PAPER

Comparison of Wound Culture and Bronchial Lavage in the Severely Burned Child

Implications for Antimicrobial Therapy

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Background: The relationship of the burn wound flora to microbial pathogens in the tracheobronchial tree has important implications for antimicrobial therapy in the severely burned patient. Management of septic complications is bolstered by surveillance quantitative wound cultures (QWC) and bronchial lavage fluid (BLF) cultures.

Objectives: To compare the organisms present in BLF with those found in QWC and to determine if QWC can predict BLF results.

Design: Results of BLF cultures from all patients who underwent bronchial lavage from January 1, 1996, to December 31, 1996, at our institution were compared with QWC data from the same date. Criteria for a positive match included an identical antibiotic susceptibility pattern and biotype. Match rates were calculated qualitatively and quantitatively.

Results: In 30 (48%) of the 62 BLF cultures, there was a match between the organism identified in the BLF and the QWC. When strict quantitative criteria were applied, the match rate was only 9 (14%) of 62. Burn size and inhalation injury had no significant effect on match rate.

Conclusions: Whereas the microbial pathogens were similar in the QWC and BLF, linear regression showed no value of QWC in predicting BLF culture results. The difference between qualitative and quantitative match rates suggests cross-colonization between the burn wound and tracheobronchial tree, but little to no cross-infection. The QWC and BLF cultures must be performed independently in determining antimicrobial specificity in the burned patient.

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BURN WOUND sepsis and pulmonary infection are 2 of the most serious causes of morbidity and mortality in thermally injured children. Before the advent of topical antimicrobial agents, burn wound sepsis invariably resulted in death of the severely burned child. Despite the routine use of agents such as silver sulfadiazine, silver nitrate, and mafenide acetate, burn wound infection still remains a potentially life-threatening complication of massive burn injury. Likewise, pneumonia has been associated with a reported mortality of up to 40% in the burned patient. This figure is elevated to 60% if there is a concomitant inhalation injury.[1] The burn wound and the lung may serve as foci for disseminated bacterial invasion and rampant septicemia.

In addition to breaching the mechanical barrier that the skin normally provides, massive burn injury is associated with a generalized state of immunosuppression,[2-4] which renders patients especially susceptible to infection of the lung and the burn wound. Furthermore, significant smoke inhalation injury impairs the mucociliary transport mechanism, which predisposes patients to invasion of the tracheobronchial tree by microorganisms. The same is true for mechanical ventilation, which has been shown to increase the incidence of pulmonary infection.[5] Together, these 4 contributing factors mandate aggressive antimicrobial treatment in the severely burned patient. The combination of early surgical debridement and improved antibiotic therapy has made a major impact on mortality due to infection in burned patients.[6]

Newer antibiotics have targeted emerging multiresistant strains of organisms. Many issues, including cost-effectiveness, therapeutic efficacy, and potential complications, must be weighed critically during antimicrobial selection. This is especially relevant in the burned patient, where a nephrotoxic drug can have an exaggerated effect on a kidney that may

SUBJECTS AND METHODS

We studied all patients who underwent bronchial lavage from January 1, 1996, to December 31, 1996. We identified 101 BLF cultures in 58 patients. There were 62 BLF cultures in 37 patients for whom QWC data were available from the same date during the hospital course for comparison. In the 39 remaining cases, there was no growth in the BLF or the burn wound, or QWC was not performed at the time of bronchial lavage. Only patients who had BLF cultures and QWC from the same date that grew quantifiable organisms were included in the study. The BLF cultures that grew at least 1 organism at greater than 1×10^3 organisms per milliliter were considered to be indicative of clinical infection, warranting specific antimicrobial therapy.[8] All bronchial lavages were performed intraoperatively at the time of excision and grafting by an anesthesiologist with extensive experience in burn care. The bronchial lavage procedure involved carefully wedging a pediatric bronchoscope into the most distal lung segment possible and lavaging with 10 mL sterile saline solution on the right and left sides. Culture results from BLF were used to direct intravenous antibiotic treatment. Specimens for QWC were also obtained intraoperatively at the time of excision and grafting and whenever there was clinical suspicion of burn wound infection based on gross appearance of the wound or conversion of a partial-thickness wound to full thickness. Any QWC growing greater than 1×10^5 organisms per gram of tissue was considered indicative of a wound at substantial risk for invasive infection.

All patients in this study had sustained acute burns, and the cultures were collected during the initial hospitalization. Children underwent the standardized care practiced at our institution. This included early excision and grafting of burn wounds, management of fluid and electrolyte balance, metabolic and nutritional support with early enteral feedings, and aggressive pulmonary toilet. Patients were initially resuscitated with lactated Ringer solution according to the formula of 5000 mL/m^2 burned body surface area (BSA) per 24 hours and 2000 mL/m^2 total BSA (TBSA) per 24 hours; half was given in the first 8 hours following injury. Bronchoscopy results from the initial admission were examined to ascertain the presence or absence of inhalation injury. Findings of mucosal erythema, hemorrhage, and ulceration with denuded respiratory epithelium were considered consistent with inhalation injury. Clinical suspicion of inhalation injury was confirmed using results of fiberoptic bronchoscopy in every case. Patients with documented inhalation injury underwent the standard inhalation injury protocol practiced at our institution, which included nebulized acetylcysteine and heparin sulfate given every 4 hours until full recovery of lung function.

Criteria for a positive match between organisms identified in BLF cultures and QWC included an identical antibiotic susceptibilty pattern and the presence of the same microbiologic biotype as determined by a series of biochemical assays. These were performed using commercially available gram-positive and gram-negative panels (MicroScan; Dade International Inc, Sacramento, Calif).

Antibiotic susceptibility patterns were determined based on minimum inhibitory concentration.The panels were incubated in a commercially available automated system (Walkaway 40; Dade International Inc). Antibiotic susceptibility patterns differing in sensitivity or resistance to 2 or fewer antibiotics were considered identical. If the antibiotic susceptibility pattern or the microbiologic biotype of the organisms identified were different between the BLF culture and the QWC, then there was no match.

already be at risk due to inadequate resuscitation.[7] Therefore, it becomes imperative that only those antibiotics that are absolutely necessary are administered, to reduce the systemic toxic effects of these drugs in a patient whose renal status may be marginal. To achieve this goal, a program of routine bacterial surveillance is often used to adjust antimicrobial therapy. This program most often consists of frequent quantitative wound cultures (QWC), bronchial lavage fluid (BLF) cultures, and blood and urine cultures as necessary. As noted previously, it is often the wound or the lung that serves as a focus for sepsis. Therefore, we concentrated our attention on both areas.

It is very tempting to assume that the microbial pathogens isolated from BLF should reflect the burn wound flora. Ideally, this would mean that antimicrobial coverage directed at the organisms found in the burn wound would also be adequate coverage for those organisms found in the tracheobronchial tree, thereby minimizing the number of different antibiotics needed to treat clinically apparent infection and reducing cumulative systemic toxic effects.

It is our hypothesis that whereas the spectrum of pathogens is similar in the burn wound and the lung, there are sufficient differences to merit independent cultures and a 2-pronged antimicrobial approach. To test this hypothesis, we decided to compare the organisms found using QWC with those found in BLF and establish guidelines for choosing appropriate antimicrobial therapy.

RESULTS

Analysis of the demographic characteristics of the patient population reveals that there were 23 males (62%) and 14 females (38%), with a mean age of 6.4 years (range, 0.5-17.5 years). Mean percentage of TBSA burned was 43.8% (range, 5%-95%). Inhalation injury was diagnosed using results of bronchoscopy in 15 patients (40%).

To best understand the relationship between the burn wound flora and microbial pathogens in the lung, we first examined the incidence of organisms that were present in both areas qualitatively, regardless of the total quantification. Looking first at the burn wound, we identified several common pathogens, as illustrated in **Figure 1**. Staphylococcal organisms were most common, followed by several gram-negative organisms such as *Klebsiella* and *Pseudomonas* species. **Figure 2** depicts the incidence of organisms cultured from BLF. A similar spectrum of organisms was encountered, with a slightly higher incidence of methicillin-sensitive *Staphylococcus aureus*. **Figure 3** and **Figure 4** represent the incidence of organisms isolated from the burn wound and the BLF when strict quantitative criteria were applied. This was

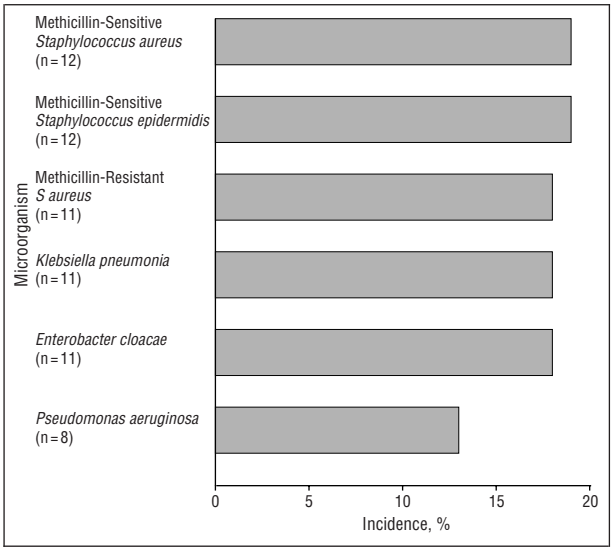

Figure 1. *Spectrum of pathogens isolated from all quantitative wound cultures.*

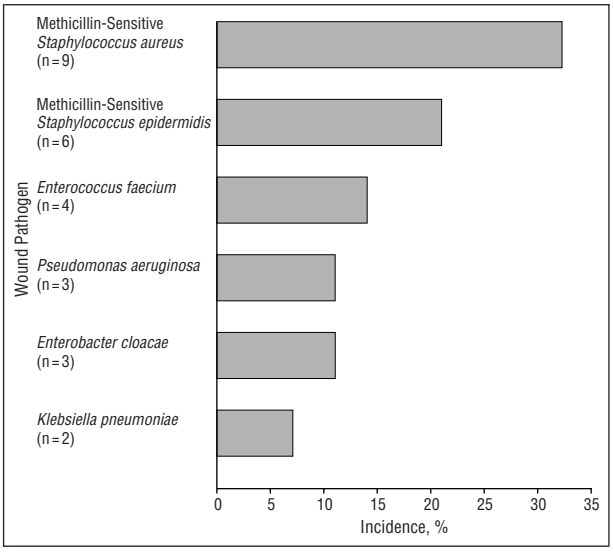

Figure 3. *Incidence of burn wound pathogens isolated at less than 1×10^5 organisms per gram of tissue.*

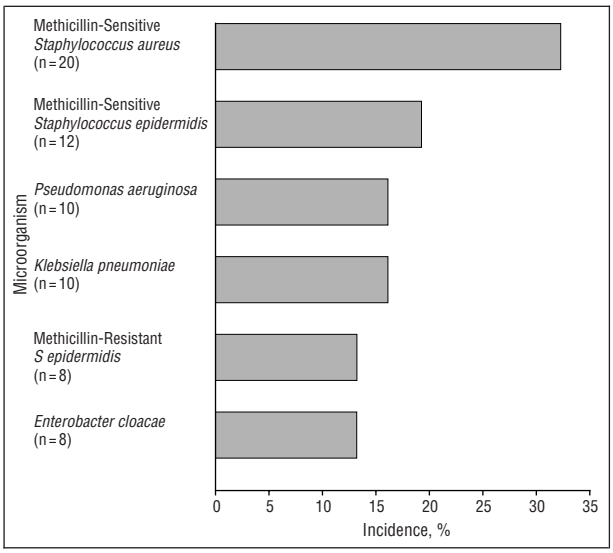

Figure 2. *Spectrum of pathogens isolated from bronchial lavage fluid cultures.*

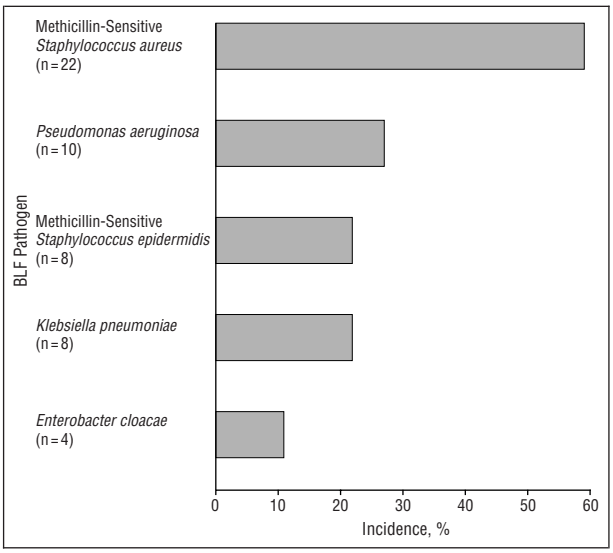

Figure 4. *Incidence of pathogens in bronchial lavage fluid (BLF) isolated at less than 1×10^3 colony-forming units per milliliter.*

1×10^5 organisms per gram of tissue and 1×10^3 colony-forming units (cfu)/mL for QWC and BLF cultures, respectively.

After analyzing the microbial spectrum of the burn wound flora and the tracheobronchial tree qualitatively and based on strict quantitative criteria for infection, the match rate was calculated for organisms found in QWC and BLF cultures. Criteria for a positive match included the presence of an identical antibiotic susceptibility pattern and an identical biochemical biotype. The overall match rate based on qualitative criteria was 30 (48%) of 62 cultures. When strict quantitative criteria were applied, the match rate was reduced to only 9 (14%) of 62 cultures. The difference between qualitative and quantitative match rates was highly significant ($P<.001$, χ^2 analysis). This is clearly illustrated in **Figure 5**. In addition to examining the match rate between organisms in QWC and BLF cultures, the incidence of the most common pathogens found simultaneously in QWC and BLF matches was analyzed. This was performed for qualitative matches (**Figure 6**) and for matches in which QWC and BLF cultures met strict quantitative criteria for infection (**Figure 7**). Next, linear regression analysis was performed for all sets of matched organisms, to determine whether the number of organisms in the burn wound could predict the number of identical organisms in the tracheobronchial tree. This analysis failed to show any predictive value of QWC with respect to BLF cultures ($r = 0.02$). Finally, we determined the effect of burn size and inhalation injury on match rate as depicted in **Figure 8** and **Figure 9**. There was no statistically significant difference in the match rates for microbial pathogens between patients with burns of greater than and less than or equal to 40% TBSA. The effect of inhalation injury was negligible.

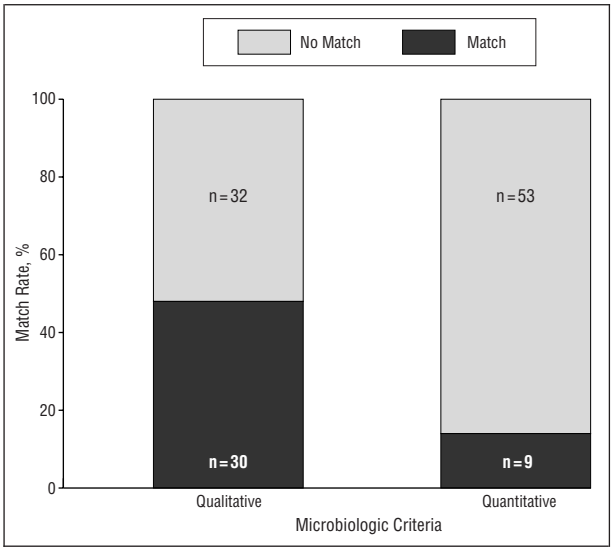

Figure 5. *Match rate for pathogens in burn wound and bronchial lavage fluid qualitatively and when strict quantitative criteria for infection were applied (P<.05).*

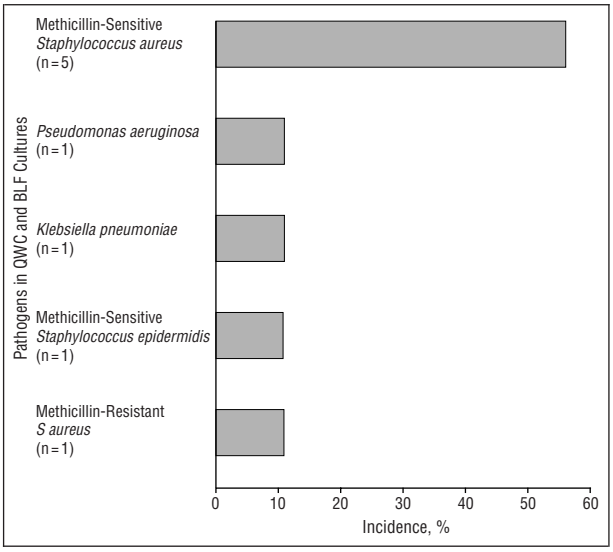

Figure 7. *Incidence of pathogens among quantitative matches between quantitative wound cultures (QWC) and bronchial lavage fluid (BLF) cultures.*

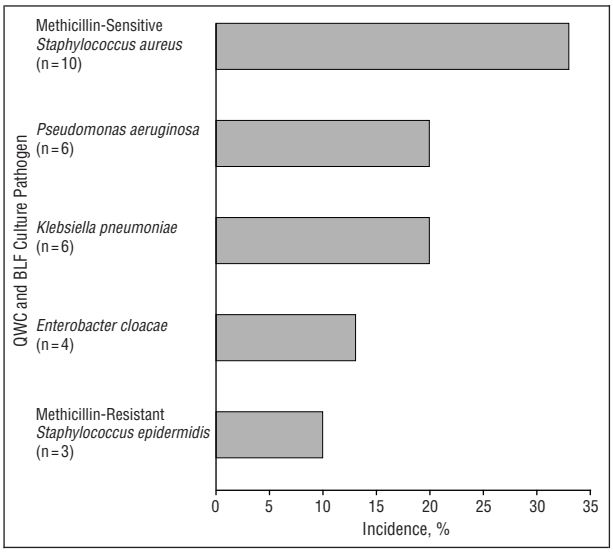

Figure 6. *Incidence of pathogens among qualitative matches between quantitative wound cultures (QWC) and bronchial lavage fluid (BLF) cultures.*

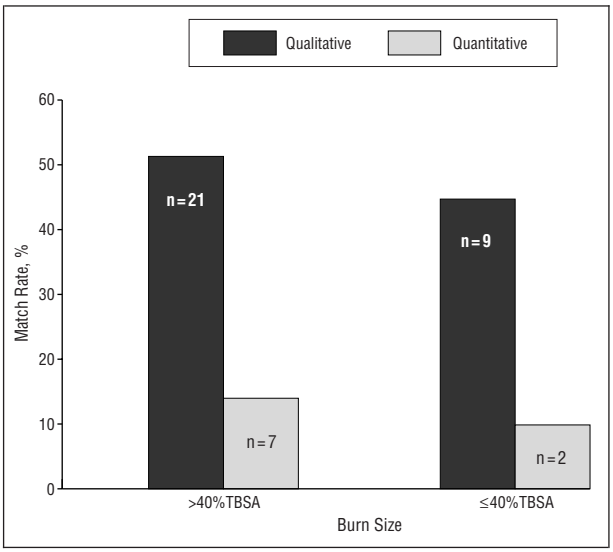

Figure 8. *Effect of burn size on match rate between quantitative wound and bronchial lavage fluid cultures. Qualitative and quantitative match rates are the same for large (>40% of total body surface area [TBSA]) and small burns (<40% of TBSA).*

COMMENT

On extensive scrutiny of the literature, we found that although many studies have addressed burn wound sepsis and pulmonary infection, there has been no previous attempt to compare the organisms cultured from these 2 important areas. There are several cogent elements of this study to recognize. The first is to realize that whereas there was a 48% qualitative match rate, there was only a 14% quantitative match rate, as seen in Figure 5. Nearly half of the time, BLF cultures were growing the identical organism as QWC. Interestingly, we find that the spectrum of pathogens is very similar in the burn wound and tracheobronchial tree. Looking at the qualitative and quantitative data in Figures 1 through 4, it is clear that methicillin-sensitive *S aureus* was the most prevalent organism, which was isolated from QWC and BLF. Methicillin-sensitive *S aureus* was responsible for more than half of the quantitative matches. Methicillin-resistant *S aureus* also makes its first appearance among the quantitative matches in Figure 7.

Figure 8 clearly demonstrates that there is no effect of burn size on match rate. This is important, because we surmised that perhaps the patients with larger burns may skew the results, since they underwent more intraoperative surveillance cultures. The match rates are nearly identical for patients with greater than and less than or equal to 40% TBSA burns.

An important consideration is that earlier studies were based on only a few biochemical reactions to identify microbial pathogens. For example, staphylococci were broadly classified into 2 groups based only on the coagulase reaction. The same is true for *Pseudomonas* species, which were classified solely based on the oxidase

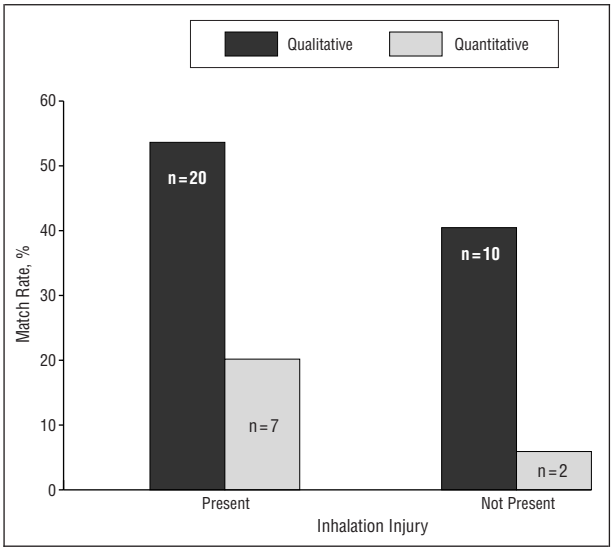

Figure 9. *Effect of inhalation injury on match rate between quantitative wound and bronchial lavage fluid cultures.*

and pyocyanic reactions. This provided for only a limited degree of specificity in determining antimicrobial susceptibility. Modern technological advances have afforded us a more in-depth approach to identification and susceptibility testing based on a wide gamut of reactions and have allowed microbiologists to fine-tune the antibiotic susceptibility pattern.

The fact that there is a 48% match rate between QWC and BLF cultures suggests a high incidence of cross-colonization between the burn wound and the tracheobronchial tree. As mentioned earlier, the match rate is reduced to only 14% when strict quantitative criteria are applied. There are several possible explanations for this, including cross-contamination by hospital personnel. Furthermore, several studies have noted a transient bacteremia that occurs following burn wound manipulation.[9] This transient bacteremia may have seeded the tracheobronchial tree with small numbers of organisms. As this bacteremia is usually transient, natural host defense, although impaired after burn injury, may have been sufficient to prevent further infection. The 14% quantitative match rate suggests that whereas there is a high rate of cross-colonization, there is little to no significant cross-infection between the burn wound and the lung.

The gram-positive and gram-negative distribution of organisms is similar between the burn wound and the tracheobronchial tree. Nineteen (58%) of the 33 organisms isolated from QWC growing less than 1×10^5 organisms per gram of tissue were gram positive, whereas 14 (42%) were gram negative. This is similar to BLF cultures growing more than 1×10^3 cfu/mL, where 30 (65%) of the 46 organisms were gram positive and 16 (35%) were gram negative. Previous work by Shannon et al[10] has shown that it is usually the gram-negative organisms that cause significant morbidity and mortality, and that the importance of methicillin-resistant *S aureus* and *Staphylococcus epidermidis* in the burn population is overrated, as they are rarely a cause of morbidity and often can be managed with monotherapy. This is in sharp contrast to the gram-negative infections, which are frequent causes of morbidity and usually require antimicrobial therapy with more than 1 agent.

The question then arises as to the implications of this study for antimicrobial therapy in the severely burned child. As noted previously, breaching of the mechanical barrier of the skin, generalized immunosupression, mechanical ventilation, and impaired mucociliary transport all mandate aggressive antimicrobial therapy in these patients. At our institution, these antibiotics are administered before burn wound manipulation to assist host defense mechanisms. Normally, patients receive empirical antibiotic therapy based on epidemiological surveillance data.[11] The antimicrobial therapy is then adjusted appropriately based on results of QWC. No further changes would be necessary, provided that the match rates between organisms from the burn wound and tracheobronchial tree were high.

Our study, however, shows that qualitative and, to a greater extent, quantitative match rates are poor. Even if the same organisms are present, the antibiotic susceptibility patterns and biotypes are different.

The implication, then, is that after appropriate antibiotic therapy has been started based on QWC, additional cultures of BLF are warranted. Antimicrobial therapy can then be adjusted based on results of susceptibility testing of the pathogens in the BLF. The clinician cannot stop after QWC and be assured of adequate coverage. Ideally, at that point, should the susceptibility pattern for gram-negative organisms in the BLF be different from those of the burn wound, appropriate antibiotics could be selected that would provide adequate coverage for the burn wound and the tracheobronchial tree to decrease cumulative toxic effects.

These bacterial surveillance cultures should only serve as an adjunct in determining antimicrobial therapy, when clinical suspicion of an infection exists. In conclusion, the pathogens in the burn wound and the BLF are sufficiently different to merit independent culture and susceptibility testing to direct antimicrobial therapy in the burned child.

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DISCUSSION

Albert T. McManus, PhD, San Antonio, Tex: I have several questions pertaining to this paper. First, I am not sure if the invasive techniques used—basic bronchoalveolar lavage and biopsy—were done for diagnostic or surveillance purposes, and I noticed, in commenting about the QWC, you mentioned that would indicate the opportunity for wound infection. What data do you have to base a quantitative lavage culture without a Gram stain or measurement of cellularity as a diagnostic tool for respiratory tract infection? Also, I assume that you were attempting to decide whether, if organisms were present in both the respiratory tract and the wound at significant cultures, that these would indicate infections at both these sites. Would it follow if there were infections but a difference in antibiotic sensitivity patterns, how would you determine the antibiotic to use with both of these conditions going on?

And finally, most people assume that the respiratory tract becomes colonized via the oral pharynx. I wonder if you have any sputum cultures or pharyngeal swab cultures to compare to the invasive lavage cultures to see whether in fact they would be of equal utility.

Dr Ramzy: Dr McManus, in answer to your first question, were the bronchoalveolar lavages performed for diagnostic purposes or for surveillance purposes, all these lavages were performed interoperatively at the time of excision and grafting routinely, so the answer to your question is surveillance. In order to answer your second question about whether there is evidence to show that bronchoalveolar lavage is efficacious in the diagnosis of pneumonia in critically ill patients, there are several papers that have shown the utility of this technique in these patients, most recently the paper by Martin Croce, which was presented at the Southern Surgical, which showed that bronchoalveolar lavage was adequate for the diagnosis of pneumonia in these cases.

To answer your next question, how would you select antibiotic therapy based on these results, the idea, if possible, is to reduce the cumulative toxicity of these drugs in these patients. Since they have marginal renal status to begin with, anything you can do to decrease the number of antibiotics needed is better. So if you culture the BLF separately, you can hopefully pick 1 agent, which can cover the organisms in both tracheobronchial tree and the burn wound.

In order to answer the last question, your point is very well taken. Clearly, many pneumonias are descending infections and not hematogenous. The data in this study don't speak directly to that issue; however, there have been reports in the past by several groups, including our own, that there is a transient bacteremia following burn wound manipulation and excision. It is possible that this transient bacteremia is sufficient to seed these areas and cause colonization, but that immune host defenses, although impaired after burn injury, are still strong enough to prevent actual invasive infection.

E. Patchen Dellinger, MD, Seattle, Wash: I wonder if you are not being a little too restrictive in the way you gathered your data and a little too negative in interpreting your results. You only called it a match if you got the same bug from the bronchoalveolar lavage and the wound on the same day. But clinically speaking, you are going to have that information at the same time also. What would be interesting to know is if the bacteria in the bronchoalveolar lavage are the same as what you cultured from the wound several days earlier. In that case, if you make a clinical judgment that your patient has a respiratory infection and look back at what you are growing from your wound 3 days to 7 days earlier, you could make a more informed choice. Knowing that you have the same bug at the same time won't help you clinically, although it may be interesting statistically.

Secondly, assuming that your match for cultures not on the same day was as good as the match you showed for cultures on the same day, 50% would not allow you the luxury of avoiding the culture of the bronchoalveolar lavage, but having a 50% chance of picking the right bug is pretty good. You could at least cover that bug that you know about for sure with your empiric therapy and then perhaps broaden from there, depending on other clinical circumstances.

Dr Ramzy: Certainly, looking at wound cultures from several days prior is a good idea for something for us to do in the future, and we will do that.

Basil A. Pruitt, Jr, MD, San Antonio: I am still a little puzzled about the clinical relevance of all this. Did any of the patients have pneumonia and did any of them have histologically documented wound infection? Was there any mortality associated with wound infection? In the absence of such, I am not sure what these cultures mean. I would anticipate that the concordance between BAL cultures and wound cultures might increase with time post injury, and ask whether that did occur?

Dr Ramzy: I did not specifically analyze the data in that way to answer that particular question, Dr Pruitt. With regard to the clinical diagnosis of pneumonia and wound infection, we did not look at any histologic tissue samples to document invasive sepsis. This was based on the QWCs, to identifying wounds that were at risk for sepsis.

Dr Pruitt: You cited Dr Croce's paper, but that was in a setting of an infiltrate and clinical signs of an infection, not just cultures.

Dr Ramzy: Your point is very well taken. As you know, sometimes the diagnosis of pneumonia in these critically ill patients is very difficult. Because of the hypermetabolic response, many of them have fever, leukocytosis, tachypnea, even in the absence of pneumonia, and certainly x-rays are helpful but, unfortunately, are difficult to interpret in the ICU setting. In fact, we recently presented a paper at the American Burn Association showing that bronchoalveolar lavage does not correlate with radiographic evidence of pneumonia, but rather with tracheobronchitis. Lavage has a role, but I agree with you; we have no way of knowing for sure whether these patients really had pneumonia.