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A SINGLE SEASON PROSPECTIVE STUDY OF RESPIRATORY VIRAL INFECTIONS IN LUNG TRANSPLANT RECIPIENTS

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ABSTRACT

Background: Respiratory viruses cause serious infections in lung transplant recipients, but only retrospective studies are available. Our objective was to prospectively study the frequency and complications of respiratory viral infections in an ambulatory lung transplant population during a single winter season using multiple diagnostic tests, including viral antigens, viral cultures and PCR of nasal washes (NW) or bronchoalveolar lavages (BAL).

Methods: Fifty lung transplant recipients were followed for respiratory viral infection from November through March. Serum was obtained at enrollment and one month after study conclusion. Patients were interviewed weekly. Forty nine episodes of respiratory symptoms in 32 patients prompted either NW (n=44) or BAL (n=5), which were evaluated by viral culture and PCR for respiratory syncytial virus (RSV) A&B, influenza (FLU) A&B, parainfluenza virus (PIV) 1,2 & 3. Viral antigens were performed for RSV and FLU. Sera were assayed for RSV (ELISA) and FLU (kinetic ELISA) antibodies. Patients' survival and the occurrence of acute rejection and bronchiolitis obliterans (BO) or bronchiolitis obliterans syndrome (BOS) were monitored for one year after the end of the study.

Results: Thirty-two (64%) of the 50 study patients had NW or BAL studied for respiratory viruses. Documented infections included eight due to RSV (1 culture, 5 PCR and 7 serological), one due to PIV (culture and PCR) and ten due to FLU (3 culture, 4 PCR and 8 serological). Four patients had serological rises to FLU without reporting symptoms. Overall 17 patients (34%) had viral infection, since two had both RSV and FLU. Four patients had lower respiratory involvement and two patients (1 RSV, 1 PIV)

were hospitalized for aerosolized ribavirin treatment. No patient required mechanical ventilation or died within 90 days. After one-year there were three deaths (6%), unrelated to respiratory virus infection and BO or BOS had occurred in 1/17 (6%) patients with respiratory viral infection and 3/33 (12%) without respiratory viral infection.

Conclusions: Respiratory viruses infected a third of ambulatory lung transplant recipients in a single season – a rate that is much higher than previously reported. Most patients on study had good outcomes, but two (12%) infected patients were hospitalized. We could not document an association between respiratory viral infection and subsequent BO or BOS. Larger prospective studies will be required to define the acute and long-term morbidity of these infections and why some patients have minor disease and others progress to more serious complications.

Key words: respiratory virus; lung transplantation; PCR

INTRODUCTION

Only a few infections caused by respiratory viruses were reported in the initial studies of infectious complications of lung transplantation (1, 2). Subsequently, studies that focused on respiratory viral infection, documented cumulative infection rates ranging from 8-21% in populations of lung transplant recipients followed over 5-7 year intervals (3-5). The average yearly incidence of respiratory viral infection in these studies was 2-3%; the mortality rate in two studies in which this was reported was 10% (3, 4). There appear to be differences in severity and outcome related to the type of viral infection. For instance, rhinovirus infections were not commonly associated with symptoms, but adenovirus infections were associated with a high rate of respiratory failure and death (5-8).

Apart from the direct morbidity and mortality caused by respiratory viral infections, there has been a concern that respiratory viral infections might also cause chronic allograft dysfunction due to bronchiolitis obliterans in lung allografts by stimulating alloimmune cells in the lung. This possibility is supported by an animal model (9). There is also clinical evidence supporting such a relationship from retrospective studies (3,10,11). In these studies the diagnoses were made by viral culture of BAL fluid in patients who underwent bronchoscopy for lower respiratory tract symptoms or a documented change in pulmonary function. Such a retrospective approach is likely to detect the most severe cases, but may underestimate the actual rate of infection. Also, patients with preexisting lung dysfunction may be more likely to be detected in such a study. Moreover, available studies have usually employed only one or two diagnostic methods to detect infection, such as culture or viral antigen testing.

Additional diagnostic tools such as serology and PCR that have been shown to increase the rate of diagnosis of respiratory pathogens in some population studies have not routinely been used (12-15).

To better understand the epidemiology of respiratory viral infections in a lung transplant population, we undertook an intensive, multiple-modality, prospective study of respiratory viral infections in lung recipients in a single winter viral season in Nashville, Tennessee. The goals of the study were to obtain an accurate rate of infection of the most important respiratory viruses in lung recipients, to document the short-term morbidity and mortality of these infections, and determine the incidence of acute rejection, new diagnoses of bronchiolitis obliterans and death in both infected and uninfected patients during a year's follow-up.

METHODS

Clinical: From November 1, 1999 until March 31, 2000, lung transplant recipients at Vanderbilt University Medical Center were recruited for a prospective evaluation of viral respiratory infection. Adult patients were eligible for enrollment if they were at least two weeks post transplant, being followed in the outpatient clinic, and lived within two hours driving time of the medical center. The study was closed after fifty patients were enrolled. No participant in the study received oral antiviral prophylaxis for influenza (ie. amantadine or ramantadine). The study was supported by a research grant from Medimmune Inc. All patients who participated in the study gave informed consent and signed consent forms approved by the Vanderbilt University Medical Center Institutional Review Board. A study nurse interviewed each patient weekly by telephone or in clinic to screen for signs and symptoms of a new respiratory infection. Symptoms monitored

included both upper respiratory tract symptoms (e.g. coryza, stuffy nose, sore throat, and sneezing) and lower respiratory tract symptoms (e.g. cough, wheezing, shortness of breath). Patients with active symptoms were seen within 48 hours in the clinic where a physical exam and a nasal wash were performed. For the nasal wash, 5 ml of non-bacteriostatic saline was instilled into each nostril and collected in a sterile cup. An aliquot of this sample was submitted to the Vanderbilt University Hospital virology laboratory for viral culture and viral antigen testing. The remainder of the nasal wash was frozen at –70 degrees Celsius for future PCR testing. In addition, all patients had serum drawn at enrollment and between 3/28/00 and 7/7/00 when they came to clinic for routine followup (mean 115.8 ± 35.4 days). Patients who underwent bronchoscopy and BAL also had lavage fluid submitted for viral culture, viral antigens and an aliquot frozen for PCR testing. A few patients were admitted directly to hospital and underwent bronchoscopy. These individuals did not have nasal washes and only BAL fluid was available for analysis. The decision to perform bronchoscopy and the treatment of the patient's illness was determined by the attending physician on the pulmonary transplant service. Patients were not routinely studied for cytomegalovirus infection unless they were less than 6 months from transplant, in which case they were managed by our standard cytomegalovirus regimen that relies on a brief two week period of antiviral prophylaxis followed by monitoring of blood antigenemia and preemptive therapy (19).

The primary outcome was the occurrence of any respiratory tract viral infection. Secondary outcomes included the occurrence of lower respiratory tract viral infection or pneumonia, as well as the need for hospitalization and death within 30 days. Patients were evaluated after the end of the study for the occurrence of acute rejection, new

diagnoses of bronchiolitis obliterans (BO) or bronchiolitis obliterans syndrome (BOS), or death for one year. The diagnosis of lower respiratory tract infection required detection of virus and the presence of new signs suggesting lower respiratory tract involvement (wheezing, rales or rhonchi over the transplant lung), together with shortness of breath, new hypoxemia or a greater than 10% drop in FEV1. The diagnosis of pneumonia additionally required the appearance of a new infiltrate on chest radiograph or computerized tomographic scan and a transbronchial biopsy showing evidence for parenchymal infection. Acute rejection was diagnosed by transbronchial biopsy and BO and BOS were diagnosed using the criteria established by the International Society of Heart and Lung Transplantation (20).

Because we performed this prospective study only during a single respiratory viral season we wanted to assess whether the rate of viral infection in the community during that year differed from other years. To this end we collected data on the frequency and proportion of positive influenza cultures and RSV antigen tests for five consecutive respiratory viral seasons from the Vanderbilt University Hospital virology laboratory. The hospital virology laboratory performs all virological testing from adults and children at Vanderbilt University Medical Center and also receives many samples from local hospitals and clinics. The data included test results for five-month intervals (November-March) for two years before and two years after the 1999-2000 viral season. We could not analyze culture data for RSV because in August 1999 the virology lab stopped performing RSV cultures when RSV antigens were positive on samples requesting RSV antigen only.

Laboratory: Nasal washes and BAL fluids were inoculated into culture tubes of Hep-2 and rhesus monkey kidney (RMK) cells (BioWhitaker Inc., Walkersville, MD) and examined for cytopathologic effect (CPE). CPE in HEp-2 cells was stained with Chemicon anti-RSV followed by FITC-conjugated goat anti-mouse IgG. RMK cells were additionally assayed for hemadsorption of guinea pig RBCs at days 5 and 10. If CPE or hemadsorption was detected, the cells were stained with Chemicon antibodies against FLU A & B and PIV 1,2 and 3, followed by FTIC conjugated goat anti-mouse IgG. Samples were additionally tested by RSV Directigen and influenza A & B Directigen (Becton Dickinson, Franklin Lakes, NJ). As performed, the viral cultures would be expected to detect adenoviruses but not rhinoviruses. Polymerase chain reactions for RSV A & B, Influenza A & B, and Parinfluenza 1,2 and 3 were performed by hexaplex PCR (Prodesse, Milwaukee, WI) as previously described (13). Pre- and post-study sera were assayed for RSV antibodies by ELISA by a previously described assay except that purified RSV F protein was substituted for G protein (21). Influenza antibodies to A/Beijing/262/95, A/Sydney/5/97 and B/Beijing/184/93 were measured by kinetic ELISA using a modification of a previously described assay (22). An increase of the kinetic ELISA of 100 mOD/min or more was used as a criterion of seroconversion. In order to exclude an effect from influenza vaccination, we excluded influenza serological results on patients who had received their influenza vaccination less than 28 days before their baseline serum draw. This led to the exclusion of twelve of the fifty patients from the serological analysis of influenza.

Statistics: Categorical variables were analyzed by chi-squared test or Fisher's exact test. Medians were analyzed with the Mann-Whitney test. Means were analyzed with Student

t testing. P-values of < 0.05 was considered significant. SPSS for Windows edition 13.0 (SPSS, Inc.; Chicago, IL) was used to calculate the statistics.

RESULTS

Table 1 and Table 2 provide information on demographics and virus detection in the 50 study patients. As seen in Table 1, the infected and uninfected groups did not differ in age, gender, underlying lung disease, type of transplant, type of immunosuppression, or in prior diagnoses of bronchiolitis obliterans (BO) or bronchiolitis obliterans syndrome (BOS). However, patients with documented infection had a longer interval to transplant surgery (median 1335 days versus 786 days; $p=0.04$ Mann-Whitney test). Thirty-two (64%) of the 50 study patients had NW or BAL studied for respiratory viruses including 44 nasal washes and 5 samples of bronchoalveolar fluid. Overall, laboratory evidence of respiratory viral infection was found in 17 (34%) of the 50 patients during the study interval. Table 2 reveals the type of virus, the method of detection and the total number of patients infected with each virus. Infections with respiratory syncytial virus and influenza were common, occurring in 16% and 20% of the study population, respectively. Two patients had multiple infections; one patient had concomitant FLU A and RSV infections and one patient had separate FLU A and RSV infections occurring approximately two months apart. Parainfluenza virus infection was only found in one patient; however, we did not have antigen or serologic testing available for this virus so this may be an underestimate of its true frequency. Adenovirus was not isolated in culture from any patient in this study. Antigen and serological testing was also not available for adenovirus. As can be seen in Table 2, PCR and serology were the most sensitive techniques for detecting infection. In the case of RSV, there was

considerable concurrence between PCR and serology; four of five patients with positive PCR had documented seroconversions. By contrast, only two of four patients with positive PCR for FLU A seroconverted to influenza A. Six patients had seroconversions to influenza A or B without having a positive PCR or positive cultures. In four of these six patients, however, no nasal wash samples were collected because the patients never reported symptoms during the study period. The other two patients were evaluated for respiratory symptoms but had negative results on their virological tests.

Of the five patients with RSV detected by PCR, 3 had type B and 2 had type A. The serology for RSV did not distinguish between RSV serotypes A and B. All four patients who were PCR positive for influenza had FLU A and three of these four infections were also confirmed by culture. The six seroconversions, however, included four patients with FLU B infection, one of whom also seroconverted to FLU A. Of the three patients who seroconverted to FLU A, two had serological rises to H1N1 Sydney, and one to H3N2 Beijing. The single parainfluenza virus that was detected by PCR and isolated in culture was PIV 1.

Table 3 shows data on patients who had significant complications associated with viral respiratory infection. Lower respiratory tract infection occurred in 4 (24%) of the infected patients and led to hospitalization in 2 (12%). In all four cases virus was detected in nasal wash, by culture and PCR in three patients and by PCR alone in one patient. One (6%) of the 17 patients had pneumonia. This patient (VU15, Table IV) underwent bronchoscopy with transbronchial biopsies and BAL one week after her nasal wash culture turned positive for parainfluenza. The biopsy showed pneumonia and parainfluenza was detected from BAL by PCR but not by culture. There were no deaths

from respiratory viral infection in this population. Both patients who were admitted to the hospital were treated with aerosolized ribavirin.

Table 4 evaluates outcomes in the year following the end of the study. There were three deaths in the study population; two occurred in patients who had respiratory viral infection during the study. One of the patients died six months after the end of the study from an intraperitoneal hemorrhage and the other patient at one year from aspiration pneumonia following a cardiac procedure. The one death that occurred in a patient without documented respiratory viral infection was related to progressive pulmonary compromise in the setting of advanced bronchiolitis obliterans. The rates of acute rejection or new diagnoses of BO or BOS in the year after the study were not different between patients with and without respiratory viral infection. However, the one case of bronchiolitis obliterans that occurred in a patient with respiratory viral infection was in a patient who had evidence of lower tract infection (patient 49, Table 3). Figures 1A and 1B show selected virological data from the Vanderbilt University Hospital virology laboratory for five consecutive respiratory viral seasons beginning in 1997 and ending in 2002. Figure 1A shows the number and proportion of positive influenza cultures. Similar data for RSV antigens is shown in Figure 1B. In both figures, data from the study year (1999-2000) is shown in the central columns. As can be seen from these figures, the number of diagnoses of RSV and influenza virus infection in the study season was not unusually high or low compared with the surrounding years.

During the five-month study interval, two lung transplant recipients who were not eligible for the study, because they had been recently transplanted and were not yet discharged from the hospital died of respiratory viral infection. One patient was

diagnosed with RSV pneumonia a few days after transplantation. In retrospect, he had mild coryza when admitted for his operation. We suspected that he had upper airway infection with RSV before transplantation and the infection spread to the lung allograft shortly after transplantation. The other patient had primary graft failure. She developed a urinary infection secondary to adenovirus nine days after transplantation, which subsequently spread to her transplanted lung. The source of her infection was not determined.

DISCUSSION

In the first decade of lung transplantation, surveys of infectious complications only made occasional note of respiratory viral infections. Over the last ten years, studies focusing on respiratory viral infections have shown that they are a cause of significant morbidity and mortality in lung transplant recipients (3-5). These studies have accurately defined the clinical presentation and more serious outcomes of respiratory viral infections in this population, but have some limitations due to their retrospective design. Most studies also did not employ more recently available diagnostic techniques such as PCR to determine the presence of viral infection. Recently, Garbino studied lung recipients with a broad panel of PCR tests for respiratory viruses. However, only patients who had both undergone bronchoscopy with available respiratory viral cultures were studied (15). Thus, it was not possible to calculate the incidence of respiratory viral infections in his population or compare infected with uninfected patients. Respiratory viruses were detected by PCR in 55% of 31 lung recipients who had been thought to have respiratory

viral infection by clinical criteria. Fifty-three percent of the detected viruses were rhinoviruses; the remainder were paramyxoviruses, orthomyxoviruses or adenoviruses.

Our study detected respiratory viral infection in one-third of clinically stable ambulatory lung transplant recipients followed intensively using multiple diagnostic modalities over a 5-month respiratory virus season. Although many of the 17 infected patients had only mild infections limited to the upper respiratory tract, the rate of lower respiratory tract involvement was 8 % (4/50) over the five-month study interval. This rate is somewhat higher than previously reported rates. For instance, the average yearly rate of lower respiratory paramyxoviral infection reported by Wendt and coworkers in a 7-year retrospective evaluation was 3% (4). Similarly, Palmer and coworkers reported an average annual incidence rate of 1.6% for the occurrence of RSV, PIV and adenovirus infection in a 5-year interval (3). Our findings do not merely reflect an unusually high rate of respiratory viral infection during the 1999-2000 season as is shown by the five years of data from the Vanderbilt virology laboratory (Figures 1A and 1B). Indeed, the rate of lower respiratory viral infection may be an underestimate of the actual yearly rate in the population, because we conducted our study only during the five-month respiratory season from November through March and focused our diagnostic efforts on the viruses which have been known to cause severe disease in lung recipients, notably respiratory syncytial virus, parainfluenzavirus, influenza and adenovirus. We specifically did not look for rhinoviruses or coronviruses. Also, metapneumovirus was not investigated, as it had not been described at the time of the study. In recent studies these viruses have emerged as probable respiratory pathogens in lung transplant recipients and should be included in future studies. (15-18) Such a study might also include techniques to detect

atypical pathogens such *as chlamydia pneumonia* and *mycoplasma pneumonia* as infection with these pathogens may mimic respiratory viral infection. (15)

In this study, the most common viral infection, influenza, was also associated with the least morbidity. Other studies have shown similar results, including recent work by Vilchez and colleagues who evaluated 15 lung transplant recipients infected and hospitalized with influenza (23). None of the influenza-infected patients in that study developed respiratory failure despite the fact that 5/15 (33%) had clinical pneumonia. Garantziotis et al. (24) described influenza pneumonia in three lung transplant recipients. All three patients had significant radiographic changes consistent with pneumonia and all recovered from their acute viral illness but developed late chronic rejection. In our study two patients had lower respiratory involvement but neither had pneumonia or required hospitalization. One of these patients (pt 49) was diagnosed with BOS less than a year after her infection. Because she was not hospitalized and did not undergo bronchoscopy ~~and so~~ her case might have been missed in a retrospective study.

A plausible explanation for the low acute influenza morbidity in our study is the high immunization rate in our transplant population. We attempt to vaccinate all lung transplant recipients at our center on a yearly basis. We were able to document influenza vaccination in at least 80% of the 50 study patients. A prospective study would be necessary to see whether consistent yearly influenza vaccination truly reduces infection rates or attenuates morbidity in lung recipients. Such a study would require that a large number of patients ~~who were~~ be monitored for the adequacy of their serological responses and followed over a number of years.

Although the overall rates of respiratory viral infection in the study were higher than in previous lung transplant reports, the rates of severe lower respiratory tract infection are similar to those studies, as evidenced by the frequency of pneumonia (2%) and hospitalization (4%). No deaths from respiratory viral infection were seen in the ambulatory study patients, most of whom were healthy. We did diagnose two deaths due to respiratory viral infection in patients who had been recently transplanted and were not eligible for entry into the prospective study. It is likely that patients are more vulnerable during this early post-transplant interval because they receive higher doses of immunosuppression, have lower pulmonary reserve and may have ischemic injury to the transplanted lung. Pohl and coworkers noted that RSV infection in children with liver transplants was more likely to be fatal if it occurred early after transplantation (25).
A number of authors have associated the occurrence of respiratory viral infection with subsequent development of BO or BOS (11). In the study by Billings the occurrence of BO or BOS was specifically linked with preceding lower respiratory tract viral infection. Our study did not show any association between respiratory viral infection and BO or BOS but most of the cases we saw had infection limited to the upper respiratory tract and there were only four cases of lower respiratory tract infection.

We are not sure why the respiratory viral infections were more common in patients who were later post transplantation but it did not appear to be due to a higher rate of BO or BOS in this group. One possible explanation is that the patients who had been transplanted more recently may have been more likely to come in for minor symptoms. They may have been more likely to be infected by less virulent organisms such as rhinoviruses as opposed to the more virulent orthomyxoviruses and paramyxoviruses. A

larger and more comprehensive prospective study, that encompassed more viruses should be able to evaluate this possibility.

This study represents one of the few prospective studies that has used multiple diagnostic modalities including PCR to evaluate the incidence and impact of respiratory viral infections in lung transplant recipients. It shows that studies that look only at clinically diagnosed cases patients may underestimate the underlying rate of respiratory tract infection. While this result is not surprising in itself, it does illustrate that a complete picture of the morbidity and immunologic consequences of respiratory viral infection in lung transplantation will only be achieved with prospective population-based studies. These studies ideally would use both conventional and molecular techniques to detect a large number of different respiratory viruses at multiple centers over multiple years.

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TABLE 1
PATIENT DEMOGRAPHICS*

Characteristic	Infected (n=17)	Uninfected (n=33)
Age (mean years ± SD)	50 ± 13	50 ± 10
Gender (M : F)	12 : 5	16 : 17
Pre-transplant diagnosis – no. (%)		
IPF	7 (41)	9 (27)
COPD	4 (24)	10 (30)
AAT	1 (8)	3 (9)
CF	2 (12)	4 (12)
PPH	2 (12)	3 (9)
Other	1 (6)	4 (12)
Immunosuppresssion no. (%)†		
Cyclosporine	16 (94)	29 (88)
Tacrolimus	1(6)	4 (12)
Azathioprine	12 (71)	27 (81)
Mycophenylate	3 (18)	5 (15)
Time post-transplant - median days (range)§	1335 (61-3104)	786 (19-2651)
Previous BO or BOS - no. (%)	2 (12)	5 (15)
Single lung transplant – no. (%)	12 (71)	24 (73)
Double lung transplant – no. (%)	4 (24)	8 (24)
Heart lung transplant – no. (%)	1 (4)	1 (3)

* IPF = idiopathic pulmonary fibrosis; PPH = primary pulmonary hypertension; COPD = chronic obstructive pulmonary disease; AAT = alpha one antitrypsin deficiency; CF = cystic fibrosis; Other = sarcoidosis, lymphangioleiomyomatosis, Eisenmenger's syndrome, and post-adult respiratory distress syndrome fibrosis. BO=Bronchiolitis obliterans; BOS= Bronchiolitis obliterans syndrome.

† One patient in both groups was enrolled in a trial comparing azathioprine and everolimus; all patients were receiving prednisone

§ p=0.04; Mann-Whitney test; all other comparisons between infected and uninfected patients were not significant.

TABLE 2

TYPE OF VIRUS, METHOD OF DETECTION AND TOTAL PATIENTS WITH INFECTION

Virus	Method of Detection				Infected Patients* (% total)
	Antigen	Culture	PCR	Serology	
Respiratory Syncytial Virus	1	1	5	7	8 (16%)
Adenovirus	N/A	0	N/A	N/A	0 (0%)
Influenza	2	3	4	8	10 (20%)
Parainfluenza	N/A	1	1	N/A	1 (2%)
				Total:	17 (34%)

* The total number of infections is less than 19 because two patients had both FLU and RSV infections during the study period

TABLE 3

SIGNS AND SYMPTOMS IN PATIENTS WITH LOWER RESPIRATORY INFECTION

Pt. ID	Virus Identified (Method)	Symptoms	Signs	Decline in $FEV_1 \geq$ 10%	Chest Radiograph Infiltrate	Lung Biopsy
VU15*	PIV (Culture/PCR)	Stuffy nose Hoarseness Dyspnea Cough	RR 24 bpm 98.9 F Rales present Wheezing	No	Yes	Yes
VU38	IA/RSVA (PCR)	Stuffy nose Hoarseness Cough	RR 24 bpm 98.6 F Wheezing	Yes	No	NP
VU49	IA (Culture/PCR)	Stuffy nose Sneezing Dyspnea Cough	RR 28 bpm 98.7 F Wheezing	No	No	NP
VU2*	RSVB (Culture/PCR Antigen/Serol)	Stuffy nose Runny nose Dyspnea Cough Pleuritic chest pain	RR 32 bpm 102.5 F Rales present Rhonchi present	No	No	NP

IA=Influenza A; PIV=Parainfluenzavirus; RSVA=Respiratory syncytial virus A; RSVB=Respiratory syncytial virus B; Serol= serology

RR = respiratory rate in breaths per minute (bpm)

FEV_1 = forced expiratory volume in 1 second

NP = not performed

* Two patients who required hospitalization and were treated with inhaled ribavirin

TABLE 4

CLINICAL OUTCOMES ONE YEAR
AFTER END OF STUDY

Outcome	Infected† (n=17)	Uninfected† (n=33)
Death (%)	2 (12)	1 (3)
Acute Rejection (%)	0 (0)	5 (15)
BO or BOS * (%)	1 (7)	3 (11)

* The denominators for this comparison are the patients who did not have prior BO or BOS (infected=15; uninfected=28)

† All comparisons p = NS

LEGENDS

FIGURE 1A – Shown is the number of positive influenza cultures (shaded bars) and the proportion of influenza positive cultures (connected line) in the Vanderbilt Hospital virology laboratory for 5 consecutive respiratory viral seasons. The study was conducted in the 1999-2000 season.

FIGURE 1B – Shown is the number of positive RSV antigens (shaded bars) and the proportion of positive RSV antigens (connected line) in the Vanderbilt Hospital virology laboratory for 5 consecutive respiratory viral seasons. The study was conducted in the 1999-2000 season.

Figure 1A

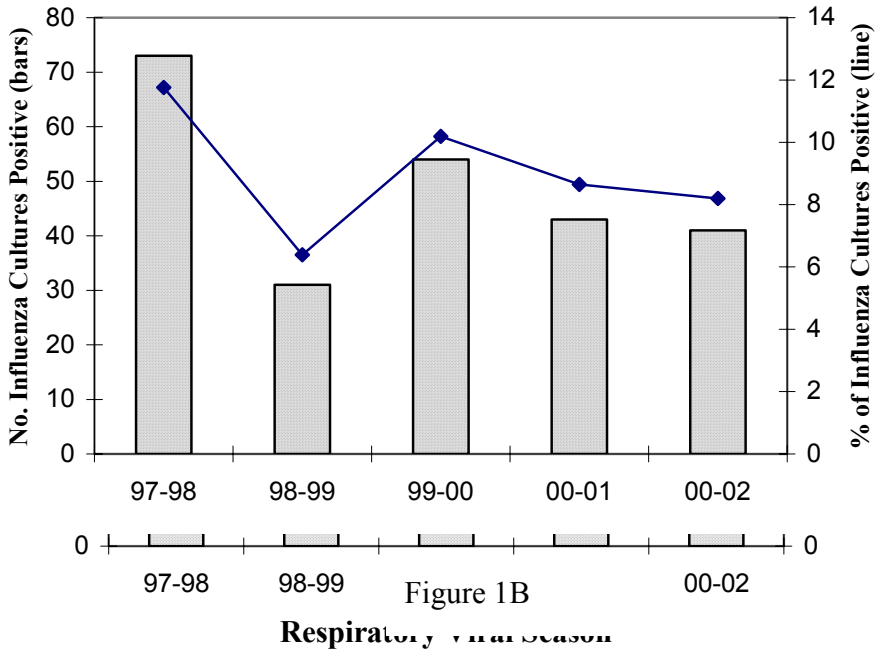
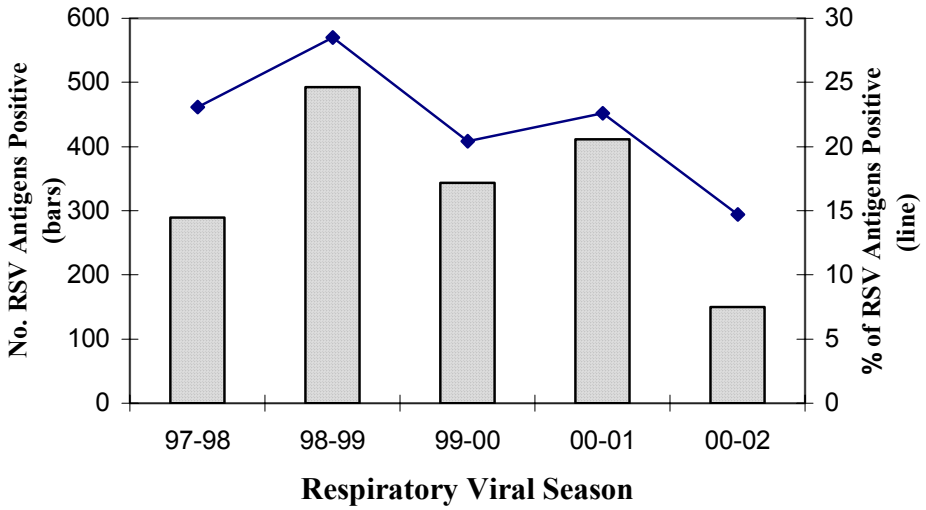


Figure 1B

Respiratory Viral Season

Figure 1B


600
500
400
300
200
100
0
30
25
20
15
10
5
0
No. RSV Antigens Positive (bars)
% of RSV Antigens Positive (line)
97-98
98-99
99-00
00-01
00-02
Respiratory Viral Season