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Endotracheal Intubation: The Role of Sterility

NORA CHEUNG,[1] GERARD BETRO,[1] GINA LUCKIANOW,[1]
LENA NAPOLITANO,[2] and LEWIS J. KAPLAN[1]

ABSTRACT

Background: **There is a paucity of data regarding whether sterile handling of endotracheal tubes (ETTs) impacts the incidence and prevalence of pneumonia in the emergency, urgent, or elective clinical scenarios. Intensive care units employ infection control and reduction schemes to reduce pneumonia rates.**

Methods: **A MEDLINE search of the English-language literature for the last 30 years was performed using the keywords "endotracheal intubation," "intubation," "pneumonia," "sinusitis," "tracheobronchitis," "nosocomial infection," and "infection." Data were limited to those papers addressing the role of sterile handling or passage of ETTs, infection with antibiotic-resistant micro-organisms, antibiotic prophylaxis, and the role of virulence determinants in supporting invasive infection. Also, a convenience sample of a single author's patients requiring tracheal intubation was undertaken. Data were acquired on tube handling, success of insertion, and subsequent occurrence of pneumonia.**

Results: **Virtually no data exist on the impact of sterile ETT handling, but unsterile manipulation of the ETT prior to insertion is common (112 of 154 intubation events). Within the limited patient sample, no conclusions may be drawn regarding the impact of unsterile handling on pneumonia rates, although sinusitis after nasotracheal intubation clearly increases the incidence of pneumonia. Biofilm generation as a facilitator of bacterial colonization of artificial airway surfaces is a ubiquitous virulence determinant that is not ameliorated by antibiotic administration.**

Conclusions: **Unsterile ETT handling and insertion techniques are not clearly associated with pneumonia induction, but physiologically sound approaches that retard biofilm production may decrease pneumonia rates.**

THE HUMAN OROPHARYNX is home to a multitude of different bacteria and fungi [1]. In sharp contradistinction, the human trachea and bronchial tree normally harbor no bacteria. Nasal or orotracheal intubation places a plastic (usually) foreign body through the oropharynx, thence between and below the true vocal cords, ideally to rest in the proximal tracheobronchial tree. Invariably, the initially sterile endotracheal tube (ETT) becomes contaminated with the patient's resident bacteria during its nasopharyngeal or oropharyngeal passage to the proximal trachea.

Our current medical climate embraces infec-

[1]Department of Surgery, Section of Trauma, Surgical Critical Care and Surgical Emergencies, Yale University School of Medicine, New Haven, Connecticut.
[2]Department of Surgery, University of Michigan Health System, Ann Arbor, Michigan.

tion-reduction measures spanning central venous catheter insertion [2], ventilator-associated pneumonia (VAP) [3], and appropriate surgical antibiotic prophylaxis [4]. These initiatives raise a number of questions regarding endotracheal intubation: (1) How does such intubation fit into the infection-reduction scheme? (2) What is the role of sterile handling of an ETT prior to oropharyngeal passage? and (3) Does endotracheal intubation merit antibiotic prophylaxis?

INFECTION-REDUCTION PROTOCOLS

Endotracheal intubation occurs in one of three settings: Emergency, urgent, or elective. Moreover, because some patients require long-term endotracheal intubation, a fourth setting may be recognized: Chronic intubation, most commonly with a tracheostomy tube. This discussion addresses the first three settings, as patients with a chronic need for intubation represent a different population with regard to airway violation, colonization, and infection risk [5]. It is increasingly clear that tracheal intubation confers an additive risk with regard to hospital-acquired pneumonia (HAP) as well as a special subset of that entity—VAP [6]. Moreover, there is an important influence of underlying disease processes and non-respiratory system intervention, as HAP rates are markedly higher in surgical than in medical ICUs [7].

Clearly, tracheal intubation is unavoidable in emergency situations such as cardiac arrest (in persons desiring to be resuscitated) and after injury leading to hemodynamic instability. Tracheal intubation frequently is unavoidable in the urgent situation as well. However, many of these patients may be salvaged using non-invasive ventilator techniques such as bilevel positive airway pressure (BiPAP) or negative-pressure ventilation [8]. Non-invasive ventilatory techniques carry a lower risk of VAP than does ventilatory support via an indwelling ETT [9]. Thus, avoiding tracheal instrumentation when possible supports infection reduction measures. Nonetheless, this posture is frequently irrelevant clinically, as many patients (especially children) presenting to an emergency department or an intensive care unit require life-saving tracheal access. The exigencies of emergency intubation may impact ideal tube handling and placement. Therefore, these subsets of patients probably will not be impacted by mechanical recommendations to reduce endotracheal intubation-associated contamination–colonization–infection.

The patient population undergoing elective intubation, on the other hand, is a prime target for focused intervention to reduce the likelihood of mechanical transfer of bacteria from the oropharynx to the tracheobronchial tree and the size of any inoculum. It is intuitive that an unobstructed view of the vocal cords will facilitate passage of an ETT through those cords with minimal contact with oropharyngeal structures. Such maneuvers will minimize the density of adherent bacteria carried inadvertently into the lower airway by an orally placed ETT. No such maneuvering is possible for nasally placed tubes, as they necessarily traverse the nasal and oral passages in intimate contact with mucosal surfaces. To date, there are few data on the effect of sterile passage of oral ETTs on subsequent rates of tracheobronchitis or pneumonia. The extant data indicate that oropharyngeal preparation with a topical solution such as povidone–iodine reduces the bacterial recovery rates from ETTs and the posterior pharynx in patients undergoing short-term tracheal intubation [10].

Regardless, there are parallels in other arenas that support the paradigm of sterile passage of ETTs. Operating room procedures are, ideally, conducted in a sterile fashion. Clearly, head and neck procedures such as sinus surgery, transsphenoidal hypophysectomy, and tracheostomy all traverse non-sterile environments. Early work by Harvey Cushing, operating in a minimal-to-no antibiotic era, achieved infection rates below 2% after transsphenoidal surgery. How do we reconcile our abiding commitment to surgical field sterility with low infection rates operating through contaminated spaces, and does that reconciliation relate to endotracheal intubation? The answer lies in host defenses.

First, one must recognize that no operation

is completely sterile. Second, operative field and patient preparation reduce surface bacteria and minimize entry of bacteria into sterile tissue planes. Third, antimicrobials serve as an adjunct to host defense in handling the bacterial inoculum that invariably results from incision and tissue handling; endogenous humoral and cellular defenses, including the important Toll-like receptor complexes, shoulder the burden of dealing with bacterial contamination to prevent invasion [11]. These observations relate to endotracheal intubation, as it must be recognized that optimal ETT placement is a clean or clean-contaminated technique, not a sterile procedure. In the majority of cases, host defenses should be able to thwart a bacterial inoculum in the tracheobronchial tree. It is intuitive, although scientific data are absent, that because it is the patient's own flora that is transmitted in the elective intubation scenario, host defenses should already recognize those bacteria, respond readily to their surface antigens, and eliminate them rapidly from the normally sterile tracheobronchial tree. If this hypothesis is correct, then the corollary should also be true: Foreign organisms present a more difficult challenge to host defenses than does the native flora. This idea may have important implications for ETT handling prior to insertion.

ENDOTRACHEAL TUBE HANDLING

Endotracheal tubes arrive in a sterile package despite their intended passage through the heavily colonized human oropharynx. Of what value, then, is the sterile packaging? The value is more theoretical than proved in that there is no study of any kind that addresses sterile handling of ETTs prior to placement. Sterile processing gives the clinician a tube devoid of non-resident bacteria, impacting the bacterial inoculum presented to the patient's tracheobronchial tree. Such a scheme may be important in the immunocompromised host whose defenses are impaired or functionally absent. Instead, there is a wealth of accumulated clinical wisdom justifying non-sterile handling of ETTs in the field by emergency medical services personnel, as well as by the emergency department, operating room, intensive care unit, and general ward. Further buttressing this observation is the absence of deleterious outcomes vis-à-vis infection with short-term nasally placed ETTs although it is clear that trans-nasal airway intubation increases the rate of tracheobronchitis and subsequent pneumonia [12].

Nonetheless, it makes sense to avoid introducing, not only non-resident bacteria, but particularly nosocomial single- or multi-drug-resistant bacteria into a patient's tracheobronchial tree. A multitude of pathogens may survive on surfaces with and sometimes without moisture, to thrive when introduced into a supportive environment [13]. Such pathogens include *Clostridium difficile* spores, *Acinetobacter* spp., *Pseudomonas* spp., vancomycin-resistant *Enterococcus* spp. (VRE), and a number of viruses and fungi [14]. Gram-negative pathogens with genetic wiring for extended-spectrum β-lactamase (ESBL) production may be grouped conveniently under the acronym SPACE (*Serratia*, *Pseudomonas/Proteus*, *Acinetobacter*, *Citrobacter*, and *Enterobacter*) [15–18]. Other pathogens may acquire plasmids for multi-drug resistance (i.e., VRE). Introducing these pathogens from the environment may be disastrous for an already critically ill patient whose immune defenses are inadequate and whose original flora has been altered by concomitant antibiotic therapy.

That non-sterile ETT handling is common is underscored by a series of convenience-sampled observations in consecutive patients requiring endotracheal intubation over the last nine months in the clinical practice of one of the authors (LJK). The observations derive from 154 operations (42 emergency, 112 elective) that necessitated endotracheal intubation and were observed directly by that author. In all 154, the sterile ETT was cannulated with a non-sterile stylet. The data on ETT handling and intubation success are displayed in Figure 1. Figure 2 depicts the breakdown of pneumonia according to the nature of the need for intubation (elective vs. emergency). Because of the small numbers, the significance of the pneumonias is not clearly related to the method of ETT handling.

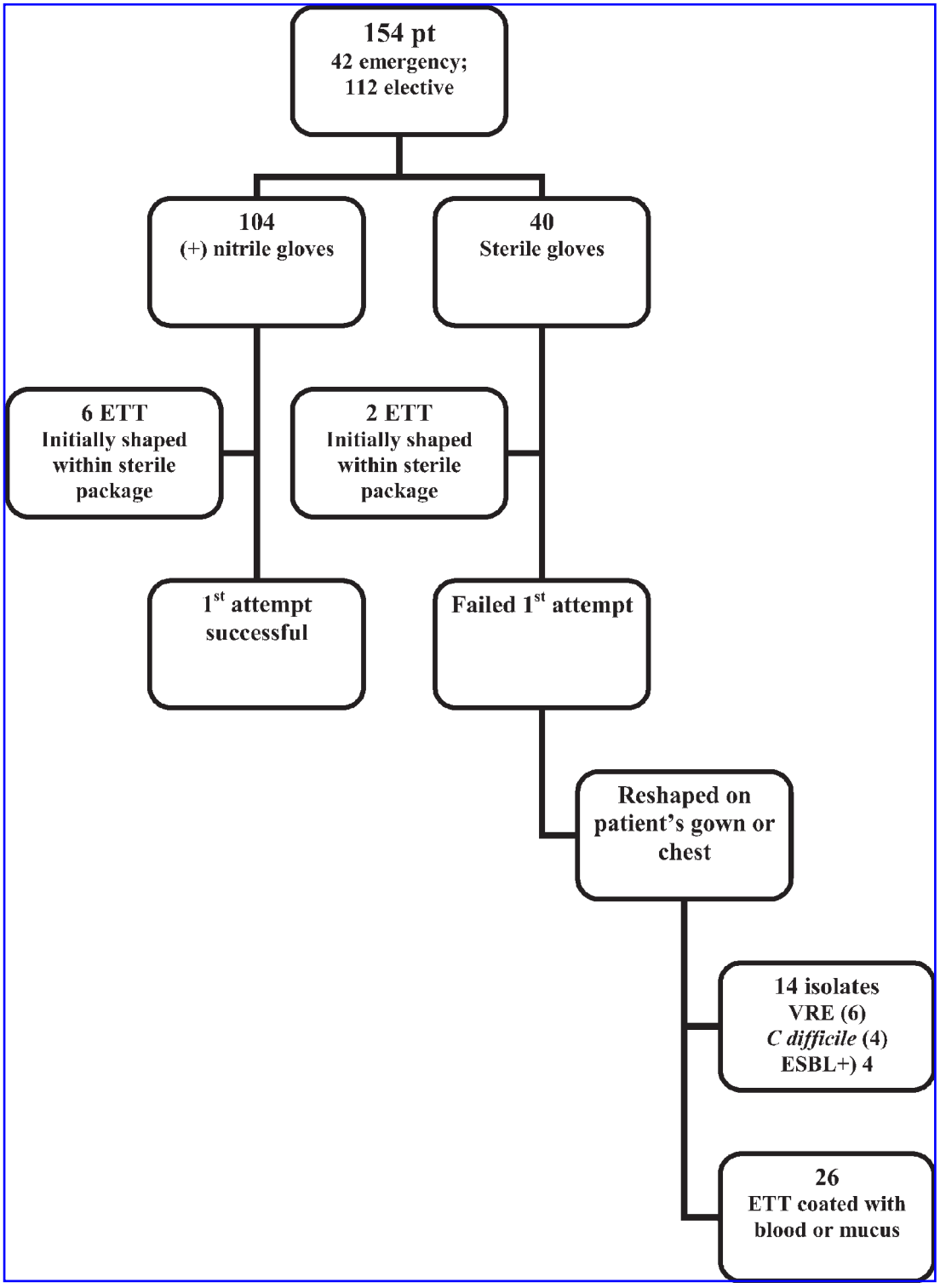

FIG. 1. Depiction of outcomes of 154 patients by urgency of intubation and endotracheal tube handling. (+) nitrile gloves = tube handling with non-sterile nitrile gloves used to manipulate medications, move patient, or touch other non-sterile surfaces; VRE = vancomycin-resistant *Enterococcus faecium* derived from blood or body cavity other than urinary tract or open wounds; *C. difficile* = *Clostridium difficile* colitis; ESBL+ = extended-spectrum β-lactamase-producing gram-negative bacillus infection; derived from pulmonary source in all instances.

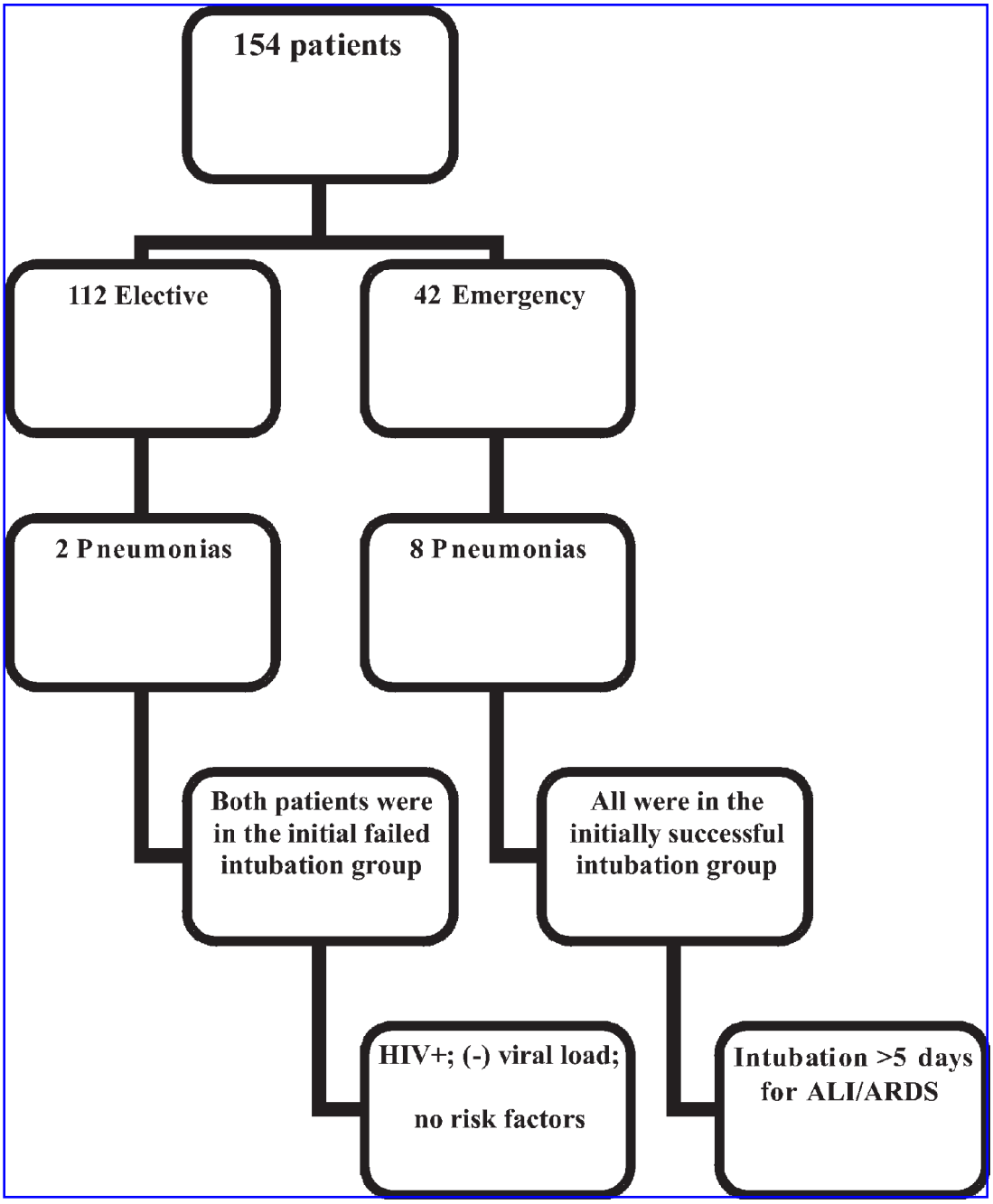

FIG. 2. Classification of patients by urgency of intubation and subsequent identification of pneumonia. HIV+; (−) viral load = infected with human immunodeficiency virus but without detectable serum titer; ALI/ARDS = acute lung injury/acute respiratory distress syndrome.

ANTIBIOTIC PROPHYLAXIS OF ENDOTRACHEAL INTUBATION

To date, no study supports prophylactic systemic antibiotics for endotracheal intubation. In fact, whereas many studies identify a higher risk of HAP and VAP with prolonged intubation, no study supports antibiotic administration to minimize that risk. Instead, mechanical measures such as head-of-bed elevation, chlorhexidine oral cleansing, and active weaning are standards of care [19]. Numerous studies document an adverse impact of antibiotic prophylaxis where none is needed or with

overly broad-spectrum agents [20,21]. Such deleterious effects include prolonged intensive care unit and hospital stays, a higher incidence of catheter-related infections, and promotion of resistant pathogens, including fungi. Most strongly associated with selection of resistant pathogens are third-generation cephalosporins and the fluoroquinolones—"collateral damage" from inappropriate antibiotic prescription practices [22–24]. Therefore, there currently is no role for systemic antibiotic prophylaxis of endotracheal intubation despite knowledge that the resident and non-resident bacteria are inadvertently but regularly inoculated into the normally sterile tracheobronchial tree. However, the reader should be aware that no study has segregated those patients with impaired host defenses from those without, nor assessed endotracheal intubation with regard to ETT handling and insertion technique.

Instead, there is a growing body of evidence that local antimicrobial control measures may be effective in reducing the bacterial burden of the tracheobronchial tree. Novel advances in tube construction and coating are being tested [25]. The combination of gentian violet and chlorhexidine (gendine) in a solution that may be applied to either ETTs or urinary catheters provides one means of preparing such devices for long-term placement [26]. Gendine provides three weeks of antibacterial activity against bronchoalveolar lavage fluid containing methicillin-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa*, and treated urinary catheters maintained potency against urine containing *Escherichia coli* for eight weeks. A provocative study in dogs comparing silver hydrogel-coated endotracheal tubes with untreated endotracheal tubes identified delayed appearance of aerobic bacteria in the endotracheal tube after a buccal *P. aeruginosa* challenge [27]. Furthermore, in dogs intubated with the coated tubes, there were decreases in the total bacterial burden in the lungs and in histologic evidence of inflammation (e.g., hyperemia, edema, cellular infiltration, and bacteria). A related study in sheep extended the observations to a smaller bacterial burden when ETTs coated with silver sulfadiazine and chlorhexidine were included in the ventilator circuit [28]. A recent study in human beings documented decreased density of bacteria on silver-coated ETTs, suggesting a potential role for silver ions in diminishing the bacterial burden on the interior of endotracheal catheters [29].

Of particular importance, silver ions may impact the biofilm that forms on the interior of endotracheal tubes. Biofilm formation has been implicated as an important step in the progression of bacterial airway colonization to invasive infection. Normal respiratory mucosa is rich in antimicrobial proteins and polypeptides that retard biofilm growth [30]. In an analogous manner, silver ions may well serve as an antibiofilm therapeutic agent. Biofilm production is a species-specific virulence determinant linked to genetic diversity [31]. Neuraminidase is produced by a host of respiratory pathogens and functions as a virulence determinant as well. Neuraminidase cleaves sialic acid residues from respiratory epithelium and uncovers bacterial adhesion targets. Strains of *Pseudomonas* whose ability to generate neuraminidase has been deleted genetically are unable to establish an invasive infection after direct inoculation into a murine respiratory system [31]. Importantly, diminished neuraminidase production also correlates with decreased biofilm generation. The clinical relevance of biofilm generation extends to nasogastric tubes (NGTs) in that there is a relation among NGT biofilm, aspiration pneumonia, and antibiotic resistance [32]. Biofilm was noted to develop on 60% of NGTs within a single day; therefore, prophylactic measures to retard biofilm genesis may be crucial in reducing nosocomial infection.

CONCLUSIONS

There is a paucity of data about sterile handling of ETTs for orotracheal intubation. It is likely that in order to detect a benefit from sterile handling, patients requiring intubation will need to be evaluated in two populations: Those who have not recently required a tracheal device, and those with an indwelling device or a recently removed device. The differences between these groups are likely related to different flora stemming from the location within a

hospital as well as concomitant antibiotic therapy. At present, limiting the introduction of non-resident flora from the environment into a patient's trachea remains grounded in sound physiology and microbiology. Sterile handling of the ETT helps maximize the success of the patient's native immune system by reducing the bacterial burden delivered to the tracheal mucosa. Future clinical trials will determine the value of ETT coating with an antiseptic agent to further reduce bacterial colonization and subsequent infection of the tracheobronchial tree.

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Address reprint requests to:
Dr. Lewis J. Kaplan
Section of Trauma, Surgical Critical Care and Surgical Emergencies
Department of Surgery
Yale University School of Medicine
330 Cedar St., BB-310
New Haven, CT 06518

E-mail: Lewis.Kaplan@yale.edu