Pulmonary Aspergillosis in Cystic Fibrosis Lung Transplant Recipients

David R. Nunley, MD, FCCP; N. Paul Ohori, MD; Wayne F. Grgurich, BS; Aldo T. Iacono, MD; Princess A. Williams, MD; Robert J. Keenan, MD; and James H. Dauber, MD, FCCP

Study objective: To define the prevalence of colonization and infection of the lower respiratory tract (LRT) with Aspergillus in lung transplant recipients with and without cystic fibrosis (CF).

Design: Retrospective review.

Setting: Large university lung transplant center.

Materials and methods: The postoperative course of 31 CF and 53 non-CF double lung or double lobar transplant recipients receiving allografts from April 1991 to February 1996 was reviewed. All recipients were subjected to surveillance bronchoscopy and biopsy at predetermined intervals and when clinically indicated. BAL fluid (BALF) and biopsy material were examined by appropriate fungal culture and staining techniques. Infection was defined by the finding of tissue-invasive disease on biopsy specimens.

Results: Seven of the 31 CF recipients (22%) had Aspergillus isolated from cultures of sputum prior to transplantation. Following transplantation, 15 CF recipients (48%) had Aspergillus isolated from either sputum or BALF, including 4 of the 7 recipients identified with the fungus prior to transplantation. By contrast, 21 of the 53 non-CF recipients (40%) had Aspergillus isolated from the LRT following transplantation, none having had the fungus isolated prior to transplantation. The prevalence of Aspergillus did not differ between these groups (p = 0.51). Infections with Aspergillus occurred in 4 of the CF recipients (27%) and did not differ from the 3 infections (14%) identified in the non-CF recipients (p = 0.36). However, three of the four infections in the CF recipients involved the healing bronchial anastomosis and occurred prior to postoperative day 60. All three of these recipients had Aspergillus preoperatively. Postoperative infection was more common in the CF recipients having Aspergillus preoperatively than in those CF recipients without preoperative Aspergillus (p = 0.02).

Conclusions: Isolation of Aspergillus from the LRT following double lung transplantation is common and generally not associated with tissue-invasive disease. Those CF recipients with Aspergillus isolated in cultures of sputum preoperatively are at risk for postoperative infections with this agent. The healing bronchial anastomosis is particularly vulnerable.

(CHEST 1998; 114:1321-1329)

Key words: aspergillosis; Aspergillus; cystic fibrosis; lung transplantation

Abbreviations: ABPA = allergic bronchopulmonary aspergillosis; BALF = BAL fluid; CF = cystic fibrosis; POD = postoperative day

Species of the fungus Aspergillus are known to often colonize the respiratory tract of patients with certain types of chronic lung disease. One such disorder is cystic fibrosis (CF) where it is estimated that by adulthood as many as 50% will have Aspergillus routinely isolated from cultures of sputum.1 In CF patients, the fungus, when present, is nonpathogenic but in a few individuals may elicit an immune response resulting in significant bronchospasm (allergic bronchopulmonary aspergillosis [ABPA]). Conversely, in certain immunocompromised individuals, Aspergillus can become a significant pathogen causing tissue-invasive disease often spreading along vascular planes and invading blood vessels (angiinvasive disease). With its inherent need for systemic immunosuppression, organ transplantation is one arena in which aspergillosis has become a significant problem, sometimes resulting in devastating pulmonary angiinvasive disease.2,3

Patients with CF constitute a rapidly growing
population that require lung transplantation. However, it is unknown whether CF lung transplant recipients who had evidence of respiratory colonization with Aspergillus prior to transplantation are at an increased risk of developing postoperative invasive aspergillosis following the initiation of long-term immunosuppression. Therefore, we retrospectively reviewed our center’s experience with those CF lung recipients who were known to have Aspergillus on culture of the sputum prior to transplantation with respect to the development of invasive aspergillosis following successful transplantation.

**Materials and Methods**

Between April 1991 and February 1996, 54 patients with CF received double lung or double lobar transplantation at our institution for end-stage pulmonary disease. A total of 31 CF recipients had serial cultures of sputum for bacteria and fungi (approximately every 6 to 8 weeks) while awaiting their transplant, had successful grafting, and survived a minimum of 14 days following the procedure. None of the CF recipients who died prior to postoperative day (POD) 14 had infections with Aspergillus. Of these 31, 11 were male and 20 were female with the average age at the time of transplant being 32 years (median, 30 years). All of the CF recipients had chronic pulmonary infections with Pseudomonas prior to transplantation.

Fifty-three double lung recipients contemporarily receiving allografts for a variety of indications were utilized for comparison and designated the non-CF group. This group consisted of 25 male and 28 female patients with the mean age at the time of transplant being 41 years (median, 42 years). The pretransplant diagnosis in this recipient group included the following: Eisenmenger’s syndrome (n = 21), primary pulmonary hypertension (n = 12), chronic obstructive lung disease (n = 10), α₁-antitrypsin deficiency (n = 4), pulmonary fibrosis (n = 3), bronchoalveolar carcinoma (n = 1), Munier-Kuhn syndrome (n = 1), and obliterator bronchiolitis (n = 1). Recipients receiving allografts for bronchiectasis (n = 7) and dysmotile cilia syndromes (n = 1) were excluded from the non-CF group. The recipients in these latter two categories were not included in the CF group because their underlying pathophysiology is not identical to CF (a group in which the incidence of Aspergillus colonization has been better defined). Likewise, these recipients were not included in the non-CF group because, unlike the other disorders in this group, they were associated with infections. To better compare the postransplant morbidity from Aspergillus in this preliminary investigation, it was decided to initially compare the CF recipients (where Aspergillus colonization prior to transplantation is more prevalent) with a group of nonseptic lung disorders (where Aspergillus colonization is not expected or well defined). All of the recipients in the non-CF group also had serial cultures of sputum for bacteria and fungi while awaiting their transplant procedure. Engraftment of the donor organs was performed utilizing the bilateral sequential technique with end-to-end bronchial anastomoses as previously described. Procedures performed for recipients of pulmonary lobes from living related donors were performed utilizing a telescoping bronchial anastomosis secondary to the relative small size of the donor bronchus.

Immediately following transplantation, routine immunosuppression was employed utilizing standard regimens consisting of cyclosporine or tacrolimus with azathioprine and corticosteroids (initially IV methylprednisolone and later oral prednisone). All of the CF recipients were empirically treated for the first 10 to 14 PODs with two antibiotics, one antipseudomonal and one antifungal. Recipients in the non-CF group received empiric systemic antibiotic therapy with clindamycin and ceftazidime for the first 7 to 10 postoperative days unless preoperative cultures of sputum suggested organisms that required specific antimicrobial coverage. No recipient received empiric systemic or aerosolized antifungal therapy. Likewise, recipients found to have Aspergillus in respiratory secretions following transplantation without accompanying tissue invasion were not routinely treated with antifungal agents.

Surveillance bronchoscopy with transbronchial biopsies was performed routinely at a minimum of every 12 weeks during the first postoperative year, every 16 weeks during the second year, and every 36 to 52 weeks thereafter. As determined by the physician, bronchoscopy was additionally performed for any deterioration in clinical status of the recipient manifested by cough, dyspnea, and/or decline in spirometric values. The average postoperative surveillance time for the CF group was 634 days (median, 506 days; range, 18 to 1,815 days) and 731 days (median, 750 days; range, 18 to 1,800 days) for the non-CF group. Endobronchial biopsies were performed for visual abnormalities noted by the physician. Grocott tissue stains to assess for fungal elements were performed on the biopsy material. All biopsy specimens were interpreted by a skilled pulmonary pathologist. BAL was performed as a routine part of each bronchoscopic procedure. If the recipient was receiving mechanical ventilatory support, the bronchoscope was passed via the endotracheal or tracheostomy tube. If the patient was spontaneously breathing, the bronchoscope was passed either through the nose and nasopharynx or the mouth and oropharynx. One percent lidocaine was used as regional anesthesia of the glottic structures. Suction was not applied to the bronchoscope until the tip was wedged into a subsegmental airway—usually in the right middle lobe or lingula. Two hundred milliliters of sterile saline solution was introduced into the airway in 50-mL aliquots. Suction was then employed, and after each aliquot, as much of the saline solution as could be recovered was aspirated from the airway into a sterile suction trap. Once the saline solution lavage fluid was recovered, this BAL fluid (BALF) was processed by an experienced technician. All recovered BALF, including the first recovered aliquot, was separated into two samples of approximately equal volume. After centrifugation of each sample, the resulting cell pellet was recovered. One pellet was resuspended in buffer solution and appropriate cell counts were obtained. The second sample with its cell pellet was forwarded to a microbiology and a cytology laboratory where the fluid was cultured using standard bacterial and fungal growth media. Appropriate staining of the BALF was performed utilizing Gram’s and calcofluor white stain.

**Definitions**

A positive culture for Aspergillus denotes the isolation of any species in this genus (ie, *Aspergillus fumigatus, Aspergillus niger, Aspergillus flavus*). Fungal infection was defined solely on the bases of allograft histology revealing characteristic invasive fungal elements. With respect to infection, biopsy material was graded as either pneumonia (alveolar airspace infiltration) or bronchitis (bronchial mucosal or submucosal infiltration). Those recipients with positive BALF or sputum cultures for Aspergillus without accompanying characteristic histologic changes on biopsy material were considered to be simply “colonized” with the fungus.

**Statistical Analysis**

Data are expressed as mean or median unless otherwise stated. The χ² and Fisher’s Exact Tests were employed for comparisons
between nominal variables utilizing 2 × 2 contingency tables. Means between study groups were compared using the Student’s t test. The Mann-Whitney U test was used to compare all unpaired data. A significant difference was determined at p < 0.05.

**RESULTS**

Figure 1 summarizes the course of the 31 CF lung recipients. Of these 31 recipients, 7 (22%) were noted to have Aspergillus isolated on at least one culture of sputum prior to transplantation. Following transplantation, 15 of the 31 recipients (48%) were found to have Aspergillus in culture of sputum or BALF by median POD 23 (range, 3 to 1,142 days). Included in these 15 recipients were 4 of the 7 CF recipients (57%) identified with Aspergillus prior to transplantation. Of the 24 CF recipients without Aspergillus isolated prior to transplantation, 11 recipients (46%) were found to have the fungus in the respiratory tract following transplantation.

Four of the 15 CF recipients (27%) with Aspergillus isolated following transplantation had histologic evidence of tissue-invasive disease identified on biopsy material. One of these recipients developed a bronchitis secondary to Aspergillus on POD 1,142 in association with a pneumonitis secondary to cytomegalovirus. This recipient did not have Aspergillus isolated on culture of sputum prior to transplantation. The remaining three recipients each developed tissue-invasive disease involving the bronchial anastomosis early in the postoperative period (POD 15, 23, and 58). In each case, the infection was secondary to *A. fumigatus*. Each of these three recipients had Aspergillus isolated from culture of sputum prior to transplantation. Two of these three recipients also had fungal cultures of their native lungs at the time of the transplant procedure that revealed *A. fumigatus*. The third recipient’s species of Aspergillus was not able to be identified on culture of the sputum prior to transplantation. Two of the recipients survived their infection after intense systemic and aerosolized antifungal therapy, while the third died of massive hemoptysis following erosion by Aspergillus into the recipient bronchial anastomotic site (Figs 2 and 3).

Therefore, of the 7 CF recipients with Aspergillus prior to transplantation, 3 (43%) developed early postoperative infections involving the bronchial anastomosis as compared with the one late postoperative infection in the group of 24 CF recipients (4%) without Aspergillus prior to transplantation. The prevalence of infection in the CF recipients having Aspergillus prior to transplantation was significantly greater than the prevalence of infection in the CF recipients without Aspergillus prior to transplantation (p = 0.02, Fisher’s exact p value) (Fig 4).

![Aspergillus Infections in CF Lung Recipients](aspergillus_diagram.jpg)

**Aspergillus Infections in CF Lung Recipients**

- **31 CF recipients**
  - *Aspergillus* pre-transplant
    - 7/31 (22%)
  - *Aspergillus* post-transplant
    - 15/31 (48%)
  - Invasive *Aspergillus* infection
    - 4/15 (27%)
    - *3 anastomosis infections (POD 15, 23 & 58)*
  - No infection
    - 11/15 (73%)
    - 1 bronchial infection
      - (POD 1142)

* identified with *Aspergillus* pre-transplant

**Figure 1.** Diagram detailing Aspergillus infections in 31 CF lung recipients.
Fifty-three contemporaneous patients received double lung transplantation for a variety of nonseptic lung disorders. Figure 5 summarizes the course of these non-CF recipients. None of these recipients had Aspergillus isolated from cultures of sputum prior to transplantation. Following transplantation, 21 of these recipients (40%) had Aspergillus isolated from sputum or BALF during postoperative surveillance. The prevalence of postoperative isolation of Aspergillus in this group did not differ significantly from the CF recipients ($\chi^2 = 0.43, p = 0.51$). The median time to isolation of Aspergillus in this recipient group was POD 292 (range, 7 to 1,160 days) and was significantly greater than the time to isolation in the CF recipients ($p = 0.02$, Mann-Whitney $U$). Three of these 21 recipients (14%) developed histologic evidence of tissue-invasive disease, 1 with pneumonia and 2 with bronchitis (POD 123, 188, and 870), but no infections of the bronchial anastomosis. The prevalence of invasive disease in these non-CF recipients was no greater than in the CF recipients ($\chi^2 = 0.86, p = 0.36$) (Fig 6).

Both fungal and routine bacterial cultures were performed on the sputum in both recipient groups prior to transplantation. The mean number of routine cultures obtained in the CF recipients was $7.13 \pm 6.16$, while the mean number of fungal cultures was $1.42 \pm 1.54$. The total number of sputum cultures obtained prior to transplantation was significantly greater in the CF recipient group ($\bar{X} = 8.55 \pm 6.81$) compared with the non-CF recipients ($\bar{X} = 1.15 \pm 2.69$) ($p < 0.001$, Student’s $t$ test).

**DISCUSSION**

Our experience illustrates two important findings. First, as with other investigations, we found that colonization of the lower respiratory tract with Aspergillus is a common occurrence following lung transplantation; the prevalence does not differ in the CF lung recipients as compared with other lung allograft recipients. However, unlike previous investigations, we experienced a statistically increased number of bronchial anastomotic infections attributable to Aspergillus in those CF recipients who had the fungus isolated in their sputum prior to transplantation.

Aspergillus is a common finding in the respiratory secretions of adult CF patients. Treatment to eradicate the fungus is unnecessary as tissue invasion has rarely been reported to occur. As many as 10% of the adult CF population will experience bronchospasm secondary to allergic bronchopulmonary aspergillosis often coincident with the finding of Aspergillus in the sputum. Even in these cases, treatment is not targeted toward elimination of Aspergillus, but rather utilizes corticosteroids to reduce the inflammatory response. However, in bone marrow and solid organ transplant recipients, the isolation of Aspergillus from bodily secretions, including the respiratory tract, has not been as innocuous. The isolation of Aspergillus from BALF and/or sputum has been shown to highly correlate with histopathologic changes of invasive pulmonary aspergillosis in bone marrow recipients, while its isolation from cultures of respiratory secretions, pleural fluid, or ascitic fluid has been correlated with invasive Aspergillus infection and poor outcome in recipients of both liver and kidney transplants. More recently, a multicenter investigation of Aspergillus infections in liver transplant recipients revealed that 50% of

**Figure 2.** Endobronchial biopsy specimen of the surgical bronchial anastomosis revealing tissue invasive Aspergillus hyphae (Grocott stain).

**Figure 3.** Postmortem examination of the lung allograft in a recipient with Aspergillus infection of the bronchial anastomosis who died of massive hemoptysis. The probe (large arrow) is through the defect in the bronchus leading to the bronchial artery. The anastomotic site is designated by the small arrow.
Aspergillus Infections in CF Lung Recipients

Figure 4. Aspergillus infections in CF lung recipients.

Aspergillus Infections in Non-CF Recipients

Figure 5. Diagram detailing Aspergillus infections in non-CF lung recipients.

those patients ultimately identified with invasive pulmonary aspergillosis had isolation of Aspergillus from sputum or BALF. Unlike the case with these organ recipients, our results, along with others, suggest that the isolation of Aspergillus from the respiratory tract occurs in 30 to 50% of CF and non-CF lung recipients, and in most cases is not associated with invasive disease. While in our investigation the total number of Aspergillus infections did not differ between CF and non-CF lung recipients, quite disturbing is the finding of increased early bronchial Anastomotic As-
pergillus infections. All of these infections occurred in CF recipients who had evidence of respiratory tract colonization with the fungus prior to transplantation, while no anastomotic infections occurred in those recipients (both CF and non-CF) without Aspergillus prior to transplantation. This suggests that those recipients with airway colonization at the time of transplantation have this potential pathogen at the site of a fresh surgical incision. The normal nutrient blood supply to the major bronchi is supplied by the bronchial arteries that are disrupted during the end-to-end bronchial anastomotic procedure. This may result in transiently devascularized tissue at the surgical site that, in the presence of immediate induction of immunosuppression, provides a excellent growth medium for Aspergillus. This early devascularization scenario would be consistent with the finding that all of these bronchial infections occurred within the first 60 days following transplantation. Furthermore, it has been suggested that the early use of corticosteroids (as has been done in our program) following transplantation may promote infections with Aspergillus in lung transplant recipients. Macrophages and granulocytes are the major immunoregulatory cells involved in the host defense against fungal infections. It has been demonstrated that corticosteroids suppress macrophage and granulocyte function while no effect has been noted from the suppression of T-lymphocyte function by cyclosporine.

Paradowski recently reported the experience of the University of North Carolina transplant center with respect to saprophytic infections. She identified 35 of 71 CF transplant recipients (52%) with preoperative airway colonization with Aspergillus. Only one CF recipient developed invasive fungal disease after transplantation. This infection, with Scedosporium apiospermum, initially involved the CNS and later the lung parenchyma. It is unknown whether this recipient was one of those colonized preoperatively. Of note, until recently the induction of immunosuppression in their program was devoid of corticosteroid use until POD 15. Also, the use of the omental wrap was employed to promote blood flow to the bronchial anastomosis. It is interesting to speculate that one or both of these practices may have contributed to the absence of fungal bronchial anastomotic infections in their series.

Our results are contingent on the accurate identification of Aspergillus in the sputum prior to transplantation and the assumption that this identifies persistent colonization of the lower respiratory tract. It is possible that our preoperative identification of CF patients with Aspergillus is flawed. Unlike the situation with the bacterium Pseudomonas aeruginosa, it is unknown whether Aspergillus persists in
the lower respiratory tract of CF patients following the initial isolation. Once colonized with *P. aeruginosa*, the organism, with very few exceptions, remains in the lower respiratory tract and can be recovered sequentially on cultures of the sputum.\textsuperscript{17–19} This is, in part, believed to be secondary to adhesion of carbohydrate moieties in the capsule of the organism with certain receptors on the respiratory epithelium.\textsuperscript{20} No such epithelial adhesion has been demonstrated with Aspergillus, and whether the organism persists in the lower respiratory tract has not been defined. Those health professionals who routinely care for patients with CF frequently observe Aspergillus in cultures of the sputum that may disappear on subsequent cultures only to reappear at a later time. It is unknown whether this is related to sputum collection techniques, laboratory culture techniques, or actually represents transient and/or relapsing colonization of the lower respiratory tract by the organism. There have been preliminary observations to suggest that culturing of the sputum has a low positive predictive value for identifying those patients who have Aspergillus in the lower respiratory tract.\textsuperscript{21} It is therefore possible that those recipients identified by culture of sputum as harboring Aspergillus in their airway preoperatively may not have had the organism at the time of the transplant procedure. It is unfortunate that our program was not consistent in its the early years in routinely culturing the native recipient lungs for fungal elements. It is known that two of the 3 recipients with bronchial anastomotic infections had fungal cultures obtained of their native lungs and both showed positive growth of Aspergillus.

Other than cultures of respiratory secretions, it may be possible to identify those CF recipients having Aspergillus prior to transplantation by the use of serologic markers. ABPA is a relatively common occurrence in CF and is typically identified by, among other criteria, an elevated total IgE level, immediate cutaneous reactivity to *A. fumigatus*, and elevated serum IgE or IgG antibodies to *A. fumigatus*.\textsuperscript{1} These markers have been used successfully in a CF recipient who had ABPA diagnosed serologically before transplantation and had these markers decrease after transplantation only to rise again with the clinical recurrence of ABPA later in the posttransplant course.\textsuperscript{22} Elevation of these serologic markers may also be beneficial in predicting Aspergillus infections prior to radiographic or culture evidence, and may be useful in monitoring the response to antifungal therapy.\textsuperscript{23,24} Whether the quantity of Aspergillus in the airway prior to transplantation is relevant to the risk of postoperative infection and whether the degree of elevation of these markers correlates with the quantity of Aspergillus is unknown.

Assuming that cultures of the sputum are accurate for identifying those lung transplant candidates harboring Aspergillus in the lower respiratory tract, there arises another potential source of error in our findings. Significantly more cultures of the sputum were obtained in the CF recipients prior to transplantation as compared with the non-CF recipients. This discrepancy in sampling could fail to accurately identify those non-CF recipients colonized with Aspergillus prior to transplantation. However, the lung diseases in the non-CF group were noninfectious disorders and those not typically associated with fungal colonization. Furthermore, the nature of these disorders was such that the subjects did not chronically produce sputum and thus the ability to obtain frequent samples was curtailed.

If cultures of the sputum revealing Aspergillus truly identify those recipients at risk for postoperative infections, there remains the question of management. Long considered the mainstay of antifungal therapy, amphotericin B clearly has some undesirable side effects. Among these, nephrotoxicity is the most worrisome. Both cyclosporine and tacrolimus are significantly nephrotoxic. In addition, any intraoperative hemodynamic instability places the recipient at risk for developing acute tubular necrosis. For these reasons, the prophylactic use of this agent following transplantation in CF recipients with Aspergillus can hardly be recommended. Amphotericin B has been used in an aerosolized formulation for the treatment of ABPA in patients with CF.\textsuperscript{25} Although there has been some anecdotal evidence of improvement with this therapy, it has not been employed to completely eradicate the fungus and controlled clinical trials of its efficacy have not been performed. Aerosolized amphotericin B has also been employed prophylactically in bone marrow transplant recipients for prevention of fungal pulmonary infections with some demonstrated success.\textsuperscript{26} Preliminary investigations into prophylactic use of aerosolized amphotericin B for prevention of fungal pulmonary infections in heart and lung transplant recipients have demonstrated some benefit.\textsuperscript{27}

Of the newer class of azole antifungal drugs, itraconazole has demonstrated *in vivo* activity against Aspergillus pulmonary infections in immunocompromised patients.\textsuperscript{28,29} Its use in transplant recipients can be complicated by drug interactions with cyclosporine, tacrolimus, and several other medications frequently employed in this patient population.\textsuperscript{30,31} These interactions, if carefully monitored, generally do not preclude its use. Some transplant centers utilize itraconazole prior to transplantation in those
CF candidates with Aspergillus isolated in cultures of sputum with the goal of eradicating or significantly reducing the amount of the fungus in the airway. It is known that the growth of Pseudomonas in the airway of the CF patient is attenuated by the use of systemic antimicrobials but that its eradication is generally not possible.32 There are no corresponding data regarding the use of itraconazole and the eradication or reduction of Aspergillus in CF patients who have the fungus isolated from sputum. One report has suggested an improvement in the treatment of ABPA in CF patients by utilizing itraconazole with systemic corticosteroids.33 It was postulated that the observed benefit of itraconazole may have been secondary to reducing the burden of Aspergillus, although this was not an outcome measure of this study. Therefore, at this time, the use of preoperative itraconazole in this patient population with the goal of fungal eradication is unprecedented.

Recently, it has been suggested that lung transplant recipients who have colonization of their airway secretions with A fumigatus within the first 6 months following transplantation are at increased risk for developing tissue-invasive disease.34 Unfortunately, in this investigation, the identification of tissue-invasive disease was not always heralded by prior recovery of Aspergillus from airway secretions. Therefore, the authors have suggested that empiric anti-Aspergillus therapy for the first 6 months following transplantation may be beneficial. The basis for this suggestion would be consistent with our observation that most invasive Aspergillus infections occurred before POD 60. As in this previous investigation, our cases of tissue-invasive disease also appear to be primarily related to A fumigatus.

In addition to a reduction of systemic immunosuppression, all three of our recipients with endobronchial Aspergillus were treated with a combination of systemic and aerosolized amphotericin B as well as with oral itraconazole. This therapy was successful in two of the three recipients, but only after several weeks of treatment.

In summary, we conclude that the isolation of Aspergillus from the lower respiratory tract is a common occurrence following lung transplantation, and in most cases is not associated with tissue-invasive disease. There is no difference in the prevalence of Aspergillus in airway secretions between CF and non-CF lung recipients. Likewise, there is no difference in the prevalence of tissue-invasive disease secondary to Aspergillus between these groups. However, there is an increase in the number of Aspergillus infections in those CF recipients known to have the fungus in their airway prior to transplantation. These infections tend to have a predilection for the site of the bronchial anastomosis. Close surveillance of the healing bronchial anastomosis is therefore crucial in these recipients. Whether differences in surgical technique, immunosuppressive drug regimens, or prophylactic use of antifungal agents impact on this finding remains to be determined.

ACKNOWLEDGMENT: The authors gratefully acknowledge the assistance of Gerene Bauldoff, RN, MSN, in the preparation of this manuscript.

REFERENCES
17. Bauernfeind A, Bertele RM, Harms K, et al. Qualitative and quantitative microbiological analysis of sputum of 102 pa-
18 Brett MM, Ghoneim AT, Littlewood JM. Prediction and
diagnosis of early Pseudomonas aeruginosa infection in cystic
1570
19 Sharma GD, Tosi MF, Stern RC, et al. Progression of
pulmonary disease after disappearance of Pseudomonas in
20 Prince A, Saiman L. Pseudomonas aeruginosa pili bind to
asialoGM1 which is increased on the surface of cystic fibrosis
21 Bauldoff GS, Nunley DR, Manzetti JD, et al. The value of
sputum cultures in predicting respiratory tract colonization
with Aspergillus in cystic fibrosis lung transplant candidates
[abstract]. Am J Respir Crit Care Med 1997; 155:A386
22 Fitzsimmons EJ, Aris R, and Patterson R. Recurrence of
allergic bronchopulmonary aspergillosis in the posttransplant
monary aspergillosis in lung allograft recipients. Eur Respir J
1996; 9:169–171
24 Tomée JF, Mannes PM, van der Bij W, et al. Serodiagnosis
and monitoring of Aspergillus infections after lung transplan¬
25 Lewiston NJ, Bidermann AA, Harvey B. Allergic bronchopul¬
monary aspergillosis plus cystic fibrosis: addition of amphi¬
tericin B aerosol to therapy [abstract]. Cystic fibrosis club
abstracts 1973: 47; cystic fibrosis research foundation 14th
annual meeting
26 Hertenstein B, Kern WV, Stefanie M, et al. Low incidence of
invasive fungal infections after bone marrow transplantation
in patients receiving amphotericin B inhalations during neu¬
reduction in the number of fungal infections after lung-, heart-lung, and heart transplantation using aerosolized am¬
28 Denning DW, Follansbee SE, Scolaro M, et al. Pulmonary
aspergillosis in the acquired immunodeficiency syndrome.
29 Denning DW, Tucker RM, Hanson LH, et al. Treatment of
86:791–800
30 Systemic antifungal drugs. Med Lett 1996; 38:10
31 Nunley DR, Dauber JH. Lung transplantation: implications
for the general internist. In: Schrier RW, ed. Advances in
internal medicine. St. Louis, MO: Mosby-Yearbook, 1996;
497–529
neutrophil elastase and elastase/α1-antiprotease complex in
cystic fibrosis: comparison to interstitial lung disease and the
effect of intravenous antibiotic therapy. Am Rev Respir Dis
1991; 143:580–588
therapies for allergic bronchopulmonary aspergillosis with itra¬
34 Cahill BC, Hibbs JR, Savik K, et al. Aspergillus airway
colonization and invasive disease after lung transplantation.
Chest 1997; 112:1160–1164