Segregation is not good for patients with cystic fibrosis

Duncan Geddes

Professor of Respiratory Medicine, Royal Brompton Hospital, Sydney Street, London SW3 6NP, UK.

E-mail: d.geddes@rbht.nhs.uk

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Introduction

This is an intentionally polarized opinion presented as part of a debate. A pro–con debate works best by exaggerating two opposing points of view as a way of stimulating an open discussion. When, however, the same debate is written down the arguments can be taken out of context and so be misleading. The middle ground between two polarized positions can be lost, and in a supremely important area such as cross-infection this can be dangerous. This article must not, therefore, be taken as definitive but rather as a contribution to a vitally important discussion about how best to run a cystic fibrosis (CF) service.

First some definitions. Segregation for this debate means cohort segregation or the clustering of people with CF either as in- or out-patients according to the bacteria that they carry. This is not the same thing as infection control. Cohort segregation may or may not be a part of the much more complex business of infection control but can never be the whole story. A clinic could have infection control without segregation. It could do this by ensuring no contact between patients as a part of best practice infection control. Conversely, it would be possible to have segregation without infection control, if for example patients came to a Pseudomonas-only clinic but the doctors did not wash their hands. The American guidelines for infection control in CF recommend strict infection control without cohort segregation while the UK prefers a combination of both and puts great emphasis on cohort segregation.

I will present two main arguments. First, that infection control is essential, complex, many faceted and far more important than cohort segregation. Second, that cohort segregation is an illusion. It is illogical, unrealistic, ignores the complexity of CF microbiology and is occasionally harmful. Also, it can deflect attention from much more important issues of good infection control and is therefore not good for our patients.

Is cross-infection a problem is CF?

Of course it is. There have been a number of catastrophic outbreaks causing huge distress among patients and staff at a limited number of CF centres. When we look closer, however, the precise causes of these outbreaks is somewhat mysterious. In the first place they are surprisingly limited in time and space. The same, or apparently the same, strains of bacteria have caused a number of deaths over a short period in one clinic but seem to have been less of a problem elsewhere. In the Melbourne outbreak[1] a 'transmissible' *Pseudomonas aeruginosa* was linked to five deaths in young children but was also found in 55% of the clinic with a much more benign outcome. The same pattern was reported from a *Burkholderia cepacia* complex (Bcc) outbreak in Edinburgh.[2] In addition, strains similar or identical to those implicated in these outbreaks have been found in clusters[3] in other CF clinics where the transmission and clinical consequences have been much less.

Following these outbreaks there has been a rush to blame the organism and by association the individuals who carry it. This reaction seems altogether too simplistic. The host bacterial interaction in CF is immensely complicated and if the same organism's behaviour is quite different in different settings then maybe these 'transmissible', 'epidemic' or otherwise stigmatized superbugs are not exactly the same. The accuracy of strain typing is beyond my expertise but the definition of an identical strain as having 80% genetic homology is worrying. Alternatively they are genuinely the same but other factors are involved and we are missing something. Of particular concern is the multiplicity of bacteria and viruses in a CF lung; this could mean that a combination of bacteria x with virus y can be disastrous when either alone is not. Whatever is going on it seems to me to be much more complicated that one vicious strain jumping from patient to patient. This leads on to the question of how these outbreaks occur.

Cross-infection – how and why

If we accept that the same organism spreads from one person with CF to another, this could happen by direct contact between patients or indirect transmission via the environment or hospital staff.

The segregationists like to blame a combination of the organism and the patient. Their argument seems to be that segregating people into a few groups by bacterial species will prevent all other routes of transmission. This seems unbelievably simplistic and it ignores a number of facts.

(1) The majority of Pseudomonas strains in CF are acquired from the environment
(2) Pseudomonads are perhaps the most abundant life form on the planet and have evolved many ways of surviving and moving from host to host other than by direct contact
(3) The hospital environment is heavily colonized by bacteria such as Pseudomonas and hospital hygiene has not always been ideal
(4) Hospital staff have been lax about infection control over the period that the cross-infection outbreaks have occurred and contact between staff and patient is at least as close and frequent as between patient and patient
(5) Hospital cross-infection is a much wider problem than a CF clinic: poor hygiene has been implicated in spread of *Clostridium difficile* and MRSA.

CF microbiology

Segregation by organism might be sensible if there were only a few bacteria involved and they remained constant. Sadly this is not the case. Clinicians receive laboratory results that mention the bacteria that are looked for and so get a false idea that CF microbiology is simple. Leaving aside the difficulties of identity and stability of the individual strains of Pseudomonas referred to above, the microbiology is horrendously complex. At the 2007 North American CF conference, examples of this complexity included reports that normal 'commensal' bacteria may play a part in CF lung inflammation; that DNA typing reveals as many as 60 species and 980 taxa in limited samples of CF sputa; and that 76% of CF sputa contain at least one fungus and 69% at least one virus. Even if this variety remained constant, and is seems pretty unlikely that it does, how do we separate people with CF into logical groups according to their sputum microbiology? Do we segregate according to a single organism, as single strain or some combination of organisms and strains? Are interactions between micro-organisms important? Do host factors matter, so that some organisms may be bad in one person but gentle in another? There seems to be too much complexity and too much ignorance for simple answers.

Practicalities of segregation

For segregation to be logical and feasible we should know what bacteria, fungi and viruses matter and which one (two, three or 60) each person is carrying. We cannot do this. In the first place the best information is always out of date. When someone with CF makes a booking for a clinic the sputum result refers to some day in the past. It may be within the last week but more often is 2–3 months previously and by the time the clinic happens it may be even longer. While in the chronic stable state the organisms may be the same, and so it may be reasonable to use out-of-date information for a routine visit, the microbiology may change at the time of a clinical deterioration. The next problem is what should be sent to the laboratory. Many people with CF do not cough sputum and so throat or cough swabs are used. These may or may not be a good reflection of what is or will later be present in the lungs. Perhaps the biggest problem is that we do not know what really matters. The history of CF has been one of blaming different bacteria. *Staphylococcus aureus* was the first, there was then a brief period of concern about *Haemophilus influenzae*, followed by a long period in which *P. aeruginosa* has dominated. Recently, new bacteria have been isolated and the importance of each is still being worked out. In the future there will be more. Finally different strains of the same species behave differently. For Bcc some genomovars are linked to clinical decline while others are not, and the same is probably true of *P. aeruginosa*. This means that segregation by species may simply miss the point. Patients with *P. aeruginosa* tend to have worse lung function and clinical status than those without and to spend more time in hospital. By putting them together in a segregated clinic we may therefore be exposing the most vulnerable to a greater risk. The Manchester clinic reported cross-infection with a new multi-resistant *P. aeruginosa* within patients segregated because they carried that bacterium.[4] They went on to claim that this proved the value of segregation, as another cohort who did not carry *P. aeruginosa* did not acquire the multi-resistant strain. These data can be used to reach the opposite conclusion, namely that the segregated *P. aeruginosa* carriers were exposed to a greater risk, while

those who were not infected in the first place avoided cross-infection by spending less time in hospital.

All these concerns and uncertainties argue that cohort segregation by bacterial species is an illusion. We do not know what bacteria a patient carries, we do not know what matters, we cannot define a few simple groups based on bacteriology which will either limit cross-infection or its consequences, and cohort segregation does not prevent cross-infection within the cohort.

It therefore seems more logical to assume that every patient is a potential risk to every other patient and that minimal contact and optimal general infection control measures are the best approach.

Does cohort segregation do harm

It can be argued that even with all these uncertainties and difficulties segregation may help a bit and anyway does no harm. Again, sadly, this is not the case. By describing some bacteria as 'transmissable' or 'epidemic' and others as not results in demonizing both the bacteria and also the people that carry them in a way that goes far beyond the evidence. *P. aeruginosa* has become, in the CF world, a dangerous 'superbug'. This means that when it is first isolated from someone with CF this is taken as a disaster and leads at best to concern and at worst to terror. In reality, the rate of decline in lung function in CF patients with *P. aeruginosa* is now less than 1% per year. There have been reports of parents preventing their children playing outside because of the fear of *P. aeruginosa* in puddles of rainwater. Let's look at some examples of what may happen if we over-stress segregation:

Story one

Two brothers stopped seeing each other because one acquired Bcc.[5] When the one with Bcc reached the terminal phase of his disease his brother wanted to see him to say goodbye. The request was refused and they never met again.

Story two, part one

A two-year-old girl with CF acquired an 'epidemic' multi-resistant strain of *P. aeruginosa*.[6] This organism was also acquired by two of her relatives, both of whom has significant illnesses as a result, although they both survived. Should the girl have been segregated from these two relatives? The rest of the story, which may provide the answer, is given at the end of the text.

The message is clear. Segregation can do harm. If it also does good then clearly a balance must be struck. However, the burden of proof rests with the segregationists.

Conclusions

- The microbiology of the lung in people with CF is very complex
- Simplistic approaches to infection control are likely to be wrong
- All contact between all people with CF carries some risk of cross-infection
- Infection control measures should be the best available and applied equally regardless of the organisms isolated
- Cohort segregation is practically difficult and at best incomplete due to ignorance of current microbiology
- The burden of proof rests with the segregationalists to show that it does more good than harm.

Story two, part two

The patient's two relatives were her parents. She remains well with normal lung function at the age of 22. In this case, strict separation of family members would have done more harm than good.

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