Prevention and Management of Infections Associated With Combat-Related Head and Neck Injuries

Kyle Petersen, DO, David K. Hayes, MD, Jeffrey P. Blice, MD, and Robert G. Hale, DDS

Maxillofacial injuries constitute 16% of all war-related injuries. This review focuses on data available from military and civilian studies to provide evidence-based recommendations for the modification of infections associated with combat-related injuries to the head and neck. The major emphasis of this review is on the study of subsequent infection, perioperative antimicrobial prophylaxis, debridement of devitalized tissue, optimal time to wound closure to achieve a water tight seal, wound irrigation with removal of debris and gross contaminants, fracture fixation, and removal of ocular foreign bodies with intravitreal antibiotics. Further studies are needed in combat-related injuries to the head and neck in military personnel to provide the highest evidence-based medicine recommendations.

Key Words: Combat, Trauma, Head, Neck, Maxillofacial, Infection.


Modern battlefield injuries to the maxillofacial region have challenged surgeons because high-velocity, high-energy missile and fragmentation weapons inflict tremendous destruction and tissue loss. War-associated traumatic injuries differ from civilian injuries in that combat firearm projectiles travel at higher velocities and cause more severe injuries. In addition, fragmentation ordnance such as shells, grenades, mines, or explosive devices are accompanied by a blast wave resulting in additional damage. Combat wounds often occur in a dirty environment. Studies have shown that animals wounded by these projectiles become colonized with bacteria from their immediate environment relatively quickly and casualty data show infections occur more frequently than in other forms of trauma.1

Maxillofacial, head, and neck structures compose about 12% of total body surface area, but retrospective analysis of 26 recent conflicts showed disproportionately higher numbers of maxillofacial, head, and neck injuries (about 16% of all war-related injuries).2 The proportion of maxillofacial injuries relative to other sites has increased in recent conflicts. Among injuries sustained in the Battle of Mogadishu, 36% of the fatal wounds were to the head and neck, consistent with the Vietnam War experience.3 In that study, Kevlar helmets did not offer protection from projectiles entering the cranium frontally through the face. It was postulated that the unprotected face of a soldier wearing body armor is not only exposed but specifically targeted by the enemy in an urban environment.

Forty percent of people with facial injuries in World War II died after evacuation.4 This high mortality rate was dramatically reduced to 1.3% during the Korean War through rapid evacuation and treatment of the wounded, to include the use of antibiotics.5 Positioning an oral surgeon at forward operating facilities resulted in improved management of casualties during the Korean War.5–8

The maxillofacial region is anatomically complex with skin and mucosa lining structures that support the upper airway, deglutition apparatus, and specialized sensory organs of sight, smell, hearing, taste, and touch. There are no large muscular masses in the face and neck, so the risk of late cavitary necrosis and subsequent possible infection is considerably lower than with other types of combat injuries. Facial injuries can be extensive but are rarely life threatening; initial management priorities are airway management, particularly tracheotomy if required, hemostasis, and treatment of shock with fluid replacement.9 The integrity of the oral cavity mucosal lining is a critical feature of the maxillofacial region. Battlefield injuries of the maxillofacial region often disrupt this mucosal lining leading to contamination of the deep structures of the face and neck with bacteria-laden saliva. However, because of the rich vascular supply, early primary closure of maxillofacial structures after conservative debridement is possible.

Combat-related infections of the maxillofacial region were first identified in the Vietnam conflict.10 A comparison of in-theater infection rates of all war wounds (3.9%) with maxillofacial injuries (7.1%) revealed a higher prevalence of infections in maxillofacial wounds despite rapid evacuation, frequent use of “prophylactic” antibiotics, and early wound care.

Ocular injuries are relatively uncommon in wartime but are increasing in numbers. In World War II they represented 2% of all injuries. In the 1967 Israeli war, they were 5.6% of injuries, and by the 1982 Israel-Lebanon War 6.8% of all
injuries. Most distressing was in the 1982 conflict, when 28% of eye injuries were bilateral. Belkin et al.11 attribute this rise in rates to increased urban warfare. The confined area of the urban battlefield concentrates airborne foreign bodies in the area of an explosion or projectile strike. There is also a pervasive nonadherence to ballistic goggle use.11 During the current Iraq war, 10% of all hospital admissions to date had ocular injuries, 82% the result of blast injuries, and 51% from explosive devices.12 Of all the ocular injuries, 64% were open globe and 20% required enucleation. Nonuse of ballistic eyewear is attributed for the current rise in these injuries. Penetrating eye injuries of the orbital fossa are unique in that they likely need neurosurgical involvement in addition to the ophthalmologist.13

The following factors have been useful in preventing infection of the traumatized maxillofacial region: early definitive treatment with debridement, irrigation, early repair of hard and soft tissues, and institution of broad-spectrum antibiotics as soon as possible.14,15 Current US Army references indicate that maxillofacial war injuries not repaired ≤12 hours or without antibiotics ≥6 hours postinjury become infected and require antibiotics for 10 to 14 days.16 Although these recommendations are not evidence based, they are nonetheless universal in current oral and maxillofacial surgery textbooks.14,15 It is possible that antibiotics play a secondary role to early debridement, stabilization, closure, and drainage of maxillofacial war wounds for preventing infections. The purpose of this review is to analyze the current literature for evidence of treatment modalities useful in preventing and managing infections of the maxillofacial, head, and neck region.

Epidemiology or Microbiology of Wound Colonization and Infection

Infection rates in maxillofacial injuries are well described. In one study of 17,690 trauma admissions to selected US military hospitals during the Vietnam War, 1,958 (11.1%) casualties had maxillofacial injuries.17 Within this group of injuries, there was a high incidence of comminuted fractures (75%) and avulsion defects (54%) of the mandible. Overall, maxillofacial infection wound rate was 7.1% in theater; further analysis of this group after evacuation from Vietnam was difficult because 68% of the casualties were lost to follow-up. In a retrospective study of 162 patients with maxillofacial injuries from time of injury in Vietnam to treatment in higher level medical facilities, 68 (42%) developed infections during some point of treatment with 13% incidence at early-care facilities, 25% at intermediate facilities, and 62% at late-care facilities.18 Eighty-two patients with mandibular avulsion-type injuries required bone grafts with infections later developing in 56.1% of those cases. Despite rapid evacuation and antibiotics, 42% of patients with severe maxillofacial injuries developed infection during the course of treatment.

In a retrospective analysis of 183 patients treated for weapon-related injuries in maxillofacial surgery clinics during the Balkans conflict (1988–2002) with special analysis of 91 patients injured during the period 1991 to 1995, 40% of the injuries were to the mandible and 6% had isolated maxillary fractures.19 From 1991 to 1995 most injuries were caused by high-velocity projectiles with 56% from bullets and 44% by explosions. Perforating wounds occurred in 70% and penetrating wounds in 30% of patients. It was noted that most wounds were infected at presentation because of delays in admission to the clinic. The average time between injury and admission to the maxillofacial surgery clinic was 7 days during war and 5 days during peacetime. Wounds became infected postoperatively with Escherichia coli and Streptococcus pyogenes in 19% of war-wounded patients, compared with 10% in nonwar wounds.

Among 210 combat casualties of the Iran-Iraq war with maxillofacial injuries, 94.3% were caused by missile and explosions, the rest resulting from motor vehicle crashes.20 The mandible, especially the anterior, was the most prominent area injured. Twenty-four cases (11%) were complicated by infection, including nine cases of osteomyelitis. Significant contributors to infection rates were delay in evacuation and lack of suitable fixation devices.

Descriptions of actual pathogens in maxillofacial infections in combat-associated trauma are rare. Providers should be aware of the pathogens involved and their potential for other system infections (e.g. pneumonia) as well as their capacity for complications (e.g. cervical osteomyelitis). In a study of 564 jaw fractures evacuated to a level IV hospital in the Philippines during the Vietnam war, 31 patients with postoperative infections were described.5 Daily cultures were performed on all patients. Pseudomonas species (spp.) and Klebsiella spp. were cultured before the first surgery in 100% of patients. Staphylococcus aureus, E. coli, and fungi (likely Candida spp.) were also reported, but rates of infection for these pathogens are not included. The authors point out that infection rates for the mandible paralleled those for other nonmaxillofacial war wounds. Another study from Lebanon noted Proteus mirabilis, Bacteroides fragilis, Peptococcus, and Peptostreptococcus in maxillofacial wound infections.21 Based on these two studies, perioperative and empiric antibiotics against these pathogens to prevent or initially treat infection might be warranted, but the evidence is very poor (CII) (grading outlined in this supplement of Journal of Trauma: “Guidelines for the Prevention of Infection After Combat-Related Injuries”).

There are no other studies of maxillofacial combat wounds describing microbiology. Because trauma wounds are by definition contaminated or dirty, it is reasonable to examine data from military or civilian nontrauma microbiology studies of surgical cases classified as contaminated or dirty to better appreciate potential pathogens of interest. Table 1 summarizes all pathogens isolated from contaminated war or civilian surgical cases. One center reported microbiology of infection from 354 primarily oncologic patients enrolled in several perioperative prophylactic antibiotic
trials. All patients were contaminated major head and neck surgical cases who received perioperative antibiotics. Infection rates were 6.5%, which is equivalent to Tinder’s reported rates of infection in Vietnam. Of the infections that occurred 1 to 23 days postop, 96% were polymicrobial, 91% aerobic, and 74% anaerobic. Fungi (100% Candida spp.) occurred in 45%, but were not treated and therefore thought to be colonizers.

Bacteroides spp. was the most common anaerobe (76%) followed by microaerophilic streptococci. Streptococcus viridans was the most common aerobe. Prophylactic perioperative antibiotics did not cause subsequent infection with resistant bacteria. Because most infections were late (>10 days postop) the authors concluded that immediate postoperative antibiotics may not prevent infections.

Another summary of 400 primarily oncologic major surgery patients from a military center has similar findings. More than 50% received perioperative cefazolin and the infection rate was 3.2%. Of those infected, 88% were polymicrobial, 45% were aerobic, and 54% anaerobic. S. viridans was again the most common aerobic pathogen followed by Lancefield group C and G streptococci and S. aureus. Peptostreptococcus spp., followed by Bacteroides spp. and Fusobacterium spp., were the most common anaerobes. Seventy-one percent of isolates were \( \beta \)-lactamase producers, which would theoretically render cefazolin ineffective.

Osteomyelitis of the cervical spine deserves mention as there are several case reports of this condition associated with war and low-velocity civilian gunshot injuries to the neck. These studies describe osteomyelitis in relation to penetrating trauma of the neck by bullets or shrapnel in six patients. Neurologic symptoms are present in only 12% to 25% of patients with osteomyelitis in this setting.
Prevention of Infection: Surgical Management

In an analysis of 31 Vietnam War casualties with mandibular comminuted fractures or avulsion defects evacuated 4 to 24 days after injury to the Philippines, all patients underwent repeated debridement, establishment of dependent drainage, and closed reduction of the fractures with indirect appliances. Mandible fractures were definitively treated with open reduction using intraosseous wire ligatures. A retrospective study of 1,357 war injuries in 1,021 patients from Beirut (1975–1984) revealed 24% of injuries to the maxilla, 18% to the mandible, 10% to the nose, 8% to the oral cavity, and 6% to the orbits. Most of the maxillary injuries were compound, comminuted Lefort type fractures; treatment consisted of debridement, soft-tissue coverage of bone, and delayed definitive management. Twenty-five percent had complications of malunion, nonunion, fistula, and infection. Most mandibular fractures were compound, comminuted with bone and soft-tissue loss; 54% were treated with closed reduction and 46% with open reduction. Seventy-four percent healed after primary surgery, 26% requiring a second surgery for malunion, nonunion, graft extrusion, or infection. Osteomyelitis developed in 6%, particularly when fractures had marked overlying soft-tissue loss. Overall infection rate was 12%, with \(S.\) aureus, \(P.\) aeruginosa, and \(E.\) coli isolated. This low infection rate was attributed to aggressive debridement, irrigation of wounds, meticulous removal of contaminates, minimal introduction of foreign synthetic material during initial surgery, coverage of bone with tension-free closure, and immediate institution of antibiotics in high-risk wounds. Based on this large case series, using all of the aforementioned techniques might be helpful in minimizing infection (BII).

In a 10-year retrospective study of 44 patients with gunshot and war wounds to the face treated in a single medical center in Iran, soft tissue and underlying bone injuries were treated with primary reconstruction in 86.3% of the cases. The mandible was the most frequently injured bone (72.7%) followed by the maxilla (34%). Closed reduction was used in 56.8%, and 22.6% had open reduction with internal fixation; the remainder required only debridement and closure of the wounds. Postoperative discharge was noted at the suture sites in 24.3% of the patients; all infections treated with daily irrigation resolved. Antibiotics were noted to play a major role in preventing infection after primary closure, but no details of type or regimen were described. The author concluded that early and conservative debridement, irrigation, fixation and immobilization, and primary closure with drainage were all important to prevent infection (BIII).

A large series of 1,135 patients injured in the face during the Iran-Iraq war revealed mixed bone and soft-tissue injuries in 72.7% of the cases. Lower facial injuries were the most common (72.6%), and compound mandible fractures occurred in 517 cases (45%). Most of the casualties with severe facial injuries were infected upon arrival at the hospitals. After resuscitation, wounds were debrided of necrotic tissue margins, visible foreign bodies, dental fragments, and small bone fragments. The wounds were then irrigated with normal saline, hydrogen peroxide, and povidone iodine. Soft-tissue wounds were closed, with or without bony repair. Bone defects were packed with gauze impregnated with glycerin and povidone iodine. Bone injuries were later addressed with Kirschner wires, bone cement space maintainers, and other temporary fixation devices (transosseous wires and arch bars). Late reconstruction involved bone grafting of defects. Perioperative antibiotics were administered but no details on antibiotic regimens were offered. Despite a reported infection rate of 11% of patients presenting for treatment, the author experienced an overall 1.15% postoperative infection rate using a closed reduction and delayed reconstruction approach, suggesting that this might be the preferred method of management to prevent infection (BII). Surgical techniques utilized are further detailed in a case report.

Clark et al. performed a retrospective study of 178 gunshot, 53 shotgun, and 15 high-energy avulsion facial in-
Injuries. Using a protocol of immediate bone stabilization, primary closure of existing soft tissue, serial debridement of devitalized tissue every 24 to 48 hours, and definitive early reconstruction of soft- and hard-tissue defects when no further necrosis was noted, 35% who underwent immediate reconstruction for comminuted mandible fractures developed localized sepsis, persistent fistula, or wound breakdown requiring further bone debridement. Furthermore, primary bone grafting was uniformly successful in the cranium and midface, but had higher failure rates when applied to the mandible. This supports our conclusion that avulsion defects of the mandible are best managed by stabilization of existing bone fragments, primary soft-tissue closure, serial debridements, and a delay of bone reconstruction for at least 8 weeks (BII).

Intraocular infections (endophthalmitis), although cited as occurring in 7% to 15% of penetrating ocular trauma, have not been seen in returning casualties from Iraq and Afghanistan. There is controversy as to the timing for removal of retained intraocular foreign bodies (IOFB), although the presence of a retained foreign body is an accepted risk factor for endophthalmitis. Management at levels I and II should be protection of the eye from further injury with a fox shield and evacuation to definitive care at level III or higher by an ophthalmologist. Some measure of visual acuity as close as possible to the time of injury provides the best prognostic indicator of recoverable vision. Simple measurements including light perception, hand motion, or finger counting provide useful information to the subsequent providers. Intraocular cultures should only be obtained by an ophthalmologist and are usually not required except in cases where endophthalmitis has already developed (BIII).

In a recent retrospective comparative interventional case series of 79 eyes in 70 patients with retained IOFB, 10% underwent enucleation because of severe injury and 84% had a vitrectomy at the time of IOFB removal.32 Time to IOFB removal was 39 days mean and 21 days median. Fifty-seven percent of IOFB were metallic, but compared with previous studies there were increasing numbers of stone or concrete IOFB noted. All patients received topical fluoroquinolones and some received i.v./PO (not described in detail); only 3.7% received intravitreal antibiotics. No prophylactic intraocular injections were performed. Zero cases of endophthalmitis were described. This is in stark contrast to the previously cited studies.47,48 This study provides good evidence that surgical extraction of retained IOFB may be delayed for weeks to months with no increased risk of endophthalmitis. Therefore, IOFB removal in forward levels is not recommended unless required to perform the initial repair (BII). It is preferentially performed at level IV. Furthermore, there is also evidence that intravitreal antibiotics are unnecessary when doing vitrectomy for retained IOFBs (BII).

Prevention of Infection: Prophylactic Antibiotics

Antibiotic prophylaxis trials are summarized in Table 2. Several well-constructed randomized trials exist; however, they do not include any trauma or war-injured patients. Among war literature, a previously cited study by Zaytoun21 routinely used cephalosporins and continued them for at least 3 days postop. In the study of Akhlaghi20 antibiotics described were either ampicillin (AMP) or penicillin; patients undergoing bone grafting procedures received postoperative cephalotin and gentamicin. Despite the use of antibiotics, Morgan and Szmyd8 showed infection remained a problem not only at initial repair but with later reconstructive procedures. Therefore, these agents might have utility, but because the duration of therapy, definition of infection and organisms encountered is not defined, the evidence to support their use is poor (CII).

Perioperative antibiotics are clearly needed for traumatic war wounds of the maxillofacial region as they present contaminated with oral secretions and environmental debris. Studies show reductions in contaminated surgery infection rates from 28% to 87% down to 6% to 20% using perioperative antibiotics. A study of prophylactic antibiotics in the setting of facial fractures showed highly significant reductions in infection rates from 42% to 8.9%, therefore, based on this evidence perioperative antibiotics are required when conducting repair of maxillofacial fracture, surgical debridement alone is inadequate (AI).33

One of the first studies to examine perioperative prophylaxis for contaminated head and neck surgery was a placebo-controlled trial of 1 or 5 days of either cefazolin or clindamycin or gentamicin.34 Eighty-three patients were evaluated in four arms and the study later expanded to 107 patients.35 Overall infection rates were 17%. Cefazolin had higher rates of infection than clindamycin or gentamicin (27% vs. 7%). All infections were polymicrobial with predominant isolates of Klebsiella spp., Enterococcus faecalis, and Serratia spp. This trial showed that cefazolin at the 500 mg every 8 hours dose was inadequate perioperative prophylaxis for contaminated head and neck surgery, there is sufficient evidence to recommend it should not be used at this dosage when treating traumatic maxillofacial, head, and neck injuries (DI). It further demonstrated that 5 days was not superior to 1 day of postoperative antibiotic coverage; flap reconstruction; however, tended to be more susceptible to infection and therefore there is evidence for extending antibiotic coverage during flap reconstructions of traumatic maxillofacial, head, and neck injuries beyond 24 hours postop (B1). A potential drawback of this study might be the small sample size in each arm.

Another randomized prospective study evaluated placebo versus two third-generation cephalosporins: cefopazone and cefotaxime, for perioperative prophylaxis.36 Doses were given preoperatively and for 24 hours postop. The placebo arm terminated after a 78% infection rate with several cases of bacteremia. This was highly significant and

Infections of Combat Casualties—Head/Neck
Table 2 Summary of Prophylactic Perioperative Antibiotic Trials in Contaminated Head and Neck Surgery

<table>
<thead>
<tr>
<th>Authors/Year</th>
<th>Type of Surgery</th>
<th>Drug</th>
<th>Dose</th>
<th>Days Perioperative Prophylaxis</th>
<th>No. Doses</th>
<th>Patients</th>
<th>Infections (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Johnson et al.36</td>
<td>Contaminated HN</td>
<td>Placebo</td>
<td>—</td>
<td>1</td>
<td>1</td>
<td>9</td>
<td>7 (78)</td>
</tr>
<tr>
<td>Johnson et al.35</td>
<td>Contaminated HN</td>
<td>Cefazolin</td>
<td>500 mg q 8h</td>
<td>1</td>
<td>4</td>
<td>21</td>
<td>7 (33)</td>
</tr>
<tr>
<td>Johnson et al.39</td>
<td>Contaminated HN</td>
<td>Cefazolin</td>
<td>500 mg q 8h</td>
<td>5</td>
<td>16</td>
<td>30</td>
<td>6 (20)</td>
</tr>
<tr>
<td>Johnson et al.40</td>
<td>Contaminated HN</td>
<td>Clindamycin</td>
<td>2 g q 4h</td>
<td>1</td>
<td>4</td>
<td>59</td>
<td>5 (8.5)</td>
</tr>
<tr>
<td>Johnson et al.35</td>
<td>Contaminated HN</td>
<td>Cefazolin</td>
<td>600 mg q 8h</td>
<td>1</td>
<td>4</td>
<td>52</td>
<td>2 (3.4)</td>
</tr>
<tr>
<td>Johnson et al.40</td>
<td>Contaminated HN</td>
<td>Clindamycin</td>
<td>600 mg q 6h</td>
<td>1</td>
<td>5</td>
<td>88</td>
<td>12 (14)</td>
</tr>
<tr>
<td>Johnson et al.35</td>
<td>Contaminated HN</td>
<td>Clindamycin/gentamicin</td>
<td>600 mg/1.7 mg/kg</td>
<td>1</td>
<td>4</td>
<td>52</td>
<td>2 (3.8)</td>
</tr>
<tr>
<td>Johnson et al.40</td>
<td>Contaminated HN</td>
<td>Clindamycin/gentamicin</td>
<td>600 mg/1.7 mg/kg</td>
<td>1</td>
<td>4</td>
<td>29</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Johnson et al.36</td>
<td>Contaminated HN</td>
<td>Cefoperazone</td>
<td>2 g</td>
<td>1</td>
<td>4</td>
<td>39</td>
<td>4 (10)</td>
</tr>
<tr>
<td>Johnson et al.36</td>
<td>Contaminated HN</td>
<td>Cefotaxime</td>
<td>2 g</td>
<td>1</td>
<td>4</td>
<td>32</td>
<td>3 (9)</td>
</tr>
<tr>
<td>Johnson et al.39</td>
<td>Contaminated HN</td>
<td>Moxalactam</td>
<td>2 g q 4h</td>
<td>1</td>
<td>4</td>
<td>59</td>
<td>2 (3.4)</td>
</tr>
<tr>
<td>Johnson et al.47</td>
<td>Contaminated HN</td>
<td>Ampicillin/sulbactam</td>
<td>1.5 g q 6h</td>
<td>1</td>
<td>5</td>
<td>81</td>
<td>11 (14)</td>
</tr>
<tr>
<td>Simons et al.36</td>
<td>Contaminated HN</td>
<td>Piperacillin/tazobactam</td>
<td>3.375 g q 6h</td>
<td>2</td>
<td>9</td>
<td>31</td>
<td>2 (6.4)</td>
</tr>
<tr>
<td>Simons et al.36</td>
<td>Contaminated HN</td>
<td>Pip/taz + pip/taz gargle</td>
<td>3.375 g/3.375 g</td>
<td>2</td>
<td>9/3</td>
<td>31</td>
<td>3 (9.7)</td>
</tr>
<tr>
<td>Miles et al.44</td>
<td>Open Mandible fx repair</td>
<td>Cefazolin + Benzathine Pen G</td>
<td>2 g + 2.4 mIU</td>
<td>1</td>
<td>1/1</td>
<td>81</td>
<td>8 (9.9)</td>
</tr>
<tr>
<td>Abubaker and Rollert43</td>
<td>Uncomplicated mandible fx repair</td>
<td>Pen G + Pen VK</td>
<td>2 mIU q 4h + 500 mg q 6h</td>
<td>5</td>
<td>4/20</td>
<td>14</td>
<td>2 (14.3)</td>
</tr>
<tr>
<td>Abubaker and Rollert43</td>
<td>Uncomplicated mandible fx repair</td>
<td>Pen G + placebo</td>
<td>2 mIU q 4h</td>
<td>1</td>
<td>4</td>
<td>16</td>
<td>2 (12.5)</td>
</tr>
<tr>
<td>Heit et al.45</td>
<td>Compound mandible fx repair</td>
<td>Ceftriaxone + Pen VK</td>
<td>1 g + 500 mg q 6h</td>
<td>7</td>
<td>2/28</td>
<td>45</td>
<td>2 (4.4)</td>
</tr>
<tr>
<td>Heit et al.45</td>
<td>Compound mandible fx repair</td>
<td>Pen G + Pen VK</td>
<td>2 mIU + 500 mg q 6h</td>
<td>7</td>
<td>7/28</td>
<td>45</td>
<td>2 (4.4)</td>
</tr>
</tbody>
</table>

HN, head and neck; fx, fracture; Amox/clav, amoxicillin/clavulanate; ticar/clav, ticarcillin/clavulanate; Pen G, penicillin G; Pen VK, penicillin VK; mg, milligrams; g, grams, mIU, million International Units; q xh, every x hours; q d, once daily.
Injuries

Wound infections were similar after perioperative antibiotics: 10% in the cefotaxime arm and 9.4% in the cefoperazone arm (equivalent to clindamycin or gentamicin despite poorer anaerobic activity and lack of \( \beta \)-lactamase inhibition). This and two similar studies with highly significant rates of infection from placebo, given ample evidence that use of no perioperative antibiotics (i.e., surgical debridement alone) is not warranted in combat-related maxillofacial surgery (E1). This study provided good evidence that third-generation cephalosporins are equivalent to clindamycin or gentamicin and can be used as perioperative prophylaxis for surgical repair of contaminated head and neck injuries (Bl).

Although 500 mg of cefazolin every 8 hours failed to protect against infection, higher doses might still be adequate. This is encouraging as most combat trauma receiving institutions stock this antibiotic and it might be utilized as prophylaxis for other injuries. A prospective randomized trial of 118 patients receiving 24 hours of high-dose cefazolin (2 g every 8 hours) versus moxalactam showed wound infections in 8.5% of patients receiving cefazolin and 3.4% of moxalactam (not significant). Wound infections were preceded by fluid collection under the flap. High-dose cefazolin (6 g/d) for 24 hours was as good as third-generation cephalosporins at preventing postop wound infections with no increased hematologic or renal toxicities and because of the excellent evidence to support use, narrower spectrum of activity than third-generation cephalosporins and utility for other injury in patients with multiple injuries is therefore preferred for perioperative prophylaxis of war-related maxillofacial infections (Bl).

Whether gram-negative coverage offered by third-generation cephalosporins is necessary is subject to debate. A prospective randomized double-blind trial of 104 patients examined 600 mg clindamycin versus 600 mg clindamycin plus 1.7 mg/kg gentamicin every 8 hours, 1 dose preop and for 24 hours postop. Infection rates were the same in each arm of the study (3.8%). The authors thought that the gram-negatives often isolated in these wounds are likely colonizers and not pathogens, because the addition of gram-negative coverage did not reduce infection rates. This is important in that gram-negative pathogens appear to be a significant portion of nonmaxillofacial wound infections in the Iraq conflict. In addition, a smaller study of clindamycin alone had excellent perioperative prophylaxis for contaminated head and neck surgery with infection rates <5%, therefore, we think there is excellent evidence that clindamycin alone is adequate prophylaxis for contaminated major head and neck surgery to the trauma setting (AI), addition of gram-negative antibiotics such as aminoglycosides or fluoroquinolones has no additional benefit and increases potential toxicity and potential for colonization with multidrug-resistant nosocomial pathogens and should be avoided (Di). Recommended agents for perioperative prophylaxis are shown in Table 3.

The optimum duration of perioperative coverage for contaminated combat trauma wounds is not defined in the literature. Again we think the data from contaminated major head and neck cancer surgeries is the data most applicable to traumatic injuries. A prospective randomized placebo-controlled multicenter trial (including military) of 1 versus 5 days of cefoperazone enrolled 142 patients undergoing major contaminated head and neck surgery. The outcome showed 19% of patients infected with 1 day of coverage versus 25% with 5 days (not significant). The majority of infections were again polymicrobial. This study provides excellent evidence that extending perioperative prophylaxis past 24 hours does not reduce infection rates and is unnecessary in contaminated head and neck surgery (AI).

### Table 3: Suggested Antimicrobials and Duration of Administration for Perioperative Use in Maxillofacial War Injuries

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose and Schedule</th>
<th>Duration of Therapy</th>
<th>Evidence-Based</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perioperative prophylaxis—( \beta )-lactam tolerant</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefazolin</td>
<td>2 g every 8 h</td>
<td>Preoperatively and then for 24 h postop</td>
<td>S3</td>
<td>The preferred agent for nonallergic patients. Presence of ( \beta )-lactamase activity does not seem to influence outcomes</td>
</tr>
<tr>
<td>Perioperative prophylaxis—( \beta )-lactam allergic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td>600 mg every 8 h</td>
<td>Preoperatively and then for 24 h postop</td>
<td>BI</td>
<td>Ideal for ( \beta )-lactam allergic patients. Adding additional gram negative coverage (i.e., a second antibiotic) does not improve outcomes (Bl)</td>
</tr>
<tr>
<td>Perioperative prophylaxis—alternate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ceftriazone</td>
<td>1 g every 12 h</td>
<td>Preoperatively and then for 24 h postop</td>
<td>BI</td>
<td>Based on studies using cefotaxime and cefoperazone. Should have similar activity (All). Not superior to cefazolin in head to head trials (AI), reserve for cefazolin or clindamycin intolerant. (All)</td>
</tr>
</tbody>
</table>

---

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.
Another prospective randomized placebo-controlled trial enrolled 30 patients with uncomplicated open mandible fractures. Perioperative intravenous penicillin G was administered for 24 hours followed by oral penicillin VK or placebo for 5 days. Rates of infection were not significant between oral penicillin and placebo (14.3% vs. 12.5%). In another prospective randomized trial of open mandibular fractures utilizing both introral and extraoral open reduction and fixation, patients received various preoperative antibiotics and then switched to either 2 gm cefazolin perioperatively plus 1 shot intramuscular benzathine penicillin 2.4 million units as postoperative prophylaxis (900 mg clindamycin intravenous and oral for 5–7 days if penicillin allergic) or no postop antibiotics. Follow-up was to 8 weeks. Of 291 patients enrolled, 181 were studied; 81 received postop antibiotics and 100 received none. There were no differences in infection rates between the two groups (8 of 81 vs. 14 of 100; p = 0.399). Based on these two studies, antibiotics in excess of those administered during the 24-hour perioperative period for mandible fractures do not appear to reduce wound infection in otherwise uncontaminated wounds and should be discontinued at 24 hours postop (AI).

The previously discussed cefoperazone trials, as well as the moxalactam and cefotaxime trials, give ample evidence that third-generation cephalosporins are adequate for perioperative prophylaxis in maxillofacial, head, and neck injury (BI). Rates of infection in the most recent cefoperazone trial were higher than clindamycin or gentamicin used in previous trials; however, suggesting other cephalosporins might be preferred over this agent. In addition to elective head and neck surgery, a prospective randomized controlled trial of ceftriaxone versus penicillin G for compound mandible fractures is described. Intravenous antibiotics were given perioperatively for 24 hours along with a dose of corticosteroid. Oral penicillin VK was then given to all patients for 1 week.

Rates of infection for the 90 patients enrolled were not significantly different between penicillin and ceftriaxone (13% in each arm and infection onset was again late (7 ± 2 days postop). Most infections (76%) were polymicrobial. This was the first trial to examine complications of antibiotics for surgical prophylaxis. Clindamycin patients had seven times more Clostridium difficile enteritis complications than AMP/S. This study showed AMP/S is equivalent to clindamycin for perioperative prophylaxis, furthermore, the addition of β-lactamase inhibitor did not provide a prophylactic advantage over clindamycin when performing contaminated head and neck surgery (BI). However, there is evidence that Clostridium difficile enteritis is less prevalent with AMP/S than with clindamycin therapy (BI).

Another randomized prospective trial of β-lactamase inhibitor antibiotics, 62 patients undergoing contaminated head and neck surgery were randomized to 48 hours of postoperative piperacillin/tazobactam (PIP/TAZ) or PIP/TAZ plus PIP/TAZ powder in 60 mL of 5% dextrose solution with a flavor packet as a gargoyle on call to the operating room and daily postoperatively. Infection rates were 6.4% for intravenous alone and 9.7% with addition of the gargle (not significant). Although this study showed some evidence that perioperative PIP/TAZ has slightly lower rates of postop wound infections than AMP/S or clindamycin in previous studies (BI), the lower rates of infection are likely a reflection of the smaller sample size and there was no direct comparison between the agents to suggest superiority. PIP/TAZ cannot be recommended as prophylaxis based on this study alone, but this does show efficacy and lends evidence for use of PIP/TAZ as empiric therapy should a wound develop subsequent infection (BIII). This study showed intravenous plus topical antibiotic prophylaxis was not superior to intravenous prophylaxis alone (BI), but topical agents require further mention.

In a retrospective descriptive study of 100 patients undergoing dental extraction and management of odontogenic abscess, 72 had surgical extractions plus 1% povidone iodine gargle with 10% povidone iodine applied to the drain site where it exited the skin, and were compared with 20 that received antibiotics alone. Patients receiving iodine had a shorter duration of antibiotic therapy (8 vs. 12 days; p < 0.05), therefore topical agents might have conferred additional reduction in wound infections over intravenous therapy. However, because this study was not randomized, not controlled, and the arms were uneven favoring betadine the evidence favoring its use is poor (CII).

Clearly more study is necessary to see if topical agents such as these or chlorhexidine truly prevent infection or potentially impede wound healing. The war literature from Vietnam and Korea describes that oral irrigation with saline enhances wound healing. Evidence supports the authors’ conclusion that early cleansing of wounds using irrigation and conservative debridement of devitalized tissue reduces foreign bodies and the bacterial load that contributes to postoperative infection (BIII). The most effective irrigation solution is not clear however.

Endophthalmitis has not occurred with any frequency in the current Iraq conflict. Broad-spectrum antibiotic use at all levels of care and early primary globe repair may play a
significant role in the prevention of this complication (Blice J, personal communication). A recent multicenter randomized double-blind trial of intracameral (anterior chamber) or intravitreal injection of gentamicin and clindamycin versus saline in penetrating eye injury at the time of primary repair sheds some light on methods to prevent endophthalmitis. Postoperative gentamicin and steroid drops were also used in this study. Intravenous gentamicin (3–5 mg/kg) was administered upon admission and every 8 hours along with cefazolin (50 mg/kg) every 6 hours and continued for 5 days after primary repair. Outcome was the development of endophthalmitis at 14 days after injury. Of 346 patients enrolled, endophthalmitis developed in 2.6% of eyes overall and significantly more upon admission and every 8 hours along with cefazolin (50 mg/kg) every 6 hours and continued for 5 days after primary repair. Outcome was the development of endophthalmitis at 14 days after injury. Of 346 patients enrolled, endophthalmitis developed in 2.6% of eyes overall and significantly more (2.3%) in controls than in patients receiving intraocular antibiotics (0.3%; p = 0.04; odds ratio 8.9). Thirty-four percent of cases were culture negative and the authors emphasized that high clinical suspicion was more important than obtaining cultures. IOFB was also associated with development of endophthalmitis in eyes not receiving intraocular antibiotics. Intravitreal injections trended toward better outcomes than intracameral (p = 0.01). Intravitreal injections of clindamycin and gentamicin, particularly intravitreal, showed evidence of preventing endophthalmitis at the time of primary repair in this study (B1). Because of potential toxicities of intraocular injections (particularly gentamicin), routine prophylactic injections of intravitreal antibiotics in penetrating trauma are not recommended on the basis of this study alone. However, it can be considered in some settings at the ophthalmologist’s discretion.

**Diagnosis of Infection**

The hallmarks of an acute infection in the maxillofacial region are readily apparent within days of an injury manifested as pain, redness, and swelling of the face or neck, trismus, dysphagia, and drainage. Systemically, fever, lymphadenopathy, malaise, and an elevated white blood cell count are hallmarks of an infection. Diagnosis of deep neck space involvement is improved with computed tomography scans or magnetic resonance imaging to image deep soft tissues. The diagnosis of osteomyelitis is made histologically by the presence of bacteria in the marrow spaces, but bone scan studies are hallmarks of an infection. Diagnosis of deep neck space involvement is improved with computed tomography scans or magnetic resonance imaging to image deep soft tissues. The diagnosis of osteomyelitis is made histologically by the presence of bacteria in the marrow spaces, but bone scan studies are helpful in imaging occult bone infection. In the literature reviewed, infection was noted as a common complication but there was scant information about infection severity (grade 1–5) or definition. Cultures of the affected deep wound bed, bone, or pus collection if present are necessary to guide antimicrobial therapy. Based on the described epidemiology, bacterial and anaerobic cultures should be obtained, fungal cultures are unnecessary, mycobacterial cultures can be considered, but mycobacterial infections were not described in the literature reviewed (BIII).

**Management of Infection**

The following factors have been identified in current oral and maxillofacial surgery textbooks as useful in the management of infection of the traumatized maxillofacial region: incision and drainage of accumulated pus, debridement of foreign bodies and necrotic tissue, stabilization of fractures, and institution of antibiotics. At several military facilities in the United States, the standard of care for a surgical wound infection is intravenous or intravenous and oral antibiotics for 10 to 14 days, or for 2 to 3 days after the wound is closed and no signs of infections are present. For osteomyelitis, especially of the mandible, 6 weeks of intravenous antibiotics are preferred. Review of literature on the management of infections in maxillofacial war wounds is consistent with these recommendations, but the length of antibiotic treatment was not studied or offered and therefore the evidence to support these recommendations is limited (CII). Empiric antibiotic treatment should be initiated at first signs of wound infection. Preferred agents should be broad in spectrum and take into account the possible pathogens described in the previous epidemiology. Because there are no described studies of particular antibiotics in these settings, agents should be selected with activity against the described pathogens, or that have been utilized in similar settings such as prophylaxis trials or human bite infection treatments. Based on its broad activity against Streptococcus spp. as well as β-lactamase-producing anaerobic pathogens, and proven utility in contaminated head and neck prophylaxis trials, we recommend AMP/S 2 g every 6 hours as the preferred initial agent for treating infection, and then tailoring therapy to organisms encountered from culture of the afflicted site once this information becomes available (BIII). For the β-lactam allergic patient, we recommend clindamycin 600 mg every 8 hours, plus moxifloxacin 400 mg daily, which should provide similar spectrum of activity (BIII). Alternatives to these two agents for intolerant patients or patients with specific allergy include PIP/TAZ 4.5 g every 8 hours, which has proven efficacy in prophylaxis trials, but the additional pseudomonas coverage it provides over AMP/S is likely unnecessary; or cefoxitin 2 g every 8 hours, which is proven in human bite treatment (BIII).

**Outcome of Infection**

The face and neck region is highly vascular and wound infections are usually contained regionally. Infections can however, result in delayed healing, deformity, fistula formation, and scarring, any of which can greatly compromise resolution. Necrotizing cervical fasciitis, acute osteomyelitis, and infected cavernous sinus thrombosis, although uncommon, are serious consequences of maxillofacial infections. Osteomyelitis, nonunion, fistula formation, and scarring were described in several case series reviewed. However, no deaths as a consequence of maxillofacial infections were noted in any of the same case series.

**DISCUSSION**

From the literature reviewed here, comminuted fracture or an avulsion defect of the mandible was identified as a
high-risk injury for infection. Except for one case series of delayed treatment with closed reduction fracture management, most used conservative debridement, early fracture stabilization, primary closure of soft tissue, drainage of wound, and administration of antibiotics. Maxillofacial war wounds were noted to become infected if there was a delay in treatment. Postoperative infection rates of 1.15% to 100% were noted in the case series reviewed, a total of 2,564 patients with maxillofacial injuries were treated, with 218 (8.5%) postoperative infections noted. Antibiotics were considered important and used in all of the case studies but the length of antibiotic coverage was not described. Two studies mentioned difficulty in obtaining stable fixation as a cause of complications. Lack of soft tissue for closing wounds was also noted to be a leading cause of complications.

When selecting a perioperative agent, we conclude that both prophylactic and empiric antibiotics should cover *Streptococcus* spp. and anaerobes for contaminated maxillofacial, head, and neck war surgery (BII) and could reduce infection rates to 3% to 7%. This conclusion is based on two retrospective epidemiologic studies of wound microbiology, one of which is a summary article of several well-designed prospective randomized trials and the second a military-specific population.23,24 Furthermore, empiric antifungal coverage for yeast or molds is not required (EII).

The need for a β-lactamase inhibitor is less clear as one article showed low infection rates with cefazolin despite the presence of β-lactamase in the majority of microbiologic isolates. Providers should consider a β-lactamase inhibitor combination such as AMP/S in refractory cases of infection (BII). They should also be aware of the potential complication of cervical osteomyelitis, although today different antimicrobial agents might be employed to manage such an osteomyelitis rather than the penicillin and gentamicin reported in the literature.

Regarding surgical management, rapid evacuation from the battlefield to a medical facility with specialists to debride, irrigate, and stabilize the wounds is a major factor in preventing infections.52 Care must be taken to conserve the inner mucosal lining during the debridement process. Antibiotics should be administered as soon as possible after injury. The highly vascularized tissues in the maxillofacial region allow for early or delayed-early primary reconstruction of the hard and soft tissues. Primary bone grafts to reconstruct defects appears successful in the upper and midface but not in the lower face.31 Bone grafting mandibular defects is best delayed until after the wound is infection-free and revascularized.27–30 Rigid internal fixation of mandibular fractures was used in one case series of severe nonwar facial injuries; the other case series used a combination of closed reduction techniques and open reduction with varying degrees of rigidity.8,20–21,27–30 Taher’s case series29 had the lowest infection rate which he attributed to avoidance of internal fixation devices. Zaytoun et al.23 also recommended the minimal use of internal devices for fracture repair to avoid complications.

In the Korean and Vietnam Wars, a team surgical approach using oral/maxillofacial surgery, neurosurgery, general/vascular surgery, and ophthalmology worked well to manage complicated maxillofacial injuries. This capability was augmented by the addition of otolaryngology during the Iraq war and remains of paramount importance.53

Our analyses of numerous previously mentioned maxillofacial, head, and neck surgery studies determined that extending perioperative antibiotics beyond 24 hours did not significantly reduce infection rates. One day of perioperative treatment significantly reduced immediate perioperative infections. Late infections still occur, and are not prevented by prolonged postoperative antibiotics. These late-onset infections are related more to the nature of injury and adequacy of tissue for surgical repair. Perioperative antibiotics should be terminated at 24 hours after primary repair of maxillofacial wounds (AI). Longer courses of antibiotics are indicated if there are signs of infection, compromise of blood supply to the affected area because of surgical approach, closure under tension because of inadequate tissue or requirement of flaps, or grafting for closure or coverage (CIII).

Overall infection rates are fairly comparable in all perioperative studies performed with the exception of the 500 mg dosing of cefazolin, which is significantly worse. Of all assessed medications currently available, moxalactam had the lowest rates of infection in head and neck surgical literature, and ceftriaxone or penicillin G followed by 1 week of oral penicillin in the mandibular fracture literature. Moxalactam is not currently available in the United States however. Advantages of clindamycin include activity against β-lactamase producers and no usage restrictions in β-lactam allergy. Clindamycin might have higher rates of *C. difficile* infection however. High-dose cefazolin and cefotaxime are good alternatives. There is a putative concern with β-lactamase production in oral anaerobes that has not proven to be true in clinical trials. Cefazolin and cefotaxime are given three times daily and are likely safe in penicillin allergy, but might have cross reactivity in 6% to 7% of cases.32 We prefer ceftriaxone over cefotaxime; however, because of its less frequent dosing schedule and similar spectrum of activity. AMP/S and PIP/TAZ are effective against β-lactamase producers, although in one study AMP/S was used three times daily, when they are traditionally given as four times daily drugs and are not useful in β-lactam allergy. We would favor the use of cefazolin, clindamycin, or ceftriaxone as perioperative prophylaxis and to reserve β-lactam/β-lactamase inhibitor combinations for empiric treatment of infection.

Five days of perioperative antibiotics do not appear to be superior to 1 day in both contaminated major head and neck surgery and mandible surgery, so providers should be advised to use the 1-day regimen. Topical oral or intraoperative irrigation antibiotics do not appear to have added value, but topical iodine might add a small value in preventing infections.

The incidence of combat-related maxillofacial infections in the current conflict, the relationship of antibiotic type and
timing of administration with the incidence of infection, the outcomes of maxillofacial infections based on severity (grade 1–5), and the epidemiology of trauma and infections of the maxillofacial region are all areas that require further study. In addition, the relationship of infection to delays in definitive surgery has not been studied except in the Ophthalmology literature. The bacteriology of current maxillofacial war wounds deserves at least a retrospective, and preferably prospective, evaluation. Rigid internal fixation of mandible fractures is thought to reduce risk of infection and deformity by preventing micromovements of the fragments. The current conflicts in Iraq and Afghanistan are the first time rigid internal fixation is being applied to maxillofacial war wounds on a large scale. It is unknown whether rigid internal fixation on maxillofacial war wounds has an effect on infection incidence, especially in comminuted fractures and avulsion defects of the mandible. This is another area that requires thorough analysis. Finally, a longitudinal study of maxillofacial combat-injured patients throughout their course of treatment would be valuable in studying the incidence of complications. Better analysis in all of these areas will improve treatment outcomes and positively impact care for those brave warriors who have made a tremendous sacrifice, having suffered a severe maxillofacial war injury in the service of their country.

ACKNOWLEDGMENTS

We thank Mrs. Diana Temple at Naval Medical Research Center for her assistance in the preparation of this manuscript.

REFERENCES


49. Valderrama LS. Clinical application of povidone-iodine oral antiseptic 1% (betadine mouthwash) and povidone-iodine skin antiseptic 10% (betadine solution) for the management of odontogenic and deep fascial space infection. *Dermatology.* 2006;212(Suppl 1):112–114.


