165 Effectiveness and safety of long-term treatment with linezolid in cystic fibrosis patients

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Treatment of chronic colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) and non-MR in cystic fibrosis patients shows a wide variability among CF units. While some caregivers prescribe continuous treatment with oral antibiotics, others only treat infectious exacerbations.

Patients and Methods: 39 CF patients were included. The mean age was 24.2 (±7.5) years. All patients were chronically colonized by *SA* (5% MR), and showed a poor clinical progress and respiratory function after receiving several conventional antibiotic cycles to treat infectious exacerbation.

Every patient was prescribed continuous treatment with oral Linezolid: 600 mg/12 h for 15–21 days every 45 days, for a minimum of one year. Serial spirometry, sputum analysis and blood analysis were determined to rule out toxicity derived from chronic treatment with Linezolid.

Results: An inflection in the pulmonary function drop in FEV1 and FVC was observed, with a recovery and slowing down of this drop after treatment. In regards to microbiology, after a treatment period of at least one-year, no resistances to Linezolid were observed. There was a significant raise of fungal colonizations with filamentous moulds (*Aspergillus*). There were no blood changes during the one-year treatment. Patients described clinical recovery with a significant decrease of cough and expectoration during the treatment with Linezolid.

Conclusion: Treatment with Linezolid cycles is effective and safe in those patients colonized by *SA* who present both a clinical and functional torpid progress with conventional treatments. Linezolid allows the stabilization of the symptoms and lung function.

166 Effect of tobramycin on *Pseudomonas aeruginosa* populations in artificial sputum media

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Persistent colonisation of the lung by Pseudomonas aeruginosa is associated with significant increases in morbidity and mortality in cystic fibrosis patients. Chronic infection with *P. aeruginosa* results in the bacteria exhibiting adaptation to the unique CF lung environment. Examples include the development of resistance to antimicrobial agents, biofilm formation and colony morphology variation. Recently artificial sputum media (ASM) has been developed to mimic the nutritional conditions within the CF lung. We investigated this novel *in vitro* model system to monitor the responses of populations of *P. aeruginosa* to antimicrobial challenge.

P. aeruginosa isolates of the Liverpool Epidemic Strain (LES) were cultured in ASM for a total of 7 days and then assessed for diversification by studying phenotypic and genotypic attributes in the presence or absence of tobramycin. After 7 days culture in the ASM there was significant evidence of divergence of isolates with respect to colony morphology and the presence of auxotrophic mutants. Interestingly there was evidence of increased production of toxic exoproducts such as pyocyanin in the presence of tobramycin. Increased levels of LES bacteriophages were also noted with antimicrobial challenge. These results demonstrate that during growth in ASM *P. aeruginosa* undergoes phenotypic diversification that resembles population behaviour in CF, and that ASM can be used to model bacterial responses to antibiotics. These adaptations may help explain the long-term success of the bacterium within CF patients.

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167 Effect of antibiotics on bacteriophage production by a cystic fibrosis epidemic strain

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Bacteriophages are viruses that can infect bacteria and integrated phages (prophages) are common amongst bacterial genomes. Using induction with norfloxacin, we have shown that each of the five prophages in the genome of the Liverpool Epidemic Strain (LES) of *Pseudomonas aeruginosa* is able to produce active progeny phage. The aim of this study was to analyse CF patient sputum samples for the presence of LES phages, and to determine the effects of CF relevant antibiotics on phage production by four LES isolates (LESB58, LESB65, LES400 and LES431).

We detected LES phages by plaque and PCR assays directly from patient sputum samples, and in some patients the level of phages increased during exacerbation. In Luria broth, antibiotics affecting the cell wall/membrane (meropenem and colistin) and protein synthesis (tobramycin and azithromycin) showed low levels of induction of phages in the four LES isolates. Conversely, ciprofloxacin, which affects DNA synthesis, caused a higher level of induction in all of the LES isolates. We found variation between the LES isolates, with isolate LESB65 consistently producing more phages than the other isolates. Phage production by LES isolates can also be detected during growth in an artificial sputum medium biofilm model.

Phages have been implicated in the adaptability and competitiveness of bacterial populations. We have shown that phages are readily detectable in CF sputum and that the choice of antibiotic may influence the levels of phage production.

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168 Accurate identification of antibiotic allergies in cystic fibrosis

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Background: Intravenous antibiotics are crucial to cystic fibrosis (CF) treatment. A history of adverse reactions undermines treatment by limiting drug choice. Drug allergy guidelines suggest that careful workup allows some suspect drugs to be used safely. In collaboration with immunology we critically evaluated suspected adverse reactions to antibiotics in our CF population.

Method: Serial attendees to our CF Unit were asked about adverse reactions to antibiotics and the drug allergy documentation checked. Based only on this information an initial decision was made on whether the relevant drugs should be used.

Past medical records of the same group were then examined in detail. If immunologically-mediated reactions were suspected specific serum allergen IgE assay, allergen skin prick, intradermal and challenge testing were employed. The putative allergies were then reclassified and drugs deemed safe following analysis were compared to those deemed safe previously.

Results: 20 of 44 patients reported adverse reactions to antibiotics with 46 'allergies' in total. The Table shows the available safe antibiotics based on each method of acquiring information ($p < 0.00001$ for a chi-square test of differences between groups). To date, antibiotics that were previously avoided have been given uneventfully in four cases.

Approach to antibiotic prescribing

	Information from history and existing drug allergy table only	Additional information from old medical notes and immunological testing
Avoid completely	33	11
Use (as normal or with limitations, e.g. at reduced dose, only after a desensitization regimen)	13	35

Conclusion: A systematic evidence-based approach to evaluating possible drug allergies is significantly improving options for treatment in our CF cohort.