120* Multiplex cytokine profile detection in young children with cystic fibrosis

S. Terheggen-Lagro[1], W. de Jager[2], B. Prakken[2], C.K. van der Ent[1]. [1]*Paediatric Pulmonology, University Medical Centre Utrecht, Utrecht, Netherlands;* [2]*Paediatric Immunology, University Medical Centre Utrecht, Utrecht, Netherlands*

In young cystic fibrosis (CF) patients with mild lung disease it is unclear whether signs of a systemic inflammatory response are present. We therefore measured plasma cytokine profiles in young, clinically stable CF patients with mild lung disease.

Twenty-eight different cytokines, chemokines and soluble adhesion molecules were measured in 47 CF children, ages 1.7–12.2 years, using a multiplex immunoassay. Sputum cultures were obtained on the same day as blood sampling and children were categorized as uninfected (n = 12), positive for *Staphylococcus aureus* and/or *Haemophilus influenzae* (n = 26) or positive for *Pseudomonas aeruginosa* (n = 9). Data were compared to those obtained from 20 healthy control children, ages 3.8–11.5 years.

All CF children displayed a pro-inflammatory cytokine profile and especially interleukin (IL)-1α, IL-4, IL-12 and tumor necrosis factor-alpha (TNF-α) were significantly higher in CF children (p-values <0.001 or <0.05). Although interleukin-8 and oncostatin M (OSM) were also higher in CF children, CC-chemokines were significantly lower than in controls. In CF children bacterial sputum culture results did not influence plasma cytokine profiles, except for soluble vascular endothelial cell adhesion molecule-1 (sVCAM-1). sVCAM-1 concentrations were significantly lower in uninfected CF children compared to *Pseudomonas aeruginosa* positive CF children (2186.8±1207.7 versus 7170.21±2129.7, p = 0.025).

Young, clinically stable CF children display a derangement of inflammatory mediator profiles. Pro-inflammatory cytokines are increased in plasma while CC-chemokines are decreased.

Supported by: Netherlands Organization for Health Research and Development (ZonMW).

121 Immunoglobulin levels in cystic fibrosis patients: influence of age and gender

L. Hanssens[1], A. Wauters[1], C. Knoop[2], S. Mulier[1], J. Duchateau[3], G. Casimir[1]. [1]*Children's CF Unit, Queen Fabiola Children's University Hospital, Brussels, Belgium;* [2]*Adult CF Unit, Erasme University Hospital, Brussels, Belgium;* [3]*Immunology Service, Brugmann University Hospital, Brussels, Belgium*

Objectives: Abnormal immunoglobulin (Ig) levels, particularly abnormal IgG levels, have been described in cystic fibrosis (CF) patients. The aim of the present study was to assess Ig levels in our CF patients and relate these to parameters of disease severity.

Methods: IgG, IgA, IgM levels were measured in 62 patients. Hyper- and hypo-IgG were compared with age- and sex-matched control patients who had normal IgG levels.

Results: Median age of patients was 15.1 years (0.9–46.6). Male/female ratio was 1:1. Mean FEV1 was 68.1% and chronic *Pseudomonas aeruginosa* status was 37.1%. Five patients had hypo-IgG (8.1%), all of them were males and less than 18 years old. Eighteen patients had hyper-IgG (29.0%), were mainly females (61.1%) and more than 18 years old (72.2%). No difference was found in any parameters of severity between hypo-IgG and control patients. Hyper-IgG patients younger than 18 years old had lower FEV1 (73.4% versus 45.6%, p < 0.04) and worse Shwachman scores. Female patients had lower FEV1 (p < 0.05) and FVC (p < 0.05) and higher levels of erythrocyte sedimentation rate (p < 0.05) and neutrophils (p < 0.05).

Conclusions: From our study we conclude that (1) Hypo-IgG is present in some young and male CF patient and does not seem to have consequences, (2) Hyper-IgG is a marker of worse clinical status (already published) and (3) this seems to be particularly true in children and thus total IgG levels may be a useful additional tool for monitoring of pediatric CF patients, (4) Unfavourable role of age and female gender in prognosis of the patients seems to be confirmed and could be explained by an increased inflammatory reaction.

122 Pro-inflammatory cytokines in serum, sputum and lavage fluid (BALF) in cystic fibrosis lungs

T.V. Bulgakova, E.A. Surkova, T.E. Gembitskaia, L.A. Jelenina, E.V. Boitsova, L.F. Kovaleva. *Pavlov State Medical University, Scientific Research Institute of Pulmonology, Saint-Petersburg, Russian Federation*

Cytokines regulation plays significant role in creation of inflammatory process and, first of all, cytokines synthesized in inflammatory site. In this study we investigated levels of pro-inflammatory cytokines IL-1β, TNFa and IL-8 in serum, sputum and lavage fluid (BALF) from 78 patients (mean age 11.85±0.82) with Cystic fibrosis (CF) at the exacerbation period of disease and at the minimum activity period of inflammatory process.

It is revealed that level of IL-8 in sputum and BALF of patients with CF exceeds the control values 30–100 times. This fact points out about local synthesize IL-8 predominance in inflammatory site. Il-1β and TNF α levels of patients with CF was significantly (p < 0.005) higher at exacerbation period of disease to compare with minimum activity period of inflammatory process. The maximum value was determined in sputum and BALF. These results predominance of local lung synthesis of pro-inflammatory cytokines takes place in patients with CF.

123* AGE and sRAGE levels in cystic fibrosis

J.W. Wilson[1], J. Forbes[2], S.J. King[1]. [1]*CF Service, The Alfred Hospital, Melbourne, VIC, Australia;* [2]*The Baker Medical Research Institute, Melbourne, VIC, Australia*

Background: Airway inflammation in CF is associated with marked remodelling and bronchiectasis. Pro-inflammatory mediators such as advanced glycation end-products (AGE) derived from carbohydrate in diet and its soluble receptor (sRAGE) may perpetuate this response in the lung and other organs such as the kidney (Westall et al, 2005).

Methods: Adults with CF (n = 58, 35 males, 86% pancreatic insufficient, mean age 33.9±7.7 years, range 23 to 62 years, mean FEV1%predicted 58.7±22. (range 20–110)) and 24 healthy adults (13 male, mean age 32.7±9.2 years, range 21–55 years) were studied. CF participants provided 1–3 serum samples each over a six month period. Serum was analysed for levels of advanced glycation end-product (AGE-CML) and sRAGE by ELISA.

Results: Median (IQR) levels for AGE-CML were 1650 (1158, 1986) nmol/mmol lysine in CF and 659 (464, 1015) nmol/mmol lysine in controls (p < 0.0001). Median (IQR) levels for sRAGE were 1190 (946, 1578) ug/ml in CF and 975 (751, 1352) ug/ml in controls (NS). FEV1%predicted was negatively correlated with sRAGE level in CF (rho = −0.45, p = 0.0005), but not with AGE-CML level (rho = −0.09, p = 0.51). No other clinical factors analysed were significantly correlated with AGE-CML or sRAGE levels (age, gender, BMI, presence of diabetes or HbA1c level).

Conclusions: The levels of sRAGE reflect ability to respond to this pathway and are associated with poorer lung function. Modification of diet in CF may reduce this mediator and tissue injury.