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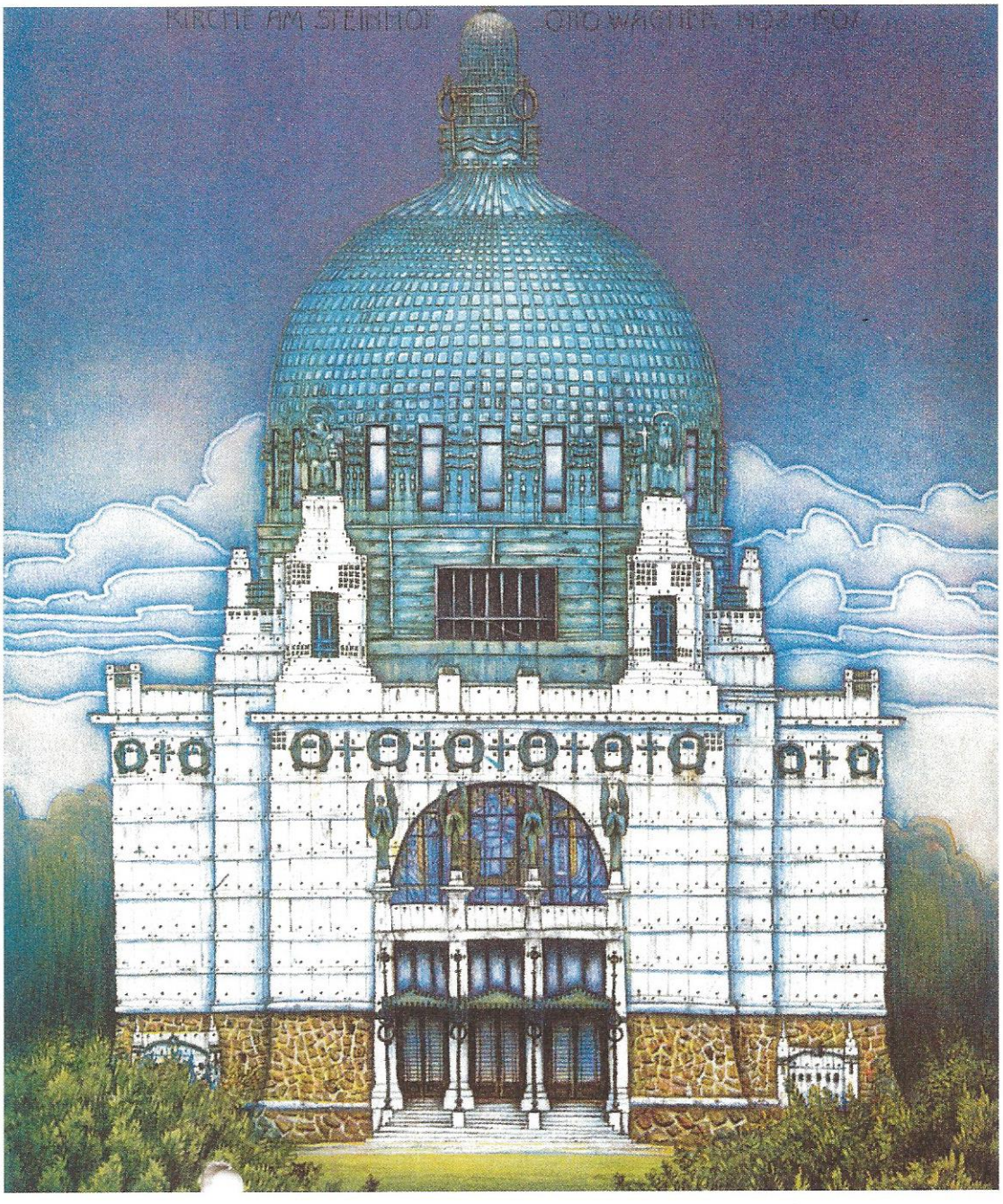

Final Programme

P 172 EFFECT OF TOBRAMYCIN SOLUTION FOR INHALATION ON CIRCULATING WHITE BLOOD CELL COUNTS IN EXACERBATING AND STABLE CF-PATIENTS

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P 173 INTENSIVE ANTIMICROBIAL CHEMOTHERAPY DECREASES THE NUMBER OF PRECIPITATING ANTIBODIES AGAINST *PSEUDOMONAS AERUGINOSA* IN CYSTIC FIBROSIS PATIENTS

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P 174 INS37217, A NOVEL $P2Y_2$ RECEPTOR AGONIST, BEING DEVELOPED FOR THE TREATMENT OF CYSTIC FIBROSIS: RESULTS FROM INITIAL PHASE 1 STUDY IN NORMAL VOLUNTEERS

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P 179 DIFFERENT ALVEOLAR MACROPHAGE RESPONSE TO *PSEUDOMONAS AERUGINOSA* BETWEEN TH2 RESPONDING BALB/c MICE AND TH1 RESPONDING C3H/HeN MICE AND THE MODULATING EFFECT OF MACROLIDES

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P 180 IgG SUBCLASS ANTIBODIES TO *SPERGILLUS FUMIGATUS:* MONITORING DISEASE ACTIVITY AND TREATMENT OF ABPA IN CF

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P 181 DEFECTIVE SLPI SECRETION IN CYSTIC FIBROSIS SALIVA

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P 182 DIFFERENT EXPRESSION OF CC AND CXC CHEMOKINE RECEPTORS IN NON-CF AND CF AIRWAY EPITHELIAL CELLS

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P 183 INFLAMMATION AND ANAEMIA IN CYSTIC FIBROSIS

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P 180 IgG SUBCLASS ANTIBODIES TO *SPERGILLUS FUMIGATUS*: MONITORING DISEASE ACTIVITY AND TREATMENT OF ABPA IN CF

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Background and aim: Allergic bronchopulmonary aspergillosis (ABPA) is characterised by a dual IgG and IgE antibody response and earlier studies have shown that determination total and subclass specific *Aspergillus fumigatus (Af)*)-IgG antibody levels is valuable in the diagnosis of ABPA in cystic fibrosis (CF) patients. Serious side effects in patients treated with itraconazole concomitantly with inhaled steroids led to withdrawal of itraconazole treatment in a number of patients with ABPA in our centre. This offered an opportunity to test the value of specific *Af*-antibody levels in monitoring disease activity and treatment response in ABPA.

Patients and methods: Serum levels of total *Af*-IgG and *Af*-IgG1, 2 and 4 were determined by ELISA using water-soluble somatic hyphal (WSSH) *Af* antigens and expressed as ELISA units (EU). Changes are expressed in % of EU. Serial determinations were done in 223 patients (83%) seen on a regular monthly basis, including measurements of forced vital capacity (FVC) and forced expired volume in 1 second (FEV1) recorded on a Pneumotach and expressed as per cent of predicted values. The study period included 2 months prior – and 12 months after discontinuation of itraconazole treatment.

Results: 30 patients were treated with itraconazole at onset of study and 5 started treatment within the period. After discontinuation 18 of the 30 patients (60%) showed a mean increase in specific *Af*-total IgG, IgG1, IgG2, IgG4 by 39, 59, 40 and 41% respectively. Serum levels were unchanged in 6 and decreased in 6 patients. FVC and FEV1 decreased in 15 patients with a mean value of 12% and 11% respectively. Lung function was unchanged in 10 and increased in 5 patients. Recurrence of clinical symptoms of ABPA with increasing levels of specific antibody levels resulted in re-administration of itraconazole in 18 of 30 patients (60%) after a mean period of 5 months. Hereafter antibody levels decreased in 15 by 31, 27, 24 and 41% (mean), remained unchanged in 2 and increased in 1 patient, and a mean increase in FVC and FEV1 by 6% and 7% respectively was seen. Lung function was unchanged in 9 (further decrease prevented) and decreased in 1 patient. A mean decrease in antibody levels in all the 5 patients who developed ABPA leading to itraconazole treatment within the study period by 26, 51, 22 and 39% respectively was seen, and FVC and FEV1 increased in 3 patients by 5 and 7% (mean). The changes were seen within few months.

Conclusions: Levels of IgG and IgG subclass antibodies to *Af* are not only useful for the diagnosis of ABPA, but also seem valuable for monitoring of disease activity as well as of treatment response.

P 181 DEFECTIVE SLPI SECRETION IN CYSTIC FIBROSIS SALIVA.

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CF is characterized by a general defect in exocrine secretion and studies of salivary secretion can be used as a non-invasive model of examination of relatively large volumes of affected exocrine glands. Since the secretory leucocyte proteinase inhibitor (SLPI) is a specific protein marker of serous secretion implicated in salivary antibacterial, antiviral and antifungal defense, we measured its concentration as well as the electrolyte and protein contents of total saliva from normal and CF individuals under resting conditions and during masticatory stimulation.

Methods: total saliva from 22 control (4-15 years old) and 13 CF (3-17 years old) were collected under resting conditions for 5 min and after chewing a piece of PARAFILM® (used for saliva stimulation) for 2 min. SLPI was assayed by ELISA and electrolytes, total proteins, and amylase were measured with classical techniques.

Results: SLPI concentration was showed to be significantly decreased in CF saliva after stimulation compared to control subjects whereas no difference in amylase stimulated secretion was observed between normal and CF. As already reported in the literature, our data showed that chloride concentration was higher in CF saliva than in control under resting conditions. Nevertheless chloride concentration does not show any differences in stimulated conditions between control and CF saliva. Our results of sodium and calcium concentration are also similar to those reported elsewhere.

Conclusion: Our results suggest a specific regulatory defect of SLPI secretion in CF salivary glands in vivo, likely to be directly related to the genetic defect. This observation rises the questions of mechanism of this specific secretory defect, the possible implication in oropharyngal microbal contamination and gives the possibility of using saliva as a model to investigate the effect of new drug therapies.

Supported by "Vaincr e la Mucoviscidose".

P 182 DIFFERENT EXPRESSION OF CC AND CXC CHEMOKINE RECEPTORS IN NON-CF AND CF AIRWAY EPITHELIAL CELLS

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Chemokines and their receptors play an important role in the process of leukocyte recruitment at sites of inflammation. The expression and function of chemokine receptors have been well characterized in leukocyte populations. Recent findings suggest that these receptors could also regulate other non-leukocyte cell functions, such as migration and proliferation. In order to investigate the expression of some of these receptors on airway epithelial cells, we performed immunocytochemistry, immunihistochemistry and quantitative RT-PCR analysis on different kind of respiratory epithelial cells, including bronchial biopsies, nasal brushings, primary cultures of nasal polyps from CF and non-CF patients, and immortalized tracheal cell lines (9HTEo$^-$ and ΣCFTE29o$^-$). Bronchial biopsies, nasal brushings and airway epithelial cell lines expressed mRNAs and protein for CCR3, CCR4, CCR6, CCR8 that are mainly receptors for eotaxin and RANTES, TARC and MDC, MIP-3α and LARC, TARC and I309, respectively. Recent findings have shown that CCR6 is also able to bind hBD1 and hBD2, two members of the β-defensin's family produced by respiratory epithelial cells and suggested to have a critical role in CF pathogenesis. Interestingly, we observed a consistent difference in the expression of these receptors between CF and non-CF cells. A quantitative analysis of mRNA expression levels indicated that there is an up-regulation of these receptors in CF cells. Expression of CXCR1, a highly specific IL-8 receptor, was also found in primary cultures of bronchial epithelial cells. Preliminary results, obtained on primary culture of nasal polyps from CF and non-CF patients, suggest that also the expression of this receptor could be impaired in CF cells. Further studies are in progress to characterize the relevance of these differences, especially in their relation with the genotype and phenotype of the patients.

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P 183 INFLAMMATION AND ANAEMIA IN CYSTIC FIBROSIS

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AIMS: Hypochromic microcytic anaemia is common in Cystic Fibrosis (CF). Differentiation between iron deficiency and inflammation is difficult. Our question was whether laboratory measurements could identify iron deficiency when inflammation was present. **METHODS:** 74 consecutive CF patients who were well and attending for annual review (AR) and 39 consecutive patients admitted to hospital for presumed infective exacerbation (IE) were selected. Full history was obtained on a structured questionnaire with details of symptoms and medication. Physical examination included measurements of weight, spirometry and oxygen saturation. Chest X-ray was taken. Red cell indices were measured on an Advia (Bayer) cell counter and ferritin by Beckmann Access immunoassay. A Wilcoxon rank sum test was used to test for differences between groups. **RESULTS:** The groups were well matched demographically. The IE group had more severe markers of inflammation , were more anaemic, with lower haemoglobin (Hb), mean cell volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), total iron binding capacity (TIBC) and serum iron (Fe). Ferritin (FER) was not as discriminatory.

Measurement	AR, N = 74 Median	AR, Range	IE, N = 39 Median	IE, Range	P value
Hb g/dl	14.4	10.5-16.5	13.1	9.4-17.0	0.0011
MCV fl	85.5	74-95	82	62-92	0.0007
MCH pg	28.25	22.9-31.4	26.45	18.6-30.2	0.0001
MCHC pg	32.7	30.1-37.0	32.1	29.7-34.0	0.003
Neut. x 10^9/l	7.5	2.8-16.7	9.7	2.7-24.3	0.0125
ESR mm/hr	9	1-73	32.5	2-94	0.0001
CRP µg/l	9	5-150	52	5-256	0.0001
Fe µmol/l	9.2	1.7-22.1	4.4	0.2-53	0.0006
TIBC	56	42-95	49	18-85	0.0003
FER µg/l	35	5-121	37	2.5-228	0.094
Albumin g/l	38	31-44	31	17-42	0.0001
% Anaemic	11		51		
% FER<20µg/l	26		2.6		

ESR = erythrocyte sedimentation rate, CRP = C reactive protein, Neut = neutrophils

CONCLUSIONS: More patients in the IE group were anaemic and had raised inflammatory markers but more in the AR group showed evidence of depleted iron stores with ferritin< 20µg/l. Inflammation may elevate ferritin, an acute phase protein, and mask iron depletion in patients with CF.