

INSTRUCTIONS FOR INFECTION CONTROL IN OUTPATIENT CARE OF PATIENTS WITH CYSTIC FIBROSIS

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Abstract

Rationale and goals: Infections of the respiratory tract with multiresistant bacteria and other pathogens lead to a poor prognosis in patients with cystic fibrosis [1, 2]. The patient-to-patient transmission of infectious agents during the clinic visit and the transmission via the hands of healthcare workers has gained increased attention in the cystic fibrosis community [3, 4]. For this reason practical and possibly evidence-based instructions for infection control measures are needed that are feasible in every day outpatient management of patients with cystic fibrosis.

Methods: For generating these instructions, a committee consisting of medical doctors and nursing staff providing care to cystic fibrosis patients, infectious diseases specialists and members of the department of infection control analyzed the patients' route through our cystic fibrosis unit during a routine clinic visit. First, the expert committee defined instructions concerning important infection control measures for each step. Next, each instruction was compared with the published literature and categorized as to its grade of evidence (I, II, 0). Instructions with grades of evidence I and II and instructions without demonstrated evidence (0) but theoretically reasonable and practically feasible, were accepted and outlined in a flow diagram. All other instructions were rejected.

Results: The expert committee defined 45 instructions for infection control measures during an outpatient visit of a cystic fibrosis patient. 43 instructions within the categories "principles", "measures before entering the clinic", "measures in the examination room" and "measures when leaving the clinic" matched the criteria mentioned above and were accepted. 2 instructions were rejected.

Conclusions: Here we report evidence-based instructions for infection control in the setting of outpatient care for cystic fibrosis patients which are feasible in every day care. Since some instructions could only be assigned low evidence grade levels, i. e. II or 0, a further clarification of these issues by scientific investigations is warranted. Unresolved issues are primarily the recommendation for or against wearing a face mask for patients with certain pathogens and the issues of colonization with *Stenotrophomonas maltophilia* and *Alcaligenes xylosoxidans*, but also with *Aspergillus spp.*. Continuous education of patients and healthcare workers as well as the validation of these practical in-

structions by a close monitoring and documentation of pathogens are of great importance.

Key words: Infection control, cystic fibrosis, outpatient care, practical instructions

INTRODUCTION

Pulmonary infections with pathogens such as *P. aeruginosa*, multiresistant strains of *P. aeruginosa* and *B. cepacia* lead to an accelerated deterioration in lung function and a reduced median survival time in patients with cystic fibrosis [5, 6, 7, 8, 9, 10]. Thus the avoidance of an acquisition of *P. aeruginosa* and other pathogens is a fundamental goal in cystic fibrosis treatment. Because of the increasing life expectancy with cystic fibrosis and due to the availability of potent oral, intravenous and inhaled antibiotics, the number of multiresistant *P. aeruginosa* strains is rising [11] and a new infection with such strains in previously *P. aeruginosa* negative patients is more difficult to treat. Other problems are associated with methicillin-resistant *S. aureus* (MRSA). The clinical and prognostic impact of MRSA infections in patients with cystic fibrosis is currently unresolved, however the prevalence of cystic fibrosis patients colonized with MRSA is increasing considerably [12]. *S. maltophilia* and *A. xylosoxidans* are gram-negative bacteria frequently recovered but their pathogenetic role is not defined yet. As there are studies showing an association of these pathogens with pulmonary exacerbations [13, 14], measures to avoid their transmission are justified.

Previous publications on infection control in cystic fibrosis patients partly imply evidence-based recommendations for the avoidance of pathogen transmission in the hospital in general [3, 4, 15]. The meta-analysis by Vonberg et al. [15] is especially important, summarizing measures for the isolation of cystic fibrosis patients with transmissible pathogens but primarily referring to the setting of a hospital ward and also omitting measures concerning MRSA which is relatively frequent among our patients (10/400 patients). According to Vonberg et al. [15], patients with *B. cepacia* need to be isolated in single patient rooms, patients with *P. aeruginosa* infection need to be separated from patients without *P. aeruginosa* and patients with multiresistant *P. aeruginosa*, *S. maltophilia* and

A. xylosoxidans are to be separated from immunocompromised patients on hospital wards and generally isolated on intensive care units. However, in cystic fibrosis care the outpatient setting has a much larger dimension and specific instructions for an evidence-based treatment with optimized infection control are still missing.

Our cystic fibrosis unit (Christiane-Herzog Ambulanz) is attended by 400 patients with cystic fibrosis. Currently, 250 patients are positive for *P. aeruginosa*, 10 for MRSA, 7 for *B. cepacia* and 3 for non-tuberculous mycobacteria. The mean patient age is 16.7 years (median 15.7, range 0.2 – 47), the mean FEV1 in lung function testing is 85.9 % (89, 20 – 147) and the mean weight for height score 105 % (104, 62 – 158). The unit is located in the main building of the hospital and has two separate entrances and waiting areas (“large” and “small”, Fig. 1). From the “large” waiting area, four examination rooms can be reached via a corridor, while there are two examination rooms directly adjoining the “small” waiting area. Each area has its own separate rooms for lung function testing and on each side physiotherapy can be administered.

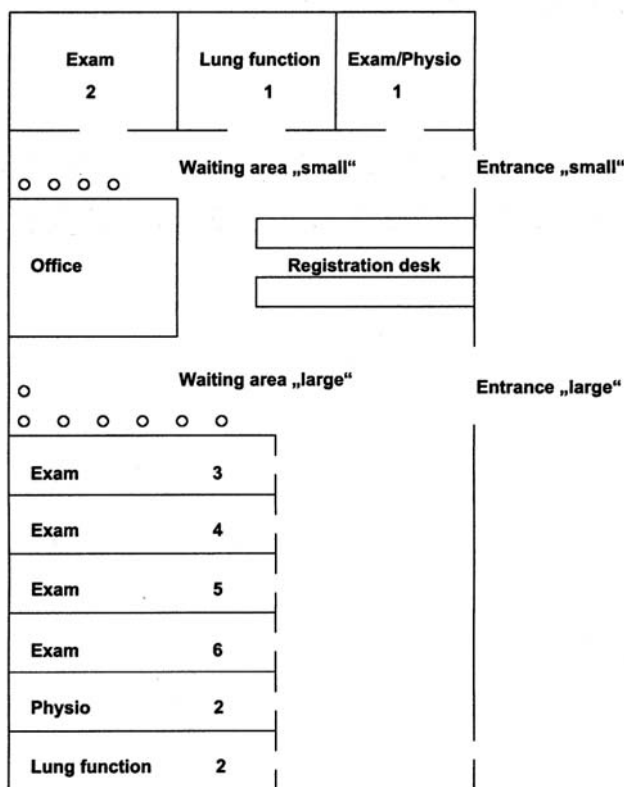


Fig. 1. Schematic ground plan of the cystic fibrosis outpatient unit (Christiane-Herzog Ambulanz).

Here we present an infection control concept for the outpatient treatment of cystic fibrosis patients which has been set up by the expert committee described below. The measures were assessed using previously published data, and they were summarized in a

flow chart depicting the stepwise sequence of a routine outpatient visit with the infection control measures found to be necessary (Fig. 2). It must be clearly stated that it is yet unclear whether this concept is efficient, sufficient or even exaggerated. Therefore its prospective evaluation is currently under way.

METHODS

Expert meeting: An expert committee (appendix 1) was formed for the generation of an infection control concept for the every-day treatment of cystic fibrosis patients in an outpatient setting. Instructions were categorized according to the patients' route from the hospital entrance to the cystic fibrosis unit, within the unit, and back out of the hospital during a routine visit. This stepwise approach allowed the analysis of every single action taking place from an infection control point of view.

Evaluation of the generated instructions: A MEDLINE-search (01/1966 – 10/2004) with the following keywords was performed: („burkholderia“ OR „cepacia“ OR „methicillin-resistant“ OR „MRSA“ OR „pseudomonas“ OR „aeruginosa“ OR „stenotrophomonas“ OR „maltophilia“ OR „alcaligenes“) AND „cystic fibrosis“ AND („transmission“ OR „outbreak“ OR „nosocomial“ OR „infection control“). Keywords were included in the search as words in the text and, if possible for the individual item, also as MeSH-terms (Medical Subheadings). Comments, letters, editorials and studies not relevant for the purpose were excluded. The results were assigned to the individual instructions according to their subject. Levels of evidence were assigned to the individual instructions according to established criteria (Table 1). All other instructions not matching one of the categories were not included in the final version of infection-control instructions and in the flow diagram. The evaluation of each instruction was finally compared with the “United States of America Cystic Fibrosis Foundation Consensus Conference on Infection Control” recommendations [3].

Table 1. Definition of evidence grades.

Grade	Supported by
IA	Well-designed, prospective, experimental and possibly randomised clinical or epidemiological studies
IB	Some prospective studies
II	Clear theoretical, clinical or experimental rationale but no prospective studies
0	No evidence for or against, but implementation allowed by theoretical and practical aspects

RESULTS

Initially we defined a total of 45 instructions and categorized them to the fields of “general principles”, “measures before entering the clinic”, “measures in

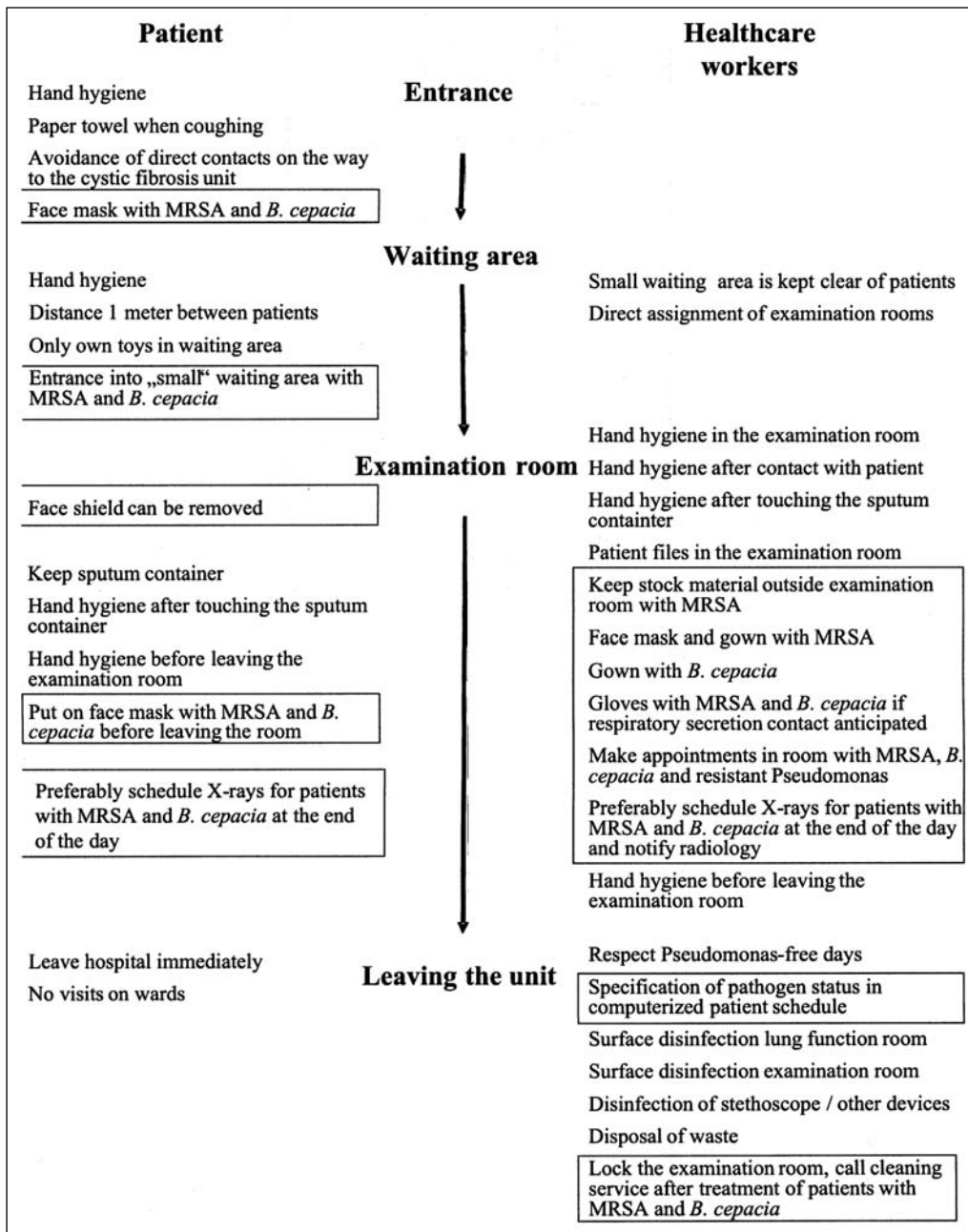


Fig. 2. Flow chart of instructions for cystic fibrosis patients and healthcare workers. Instructions applying to patients with MRSA and *B. cepacia* are depicted in frames

the examination room” and “measures when leaving the clinic”. The MEDLINE-search described above gave 242 hits, 64 of which were classified as relevant and assigned to the different instructions. One citation could thereby be assigned to several instructions. After evaluation of the instructions according to their level of evidence, a final version of the recommendations with 43 instructions was obtained. Levels of evidence for 7 instructions could only be assigned after comparison with the US-American recommendations for infection-control in cystic fibrosis care [3]. For 2 instructions no or not sufficient evidence could be obtained or suggestions did not seem to be feasible in every day practice, so that they were not included in the final version. One of these concerned the prescription of disinfectants to patients for hand hygiene before entering the hospital and the other face shields

for patients with *B. cepacia* and MRSA in the examination room.

Hygiene Instructions for Outpatient Care of Cystic Fibrosis Patients:

General principles:

- Every patient with cystic fibrosis may have transmissible pathogens in his or her respiratory secretions. Therefore basic infection-control measures must generally be applied (IA - 16, 17, 18).
- The hands of patients and healthcare workers are the main cause for pathogen transmission. If a strict hand hygiene is pursued, a considerable amount of problems can be avoided (IA - 19, 20).
- The clinically most relevant pathogen in cystic fibrosis is *P. aeruginosa*. Outpatient care therefore is

divided into *P. aeruginosa*- and *P. aeruginosa*-free days. Patients who are infected with *P. aeruginosa* get appointments on *P. aeruginosa*-days and *P. aeruginosa*-free patients get appointments on *P. aeruginosa*-free days (II).

- Appointments for *P. aeruginosa* positive patients on *P. aeruginosa*-free days are an exception and a very strict spatial separation has to be performed. The same applies to appointments for *P. aeruginosa*-free patients on a *P. aeruginosa*-day (IB - 16). A clear specification of the *P. aeruginosa* status in the computerized patient schedule and the availability of the latest bacteriology result are essential (II).
- Patients with MRSA or *B. cepacia* infection are preferably scheduled at the end of an individual clinic day. If this is not possible for reasons of organization, an adequate amount of time between these patients' and other patients' appointments has to be guaranteed to avoid contacts and to ensure sufficient disinfection of the examination room (IB - 21-25).
- After shaking hands between patients and healthcare workers or other patients proper hand hygiene has to be performed by both parties (IA - 26, 27, 28).
- Continuous education of patients and healthcare workers about the reasons and proper performance of infection control is essential for the success of infection control measures. This can be achieved by training courses, discussion rounds, parent- and patient classes as well as by printed information material (II).
- All hand hygiene measures apply to companions of cystic fibrosis patients during the outpatient visit equally (IA - 26, 27, 28).
- Waiting times in the waiting areas must be minimized. If possible, an examination room is assigned to all cystic fibrosis immediately after registration in the unit (0).
- Patients with MRSA or *B. cepacia* are considered positive until three negative throat swabs or sputum samples have been obtained on routine outpatient visits scheduled every three months (0).
- X-rays and other examinations for patients with MRSA or *B. cepacia* are scheduled at the end of the day and the department is notified (IA - 3, 4).

Measures before entering the clinic:

- Distributors containing alcohol-based hand washing solution are placed at the entrances of patient registration, the cystic fibrosis unit itself and at the entrance to each examination room (IA - 20).
- On entering the hospital building, patients with MRSA and *B. cepacia* put on a face shield and keep it on until they reach the examination room. (0).
- All cystic fibrosis patients and their family members perform hand disinfection at the entrance of patient registration (IB - 27, 29-31).
- All cystic fibrosis patients are called upon to cover their mouth with a paper tissue when coughing and to dispose it in the provided collection cans (II).
- On their way to the cystic fibrosis unit, all patients are allowed to use the same itinerary, however a direct contact < 1 meter should be avoided (II).

Measures in the cystic fibrosis unit:

- All cystic fibrosis patients and their companions perform hand disinfection at the entrance of the cystic fibrosis unit (IB - 27, 29-31).
- All cystic fibrosis patients keep a distance of at least 1 meter from each other in the waiting area of the cystic fibrosis unit (IB - 26).
- Children toys are removed from the waiting area of the cystic fibrosis unit. If desired, patients can bring own toys (II).
- If patients with MRSA, *B. cepacia* and multiresistant *P. aeruginosa* strains are expected, the "small" waiting area (Fig. 1) is to be kept clear of other cystic fibrosis patients 5-10 minutes before (0).
- Patients with MRSA, *B. cepacia* and multiresistant *P. aeruginosa* strains always directly go to the separated waiting area ("small") and check in there (IB - 21-25).
- Patients with MRSA, *B. cepacia* and multiresistant *P. aeruginosa* strains do not wait in the waiting area. They are immediately assigned an examination room in the "small" part (Fig. 1) of the cystic fibrosis unit (IB - 21-25).
- Patients with MRSA, *B. cepacia* and multiresistant *P. aeruginosa* strains have the possibility to perform spirometry with a portable device in the examination room. If complete lung function testing is required, sufficient time for disinfection of the lung function room must be reserved (0).
- Inner parts of the lung function testing device do not need to be disinfected after usage since always disposable filters are used (II). Surfaces in the body box and in the lung function room need to be disinfected according to infection-control standards (IB - 32-35).

Measures in the examination room:

- Healthcare workers perform hand hygiene using the distributors containing alcohol-based hand washing solution before entering and when leaving the room (IA - 19, 20).
- Before and after each hand contact with the patient, healthcare workers perform proper hand hygiene (IB - 19, 20).
- Patient files of all cystic fibrosis patients can be taken along into the examination room (0).
- Patients with MRSA and *B. cepacia* can remove their face mask in the examination room (0).
- Prior to treatment of patients with MRSA, the wheeled car with stock supplies is removed from the examination room. Only material required for planned examinations and procedures is kept in the room (0).
- When caring for patients with MRSA, healthcare workers wear a face mask and a disposable gown (IB - 21, 36).
- When caring for patients with *B. cepacia* and multiresistant *P. aeruginosa* strains, healthcare workers wear a disposable gown (0).
- When contact with respiratory secretions in patients with *B. cepacia* and MRSA can be anticipated, healthcare workers additionally wear gloves (0).
- Patients bringing a sputum sample to the office visit, keep it until it can be disposed in a second clean outer container for further handling and transportation (0).

- After touching a sputum container, patients and healthcare workers need to perform hand disinfection (IA).
- Appointments for all patients are made using the computers in the examination rooms so that another contact with other patients in the reception area is avoided (IA).
- Prescriptions are printed by the nursing staff. The patients chip cards are first disinfected and then taken out of the examination room (0).

Measures when leaving the clinic:

- Before leaving the examination room, patients perform hand disinfection using the distributors placed in the room (IB - 27, 29-31).
- All cystic fibrosis patients directly leave the hospital. Visits of other patients (e. g. on hospital wards) are to be omitted (0).
- Materials to draw blood in patients with MRSA, *B. cepacia* and multiresistant *P. aeruginosa* strains and all other patients are disposed in plastic containers according to standard recommendations (IA).
- Waste from patients with MRSA, *B. cepacia* and multiresistant *P. aeruginosa* strains and all other patients as well as all used gowns are disposed according to standard recommendations (IA).
- Stethoscope and other devices are disinfected after usage in all cystic fibrosis patients (IA - 32, 37, 38).
- Stretcher, chairs, table etc. as well as the computer keyboard is disinfected by the nursing staff according to standard recommendations after each visit of a cystic fibrosis patient (IB - 32-35).
- After MRSA and *B. cepacia* patients, the room is locked and the cleaning service is called for complete disinfection of the room (IB - 32-35).

For further clarification, these practical instructions are depicted in a flow diagram showing the different steps and infection control measures during routine outpatient visits (Fig. 2).

DISCUSSION

Certain infection control measures and strategies to avoid the transmission of pathogens have been used for decades in our hospital however these were not systematically compiled and taught to patients and healthcare workers. To define these measures more precisely, an expert committee suggested common sense based recommendations for infection-control measures in outpatient care for cystic fibrosis patients which could reliably be implemented in every day care. These recommendations were then evaluated as to their level of evidence and practicability. This resulted in 43 instructions that can be judged as feasible and reasonable for daily work with cystic fibrosis patients.

All members of the cystic fibrosis team (nursing staff, medical doctors, and other healthcare professionals (social workers, physiotherapists, dietician, diabetes specialist)), as well as the patients and their families were introduced to these measures. Potential problems that might arise with the implementation and usage of this infection-control concept in every day clinical

work, were broadly discussed. The instructions are used on a daily basis since December 1st 2004. The advantage of such an approach is the very precise description how to behave, fitting exactly into the environment where the instructions are to be realized and the possibility for all staff members and the patients, to control these measures and to judge on the adherence to them.

Even though the efficacy of single instructions with the evidence grade I is clearly supported by well-designed controlled clinical trials, no evidence exists for the efficacy of such a general concept up to now. Therefore the evaluation of the potential success or failure achieved by these instructions in optimizing outpatient cystic fibrosis care from an infection-control standpoint is a primary goal. This validation can only be achieved by a careful monitoring of previously known or newly detected pathogens in sputum or oropharyngeal cultures of cystic fibrosis patients. Such surveillance can be realized quite easily since cultures of respiratory secretions or oropharyngeal swabs are obtained routinely during each outpatient visit. Changes in individual patients must be monitored systematically and at fixed time intervals, to look for deviations in the course. In fact, such an approach is complementary to §23 [1] of the German federal infection-control act (IfSG), which directs that all transmissible agents with special resistances and multiresistance have to be documented and evaluated with respect to their clinical relevance. In this context we currently introduced a program for routine genotyping of all newly isolated MRSA and *B. cepacia* strains. For logistic and financial reasons routine genotyping can not be performed on all *P. aeruginosa* pathogens.

The success of each infection-control measure is highly dependent on the adherence of the persons involved. This makes continuing education of patients and healthcare workers on infection-control measures an essential component of the program. Within the last six months, our institution provided two separate events for healthcare workers covering this subject apart from the expert meeting (education program of the Department of Infection control for nursing staff and doctors, quality control meeting of the Bavarian cystic fibrosis units), so that the importance of infection-control was repeatedly recalled. Every participant including the patients, with special emphasis on the nursing staff, is responsible for pointing out the importance of infection-control measures and the adherence to them. Patients need to get written and oral explanations why for instance appointments are scheduled on special days of the week (e. g. on a *P. aeruginosa*-day or on a *P. aeruginosa*-free day) or that new dispensers for hand washing solution have been put up or why hand hygiene is important and how it is performed correctly. All measures are explained to all the patients with the help of a video sequence showing the stepwise sequence of a routine outpatient visit with respect to the infection control measures in and out our facility during a routine visit. This material is available online and as a CD handed to the patients. In addition to this, all patients receive printed information material on the infection-control instructions, so that he or she can read about the background of these changes

and novelties at home. As children are treated in our cystic fibrosis unit, playful methods of education constitute important measures for the correct implementation of the new instructions.

The introduction of infection-control instructions in outpatient cystic fibrosis care also implies relatively restrictive measures (e. g. face masks for patients with MRSA and *B. cepacia* or the treatment of MRSA and *B. cepacia* patients in separate areas of the unit) which might sometimes cause emotional problems. The fact that the doctor is wearing a gown or a face mask can be perceived as discriminatory by the patient, especially when a pathogen such as MRSA is detected for the first time. This can have intense psychological consequences for the patient. Prejudice, second-class treatment and disgust will be reproaches the treating healthcare workers will be confronted with. Negative patient feelings can also have an impact on compliance, so that medical advices will not be taken seriously any more or not followed in defiance. Outpatient visits of individual patients with certain pathogens might become less frequent. Grief, depression and deterioration of the health status neglecting necessary therapies might result in certain patients. An alternative to counter such problems is currently practiced in the cystic fibrosis unit of the University Children's Hospital in Vienna where specifically every patient is given the opportunity to wear a face mask when entering the hospital. Again, continuous education of all patients plays an important role with respect to this potential consequence of infection-control measures as well as honesty and empathy among the medical staff.

Another specific problem with regard to infection control in cystic fibrosis is to what extent these instructions are applicable to other pathogens which are detected less frequently in patients with cystic fibrosis. Non-tuberculous mycobacteria are associated with a more rapid clinical deterioration in cystic fibrosis [39] and a colonization with *Aspergillus fumigatus* predisposes to allergic bronchopulmonary aspergillosis. Even though the negative clinical impact of these pathogens is clearly confirmed, data concerning the transmission routes of these agents are rare and the need for specific infection control measures is less clear. For instance, in our cystic fibrosis unit, patients with non-tuberculous mycobacteria are treated like patients with *B. cepacia*. However this decision is arbitrary and a definite clarification of this issue can only be achieved by further investigations on the biology of these organisms. In our situation, the prospective evaluation of our 43 instructions on practical infection control measures in outpatient cystic fibrosis care with regard to more commonly detected pathogens is of primary importance and currently underway.

In summary, instructions for infection control measures for every day outpatient management of patients with cystic fibrosis which are readily realized on a routine basis, were initially generated by an expert committee. Next, each instruction was categorized as to its grade of evidence. Instructions with high grades of evidence and those theoretically reasonable and practically feasible were accepted. All other instructions were rejected. Unresolved issues primarily concern the recommendation for or against wearing a face mask

for patients with certain pathogens and the issues of colonization with *Stenotrophomonas maltophilia* and *Alcaligenes xylosoxidans*, but also with *Aspergillus spp.*. All measures were explained to all the patients and the health care workers with the help of written material, video material and during meetings of patients cohort-ed according to their microbiological status. Continuous education as well as the validation of these practical instructions are ongoing.

Appendix 1

Infection control team of the cystic fibrosis unit:

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