Cross-infection risk in patients with bronchiectasis: a position statement from the European Bronchiectasis Network (EMBARC), EMBARC/ELF patient advisory group and European Reference Network (ERN-Lung) Bronchiectasis Network

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Risks of cross-infection in bronchiectasis are small, and should not currently restrict access to specialised care http://ow.ly/dkVl30hcu5p

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Introduction

Involving patients in the design, conduct and dissemination of clinical research, clinical guidelines and education projects is highly beneficial, and is a priority for funders and societies such as the European Respiratory Society (ERS) [1]. Bronchiectasis is a lung condition associated with chronic cough and sputum production that is rapidly increasing in prevalence in Europe [2]. It is a neglected disease, but recent initiatives including the European Bronchiectasis Registry and research network (EMBARC) and the European Union supported European Reference Network for Rare Pulmonary Diseases (ERN-LUNG) are beginning to raise the diseases profile and stimulate new research [3, 4]. Patient involvement has been, and remains, central to these projects including the recently published European bronchiectasis guidelines which were developed with patients as members of the panel [5].

Patient with bronchiectasis are frequently chronically infected with bacterial pathogens [6]. Recent publications have raised the concern that bacteria such as *Pseudomonas aeruginosa* could be transmitted between patients (cross-infection) [7–10]. EMBARC, ERN-Lung and European Lung Foundation (ELF) activities in bronchiectasis involve face-to-face meetings involving multiple patients, and the recent ERS guidelines recommended that bronchiectasis patients should be involved in group activities, such as pulmonary rehabilitation, where they may come into contact with other patients [5]. Consequently we conducted a review of the risk of potential transmission of pathogens in bronchiectasis in order to guide international bronchiectasis patient activities.

Recommendations in cystic fibrosis

The risk of cross-infection with pathogens such as *Pseudomonas aeruginosa,* methicillin-resistant *Staphylococcus aureus* (MRSA) and *Burkholderia cepacia complex,* and most recently *Mycobacterium abscessus*, is a matter of concern in patients with cystic fibrosis bronchiectasis (CF) [11–16].

As a result of compelling evidence of transmission of these organisms between people with CF and, in the case of *Burkholderia cepacia* complex organisms and *P. aeruginosa*, the identification of transmissible "epidemic" strains, clear guidance has been published which recommends restrictions on contact between CF patients [15, 16]. These guidelines recommend that universal precautions should be taken with individuals with CF and clinics should be cohorted, separating patients with *B. cepacia* complex infection, *P. aeruginosa* and other infections. All direct contact whether inside or out of the hospital between individuals with CF should be avoided [15, 16] CF physicians are also advised to practise rigorous hand hygiene and other measures since microorganisms can survive on surfaces, hands or clothing for several hours [14, 17]. For patient support events and conferences, participation by CF patients is heavily restricted. The CF Trust in the UK limits participation strictly to a single CF patient for indoor events and has strict regulations for outdoor events. Virtually all international guidelines for CF advocate similar measures to reduce the risk of cross-infection [15, 16]. These are clearly recommendations that individuals with CF may choose not to adhere to, or may be unable to adhere to, for example where patients are siblings. For institutional events and in healthcare facilities, however, the principal of restricting access to minimise exposure to other people with CF is very important and widely implemented.

Cross-infection in bronchiectasis

Cross-infection, particularly with *P. aeruginosa* is also a potential concern in bronchiectasis not due to CF because of evidence that *P. aeruginosa* infection is associated with an increased risk of death, exacerbation and worse quality of life [18]. The ERS bronchiectasis guidelines did not address the issue of cross-infection [5]. This reflects the lack of evidence, which prevents recommendations being made in an evidence-based guideline. Of note, the current Spanish Society of Pneumology and Thoracic Surgery (SEPAR), the British Thoracic Society and guidelines from Australia and New Zealand also make no specific recommendations regarding the risk of cross-infection [19–21]. The ERS guidelines do, however, emphasise the importance of specialised care for the management of bronchiectasis, which is best delivered within specialised centres seeing a large number of patients and recommend that patients with bronchiectasis and significant breathlessness attend pulmonary rehabilitation [5, 22–25]. Pulmonary rehabilitation and specialist outpatient clinics are environments where patients with bronchiectasis will inevitably come into contact with other patients with a theoretical risk for cross-infection with respiratory pathogens.

What is the evidence for the risk of cross-infection in bronchiectasis?

Bronchiectasis and CF are two quite distinct conditions, with a different spectrum of microbiology and a different pathophysiology [26]. *B. cepacia* complex, the most feared transmissible pathogens in CF, are very rarely cultured in bronchiectasis [22–27]. While infection with *P. aeruginosa* is almost universal in CF over a patient's lifetime, *P. aeruginosa* affects only 20% of patients with bronchiectasis in Europe [5, 18, 23, 27]. It may be speculated that only a proportion of patients with bronchiectasis are susceptible to persistent

P. aeruginosa infection which tends to be concentrated in patients with more severe and extensive bronchiectasis [27].

We conducted a scoping review using Pubmed (using search terms "cross-infection" OR "transmission" AND "bronchiectasis", supplemented by searches of American Thoracic Society, ERS, BTS and World Bronchiectasis Conference abstracts 2014–2017; searches were limited to articles in English only and no date limits were applied). Any article type was accepted including case reports and case series. The primary search identified 117 articles, and an additional eight abstracts and four papers were identified as potentially relevant in supplementary searches. Review of the full manuscripts/abstracts excluded 123 articles/abstracts that did not report on cross-infection, leaving six potentially relevant articles. These are discussed below.

Based on this literature review, reports of cross-infection in bronchiectasis to date are extremely rare. Acquisition of a multidrug resistant strain of *P. aeruginosa* in a 14-year-old boy with bronchiectasis due to chronic aspiration was reported by Robinson *et al.* [28] in 2003. The patient had shared accommodation and physiotherapy facilities with a CF patient harbouring a genetically identical strain making transmission likely [28]. In contrast, a study of 64 *P. aeruginosa* isolates from 16 patients with bronchiectasis in Spain found no evidence of cross-infection, based on the high degree of genetic dissimilarity between each isolate [29].

De Soyza *et al.* [7] performed a single centre study of 56 isolates and 36 bronchiectasis patients. They identified that the vast majority of *P. aeruginosa* isolates appeared to be acquired from the environment but could not exclude cross-infection in two cases. Genetic similarity between strains does not prove cross-infection, since acquisition from a common environmental source is also possible [7]. A lack of longitudinal "before and after" data also means we do not know if these strains represented a new infection by *P. aeruginosa*, or acquisition of a new strain among many in a patient already infected with *P. aeruginosa*. It is also not known whether any acquisition is associated with a clinical deterioration [7].

Most recently, Hilliam *et al.* [8] performed a multi-centre study using whole genome sequencing of 189 isolates from 91 patients attending 16 UK bronchiectasis centres. In this study there were five examples of strains from different patients that were genetically similar but again did not have the epidemiological or longitudinal data to prove transmission *versus* common source acquisition. The authors concluded that there was no evidence to suggest a widespread transmissible strain in the UK bronchiectasis community, and that the *P. aeruginosa* lineages that are common in bronchiectasis are generally those that are also highly abundant in the environment [8]. In a study reported in abstract form only, variable number tandem repeat (VNTR) typing was used on 144 isolates from 84 patients with bronchiectasis [9]. This study identified three cases of bronchiectasis patients infected with epidemic strains apparently acquired from CF patients during inpatient stays [9]. No evidence of transmission from bronchiectasis patients to other bronchiectasis patients was identified. A recently published cohort study from the UK identified three patients sharing strains likely to have been acquired through cross-infection [10]. All three patients were known to be chronically infected with *P. aeruginosa* prior to the presumed acquisition event [10]. Based on the apparently infrequent nature of transmission, the authors of this study did not advocate a change in infection control policy [10].

Interpretation

The above review identifies that cross-infection with *P. aeruginosa* has occurred in bronchiectasis patients but that:

1) Such events are rare, and there is so far insufficient evidence to establish if new acquisition of *P. aeruginosa* infection (*versus* acquisition of new strains in patients already infected with *P. aeruginosa*) has occurred.

2) There is insufficient evidence to show that cross-infection is associated with clinical deterioration.

3) Epidemic and highly transmissible strains have not been identified in the bronchiectasis population, except in one study where these were shown to be likely acquired from CF patients.

4) The strongest evidence for transmission overall and transmission of multidrug resistant or highly virulent strains in particular appears to be from CF patients to bronchiectasis patients, rather than within the bronchiectasis population. EMBARC data suggests that 10% of bronchiectasis patients in Europe are managed in CF clinics, while 45% are managed in centres with shared facilities for CF patients [30].

5) The current studies are inadequate in terms of numbers of patients and availability of clinical data and longitudinal follow-up. There are no studies addressing cross-infection with *Staphylococcus aureus*, MRSA, nontuberculous mycobacteria, or less common organisms in bronchiectasis.

Patient perspective

The EMBARC/ELF patient advisory group discussed this issue with a panel of clinicians at the 2nd World Bronchiectasis Conference in Milan, facilitated by the ELF. The discussions revealed that patients have diverse views on the importance of cross-infection. Patients infected with organisms such as *P. aeruginosa* or *S. aureus* are concerned about the risk of transmitting this to other patients or indeed to immunosuppressed patients and would value guidance on how to reduce any such risk. The majority of patients regarded the risk of acquiring new organisms from other patients as small, and an acceptable risk if the alternative is a lack of availability of peer support, specialised clinics and services such as pulmonary rehabilitation. The majority of patients thought they had a right to know about the risks so that they could make an informed decision about, for example, attending patient support group events. Many patients expressed concern that their condition would be stigmatised if they are required to wear masks or are unable to be in contact with others. In general, patients expressed frustration that infection control measures are often neglected in terms of their general management. Exacerbations resulting from exposure to relatives, members of the public or other patients with viral infections is a more frequent and regular problem for patients, and measures to avoid acquiring such infections are rarely discussed with patients.

Working group consensus

In the absence of high quality evidence, it is not possible to make strong recommendations about current practice with regard to infection control in patients with bronchiectasis. Nevertheless, clinicians need to make decisions about how to manage this issue in their clinics, while EMBARC, ERN-Lung and ELF must develop policies on how to manage any potential risk during patient meetings and events. The following represents a pragmatic consensus developed by the panel in response to these issues.

First, in relation to possible transmission from individuals with CF to individuals with bronchiectasis, detailed guidelines on infection control in patients with CF are already available from relevant national and international societies [15, 16, 31]. Where bronchiectasis patients are managed within a CF service we suggest managing these patients according to the same strict infection control procedures as patients with CF. This would suggest that patients with bronchiectasis should avoid sharing outpatient waiting rooms, clinic rooms or hospital bays with patients with CF. For the purposes of patient support group meetings, congresses or other events, patients with bronchiectasis should not have direct contact with individuals with CF.

Within bronchiectasis clinics, a balance must be found between the theoretical risk of cross-infection, and the risk of adversely impacting patient care. Patients with bronchiectasis benefit from specialist care in centres that see a large number of patients. Cohorting patients by organism is likely to be impractical in many hospitals in the absence of specific funding for this. Cohorting is also difficult to justify since our review did not identify a single confirmed case of new infection with *P. aeruginosa* acquired from a fellow patient with bronchiectasis. It is our judgement that there is currently not sufficient evidence to recommend separation of bronchiectasis patients with *P. aeruginosa* infection. Similarly, there are clear benefits of pulmonary rehabilitation with the evidence demonstrating improved exercise capacity, improved quality of life and reduced exacerbations [5]. These benefits outweigh the theoretical risk that attending a pulmonary rehabilitation class with other patients could expose the patient to the risk of transmission of a microorganism. Care for bronchiectasis in Europe is currently heterogeneous and predominantly inadequate with data suggesting most patients do not receive what may be regarded as the basic components of bronchiectasis care, such as chest physiotherapy, sputum culture, antibiotic therapy and self-management [32]. In this context, precious resources should be directed at improving basic medical management.

In the event of suspected transmission or a suspected outbreak we recommend seeking expert microbiological help and that facilities to investigate potential outbreaks using molecular methods should be made available.

We recommend that discussing the topic of infection control, including avoiding infections as well as the risk of transmission should be part of the bronchiectasis clinic consultation for all patients.

For patient support groups, research initiatives and social events, the balance of risks and benefits must be carefully weighed on a case-by-case basis. The value to patients of participation in such events is clear, and the need for advocacy and support in a disease like bronchiectasis is acute. Therefore, in the absence of evidence of harm, we do not currently advocate preventing patients from participating in such activities. We nevertheless have adopted the following recommendations for EMBARC/ELF events:

1) Patients should be informed that contact with other patients may carry a risk of transmission of infection. This allows patients to make an informed decision about whether to participate in such events.

2) All participants at such events should practise rigorous hand hygiene measures and patients should aim to minimise the production of potentially infectious aerosols by conducting chest clearance at home prior to attending and by covering their mouth while coughing.

3) Since shaking of hands is known to be a primary source of pathogen transmission in other areas, hand shaking at events or in hospital is discouraged.

4) Venues should have adequate space and ventilation.

5) Basic infection control measures to reduce close contact between patients should be practised, *e.g.* avoid sharing food/drinks/mobile phones and avoid activities promoting close physical contact.

6) Patients should not attend events with other patients if they are unwell, or have a current exacerbation.

7) We suggest that of patients who may be at higher risk of cross-infection, *e.g.* immunocompromised patients, or patients with multidrug resistant organisms should seek advice from their care team about the advisability of attending events.

8) Use of electronic or virtual means of communication (teleconferences, webinars, *etc.*) should be considered where available.

Patients are also concerned to reduce their risk of exacerbation by reducing the acquisition of viral and other infections. We identified no evidence that infection control measures can prevent exacerbations. We therefore suggest that patients are advised to practise standard hygiene measures, such as hand washing before meals and that patients should avoid contact where possible with children and adults with active viral infections. Patients should be encouraged to receive influenza and other vaccinations in line with national recommendations. It was discussed that some patients in online forums recommend face-masks to reduce infection risk in bronchiectasis. The panel recommended against the use of facemasks due to a lack of evidence for their effectiveness and the risk of stigmatising bronchiectasis patients.

Finally, the topic of cross-infection is a key research priority in bronchiectasis. Cross-infection was identified by both patients and physicians as one of the 55 key research questions in the field of bronchiectasis, In the EMBARC "roadmap" published in 2016 [24]. We strongly recommend that large scale longitudinal studies are performed to ascertain the incidence and clinical implications of cross-infection in bronchiectasis.

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