



Use of Selective Fungal Culture Media Increases Rates of Detection of Fungi in the Respiratory Tract of Cystic Fibrosis Patients

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ABSTRACT The prevalence of fungi in the respiratory tracts of cystic fibrosis (CF) patients has risen. However, fungal surveillance is not routinely performed in most clinical centers in the United States, which may lead to an underestimation of the true prevalence of the problem. We conducted a prospective study comparing the rates of detection for clinically important fungi (CIF), defined as *Aspergillus*, *Scedosporium*, and *Trichosporon* species and *Exophiala dermatitidis*, in CF sputa using standard bacterial and selective fungal culture media, including Sabouraud dextrose agar with gentamicin (SDA), inhibitory mold agar (IMA), and brain heart infusion (BHI) agar with chloramphenicol and gentamicin. We described the prevalence of these fungi in an adult CF population. A total of 487 CF respiratory samples were collected from 211 unique participants. CIF were detected in 184 (37.8%) samples. Only 26.1% of CIF-positive samples were detected in bacterial culture medium, whereas greater rates of detection for fungi were found in IMA (65.8%; $P < 0.001$), in SDA (at 30°C, 64.7%; $P = 0.005$), and in BHI agar (63.0%; $P = 0.001$). The prevalences of *Aspergillus* and *Scedosporium* species were 40.8% and 5.2%, respectively, which are greater than the nationally reported prevalence numbers of 20.4% and 1.9%. Selective fungal culture media and longer incubation periods yielded higher rates of detection for CIF in CF sputum samples compared with that detected in bacterial culture medium, resulting in an underdetection of fungi by bacterial culture alone. The prevalence of fungi in CF may be better estimated by using selective fungal culture media, and this may translate to important clinical decisions.

KEYWORDS fungi, cystic fibrosis, fungal culture, inhibitory mold agar, brain heart infusion agar, Sabouraud dextrose agar, *Aspergillus*, *Scedosporium*, *Trichosporon*, *Exophiala*

Cystic fibrosis (CF) is the most common deadly autosomal recessive disease in Caucasians, affecting approximately 70,000 individuals worldwide. CF is a multiorgan disease that results from the dysfunction of the cystic fibrosis transmembrane conductance regulator gene in the epithelial cells of the sinopulmonary, pancreatic, hepatobiliary, intestinal, skin, and reproductive systems (1). Recurrent infections and bronchiectasis of the lower respiratory tract lead to respiratory failure, the leading cause of death in CF. However, a greater understanding of chronic infections and antimicrobial treatments have transformed the life expectancies of individuals with CF to greater than 40 years of age. The vast majority of antimicrobial therapies in CF are directed

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toward bacteria, including *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Burkholderia cepacia* complex.

The presence of fungi isolated from CF respiratory secretions has significantly risen. The prevalence of *Aspergillus* species, the most common filamentous fungi in the CF airway, has increased from 6% to 12% over the past 2 decades (2, 3). In addition, *Scedosporium*, *Trichosporon*, and *Exophiala* species have been increasingly detected in CF sputa (4–11). Furthermore, there is increasing evidence that the chronic presence of *Aspergillus*, *Scedosporium*, *Trichosporon*, or *Exophiala* species in CF individuals is associated with pulmonary morbidity, including respiratory symptoms and pulmonary exacerbations, and even death in the post-lung transplant population (5–9, 11, 12). The reported prevalences in CF centers have ranged from 0 to 36% and 0 to 9% for *Aspergillus* and *Scedosporium*, respectively (3, 13, 14). The variability observed may be due to differences in the clinical practice of fungal surveillance and to a lack of standardized laboratory practices for detecting fungi in CF respiratory specimens (15, 16). The presence of rapidly growing Gram-negative organisms, such as *Pseudomonas aeruginosa*, can interfere with the isolation of potentially clinically significant fungi in standard culture media (5). Despite this, on the basis of pilot survey data, 80% of microbiology laboratories do not routinely perform mycological examinations with selective fungal media in CF respiratory samples, unless they are requested by clinicians (Hong, unpublished data). As a result, only molds and yeasts isolated in bacterial culture medium are reported. Some clinicians order targeted fungal respiratory culture when the suspicion for atypical infection is high, but it is unclear how often this occurs. Our survey data also demonstrated that approximately 57% (95% confidence interval, 18 to 90) of clinicians in the United States report regular monitoring of fungi in CF patients. However, given the small sample size and populations limited to large academic centers, this is likely an overestimation of fungal surveillance in U.S. CF centers.

Previous data suggest that nonselective conventional culture media are insufficient for accurately diagnosing fungal infections, and more selective fungal culture media are associated with an increased identification of fungi in CF sputa (17–21). However, a direct comparison of the rates of detection for fungi by standard bacterial culture medium (based on the infection control guidelines by the Cystic Fibrosis Foundation [CFF]) and by selective fungal media have yet to be performed in a United States CF cohort (22). Accurate diagnoses of fungal infections in the CF population may have significant clinical implications, particularly for sick individuals and among candidates for lung transplantation.

The objective of our study was to evaluate the performances of bacterial and selective fungal culture media in the detection of clinically important fungi (CIF) seen in the CF respiratory tract. We hypothesized that selective fungal culture media would demonstrate greater rates of detection of fungi, and thereby, more accurately describe the prevalences of *Aspergillus*, *Scedosporium*, *Trichosporon*, and *Exophiala* species in an adult CF population.

RESULTS

A total of 501 independent respiratory samples were collected, and 487 were analyzed. Ten samples were inoculated in only two of the three culture media in the selective fungal research protocol and were omitted from analysis due to deviations from the protocol. Four samples were inoculated on expired culture medium and were excluded from the analysis. The study included 211 unique subjects with a mean of 2.28 samples per subject during the 12-month period. Filamentous fungal or yeast species were detected in 223 of 487 (45.8%) samples. Sixty specimens (12.3%) were polymicrobial (with two or more fungi). CIF were isolated from a total of 184 (37.8%) samples, with *Aspergillus* species being the most common.

Cohort characteristics. We compared the baseline demographic and clinical characteristics of individuals from whom CIF were isolated during the study period with those of individuals from whom they were not (Table 1). The demographic characteristics were similar in both groups. Disease characteristics representing the severity of

TABLE 1 Baseline characteristics of CIF-positive and CIF-negative patients^a

Characteristic	CIF positive (n = 101)	CIF negative (n = 110)	P value
Mean age (yr)	33.2	32.4	0.60
Female sex (no. [%])	49 (48.5)	58 (52.7)	0.50
F508del/F508del (no. [%])	50 (49.5)	63 (57.3)	0.15
FEV ₁ (% predicted [mean ± SD])	62.3 ± 23.3	66.1 ± 23.2	0.23
Pancreatic insufficiency (no. [%])	88 (87.1)	93 (84.6)	0.70
<i>Pseudomonas</i> colonization (no. [%])	89 (88.1)	88 (80.0)	0.14
Treatment (no. [%])			
Inhaled antibiotic ^b	82 (81.2)	76 (69.1)	0.05
Chronic oral antibiotic ^c	28 (27.7)	15 (13.6)	0.01
Azithromycin	71 (70.3)	76 (69.1)	0.93
Antifungal ^d	7 (6.9)	7 (6.4)	0.88

^aCIF, clinically important fungi defined as *Aspergillus*, *Scedosporium*, *Trichosporon*, and *Exophiala* species.

^bTobramycin powder/solution, aztreonam, colistin, or ceftazidime.

^cSulfamethoxazole/trimethoprim, minocycline, doxycycline, or linezolid.

^dItraconazole, voriconazole, or posaconazole.

disease, including F508 genotype, pancreatic insufficiency, and pulmonary function defined as the predicted percent of forced expiratory volume in 1 s (FEV₁), were similar in both groups. However, chronic nonmacrolide oral antibiotic and inhaled anti-pseudomonal inhaled antibiotic exposures were greater in the CIF-positive group compared to those in the CIF-negative group (oral antibiotic, 27.7% versus 13.6%, respectively, *P* = 0.01; inhaled antibiotic, 81.2% versus 69.1%, respectively, *P* = 0.05).

Prevalence of clinically important fungi. CIF were isolated from samples from 101 (47.9%) individuals during the study period. The prevalences of each of the organisms are summarized in Fig. 1. The prevalences of *Aspergillus* and persistent *Aspergillus* were 40.8% and 17.1%, respectively, with *Aspergillus fumigatus* as the predominant species. The prevalences of *Scedosporium*, *Exophiala*, and *Trichosporon* species were lower at 5.2%, 4.7%, and 3.3%, respectively. Of note, other filamentous fungal species were detected in the study. *Rasamsonia* species, an emerging pathogen seen in the CF airway (23), were found in samples from 2 (<1%) individuals in the cohort. *Paecilomyces variotii* (4.3%), *Penicillium* (11.2%), and other uncommon filamentous fungi, including *Rhizopus*, *Libertella*, *Rhinochadiella*, *Cercospora*, and *Basidiomycete* species, were also seen.

Performance of selective fungal media for detection of *Aspergillus*, *Scedosporium*, *Trichosporon*, and *Exophiala*. A total of 184 samples were found to have CIF isolates. The performances of each of the culture media are summarized in Table 2. Among these, CIF were detected in bacterial cultures from 48 (26.1%) samples. CIF were detected at 37°C with Sabouraud dextrose agar with gentamicin (SDA), a selective fungal culture medium, in 103 (56.0%) samples, which was statistically significantly greater than the rate of detection in bacterial culture medium (26.1%, *P* < 0.001). When

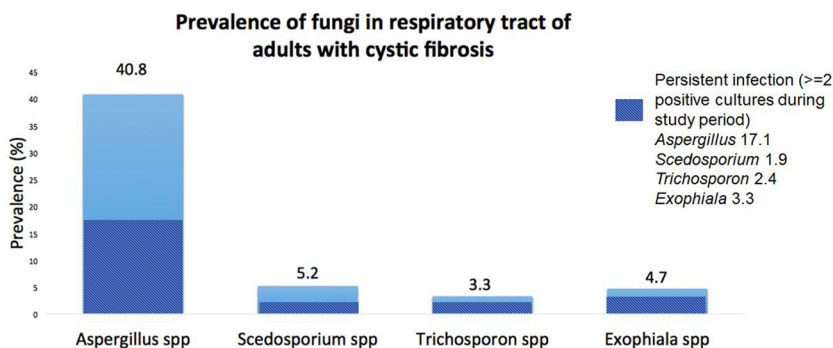


FIG 1 Prevalences of clinically important fungi in samples from adults with cystic fibrosis.

TABLE 2 Detection of CIF in bacterial culture and selective fungal culture media^a

Medium ^b	No. of samples with fungi detected (%)	P value
Bacterial culture	48 (26.1)	reference
SDA at 37°C	103 (56.0)	<0.001
SDA at 30°C	119 (64.7)	0.005
IMA	121 (65.8)	<0.001
BHI agar	116 (63.0)	0.001
Combination of IMA, SDA at 30°C, and BHI agar	156 (84.8)	<0.001

^aCIF, clinically important fungi defined as *Aspergillus*, *Scedosporium*, *Trichosporon*, and *Exophiala* species.

^bSDA, Sabouraud with gentamicin; IMA, inhibitory mold agar; BHI, brain heart infusion.

comparing the performances of each of the selective fungal media to the rates of detection of CIF utilizing bacterial medium (26.1%), we found that each of the fungal media had significantly higher rates of detection; in SDA at 30°C, CIF were detected in 119 samples (64.7%, $P = 0.005$), in inhibitory mold agar (IMA), CIF were detected in 121 samples (65.8%, $P < 0.001$), and in brain heart infusion (BHI) agar, CIF were detected in 116 samples (63.0%, $P = 0.001$).

We further analyzed the performances of selective fungal media for detecting each of the CIF: *Aspergillus*, *Scedosporium*, *Trichosporon*, and *Exophiala* (see Table S1 in the supplemental material). A total of 144 samples were positive for *Aspergillus* species, with *Aspergillus fumigatus* isolated from 134 (93%). *A. terreus*, *A. niger*, *A. flavus*, and *A. nidulans* were also observed. The rate of detection of *Aspergillus* by bacterial culture medium was 30.6%. In comparison, the rates of detection were greater with each of the selective fungal culture media: SDA at 37°C (54.9%, $P < 0.001$), SDA at 30°C (50.0%, $P < 0.001$), IMA (50.0%, $P = 0.001$), and BHI agar (47.9%, $P = 0.003$). Twenty-five of the 144 *Aspergillus*-positive samples were identified by bacterial culture medium only. Among the 20 samples positive for *Scedosporium apiospermum* ($n = 17$) and *S. prolificans* ($n = 3$), bacterial culture medium detected three of the 20 (15%), whereas the rates for detecting *Scedosporium* using selective fungal media were greater. Of the 17 *Trichosporon*-positive samples, only a single specimen (5.9%) was detected by bacterial culture. SDA at 30°C and 37°C, IMA, and BHI agar performed well in comparison to bacterial medium. Finally, we failed to detect any *Exophiala*-positive specimens after incubating bacterial cultures for 3 days. On the contrary, IMA had a high rate of detection (95.7%), whereas the rates of detection with SDA at 30°C and 37°C and BHI agar were slightly lower.

Mean time-to-detection of *Aspergillus*, *Scedosporium*, *Trichosporon*, and *Exophiala*. The mean times-to-isolation of CIF on bacterial culture medium and SDA at 37°C for a maximum incubation period of 3 days were 2.35 days and 2.21 days, respectively (Table 3). For SDA at 30°C, IMA, and BHI agar incubated for 14 days, the mean times-to-isolation of CIF were 3.49, 3.85, and 3.43 days, respectively, and did not exceed 4 days for each of the media. Upon examining each of the CIF, we found that *Aspergillus* grew in 3.48 days on IMA, *Scedosporium* in 3.61 days, *Trichosporon* in 2.75 days, and *Exophiala* in 5.87 days (see Table S2). Mean times-to-isolation for each of the CIF were similar to those on BHI agar and SDA at 30°C.

TABLE 3 Time-to-detection of CIF in bacterial culture and selective fungal culture media^a

Medium ^b	Time-to-detection (days) (mean \pm SD)	P value ^c
Bacterial culture	2.35 \pm 1.12	reference
SDA at 37°C	2.21 \pm 0.51	0.48
SDA at 30°C	3.49 \pm 1.76	0.002
IMA	3.85 \pm 2.18	0.003
BHI agar	3.43 \pm 1.89	0.003

^aCIF, clinically important fungi defined as *Aspergillus*, *Scedosporium*, *Trichosporon*, and *Exophiala* species.

^bSDA, Sabouraud with gentamicin; IMA, inhibitory mold agar; BHI, brain heart infusion.

^cBased on pair-wise comparisons.

DISCUSSION

Our study is the first to examine and compare the rates for detecting fungi in the CF airways of individuals in a North American CF cohort utilizing various culture media. The results of our study suggest CIF in CF patients vulnerable to fungal isolation in the respiratory tract are underdetected when using bacterial culture medium alone for fungal surveillance. Furthermore, when combinations of selective fungal media are used, the prevalence of CIF is notably greater than the known prevalence reported in the CFF registry (3).

The prevalence of CIF in our cohort was greater than 40%. Only one-quarter of the clinically significant fungal organisms were successfully detected in standard bacterial culture medium. Selective fungal culture media and prolonged incubation periods provided statistically significantly better rates of detection of CIF than did bacterial culture. *Aspergillus* species were best detected when utilizing SDA at an incubation temperature of 37°C. *Aspergillus* was isolated from one-third of the positive samples by bacterial culture. For other clinically significant fungi, bacterial culture performed poorly compared with the selective fungal media. Fifteen percent of the *Scedosporium* isolates were detected on bacterial culture media. Similarly, the rates of detection of *Trichosporon* and *Exophiala* from bacterial culture media were 5% and 0%, respectively. Among each of the CIF, the greatest rates of detection were found using a combination of IMA, SDA, and BHI agar, which may support a multimodal approach for selective fungal culturing. Although statistical comparisons between SDA, IMA, and BHI agar were not performed, with the exception of *Exophiala dermatitidis*, the rates of detection of each of the selective fungal media for *Aspergillus*, *Scedosporium*, and *Trichosporon* species appeared similar. Among the *Exophiala*-positive samples, a higher rate of detection occurred on IMA than on SDA or BHI agar. These data suggest that CF centers without formal mycological examinations involving selective fungal media may have unidentified cases of fungal respiratory infection or colonization in CF patients, particularly for *Scedosporium*, *Trichosporon*, and *Exophiala* species.

The prevalences of *Aspergillus* (40.8%) and *Scedosporium* (5.2%) were greater in our study than in the national registry data of CFF-accredited centers in the United States (43). The prevalences of *Aspergillus* and *Scedosporium* species in adults with CF has been reported as 20.4% and 1.9%, respectively (24). The prevalence numbers from our study are comparable to those from studies performed utilizing selective fungal media, such as SDA, but are not as high as those experimenting with *Scedosporium*-selective media (SceSel+) containing benomyl and dichloran, which have been reported to be as high as 10 to 16% (15, 17, 18, 20, 25). The prevalences of *Trichosporon* and *Exophiala* are not well described in the CFF registry. Epidemiologic data have demonstrated the prevalence of *Trichosporon* to be an estimated 2.1% in an American cohort (4, 11). The prevalence of *Exophiala* in the United States has not been described.

A number of previous studies have investigated new culturing methods and selective media for fungal species in the CF population. Nagano et al. conducted experiments to develop novel selective media for isolating yeasts and filamentous fungi and determined that SDA plus antibiotics (including co-trimethoxazole, chloramphenicol, ceftazidime, and colistin) and self-formulated Medium B+ performed with high sensitivity (96%) and specificity (82%) for the detection of fungi in CF sputa (26). Several groups have demonstrated the superior performance of SceSel+ agar containing benomyl for isolating *Scedosporium* species (18, 25, 27). A multicenter study in Europe and Australia comparing the performances of semiselective fungal media in 469 samples of CF sputum found yeast potato dextrose agar, SceSel+ agar, and B+ medium to be among the most sensitive for detecting fungi, including *Aspergillus*, *Scedosporium*, and *Exophiala* species (28). One limitation of these studies is that those selective media are not commercially available, which may prevent clinical laboratories from implementing and further standardizing laboratory protocols for fungal isolation. Despite these data and the known variability of fungal prevalence numbers secondary to nonuniform laboratory protocols, Europe and the United States lack a standardized

approach for mycological examination (15, 16). In contrast to previous studies, we directly compared rates of detection between bacterial culture medium and commonly available selective fungal media and demonstrated the suboptimal performance of bacterium-specific culture medium to detect clinically significant molds and yeasts in CF sputum samples. Our findings suggest that, in the adult CF population vulnerable to respiratory fungal infection and colonization, clinicians should not solely rely on bacterial culture to make accurate fungal diagnoses.

The duration of time from inoculation to the detection of a fungal isolate was studied to determine an optimal incubation period to maximize the detection of fungi. The mean time-to-isolation of CIF utilizing selective fungal culture media at 30°C was approximately 3.5 days, which is comparable to results from previous studies (18). Upon examining the mean time-to-detection for each fungal species group during the 2-week research protocol, the observed times were notably different between fungal species. *Trichosporon* was isolated after a short period of incubation, whereas *Exophiala dermatitidis* was recovered at a mean time approaching 6 days on IMA (see Table S2). These data suggest that an incubation period of 7 days may be sufficient for detecting the majority of fungi in CF sputa.

Currently, the standard of care protocol for analyzing CF respiratory specimens in clinical microbiology laboratories involves conventional culture techniques. Although there is evidence that culture-independent tests, such as molecular sequencing, improve the sensitivity for diagnosis, these approaches are not yet universal or widely accessible to a vast majority of clinical laboratories (29, 30). In addition, the clinical relevance of the presence of DNA from organisms has yet to be demonstrated.

Evidence suggests there may be a subset of CF patients who are at greater risk of developing fungal infections and colonizations of clinical significance. The use of inhaled antibiotics, anti-staphylococcal oral antibiotics, macrolide therapy, and inhaled corticosteroids have been associated with filamentous fungal isolation, predominantly *Aspergillus* (4, 5, 31–36). In our cohort, individuals from whom CIF were isolated during the study period had greater usages of chronic anti-methicillin-resistant *Staphylococcus aureus* (MRSA) oral antibiotics and chronic inhaled anti-pseudomonal antibiotics at baseline than those from whom CIF was not isolated. These associations may further guide clinicians in assessing the presence of fungi, such as *Aspergillus*, *Scedosporium*, *Trichosporon*, or *Exophiala* species, by utilizing more accurate selective fungal culture in a subpopulation of patients that may be more vulnerable to developing these infections.

There are limitations to note in our study. First, the study population was limited to adults who were able to expectorate sputum, affecting the generalizability to the entire CF population. However, several studies indicate that fungi are more prevalent in older adults than in children with CF (4, 5, 37, 38). On the basis of CFF registry data, the mean age for acquiring a persistent isolation of *Aspergillus* was 17.3 years (Hong, unpublished data). Second, the incubation period for bacterial culture medium could not be extended beyond a 3-day duration. As a result, the comparison data between bacterial culture medium and selective fungal media should be interpreted cautiously. Nevertheless, one could infer that the overall standard lab practice of bacterial culture for a 3-day incubation period has a lower rate of detection for CIF compared with that from a selective fungal media protocol involving a longer incubation period. Furthermore, we were unable to determine true test characteristics, including sensitivity and specificity, due to the lack of a gold standard test for a true fungal diagnosis. Although several diagnostic tests have proved to have better performances in diagnosing certain fungal species in cystic fibrosis, such as sputum galactomannan and molecular testing, these are not routinely performed in the clinical laboratory setting (30, 39). Finally, there may be unmeasured confounders that may affect the likelihood of fungal isolation on bacterial culture, such as acute oral or intravenous antibacterial therapy for treating pulmonary exacerbation at the time of the specimen collection. However, the association between intravenous (i.v.) antibiotic use and *Aspergillus* isolation has been controversial (35, 40).

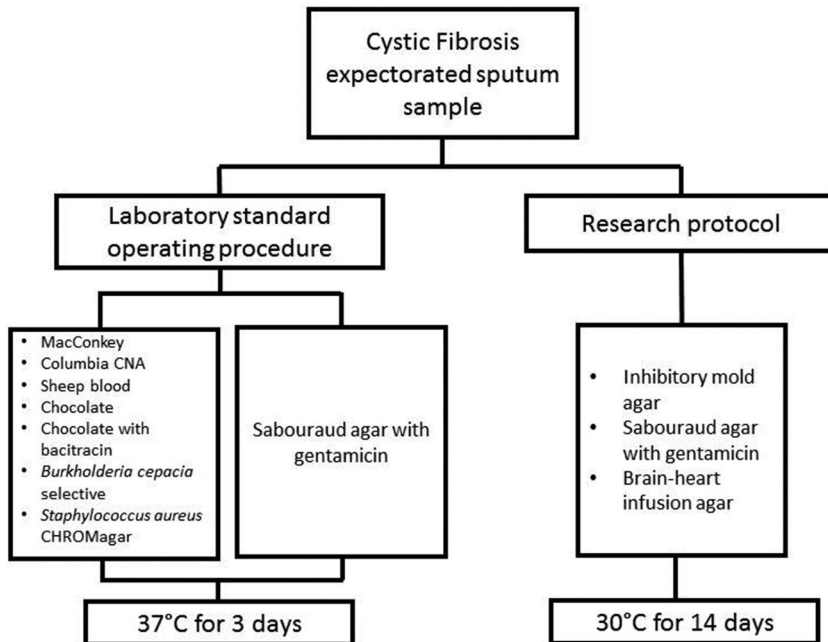


FIG 2 Flow diagram depicting the study design.

In conclusion, the clinical impact of certain filamentous fungi and yeast in CF remains debatable despite increasing data suggesting respiratory morbidity. However, accurate diagnoses are necessary to truly understand the clinical outcomes associated with fungal disease. Our study suggests the current practices of some CF clinicians and clinical microbiology laboratories may be limiting the fungal diagnoses if selective fungal culture methods are not utilized. These data suggest that a combination of selective fungal culture media, including IMA, SDA, and BHI agar, incubated for approximately 7 days would result in a greater isolation of CIF in a CF population. Further study is needed to guide the development of a standardized approach to detect fungi in the CF airway.

MATERIALS AND METHODS

Study design and participants. This was a 12-month prospective study involving the collection and analysis of expectorated sputa from adult CF patients at the Johns Hopkins Hospital in Baltimore, Maryland, USA. Consecutive expectorated sputum specimens were collected from patients in the outpatient clinic, regardless of clinical status, and underwent analysis by the Johns Hopkins clinical microbiology laboratory. Eligibility criteria included subjects with a baseline age of 18 years or older and with the ability to expectorate sputum. A minimum sputum sample volume of 0.5 ml was collected. Liquefaction, sonication, or other specimen modification procedures were not performed. All plates were inoculated with equal volumes of sputum specimens. Each specimen underwent two protocols simultaneously: (i) a standard laboratory protocol involving inoculating on the bacterial culture medium recommended by the CFF (MacConkey, Columbia CNA, sheep blood, chocolate with and without bacitracin, *Burkholderia cepacia* selective, or *Staphylococcus aureus* CHROMagar, [Remel, Lenexa, KS]) (22, 41) plus SDA (Remel, Lenexa, KS) and incubating for 3 days at 37°C and (ii) a selective fungal research protocol involving inoculating on IMA (Hardy Diagnostics, Santa Maria, California), SDA, and BHI agar with gentamicin and chloramphenicol (Becton Dickinson, Sparks, Maryland) and incubating for 14 days in 30°C (Fig. 2). The cultures were evaluated daily for the presence of fungal isolates. When we detected a fungal isolate, it was identified by colony characterization and morphological examination via microscopy, and if necessary, by DNA sequencing procedures (sequence analysis of 26S to 28S rDNA and internal transcribed regions using the Applied Biosystems 3500 genetic analyzer) (42). We collected the clinical and demographic information of the subjects. The primary outcome was the rate of detection of CIF, defined as *Aspergillus*, *Scedosporium*, *Trichosporon*, and *Exophiala* species. The selection of these organisms was based on published literature associated with increased respiratory symptoms, pulmonary exacerbations, and post-lung transplant complications (5–7, 10–13, 31). All filamentous fungi that were isolated were recorded. The secondary outcome was the mean time-to-detection, defined as the number of days from inoculation of the specimen to the isolation of fungi.

Statistical analysis. The detection rate of each culture medium was determined by the proportion of positive culture diagnoses for the respective medium over the total number of positive culture

diagnoses. A positive culture was defined by the isolation of CIF in one or more of the culture media (bacterial culture media, SDA, IMA, or BHI agar). Prevalence was calculated based on the percentages of fungi detected in an individual subject in the cohort. Persistent isolation of fungi was defined as two or more occurrences of the same fungi during the study period. A descriptive analysis of the baseline cohort was performed using calculations of means and standard deviations for continuous variables and proportions for categorical variables. Demographic and clinical variables used in the analysis included: age, sex, F508del genotype, pancreatic insufficiency, FEV₁ percent predicted, *Pseudomonas aeruginosa* colonization, and the use of inhaled anti-pseudomonal antibiotics (tobramycin powder/solution, aztreonam, colistin, and ceftazidime), nonmacrolide oral antibiotics (defined as anti-staphylococcal oral antibiotics, including sulfamethoxazole/trimethoprim, minocycline, doxycycline, and linezolid), azithromycin, and antifungals (itraconazole, voriconazole, and posaconazole). The rates of detection of fungi were compared between standard bacterial culture medium and selective fungal media (IMA, SDA, and BHI agar) using chi-square and Fishers exact tests. We used two sample *t* tests and Wilcoxon rank-sum tests to assess differences in the mean time-to-detection in the bacterial versus selective fungal media.

SUPPLEMENTAL MATERIAL

Supplemental material for this article may be found at <https://doi.org/10.1128/JCM.02182-16>.

TEXT S1, PDF file, 0.03 MB.

TEXT S2, PDF file, 0.03 MB.

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