**217** Relationship between *Pseudomonas* antibody levels, clinical wellbeing and the Leeds criteria for infection status

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**Introduction:** *Pseudomonas* antibody measurements are a method of monitoring *P. aeruginosa* infection status. The Leeds criteria are based on microbiological culture results from respiratory samples. The aim was to determine if there is any correlation between serology and microbiology in defining *Pseudomonas* infection.

**Methods:** *Pseudomonas* antibodies were measured using a Genesisc diagnostic ELISA kit and partially purified lipopolysaccharide antigens. The Leeds criteria categorises patients as ‘never’ had *P. aeruginosa* infection, ‘free’ of infection for at least 12 months, ‘intermittently’ infected or ‘chronically’ infected. Data were retrieved from all patients (excluding Bcc and post-transplant) attending the Leeds Paediatric and Adult Units in 2007.

**Results:** One hundred and twenty six children and 271 adults were categorised as follows: ‘never’ - paediatrics 10%, adults 17%; ‘intermittent’ - paediatrics 42%, adults 19%; ‘free’ - paediatrics 39%, adults 6% and ‘chronic’ - paediatrics 9%, adults 58%. In the ‘never’ group 92% of children and 100% of adults had normal antibody levels (<8U/ml). In the ‘chronic’ group 100% of children and 96% of adults had raised antibody levels. In children there was a significant correlation between antibody level and age (p<0.02), but no correlation with weight, height, or BMI standard deviation scores. In the adults there was a significant correlation between antibody level and both FEV1 and BMI (p<0.001). Adult FEV1 levels rose from a median 49% predicted in the ‘chronic’ group to 78% predicted in the ‘never’ group (p<0.001).

**Conclusions:** *Pseudomonas* antibody levels accurately reflect the infection status categories in paediatric and adult populations.

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**218** Potential role of EPI-hNE4 treatment in CF patients


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EPI-hNE4, a specific inhibitor of human neutrophil elastase (hNE), has been proposed for treatment of cystic fibrosis (CF) lung disease because it may reduce hNE-induced lung tissue damage. Interestingly, it has been reported that the Epithelial Na+ Channel (ENaC), which is responsible for Na+ hyperabsorption in CF airways, could be activated by tryptase-like serine proteases such as Channel-Activating Proteases (CAP) expressed by airway epithelial cells or hNE released by neutrophils. EPI-hNE4 could then be useful in the treatment of CF lung disease by inhibiting hNE-induced increase in ENaC activity, in addition to its anti-elastolytic activity.

We evaluated by short-circuit current (Isc) measurements the effects of hNE and EPI-hNE4 on ENaC-mediated ENaC activity in primary cultures of human nasal epithelial cells. ENaC activity and this effect was completely abolished in the presence of EPI-hNE4. These results indicate that hNE can activate in vitro ENaC and Na+ absorption in CF and normal HNEC, but that this effect is only seen after blockade of endogenous CAP activity. Thus, the pathophysiological importance of hNE-induced activation of ENaC in CF airways in vivo most likely depends on the level of CAP expression and activity in airway epithelial cells. Finally, the potent inhibitory effect of EPI-hNE4 on hNE-mediated ENaC activation observed in our experiments suggests that EPI-hNE4 could be of interest to reduce ENaC hyperactivity in CF airways in association with an inhibitor of CAP activity.

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**219** Mannose-binding lectin – polymorphisms and modifying effect on CF

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CF patients are exposed to a lifelong and large burden of antibiotics. The goal of this project was to analyse the characteristics of allergic (immunopathologic) and non-immunopathologic (toxic) reactions in CF.

We analysed all adverse drug reactions to antibiotics, which were noted routinely on a side-effect sheet in the patients charts, during 2002 to 2004 in 379 CF patients attending the unit. In addition, we sent a questionnaire to all patients and compared the results with those from the charts.

251 questionnaires were returned and could be utilized, yielding a response rate of 66%. Of the 251 patients with questionnaires and chart records available, 80 experienced 187 reactions, of which 63 were immunopathologic, the others were classified as toxic. To specify the immunopathologic reactions further, these were divided into two categories (reproducible on exposition; n=16), very likely (no re-exposure tried, but no other explanation for the symptoms observed, n=41). Of the immunopathologic reactions 47 (75.6%) were limited to the skin, and 4 (6.3%) to the skin and the respiratory tract. Shock (n=2) or fever were noted only with iv treatment. A reduced frequency of immunopathologic reactions during iv treatment with cephalosporins was noted in patients with continuous oral cephalosporins (intake over 50%/year) treatment, in contrast to sporadic treatment (less than 50%/year).

It is important to identify immunopathologic reactions. This helps to maintain the repertoire of drugs available for a specific patient. Intermittent intake of cephalosporins was associated with more reported allergic reactions to iv- cephalosporins than continuous treatment.

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**220** Reduced frequency of reactions in patients with cystic fibrosis and continuous treatment with oral cephalosporins?

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