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## Effects of Environment on Infection in Burn Patients

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**Burn patients in an early cohort (n=173) treated in an intensive care ward without separate enclosures were compared with a later cohort (n=213) treated in a renovated unit with separate bed enclosures. The number of patients developing infection was significantly reduced in the late group. Observed mortality was compared with mortality predicted on the basis of burn size and age alone. Reduction in observed compared with predicted mortality, inapparent in the early group, was seen in the late group and was restricted to the subgroup of patients with predicted mortality of 25% to 75%, in which the observed mortality of 28.3% was less than the predicted mortality of 48.7%. The incidence of infected patients was reduced from 58.1% in the early cohort to 30.4% in the late cohort. In comparison of the early cohort with the late cohort, the overall proportion of patients with bacteremia was reduced from 20.1% to 9.4%, while the incidences of both pneumonia and burn wound invasion remained unchanged. *Providencia* and *Pseudomonas* species, endemic in the early cohort, were eliminated in the late cohort. Reduction of infection by environmental manipulation in burn patients was possible and was associated with improved survival.**  
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prevention of infection is particularly important. Various isolation measures to minimize or eliminate cross-infection in these individuals have met with moderate success.<sup>2</sup> In a previous report from the US Army Institute of Surgical Research, Fort Sam Houston, Tex, we recorded our ability to prevent the transmittal of endemic strains of bacteria from one group of patients to another receiving treatment in a separate, nearby, renovated unit.<sup>3</sup> In the present study, we report the effect of such environmental changes on infection and mortality in these two cohorts.

### PATIENTS AND METHODS

During the one-year period from May 1982 through April 1983, a total of 173 patients were treated in an open intensive care ward. During the subsequent year, April 1983 through May 1984, a total of 213 patients were cared for in a renovated unit having individual patient rooms. Details of the physical plans of the old and renovated units, implementation of measures for the prevention of cross-contamination between cohorts, and the culture techniques used for bacterial isolation in these patients have been reported.<sup>3</sup> Briefly, the patients in the early group were treated in an open intensive care unit with limited facilities for hand washing; the patients in the later group were managed mostly in single rooms, each with a sink, in a separate renovated unit (Fig 1). The total of 19 sinks in the renovated unit (compared with five in the older unit) provided greater opportunity for hand washing. In both time periods, all personnel wore gowns, caps, masks, and sterile gloves while providing patient care. During a two-month transition period when both units were operational, a planned flow of personnel and equipment was utilized to avoid contamination of the new cohort with organisms from the antecedent one. Physicians changed their outer attire when going from one unit to the other. Separate nursing staffs worked in each unit. Flow of equipment and other support personnel required on both units on the same day progressed from the renovated to the open unit.

Fluid resuscitation of all patients proceeded according to a modified Brooke formula,<sup>4</sup> and nutritional support based on predicted metabolic needs was implemented. Topical burn wound

Significant advances over the past four decades in fluid therapy, burn wound management, and diagnosis and treatment of infection have resulted in an overall improvement in the survival of burn patients. Mortality in burn patients with sepsis, however, has remained relatively unchanged.<sup>1</sup> In immunocompromised burn patients, the

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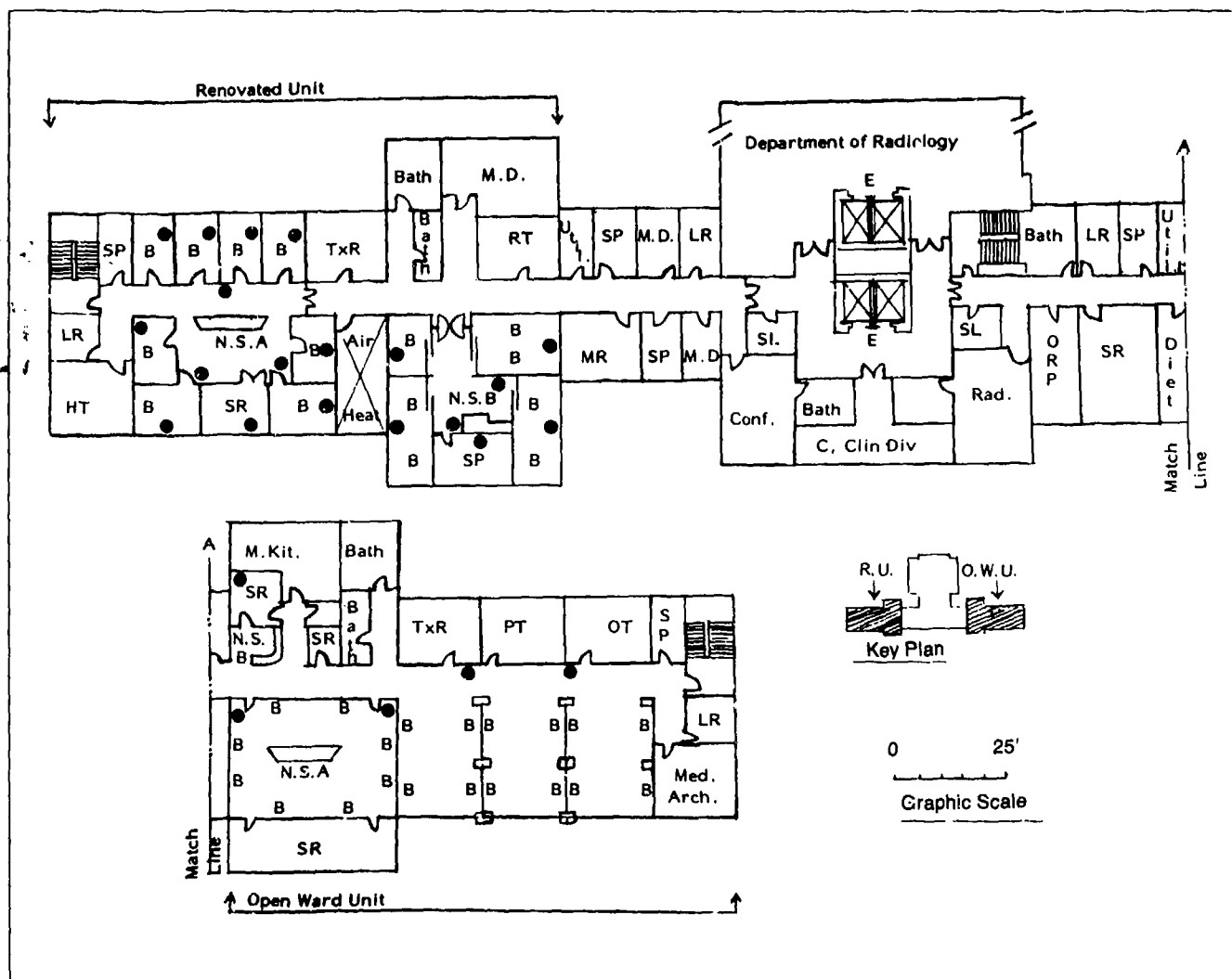


Fig 1.—Floor plan. A indicates match lines for continuity; Air-Heat, air conditioning and heating equipment (room usually closed); B, patient bed; Bath, bathroom; C, Clin Div, chief, clinical division; Conf, conference room; Diet, dietitian's office; E, elevators; HT, Hubbard tank; LR, locker room; M Kit, metabolic kitchen; MR, metabolic studies room; MD, doctor's office; Med Arch, medical archives; NSA, nurses' station, acute-care patients; NSB, nurses' station, intermediate-care patients; OT, occupational therapy section; ORP, anesthesiologist and operating room personnel; OWU, open ward unit; PT, physical therapy section; Rad, radiology office; RT, respiratory therapy section; RU, renovated unit; SL, linen storage; SP, support personnel; SR, supply room; TxR, treatment room; Util, utility room; solid circles, sinks.

therapy consisted of alternate applications of mafenide acetate cream and sulfadiazine silver cream at 12-hour intervals.<sup>5</sup> All patients were assessed daily by detailed physical examination and appropriate laboratory tests.

Infection developing beyond the third day after admission to this institute was considered nosocomial and was prospectively recorded. Data collected included causative organisms and the occurrence of bacteremia, pneumonia, burn wound infection, or urinary tract infection. For analysis, any patient diagnosed as having infection at a single site or multiple sites at one or more times was considered infected. For analysis of total occurrence of infection, infections at different sites and times were considered as separate occurrences.

### Diagnosis of Infection

The diagnosis of pneumonia in patients with purulent sputum was based on the presence of characteristic physical findings complemented by chest roentgenography, sputum examination, and sputum culture. Sputum smears or, when sputum samples were unsatisfactory, smears of endobronchial aspirate, were examined using a Gram's stain. The presence of bacteria, more than 25 white blood cells and fewer than 20 epithelial cells per high-power field, was considered diagnostic for respiratory tract infection. Diagnoses of invasive burn wound infection were based on histologic demonstration of invasion of viable tissue by microorganisms in biopsy specimens taken from representative areas of the burn wound.<sup>6,7</sup> Blood cultures were obtained in all patients clinically

	n	Burn Size, %	Age, yr	Predicted Mortality, %	Observed Mortality, %	Infection, %
All patients						
Early group	173	28.7	29.7	26.0	26.0	28.9
Infection	50	44.4	38.4	49.4	50.0	100
No infection	123	22.3	26.1	16.5	16.3	0
Late group	213	30.4	32.6	29.6	22.5*	19.2†
Infection	41	50.4	43.8	66.0	61.0	100
No infection	172	25.7	29.9	20.9	13.4*	0
Patients with predicted mortality of 25%-75%						
Early group	31	42.8	35.6	48.5	38.7	58.1
Infection	18	45.0	37.6	51.8	38.9	100
No infection	13	39.8	32.9	44.0	38.5	0
Late group	46	39.8	41.5	48.7	28.3*	30.4‡
Infection	14	41.0	44.3	51.2	50.0	100
No infection	32	39.2	40.3	47.6	18.8*	0

\* $P < .05$  vs predicted mortality.

† $P < .05$ .

‡ $P < .02$  vs early group.

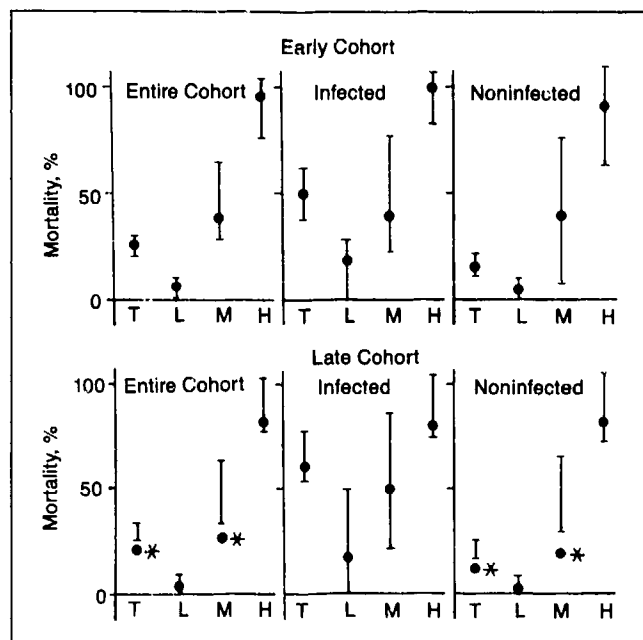


Fig 2.—Mortality in each cohort, subdivided according to presence or absence of any infection in individual patients (panels, left to right) and within panels according to predicted mortality: T, 0% to 100%; L, 0% to 25%; M, 25% to 75%; H, 75% to 100%. Vertical bracketed lines indicate 95% confidence limits of predicted mortality; solid circles, observed mortality; asterisks,  $P < .05$ , observed vs predicted mortality.

suspected of having sepsis. A diagnosis of urinary tract infection was made in patients with symptomatic bacteriuria requiring antimicrobial therapy.

#### Use of Antibiotics

Perioperative antibiotic coverage was routinely provided, with two to three doses of amikacin sulfate and vancomycin hydrochloride in all patients undergoing excision and grafting. During both study periods, amikacin, a  $\beta$ -lactam agent, and vancomycin

were commonly employed for initial treatment of a patient with clinically significant sepsis. One or more of those agents were employed, as dictated by results of smears or cultures, for initial treatment of pneumonia or bacteremia. Antibiotic therapy was thereafter modified if, on culture, the organisms were found to be resistant, or developed resistance during the eight- to ten-day course of treatment, or if there was no clinical or bacteriologic improvement despite in vitro sensitivity of the organisms to the prescribed antibiotics. Patients with invasive burn wound infections received subeschar clysis with ticarcillin disodium before excision of the burn wound.<sup>8</sup>

#### Statistical Analysis

Observed mortality was compared with predicted mortality determined by a previously developed logistic regression of mortality based on total burn size and age in over 6,000 patients treated at this institute during the past 33 years. The observed and predicted mortalities in the present study were assessed in the entire early and late cohorts and in subgroups after stratification according to predicted mortality. The observed mortality for any group was compared with the group's predicted mortality by determining the 95% confidence interval about the predicted mortality with use of a binomial expansion.<sup>9</sup> If the 95% confidence interval did not include the observed mortality, the difference between observed and predicted mortalities was considered significant. Infection incidence between groups and the occurrence of infection caused by various categories of organisms were compared by the use of the G test<sup>4</sup> with Williams' correction.<sup>10</sup>

#### RESULTS

Table 1 shows that in the late group, observed mortality was significantly lower than predicted mortality, with a parallel reduction of incidence of infection. Division of the groups into those who did or did not experience infection showed that the improvement in mortality in the late cohort was found to be confined to the noninfected patients (Table 1, upper panel). On further partitioning, this improvement was found to be restricted to patients whose probability of death (predicted mortality) ranged from 25% to 75%, as is shown in Fig 2 and in the lower panel of Table 1. Figure 2 shows that the observed mortality did not differ signifi-

	n	% of Patients			
		Pneumonia	Bacteremia	Burn Wound Invasion	Urinary Tract Infection
Early group	173	19.4	20.8	8.7	7.5
Late group	213	17.4	9.4*	6.1	2.3†

\*P<.01 vs early group.  
†P<.05 vs early group.

	No. (%) of Infections	
	Early Group	Late Group
Gram-negative enteric species	45 (25)	38 (37)*
<i>Providencia stuartii</i>	18 (10)	0 (0)†
Gram-negative nonenteric species	47 (26)	9 (9)†
<i>Pseudomonas aeruginosa</i>	43 (25)	4 (4)†
Gram-positive cocci	50 (28)	41 (39)*
<i>Staphylococcus aureus</i>	18 (10)	34 (33)†
<i>Candida</i> species	38 (21)	16 (15)
<b>Total</b>	<b>180 (100)</b>	<b>104 (100)</b>

\*P<.5 vs early group.  
†P<.001 vs early group.

cantly from predicted in patients with lower (0% to 25%) or higher (75% to 100%) expected mortality or in any subgroup within the set of infected patients. Table 2 shows that the types of infection reduced in the late cohort were bacteremia and urinary tract infection. Table 3 shows that infections with *Pseudomonas aeruginosa* and *Providencia stuartii* were markedly reduced or eliminated in the late cohort. Even the four occurrences of *Pseudomonas* in the late cohort were not of the multiple drug-resistant type 15 endemic in the early group. Infections with other enteric organisms and gram-positive cocci constituted a larger proportion of all infections in the late group.

#### COMMENT

Our previous report on a portion of these patients showed that, with the institution of preventive measures and change in the physical plant and staffing pattern, drug-resistant strains of bacteria could be contained in a patient care unit where they were endemic and that cross-infection with those organisms of patients cared for in a separate renovated unit was prevented.<sup>3</sup> In the present study, we have examined the impact of those previously described preventive measures on the clinical outcome of the two cohorts of patients. Our results indicate that the late group of patients had both a reduced incidence of infection and an improved survival beyond that anticipated for their age and burn size. Reduction of mortality in the later period was confined to the subgroup of patients who remained infection free, and this beneficial effect was discernible mainly in the subset of patients in the midrange of probability of mortality. Mortality among the infected patients in both groups closely approximated their age and burn size-related expected mortality. These findings suggest that prevention of infection was the principal contributor to the observed

improvement in survival. In susceptible individuals, such as our patients, it has been shown that those measures that minimize cross-contamination are also effective in preventing clinical infection.<sup>11</sup>

It is not surprising to observe less mortality in noninfected patients than that predicted on the basis of a predictor generated from a large population of both infected and noninfected patients. It is interesting, however, that only the late group of noninfected patients had significantly less mortality than expected; the early group of noninfected patients did not. The most likely reason for this discrepancy of predicted mortality of 25% to 75% is the altered distribution of patients without infection in the late group (70% vs 42%), which increased the power of testing and made observation of a difference between observed and predicted mortalities statistically significant (Table 1, lower panel). In comparison of the entire cohorts, apparent lack of improvement in observed mortality over predicted mortality in noninfected early patients still rests on the 25% to 75% subset, which of course is diluted with the patients in the nonresponsive predicted mortality ranges outside 25% to 75%.

An alternative explanation of the reduced mortality of noninfected patients in the late but not the early period could be general improvement in overall patient care during that period.<sup>12</sup> We consider this unlikely because infection-unrelated care was the same in both cohorts, as was the 1:1 nurse-patient ratio in both intensive care units.

The incidence of bacteremia in the early group of patients in the present study was similar to that reported previously in burn patients from this unit.<sup>13</sup> It is conceivable that the drug-sensitive bacteria prevalent in the late period were more effectively controlled by topical burn wound therapy and that the perioperative antibiotics more readily eliminated those organisms from the systemic circulation. This might explain the remarkable reduction in the occurrence of bacteremia in the late group of patients. The difference in frequency of urinary tract infection between the two groups remains unexplained, although the use of catheters was similar in both cohorts.

The present investigation demonstrates that bacterial ecology, incidence of nosocomial infections, and mortality in burn patients were favorably influenced by changing the patient environment and implementing preventive measures. Although we were able to demonstrate that the reduction of infection in burn patients was closely associated with improvement in survival, lack of concurrent controls prohibits concluding that a causal relationship existed, although one is strongly suggested.

As anticipated, at either extreme of expected mortality, neither the presence nor the absence of infection exerted demonstrable influence on patient outcome. The patients in the midrange of probability of expected mortality appear to be responsive to therapeutic endeavors and should be selected as the reference population for future clinical studies of the impact of infection on mortality in burned patients.

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## Discussion

EDWIN A. DEITCH, MD, Shreveport, La: The authors' study is a logical extension of the work presented before this society last year by Dr McManus. In last year's study this group documented that patients who are treated in open wards are more likely to become cross-contaminated with pathogens that are more drug resistant and virulent than patients who are treated in isolation rooms. The assumption based on this study is that if the incidence of drug-resistant bacteria colonizing the wound can be reduced, perhaps the mortality rate would also be reduced. This year's study tests that assumption.

Dr Shirani has basically told us two things: first, that intensive care unit patients treated on an open ward get more infections than patients treated in individual rooms; and second, that by treating patients in individual rooms the mortality rate can be reduced.

Although this is logical and really is a very attractive hypothesis, there are a few points that need to be clarified before the conclusions can be accepted. First, in the mortality statistics used in the present study the controls were historical. It would have been possible (and still is possible) to statistically compare these groups directly rather than using historical controls.

Second, the prediction of mortality was based on only two variables, age and percent of burn. Other variables are important, such as extent of third-degree burn associated injuries and inhalation injury. Since some of these factors can be as important as the percent of burn and age, I wonder if you have compared the two groups to exclude difference in these confounding factors, as an explanation for the demonstrated differences in mortality.

As a corollary question, could you go through the cause of death of those patients who were not infected and died to see if the two groups were comparable, since the noninfection mortality rates were different between the two groups.

Last, I am really very puzzled by some of the findings in the study. First, since the incidence of drug-resistant bacteria colonizing the wound was reduced, why was the mortality rate of the patients who got infected so high? Additionally, the mortality was higher in the group that were put in individual rooms than the ward patients, why was that? Last, the pattern of infection that occurred was not one I would have expected in patients who were being successfully protected from contamination. I would have expected a reduction in burn wound sepsis and perhaps a reduction in pneumonias due to reduced colonization. Reduction in urinary tract infections and reduction in bacteremias are more associated with indwelling devices and may be more related to technique.

STANLEY LEVENSON, MD, Bronx, NY: I have enjoyed Dr Shirani's presentation. I wonder if he would give us as much detail as possible about the causes of death in those patients he described as noninfected.

DONALD E. FRY, MD, Cleveland: I am always interested in why isolation rooms may or may not reduce infection rates. Certainly the number of bacteria that are carried to the bedside are relatively

small compared with the total number of bacteria that the patient has endogenously, so I might expect isolation to affect the exposure to resistant organisms. I might not expect it to affect the frequency of infection.

I am curious whether isolation rooms serve as a reminder for our personnel to exercise overall better behavior, and as such it is the modification of behavior rather than isolation per se that makes the difference. If you really believe, then, that isolation makes the difference, I am wondering if you are willing to take the next quantum leap, and that is to do what Gerald Bodey has done with children who have leukemia, and that is to install laminar airflow to reduce airborne contaminants and to use oral erythromycin and neomycin in an attempt to sterilize the gastrointestinal tract of these patients next.

N. JOEL EHRENKRANZ, MD, Miami: Accepting the methodological problems that have been pointed out, I want to congratulate the authors on very important observations, and I would like to make a little link in the scenario that I hope they will agree with.

I think what we may be seeing is a problem in patient placement, and that the key factor is urinary tract infection. As pointed out a few years ago in an outbreak of urinary tract infections studied by Hennikens and others at the Miami Veterans Administration, patient placement can be critical. If there were two catheterized patients and one had a urinary tract infection, the other became infected relatively soon. I would say that maybe what is happening here is that by blocking that transmission, either urinary tract to urinary tract or urinary tract to gut colonization, you have prevented cross-infection.

You have opened the way for providing a scientific basis to what a great many people do on an empiric basis.

RICHARD P. WENZEL, MD, Charlottesville, Va: I have enjoyed this article because many of us are interested in this type of unit. However, there are a number of aspects of the presentation I don't understand, and in order to convince colleagues I think we need to get some more details.

Looking at the two groups and the mortality of 25% vs 23%, I find it hard to understand that there is a statistically significant difference, and I need some encouragement from the authors. On the other hand, what is surprising is that when we look at the bacteremia rate, that on the other hand was reduced 50%, from 20% down to 10%, and I would have thought that if infections matter we would have seen a much more significant reduction in the overall mortality.

We really don't know much about the environment. One aspect in terms of cross-infection would be whether similar opportunity existed, for example, once *Providencia* got into that particular new area, perhaps then it would spread just as much as it did in the old area; but apparently zero percent got there to begin with. The authors also didn't comment about the increase in *Staphylococcus aureus* infections that we are beginning to see.

Last, it is important for us to be assured that the nursing-patient ratios were the same in both groups. In fact, if they were quite different in the new group, it might not be the physical plant but the actual patient care that changed.

CARL W. WALTER, MD, Boston: I wonder whether the authors investigated the carrier rate among the personnel in these two contrasting units. I would warrant that, like other studies, the carrier rate in isolated rooms was about the same as the carrier rate in operating rooms, whereas in the previous open ward their carrier rate was probably three or four times that which they found in the isolated unit.

I think it is time we looked at the occupational hazard of the people who work in this kind of situation. It is much higher than we ever suspected. We never seem to follow up and do it. The data are lost in the employee care clinic and are never reported back.

DR SHIRANI: Dr Deitch, you asked why there was a reduced incidence of infection in patients treated in single rooms. We don't have any specific answer for that. As Dr Fry pointed out, it may be behavior modification. When people moved to the new unit, everyone was anxious about reducing the rate of infection, and they might have been more careful in preventing transmission of bacteria from patient to patient. The bacteria that were present on the old unit were mostly drug resistant. When we moved to the new unit, patients were brought in with bacteria that were mostly drug sensitive, and it is possible that the therapy that was in use and prophylactic antibiotics and perioperative antibiotics might have cleared some of those bacteria. We were not able to see bacteremia in those patients as often as we saw it in the other patients.

It should be no surprise that mortality in uninfected patients was lower. That is what we would all expect. We compared these patients with the predictor based on our experience with over 6,000 patients treated during the past 33 years. It takes into account all the infected and noninfected patients, patients with associated injuries, patients with inhalation injuries, and patients with extensive third-degree burns; so, it gives a pretty good prediction just based on age and burn size depending on the previous experience. That was the reason we compared these mortalities with the predictor rather than comparing the two groups together.

That partly answers Dr Wenzel's question, that he could not see the difference in mortality between the early and later groups. The differences lie between the predicted mortality and the observed mortality between the two groups. Comparisons were made between the predicted and the observed mortality.

Dr Levenson raised a very good question, why those people who were not infected died. We do not know why. One might speculate that if the physiologic and healing reserve for an individual is overwhelmed by injury, this somehow prevents ultimate compensation and death supervenes. Infection may be an "epiphenomenon" in that set of patients who would die anyway, explaining death without infection in some patients. Alternatively, it might have been possible that occult infections, possibly viral, contributed to death in some of those patients. We do not have the necessary data to address that. We have not analyzed the postmortem findings, as it would be more germane to try to find evidence for infection pre mortem and then assess its damage.

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