between nNO and MCSA ($R = –0.30$) and between nNO and PNIF ($R = –0.48$).

*Conclusions.* NO values in NP patients are lower than those found in general population. The negative correlation between nNO and MCSA and between nNO and PNIF suggests that nasal obstruction accounts for the unexpected low nNO values detected in an airway disease characterized by the presence of an active inflammation. AR can be used in all NP patients. In contrast, PNIF cannot be used in a quarter of NP patients.

## 11:00-12:30 Oral Session 2
### Verdi Room Rhinitis
### Chairpersons: Gianni Passalaqua (I) and Stephen R Durham (UK)

**Introductory Lecture 2. Allergen Immunotherapy**

**Author:** Durham SR

**nstitution, city and country:** National Heart and lung Institute. Imperial College and Royal Brompton Hospital, London, UK

Immunotherapy is indicated in IgE-dependent diseases including allergic rhinitis and selected cases of bronchial asthma who fail to respond to usual therapy. Immunotherapy is especially indicated in hymenoptera venom anaphylaxis. Immunotherapy is the only treatment that induces longterm remission following discontinuation in adults and has been shown to prevent progression of rhimitis to asthma and the onset of new sensitisations in children.
Immunotherapy induces so-called 'blocking IgG antibodies, particularly of the IgG4 subclass. Recent evidence has confirmed that this IgG has 'functional'activity in both suppressing mast cell activation and inhibiting IgE-facilitated allergen presentation to T cells. Immunotherapy inhibits the recruitment and activation of effector cells at mucosal sites, including mast cells basophils and eosinophils in the nasal and bronchial mucosa.
All of these effects may be considered secondary to the influence of immunotherapy on allergen-specific T cells. Thus, immunotherapy has been shown to induce immune deviation of Th2 in favour of Th1 cells and to induce downregulation of Th2 responses possibly via induction of T regulatory cells.
New knowledge on mechanisms of immunotherapy is important for the development of immunoassays to predict efficacy, when to stop treatment and possibly to predict relapse etc., and for development of novel approaches, including adjuvants (CpG, MPL) and alternative routes, the most promising being sublingual immunotherapy.

*References*

1. Nouri-Aria KT, Wachholz PA, Francis NJ, Jacobson MR, Walker SM, Wilcock LK, Staple SQ, Aalberse RC, Till SJ, Durham SR. Grass pollen immunotherapy induces mucosal and peripheral IL-10 responses and blocking IgG activity. J Immunol 2004;172:3252-9.
2. Robinson DS, Larche M and Durham SR. Tregs and allergic disease. The Journal of Clinical Investigation 2004;114:1389-97.
3. Till SJ, Francis JN, Nouri-Aria KT and Durham SR. Mechanisms of immunotherapy. J Allergy Clin Immunol 2004;113:1025-34.
4. Wilson DR, Torres Lima M, Durham SR. Sublingual immunotherapy for allergic rhinitis: systematic review and meta-analysis. Allergy 2005;60:4-12.

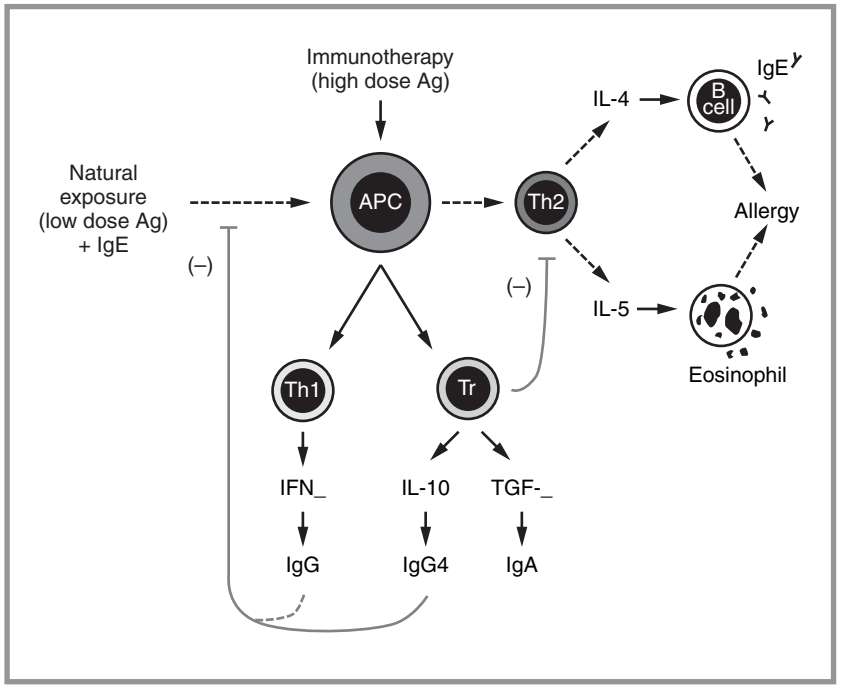


**Figura 1.** Hypothesis: Injection immunotherapy acts by inducing immune deviation in favour of Th1 responses and/or the production of T regulatory cells. Both have the potential to downregulate allergen-specific Th2 responses, and induce 'protective' antibody responses. *(J Clin Invest 2004;114:1389-97).*

**Title:** Expression profiling of the response of airway epithelial cells to house dust mite extract
**Authors:** Vroling AB, van Drunen CM, Fokkens WJ
**Institution, city and country:** AMC, Amsterdam, The Netherlands

*Background.* Epithelial cells are the first line of defense in the airways. Besides being a physical barrier for pathogens and allergens, they are also capable of producing mediators in response to these environmental factors. These mediators may contribute to the immune response, since a number of them were reported to have an immuno-modulatory function.
*Objectives.* In our research we want to examine the response of airway epithelial cells to house dust mite allergen in detail. We hope that a better understanding of the processes that take place in the local tissue will lead to new targets for medication.
*Methods.* H292 cells were cultured and exposed to house dust mite extract for 24 hours; RNA was isolated from these cells and used for microarray analysis and PCR. All experiments were done in triplicate. Microarray results were analyzed using Rosetta Resolver.
*Results.* After exposure to allergens, 3491 out of 46195 genes were significantly different between allergen exposed and control group, and of these 3491 genes 1088 were more than two-fold up- or down-regulated. Interestingly, among the most up-regulated genes are a large number of soluble factors, amongst which are chemokines (CCL-8 and -20, CXCL-1, -2 and -3), cytokines (IL1β, IL6, IL11), anti-inflammatory factors (PTX3, IL13Ra, TNFα-IP3) and factors that are involved in repair of the mucosal tissue (LOXL2, NID2, HBEGF, MUC5AC and MUC5B)
*Conclusions.* Airway epithelial cells respond to allergen by expressing a wide variety of mediators that may modulate the immune system. Future research will focus on which mediators are differentially regulated by allergen in epithelium from allergic rhinitis or healthy controls.

**Title:** Leukocyte-lymphocyte phenotyping of persistent allergic and idiopathic non-allergic rhinitis by nasal flow cytometry
**Authors:** Rondon C, Romero JJ, Lopez S, Rodriguez R, Fuentes S, Antunez C, Blanca M
**Institution, city and country:** Allergy Service and Research Laboratory, Carlos Haya Hospital, Málaga, Spain

*Background.* Flow cytometry, a tool to identify cell populations, has been employed little in allergic rhinitis. The aim of this study was to evaluate the use of nasal flow cytometry (NFC) for the differential diagnosis of persistent allergic rhinitis (PER) and persistent idiopathic non-allergic rhinitis (PINAR).
*Methods.* The study included 52 patients with symptomatic persistent rhinitis (24 patients with PER and 28 patients with PINAR), and eighteen healthy controls. Exclusion criteria were: Immunological disease, chronic sinusitis, nasal polyposis, respiratory infections in the previous month, and treatment with corticosteroids or antihistamines in the previous three weeks. Skin prick test (SPT), serum total IgE (nefelometry method), specific IgE to Dermatophagoides pteronyssinus (CAP System method), nasal lavage and cell count by flow cytometry with monoclonal antibodies (CD16-FITC, CD8-FITC, CD4-PE, CD33-PE, CD3-PerCP, and CD45-APC) were performed in all subjects.
*Results.* NFC enabled identification of leukocyte and lymphocyte subsets in the three groups. Patients with PER showed a significant increase in eosinophils (36.7%), lymphocytes (0.8%) and CD3+CD4+ T cells (21.9%) compared with the PINAR and control groups ($p < 0.05$), a significant increase of CD3+CD4+/CD3+CD8+ compared with PINAR ($p < 0.05$) and a significant increase in the CD3+ T cell population (0.40%) compared with the control group ($p = 0.004$). Patients with PINAR also showed a significant increase in the CD3+ T cell population (0.30%) compared with normal subject ($p < 0.05$), but less than patients with PER.
*Conclusions.* NFC proved useful for differentiating PER and PINAR, by defining a different leukocyte-lymphocyte phenotype in both groups. Further studies are needed to better identify the pathophysiology of PINAR.

**Title:** *Ex-vivo* nasal challenge model to investigate mast cell activation
**Authors:** Patou J, Holtappels G, Gevaert P, Van Cauwenberge P, Bachert C
**Institution, city and country:** Upper Airway Research Laboratory, Dept. of Otorhinolaryngology, Ghent University, Ghent, Belgium

*Background.* There are several *in vitro* cellular systems available for the study of mast cell biology, such as mast cell cultures of human peripheral or cord blood, or mast cell lines (HMC-1, LAD1-2), established from bone marrow aspirates. It is also possible to stimulate human tissue after enzymatic dispersion. However, mast cell lines could exhibit different responses from primary tissue mast cells, and after enzymatic digestion, receptors might be damaged. We therefore aimed to develop an *in vitro* model of allergen challenge in inferior turbinates and nasal polyps without the use of enzymatic digestion.
*Methods.* Surgical samples were collected from patients with nasal polyposis (n = 7) and inferior turbinates from patients who underwent septoplastic surgery (n = 9). Tissue cubes of 1 $mm^3$ were primed with IgE and then stimulated with ionomycine (positive control), anti-IgE 10 µg/ml and anti-IgE 100 µg/ml. Supernatants were analyzed for concentrations of histamine, $LTE_4/C_4/D_4$ and $PGD_2$ release.
*Results.* We were able to stimulate the mast cells in tissue cubes from both inferior turbinates and nasal polyps. There was a dose response for histamine, $LTE_4/C_4/D_4$ and $PGD_2$ in both inferior turbinates and nasal polyp tissue. The release of histamine, $LTE_4/C_4/D_4$ and $PGD_2$, corrected for baseline, was significantly higher in nasal polyps versus inferior turbinates.
*Conclusion.* We were able to develop a nasal challenge model without the use of enzymatic digestion. The releases of histamine, $LTE_4/C_4/D_4$ and $PGD_2$ were significantly higher in NP versus inferior turbinates.

**Title:** Clinical response to grass pollen allergen challenge is less in subjects with concurrent house dust mite allergy
**Authors:** Reinartz SM, Jansen A, van Drunen CM, Fokkens WJ
**Institution, city and country:** Dept. of Otorhinolaryngology, Academic Medical Center, Amsterdam, The Netherlands

*Background.* Nasal allergen provocation (NP) is a valid method for studying pathophysiological mechanisms in allergic rhinitis. However, an important difference with natural exposure is the increasing responsiveness to allergen after repeated exposure, also known as priming effect. It is unknown whether minimal persistent allergic inflammation caused by perennial disease also leads to increased responsiveness to other allergens.
*Objectives.* In this study we investigated the responsiveness to allergen-specific nasal challenge in seasonal versus perennial allergic rhinitis subjects and also compared to healthy controls.
*Methods.* The following groups were studied outside the grass pollen season: 1. Subjects with SAR and single sensitization to grass pollen (GP), challenged with GP extract; 2. Subjects with PAR and sensitization to house dust mite (HDM), challenged with HDM extract; 3. Subjects with PAR and multiple sensitization, to at least GP and HDM allergen, challenged with either GP or HDM extract; 4. Subjects without rhinitis symptoms with sensitization to an aero-allergen; 5. Healthy controls. Nasal and bronchial symptoms, peak nasal inspiratory flow (PNIF) and peak expiratory flow (PEF) were measured at baseline and during 24 hours following NP.
*Results.* All allergic subjects had a significant increase in total nasal symptom score after NP, as compared to the healthy controls (5) and the sensitized subjects (4). However, NP with GP extract lead to a significantly higher total nasal symptom score in subjects with isolated GP allergy (1) as compared to multiple-sensitized subjects (3). Correspondingly PNIF decreased after NP in all allergic subjects, with a significantly larger decrease in the subjects with isolated GP allergy (1).
*Conclusions.* These data show that concurrent HDM allergy leads to a decreased responsiveness to GP allergen challenge. It is not clear yet whether minimal persistent allergic inflammation can have a tolerogenic effect on responsiveness to other allergens.

## 13:45-14:30 Special Lecture 1
## Verdi Room The Sense of Smell
## Chairperson: Joaquim Mullol (E)

**Author:** Rawson N
**Institution, city and country:** Monell Chemical Senses Center, Philadelphia, PA USA

Our sense of smell has traditionally been considered our least important and least developed sense compared to other species, yet we can detect and discriminate among thousands of volatile chemicals at concentrations below the limit of detection of any instrument. Smell loss negatively affects mood, diet and lifestyle, yet there are no reliable treatments for smell loss – a condition experienced by nearly 20 million people in the United States alone. Understanding the biological bases for smell and how it is affected by diseases and age will help identify therapeutic approaches and improve quality of life for these patients.

Spurred by the Nobel-winning discovery in 1991 of the gene family encoding odorant receptors, evidence supports a model for odor detection in which individual receptor cells express one of a large family of receptor proteins that are activated by a few structurally related odors. In humans, a family of about 350 genes encoding these receptors accounts for an exquisitely sensitive and discriminating chemical detector system. The spatio-temporal pattern of receptor cell activity is carried to the olfactory bulb, to form the basis for odor quality.

Airflow dynamics, mucus solubility, blood flow and adsorption across the nasal epithelium influence odor binding and clearance, along with adaptation and resensitization. Cellular mechanisms for translating odor binding into an electrical signal to the brain are also subject to modulation. These processes can be altered dramatically by diseases, medications, trauma, inflammation and aging to reduce or eliminate the ability to smell.

Non-neural cells within the epithelium regulate ion concentrations and degrade odorants and may modulate receptor cell function. Blood borne or locally secreted signals influence neurogenesis and receptor cell sensitivity. These elements are also susceptible to disease processes.

A better understanding of the effects of inflammation, surgical manipulation and diseases on the biology of smell will help to develop therapies to treat smell loss.

## 14:30-16:00 Oral Session 3
## Verdi Room Treatment of Nasal Diseases
## Chairpersons: Kees van Drunen (NE) and Glenis Scadding (UK)

**Introductory Lecture 3. New Target in the Treatment of Nasal Disease**

**Author:** Scadding G
**Institution, city and country:** Royal National Throat, Nose and Ear Hospital, London, UK

In the past decades many major advances have occurred in the understanding of the immunopathology of allergic rhinitis, however we all still have patients who are unsatisfied with their treatment for this disorder. The situation is worse for other forms : non-allergic rhinitis has many different pathologies, most poorly comprehended and ineffectively treated. We still lack effective therapy for the common cold- arguably the single most important contributor to respiratory ill health with its secondary effects upon asthma, sinuses, polyps, middle ears, lower airways etc.
Rhinosinusitis burdens some 15% of the population and is a very common reason for primary care consultations. Advances in diagnosis and treatment occurred with improvements in sinus imaging ( CT scans), examination (nasendoscopes) and surgery ( FESS), but our clinics are still full of persistently symptomatic individuals and a dispute exists over the pathogenesis of CRS .Recent observations suggest possible genetic factors involving mucus- these need confirmation and could lead to improved treatment. Primary disorders of muco-ciliary clearance such as ciliary dyskinesia require increased understanding- especially of the link with nitric oxide via which effective help may be forthcoming.
Beyond the rhinitis/ rhinosinusitis spectrum there are the granulomatous diseases which cause severe symptoms and for which no provoking antigen has yet been identified. Similarly nasal and sinus tumour sufferers would benefit from greater awareness of causation and better targeted treatment. Finally olfactory defects, often downplayed by those unaffected , cause misery to others who are. Therapy for ,or better still, prevention of post viral anosmia/cacosmia would relieve suffering and might also lead to prevention of some intracerebral pathologies in which the CNS is accessed via the nose.
There is much work to be done.

**Title:** Effectivennes of endosinual treatment and prognostic factors of sinus lavage in patients with chronic maxillary sinusitis
**Authors:** Drvis P, Baudoin T, Grgic M, Zurak K, Ajduk J, Kalogjera L
**Institution, city and country:** Dept. of ENT-Head and Neck Surgery, University Hospital Sestre Milosrdnice Vinogradska. Zagreb, Croatia

*Background.* The aim of the study was to evaluate subjective outcomes in patients with chronic maxillary sinusitis after steroid/antibiotic endosinusal treatment. The study was designed to evaluate correlations between tryptase, eosinophil cationic protein (ECP), myeloperoxidase (MPO), immunoglobulin E (IgE) and interleukin 5 (IL-5) in sinus lavage and sinusitis symptom scores, and to test the hypothesis that their pretreatment levels in sinus lavage could predict response to endosinusal steroid/antibiotic treatment.
*Methods.* 30 patients with chronic maxillary sinusitis were recruited for the study. Patients were treated endosinusally with 2 mg of dexamethasone and 40 mg of gentamycine per maxillary sinus for 5 days. Patients rated sinusitis symptoms and completed a self-administered questionnaire at inclusion and 30 days after the treatment. Sinus lavage at inclusion was analysed for tryptase, ECP, MPO, IgE and IL-5 concentration. The improvement rate (IR) of sinusitis symptom scores was calculated as difference between the pretreatment and posttreatment scores. Patients were categorised as responders or nonresponders according to the degree of IR.
*Results.* Significant improvement was noted for sinusitis symptoms score ($p < 0.01$). There was positive correlation between baseline IL-5 level in sinus lavage and improvement rate of sinusitis symptoms score ($p < 0.01$). Difference in baseline level in sinus lavage between responders or nonresponders was significant for MPO and ECP ($p < 0.01$), but not for tryptase and IgE. Responders had higher level of IL-5, MPO and ECP in sinus lavage than nonresponders.
*Conclusions.* Steroid/antibiotic endosinusal treatment in patients with chronic maxillary sinusitis was proven effective in reducing subjective sinusitis symptoms. Improvement rate to endosinusal treatment is expected to be higher in patients with increased level of IL-5, MPO and ECP in maxillary sinus lavage and their increased concentrations in sinus fluid might be predictor of a good response to endosinusal treatment of maxillary chronic sinusitis.

**Title:** Presence of local specific IgE antibodies in nasal lavage of patients with persistent idiopathic rhinitis
**Authors:** Rondon C, Romero JJ, Lopez S, Doña I, Robles S, Rodriguez JL, Blanca M
**Institution, city and country:** Allergy Service and Research Laboratory, Carlos Haya Hospital, Málaga, Spain

*Background.* Patients with typical symptoms of persistent allergic rhinitis (PER) but with skin-prick test (SPT) and serum-specific IgE negative are often diagnosed clinically with persistent idiopathic non-allergic rhinitis (PINAR).
*Objectives.* The aim of this study was analyse the presence of specific-IgE to Dermatophagoides pteronyssinus (DP), the most prevalent aeroallergen in our area, in nasal lavage fluids from these patients, and to compare the results with PER patients and healthy controls.
*Methods.* 15 healthy controls, 24 patients with PER and 28 patients with PINAR were examined during the symptomatic period. Exclusion criteria were: Immunological disease, chronic sinusitis, nasal polyposis, respiratory infections in the previous month, and treatment with corticosteroids or antihistamines in previous three weeks. Nasal lavage was performed in all subjects. The presence of total and specific-IgE to DP was analyzed by nephelometry and CAP-System, respectively, in nasal lavage fluids. Cell analysis was done by flow cytometry with monoclonal antibodies (CD16-FITC, CD8-FITC, CD4-PE, CD33-PE, CD3-PerCP, and CD45-APC). A nasal allergen provocation test with DP (NAPT) was performed in nine subjects (three from each study group).
*Results.* In the PINAR group, three patients showed nasal-specific IgE to DP (10.7%), positive NPT and a similar leukocyte-lymphocyte phenotype to the PER group (eosinophils 34%, neutrophils < 10% and lymphocytes 0.7% of total leukocytes, and CD3+/CD4+ 21% of total lymphocytes).
*Conclusions.* The measurement of specific IgE in nasal lavage fluid can be used to optimise the diagnosis of allergic rhinitis, especially in patients with negative SPT and serum-specific IgE. Allergic rhinitis is a highly prevalent disease and frequently shows multi-sensitization. NAPTA, the diagnostic gold standard in allergic rhinitis, cannot be used in most patients.

**Title:** Amphotericin B nasal lavages: no solution for chronic rhinosinusitis

**Authors:** Ebbens FA[1], Scadding G[2] Bachert C[3], Mullol J[4], Van Zele T[3], Badia L[2], Hellings PW[5], Lund VJ[2], Fokkens WJ[1]

**Institution, city and country:** [1]Dept. of Otorhinolaryngology, Academic Medical Center, Amsterdam, The Netherlands, [2]Dept. of Rhinology, Royal National Hospital, London, United Kingdom, [3]Dept. of Otorhinolaryngology, University Hospital Ghent, Ghent, Belgium, [4]Rhinology Unit, ENT Dept., Hospital Clinic, Barcelona, Spain, [5]Dept. of Otorhinolaryngology, University Hospital, St. Rafael, Leuven, Belgium

*Background.* Chronic rhinosinusitis (CRS) with or without nasal polyposis (NP) is a common clinical condition and presents a vexing clinical problem for the treating physician. Recently, investigators from the Mayo Clinic hypothesized that immune responses to fungi play an important role in the pathogenesis of CRS with or without NP by triggering eosinophilic inflammation in susceptible individuals. On the basis of this hypothesis, Ponikau et al have suggested that intranasal treatment with an antifungal agent (amphotericin B) is an appropriate treatment for patients with CRS. In 2 uncontrolled trials, such therapy was reported as successful. In contrast, a recent double-blind placebo-controlled single-center study, including only 30 patients, only small differences between amphotericin-treated subjects and placebo-treated subjects could be observed. In order to clarify the role of intranasal antifungal drugs in the treatment of CRS we conducted a large double-blind placebo-controlled study.

*Methods.* Double-blind placebo-controlled multicenter trial study using amphotericin B to treat 116 randomly selected patients with CRS and/or NP. Patients were instructed to instill 25 ml amphothericin B (100 µg/ml) or placebo to each nostril twice daily for 3 months. Primary outcomes included total VAS (Visual Analogue Scale) score (sum of nasal blockage, rhinorrhoea, facial pain, postnasal drip and anosmia) and the amount of mucosal disease as assessed by endoscopic examination in a standardised manner. Secondary outcomes included Peak Nasal Inspiratory Flow (PNIF), polyp scores, quality of life (SF-36, RSOM-31) and patient symptom scores.

*Results.* Analysis was based on intention-to-treat and involved all patients randomly assigned. Median VAS scores, SF-36 and RSOM-31 data, PNIF values and polypscores were similar in both treatment groups at the time of randomization and no significant differences were observed after 13 weeks of treatment.

*Conclusion.* Amphotericin B nasal lavages are no solution for patients with CRS.

**Title:** Rupatadine inhibits cytokine production and NF-κB activity by a histamine H1 receptor-dependent mechanism

**Authors:** Barrón S, Roman J, Michelena P, Ramis I, Merlos M

**Institution, city and country:** J. Uriach y Compañia S.A., Barcelona, Spain

*Background.* Second generation antihistamines are claimed to display anti-inflammatory activity apart from $H_1$ receptor ($H_1$-R) blockade. Increasing evidence, however, shows that this activity is due to a great extend to a direct effect on the $H_1$-R. The present work compares the effect of rupatadine with other antihistamines on allergic inflammation and assesses the relationship between this effect and binding affinity.

*Methods.* Human umbilical vein endothelial cells (HUVEC) were pre-incubated with antihistamines prior to activation with histamine. Afterward, IL-6 and IL-8 production and NF-κB activation were measured. Antihistamine binding affinity and constitutive activity of $H_1$-R were assessed using chinese hamster ovary (CHO) cells transfected with the human $H_1$-R cDNA.

*Results.* Rupatadine inhibited NF-κB activity induced by histamine on HUVEC. The increase in activity of NF-κB induced after an overexpression of $H_1$-R in CHO cells was also inhibited by rupatadine. The production of IL-6 and IL-8, both regulated by NF-κB, was inhibited in a different extent by all tested antihistamines. $IC_{50}$ values for IL-6 production were 0.046, 0.10, 2.2 and 21 nM for rupatadine, desloratadine, levocetirizine and fexofenadine, respectively. $IC_{50}$ values for IL-8 production were 0.040, 0.12 and 2.4 nM for rupatadine, desloratadine and levocetirizine, respectively, whereas fexofenadine failed to reach 50% inhibition. Rupatadine Ki was 1.4 nM in binding assay. Desloratadine, levocetirizine and fexofenadine Ki were 1.6, 9.5 and 40.3 nM, respectively. In both functional and binding assays the relative order of potency was maintained.

*Conclusions.* Rupatadine was more potent than the other tested antihistamines in reducing IL-6 and IL-8 production. This effect was correlated with rupatadine's higher affinity for the $H_1$-R.

## 16:00-17:00 Symposium 1
## Verdi Room Global Alliance against Chronic Respiratory Disease (GARD)
## Chairperson: Jean Bousquet (F)

**Title:** Why GARD?
**Author:** Dahl R
**Institution, city and country:** Denmark

**Abstract not available**

**Title:** World Health Organization and GARD
**Author:** Khaltaev N
**Institution, city and country:** Dept. of Noncommunicable Diseases and Health Promotion, WHO, Geneva, Switzerland

Respiratory conditions impose enormous burden on society. According to WHO, the top five respiratory diseases account for 17.4% of all deaths and 13.3% of all disability-adjusted life years (DALYs). Preventable chronic respiratory diseases (CRD) are major global health problem. Over 1 billion people of all ages (from infancy to old age) suffer from preventable CRD in all countries of the world. More that 500 million of these live in developing countries or deprived populations. Preventable CRD are increasing in prevalence, particularly in children and the elderly.

The enormous human suffering caused by chronic respiratory diseases (CRD) has been recognized by the Fifty-Third World Health Assembly which requested the Director General to continue giving priority to the prevention and control of CRD with special emphasis on developing countries and other deprived populations and "to coordinate, in collaboration with the international community, global partnerships and alliances for resource mobilization, advocacy, capacity building and collaborative research" for prevention and control of non-communicable diseases, including CRD (resolution WHA 53.17, May 2000).

The need for a global alliance against CRD was first highlighted by experts attending the "WHO Consultation Meeting on the Development of a Comprehensive Approach for the Prevention and Control of Chronic Respiratory Diseases" (WHO-HQ, Geneva, 11-13 Jan 2001; WHO/NMH/MNC/CRA/01.1), and was subsequently further recognized by the *WHO Strategy for Prevention and Control of CRD (WHO/MNC/CRA/02.1)* as well as by the participants in the WHO meeting on "Surveillance, Prevention and Control of Chronic Respiratory Diseases at Country Level" (WHO-HQ, Geneva, 17-19 June 2004).

The Global Alliance against Chronic Respiratory Diseases (GARD) is a voluntary alliance of internationally recognized organizations, institutions, and agencies from developing and developed countries aimed at sharing expertise, identifying problems, promoting solutions, coordinating activities and working towards the common goal of fighting chronic respiratory diseases. GARD specific goals are focused on the improvement of collaboration among

international organizations, agencies and institutions involved in the surveillance, prevention and control of CRD with special emphasis on developing countries, with a view to:

a) Encouraging and facilitating information exchange;
b) Fostering the establishment of cooperative arrangements aimed at reducing the burden of chronic diseases;
c) Promoting the quality and affordability of patient care and improving the education and training of health care personnel dealing with CRD.

More than 40 organizations in the area of respiratory medicine, general practice, allergy, patient organizations, public health, WHO collaborating centers agreed to collaborate in facilitating progress in the following areas:

– increasing awareness of the importance of the burden of CRD, which should be regarded as significant diseases and a serious global health problem by all;
– fostering country focused initiatives for surveillance, prevention and control of chronic respiratory diseases;
– improving the quality and the affordability of care to patients with CRD in developing countries;
– improving the education and training of health care workers and personnel dealing with CRD; and
– integrating or coordinating initiatives that governmental and international nongovernmental organizations are currently undertaking in developing countries, thus avoiding duplication of efforts and wasting of resources.

**Title:** GARD mission
**Author:** Bousquet J
**Institution, city and country:** Montpellier, France

**Abstract not available**

## 16:00-17:00 Symposium 2
## Rossini Room European Consensus on Rhinosinusitis and Nasal Palyposis (EP3OS)
## Chairpersons: Wytske Fokkens (NL) and Valerie Lund (UK)

**Title:** Definitions and Classification
**Author:** Lund V
**Institution, city and country:** Professor of Rhinology, University College, London, UK

In recent years many attempts have been made to define and classify inflammatory conditions in the nose and paranasal sinuses[1-3] It is generally recognised that rhinitis and sinusitis overlap both anatomically and pathophysiologically and as a consequence the term 'rhinosinusitis' has been widely accepted. A robust definition for all clinicians has proved more difficult and usually relies on symptomatology and duration of disease. Terms such as 'acute', 'subacute', 'chronic' etc are based on duration with arbritary cutoffs at 4 or 12 weeks. A more pragmatic approach[4] modifies definitions according to the clinical audience ie epidemiologist, primary or secondary care or for research purposes. Furthermore an unresolved debate continues on the relationship of nasal polyposis and rhinosinusitis.

At its simplest, rhinosinusitis (including nasal polyposis) is inflammation of the nose and sinuses characterised by two or more symptoms: blockage/congestion, discharge, facial pain/pressure and/or reduced olfaction. Ideally these are corroborated by endoscopic signs and/or CT changes. Duration remains a relatively insensitive division of < or > 12 weeks but severity of disease may be quantified using a simple visual analog score, emulating the approach taken by ARIA[5].

Many forms of inflammation may be considered in the classification of rhinosinusitis, including the pathogens, predisposing factors and associated systemic diseases, both congenital and acquired.

There are no 'rights' or 'wrongs' in defining and classifying disease – this is merely an attempt to provide a logical approach to facilitate diagnosis, treatment and research into a common condition which in many respects, remains surprisingly obscure.

*References*

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**Title:** Acute RS. Diagnosis and EBM treatment
**Author:** Stierna P
**Institution, city and country:** Professor, Dept. of Otorhinolaryngology, Karolinska University, Stockholm, Sweden

The reported incidence of acute bacterial rhinosinusitis varies depending on wether the diagnosis is based on symptoms and/or clinical examination. Antral puncture increases the diagnostic possibility as compared to clinical examination and radiography. Sinusitis often complicate the common cold where ostial factors and/or preceeding eosinophilic inflammation (allergy?) is involved. The most common bacterial species isolated are *Streptococcus pneumoniae*, Hemophilus influencae and Moraxella catarrhalis and the prevalence of antibacterial resistance appears to be associated with local antibiotic consumption. Local impairment of host defence includes reduced mucociliary clearance and decreased local immunological defense. In acute maxillary sinusitis confirmed radiographically or by aspiration there is support for the use of penicillin or amoxicillin for 7-14 days but benefit should be weighed against the potential for adverse effect. When diagnosis is based on symptoms, antibiotics are indicated only after increasing problems after 5 days or problems longer than 10 days and with moderate to severe symptoms. In failure of treatment for moderate/severe disease diagnosis should be re-checked and referral to an ENT surgeon is considered. Addition of topical steroid to antibiotics may be used especially if background eosinophilic mucosal disease is suspected on anamnestic data. Decongestion provides relief in nasal breathing and nasal saline douche may provide symptomatic relief.

**Title:** Chronic RS and Nasal Polyps. Diagnosis and EBM treatment
**Author:** Fokkens W
**Institution, city and country:** AMC, Amsterdam, The Netherlands

Rhinosinusitis is a significant health problem which results in considerable direct medical costs and severe impact on lower airway disease and general health outcomes. Rhinosinusitis is one of the most common diagnosis for which an antibiotic is prescribed accounting to more than 20% of all adult antibiotic prescriptions in the USA. When reviewing the current literature on chronic rhinosinusitis, it becomes clear that giving an accurate estimate of the prevalence of CRS remains speculative, because of the heterogeneity of the disorder and the diagnostic imprecision often used in publications. However the data available point to chronic rhinosinusitis as one of the leading forms of chronic disease. Whatever the precise epidemiology, the burden of rhinosinusitis on health and economics warrants optimal comprehension of the available knowledge to improve the diagnosis and treatment of our patients.

The last decade has seen the development of a number of guidelines, consensus documents and position papers on the epidemiology, diagnosis and treatment of rhinosinusitis and nasal polyposis. Although of condiderable assistance none of these documents were evidence based. Contrary to diseases like allergic rhinitis and acute otitis media where treatment is mostly based on high levels of evidence, the level of evidence in treatment schemes of rhinosinusitis are usually still quit low.

Contrary to diseases which are treated only medically it is a challenge to integrate available knowledge on surgical and medical treatment in a complicated treatment modality as chronic rhinosinusitis. Some ENT surgeons think that it is impossible to imply evidence based medicine in surgery. However evidence-based medicine is not restricted to randomised trials and meta-analysis. It involves tracking down the best external evidence with which to answer our clinical questions. And if no randomised trial has been carried out for our patient's predicament, we follow the trail to the next best external evidence and work from there. It should be remembered that EBM is the process that is followed to use the evidence.

The European position paper on rhinosinusitis and nasal polyps (EP3OS), published with this edition of the Journal, was jointly written by a taskforce of experts in the field invited by the European Academy of Allergology and Clinical Immunology (EAACI). The EP3OS document is approved by the EAACI and the European Rhinologic Society (ERS).

The present document is intended to be state-of-the art 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 theavailable 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.

We trust that this position paper will help collegaes diagnosing and treating patients with rhinosinusitis to make optimal choices for their patients. Moreover we hope that it inspires investigators in rhinosinuisiitis to fill the gaps in our knowledge with high quality research.

## 9:00-10:30 Oral Session 4
## Verdi Room Glucocorticoids
## Chairpersons: Jean-Baptiste Watelet (BE) and Laura Pujols (E)

### Introducctory Lecture 4. Regulation of glucocorticoid receptors

**Authors:** Pujols L, Mullol J, Picado C
**Institution, city and country:** Servei d'Otorinolaringologia and Servei de Pneumologia i Al·lèrgia Respiratòria, Hospital Clínic i Universitari, Barcelona, Catalonia, Spain

Inhaled and intranasal glucocorticoids are the most common and effective drugs for controlling symptoms and airway inflammation in respiratory diseases such as asthma, allergic rhinitis, and nasal polyposis. The last few years have seen a growing understanding of the mechanisms of glucocorticoid action and, in particular, the receptor that mediates glucocorticoid actions, the glucocorticoid receptor (GR). The objective of the present lecture is to provide an update on the GR gene, the expression and regulation of its gene products, namely GRα and GRβ, as well as their alterations in pathological states. GRα is responsible for the induction and repression of target genes, it is expressed in virtually all human cells and tissues, and its expression is known to be downregulated by glucocorticoids. GRβ has been found to act as a dominant negative inhibitor of GRα-mediated transactivation in *in vitro* studies with transfected cells, but it does not appear to have a significant inhibitory effect on GRα-mediated transrepression. In addition, for most tissues the expression of GRβ, at least at the mRNA level, is extremely low compared with that of GRα. Some pro-inflammatory cytokines appear to upregulate the expression of GRβ, and increased GRβ expression has been reported in diseases associated with glucocorticoid resistance or insensitivity, such as bronchial asthma, nasal polyposis, and ulcerative colitis. However, the possible role of GRβ in modulating glucocorticoid sensitivity and/or resistance *in vivo* has been highly debated and it is not yet clear.

**Title:** Effects of glucocorticoids on mucin expression in human nasal polyps

**Authors:** Martínez-Antón A, de Bolós C, Garrido M, Roca-Ferrer J, Oliveras G, Barranco C, Alobid I, Xaubet A, Picado C, Mullol J

**Institution, city and country:** Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Serveis d'Otorinolaringologia and Pneumologia, Hospital Clínic, Barcelona, Catalonia, Spain

*Background*. Mucus hypersecretion is a hallmark of airway inflammatory diseases including nasal polyposis. Glucocorticoids (GC) are the recommended therapy for decreasing size and inflammatory component of nasal polyps, but their effect on mucin production is not well established.

*Objective*. To investigate the effect of oral and topical GC on mucin gene expression in nasal polyps from different origins.

*Methods*. Nasal polyps were obtained from patients without (NP; N = 10) and with aspirin-tolerant (NP-ATA; N = 7) and intolerant (NP-AIA; N = 6) asthma. Patients were treated with oral prednisone for 2 weeks (30 mg/day) and intranasal budesonide for 12 weeks (400 µg/12hr). NP biopsies were obtained before (B0) and after 2 (B2) and 12 (B12) weeks of treatment. Immunohistochemistry for MUC1, MUC4, MUC5AC, MUC5B and MUC8 was performed. Data is expressed as median and 25-75 percentiles of positive cells. Statistical significance was set at $P < 0.05$.

*Results*. At B0, MUC5AC (40; 22.5-58.8) and MUC8 (100; 90-100) levels were higher in NP from asthma patients than in NP from non-asthmatic (20; 10-30 and 75; 55-92.5, respectively). At B2, MUC1 (97.5; 90-100) and MUC4 (100; 90-100) were increased ($p < 0.05$) in NP-ATA patients compared to basal levels (70; 60-80 and 80; 60-100, respectively). At B12, MUC5AC (40; 35-60 *vs*. 5; 1.3-10) and MUC5B (45; 12.5-56.3 *vs*. 2.5; 1.3-6.3) were decreased ($p < 0.05$) in NP-ATA patients, while MUC8 was increased ($p < 0.05$) in both NP (100; 100-100) and NP-ATA (100; 100-100) compared to basal levels (75; 55-92.5 and 90; 60-100, respectively).

*Conclusions*. These results suggest that: 1) GC have a stimulatory effect on membrane mucins (MUC1, MUC4) while an inhibitory effect on secreted mucins (MUC5AC, MUC5B); and 2) polyps from ATA patients have a good response to GC while NP-AIA patients are resistant to steroid treatment.

**Title:** Topical capsaicin or furosemide *vs.* oral steroid in the management of nasal polyposis

**Authors:** Kalogjera L, Kroflic B, Baudoin T, Coer A, Ferencic Z

**Institution, city and country:** ORL Dept., University Hospital Sestre milosrdnice and Pathology Dept. Pliva Research Institute, Zagreb, Croatia. ORL Dept., General Hospital, Celje, Slovenia, Institute of Histology, Med. Univ. Ljubljana, Slovenia

*Background*. Long term topical furosemide or capsaicin treatment offers better nasal polyp recurrence protection than placebo.

*Objectives*. The aim of the study was to compare the outcomes of a short term topical capsaicin and furosemide with oral steroid treatment in terms of nasal symptom scores, polyp size, inflammatory cells and oedema reduction.

*Methods*. Forty nasal polyp patients were randomly allocated to 7-day treatment with either oral methyprednisolon (1mg/kg/day) or nasal furosemide (20 mg/day), while 16 patients with massive polyposis received topical capsaicin (30-100 mmol solution) in 5 consecutive days. Nasal symptoms and polyp scores followed by a biopsy of the most superficial polyp were done before and after the treatment. Eosinophils and mastocytes were counted and scored in 10 high power fields (400x) per slice throughout the specimen and edema was measured.

*Results*. Subjective and endoscopy scores did not differ significantly between the furosemide and steroid groups, but endoscopy scores were significantly higher in capsaicin group before and after the treatment. All subjective and endoscopy scores were significantly improved after the treatment in all groups. There was no significant difference in subjective scores between the groups before the treatment and after the treatment, except for olfaction, which was better improved in steroid than capsaicin, but not than in furosemide group. However, reduction of endoscopy scores before and after the treatment was not different between the groups. Steroid significantly reduced eosinophils, with no effect on mastocytes and edema. Furosemide and capsaicin had no effect on inflammatory cells, but furosemide reduced oedema.

*Conclusions*. Topical capsaicin and furosemide 7-day treatment have significant impact on nasal symptoms and polyp size reduction, which is comparable to the effect of oral steroid. Steroid treatment significantly reduced eosinophil infiltration, while no effect on inflammatory cells was demonstrated for furosemide and capsaicin.

**Title:** Techniques of internasal drug use
**Authors:** Rapiejko P, Wojdas A, Ratajczak J, Szczygielski K, Jurkiewicz D
**Institution, city and country:** Military Institute of the Health Services, Warsaw, Poland

*Objective.* The aim of the study was to assess the incidence of changes in nasal mucosa in patients treated with long term intranasal corticosteroids and to determinate reasonability of intranasal drops administration in symptomatic treatment of nasal catarrh.
*Methods.* The study included the total of 1962 patients. Within this group, 612 patients treated with intranasal corticosteroids underwent full laryngological examination to evaluate the status of nasal mucosa. In the group of 1350 users of web-based Allergologic Courier, who had used intranasal drops because of "runny nose" within last 3 months before the examination, a questionnaire survey was performed.
*Results.* The study results reflect poor knowledge the methods of nasal drops administration among patients, as well as low effectiveness of educational initiatives led by physicians and pharmacists. In 25 persons from 367 examined (6.81%) who used steroid spray locally, and who showed up in laryngological outpatient clinic, nasal mucosal damage was diagnosed for the first time. Mucosal damage was most frequently located in the right nasal septal mucosa – in 21 patients (5.72% of total patients) that was connected with improper nasal inhaler positioning and right hand movements directing it towards septum in the right nasal meatus. Among patients, who have remained under regular laryngological care in outpatient clinic (all of them are instructed of drug administration technique), only 5 persons (2.04%) out from 245 in the study group presented changes in nasal mucosa. No differences between changes occurrence on each side of nasal septum were found.
*Conclusion.* Without proper training, only 8.52% from 1350 examined persons had been taking nasal drops in a proper manner to achieve its effectiveness.

**Title:** *In vivo* regulation of glucocorticoid receptor isoforms in human nasal polyps by systemic and intranasal glucocorticoids
**Authors:** Pujols L, Mullol J, Benítez P, Alobid I, Fuentes M, Martínez A, Roca-Ferrer J, Ramírez J, Picado C
**Institution, city and country:** Serveis d'Otorinolaringologia and Pneumologia, IDIBAPS, Hospital Clínic, Barcelona, Catalonia, Spain

*Background.* The poor response of some nasal polyp patients to glucocorticoid (GC) therapy may be due to abnormal expression of GC receptor (GR) α and β or to GC-induced GRα downregulation.
*Objective.* To examine the *in vivo* regulation of GRα and GRβ in nasal polyp patients treated with GC, and to study the relationship between the clinical response to GC and GR expression.
*Methods.* Nasal polyp patients (n = 50) were treated with both oral prednisone (30 to 5 mg/day) and intranasal budesonide (400 mg/day) for 2 weeks and compared with 14 untreated patients. GC-treated patients continued intranasal budesonide treatment for 10 additional weeks. Nasal polyp biopsies were obtained before (B0) and after 2 (B2) and 12 (B12) weeks of treatment. Healthy nasal mucosa (n = 11) was used as control. Nasal symptoms (obstruction, smell, rhinorrhea and sneezing) and polyp size were evaluated. GRα expression was determined by RT-PCR (10e5 mRNA copies/μg total RNA) and immunohistochemistry (% immunoreactive cells). Data are expressed as median and 25-75th percentile.
*Results.* At B0, nasal polyps expressed less GRα mRNA (1.4, 0.4-1.9; $p < 0.05$) and protein (37, 28-53; $p < 0.01$) than nasal mucosa (2.5, 1.3-2.9 and 60, 51-72, respectively). At B2, increased GRα mRNA (2, 1-2.7; $p < 0.01$) and protein (55, 27-71; $p = 0.09$) were found compared to B0 (1.2, 0.7-2; 36, 26-46, respectively). At B12, GRα mRNA (1.2, 0.6-2.6; NS) and protein (37, 18-65; NS) were similar to B0. GRβ expression was almost undetectable and unaltered by GC treatment. No correlation was found between GRa levels and nasal symptoms or polyp size.
*Conclusion.* GRα is downregulated in inflamed nasal tissue. GR expression is not involved in the patients' response to GC. Neither systemic nor intranasal GC downregulate the GR *in vivo*.

## 11:00-12:30 Oral Session 5
## Verdi Room United Airways: nose and bronchi
## Chairpersons: Wytske Fokkens (NE) and Manel Jordana (CA)

**Introductory Lecture 5. Upper and lower airway interactions**

**Author:** Jordana M
**Institution, city, country:** McMaster University, Hamilton, Canada

Much has been learned over the last decade about airway inflammation in asthma. However, much remains to be elucidated about the determinants and the mechanisms of allergic sensitization as well as the connection between inflammation and the structural-functional phenotype typical of asthma. The inherent complexity of these issues is such that gaining insight in the context of human research is exceedingly challenging. In contrast, experimental modeling of allergen exposure affords the opportunity to carefully dissect and manipulate this complexity.

To date, most of the research carried out in experimental models has used ovalbumin (OVA) as a surrogate allergen. The innocuous nature of OVA has forced investigators to devise strategies to generate immunity. Typically, this is accomplished by introducing OVA into the peritoneal cavity in conjunction with an adjuvant, generally aluminum hydroxide. It is then apparent that this procedure intrinsically prevents understanding the requirements for inducing allergic sensitization.

In the course of this presentation, data will be shown to illustrate models of respiratory mucosal sensitization using common aeroallergens such as house dust mite and ragweed. Evidence will be presented indicating that the dose, the length of exposure, the presence of additional specific immune signals in the airway microenvironment and the genetic background determine whether an antigen/allergen will elicit allergic sensitization as well as the structural and functional impact of allergen exposure. Finally, we will introduce some evidence on the impact of, specifically, ragweed exposure in the nasal mucosa.

**Title:** Pulmonary upregulation of IL-4 and IL-13 mRNA following selective nasal allergen provocation in a mouse model of airway allergy
**Authors:** Hens G, Meyts I, Verbinnen B, Cadot P, Dilissen E, Bullens D, Jorissen M, Ceuppens J, Hellings P
**Institution, city, country:** ENT Dept., University Hospitals Leuven and Lab of Experimental Immunology, Catholic University, Leuven, Belgium

*Background*. During recent years, the concept of "united airways allergy" has become widely accepted, mainly because of the convincing epidemiological data linking allergic rhinitis and asthma. However, the mechanisms responsible for nasobronchial interaction remain largely unknown.
*Objectives*. We used a mouse model to unravel the extent and the mechanisms of nasobronchial interaction in airway allergy.
*Methods*. In a chronic mouse model of ovalbumin induced allergic airway inflammation, w/e performed selective nasal and bronchial allergen provocations following complete anatomical separation of upper and lower airways by means of a tracheotomy.
*Results*. Selective nasal allergen provocation induced IL-4 and IL-13 mRNA expression in lung tissue. Selective bronchial allergen provocation caused a more pronounced upregulation of pulmonary IL-4 and IL-13 mRNA. Moreover, local bronchial allergen contact was required for upregulation of pulmonary IL-5 mRNA and eotaxin-1 mRNA. Shortly after nasal provocation, IL-4 levels were increased in serum, while bronchial provocation enhanced serum levels of IL-4, IL-5 and IL-13.
*Conclusions*. Nasal allergen provocation following separation of upper and lower airways by means of a tracheotomy, induces pulmonary IL-4 and IL-13 mRNA, possibly via induction of IL-4 in the systemic circulation. Local bronchial allergen contact however is required for the full phenotype of allergic inflammation with upregulation of Th2-cytokines and eotaxin.

**Title:** Nasal pathology in bronchiectasis
**Authors:** Guilemany JM, Centellas S, Alobid I, Garcia-Piñero A, Angrill J, Bernal-Sprekelsen M, Picado C, Mullol J
**Institution, city and country:** Rhinology Unit, Dept. of ENT and Pneumology, Hospital Clínic, University of Barcelona, IDIBAPS, Barcelona, Spain

*Background*. Bronchiectasis is an uncommon disease with the potential to cause devastating complications. Associations between upper and lower airway diseases have been demonstrated in allergic rhinitis/nasal polyposis and asthma, chronic obstructive lung disease and chronic rhinosinusitis.
*Objectives*. a) To investigate the prevalence of nasal symptoms, nasal polyposis, and sinusal occupation in patients with bronchiectasis. b) To investigate the impact of bronchiectasis with/without nasal polyposis on quality of life.
*Methods*. Seventy patients with stable non-cystic bronchiectasis were evaluated for nasal symptoms (RASP, 0-3), nasal polyp size (endoscopy, 0-3), sinusal occupation (CT, 0-24), and quality of life (SF-36).
*Results*. All patients have nasal symptoms. Anterior (100%) and posterior (91%) rhinorrhea, nasal obstruction (90%), and sneezing (72%) were reported by patients as the major complaints, with intensity ranging 1.6-2.1. Nasal polyps of a moderate size (1.5 ± 0.3) were found by nasal endoscopy in 31.3% of patients. Sinusal CT was abnormal in all patients, with a CT score of 9.5 ± 0.5, predominantly in the maxillary sinus (2 ± 0.5), ethmoid sinus (1.9 ± 0.7), and osteomeatal complex (3 ± 0.9). There was a correlation between nasal polyp size and sinusal occupation ($R = 0.456$; $p < 0.05$). Patients with BQs had significantly worse QoL scores in SF-36 summaries (PCS: 46.5 ± 1.9; MCS: 39.7 ± 1.8) in comparison with the Spanish general population, (PCS: 82.7 ± 2; MCS: 84.5 ± 1.9). Males reported significantly higher quality of life scores on physical functioning and social functioning than females did.
*Conclusion*. All patients affected with BQs presents nasal symptoms and CT occupation while more than 30% presents nasal polyposis. We conclude that patients with bronchiectasis should be evaluated by an ENT-specialist to discard the presence of chronic rhinosinusitis and nasal polyposis.

**Title:** Influence of air pollution on symptoms of seasonal allergic rhinitis and bronchial asthma

**Authors:** Jadczak M, Rapiejko P, Lipiec A, Dzaman K, Jurkiewicz D

**Institution, city and country:** Military Institute of the Health Services, Warsaw, Poland

*Objective.* We sought to investigate the influence of air pollution on intensity of symptoms of allergic disease.

*Methods.* 350 inhabitants of Warsaw-Bielany district, allergic to birch and grass pollen allergens were included in the study. Their symptoms within the period between January and December 2002 were analysed. Mould spores and pollen count was concomitantly examined. Patients' symptoms score and moulds and pollen count was compared with measurements of gaseous pollutants and particulates concentration in the aforementioned district. The analyzed pollutants included: gaseous –CO, $CO_2$, $CH_4$, volatile organic compounds (VOCs), $NO_2$, $NH_3$, $SO_2$, $SO_4$, $H_2S$ and most dangerous respirable particles of 2.5 µm and smaller. Particulates are usually the most apparent from airpollution and often act as nuclei or absorbents for other atmosferic pollutans. Air pollution by chemical substances and particulates varied with time and depended on weather conditions and season of the year.

*Results.* The highest values of particulates fallout were observed in the last 10 days of August and September, what was the result of massive fires of forests and peatbogs in south-eastern Poland and Russia. Hazel pollinating season in 2002 in Warsaw started in January, whereas alder in the middle of February. Plant pollinating season in 2002 in Warsaw ended in October. In patients allergic to birch and grass pollens a clear correlation between pollen count and intensity of symptoms of allergic rhinitis and asthma was noticeable. Exacerbations of symptoms were also observed when the gaseous pollutants concentration was high.

*Conclusion.* Intensity of symptoms of allergy is strongly dependent on aeroallergens concentration. However, the influence of air pollution on exacerbation of those symptoms is noticeable.

**Title:** *Staphylococcus aureus* enterotoxin b aggravates allergic rhinitis and asthma in a mouse model

**Authors:** Hellings PW[1,2], Hens G[1,2], Meyts I[1], Bullens D[1], Van Oirbeek J[1], Gevaert P[4], Jorissen M[2], Ceuppens JL[1], Bachert C[4]

**Institution, city and country:** [1]Laboratory of Experimental Immunology, [2]Dept. of Otorhinolaryngology-Head and Neck Surgery, [3]Dept. of Internal Medicine, University Hospitals Leuven and [4]Dept. of Otorhinolaryngology, University Hospital Ghent, Belgium

*Background.* The role of *Staphylococcus aureus* enterotoxins (SAE) in airway inflammation remains largely elusive. In view of their superantigenic activity, SAE may activate inflammatory cells residing in the airway mucosa, eventually contributing to the manifestation of airway diseases like allergy and infection. We took advantage of a mouse model of allergic rhinitis and asthma to study the effect of nasal and bronchial contact with SEB on the allergic phenotype.

*Methods.* Male BALB/c mice were sensitized to ovalbumin (OVA) from day 1 till 13 on alternate days and subsequently exposed to aerosols containing either saline or OVA from day 33 till 37. Saline or 500 ng of *Staphylococcus aureus* enterotoxin B (SEB) was applied either into the nose or bronchi on days 33, 35 and 37. Mice were sacrificed on day 38 for analyses.

*Results.* Nasal application of SEB increased nasal as well as bronchial total inflammatory cell counts, as evaluated in nasal lavage (NL) and broncho-alveolar lavage (BAL) fluids and on H&E-stained histologic sections of nasal and bronchial mucosa. Differential cell counts showed a prominent nasal and bronchial eosinophilic influx by mucosal contact with SEB. Increased bronchial eosinophilia by nasal and bronchial application of SEB occurred together with enhanced expression levels of IL-4, IL-5 and IFN-γ. Also the expression levels of the so-called anti-inflammatory cytokines IL-10 and TGF-β, and chemokine eotaxin-1 were increased by SEB. Nasal application of SEB also enhanced the titers of OVA-specific IgE in serum. Interestingly, bronchial application of SEB increased not only bronchial but also nasal eosinophilia, suggestive of a systemic immune response following mucosal contact with SEB.

*Conclusion. Staphylococcus aureus* enterotoxin B induces airway inflammation in both nose and bronchi and aggravates the allergen-induced eosinophilic inflammation.

## 13:45-14:30 Special Lecture 2
## Verdi Room Leukotrienes in Upper Airways
## Chairperson: César Picado

**Author:** Bjermer L
**Institution, city and country:** Dept. of Respiratory Medicine and Allergology, University Hospital, Lund, Sweden

Cysteinyl leukotrienes ($LTC_4$,$LTD_4$ and $LTE_4$) are potent inducers of airway inflammation and the effect is mainly mediated through interaction with the $cysLT_1$ receptor, present on inflammatory and constitutive cells in the upper and lower airways. In order to understand the effect mediated by cysteinyl leukotrienes it is important to consider similarities and differeneces between the upper and lower airways. Moreover, leukotrienes are participating in a complex scenario of Eicosanoid related effects involving prostaglandins, leukotrienes and lipoxins. All these eicosanoids are using arachidonic acid as a main substrate and the pathophysiological effect may is not dependent on one single mediator, but more on the final composition of mediators produced.

The main effect by Cysteinyl leukotrienes in the nose seems to be induction of eosinophilic inflammation and nasal blockage, while phenomenon as itching and sneezing seems more related to the effect induced by histamine[1]. Provocation with LTD4 in the nose was found to be 5000 more potent then histamine in inducing nasal blockage[2]. This is consistent with the finding of CysLT1 receptors on inflammatory cells and on vascular endothelium in the nose.

Chronic rhinitis will eventually lead do nasal polyposis, especially when Aspirin intolerance is present. Patients with ASA intolerance (AI) have higher levels of Cys-LT's in nasal lavage and in Urine[3]. In contrast to ASA tolerant patients (NAI) both eosinophils and mast cells seems to be a major source of Cys-LT production and the numbers of Cys-LT1 receptors are strongly up regulated in AI patients (Data on file). PgE2 is produced through COX2 pathway and may counteract the effect by Cys-LT's. Interestingly, patients with nasal polyps have reduced numbers of COX2 positive cells and reduced tissue concentration of $PgE_2$ [4].

Lipoxines ($LTXA_4$ and $LTXB_4$) are formed through the 12 or 15-lipoxygenase pathway. There role is not fully understood, but are today believed to suppress or counteract the effect induced by Cys-LT's. In asthma they prevent eosinophilic chemotaxis and proliferation and promotes apoptosis, thus facilitating resolution of inflammation[5]. In AI patients, 15-LO is down regulated compared to NAI patients and controls.

Thromboxane A2 is another mediator with the ability to interact with the inflammatory response induced by Cys-LT's. $TXA_2$ and $LTD_2$ exhibit synergistic late allergen induced airway response[6], and the combination of an $TXA_2$ antagonist and the LTRA receptor antagonist Montelukast was shown to be very effective in preventing allergen induced bronchoconstriction in a human lung slice model[7]. Similar combined mode of action has been shown in an animal rhinitis model[8]. Thus to understand the role by Leukotrienes in airway inflammation and in the nose, it is also important to consider interactive influences by other eicosanoids involved.

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## 14:30-16:00 Oral Session 6
## Verdi Room Inflammatory mediators. Joint Session with the JMA Section
## Chairpersons: Peter Hellings (BE) and Philippe Gevaert (BE)

**Introductory Lecture 6. Eosinophils and IL-5 in upper airways. Dead or Alive?**
**Author:** Gevaert P
**Institution, city and country:** Ghent University Hospital, Ghent, Belgium

A vast majority of bilateral nasal polyps (NP) are associated with a prominent eosinophilic inflammation. Characterisation of NP suggests a central deposition of plasma proteins regulated by the subepithelial, mainly eosinophilic inflammation, as pathogenetic principle of polyp formation and growth. The accumulation and activation of eosinophils is favoured by the low concentrations of TGF- $\beta_1$ and overproduction of IL-5 and eotaxin in NP tissue. Although elevated IgE levels are found in NP, total IgE and IgE antibodies in NP tissue was unrelated to skin prick tests, but correlated with the degree of eosinophilia. In addition, we demonstrated the organisation of secondary lymphoid tissue in NP tissue and a polyclonal hyper-immunoglobulinemia E associated with the presence of IgE specific to *S. aureus enterotoxins*, colonization with *S. aureus,* and increased eosinophilic inflammation in a relevant subgroup of NP patients.
The ultimate way to test the role of IL-5 and eosinophils in the pathogenesis of nasal polyposis, is by antagonizing IL-5 in an interventional study in NP patients. We demonstrated shrinkage of nasal polyps in half of the verum-treated patients for up to four weeks after intravenous injection of a single dose of an anti-human IL-5 monoclonal antibody. When carefully analysing responders and non-responders, only those nasal polyps with elevated baseline levels of IL-5 in nasal secretions seemed to benefit from anti-IL-5 treatment. Remarkably, the degree of eosinophilia at baseline was not different between responders and non-responders. Our data show that at least in 50% of the nasal polyps, IL-5 and eosinophils play a key role (IL-5-dependent) in sustaining polyp size, whereas in the other group, eosinophilia may be more dependent on other factors (IL-5-independent). These insights in the regulation of IL-5 and eosinophilia in NP, (re-)open therapeutic perspectives in nasal polyposis based on eosinophil-selective targets.

**Title:** Eicosanoid metabolism and eosinophilic inflammation in nasal polyp patients with immune response to *Staphylococcus aureus* enterotoxins
**Authors:** Perez-Novo CA, Claeys C, Van Zele T, Van Cauwenberge P, Bachert C
**Institution, city and country:** Ghent University Hospital, Ghent, Belgium

*Background*. *Staphylococcus aureus* derived enterotoxins (SEs) have been implicated in the pathogenesis of airway inflammatory diseases, esp. nasal polyposis. However, the exact role of these molecules in the regulation of eicosanoid synthesis in this pathology remains unexplored.
*Objective*. We studied the possible impact of SE-induced immune responses on the eicosanoid production in nasal polyp (NP) patients.
*Methods*. Tissue sample homogenates from NP patients, with (NP-SEs(+)) and without detectable IgEantibodies to SEs (NP-SEs(–)) (ImmunoCap system), were assayed for IL-5, MPO, LTC4/D4/E4, LTB4, LXA4, total IgE and ECP.
*Results*. Inflammatory makers, eicosanoids and total IgE were significantly increased in NP-Ses(+) compared to NP-SEs(–) tissues, with the exception of MPO, which was similar in both groups. Eicosanoid concentrations correlated to IL-5 and ECP, however, only cysleukotriene levels correlated with IgE-antibodies to SEs, independently of allergy and asthma.
*Conclusions*. Eicosanoid synthesis is upregulated in polyp tissue of patients with immune response to SEs and seems to be related to the inflammatory reaction induced by these enterotoxins.

**Title:** Leukocyte populations and eosinophilic cationic protein level in nasal lavage from patients with persistent allergic rhinitis: correlation with symptom severity
**Authors:** Rondon C, Romero JJ, Rodriguez R, Lopez S, Antunez C, Torres MJ, Blanca M
**Institution, city and country:** Allergy Service and Research Laboratory, Carlos Haya Hospital, Málaga, Spain

*Background*. The aim of this study was to analyse the possible correlations between symptom severity, cell populations and ECP level in nasal lavage of patients with persistent allergic rhinitis (PER).
*Methods*. The study included 24 patients with PER due to Dermatophagoides pteronyssinus and 18 healthy controls. Exclusion criteria were: Immunological disease, chronic sinusitis, nasal polyposis, respiratory infections during the previous month, and treatment with corticosteroids or antihistamines during the previous three weeks. Nasal symptoms (blockage, rhinorrhea, itching and sneezing) were scored for seven days prior to nasal lavage, using the following scale: 0-no symptoms, 1-mild, 2-moderate, and 3-severe. The PER severity was expressed as total nasal score (TNS) and was classified as Mild (0-4), Moderate (5-8), or Severe (9-12). ECP and cell phenotype were measured by CAP-FEIA and nasal flow cytometry (NFC), respectively.
*Results*. The most frequent symptoms were rhinorrhea and sneezing (95.8% of cases). TNS showed a significant positive correlation with lymphocyte ($r = 0.51$; $p < 0.05$) and CD4 T cells ($r = 0.57$; $p = 0{,}007$), but no significant association with neutrophils or ECP. Patients with severe TNS had a significant negative correlation between ECP and eosinophils ($r = 0.82$; $p < 0.05$).
*Conclusions*. In nasal lavage from patients with PER, the severity of the symptoms showed a positive correlation with lymphocytes, CD4 T-cells, neutrophils and ECP, and a negative correlation with eosinophils. The negative correlation between eosinophils and ECP in nasal lavage could be related to an increased cytolysis and apoptosis of intraluminal eosinophils and/or a lack of transepithelial migration, as has been reported by others for rhinitis and nasal polyposis.

**Title:** Surgical therapy of nasal polyposis has no influence on the postoperative production of cytokines
**Authors:** Wagenmann M, Mansour N, Chaker A
**Institution, city and country:** HNO-Klinik, Universität Düsseldorf, Germany

*Background.* The amount of cytokine production in nasal polyposis not only correlates with the preoperative situation and the inflammatory status but also with the postoperative outcome.
*Objectives.* To analyze this interrelation further, we prospectively investigated the production of Th1- and Th2-cytokine production in nasal mucosa after endoscopic sinus surgery for 6 months in 25 patients with bilateral nasal polyps.
*Methods.* Preoperatively, as well as 1, 2, 3, and 6 months postoperatively nasal curettages were performed in the middle meatus and the production of cytokines in the harvested cells was quantified using ELISPOT-assays. Additionally, clinical parameters (symptomscores, polyp scores (Lildtholt 1997)) were recorded. Data was analyzed with non-parametric statistical tests (One-way ANOVA, Bonferroni's multiple comparison test).
*Results.* From the first to the sixth postoperative month, symptomscores were significantly improved ($p < 0.001$), and polyp scores were significantly reduced ($p < 0.001$). At all timepoints the production of the cytokines IL-4 and IFN-γ was detectable in all samples. But unlike the clinical parameters we observed no significant changes in the number of cytokine producing cells at all timepoints ($p > 0.5$).
*Conclusions.* These results underline the relevance of the chronic inflammatory nature of nasal polyps since the increased production of central cytokines persists despite an amelioration of the symptoms and a reduction of polyp scores. This points to the importance of anti-inflammatory treatment even after clinically successful surgery of nasal polyps.

**Title:** The expression of endothelial L-selectin ligands in nasal mucosa and nasal polyps in patients with nasal polyps
**Authors:** Toppila-Salmi S, Ebbens FA, Renkonen J, Renkonen R, Mullol J, van Drunen CM, Fokkens WJ
**Institution, city and country:** Dept. of Otorhinolaryngology, Tampere University Hospital, Tampere, Finland, Dept. of Otorhinolaryngology, Academic Medical Center, Amsterdam, The Netherlands, Dept. of Bacteriology and Immunology, University of Helsinki, Helsinki, Finland, Rhinology Unit, Dept. of Otorhinolaryngology, Barcelona, Spain

*Background.* Nasal polyps are characterized by abundant presence of leukocytes. L-selectin on leukocytes and its endothelial glycosylated ligands initiate leukocyte infiltration into inflamed tissues.
*Objective.* The aim was to study the expression of functionally active endothelial L-selectin ligands in nasal polyps and sinus mucosa in different patient subgroups. Secondly, the correlation between the expression of functionally active endothelial L-selectin ligands and the number of leukocytes was studied.
*Methods.* Nasal polyp or nasal mucosal specimens (99) from different subgroups of nasal polyposis and 25 nasal mucosal specimens from normal subjects were immunohistochemically stained with monoclonal antibodies against different subtypes of leukocytes. Vessels were stained with monoclonal antibodies against CD34 together with functionally active glycan-decorated L-selectin ligands (sialyl Lewis x; mAb HECA-452 or sulphated extended core 1 lactosamine; mAb MECA-79). The number of positive leukocytes and vessels are expressed per $mm^2$.
*Results.* The percentage of mAb MECA-79+ vessels was significantly decreased in antrochoanal polyp tissue compared to polyp tissue from patients with or without cystic fibrosis diagnosis. Interestingly, the number of mAbMECA-79+ vessels correlated significantly with the number of neutrophils and basophils but not eosinophils, mast cells, and macrophages in lamina propria of "normal" polyp. Our results suggest that functionally active L-selectin ligands expressed in polyp tissue might guide leukocyte traffic into polyps thus contributing to the aggravation of the inflammation. Endothelial sulfated sialyl Lewis x glycans are highly expressed in nasal mucosa and polyp tissue from different origin, except antrochoanal polyps.
*Conclusion.* Thus, the pathogenesis of antrochoanal polyps might differ from that of "normal" polyps.

## 16:30-17:30 Symposium 3
### Verdi Room The Sense of Smell in upper airway diseases
### Chairpersons: Nancy Rawson (USA) and Joaquim Mullol (E)

**Title:** Epidemiologic study of olfaction in the Catalan population. OLFACAT Study
**Author:** Alobid I
**Institution, city and country:** Rhinology Unit, ENT Dept., Hospital Clínic, Barcelona

*Introduction.* The sense of smell plays an important role in determining the flavour and palatability of foods and beverages, as well as in the warning of fire, toxic vapors, and spoiled foodstuffs. Their dysfunction has been associated with aging and with a broad range of diseases and anomalies. Few epidemiologic studies evaluate the status of olfaction in the general population. The aim of this study was to analyze the state of the sense of smell in the Catalan population.
*Material and methods.* four microencapsulate odorants (rose, banana, musky, and mercaptan) were included in a smell survey sent through a local newspaper to 260,000 Catalan homes. Demographic information (15 questions) and an odour questionnaires were included.
*Results.* 10783 surveys (4%) were answered and returned. More women (65.5%) than men (34.5%) answered the survey. The survey profile was a woman of 43 years with medium-high educational level and living in a city. Women detected and correctly identified the odours more than men. Anosmia was reported by 0.5% of population and hyposmia by 17%. All 4 odours were detected by 75% of population but only 25% identified all of them. Odours detection showed a mean age-related decline. Memory and identification of odors increased through fourth decade and then decline at sixth decade. Factors associated with the risk of anosmia were: gender for detection, and mean self-rated smell ability for memory; and self-rated smell ability and head injuries for identification. Factors associated with risk of hiposmia were: gender, age, self-rated smell ability for detection; all of these and allergy and smoking for memory; and gender, age, allergy, and self-rated smell ability for identification.
*Discussion.* these results suggest that: a) The sense of smell is better in women than in men; b) One of each five people has smell alteration; c) Odour detection has an age-related decline, mainly after 50 years; and d) Identification and memory of odours increase up to 40 years suggesting an important educational pattern.

**Title:** Psychophysical and behavioral perspective
**Author:** Hummel T
**Institution, city and country:** Smell & Taste Clinic, Dept. of ORL, University of Dresden Medical School, Fetscherstrasse 74, 01307 Dresden, Germany

Olfactory disorders are common in the general population, but research on consequences and treatment of these disorders has been lacking. Not until recently, when standardized tools for assessment of olfactory loss and changes in quality of life due to olfactory disorders have become available, have systematic investigations been conducted. This paper presents the most important roles that olfaction plays in humans, it describes olfactory disorders with respect to definitions, etiologies, diagnosis and treatment, and reviews the scientific literature on consequences of olfactory disorders. Current data suggest that quality of life, regarding safety issues and interpersonal relations, as well as food behavior/nutritional intake are severely altered in a large proportion of patients with olfactory disorders.

**Title:** Basic Research Perspective: Cell biology of Olfactory Loss in Rhinosinusitis

**Authors:** Rawson NE, Yee KK, Pribitkin E, Cowart B
**Institution, city and country:** Monell Chemical Senses Center, Philadelphia, PA USA, Thomas Jefferson University, Dept. of Otorhinolaryngology, Philadelphia, PA USA

*Background*. Chronic rhinosinusitis (CR) affects at least 33 million people each year and is a significant cause of olfactory dysfunction in these individuals. Under normal conditions, inflammation may occur as a healthy response to nasal infections or injuries. However, in a subset of people, this inflammation leads to a chronic condition in which the inflammatory process persists after recovery from the overt infection or injury. In these situations, the degree of tissue damage may exceed the ability of the olfactory system to recover and odor perception is impaired. Some of these patients may be temporarily aided by topical or systemic steroid treatment,or surgery, but these approaches are of limited efficacy and carry associated risks. Currently there is no effective cure for this disease.
*Objective*. To understand the cellular and molecular mechanisms underlying olfactory epithelial damage in CR and to identify a profile of inflammatory mediators, cell biological and clinical characteristics to enable predictions of olfactory recovery with treatment and identify therapeutic targets for individuals not responsive to current approaches.
*Methods*. We use a multidisciplinary strategy to study the morphological, neuronal and inflammatory changes in the olfactory mucosa of CR patients. Baseline and post-treatment data are obtained on medical status, nasal anatomy and mucus motility, olfactory abilities and lifestyle/exposure history of patients with CR. Anatomical and airflow data will be used to model odor deposition and transport.
*Results*. Immunocytochemistry for markers of proliferation and differentiation indicate that basal cell division continues, with some differentiation to mature olfactory neurons. However, a superficial layer of keratinized epithelium appears to block normal extension of neuronal dendrites to the lumenal surface.
*Conclusions*. These studies will help illuminate the mechanisms underlying regeneration in the olfactory system and suggest targets for therapy aimed at ending the non-reactive inflammatory cycle. Funded in part by NIH DC006760 and DC000014.

## 16:30-17:30 Symposium 4
## Rossini Room The role of infection in Rhinosinusitis: fungi or enterotoxins?
## Chairpersons: Glencis Scadding (UK) and Herbert Riechelmann (G)

**Title:** The fungal hypothesis
**Author:** Ponikau J
**Institution, city and country:** Gromo Institute for Airway Inflammation, USA

This presentation will focus on the role of certain airborne fungi in inducing the eosinophilic inflammation in CRS.
We are basing our new understanding of the role of fungi in the pathophysiology of CRS on the following findings:
- CRS is strongly associated with an eosinophilic inflammation.
- Patients as well as healthy controls nasal and sinus secretions are colonized with fungi.
- The immune system (lymphocytes) in patients, but not healthy controls, react to certain fungi with the production of cytokines, which elicit the eosinophilic inflammation.
- This abnormal immune response occurred regardless from the allergy status of the patient.
- The same fungi induced the degranulation of eosinophils.
- The degranulation activity is induced by a 60 kDa antigen from Alternaria alternata, is highly heat labile, and works protease dependant through a G protein-coupled receptor
- Eosinophils in CRS patients migrate into the mucus and target fungi *in vivo*.
- During that attack, eosinophils release toxic proteins onto the fungi, which also erodes the epithelium and explains the secondary bacterial infections.
- This attack is reproducible *in vitro*, but dependant on a signal from CRS patients' PBMCs. Healthy control PBMCs lack this signal.
- Intranasal antifungal medication reduce the patients symptoms, the inflammatory thickening of the mucosa and the eosinophilic inflammation.

**Title:** The enterotoxin hypothesis
**Author:** Bachert C
**Institution, city and country:** University of Ghent, Belgium

**Abstract not available**

**Title:** Treatment of infections in Rhinosinusitis. The future
**Author:** Stierna P
**Institution, city and country:** Professor, Dept. of Otorhinolaryngology, Karolinska University Hospital, Huddinge, Stockholm, Sweden

Rhinosinusitis may precipitate from a viral common cold probably in a subgroup of patients with a co-morbid mucosal disease but is still relatively rare at least presenting as a purulent infectious sinusitis. For acute sinusitis the bacteriology and their role in induction is established. Bacteria, respiratory viruses of fungi may also influence individual responses by either causing infection or by colonization and thereby through individual immune responses perpetuate the events of sinusitis. The persistence of the inflammatory response in sinusitis is not only dependent on individual differences in host immune responses, but also on specific influence of these responses by local microbes. Understanding and differentiating infectious and non-infectious inflammatory stimuli are critical to understanding sinusitis. The bacteria complicate the chronic sinusitis process by being opportunistic or colonizing and as may be seen from latest years of research on fungus and S. aureus colonization. Emerging data speaks towards aberrant immune responses and locally reduced host defence, as major factors in the pathogenesis of chronic tissue pathology in long-standing sinusitis. Experimental data from treatment with glucocorticosteroids indicate that these may have strong antibacterial effects being dose-timing dependent in relation to take, initiation, plateau and resolution of the specific microbial infection. This knowledge may also open avenues for more specific anti-inflammatory and anti-allergic treatment exhibiting anti-bacterial properties such as for example specific decoy oligodeoxynucleotides.

**17:40-19:00 Symposium in Spanish**
**Verdi Room Rhinitis and Rhinosinusinusitis research in Spain. Simposio Conjunto de los Comités de Rinitis de la SEAIC y de Rinología y Alergia de la SEORL/Joint Symposium of the Rhinitis (SEAIC) & Rhinology (SEORL) Committees**
**Chairpersons: Ignacio Antépera (E) and Joan Ramon Montserrat (E)**

**Title:** ARIA classification of rhinitis depending on its severity
**Author:** Sastre J
**Institution, city and country:** J. Sastre on behalf ESPRINT Study group, Fundación Jiménez Diaz, Servicio de Alergia, Madrid, Spain

*Background.* The recent Allergic Rhinitis (AR) and its Impact on Asthma (ARIA) recommendations have proposed a new classification for severity of AR. It is subdivided in mild or moderate-severe on basis on several criteria mostly related with parameters used in quality of life (QOL) questionnaires.
*Aim.* In a study (ESPRINT) to evaluate a new questionnaire of QOL in Spanish population with AR the new ARIA classification on severity of AR was compared with several aspects of QOL items. To explore the possibility to split moderate and severe on basis of QOL itmes affected. To investigate if any QOL parameter is more relevant to classify severity of the disease
*Material and methods.* 1-2 QOL items affected were considered as moderate rhinitis, 3 or 4 affected were considered as severe rhinitis.
*Results.* 399 patients with AR were included in the analysis. 60% of patients had persistent AR and 40% intermittent AR. Number of patients with none, one, two, three and four affected items of QOL questionnaire were as follow: 12 (3,0%),58 (14,5%),95 (23,8%),115 (28,8%) and 119 (29,8%) respectively. Classification on severity according to ARIA and ESPRINT study related with frequency of symptoms are shown in table 1 and 2. Classification on severity according to ESPRINT study are shown in table 2. Around 60% of patients had affected 3 or 4 QOL items.
*Conclusion.* it is possible to split moderate and severe AR on basis of number of QOL items affected.

**Title:** Rhinitis and Exercise
**Author:** Valero Santiago AL
**Institution, city and country:** Unidad de Alergia, Servicio de Neumología y Alergia Respiratoria, ICT, Hospital Clínic i Universitari de Barcelona, España

Previous studies have reported that exercise causes a decrease in nasal resistance in both healthy subjects and in patients with rhinitis. This change appears to be mostly account for a nasal vasoconstrictor response that results in a decrease in the volume of venous sinusoids. Vasoconstriction occurs both when the subject breathes through the nose and through the mouth. Moreover, isocapnic hyperventilation does not induced vasoconstriction. These findings suggest that vasoconstriction of nasal vessel is not due either to local reflexes or to the increased ventilation during exercise. The change in nasal resistance takes place immediately after the beginning of exercise and goes back to baseline values within 30 to 40 minutes. The magnitude of the change in nasal resistance is proportional to the intensity of exercise: the bigger the effort, the greater the change.
In contrast to the nose, exercise-induced bronchoconstriction usually occurs in asthma patients. The concept of "united airways" is based on the notion that both asthma and rhinitis share common mechanisms. It is still unclear why the response of the nose and of peripheral airways is so disparate in patients with rhinitis and with asthma. This finding appears to be one exception of the "one airway, one disease" theory.

**Title:** Mucociliary pathology in the nose and paranasal sinuses
**Author:** Armengot M
**Institution, city and country:** Hospital General Universitario, Facultad de Medicina, Valencia, Spain

Mucociliary system is one of the most important local defence mechanisms of respiratory tract. Several noxas, including microorganisms that penetrate with respiratory airflow are deposited in the nasal mucosa. Mucociliary flow carries these dangerous elements to the digestive tract where they are eliminated. Also, the mucociliary flow lets the paranasal sinuses to be health and provides fresh and clean mucus to nasal mucosa.
Mucociliary dysfunction generates stasis of airway secretions and this allows microorganism's proliferation and respiratory infection. Alterations can affect cilia o secretions and can be congenital or acquired. Early diagnosis of congenital mucociliary dysfunction provides possibility of treatment from childhood and to avoid or delay chronic and irreversible damages, as bronchiectasis or chronic sinusitis.
Diagnosis of mucociliary diskinesia is of interest and is mostly based on studies of mucociliary transport, ciliary beat frequency and ultraestructure. Nasal fosse are of many interest for these studies, because easy accessibility.

**Title:** Regulation of mucus nasal secretion
**Author:** Roca-Ferrer J
**Institution, city and country:** IDIBAPS, Hospital Clínic, Barcelona, Spain

Nasal secretions are originated from glandular structures, plasma exudation, and structural and inflammatory cells. Nasal secretions play a prominent role humidifying and cleaning the inspired air.
In physiological conditions mucus secretion is under the control of a variety of mechanisms, but parasympathetic and sensory nervous system seem to exert the prominent role. However, during inflammatory diseases, such as allergic rhinitis and chronic rhinosinusitis, several mediators released by structural and inflammatory cells also regulate nasal hypersecretion.
The mucus secretion is stimulated directly by some neuropeptides and neurotransmitters released by parasympathetic and sensory nerves. Parasympathetic activity is also stimulated by sensory nerves, histamine and inflammatory cell derived proteins such as the major basic protein (MBP). Despite the mechanism is still not well known, during viral infections the mucus secretion is increased by cholinergic mechanism. Several arachidonic acid metabolites and cytokines released by structural and inflammatory cells stimulate the glandular secretion. Other inflammatory cell derived proteins such as elastase and eosinophil cationic protein (ECP) also stimulate the mucus secretion.
The treatment of diseases associated with nasal hypersecretion includes corticosteroids, antihistamines, and anticholinergic drugs. They act through several mechanisms such as directly inhibiting the glandular secretion (blocking muscarinic receptors or dismissing the mucus production/secretion), and inhibiting the effect of segregagogues (decreasing the inflammatory mediators production/secreti on, reducing inflammatory cell infiltration, upregulating enzymes that degrade proinflammatory proteins).
In conclusion, the study of the regulation of mucus secretion in health and disease will be very useful in order to improve the current therapies of upper airway inflammation.

## 9:00-10:30 Oral Session 7
## Verdi Room Chronic Rhinosinusitis and Nasal Polyps. One or two deseases?
## Chairpersons: Claus Bachert (BE) and Herbert Riechelmann (G)

**Introductory Lecture 7. Chronic rhinosinusitis and nasal polyps. One or two diseases?**
**Author:** Riechelmann H
**Institution, city and country:** University of Ulm, Germany

Clinical manifestations of rhinosinusitis include acute rhinosinusitis, chronic rhinosinusitis (CRS) with nasal polyps and CRS without polyps. It is unclear, whether CRS with nasal polyps and CRS without nasal polyps represent different diseases or just different stages of one single disease. In three independent prospective clinical studies, various cytokines and cell differentiation markers were compared in nasal secretions and mucosal specimens of individuals without rhinosinusitis, of patients with acute community acquired rhinosinusitis, and of CRS patients with and without polyps. Irrespective of the clinical manifestation, all biomarkers assessed were increased in patients with rhinosinusitis when compared with controls. Moreover, a Th1 skewed inflammation was consistently found in acute rhinosinusitis and CRS without polyps, whereas patients with CRS and nasal polyps revealed a Th2 pattern of inflammation. Although not evidentiary, clinical characteristics, immunohistochemical features and cytokine profiles suggest that chronic CRS with and without nasal polyps represent two different disease entities.

**Title:** Systemic and local immunoglobuline production in chronic rhinosinusitis with and without nasal polyps

**Authors:** Van Zele T, Gevaert P, Holtappels G, Van Cauwenberge P, Bachert C

**Institution, city and country:** University Hospital Ghent, Ghent, Belgium

*Background*. Chronic rhinosinusitis with nasal polyps is a persistent inflammation characterized by a local hyper-immunoglobulinemia E and the presence of specific IgE to *Staphylococcus aureus* enterotoxins (SAE).
*Objective*. We aimed to study the systemic and local production of other immunoglobulines (A, G and M) in relation to plasma cells, B cells and specific IgE to SAE.
*Methods*. Concentrations of IgE, IgG, IgM, IgA (immunonefelometry) and specific IgE to SAE (Uni-CAP) were determined on tissue homogenates and serum from 18 chronic rhinosinusitis patients with nasal polyps (NP), 13 chronic rhinosinusitis without nasal polyps (CRS) and 13 control patients. Tissue cryo-sections were stained for CD20 and CD138.
*Results*. IgA, IgG and IgE concentrations were significant higher in tissue homogenates of NP compared to CRS and controls. No significant differences were observed in serum levels of IgG, IgA, IgM and IgE between the three groups. NP with specific IgE to SAE had significant higher concentrations of IgG and IgE than those without specific IgE production. Furthermore plasma cell counts (CD138+) were significantly higher in NP tissue compared to controls or CRS.
*Conclusions*. The difference in IgE, IgG and IgA expression between nasal polyp tissue and serum together with increased numbers of plasma cells suggest a local production of these immunoglobulins in NP. The presence of a local immune response to SAE is associated with a higher production of IgE and IgG, but not IgM, indicates a chronic microbial trigger, reflecting the possible influence of SAEs Ig production and Ig switching.

**Title:** Local and systemic impact of bacteria on granulocyte activation in asthmatics with chronic rhinosinusitis

**Authors:** Kalogjera L, Vagic D, Bukovec Z, Baudoin T, Grbac I

**Institution, city and country:** Dept. of ORL Head & Neck Surgery, Endocrinology Lab, Dept. of Pulmonology, University Hospital Sestre Milosrdnice, Zagreb, Croatia

*Background*. Although bacteria are often isolated from chronically inflammed sinuses, their role in pathogenesis and persistence of inflammation is not clear. Serum levels of eosinophil cationic protein (ECP) are elevated in asthma exacerbations compared to remission period. It is suggested that some bacterial antigens may have negative impact on lower airways in the united airway disease.
*Objectives*. The aim of the study was to compare markers of activations of eosinophils and neutrophils in the serum and maxillary sinus fluid of asthmatic patients with chronic maxillary sinusitis in respect of bacterial isolates from the sinuses.
*Methods*. Levels of ECP (fluoroenzyme immunoassay) and myeloperoxidase (MPO) (radioimmunoassay) were analysed in the the serum and sinus lavages of 18 patients with mild to moderate stable asthma, and chronic rhinosinusitis ( > 3 months symptoms with > 10 mm mucosal thickening in maxillary) and poor response to long-term conservative (antibiotic/topical steroid treatment Following inferior antral puncture lavages (5 cc saline) and swabs were taken and cultivated for aerobic and anaerobic growth. Patients with acute exacerbation of rhinosinusitis, nasal polyposis and systemic steroid treatment were excluded.
*Results*. Bilaterally sterile samples were found in 6, commensals in 1, and pathogens in 11 patients (3 unilaterally, 9 bilaterally), *Staphylococcus aureus*, followed by anaerobes and Pseudomonas aeruginosa were most often isolates. Serum ECP level (22,1 ± 14,6 *vs*. 6,82 ± 2,34 mcg/l) was significantly higher in patients where pathogens where isolated (p = 0,025), while MPO was not (413,61 ± 256,62 *vs*. 266,61 ± 171,34). However, MPO levels where significantly higher in the infected sinus lavages (p = 0,004), while ECP was not, although correlation between ECP and MPO in the infected sinus lavages was significant (r = 0,65, p = 0,002).
*Conclusions*. These results suggest that bacterial presence in the chronically inflammed sinuses may a) have impact on local neutrophil activation, b) elevate systemic marker of asthma severity, even in the stable stage of the disease.

**Title:** Epidemiology of Nasal Polyps - The Skövde Population-Based Study
**Authors:** Johansson L, Brämersson A, Holmber K, Melén I, Bende M
**Institution, city and country:** Dept. of Oto-Rhino-Laryngology, Central Hospital, Skövde, Sweden

*Objective.* To investigate the prevalence of nasal polyps in an adult Swedish population in relation to age, gender, asthma, and aspirin intolerance.
*Methods.* A random sample of 1900 inhabitants over the age of 20, stratified for age and gender, was drawn from the municipal population register in Skövde, Sweden, in December 2000.
*Results.* 1378 was investigated and 38 (2.7%) of them had nasal polyps (NPind) found by nasal endoscopy. OR asthma *vs.* not asthma was 5.20 [95 % CI 2.48; 10.89] and OR men *vs.* women was 2.70 [95% CI 1.33; 5.50]. The NPind was compared with the clinical patterns of 44 patients with nasal polyp disease (NPpat). Further comparisons were made with 38 matched controls from the general population based study without nasal polyps (Cind). Upper and lower airway symptoms were registered. Polyp size, peak-nasal inspiratory flow (PNIF), olfactory function, measured by the Scandinavian Odor-Identification Test (SOIT) was investigated. The NPpat experienced more symptoms of nasal blockage, reduced sense of smell, more extensive polyps, reduced PNIF compared to the NPind. On the other hand had the NPind more frequent symptoms of asthma, reduced sense of smell, aspirin intolerance, and reduced olfactory capability compared to the Cind.
*Conclusion.* The overall prevalence of nasal polyps was 2.7 %. The most predictive factor for nasal polyps was increasing age followed by asthma. The co-existence with asthma symptoms, reduced sense of smell indicates that these nasal polyps may be a significant component of a general respiratory disease.

**Title:** Nitric oxide: a new concept in chronic rhinosinusitis pathogenesis.
**Authors:** Naraghi M, Farajzadeh Deroee A, Ebrahimkhani MR, Kiani S, Dehpour AR
**Institution, city and country:** Dept.s. of Otorhinolaryngology & Pharmacology, Tehran University of Medical Sciences, Tehran, Iran

*Background.* Nitric oxide (NO) has variety of effects in nasal cavity and pathophysilogy. NO in nasal cavity seems to play an important role in inflammation. NO is increased in common cold but decreased in acute and chronic rhinosinusitis (CRS). Although iNOS expression is increased in Nasal Polyposis (NP), NO is paradoxically decreased in NP.
*Objectives.* We hypothesized that NO and NO metabolites are increased in CRS inside the sinus cavity and pathologic events may be due to this increment.
*Methods.* This study was performed on 37 cases in 3 groups: 1-Control (n = 12), 2- CRS patients with NP (n = 14), 3-CRS patients without NP (n = 11). Group 1 was patients underwent Functional Endoscopic Sinus Surgery (FESS) due to any other reason than rhinosinusitis. Groups 2&3 were patients who did not respond to medical therapy and underwent FESS. The maxillary sinuses of groups were lavaged with sterile distilled water during FESS and NO metabolites were measured in the lavage fluid.
*Results.* NO metabolites level (mean ± SEM) was 8.08 ± 1.43 µmole/l in the lavage fluid of the control group and 18.04 ± 3.51, 16.78 ± 2.91 µmole/l in group 2&3 respectively which were higher than the control group (P 1 *vs.* 2 < 0.01 and P 1 *vs.* 3 < 0.01). The difference between groups 1&2 was not significant (p = 0.12)
*Conclusions.* NO production is increased in 2 major variants of CRS due to inflammatory cells in sinus cavity. Secretions and inflamed mucosa of sinus inhibit diffusion of gaseous NO to the air-filled sinus cavity. Additionally, ostial obstruction does not allow NO to reach nasal cavity. This high amount of NO dissolves and metabolizes in the sinus. These all cause a decrease in nasal gaseous NO in CRS despite of increased levels of NO production. NO seems to play an important role in creating the vicious cycle of CRS pathogenesis.

## 11:00-12:00 Symposium 5

**Verdi Room** **Functional Genomics and Proteomics in Rhinology Research. Joint Symposium with the Interest Group on Genomics and Proteomics**

**Chairpersons:** Mikael Benson (SE) and Marek Kowalski (PL)

**Title:** Microarray research in rhinology
**Author:** Benson M
**Institution, city and country:** Dept. of Pediatrics, Queen Silvia Children's Hospital, Göteborg, Sweden

DNA microarray technology permits simultaneous analysis of expression of all genes. Potentially, this could help to identify new genes, pathways and disease mechanisms. DNA microarray studies of nasal biopsies and cells from patients with intermittent allergic rhinitis have shown increased expression of "new" pro-inflammatory genes that are not often described in the context of Th2-mediated diseases. By contrast, other studies have described decreased expression of anti-inflammatory genes, for example uteroglobin. This gene has also been implicated in microarray studies of nasal polyposis. The large number and functional diversity of genes identified in DNA microarray studies leads to the question if it is possible to gain an overall functional understanding of the complex pathogenic mechanisms. One approach to may be to search for groups of functionally related genes. The underlying assumption is that if many genes of the same function move in the same direction the likelihood of biological relevance increases. For example, decreased expression of an anti-inflammatory pathway was described in allergic rhinitis. Large-scale studies of cancer indicate that it may be possible to develop disease models that simultaneously describe many different pathways. It remains to be seen if this can be applied to rhinology. Another approach is to search for gene expression signatures that serve as "diagnostic fingerprints". This was recently applied in a study of nasal epithelium from patients with asthma. It is possible that new bioinformatic methods will simplify analysis of DNA microarray data and that this will increase the use of microarray technology in rhinology.

**Title:** Disease Phenotyping
**Author:** Brutsche M
**Institution, city and country:** Universitätsspital Basel, Basel, Switzerland

There is a complex relationship between genotype and phenotype, which complicates the molecular investigation of complex genetic disorders like rhinitis/rhinosinusitis and asthma. The precise definition of phenotype(-s) used in molecular studies are not rarely decisive for the overall study outcome. Every investigator will sooner or later make this experience. It is, therefore, important to reflect on the genotype-phenotype problem before conducting the study. Different examples including the particular situation of atopy and asthma are discussed to illustrate this problem. Four different strategies are discussed to overcome falsely negative phenotype-genotype interactions: 1. to test different phenotypes simultaneously, 2. to adopt laboratory-based phenotypes, 3. to analyse mechanism-based phenotypes, and 4$^{th}$ to go for gene expression/proteomic-based phenotypes.

**Title:** Challenges in Proteomics
**Author:** Bischoff R
**Institution, city and country:** University of Groningen, Centre of Pharmacy, Dept. of Analytical Biochemistry, Antonius Deusinglaan 1, 9713 AV Groningen, The Netherlands

Proteomics research, as practiced today, has opened many possibility for the discovery of disease-relevant proteins. However, proteomics technology is still not able to display a complex proteome of a mammalian cell, tissue or whole organism in a comprehensive manner. This is due to the enormous dynamic range of protein concentrations, especially in body fluids, and the wide variety of physico-chemical properties of proteins ranging from integral membrane proteins to highly complex glycoproteins.

In order to tackle this problem, there is an ongoing development in the area of proteomics technology beginning with better sample preparation and continuing with separation and mass spectrometric detection and identification. While two-dimensional gel electrophoresis was the method of choice in proteomics for a long time, it is slowly being replaced by techniques like multi-dimensional HPLC-MS[1], chip-based mass spectrometry[2] and affinity-based enrichment and detection techniques like protein arrays[3]. Still none of these methods allow full coverage of a complete proteome and the choice of methodology for a given biological problem is crucial.

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## 12:00-13:30 Symposium 6
## Verdi Room Eicosanoids in rhinitis and rhinosinusitis: prostaglandins or leukotrienes?
## Chairpersons: César Picado (E) and Leiff Bjermer (SE)

**Title:** Lipoxygenase pathways
**Author:** Kowalski ML
**Institution, city and country:** Dept. of Immunology, Rheumatology and Allergy, Medical University of Lodz, Lodz, Poland

Cysteinyl leukotriens generated on lipoxygenase pathway of arachidonic acid metabolism have been identified in the nasal mucosa and nasal secretions and tend to be generated in increased amounts in the tissue from patients with rhinitis and rhinosinusitis suggesting their potential role in the pathogenesis of nasal inflammation and symptomatology. Leukotrienes have been proposed to play a pivotal role in patients with aspirin-sensitive rhinosinusitis and nasal polyps. Basal levels of peptidoleukotrienes in the urine of ASA-sensitive patients are elevated, and further increase during ASA-induced reaction. LT1 receptors are over expressed in the nasal mucosa of ASA-sensitive patients , and are down-regulated following desensitization with aspirin, suggesting that their over expression may contribute to the mechanism of ASA-sensitivity[1]. On the other hand leukotriene antagonists only partially prevent ASA-induced reactions and are not more effective in improving bronchial or nasal symptoms in ASA-sensitive than in ASA-tolerant patients thus questioning the pivotal role of leukotrienes in this form of rhinosinusitis[2].

More recent observations indicate, that 15-lipoxygenase pathway may be also involved in the pathogenesis of chronic rhinosinusitis . Lipoxin A4 and 15-HETE are released from airway epithelial cells or nasal polyps fragments and 15-HETE generation further increases following aspirin challenge in ASA-hypersensitive patients suggesting potential role for 15-lipoxygenase metabolites in the pathophysiology of rhinosinusitis[3,4] Development of more specific and potent antagonists of lipoxygenase pathways may be important for further assessment of contribution of LOX metabolites to the pathogenesis of rhinitis and rhinosinusitis

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**Title:** The Cyclo-oxygenase Pathway
**Author:** Picado C
**Institution, city and country:** Servei de neumologia, ICT, Hospital Clínic, Barcelona, Spain

In some asthma patients, non-steroidal anti-inflammatory drugs (NSAIDs) can induce bronchospasm, rhinorrhea and nasal obstruction. These reactions seem to be caused by the inhibition of cyclo-oxygenase 1 (Cox-1), which in turn activates the lipoxygenase pathway; this thus increases cysteinyl leukotrienes (Cys-LT) released, responsible for bronchospasm, rhinorrhea and nasal obstruction. With regard to the metabolism of arachidonic acid in NSAID-intolerant asthmatic patients, the following changes have been observed in the Cox pathway: 1) A low production of prostaglandin $E_2$ ($PGE_2$); 2) a deficient Cox-2 regulation, and 3) a reduced production of metabolites (lipoxins) released through the trans-cellular metabolism of arachidonic acid. Up to now, there is no explanation to connect these observations, although an anomaly in the regulation of Cox-2 may probably explain part of it. The reduced activation of Cox-2 is certainly responsible for the low production of $PGE_2$. Given that $PGE_2$ controls Cys-LT production, it is possible that the increased Cys-LT synthesis in asthmatics intolerant to NSAIDs is partly due to the low production of $PGE_2$. It may be that in these patients Cys-LT synthesis is controlled, although ineffectually, by Cox-1, which would explain the sudden release of Cys-LT after being inhibited by an NSAID. This could also explain why inhibition of Cox-2 does not cause bronchospasm. Since the enzyme is not activated, it has no controlling effect over the synthesis of Cys-LT and, therefore, its inhibition causes no such release. Finally, the reduced production of lipoxins in NSAID-intolerant asthmatics could also result either from the down-regulation of Cox-2 or from an altered sensitivity of this enzyme to the effect of NSAID in these patients.

**Title:** Aspirin Desensitization
**Author:** Scadding G
**Institution, city and country:** Royal National Throat, Nose and Ear Hospital, London, UK

Patients with aspirin sensitive nasal polyps and asthma are often difficult to treat by standard anti- inflammatory therapy with or without surgery. Aspirin sensitive patients exhibit a refractory period after aspirin challenge ,during this time no further deterioration occurs in their condition.

Oral aspirin desensitisation has been shown to be effective in reducing symptoms and the need for operation, hospital admission and oral corticosteroids. High dose therapy sufficient to desensitize has significant side effects, mostly on the gastrointestinal tract, with reports of severe bleeding. Lower doses such as 100mg daily are now being used with some evidence of benefit, although the patient population in these studies is not characterized as aspirin sensitive by aspirin challenge..

An alternative method is topical lysine aspirin , the only truly soluble form of aspirin, applied intranasally. Initial open studies using 2mg weekly in addition to other treatments were indicative of benefit in both aspirin tolerant and sensitive patients. A double blind, placebo- controlled crossover study in aspirin sensitive patients using only lysine aspirin did not demonstrate any effect on the nasal airway. However addition of intranasal lysine aspirin up to 50 mg intranasally daily to routine therapy does reduce polyp size and does not adversely affect asthma. It does not reduce nasal running, itching or sneezing.

The mechanism of desensitisation probably involves reduction of leukotriene receptors.

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**Title:** Antileukotriene drugs
**Author:** Bjermer L
**Institution, city and country:** Dept. of Respiratory Medicine & Allergology University Hospital, Lund, Sweden

The rational for antileukotriene treatment in the nose are several. Leukotrienes and especially the Cysteinyl leukotriens LTC4, LTD4 and LTE4 are involved in allergic rhinitis as well as in the development of adenoids and nasal polyps[1]. Moreover, there is a distinct link between upper and lower airways and having rhinitis represents a risk factor for later asthma development, regardless of atopic status[2]. The nose has an important conditioning role of the air entering the lower airways and an untreated rhinitis is a risk factor for worsening asthma control[3]. Moreover, rhinitis is associated with sleep disturbances, probably one important factor negatively affecting quality of life[4,5]. Finally, mucosal thickening influencing the Eustachian tube facilitates the occurrence of and aggravates the course of media otitis, when it occurs. Thus, the treatment goals can be defined as:

1. Reducing rhinitis symptoms and facilitating nose breathing.
2. Improving asthma control
3. Reducing adenoid and polyp growth
4. Improving sleep quality
5. Prevent and treat otitis media

The use of anti-leukotriene therapy has been documented in all this conditions[6-10]. The observation that steroids do not suppress the production of CysLT's[11] advocates the use of combination of anti-leukotriene therapy and steroids in more advanced rhinitis, especially when polyps are present[9]. Moreover, it also seems rational to combine an anti-histamine and anti-leukotriene therapy as both mediators exhibit different pathophysiological activities[12].

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**Vivaldi Room:** Poster Presentation
**Poster Discussion:** Friday 10th, 10:30-11:00 and 16:00-16:30
**Chairpersons:** Manuel Bernal-Sprekelsen (E) and Isam Alobid (E)

**Poster 1:** Snoring and its association with asthma in Tehrani adolescents
**Authors:** Bidad K, Anari Sh, Moaieri H, Gholami N, Zadhush S
**Institution, city and country:** Immunology, Asthma and Allergy Research Institute Children Medical Center Tehran University of Medical Sciences Tehran, Iran

*Introduction.* Snoring during sleep is an important manifestation of obstructive sleep apnea syndrome (OSAS). Although clinical history is not sufficiently sensitive and specific to distinguish primary snoring from OSAS, snoring is indicative of upper airway obstruction and may be associated with the presence of diurnal symptoms. Snoring can occur alone or be the presenting feature of OSAS and other common chronic conditions such as allergic rhinitis. Some studies have shown that snoring is significantly increased in children with asthma.
*Objectives.* The aim of our study was to evaluate the prevalence of snoring and its diurnal symptoms in Tehrani adolescents and to examine the relationship between snoring and its related symptoms with asthma and allergy.
*Methods.* A population-based cross-sectional study was conducted in Tehran. Multistage randomized sampling was used for data collection. School students in the age group of 11-17 years (n = 2900) were studied. Body mass index (BMI) was measured. Information was collected via a structured face-to-face interview, based on a standardized validated questionnaire. In addition to the asthma-related symptoms, questions relating to OSAS symptoms were added. All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS).
*Results.* The prevalence of snoring was 7.9% (4.8% in girls and 12.4% in boys). The prevalence of snoring was significantly higher among males ($P < 0.05$). Snoring was positively associated with asthma. Overweight/ obese adolescents had significantly higher rates of snoring and asthma. Prevalence of daytime symptoms including lethargy and tiredness increased significantly across the snoring group.
*Discussion.* Snoring is a significant problem for children and may be associated with diurnal symptoms. We conclude that the prevalence of symptoms suggestive of obstructive sleep problems is relatively high in children of this country. This highlights the need for awareness among physicians about the problem of obstructive sleep-disordered breathing, especially in children with asthma, and for the need for further studies to measure prevalence of sleep breathing disorders among Iranians.

**Poster 2:** Role of specific immunotherapy in allergic rhinitis patients
**Authors:** Akta E, Korkut AY, Gedikli O, Eren SB
**Institution, city and country:** Dept. of Otorhinolaryngology-Head and Neck Surgery, Vakıf Gureba Teaching and Research Hospital, Istanbul, Turkey

*Background.* The treatment of allergic rhinitis (AR) patients focuses primarily on environmental control, pharmacologic treatment, immunotherapy and education. Immunotherapy reduces AR symptoms and medications requirements.
*Objective.* The aim of this study is to evaluate the effectiveness of specific immunotherapy (SIT) in patients with allergic rhinitis using symptom scores and laboratory parameters.
*Methods.* Totaly 52 patients admitted to Vakif Gureba Hospital with symptoms of AR between 1999 and 2004. Skin tests were performed to determine allergic agents in patients with diagnosis of allergic rhinitis. The study included all grass and mite allergic patients. SIT was started in 52 patients in whom symptoms persist although medical treatment after three months. Symptoms were classified in 4 point scale regarding of the severity. Specific IgE radioallergosorbent test (RAST), total immunoglobulin E (IgE) and eosinophil cationic protein (ECP) levels and prick test results were determined. Severity of the symptoms and laboratory parameters were determined after 5 years in follow-up. Results were analyzed statisticaly.
*Results*. The score of symptoms including nasal pruritus, rhinorrhea, sneezing, nasal congestion and eye symptoms reduced significantly in follow period ($p < 0.01$). Skin reactions in prick test reduced after five years of SIT in house dust mite allergy ($p < 0.01$) and grass allergy ($p < 0.05$). Although there was a significant reduction in total IgE and ECP levels in grass allergy ($p < 0.05$), the reduction was not noteworthy in mite allergy ($p > 0.05$) after five years of SIT. In mite allergy RAST levels reduced significantly ($p < 0.01$).
*Conclusions.* This study showed that SIT provides clinical improvement in allergic rhinitis patients. It also demonstrated significant efficiency in laboratory parameters.

**Poster 3:** Image analysis in computer system of pollen recognition
**Authors:** Rapiejko P, Wawrzyniak ZM, Jachowicz RS, Jurkiewicz D
**Institution, city and country:** Military Institute of the Health Services, Warsaw, Poland

*Background.* In allergology practice and research, it would be convenient to receive pollen identification and monitoring results in much shorter time than it comes from human identification.
*Objective.* The goal of such attempt is to provide accurate, fast recognition and classification and counting of pollen grains by computer system for monitoring.
*Methods.* The isolated pollen grain are objects extracted from microscopic image by CCD camera and PC under proper condition for further analysis. The algorithms are based on the knowledge from feature vector analysis of estimated parameters calculated from grain characteristics including morphological features, surface features and other applicable estimated characteristics. Segmentation algorithms specially tailored to pollen object characteristics provide exact descriptions of pollen characteristics already used by human expert. The specific characteristics and its measures are statistically estimated for each object. Some low level statistics for estimated local and global measures of the features establish feature space. Some special care should be paid on choosing these feature and on constructing the feature space to optimize the number of subspaces for higher recognition rates in low-level classification for type differentiation of pollens grain.
*Results.* The results of estimated parameters of feature vector in low dimension space for some pollen types are presented as well as some effective and fast recognition results of performed experiments for different pollens.
*Conclusion.* The findings show the evidence of using proper chosen estimators of central and invariant moments (M21, NM2, NM3, NM8, NM9) of tailored characteristics for good enough classification measures (efficiency > 95%) even for low dimensional classifiers (3) for type differentiation of pollens grain.

**Poster 4:** To evaluate systemic and local side effects in specific immunotherapy
**Authors:** Gedikli O, Akta E, Korkut AY, Eren SB
**Institution, city and country:** Dept. of Otorhinolaryngology-Head and Neck Surgery, Vakıf Gureba Teaching and Research Hospital, Istanbul, Turkey

*Background.* Immunotherapy is a specific therapy for allergic rhinitis and several reports have documented the safety and efficacy of this treatment. But systemic reactions occur in as little as 1% of patients receiving traditional specific immunotherapy.
*Objective.* The goal of this study was to evaluate safety of specific immunotherapy.
*Methods.* Totaly 58 allergic rhinitis patients (31 male and 27 female), median age 24.8 yr, were enrolled in this five-year prospective study. All the patients were treated with injections of the following allergenic extracts: 52 of house dust mite, 13 of grass. A total of 4167 injections were administered. Systemic or local side-effects and emergency treatments were recorded and the following dose was regulated.
*Results.* 68 episodes of allergic side-effects occurred, 36 systemic (52.9%) and 32 local (47%). Most of these reactions occur during the initial incremental dose period. 66.6% of systemic reactions occurred in patients who had a history of asthma based on clinical diagnosis. Systemic reactions occurred in 23 patients treated with house dust mites extract (0.83% of the injections), in 1 patient with grass extract (0.02% of the injections). One of them suffered anaphylactic shock. There was no mortality. The rate of systemic reactions, according to the number of the total injections was 0.86%.
*Conclusion.* Systemic reactions are definite side-effects of immunotherapy. Most reactions are mild and emergency treatment is essential in management of these reactions. Asthma is a major factor in the development of systemic reactions, and therefore these patients need particular caution.

**Poster 5:** The development of immunological method of Alt a 1 allergen detection
**Authors:** Rapiejko P, Bialek S, Lipiec A, Samolinski B
**Institution, city and country:** Military Institute of the Health Services, Warsaw, Poland

*Background*. Current allergology practice uses established methods for determination of pollen grains and spores concentration, being allergens source. When allergen leaves pollen grain or spore, a discrepancy between actual concentration of airborne allergen and concentration of the carrier, i.e. pollen grains or spores, may occur. It takes place mostly during rains and when pollen grains and spores are exposed to varying physicochemical conditions.
*Methods*. The authors present methodology of measurement of Alt a 1 allergen concentration using an immunological method with the usage of monoclonal antibodies anty Alt a 1. Alternaria spores concentration were measured using Lanzoni volumetric spore trap and MAS 100 method aiming at verification and standardization of the method. Studies were performed in a 18 cubic meter chamber.
*Results*. The authors present findings from preliminary studies which are aimed to verify an immunological method of determination of Alternaria alternata Alt a 1 allergen in the air. In this study, immunological analyzer by Burkard utilizing microwell technology was used for determination of particles suspended in atmospheric air.

**Poster 6:** Vomeronasal organ occurrence in adult humans
**Authors:** Rapiejko P, Jurkiewicz D, Zielnik-Jurkiewicz B
**Institution, city and country:** Military Institute of the Health Services, Warsaw, Poland

*Background*. The influence of chemical substances (feromones) on human emotional and physical condition has fascinated psychologists, sexuologists and laryngologists since centuries. Literature conveys inconsistent information on vomeronasal organ (VNO) occurrence in humans. This organ is often called Jacobson's, and 2 symmetrical openings leading into it, located on both sides of septum, are called Ruyasch's ducts.
*Objective*. The aim of the study was to analyze vomeronasal organ occurrence in humans in relation to age and sex.
*Methods*. The study was conducted in a group of 482 patients, aged 18?79 years. All patients underwent routine ENT examination including rhinoscopy, nasal cavity examination with usage of 2.5x magnification lens (surgical glasses) and surgical microscope with 10x magnification. All persons had nasal cavities examined endoscopically. Every time presence of vomeronasal organ openings, along with localization, size and symmetr! y of these was noted. Persons, who presented Jacobson's organ, were asked to fill a questionnaire concerning influence of smells on erotic sensations.
*Results*. Vomeronasal organ was present in 221 persons, that is, 45,9%. In 87% of cases vomeronasal organ opening size was smaller than 0.2 mm, what restricted its visibility to usage of magnifying lens, microscope, or endoscope. In 12,2% of cases only vomeronasal organ ducts openings were well visible in routine rhinoscopy without magnification. Vomeronasal organ was found more often in men than women. VNO was significantly more rare in patients with nasal septal deviation. In these cases, vomeronasal organ was usually found unilaterally, in all the cases on the concave side of deviated nasal septum.

**Poster 7:** Inflammation and tissular remodeling in upper and lower airway mucosa using a fibroblast *in vitro* model

**Authors:** Roca-Ferrer J, Alobid I, Pujols L, Pérez M, Oliveras G, Xaubet A, Picado C, Mullol J
**Institution, city and country:** Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Serveis d'Otorinolaringologia and Pneumologia. Hospital Clínic, Barcelona, Catalonia, Spain

*Background.* Asthma and nasal polyps are inflammatory diseases characterized by inflammatory abnormalities that also involve fibroblast proliferation.
*Objective.* To examine the influence of inflammation on *in vitro* proliferation of fibroblast isolated from human nasal mucosa (NM), nasal polyps (NP) and bronchial mucosa (BM).
*Methods.* Fibroblasts were isolated from samples obtained during nasal endoscopic surgery or bronchial endoscopic biopsies. Fibroblasts were incubated with culture media alone, 10 ng/ml cytokines (IL-1beta, TGF-beta and TNF-alpha) or 1-5-10% fetal bovine serum (FBS) for 2 to 5 days. Proliferation was assessed by XTT method. Results are expressed as median and 25-75$^{th}$ percentile of percentage of proliferation compared to media alone. Statistical significance was set at $p < 0.05$.
*Results.* Proliferation was significantly induced by 1-10%FBS in NM, NP and BB fibroblasts at 2 and 5 days. At day 2, not significant differences were found when comparing the FBS-induced proliferation of NM, NP or BB fibroblasts. At day 5, the 10%FBS-induced proliferation was significantly higher ($p < 0.05$) in NP (528%; 343-712; $n = 11$) than in BB (319%; 230-430; $n = 6$). No significant differences were found when comparing NM (10%FBS: 350%; 255-532; $n = 10$) with NP or BB proliferation. Cytokines only induced proliferation of NP fibroblasts at day 5 (50%; 15-87, $n = 11$, $p < 0.05$).
*Conclusion.* Proliferation ratio in response to FBS is lower in fibroblasts isolated from BM than from NP. The cytokines may stimulate only the proliferation of NP fibroblasts. Therefore, the fibroblast proliferation induced by inflammation might be different between lower and upper airways.

**Poster 8:** Evaluation of the pneumatization of paranasal sinuses in mice

**Authors:** Prades E, Rojas S, Garrido M, Tortosa M, Bernal-Sprekelsen M
**Institution, city and country:** Servei d'Otorinolaringologia, Hospital Clínic, Barcelona, Spain

*Background.* Several investigators have studied normal anatomy of paranasal sinuses of mice in order to obtain animal models of rhinosinusitis. We describe the development of paranasal sinuses lasting from 6 to 9 week-old mice.
*Objective.* To survey normal murine sinonasal anatomy.
*Methods.* 8 healthy, 6 to 9 week-old, female Balb /c mice (Charles River Lab, Boston, USA) were sacrificed with euthanasia dose of Ketamine and Xylazine, administered via intraperitoneal injection. Sequential 10 µm sections of the paranasal sinuses were taken in the coronal plane at 250 µm intervals and stained with Hematoxilin-Eosin. All histological figures were digitally captured and imported with Reconstruct (free software for serial section microscopy, Fiala JC, Boston University, Boston, USA).
*Results.* Anatomical study revealed a rudimentary maxillary sinus, bilateral ethmoid cells, nasal passage and turbinates. The volume and area surface of paranasal sinuses is 20% higher in 9-week old mice than in 6-week-old mice. The Surface-Volume rate ($mm^2/mm^3$) is 7% higher in older mice. This indicates there is an increased complexity of paranasal sinuses that allows containing more mucosal surface.
*Conclusions.* Reconstruct is a recommendable free editor for serial section microscopy. It allows us to define volumes and surface in our model. Main growth of paranasal sinuses in the studied mice occurs in early stages of life. Murine paranasal sinuses seem to offer a good target for further studies, e.g. animal model rhinosinusitis.

**Poster 9:** Rabbit anatomy of the nasal and paranasal cavities in experimental work
**Authors:** Huvenne W, Van Cauwenberge P, Bachert C
**Institution, city and country:** ENT Dept., Ghent University Hospital, Upper Airway Research Laboratory, Ghent, Belgium

*Background.* Sinusitis in humans is a heterogeneous disease. Many variations in etiology, bacteriology, stage of disease and treatment occur. Animal models have the advantage of bypassing a lot of these variables while studying sinusitis, but it is important to be aware of the anatomical differences and similarities of the nasal and paranasal cavities between experimental animals and humans.
*Methods.* After literature research, 4 rabbits were sacrificed to perform CT-scans, endoscopic examination and dissection of the nasal and paranasal cavities.
*Results.* The major structures of importance when studying experimental sinusitis are the turbinals and the sinuses. The richly arborescent maxilloturbinal can be regarded as the inferior turbinal in humans. The ethmoïd part of the nasal cavity is filled by its turbinals: four endoturbinals and four ectoturbinals. The endoturbinals can be regarded as the middle turbinal in humans. Regarding the sinuses, the maxillary sinus is of greatest importance, as rabbits don't have frontal or sfenoïdal sinusses. Ethmoïdal cells are represented by the open spaces between the ethmoturbinals. The maxillary sinus and the nasal marsupium (pouch) form one large cavity, which forms a wider area than the nasal cavity itself. The orifice of the rabbit maxillary sinus is a large canal, totally different from the human sinus ostium.
*Conclusions.* Rabbit anatomy of the nasal and paranasal cavity is rather different from humans. To obtain satisfying results from experimental work, it is necessary to be aware of these anatomical differences but at the same time notice the similarities.

**Poster 10:** Influences of allergic rhinitis to the outcome of functionell, endoscopic sinus surgery
**Authors:** Meuret S, Müller H, Strauß G, Dietz A
**Institution, city and country:** ENT clinic, University Leipzig, Germany

*Background.* the exact pathogenesis of nasal poyposis (NP) is still unknown. Empiric data show that patients that suffer from NP and allergic rhinitis (AR), do not benefit as much from functionell, endoscopic sinus surgery (FESS) than patients without AR.
*Objectives.* In this study we want to present our expirience in FESS in patients with AR.
*Methods.* 120 patients were included and devided into three groups: 1- 45 patients with AR without NP and without FESS; 2-43 patients with AR and NP and FESS a) 32 patients with SIT b) 11 patients without SIT; 3- 32 patients with NP without AR In our protocol we included a score of symptoms, the endoscopis findings and a CCT of the sinuses.
*Results.* In general, patients in group 3 have a better outcome of FESS than patients in group 2. Group 2a benefit more of FESS than group 2b.
*Discussion.* In this investigation, we can show that there is a tendency that patients with NP and AR who are treated by SIT have a better outcome of FESS than patients without AR.

**Poster 11:** Intranasal schwannoma treated by endoscopic excision (case report)
**Authors:** Korkut Y, Akta E, Gedikli O, Eren SB
**Institution, city and country:** Istanbul,Turkey

Abstract Although between 25 and 45 % of all schwannomas occur in the head and neck region, nasal and paranasal sinus presentations are rare in the literature. We report the case of a 67-year-old woman with a nasal schwannoma. Computerized tomography (CT) showed the mass completely occluding the nasal passage with evidence of a secondary maxillary sinusitis. A preoperative biopsy was suggestive of benign schwannoma. She underwent a complete intranasal excision of the mass which arising from the cribriform plate. The patient is asymptomatic and without endoscopic evidence of recurrence 4 years after surgery. This case demonstrates to achieve complete endoscopic excision of the nasal schwannoma like other benign nasal tumors.

**Poster 12:** Rhinitis symptoms caused by rubber gloves components
**Authors:** Jadczak M, Rapiejko P, Dzaman K, Jurkiewicz D
**Institution, city and country:** Military Institute of the Health Services, Warsaw, Poland

The aim was to investigate the prevalence if rhinitis evoked by rubber particles in health service workers.
*Material and Methods.* 83 health service workers with hyperreactivity to rubber gloves particles, 450 patients suffering from seasonal allergic rhinitis and 360 perennial allergic rhinitis sufferers took part in the study. ENT and allergologic examination was performed as well as skin prick test for latex immediate type allergy. Health service workers underwent patch test with contact allergens (TMTD, 2MBT, Nonox 2A). The relation of rhinitis symptoms to rubber gloves and airborne tire particles high concentration exposure was analyzed.
*Results.* 4,8% of health service workers, 1,1% of seasonal allergic rhinitis patients and 1,6% of perennial allergic rhinitis patients presented positive skin prick test with latex allergen. 27,7% of health service workers developed rhinitis symptoms following rubber gloves contact, but only 6,0% of health service workers presented positive sIgE (latex). 5,3% of health service workers suffered from rhinitis in days with high airborne tire particles concentration (over 5000/m3).
*Conclusions.* We conclude that immediate type allergy (rhinitis or contact urticaria) to rubber gloves latex is probably more often than prevalence of positive skin prick tests to one of latex allergens. High airborne tire particles (over 5000/$m^3$) exposure can cause rhinitis symptoms in some patients with hyperreactivity to rubber gloves particles.

# GENERAL INFORMATION

## TRAVEL GRANTS

The Congress has conceded the following grants:

| | | | |
|---|---|---|---|
| Katyoon Bidad | Iran | Susanne Reinartz | The Netherlands |
| P. Drvis | Croatia | Mazyar Shadman | Iran |
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| Joke In't Veen | The Netherlands | Aram Vroling | The Netherlands |
| Asunción Martínez | Spain | Huvenne Wouter | Belgium |
| Joke Patou | Belgium | | |

## PRACTICAL INFORMATION

SERIN Symposium will take place in Fira Palace Hotel well communicated with any place in Barcelona. Metropolitan area by bus, metro and train, and at 8 km from the Barcelona International Airport.

## GALA DINNER

Gala dinner will be celebrated at 21:00h in Can Cortada, located at Av. Estatut de Catalunya, s/n.
Buses will depart from Fira Palace hotel at 20.30 and the ticket will be required to enter.

## MEALS

The Conference fee includes lunches and all coffee breaks.
The tickets for these meals can be found inside the conference bag. People who wish to buy additional tickets should contact directly the congress Secretariat.
The conference lunches will be served at the Fira Palace Hotel

## REGISTRATION

The registration of the conference participants will start on Thursday morning, February 9th, at 8:00am, at Fira Palace hotel. It will close at 5:30 pm and reopen Friday morning at 08:30am.

*On-site registration:* Will be accepted but dealt with on a "first come-first served" basis. On-site registration can not guaranteed to receive all congress documents.

## WELCOME RECEPTION

All participants are invited to a Welcome Reception which will take place at Fira Palace hotel.

## SCIENTIFIC INFORMATION

Audiovisual material: Will be set up in front of Rossini Room.
The CD-ROM, DVD or a USB should be submitted as minimum 2 hours before the session starts.

*Posters:* Posters will be displayed in the specific place (The platform number matches with the number of the poster). Poster will be placed in the Vivaldi Room the February 9th from 8am – 9am. All posters must be set up by 9.00am and dismantle the February 11th between 12am-14.45am, All posters must remain in place until 12:00am.

*Oral presentation:* The time for oral presentation will be 10 minutes plus 5 minutes for discussion.
Please see your chairman 10 min before the session starts.
Changes in the Congress Programme: In the event of cancellations by speakers or other changes in the main Congress Programme, no full or partial refund of the registration fee can be made.

## GENERAL INFORMATION

Liability and Insurance: Neither the organizing committee nor the SERIN nor Grupo Pacífico nor Fira Palace hotel will assume any responsibility for damage or injuries to persons or property during the Congress pre and post travel. It is recommended that delegates and accompanying persons arrange for personal and health insurance.

*About Barcelona:* Barcelona, located at the Mediterranean see in the very north of the Spanish coast, is certainly a most cosmopolitan and economically active city. It has always proved its will to be modern, to follow the latest international tendencies or be ahead of them. This is evident, specially in architecture, which so well reflects the general approach to life in this always pulsating city.

*Climate:* Being located on the shores of the Mediterranean, Barcelona enjoys a warm, welcoming climate and pleasant temperatures all year round.

*Currency & exchange:* As a member of the European Monetary System the € [euro] is the Spanish currency.
Major credit cards are accepted in most hotels, shops and restaurants. Traveller cheques and currency can be changed at hotels or at a bank - these are open Monday to Friday from 08h30 to 14h00. Automatic changing and cash dispensing machines linked to international networks are also widely available.

*Electrical current:* European type 2 pin sockets with 220 volts AC at 50 cycles are used.

*Language:* The official languages are both Spanish and Catalan. English and French are widely spoken in touristic services.

*Local time:* Mainland Spain is the Central European Standard Time [Paris –Roma –Berlin –....]

*Meals, shopping, etc.:* In Barcelona, as in the rest of Spain, people normally have their meals later than in other European countries. People sit down for lunch between 13:00 and 15:00 in and for dinner between 21:00 and 22:00.
Shops in Barcelona open their doors between 9:00 and 10:00 in the morning, and generally close for lunch at 13:30 or 14:00. They open again in the afternoon between 16:00 and 17:00 and remain open until 20:00 or 20:30 in the evening. Nevertheless, it should be noted that many shopping centres and larger establishments do not close at midday. Many shops and all department stores and shopping centres open Saturday afternoons, while all shops close Sundays, except for a few dates when they are permitted to open.
Sales tax [VAT] is included in prices quoted. For non E.U. residents, tax free shopping schemes are available in many shops, which gives substantial savings to visitors.

*Medical care:* Clinics and hospitals provide round the clock emergency service. The national emergency phone number is 112.
Spain has reciprocal health care agreements with EU and many other countries. Please check that you carry the corresponding documents with you.

*Museums, parks, gardens, remarkable churches & palaces, cultural activities, etc.:* Barcelona's reputation as a world centre for art, architecture and design is growing yearly with a plethora of cultural activities on offer.
Please, refer to Barcelona Official Web-page for updated detailed information (http://www.bcn.es).
Once you are in Barcelona, Barcelona's main tourist offices can be found in Plaça de Catalunya, Plaça Sant Jaume and in Barcelona International Airport. Opening hours vary, but are generally between 9:00-20:00. English speaking staff will always be available. There is a cultural information desk at Palau de la Virrena, La Rambla 99 (tel:+34) 93 301 7775).

*Post & telecommunications:* Automatic direct dial telephone service is available to and from most countries in the world. Spanish International Country Code is (+34); International access code dialling from Spain is "00" (then dial Country Code, Area Code, etc.). Additionally, to make a phone call from Hotels, etc. you may need to dial first specific codes to get external line.
Public phones accept either a pre-paid card, or coins. Credit systems such as AT&T are also available in specific places like airports, etc.
Barcelona Central Post office is located in Pza. Antonio López and it is open to the public from 08:30 to 21:30 from Monday to Saturday.

*Public transportation:* Barcelona boasts a very comprehensive public transport network made up of a metro system plus trains, buses, cable cars and funicular railways. Please, refer to http://www.tmb.net for complete information about transport in the metropolitan area... and notice that you can take profit of several multi-journey combinations.
Trains and express bus services also link the main towns of the country. Please refer to your travel agency and/or to the Tourist Information Services.

*Religious services:* At http://www.iese.edu/studenthome/AH/htmls/hba44_06.html you will find some places of worship, which may have services in languages other than Spanish and Catalan.

*Security:* Barcelona is a touristic city. Although it is very unlikely to suffer from any act of violence (crime rates are lower than in most populated cities in the EU), logically, you have to be aware about pickpocketing. Please take care of your personal belongings and documents, specially in the most touristic areas (General emergencies: 112; Medical emergencies: 061; Guardia Urbana (Local Police): 092; Main Lost and Found Office: 93 402 31 61).

*Tipping:* Because the service charge is normally included in most bills, tipping is not compulsory.
If the service you receive is particularly good, however, it is customary to leave a small additional amount. With regard to taxi drivers, it is usual to round the payment up.

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Tel: +34 93 238 87 77
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