Pneumonia in Patients With Severe Burns*
A Classification According to the Concept of the Carrier State

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Objective: To establish baseline values of pneumonia incidence and mortality and to distinguish primary endogenous from secondary endogenous and exogenous pneumonias in a homogeneous patient population with severe burns.

Design: Cohort study.

Setting: A six-bed burn ICU.

Patients: All patients of ≥ 14 years admitted to the ICU between January 1995 and June 1996 with a total body surface area burn of ≥ 20%.

Intervention: Collection of data on surveillance samples from throat and rectum on admission and twice weekly afterward, and pneumonias during the ICU stay.

Measurements and results: Fifty-six patients fulfilled the criteria of the study. Mean age was 43 ± 19.8 years; total body surface area burn, 41 ± 18.2%; the area of full-thickness burn was 24 ± 17.7%. Forty-one patients required mechanical ventilation. Twenty-seven patients (48%) experienced 37 episodes of pneumonia. Twenty-one pneumonias were of primary endogenous development, i.e., caused by potential pathogens carried in the admission flora. There were 14 secondary endogenous and 2 exogenous infections caused by microorganisms acquired on the burn unit. Inhalation injury was identified in 26 patients. The pneumonia rate was two times higher in the subset of patients with inhalation injury compared with the group of patients without inhalation injury (p < 0.001). Overall mortality was 25%.

Conclusions: This study shows that pneumonia in burn patients is mainly an endogenous problem. Interventions that prevent the development of endogenous infections deserve prospective evaluation in patients with severe burns.

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Key words: anti-infective agents; burn units; burns; infection control; inhalation; mechanical ventilation; pneumonia

Abbreviations: CI = confidence interval; FTB = full-thickness burn; MRSA = methicillin-resistant Staphylococcus aureus; SDD = selective decontamination of the digestive tract

Infection, in particular pneumonia, is a major cause of morbidity and mortality in burn patients.1–4 Prospective studies conducted between 1992 and 1998 show infection rates of up to 50%, with a pneumonia rate of 65% in burn patients requiring mechanical ventilation.5–8 The expected increase in mortality owing to pneumonia has been estimated to be 25% in a retrospective cohort study.2

New insights obtained from critically ill patients requiring mechanical ventilation show that pneumonia can be classified according to three different types to implement specific prevention measures.9,10 Endogenous pneumonias are distinguished from pneumonias of exogenous development. A pneumonia is defined as an endogenous infection of the lower airways if the causative bacteria are present in the patient’s oropharyngeal or GI flora. The pneumonia is primary endogenous when the microorganisms are present in the ICU admission flora. A secondary endogenous pneumonia is defined as a pneumonia caused by microorganisms not carried by...
the patient on admission to the ICU but acquired later on the unit. The microorganisms associated with the ICU ecology are firstly acquired in the oropharynx, followed by carriage and overgrowth in the digestive tract. Subsequently, infection of the lower airways may occur. An exogenous pneumonia is a pneumonia caused by bacteria associated with the ICU ecology that are not carried by the patient in the oropharynx or GI flora. The causative microorganisms are directly introduced into the lower airways, e.g., via a tracheostomy, bypassing the oropharynx.11,12

Each of these three types of infection requires a different prophylactic intervention. Only systemic antibiotics prevent primary endogenous infections, whereas topical antibiotics have been shown to eradicate, if already present, or prevent carriage and subsequent secondary endogenous infections. A high level of hygiene is required to control exogenous infections. Finally, regular surveillance samples of throat and rectum are essential in monitoring the efficacy of the topical antibiotics and in distinguishing endogenous from exogenous infections. These four components—a short cycle of systemic antibiotics, oral nonabsorbable antibiotics, hygiene, and surveillance cultures—together form the protocol of a strategy termed selective decontamination of the digestive tract (SDD),13 which has been shown to significantly reduce morbidity and mortality in critically ill patients.14,15

A prospective cohort study in patients with severe burns was undertaken between January 1995 and December 1996 in the burn unit of the University Hospital of Getafe, Madrid, to establish the rates of pneumonia morbidity and to distinguish primary endogenous from secondary endogenous and exogenous pneumonias in a homogeneous patient population with severe burns.

**Materials and Methods**

**Patients**

All patients ≥ 14 years of age admitted to the burn unit between January 1995 and December 1996 and with a total body surface area burn of ≥ 20% were consecutively enrolled in the study. Exclusion criteria were immunosuppression, pregnancy, ICU length of stay < 5 days, and ICU admission > 48 h after burn trauma.

All patients were cared for in single-bed rooms with a negative pressure. They were resuscitated using the modified Parkland formula.16 Enteral nutrition was commenced within the 24 h of injury and gradually increased during the first 3 days. Nutritional requirements were empirically estimated according to Curreri et al.17 Excision and graft of the burn wound usually began within the first 5 days. Burn wounds were treated with closed dressings and daily application of silver sulfadiazine or iodine-povidone ointment.

**End Points**

I. Primary
A. Infection rates of pneumonias
B. Microorganisms involved in pneumonias
C. Classification of infections according to the carrier state

II. Secondary
A. Mortality rates

**Infection Control Methods**

The isolation practices implemented in the burn unit included hand washing before each patient contact, washing hands and changing gloves between sequences of care, and wearing gloves in case of contact with burn wound body substances.18

**Antibiotic Policy**

Systemic antibiotics, cefotaxime plus an aminoglycoside, were administered empirically when clinical signs of infection developed and were adjusted according to the microbiological results. Infections caused by Gram-positive bacteria were treated by monotherapy with a β-lactam. Burn patients with a Gram-negative infection received a combination of cefotaxime and an aminoglycoside. Cefotaxime was replaced by ceftazidime when the infection was caused by *Pseudomonas aeruginosa*.

**Microbiological Methods**

A surveillance set comprised throat and rectal swab taken on ICU admission and twice weekly afterward. All surveillance samples were processed according to a previously described method.19 Semiquantitative estimation of bacterial concentrations was made by grading growth density from the four-quadrant method combined with enhancement broth on a scale of 1+ to 5+, as follows: growth only in broth = 1+ (comparable to 1 to 10 cfu/mL), growth in the first quadrant of solid plate = 2+ (10<sup>3</sup> cfu/mL), in the second quadrant = 3+ (10<sup>4</sup> cfu/mL), in the third quadrant = 4+ (10<sup>5</sup> cfu/mL), and on the whole plate = 5+ (> 10<sup>6</sup> cfu/mL).

Diagnostic samples of tracheal aspirate were taken on clinical indication only and were processed using standard microbiological methods.

**Definitions**

Inhalation injury was suspected in patients with facial and neck injuries and in patients who suffered burns in an enclosed space. All suspected patients underwent bronchoscopy. The diagnosis of inhalation injury was made by demonstration of inflammatory changes in the respiratory tract such as mucosal erythema, edema, ulceration, or submucosal hemorrhages.2

Pneumonia was defined as the presence of new (or progressive) pulmonary infiltrates persisting for > 48 h on chest radiograph in addition to at least two of the following criteria: (1) temperature ≥ 38.5°C or hypothermia < 35.0°C; (2) leukocytosis ≥ 10,000/µL or leukopenia < 3,000/µL; and (3) isolation of potential pathogens in high concentration of ≥ 4+ using semi-quantitative culture from unprotected purulent tracheal aspirates.21

Pneumonias were classified11,12,22 as primary endogenous when they were caused by microorganisms that were already carried in the throat or gut on admission to the ICU, secondary endogenous when they were caused by microorganisms not carried on admission but acquired in the throat and gut later during the stay.
in the ICU, and exogenous when they were caused by microorganisms that were never present in throat and rectal swabs.

**Statistical Analysis**

Data are presented as mean (SD), median, range, differences, and relative risk with 95% confidence intervals (CIs). Comparison between groups was performed using Wilcoxon test or Fisher's Exact Test when appropriate. The severity of the burn trauma was estimated using the expected mortality scoring model of Smith et al.23

The study was approved by the Institutional Board for Clinical Research.

**RESULTS**

Fifty-six patients fulfilled the criteria for inclusion in the study. Table 1 shows the patient demographics. Mean age (± SD) was 43 ± 19.8 years, mean total burn area was 41 ± 18.2% of the total body surface, and the mean full-thickness burn (FTB) area was 24 ± 17.7% of the total body surface. Inhalation injury was identified in 26 patients (46%). Forty-one patients (73%) required mechanical ventilation for a median of 14 days. The observed mortality was 25% (14 patients). The expected mortality was 34% (95% CI, 27 to 42%). Patients died at a median of 17 days.

Twenty-seven patients (48%) experienced 37 episodes of pneumonia: 21 episodes (57%) were primary endogenous, 14 (38%) were secondary endogenous, and 2 (5%) were exogenous. The cumulative incidence of ventilator-associated pneumonia was 69% with a rate of 48.0 per 1,000 ventilation days. Nineteen patients with inhalation injury had 29 episodes of pneumonia: 16 primary endogenous and 13 secondary endogenous. The cumulative incidence of pneumonia was 73%, and the rate was 56.6 pneumonias per 1,000 ventilator days. The two patients with primary endogenous pneumonia caused by MRSA and Acinetobacter spp were referrals from other hospitals. Systemic antibiotics were given to treat primary endogenous pneumonia at a median of 3 days (range, 1 to 7 days) after ICU admission. There were a total of 14 secondary endogenous pneumonias caused by MRSA (10 cases), *P. aeruginosa* (3 cases), and *Enterobacter cloacae* (1 case). Of the 14 secondary endogenous pneumonias, 10 developed in patients who had had a previous episode of primary endogenous pneumonia. The median time of onset was 16 days after admission to the unit. The association between primary and secondary endogenous pneumonia was significant (p < 0.01). An exogenous pneumonia caused by *S. aureus* and *P. aeruginosa* was diagnosed in two patients.

The analysis of risk factors associated with mortality is shown in Table 3. The two factors that showed a statistically significant association with death were primary endogenous pneumonia (relative risk, 2.25; 95% CI, 1.21 to 4.17) and FTB area (difference, 14%; 95% CI, 3.3 to 24.3%). Other factors with differences close to statistical significance (p < 0.1) were age (difference, 14 years; 95% CI, −1.1 to 23.9 years) and total body burn area (difference, 8%; 95% CI, −3.3 to 19.0%).

**Table 1—Demographics**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean (SD)</th>
<th>Median</th>
<th>Range</th>
<th>Proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>43 (19.8)</td>
<td>41</td>
<td>15–88</td>
<td>26 (46)</td>
</tr>
<tr>
<td>Total burn area, %</td>
<td>41 (18.2)</td>
<td>38</td>
<td>20–85</td>
<td>41 (73)</td>
</tr>
<tr>
<td>FTB, %</td>
<td>24 (17.7)</td>
<td>20</td>
<td>0–85</td>
<td></td>
</tr>
<tr>
<td>Inhalation injury</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients requiring mechanical ventilation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days of mechanical ventilation</td>
<td>19 (13.6)</td>
<td>14</td>
<td>3–67</td>
<td></td>
</tr>
<tr>
<td>Length of stay, d (all patients)</td>
<td>28 (19.3)</td>
<td>23</td>
<td>6–91</td>
<td></td>
</tr>
<tr>
<td>Length of stay, d (survivors)</td>
<td>30 (18.0)</td>
<td>20.5</td>
<td>6–77</td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
<td></td>
<td>14 (25)</td>
</tr>
</tbody>
</table>

*Data are presented for 56 patients.
The five main findings emerging from this prospective trial in burns are the following: (1) practically all pneumonias (95%) were endogenous, both primary and secondary; (2) more than half of the burn patients requiring mechanical ventilation (57%) developed a primary endogenous pneumonia at a median of 3 days; (3) the pneumonia rate was two times higher in the group with inhalation injury compared with the group without inhalation injury; (4) all but two primary endogenous pneumonias were caused by community-acquired bacteria, including *S aureus*, *S pneumoniae*, and *H influenzae*; and (5) secondary endogenous pneumonias occurring at a median of 16 days were usually preceded by a primary endogenous pneumonia.

The burn trauma not only affects the skin but also the lower airways, in particular in patients with inhalation injury. Severely burned patients who require mechanical ventilation—even without inhalation injury—show high pneumonia rates because of serious immunodepression after the burn trauma.24

In our study, the pneumonia rate was 31.3 episodes per 1,000 ventilation days in the subset of patients who did not suffer inhalation injury. The mucosal damage caused by smoke inhalation further increases the risk of pneumonia.2

Aspiration of contaminated oropharyngeal secretions is the first step in the pathogenesis of lower airways infections. *S pneumoniae*, *H influenzae*, and *S aureus* are the classic community-acquired bacteria carried in the oropharynx of previously healthy individuals. They are the microorganisms involved in primary endogenous pneumonia. In more than half

**Table 2—Classification of 37 Pneumonia Episodes in 27 Severely Burned Patients Using the Criteria of the Carrier State***

<table>
<thead>
<tr>
<th>Digestive Tract Carrier State</th>
<th>Primary Endogenous ( (n = 21) )</th>
<th>Secondary Endogenous ( (n = 14) )</th>
<th>Exogenous ( (n = 2) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oropharynx</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>On ICU admission</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>S aureus</em> ( (n = 11) )</td>
<td>( S aureus \ (n = 11) )</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>S pneumoniae</em> ( (n = 6) )</td>
<td>( S pneumoniae \ (n = 6) )</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>H influenzae</em> ( (n = 6) )</td>
<td>( H influenzae \ (n = 6) )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRSA ( (n = 1) )</td>
<td>MRSA ( (n = 1) )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acinetobacter ( spp \ (n = 1) )</td>
<td>Acinetobacter ( spp \ (n = 1) )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acquired</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRSA ( (n = 10) )</td>
<td>MRSA ( (n = 10) )</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>P aeruginosa</em> ( (n = 2) )</td>
<td><em>P aeruginosa</em> ( (n = 3) )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gut</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>On ICU admission</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRSA ( (n = 1) )</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acinetobacter ( spp \ (n = 1) )</td>
<td>Acinetobacter ( spp \ (n = 1) )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acquired</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRSA ( (n = 6) )</td>
<td>MRSA ( (n = 6) )</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>P aeruginosa</em> ( (n = 2) )</td>
<td><em>P aeruginosa</em> ( (n = 1) )</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>E cloacae</em> ( (n = 1) )</td>
<td><em>E cloacae</em> ( (n = 1) )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No carriage</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Of 37 pneumonia episodes, 35 episodes (95%) were caused by microorganisms carried by the patients, supporting the endogenous pathogenesis of pneumonia in severely burned patients.

**Table 3—Univariate Analysis of Factors Associated With Mortality***

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Nonsurvivors ( (n = 14) )</th>
<th>Survivors ( (n = 42) )</th>
<th>Difference ( (95% \ CI) )</th>
<th>Relative Risk ( (95% \ CI) )</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>54 ± 24.2</td>
<td>40 ± 17.2</td>
<td>14 (−1.1 to 23.9)</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>Total burn area, %</td>
<td>47 ± 20.3</td>
<td>39 ± 17.2</td>
<td>8 (−3.3 to 19.0)</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>FTR, %</td>
<td>34 ± 21.0</td>
<td>20 ± 15.2</td>
<td>14 (3.5 to 24.3)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Inhalation injury</td>
<td>9 (64)</td>
<td>16 (40)</td>
<td>1.59 (0.93 to 2.71)</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td>Primary endogenous pneumonia</td>
<td>9 (64)</td>
<td>12 (29)</td>
<td>2.25 (1.21 to 4.17)</td>
<td>0.02</td>
<td></td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD or No. (%) unless otherwise indicated.

**Discussion**

The five main findings emerging from this prospective trial in burns are the following: (1) practically all pneumonias (95%) were endogenous, both primary and secondary; (2) more than half of the burn patients requiring mechanical ventilation (57%) developed a primary endogenous pneumonia at a median of 3 days; (3) the pneumonia rate was two times higher in the group with inhalation injury compared with the group without inhalation injury; (4) all but two primary endogenous pneumonias were caused by community-acquired bacteria, including *S aureus*, *S pneumoniae*, and *H influenzae*; and (5) secondary endogenous pneumonias occurring at a median of 16 days were usually preceded by a primary endogenous pneumonia.

Discussion...
of the burn patients, the first pneumonia was followed by a secondary endogenous pneumonia caused by nosocomial microorganisms, including MRSA and *P aeruginosa*. The observation that superinfections are practically always preceded by a first infection of the same internal organ was supported by the significant association between primary and secondary endogenous pneumonia.

All prospective studies on infection in burn patients use the traditional criteria for classifying both nosocomial infections and their causative microorganisms. The distinction between Gram-positive and Gram-negative microorganisms and a time cutoff are the traditional bases for distinguishing infections in burn patients. However, these criteria do not relate to the burn patient and may not be helpful for the prevention of infections in burn patients requiring intensive care. This prospective study distinguished community-acquired from hospital-acquired bacteria, rather than Gram-positive from Gram-negative microorganisms. Eight early pneumonias were caused by Gram-negative bacilli (*H influenzae* [n = 6], Acinetobacter spp [n = 1], and *P mirabilis* [n = 1]), whereas Gram-positive cocci, invariably MRSA, were responsible for 10 late pneumonias. The traditional distinction as to whether infections are nosocomial or not is primarily made by the time when signs and symptoms of infection start, *i.e.*, ≥ 72 h after admission to the burn unit. A total of nine pneumonias, invariably of primary endogenous development, would have been discarded if the 72-h cutoff had been applied to the study population. Moreover, a time cutoff is used on the assumption that early infections, mainly primary endogenous pneumonia, cannot be prevented in intensive care facilities. This concept contrasts with the beneficial effects of SDD, which comprises early administration of parenteral antibiotics combined with oral nonabsorbable antimicrobials in critically ill patients.

The classification used in this study is based on the carrier state detected by surveillance samples of the throat or gut. That approach allows the distinction between infections caused by potential pathogens brought into the burn unit by the patient (primary endogenous) and infections caused by microorganisms related to the burn unit (secondary endogenous and exogenous). Primary endogenous pneumonias (57%) cannot be controlled or prevented by the traditionally recommended measures of hand washing and isolation. Only secondary endogenous (38%) and exogenous (5%) pneumonias are to be considered true nosocomial infections caused by breaches of hygiene. Exogenous infections were remarkably uncommon in this study. The observation that 95% of microorganisms, including MRSA, were first acquired and carried in the throat and gut before infecting lower airways is of utmost importance. The mainly endogenous pathogenesis of pneumonia in patients with severe burns suggests that prophylactic SDD aiming at the eradication, if initially present, and at the prevention of oropharyngeal and GI carriage of potential pathogens may be effective in controlling pneumonias in those patients.

The observations made from this cohort study are in line with a previous study that provided low-level evidence suggesting that burn patients may benefit from SDD in terms of both morbidity and mortality. A randomized controlled trial in burn patients is underway, to appropriately test the hypothesis that SDD may reduce morbidity and mortality in patients with severe burns.

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