155 Development of a low dose nasal infection model with *Pseudomonas aeruginosa* in mice

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Strategies that prevent chronic *Pseudomonas aeruginosa* infection in Cystic Fibrosis patients are desirable. Vaccination would be a sensible approach. A meaningful animal infection model that represents protection at the airway mucosa surface is still lacking, since present models tend to mimic chronic or lethal airway infection with high doses of *P. aeruginosa*. Consequently, we pursue a model of low dose nasal inoculation and longitudinal investigation of physiologic parameters to monitor the onset of infection.

Using head-out spirometry we are able to monitor *P. aeruginosa* infections as low as 5×10^4 CFU PA14 in C57BL/6 mice. 18 relevant respiratory parameters including respiration rate, tidal volume and midtidal expiratory flow at 50% are analyzed over a course of 8 days post infection. One of the most sensitive parameters is tidal volume which dropped by 62% within 4 hours post infection with recovery after 7 days. A clear dose-dependency could be monitored. Additionally a number of physiological parameters are checked to monitor the state of infection. In the near future the protectivity of a vaccine against P.aeruginosa will be investigated in C57BL/6 and isogenic CFTR-deficient mice.

Additionally, to monitor the infection in vivo, bioluminescent pseudomonads, including the clinically important strains PAO1 and TB were developed using transposon mutagenesis (mini-ctx-lux). First infection experiments in C57BL/6 mice showed that a lung infection with bioluminescent pseudomonads can be monitored until clearance after 24 hours.

We conclude that this infection model holds promise for assessment of airway pathology which better mimicks the clinical situation.

156* Genotype based evaluation of eradication treatment of new *P. aeruginosa* infections in CF patients

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Introduction: Longitudinal data on genotypes of PA strains after eradication treatment are limited. We followed CF patients after a first ever PA isolate and evaluated the PA free time period after eradication therapy and the efficacy of this treatment relying on comparison of the genotypes of subsequent PA isolates.

Methods: From June 2002 till December 2008 sputa or nasopharyngeal aspirates were cultured prospectively from 41 CF patients with a first ever PA isolate. Eradication treatment consisted of oral ciprofloxacin and inhaled tobramycin or colimycin for 3 months Genotyping of PA was carried out by RAPD-analysis.

Results: Eradication treatment was successful in 34(83%) patients. Twenty out of these (59%) reacquired PA after a median period of 12 months, with 4 patients becoming chronically colonized after a median time of 13 months. At present, 14 patients (34%) remain PA free after a median follow-up period of 3 year 2 months.

Fifteen of the 27 patients (55%) with at least a second isolate showed an identical PA genotype. Patients becoming chronicically colonized during the study period had a significantly shorter PA free interval between the first ever and second isolate compared to not chronically colonized patients with at least 2 isolates (p 0.041).

Conclusion: Our findings of eradication success and median time to recurrence after a first positive PA culture were comparable to other studies. More long lasting eradication however was achieved. An identical PA in the second positive culture and a short PA free interval are ominous signs of impending chronic colonization.

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157* Interim outcomes of a *Pseudomonas aeruginosa* (Pa) eradication protocol in young children in the Australasian Cystic Fibrosis Bronchoalveolar Lavage (ACFBAL) Study

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Background: Eradication of early Pa infection is now standard practice, although many different protocols are used and controversy remains over long term effects.

Objective: To determine the efficacy of a Pa eradication protocol in children <5 yrs.

Methods: Data on Pa acquisition ($\geqslant$ 1000 CFU/mL for BAL group; +ve oropharyngeal specimen for std group) were collected prospectively as part of an ongoing multicentre RCT designed to examine BAL-directed therapy in children diagnosed with CF by newborn screening. 168 infants were randomized at a mean of 3.6 (SD 1.6) mths of age (84 BAL, 84 Std therapy). Final outcomes for all children at 5 yrs included BAL. A standardized Pa eradication protocol was used across all sites for both arms of the study: 2 wks IV anti-pseudomonal antibiotics then 1 mth oral ciprofloxacin + 2 mths nebulised TOBI®.

Results: By 31/12/07, 85/168 patients had >1 episodes of Pa eradication treatment. 51 children were reinfected (mean 402 (range 35–959) days between episodes). Average age of Pa acquisition was 2 (SD 1.3) yrs. After a single eradication treatment, Pa was cleared 93% of the time. 10/100 children were Pa +ve at end of study BAL at age 5 yrs. A. fumigatus and S. maltophilia were more frequently cultured from the end of study BAL if eradication treatment had been given (14/56 v 1/44 $p=0.002$; 6/56 v 0/44 $p=0.033$ respectively).

Conclusions: Early, aggressive treatment is successful at eradicating Pa but may be associated with emergence of A. fumigatus and S. maltophilia.

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158 Eradication of *Pseudomonas aeruginosa* in adults with CF

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Eradication of new new isolates of P aeruginosa(PA) is a key part of management in CF. However most of the data on eradication therapy relates to children. In this study we report the outcomes of eradication therapy in an adult population. Adults with CF and a first sputum isolate of PA from 1999 to 2007 were studied. The mean age of this group was 30 years and 59% were male. Seventeen patients had a new isolate of PA during this period of study. Nine patients were treated with oral Ciprofloxacin (Cip) and nebulised Colomycin (Col) for 3 months, four were treated with intravenous anti-pseudomonal antibiotics for 14 days and then received 3 months of Col. A further four patients received other combinations of oral Cip and nebulised antibiotics. In 11(65%) patients successful eradication was achieved with a negative sputum culture within 6 weeks of commencing treatment and at least 3 negative sputum cultures in the subsequent 6 months with the first treatment. In the six patients who continued to isolate PA after 4 weeks, second line therapy was initiated in 4 cases using intravenous antibiotics and in 2 nebulised Tobramycin. Following this, in a further 3 patients PA was successfully eradicated. All patients who had successful eradication had negitive sputum cultures by 6 weeks and remained negitive for 12 months. The median time to eradication was 1 month and median time to a new isolate of *P. aeruginosa* was 31 months. There was no significant change in FEV1 demonstrated at 12 months. Conclusion: Eradication of *P. aeruginosa* was successful in 84% of all patients isolating *P. aeruginosa* infection. Aggressive treatment of new infection of *P. aeruginosa* in adults is successful in the majority of patients and is of similar efficacy to the reported success in paediatric populations.