Prevention of Infections Associated With Combat-Related Thoracic and Abdominal Cavity Injuries

AQ: 1

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Abstract: Trauma-associated injuries of the thorax and abdomen account for the majority of combat trauma-associated deaths, and infectious complications are common in those who survive the initial injury. This review focuses on the initial surgical and medical management of torso injuries intended to diminish the occurrence of infection. The evidence for recommendations is drawn from published military and civilian data in case reports, clinical trials, meta-analyses, and previously published guidelines, in the interval since publication of the 2008 guidelines. The emphasis of these recommendations is on actions that can be taken in the forward-deployed setting within hours to days of injury. This evidence-based medicine review was produced to support the *Guidelines for the Prevention of Infections Associated With Combat-Related Injuries: 2011 Update* contained in this supplement of *Journal of Trauma*.

Key Words: Combat, Trauma, Thorax, Abdomen, Infection, Prevention.

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The ominous nature of penetrating thoracic or abdominal wounds was recognized by ancient physicians, who observed that even those who survived the initial injuries were likely to succumb if infection ensued. The higher velocity penetrating thoracoabdominal injuries of modern warfare were initially distinguished by such high mortality rates that US Civil War patients with these injuries were often treated expectantly.[1] Even now, combat injuries to the chest and abdomen, although not as frequent as extremity injuries, are more commonly serious or fatal and more frequently associated with infectious complications than other sites of injury.[2–4]

Among 486 autopsies from Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF, in Afghanistan), 83% of deaths were from penetrating injury and 50% of deaths were attributed to truncal hemorrhage (includes thorax and abdomen), making it the leading cause of death.[4] Another study looking at the cause of death among 82 US Special Operations Forces in Iraq revealed that truncal hemorrhage accounted for 47% of the mortalities.[5]

Management of thoracoabdominal wounds has evolved along with the development of more lethal weaponry and more effective protective equipment. The use of body armor in OIF/OEF, and a shift from bullet wounds to blast injuries from improvised explosive devices (IEDs) have presented new challenges for these treating potentially massive injuries.[6–8] We focus on initial management of chest and abdominal wounds to prevent infection. The data reviewed places emphasis on combat-related studies and case series, especially those from 2007 through 2010 (since the last review).[9]

METHODS

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A Medline search using PubMed from the US National Library of Medicine National Institutes of Health was performed using the key words "abdominal," "thoracic," "military," "combat," "infection," "prevention," "empyema," "hemothorax," "thoracostomy," "irrigation," "antimicrobial," "culture," "bacterial," "wound infection," "splenectomy," "immunization," "sepsis," "meningococcus," "pneumococcus," and "hemophilus" with an emphasis on June 2007 through January 1, 2011. We also crossed referenced published bibliographies for additional manuscripts. In addition, we analyzed ongoing research projects with data published in abstract form or preliminary draft manuscripts for inclusion in the guidelines.

THORACIC WOUNDS

Chest trauma is the second most common cause of traumatic death in the United States (after head trauma) and accounts for approximately 20% of these deaths.[10] Penetrating chest wounds, especially when associated with abdominal injury or esophageal perforation, have been associated with high mortality rates.[2] Borden,[11] in a presentation to the Association of Military Surgeons in 1900, discussed the increased mortality associated with penetrating thoracic wounds caused by high velocity and large caliber rounds

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versus those associated with low velocity and small caliber rounds. A similar comparison exists today between the generally low velocity stab and small caliber gunshot wounds to the chest described in the civilian sector versus the large caliber, high velocity penetrating injuries, and high energy blast injuries experienced in the current military experience. Propper et al.,[12] in a recent review of the data from the US Joint Theater Trauma Registry (JTTR) from Iraq and Afghanistan, revealed that among 33,755 casualties, thoracic injuries were experienced by only 4.9%. This is in contrast to data from Vietnam where 20% of hospital admissions were for thoracic wounds.[13] The OIF/OEF chest wounds are notable for fewer penetrating truncal injuries (40%) and more blast injuries (46%); a contrast from the predominance of bullet and shrapnel penetrating injuries in previous conflicts. The Spanish Army Hospital in Afghanistan noted that 17% of ICU admissions were due to thoracic injuries and that thoracic blast injuries were more likely to require ICU admission than wounds from firearms.[14] In OIF/OEF, lung contusion is the most prevalent thoracic injury, experienced in 32% of cases, with traumatic pneumo- or hemothorax experienced in 19% (Table 1).[12]

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The increase in blast injuries to the chest may explain the significant increase in the mortality associated with thoracic wounds in OIF/OEF (12%) versus Vietnam (3%).[12,13] Although body armor prevents most penetrating thoracic injuries, it does not diminish high energy blast effects. A British study of IED injuries among UK and US forces in Iraq and Afghanistan determined that only 10% of those injured by IEDs suffered torso wounds and a US study found that 80% of thoracic wounds were caused by explosions.[7,15,16]

TABLE 1. Breakdown of 1,660 Thoracic Injuries Sustained in OIF/OEF (Modified From *Ann Thorac Surg.* 2010;89:1032–1036)

Diagnosis	N (%)
Lung contusion	518 (31.8)
Traumatic pneumothorax/hemithorax	316 (19.4)
Rib fracture	215 (13.2)
Diaphragm injury	123 (7.5)
Open chest wound	110 (6.7)
Lung laceration	91 (5.6)
Innominate/subclavian injury	43 (2.6)
Other open thoracic injury	36 (2.2)
Other closed thoracic injury	22 (1.3)
Sternum fracture	22 (1.3)
Intercostal/mammary artery injury	22 (1.3)
Heart laceration	21 (1.3)
Larynx/trachea fracture	19 (1.2)
Esophageal injury	17 (1.0)
Open tracheal wound	12 (0.7)
Flail chest	12 (0.7)
Thoracic vein injury	7 (0.4)
Pharyngeal wound	6 (0.4)
Pulmonary vein injury	4 (0.2)
Vena cava injury	4 (0.2)

Regardless of the etiology of the penetrating wound to the chest, the need to evacuate debris and clot and close open wounds to prevent infection has been a standard practice for over a century, as development of infection was frequently associated with death if a patient survived the initial trauma.[17] The role for postinjury antimicrobials and the duration of their administration in the management of thoracic injuries and thoracostomy has been controversial throughout the antimicrobial era.[18,19]

Prevention of Infection in Traumatic Thoracic Wounds

Famous Second World War surgeon Major Thomas Burford, in his treatise on posttraumatic empyema opines, "Of all the tragic sequelae of war, few are more distressing than the problems of those whose injuries result in chronic intrapleural sepsis. These unfortunates are inevitably found in large numbers through the postbellum years either doggedly submitting to one major operative procedure after another, or resignedly suppurating through a shortened life-span of chronic invalidism."[20]

Prompt surgical intervention with debridement and evacuation of hemothorax combined with appropriate use of antimicrobials has significantly reduced the morbidity and mortality associated with combat-associated chest trauma from 63% in the Civil War to less than 5% in the last 50 years.[1,12,21]

Tube thoracostomy, video-assisted thorascopic surgery, or thoracotomy is used to reexpand the lung and drain fluid, debris, and blood from the chest. Blood accumulating in the pleural space, particularly if a large volume, will form a clot. Retained clot (residual hemothorax), if not evacuated, will organize and adhere to the lung and pleura. Retained hemothorax is difficult to remove, forms a nidus for infection and fibrosis, and is the predominant risk factor for infection after thoracic trauma.[22,23]The incidence of empyema in chest wounds has, in most studies, been higher in combat-related injuries than in civilian, peacetime injuries.[18]

Empyema, although more common after penetrating chest injuries than after blunt chest trauma, may occur with either mechanism of injury (or even in the absence of chest trauma). Some etiologies of empyema are summarized in Table 2.[18,24] The incidence of posttraumatic empyema after chest injuries varies from 2% to 25%, but in most recent series is less than 5%.[19,24–28] Mandal et al.[27] reviewed 5,474 trauma patients (4,584 with penetrating trauma and 890 with

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TABLE 2. Etiologies of Empyema After Chest Trauma[18,24]

Direct infection from the penetrating injury and debris in the pleural cavity
Iatrogenic introduction during the performance of thoracostomy
Diaphragmatic disruption and intra-abdominal wound contamination
Secondary infection of undrained or partially drained hemothoraces
Hematogenous spread from infection outside the chest
Development of a parapneumonic empyema from a posttraumatic pneumonia
Pulmonary contusion

blunt injuries) who required tube thoracostomy in Los Angeles over a 24-year period. Among the patients with isolated thoracic trauma, only 1.6% developed posttraumatic empyema and the only significant associated risk factor was retained hemothorax. In a retrospective study of 71 patients who developed empyema (of 2,261 trauma patients with thoracostomy), factors associated with increased risk of empyema included longer duration of thoracostomy, length of ICU stay, presence of contusion, and need for exploratory laparotomy. Retained hemothorax was associated with an odds ratio of 5.5 and was the greatest risk factor observed for development of empyema.[25] Approximately all studies have demonstrated that penetrating chest wounds are more frequently associated with empyema than blunt trauma.

A trauma patient with a pneumothorax or hemothorax requiring tube thoracostomy should have the procedure performed as soon as it is possible to safely do so. In combat settings, medics and corpsmen responding to an injured troop in the field may not have adequate training to perform tube thoracostomy. In the civilian setting, mobile trauma teams have increasingly included a provider with tube thoracostomy training, so it can be performed in the field if the patient is in extremis. In the noncombat literature, there has been considerable controversy regarding the setting and appropriate level of training for a provider to perform tube thoracostomy. Some studies have demonstrated increased complication rates, especially residual hemothorax or empyema, when chest tubes have been placed by providers other than surgeons.[29] Other studies have concluded, there is little difference in outcome with different providers.[30,31] Regardless of who performs tube thoracostomy, it is important to reassess for adequacy of drainage of hemothorax (and possible migration of the tube during transport of the patient) as early evacuation of residual clot is important to diminish risk of developing an empyema.[32]

Postinjury Antimicrobials

Rationale

The role of postinjury antimicrobials in chest trauma to prevent empyema and, to a lesser degree, pneumonia, has remained controversial for decades.[33] As noted previously, in most series the incidence of posttraumatic thoracic infection is low, making significant differences in infection rates between groups administered or not administered postinjury antimicrobials difficult to determine. Individual randomized controlled trials have been underpowered and meta-analyses have reached contradictory conclusions. Overall, eight studies favored the recommendation for postinjury antimicrobials,[26,34–38] contrasting with three not supporting routine use.[27,33,39,40] The meta-analyses have struggled with which of the numerous studies to include due to differences in the choice, dosage, and duration of antimicrobials used and consideration of pneumonia versus empyema (should empyema be considered separately from concomitant pneumonia).[19,33,41] Most authors have concluded that another randomized controlled trial is required to definitively address the issue, but approximately 2,500 patients would be needed to power such study properly.

In 2000, the Eastern Association for the Surgery of Trauma (EAST) guidelines concluded, there were insufficient data to support the use of prophylactic antibiotics for tube thoracostomy as the standard of care or to suggest they reduce the incidence of empyema, but did recommend prophylactic use of a first-generation cephalosporin to reduce the incidence of pneumonia, recommendations that only increased the controversy.[18,42] Guidelines from the British Thoracic Society in 2010 recommended consideration of prophylactic antibiotics in trauma, especially with penetrating chest injuries.[43]

Antibiotic selection

Recommendations for postinjury antimicrobial therapy are to prevent early infection and sepsis, not for the empirical treatment of established infections after chest trauma. The majority of wounds, especially thoracic wounds, are not contaminated with resistant organisms at the time of injury.[44] Most of the organisms isolated have been staphylococcal and streptococcal species.[24,45,46] Although a wide range of organisms have been reported in association with posttraumatic empyema and reports of multidrug-resistant (MDR) gram-negative bacteria and methicillin-resistant *Staphylococcus aureus* have appeared after combat injury, these have been primarily isolated from patients days or weeks after their injury with a sufficient interval of time for acquisition of resistant bacteria from the healthcare system.[28] Empiric antimicrobial coverage for these resistant organisms at the time of injury is therefore not recommended.

Randomized control trials have used a wide range of antimicrobial agents, including amoxicillin, doxycycline, clindamycin, and cephalosporins, at various dosing interval and duration. Although there is not clear evidence that one regimen is preferable to another, cefazolin has been the antimicrobial most frequently studied. Even in a study that markedly under-dosed cefazolin (500 mg intravenously every 8 hours), there was a significant decrease in early pneumonia but not empyema.[26] Cefazolin is also inexpensive, widely available, and is recommended in our guidelines for postinjury treatment for injuries at other sites.[47] Use of a higher dose, 2 g every 6 hours to 8 hours is emphasized, especially in patients who have prolonged surgical procedures and/or significant blood loss. Dosage for children less than 40 kg should be 20 mg/kg to 30 mg/kg IV every 6 hours to 8 hours (up to a maximum of 100 mg/kg/d). Chest wounds with evidence of esophageal perforation have a much wider variety of bacterial contamination that should prompt use of the same antibiotic recommendations as in abdominal wounds (see below).

Duration

Duration of postinjury antimicrobial coverage for surgery, regardless of the site, has remained controversial but prolonged courses, even after severe trauma, are increasingly recognized for their association with MDR organisms if infection develops.[48] Postinjury antimicrobial regimens in chest trauma have ranged from a single dose before tube thoracostomy to continuation of antibiotics for the duration of chest tube drainage. Recommendations from the National Surgical Infection Project for patients undergoing routine

preoperative thoracic surgical procedures (not related to trauma) recommend 24 hours of therapy with cefazolin or cefuroxime.[49] There are no randomized controlled trials assessing the duration of antimicrobials specifically for thoracic trauma without tube thoracostomy. Velmahos et al. retrospectively assessed 250 severely traumatized patients, including 74% who underwent a thoracic or abdominal surgical procedure. Patients received either 1 day of a single antimicrobial or one or more antimicrobials for more than 24 hours, typically 3 days to 5 days. The only significant difference in outcome between the groups was the increased incidence of antimicrobial-resistant bacteria cultured from 50% of those with longer regimens versus 35% of those on short-term regimens.[46] There are no data in trauma to suggest any added advantage to longer durations of postinjury antimicrobials beyond 1 day and a single dose preprocedure is often advocated.

Redosing of antimicrobials in prolonged surgery or in cases of extensive blood loss

To remain effective in preventing infection, a postinjury antimicrobial should maintain a concentration sufficient to inhibit or kill bacteria. Massive blood loss can be associated with thoracoabdominal injuries due to disruption of the great vessels and/or lengthy surgical repair of extensive injuries. A 1,500 mL to 2,000 mL blood loss (or more) accounts for 30% to 40% of a patient's blood volume and replacement of that volume of blood suggests that serum antimicrobial concentrations may be diminished. Many surgeons have addressed this by empirically decreasing the dosing interval in cases requiring a significant volume of blood products. Evidence to support this practice has been somewhat conflicting. Cefazolin drug levels have been the most studied. As cefazolin does not enter red blood cells, it is the loss of plasma, not total blood volume that is responsible for any decrement in the plasma concentration. A number of the studies that demonstrated little change in serum levels of cefazolin were associated with smaller volume blood losses (1,200 mL or less).[50–52] Meter et al.[53] prospectively studied 18 patients undergoing hip surgery and assayed cefazolin levels 48 hours before operation and during surgery. Even though the average blood loss was 1,137 mL, there was no clinically significant decrement in cefazolin levels. Furthermore, Meter et al. extrapolated their pharmacokinetic data to calculate that even with a blood loss of 5,000 mL, there would be adequate serum levels of cefazolin. Swoboda et al.[54] prospectively studied 11 patients undergoing spinal surgery and performed pharmacokinetic measurements of serum and tissue concentrations of cefazolin and gentamicin throughout the procedure and concluded that additional doses of cefazolin should be administered in cases with more than 1,500 mL of blood loss or surgery longer than 3 hours.

The pharmacokinetics for most antimicrobials have not been adequately assessed in trauma patients and the data are insufficient to support specific recommendations for altering dosing regimens for other agents.[55]

The 2000 EAST guidelines for postinjury antimicrobials in penetrating abdominal trauma concluded that there were insufficient data for evidence-based recommendations but advised that in cases of massive hemorrhage, antibiotic dose should be doubled or tripled and repeated after every tenth unit of blood product transfusion.[56]

Although data are conflicting, it appears that hemorrhage of more than 1,500 mL and development of shock may be associated with altered pharmacokinetics of antimicrobials and potentially inadequate serum concentrations. Our recommendation is for redosing of antimicrobials after large volume blood product (1,500–2,000 mL of blood loss) resuscitation has been completed, regardless of when the last dose of antimicrobial was administered.

Our review of the literature does not support change to the recommendations for thoracic trauma postinjury antimicrobials made in the 2008 guidelines.[47] Although the subject remains controversial, the majority of studies have demonstrated a reduction in both empyema and pneumonia in patients administered antimicrobials postthoracic trauma. The administration of a single dose of cefazolin (2 g IV) before tube thoracostomy or thoracotomy and, if desired, continued (every 6–8 hours) for no more than 24 hours after the procedure, may reduce infectious complications without significant selective pressure on colonizing bacteria yielding antimicrobial resistance.

ABDOMINAL WOUNDS

In 1898, Cousins,[57] a British surgeon, described resuscitation of a patient after an abdominal gunshot wound with "subcutaneous strychnine and brandy." Surprisingly, the patient "rallied" with this medical intervention and went on to laparotomy, debridement, irrigation, and a successful repair of a gastric perforation, to ultimately survive. Although preoperative management has advanced considerably in the last century, many of the surgical principles remain current.

In the US Civil War, penetrating abdominal injuries were associated with death in 87% of cases; poor outcomes were so uniform that surgical intervention was uncommon. As general anesthesia with ether became widely available, surgeons could perform longer, more intricate procedures, and by the close of the 19th century, early surgical intervention for thoracic and abdominal injuries was becoming accepted as potentially lifesaving. Surgeons faced a massive number of injuries in World War I and the British Army's review of data from penetrating combat wounds to the abdomen demonstrated that early surgical intervention was associated with approximately 50% survival and, by 1916, mandated early surgical exploration after penetrating abdominal injury during the remainder of the war.[58] The Belgian surgeon Depage[59] noted that rapid access to surgical intervention was critical in abdominal wounds and that moving "advanced dressing stations" to within 2 km to 3 km of the front, along with adequate debridement and irrigation decreased mortality from 65% to 45%. Even as antibiotics became available in the 1940s the importance of prompt irrigation, debridement, and repair to prevent development of infection have remained paramount.[60–63]

During the First World War operating on patients in shock was associated with worse outcomes and postponement of surgery to treat shock was advocated by some surgeons.[61]

As the concept of delay of definitive repair in patients evolved in the 1980s and 1990s to "Damage Control" surgery, the appropriate timing for closure of the abdomen and selection of suitable prophylactic antimicrobials of narrow versus broad spectrum antibiotics have remained areas of discussion.[64] Although severe abdominal trauma may be associated with multiple intestinal perforations, injuries not causing intestinal perforation have a much lower incidence of infectious complications.[65]

Abdominal trauma in the wars in Iraq and Afghanistan occurred in similar proportions to those seen in the Second World War, Korea, and Vietnam.[2,13,16] In OEF/OIF, abdominal wounds constituted 9.4% of 6,609 wounds recorded by the US JTTR. A total of 81% of abdominal injuries were caused by explosions, 17% by gunshots, and 2% by motor vehicle collisions.[16] Casualties earlier in the war were more likely to have suffered gunshot wound than blast abdominal injuries.[66] Hospital data regarding injuries are skewed by inclusion of only those patients that survive to admission. Because abdominal injuries, like thoracic injuries, may be associated with significant hemorrhage that cannot easily be halted by compression (or having a tourniquet applied) in a tactical setting, many personnel with abdominal injuries die around the time of injury. Among 486 autopsies from OEF/OIF, 83% of deaths were from penetrating injury and 50% of deaths were attributed to truncal hemorrhage (includes thorax and abdomen), making it the leading cause of death.[4]

The incidence of postinjury infection in penetrating abdominal injury reported in the literature ranges from 4% to 31%.[67–70] A study of 211 injured patients cared for on the USNS Comfort during the first months of the Iraq War found 30% of abdominal injuries were infected, yielding an odds ratio of 2.7 for an abdominal injury to develop an infection (this series was primarily civilian Iraqis, not US troops).[28] In civilian studies, Nichols et al.,[65] in a study of 145 patients with abdominal trauma and gastrointestinal perforation, identified increased age, injury to the left colon requiring colostomy, large numbers of intraoperative blood products and a larger number of injured organs as factors associated with an increased risk of postoperative infections. Croce et al.[71] and later O'Neill et al.[69] found a significantly increased number of infections in patients with concomitant gastric and colonic perforation over those with isolated colonic perforation. More recently, Salim et al.[70] analyzed outcomes of 178 cases of penetrating stomach and small bowel injuries and reported 50% of combined stomach and colon perforations developed postoperative infections while only 16% of isolated gastric injuries developed an infection.

The organisms responsible for infections after penetrating abdominal trauma have been well characterized in numerous studies and are most commonly *Escherichia coli* and other *Enterobacteriaceae*, *Streptococci* (including *Enterococcus* spp.) and *Bacteroides* spp. Colonic perforations are more likely to be associated with *E. coli* and *Bacteroides* spp., while *Enterobacter cloacae* and *Klebsiella* spp. are seen more commonly in gastric and small bowel injuries. *Candida* spp. have been reported in 20% of infections in a recent study.[67,69,70] Although there has been understandable concern about the prevalence of MDR gram-negative bacteria, including extended-spectrum β-lactamase (ESBL)-producing *E. coli, Klebsiella* spp., and *Enterobacter* spp. and MDR *Acinetobacter baumannii* in abdominal infections, it appears that most of these resistant organisms have been acquired from the healthcare system and not at the time of injury.[28,44] They are, therefore, not targets of antimicrobial prophylaxis.

Prevention of Infection in Traumatic Abdominal Wounds

Postinjury Antimicrobials

Rationale

Penetrating abdominal injury is so frequently associated with bacterial contamination that postinjury antimicrobials have become the standard of care.[72] Unlike thoracic trauma, routine administration of postinjury antimicrobials in penetrating injuries to the abdomen had come into practice during the Korean War and was well established by the 1970s. In 1972, Fullen et al.[73] conducted a retrospective study of 295 patients who underwent laparotomy after penetrating abdominal injury first demonstrated that antimicrobials administered preoperatively were associated with significantly lower rates of secondary infection. They observed fewer infectious complications in those who received antimicrobials preoperatively (7%) than when given intraoperatively (33%) or postoperatively (30%). Subsequent studies by Thadepalli et al.[74] compared presurgical administration of kanamycin plus cephalothin with the expanded anaerobic coverage provided by kanamycin plus clindamycin and saw significantly fewer postoperative infections (27% vs. 10%) in the clindamycin group. The kanamycin plus cephalothin group experienced anaerobic infections in 21% versus only 2% in the patients treated with kanamycin/clindamycin. These high quality studies supported recommendations and guidelines decades later.[56,75] The use of postinjury antimicrobials in abdominal trauma has become the standard of care and subsequent studies over the next 40 years have not been placebo-controlled, but comparisons between different regimens and have included combinations of nearly every antimicrobial class, dosage, and duration.

Despite near universal acceptance and guideline recommendations, Brand et al.,[76] in a 2009 Cochrane Review determined that none of more than 500 references reviewed constituted a randomized controlled trial that fulfilled their strict inclusion criteria. They therefore concluded that recommendations in guidelines for postinjury antimicrobials in abdominal trauma are based on expert opinion rather than firm evidence from clinical trials. We disagree with their conclusions. It is our opinion that there are adequate trials to support our recommendations.

There has also been considerable controversy about the choice of antimicrobials recommended for postinjury administration (and for treatment of established infections) after perforating abdominal injury. The Surgical Infection Society and the Infectious Diseases Society of America Guidelines Committee, in both 2002 and 2010, in making recommendations for treatment of established intra-abdominal infections concluded that there were insufficient data to recommend a

single regimen as superior to others based on efficacy.[75,77] A similar conclusion can be drawn for postinjury regimens. Many of the trials comparing postinjury regimens were not designed to detect therapeutic superiority and were underpowered to even detect a significant difference between the treatment groups. There have been scores of different antimicrobial combinations compared, many of which were reviewed in forming the EAST Practice Management Guidelines for postinjury antimicrobial use in penetrating abdominal trauma in 2000.[56,78–82]

Although many different antimicrobials, either alone or in combination, can be considered for postinjury administration in abdominal penetrating trauma, there are some factors that should be considered in the determination of which drugs to use. An ideal regimen provides antimicrobial coverage for enteric gram-negative bacteria, primarily the *Enterobacteriaceae*, *Streptococci*, and anaerobes, predominately *Bacteroides* spp. Metronidazole remains overall a highly effective anaerobic antimicrobial. A number of recent studies suggest that clindamycin is inferior to metronidazole, carbapenems, and moxifloxacin for treating anaerobic infections due to its poor coverage of *Bacteroides* spp., the primary cause of anaerobic infection in penetrating abdominal wounds, and other clinically relevant anaerobes such as *Prevotella* spp.[83–88] In the 10 years since the EAST Guidelines were published, there have been additional studies performed and a trend toward the recommendation of a single dose of a single agent for prophylaxis. Both ertapenem and moxifloxacin have been shown to have at least comparable efficacy with established single- and dual-drug regimens in prophylaxis for elective (nontrauma) surgery and treating established intra-abdominal infections.[89,90] Ertapenem was superior to cefotetan in a randomized double blind trial for elective colorectal surgery, a difference likely due to the modest anaerobic activity of cefotetan.[91] Assumptions that drugs with demonstrated efficacy in elective abdominal procedures will perform equally well in severe trauma cases must be made cautiously. Serum levels and pharmacokinetics of ertapenem and moxifloxacin have been performed in healthy adults, not in critically injured patients who may have experienced massive hemorrhage and shock. There are no data on the pharmacokinetics of ertapenem in the trauma patient and relatively little experience with its use in trauma patients. The pharmacokinetics of ertapenem in eight critically ill patients with sepsis demonstrated wide variability in comparison with healthy volunteers with suboptimal serum drug concentrations observed in some patients. The authors questioned whether it was even appropriate to use ertapenem in septic patients.[92] Moxifloxacin has been more thoroughly evaluated than ertapenem. For example, in one study of 10 patients with peritonitis, serum, and peritoneal concentrations of moxifloxacin were measured. The peritoneal fluid achieved higher concentrations than plasma and exceeded the minimal inhibitory concentration for the most common pathogens.[87] Moxifloxacin was also studied in two comparison trials in the treatment of complicated intra-abdominal infections and found to be comparable with ceftriaxone plus metronidazole.[77,90] There are no data for the use of moxifloxacin in postinjury for abdominal wounds.

A combination of cefazolin and metronidazole is recommended in the updated guidelines.[47] This selection is based on evidence of the efficacy of these agents, years of experience with their use in a variety of surgical scenarios, and because they are used for postinjury treatment for other injury types. Use of this combination allows a more limited number of agents to be stocked in a forward deployed setting, especially in this setting where there is no evidence that any alternative regimens are more efficacious. Either ertapenem or moxifloxacin are acceptable alternative agents for postinjury antimicrobial therapy. These agents provide simple regimens that may be preferred by some surgeons, or in some situations. Neither ertapenem nor moxifloxacin have good data supporting their use in trauma patients. Furthermore, limiting use of quinolones, carbapenems, and expanded-spectrum cephalosporins should decrease the selective pressure on enteric bacteria and development of resistance should a postoperative infection develop.

Although there has been understandable concern about the prevalence of MDR gram-negative bacteria, including extended-spectrum β-lactamase (ESBL)-producing *E.coli, Klebsiella* spp., and *Enterobacter* spp., and MDR *Acinetobacter baumannii* in established abdominal infections, it appears that most of these resistant organisms have been acquired by transmission from the healthcare system,[28] and not at the time of injury.[27] Empiric coverage for these resistant organisms in postinjury regimens is not recommended.

Redosing of antimicrobials (see discussion in thoracic section) should be considered after large volume resuscitation with blood products (1500–2000 mL) has been completed, regardless of when the previous dose was administered.

Antibiotic impregnated beads, cement, and sponges have been used by surgeons to prevent infections in a variety of capacities. A gentamicin collagen sponge has been approved for surgical implantation in many countries and has been used in over a million patients. Bennett-Guerrero et al.[93] randomly assigned 602 patients undergoing colorectal surgery to either have placement of two gentamicin-collagen sponges or no sponges and paradoxically observed a significant increased incidence in superficial surgical-site infections (30% in the sponge group and 21% in controls). Antibiotic sponges should not be considered as part of a prophylactic regimen in abdominal trauma surgery. Topical antimicrobials have also been widely studied and appear of no added value if systemic postinjury antimicrobials are provided.[94]

Duration of postinjury antimicrobials

The pharmacologic goal of antimicrobials in abdominal trauma is to ensure a sufficient concentration of a suitable agent is present in the peritoneal cavity during the vulnerable period before the establishment of infection. At laparotomy the perforation is closed, the field is irrigated to reduce peritoneal contamination and no further antimicrobials should be required.[56] Straightforward as this goal is, the optimal duration of postinjury antimicrobials in penetrating abdomi-

nal trauma has remained controversial. A number of studies have demonstrated that longer courses (greater than 24 hours) offer no advantage over shorter (less than 1 day) regimens.[95–98] Dellinger et al.[98] randomized 116 patients with confirmed penetrating injuries of the bowel to either 12 hours or 5 days of postinjury antimicrobials, 24% developed a postoperative infection, but there was no difference in the incidence of infection between the two groups. In a larger prospective study of 515 patients, Fabian et al.[96] randomized patients to 1 day or 5 days of antimicrobial coverage and again found no difference in the incidence of infection between the two groups even in those with the more severe colonic perforations. The EAST guidelines that were published in 2000 recommend that the chosen postinjury antimicrobial dose be administered once preoperatively and, if there is no evidence of gastric or bowel perforation at laparotomy, limit administration to a single dose. If gastric or bowel perforation is identified, then antimicrobials are continued for no more than 24 hours.[56] Despite recommendations for short-course regimens, there is reluctance to adhere to these recommendations, especially when there has been colonic perforation. Delgado et al.[68] observed that postinjury guidelines for penetrating abdominal injury were exceeded in 78% of cases and even observed a trend toward increased infections in those patients who had received prolonged antimicrobials.

SURGICAL MANAGEMENT

Recommendations

For patients with abdominal and thoracic injuries, the skin should not be closed if there is a colon injury or extensive devitalized tissue due to extensive contamination, shock, or residual injured tissue at the incision site. Similarly, skin incisions should not be closed even if possible in the presence of massive blood transfusion, ongoing hypotension, hypoxia, reperfusion injury, multiple other injuries, high velocity injury, or extensive local tissue damage.

Early primary repair of complex or destructive colonic injuries should not be performed especially if associated with massive blood transfusion, ongoing hypotension, hypoxia, reperfusion injury, multiple other injuries, high velocity injury, or extensive local tissue damage.

If the abdomen is left open, the possibility of partial or complete closure should be considered at each subsequent laparotomy. Scheduled laparotomies should be performed in patients managed with an open abdomen technique at 24-hour to 48-hour intervals.

Since the original recommendations, several additional studies in combat casualties have been published which serve only to further confirm the original guidelines.[9,99,100] One study by Duncan et al.[101] documented the outcome of 23 combat casualties with colorectal injuries. Management of these injuries resulted in 30% undergoing primary repair, 13% undergoing resection and anastomosis, and 57% undergoing diversion with colostomy. Four of these patients were initially managed operatively via a "damage control" laparotomy, and in each case, they were ultimately managed with colostomy as definitive treatment for their colon or rectal injury. Of note, 30% of patients treated with either primary repair or resection and anastomosis went on to develop a leak and required diversion, compared with none in the diversion group. The authors concluded that based on injury severity, the complex nature of triage and medical evacuation and the multiple levels of care involved for injured military personnel, temporary stoma usage in patients with penetrating colorectal injuries should play a greater role in the military population than in the civilian environment. In a slightly larger study done by Vertrees et al.,[102] the authors retrospectively evaluated 65 patients with major colon injuries, 92% of whom had penetrating injuries. The authors documented a primary repair rate of 57% and a 43% diversion rate. Failure of repair occurred in 16% and was more likely in those with concomitant pancreatic, gastric, splenic, diaphragmatic, and renal injuries. In a subset of patients who underwent colon injury damage control (n = 27), delayed anastomoses were performed in 10 patients and 17 patients were treated with diversion. In the damage control subset, 50% (n = 5) of the patients undergoing delayed anastomoses went on to develop a leak and ultimately required a second diversionary procedure. The authors concluded that primary repair of war-related colon injuries could be performed safely in a selected patient population in the absence of concomitant organ injury, as was evident in the damage control group.

Finally, Cho et al.[103] retrospectively reviewed 133 patients who sustained colonic injuries from penetrating (71%), blunt (5%), and blast (23%) mechanisms. Authors divided the cohort into three groups: initial primary repair (32%), initial diversion (44%), and initial damage control (23%). All three groups had similar colon-related complication rates (14%, 15%, and 20%), and there were no identified risk factors on multivariate logistic regression analysis for colon-related complications. On discharge from the institution, a total of 62% of the study cohort had undergone a diversion and 38% had undergone either a primary or a delayed repair. The authors concluded, similar to other articles, that in a combat setting, primary repair is feasible with acceptable complication rates in selected cases.

For severe blunt and penetrating abdominal injuries, damage control principles are indicated and the resulting open abdomen requires careful management to prevent infection and promote healing. Several recent studies have advocated the use of negative pressure wound therapy (NPWT, also called vacuum-assisted closure devices) in the management of these patients.[104–106] Miller et al.[107] studied the use of NPWT in a prospective, single center, comparative protocol. The authors concluded that the rate of successful primary fascial closure (88%) and the time to fascial closure were both significantly improved with the use of NPWT compared with historical controls. No enterocutaneous fistulas were reported. However, patients required frequent trips to the operating room for NPWT changes (every 24–72 hours until fascial closure). In a similar study, Suliburk et al.[108] documented a fascial closure rate of 86% in patients with open abdomens treated with NPWT. No enterocutaneous fistulas were reported and time to fascial closure was 7.0 days ± 1 days. Recent studies in combat casualties undergoing aeromedical evacuation using NPWT documented their safe use

during flights and a similar benefit in wound closure.[109,110] The use of these devices appears to be both safe and effective in patients with open abdomens.

IMMUNIZATION IN THE EVENT OF SPLENECTOMY

Recommendation

Immunize with pneumococcal, *Hemophilus influenza* type b (Hib), and meningococcal vaccines as soon as the patient is clinically stable and preferably within 2 weeks of splenectomy. A single booster dose of pneumococcal vaccine should be administered 5 years later. A booster dose of meningococcal vaccine should be administered 2 months after the initial dose and every 5 years thereafter.

Rationale

Overwhelming postsplenectomy infection (OPSI) is a rare and potentially fatal condition that can develop weeks to years after splenectomy. Although these infections have been associated with many different bacteria, the encapsulated organisms, especially *Streptococcus pneumoniae* (50–90% of cases),[111] *Hemophilus influenzae* type b (Hib), and *Neisseria meningitidis* are the most likely to cause severe, invasive disease in individuals with asplenia. Patients suffering from OPSI may progress from good health to death in only 12 hours to 18 hours.[112] The greatest risk of OPSI is in children, especially those younger than 2 years of age, but fulminant sepsis may occur at any time, with OPSI being reported from 24 days to 65 years postsplenectomy.[111] A meta-analysis of literature from 1952 to 1987 of 5,902 patients found an incidence of 4.4% and mortality of 2.2% in children younger than 16 years. In adults, the incidence was 0.9% with a mortality of 0.8%.[113] There is a lower incidence of OPSI in adults who have had a splenectomy posttrauma versus splenectomy for neoplasm or other medical diagnoses. Another extensive review estimated that asplenic patients did not experience a significant increase in the risk of sepsis beyond that in the general population, but that there was a 58-fold increased risk of death among asplenic patients who developed sepsis.[114] Although there are not adequate randomized control studies to yield strong evidence to support immunization against these agents after splenectomy, the practice is currently recommended by the Surgical Infection Society,[115] the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (Table 3),[116] and in the Clinical Practice Guidelines of the Joint Theater Trauma System for patients postsplenectomy.[117] T3

Pneumococcal Immunization

There is evidence that immunization after splenectomy yields antibody titers up to 50% lower than when administered before splenectomy (although there are contradictory studies).[118,119] Furthermore, the timing for immunization after a traumatic splenectomy remains controversial. The randomized clinical trials are only for pneumococcal vaccine and have had some conflicting findings.[120] In a series of studies using the 23-valent pneumococcal polysaccharide vaccine after splenectomy for trauma, Shatz et al.[121,122] found that immunization given at days 1, 7, 14, or 28 after splenectomy were all associated with an immune response. The antibody levels achieved with immunization at days 7 or 14 were significantly lower, probably reflecting the suppression of the immune system immediately after trauma and surgery. Although immunization after splenectomy yields lower functional antibody titers than when administered with an intact spleen, the antibody levels achieved at 14 days postsplenectomy were equivalent to those at 28 days after surgery. Other human studies have failed to demonstrate any significant difference in antibodies in immediate versus delayed immunization.[119] With both polysaccharide and conjugate vaccines available, there remains no strong evidence to use one vaccine over the other. The current recommendations from the ACIP are to administer the 23-valent polysaccharide pneumococcal vaccine in asplenic children and adults. Additionally, asplenic children should be administered the pneumococcal conjugate vaccine on the same schedule as is recommended for children with an intact spleen.[123] Studies in both Britain[111] and the United States[124] have demonstrated that despite recommendations for the use of all three vaccines that immunization often does not occur.

Meningococcal Immunization

Asplenic persons who develop meningococcal infection have mortality rates of 40% to 70%. A study with a meningococcal conjugate vaccine demonstrated that 20% of asplenic persons do not develop adequate serum bactericidal activity after a single dose of vaccine but a second dose 2 months later reduced those with inadequate titers to 7%.[125,126] ACIP meningococcal recommendations for those with asplenia have recently been modified and now recommend a two-dose primary series with the second dose of meningo-

TABLE 3. Recommended Immunizations After Traumatic Splenectomy (ACIP)[116,126]

Vaccine	Primary Series	Repeat Vaccination
23-valent Pneumococcal polysaccharide	When clinically stable, preferably within 2 wk of splenectomy (children <5 yr should receive age appropriate Pneumococcal conjugate vaccine in addition)	Single repeat dose 5 yr later
Polysaccharide protein conjugate *Hemophilus influenzae* b	When clinically stable, preferably within 2 wk of splenectomy	No recommendation for repeat
Quadrivalent Meningococcal conjugate vaccine	When clinically stable, preferably within 2 wk of splenectomy for first dose, second dose 2 mo later	Every 5 yr (at the earliest opportunity if a 1-dose primary series was administered, then every 5 yr)

coccal vaccine administered 2 months after the initial dose and then a booster dose every 5 years. Those who have previously received only a single-dose primary vaccine should receive a second dose at the earliest opportunity and subsequently every 5 years.[126]

Hib Immunization

The data for use of the Hib vaccine after splenectomy is lacking although expert opinion recommends its administration. A single primary dose is recommended, and there are no data regarding subsequent booster doses.

Additional Considerations After Splenectomy

It is important that asplenic patients and their providers are made aware of the increased risk for infections, the recommendations for repeat immunization and the increased risk of sepsis. The role of postsplenectomy antibiotic prophylaxis remains controversial, especially in adults who have been vaccinated. In children, especially younger than 5 years, the incidence of sepsis is so increased that the American Academy of Pediatrics recommends daily antibiotic prophylaxis penicillin be considered, particularly for the first year after splenectomy.[115,127]

RESEARCH GAPS

Trauma is inherently a difficult area in which to perform randomized controlled trials. The lack of adequately powered studies to answer questions such as the optimal antimicrobial regimens for postinjury administration in abdominal trauma will therefore remain controversial. Likewise, the pharmacokinetics of antimicrobials in severe, combat injuries has not been adequately assessed. Generalizing antimicrobial recommendations made for elective thoracoabdominal surgery to the severely traumatized patient may be inaccurate and further research in this population will potentially make recommendations for use of newer agents possible.

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