with severe asthma. Our findings would at first glance seem to speak against this proposal. Thus, there was a significant accumulation of subjects with neutrophilic inflammation amongst the patients with severe asthma in the ENFUMOSA study and this was not seen in the group with mild-to-moderate controlled persistent asthma investigated with the same procedures. However, as discussed in the Editorial [4] accompanying our paper [5], there are subgroups of subjects with severe asthma that have eosinophilic inflammation. As it is established that mild-to-moderate allergic asthma is most commonly associated with an eosinophilic inflammation, our findings could lead to a hypothesis that eosinophilic asthma provides relative protection against progression into severe disease. This would also fit with the observation that atopy was less common among the subjects with severe asthma, as documented in the ENFUMOSA study.

Rather than speculating further, or engage in the debate on whether the eosinophil is pro- or anti-inflammatory, or both, the ENFUMOSA group has already embarked on the longitudinal study that P.G. Gibson and J.L. Simpson suggest. We are in the middle of the Longitudinal Assessment of Clinical Course and BIOMarkers in Severe Chronic AIRway Disease (BIOAIR) study, a large Pan-European and partly European Union sponsored effort, where genotypes, biomarkers and clinical characteristics are followed in three groups of patients with mild asthma, severe asthma and chronic obstructive pulmonary disease. Following an intensive cross-sectional baseline characterisation of the subjects, they are monitored with repeated measures of biomarkers, airway function and a large panel of other investigations over at least 1 yr. We hope that these data may help clarify some of the hypotheses that arose from the ENFUMOSA study. The BIOAIR study will be completed in 2005 and we hope to be able to report on the findings soon after. We find it particularly important in the BIOAIR study to have repeated measurements of the different variables across 12 months, as many hypotheses concerning pathogenesis are based on cross-sectional observations in relatively small study populations, rather than demonstrating consistent differences that are preserved over time. We hope that the results of the BIOAIR study, which also includes a double-blind placebo-controlled oral steroid intervention, may provide data to help us respond more comprehensively to P.G. Gibson's and J.L. Simpson's question concerning the classification and pathogenesis of asthma.

We would finally like to broaden the view beyond the debate of eosinophilic and noneosinophilic inflammation. The different asthma phenotypes are the result of complex gene-environment interactions where we currently, despite exciting recent progress, only see the tip of the iceberg. It is likely that small differences in genotype may determine how common environmental influences produce varying phenotypes. Along these lines, it was recently observed that a specific and functionally important polymorphism of the cell surface receptor used by hepatitis A virus may protect individuals from development of atopy after hepatitis infection [6]. Many similar observations are likely to follow and may in the future help us to identify the genetic and environmental causes of distinct expressions of the heterogenous syndrome of asthma.

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Host response to transmissible *Pseudomonas aeruginosa*

To the Editor:

The recent study by JONES *et al.* [1] was interesting in that it found no significant difference in local airway or systemic inflammation between cystic fibrosis patients colonised with either transmissible or nontransmissible strains of *Pseudomonas aeruginosa*. At face value these results appear reassuring, although the authors do rightly raise a note of caution. One factor that was not considered in this article is the effect of bacterial load within the airways, but this must surely be the denominator when one is trying to identify a significant difference in host response. There is also anecdotal evidence that the host inflammatory response at the time of first acquisition of transmissible *P. aeruginosa* or *Burkholderia*

cepacia may be what determines subsequent outcome *i.e.* some patients become extremely unwell and die whereas the majority seem to remain relatively well. Presumably some sort of *status quo* is reached between host and organism and perhaps what we are seeing in the study by JONES *et al.* [1] is in fact a survivor effect. The experience of ARMSTRONG *et al.* [2], where a number of deaths occurred shortly after acquisition of a transmissible strain goes some way toward supporting this hypothesis. However, the long-term outcome in those other children in the study by ARMSTRONG *et al.* [2] who were similarly infected remains unknown, but hopefully longitudinal follow-up in these individuals will add further weight to the reassurance by JONES *et al.* [1].

In the meantime, until there is evidence to the contrary,

efficient segregation based on molecular typing of *Pseudomonas aeruginosa* would seem to be the only appropriate management strategy for our cystic fibrosis patients.

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From the authors:

D.W. Reid and colleagues state that there is anecdotal evidence that the host inflammatory response at the time of acquisition may be what determines subsequent outcome, and propose that the results of our own study may be influenced by a survivor effect. However, unlike the clinical situation of a rapid deterioration and death sometimes seen among a proportion of cystic fibrosis (CF) patients who develop infection with transmissible strains of *Burkholderia cenocepacia*, we have not observed a similar rapid decline in the patients who have recently become infected by a transmissible *Pseudomonas aeruginosa*. D.W. Reid and colleagues also

reflected on the experience of ARMSTRONG *et al.* [1]. However, there are likely to be differences between our own experience and that of ARMSTRONG *et al.* [1]. Firstly, ours is an adult CF centre, whilst the report of ARMSTRONG *et al.* [1] concerns paediatric CF patients. Secondly, the vast majority of our patients were infected with sporadic *P. aeruginosa* strains before acquiring a transmissible strain; it is likely that the CF patients in the report by ARMSTRONG *et al.* [1] were all previously *P. aeruginosa* naïve before developing infection with their clonal strain. Finally, it is possible that individual transmissible *P. aeruginosa* strains may differ in their pathogenicity.

It is clear that prospective studies of the clinical outcome for cystic fibrosis patients who harbour transmissible strains of *Pseudomonas aeruginosa* are needed before we can reach any firm conclusions of the clinical effects of *Pseudomonas aeruginosa* cross-infection in cystic fibrosis. We firmly agree with D.W. Reid and colleagues that until there is evidence to the contrary, cross-infection control measures should include segregation based upon the results of molecular fingerprint typing of isolates.

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The use of computer-animation programs during spirometry in preschool children

To the Editor:

We read with interest the paper by GRACCHI *et al.* [1] describing the use of computer-animation programs as a device to improve reproducibility in acquiring forced expiratory manoeuvres in 4–8-yr-olds. The study was simple and well designed but the possibility both that the computer-animation programs were not used to their full potential and that the European Respiratory Society "adult" reproducibility criteria are too strict for preschool children must be raised [2, 3].

While we agree that the use of computer-animation incentive programs offers little advantage in the 6–8-yr-old group, younger children cannot always understand, process and carry out multistep tasks. In such children, using a combination of the computer-animation programs will allow the production of a prolonged forceful expiration to be broken down into smaller steps. We find starting with the candles, to achieve maximal peak flow, and then progressing to the balloons or bowling alley games (prolonging the forced expiration) with individualised target modification provides maximum encouragement for each child according to their ability and lung function.

Individualised target modification is necessary as the animations are preset at a target of 120% predicted for both peak expiratory flow and forced vital capacity, a target that is only appropriate if based on suitable reference data for that age group. Any underestimation of predicted values (which, given the paucity of data from healthy 4–8-yr-olds, is quite likely to occur) will mean that the child reaches the animation target before they have truly reached their maximum, thereby losing the incentive to try any harder as they will not be able to see any improvement in their performance. Likewise, on some occasions it may be appropriate to reduce the target % initially in order to encourage the younger children or those with poor coordination to aim for a target that is achievable, thereby encouraging them to try harder next time, and to prevent them giving up.

When comparing the proportion of children in the study by GRACCHI *et al.* [1] who were able to achieve certain reproducibility criteria under the different measurement conditions it is important to note the following: 1) none of the observed differences were significant; 2) most of the children produced forced expiratory parameters within <0.1 L, rather than within 5% of each other, the former equating to a