CPD article

Emergency management of open fractures

Open fractures are associated with an increased risk of complications, such as infection or nonunion, and present a therapeutic challenge. The incidence of such complications is directly influenced by how they are treated in the first several hours after presentation. As such, the focus of this article is to adopt an evidence-based approach to guide open fracture emergency management and minimise complication rates. Upon initial presentation, the potential for concomitant life-threatening injuries should be investigated and the patient stabilised as necessary. Critical components of emergency management that have been shown to impact on complication rates include initial classification of the fracture, the prompt instigation of broad-spectrum systemic antibiotic therapy, the use of local antibiotics in select cases and copious wound irrigation using sterile saline. As long as antibiosis is attended to appropriately, small delays in wound debridement do not translate to increased complication rates and waiting for an experienced surgical team is recommended. In cases with no severe tissue damage or contamination, primary wound closure results in lower infection rates and can be recommended. In cases where primary closure is not an option, the wound should be sealed to prevent contamination with nosocomial pathogens.

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An open fracture is defined as any fracture accompanied by a break in the skin that communicates with the fracture or its associated haematoma. They are characterised by contamination of the fracture site with microorganisms, and sometimes the introduction of foreign bodies into the wound (Zalavras, 2003). Moreover, depending on the severity of injury, there may be extensive damage to the soft tissue envelope and bone vascularity, which compromises healing potential. As a result, open fractures are associated with an increased risk of complications such as infection and nonunion and present a therapeutic challenge. The incidence of such complications is directly influenced by the emergency treatment approach and as such, the focus of this article is to help practitioners optimise their emergency management of open fractures and minimise complication rates.

The goals of open fracture management are prevention of infection, fracture union and restoration of function. These goals are best achieved by careful patient and injury assessment, including:

- Fracture classification
- Early administration of systemic antibiotics
- Supplementation with local delivery of antibiotics in severe cases

- Thorough irrigation
- Surgical debridement
- Wound management, with soft tissue coverage if needed
- Stable fracture fixation (Zalavras, 2017) (*Figure 1*).

Pet owners are often anxious about a number of issues such as total length of treatment, the number of anaesthetics required, the quantity and frequency of re-checks, length of hospital stay, the likelihood of returning to an acceptable level of function and the risk of associated complications. The ability of veterinarians to provide guidance on these important issues is dependent upon experience and evidence. Unfortunately, evidence in the small animal literature regarding open fracture management is relatively lacking, prompting extrapolation from human medicine where appropriate. More evidence, specific to small animals, is required, but this review article uses the most recent information available, in conjunction with the most up-to-date data from human medical literature and the personal experience of the authors, to provide a comprehensive, evidence-based guide to emergency management of open fractures.

Patient evaluation and stabilisation

Patients presenting with an open fracture must be carefully assessed. Open fractures are typically the result of high-energy
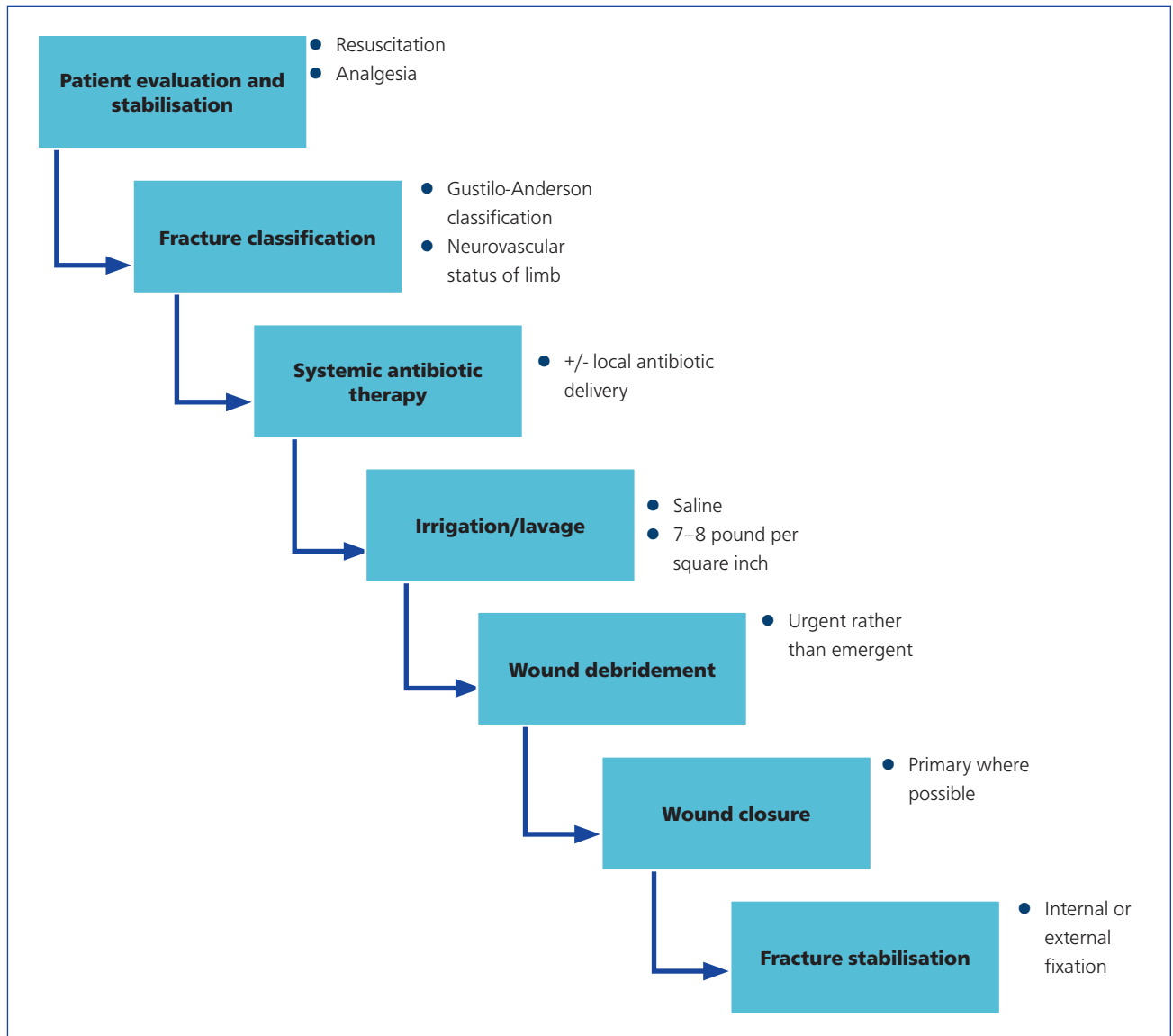
Figure 1. Summary flow chart demonstrating the key steps in the management of open fractures.

trauma (Anderson and Gustilo, 1980), such as automobile accidents, so any potentially life-threatening injuries should be investigated before addressing injuries to the limbs. A detailed and systematic evaluation of all organ systems should be performed, and resuscitation measures initiated where appropriate. Analgesia must also be attended to, although if possible, it is beneficial to withhold opioid medications until after the neurological status of the injured extremity has been assessed. While elaboration on this aspect of care is beyond the scope of this article, it represents a critical component of care which cannot be overlooked. While the assessment and resuscitation is ongoing, and until irrigation, debridement and wound care can be performed, a temporary sterile dressing should be applied to cover the open fracture wound and limit the risk of nosocomial infection.

While high-energy trauma is the archetypal history for open fractures, it remains possible for less severe open fractures to occur with low-energy trauma. As such, all fracture patients

should be assessed carefully for any evidence of an open wound that may communicate with the fracture site. Any soft tissue wound in proximity to a fracture should be treated as an open fracture until proven otherwise. The wounds associated with open fractures may be very small, so the limb may need to be clipped to identify them (*Figure 2*). Timely detection of such wounds, and the instigation of appropriate emergency management, can have a significant impact on the prognosis following such injuries.

Once stabilised, a full examination of the affected limb is performed. As a minimum, emergency management of the open fracture should include:
- Assessment and documentation of the neurovascular status of the injured limb
- Evaluation of the size, location and degree of gross contamination of the open fracture wound, leading to an initial classification of the fracture

- Placement of sterile, water-soluble lubricant within the wound, clipping of the hair widely and cleansing the peri-wound area with a 4% chlorhexidine solution
- Wound irrigation, removal of gross contamination and application of a sterile dressing. A full description of all the potential dressing types available is beyond the scope of this article but depending on wound characteristics, low adherent dressings, semipermeable films, hydrocolloids, alginates (with a secondary dressing), foam dressings or antimicrobial dressings may be appropriate
- Gross realignment of the fractured limb and, for fractures distal to the elbow or stifle, immobilisation with external coaptation. In the majority of cases, a traditional Robert Jones bandage is sufficient to minimise oedema and provide stability, thereby assisting with analgesia. In select cases, this may be reinforced with a splint or bivalved cast for additional stability but this is generally unnecessary as a temporary first-aid measure
- Systemic antibiotic therapy
- Imaging to characterise the fracture so that fixation can be planned

Fracture classification

Open fractures vary in severity depending on the mechanism and energy of injury. Classification systems have been developed to describe the injury, guide treatment, determine prognosis and compare various treatment methods. The classification system of Gustilo and Anderson (1976), subsequently modified by Gustilo et al (1984), has been extensively used in both human and veterinary medicine.

The Gustilo-Anderson classification was the first of its kind; a system through which clinicians could classify open fractures with some degree of reliability. The original article defined type I fractures as those with skin wounds <1 cm in length, which were clean with no overt evidence of contamination or infection (Gustilo and Anderson, 1976). Examples of type I fractures can be seen in *Figure 2*. Type II fractures involved lacerations >1 cm but without extensive soft tissue damage, flaps or avulsions. Another commonly included criterion was that type I fractures were generally created from inside to out, while type II fractures more commonly were created from outside to in. Type III fractures were defined as either segmental, with extensive soft tissue damage, or traumatic amputations. Special consideration was given to those involving gunshot injuries, or those requiring vascular repair.

Although the original description has stood the test of time, studies have highlighted that the way in which the classification was created and validated was not scientifically sound (Trompeter et al, 2020). The pooling of retrospective and prospective data, the use of a single outcome measure (infection) and the highly subjective descriptors for each group highlight significant limitations of the original system (Trompeter et al, 2020). Another limitation was that too many types were grouped together. The original severe type III covered a huge spectrum of injuries and in 1984, Gustilo expanded it into three subgroups. Type IIIa fractures were defined as having severe crushing soft tissue injuries and high degrees of contamination, yet were still closeable. Type IIIb were defined as having a loss of soft tissue cover and typically required

Figure 2. Images of the lateral aspect of the hock of a domestic medium hair cat with an open fracture of the lateral malleolus (left), and the lateral aspect of the humerus of a German Shorthaired Pointer with an open humeral fracture (right). Owing to the small size of the wounds, neither was immediately evident upon physical examination. Wounds only became evident upon clipping of the area.

a soft tissue flap, and type IIIc fractures had an associated arterial injury requiring repair. However, the significant use of subjective language that persists within this classification scheme remains a limitation (Trompeter et al, 2020). Gustilo further evolved the descriptions from the original paper, adding more subjective detail (Gustilo et al, 1990). Descriptions such as 'extensive stripping of periosteum' and 'massive' contamination appear. However, it remains impossible to quantify these terms and again this classification system is let down by subjective interpretation. This explains the major limitation of this system, in that the inter-observer reliability has been shown to be poor with only moderate (kappa 0.59) (Horn and Rettig, 1993) and average agreement of 60% (Brumback and Jones, 1994).

Despite these limitations, the Gustilo–Anderson classification scheme remains the most commonly used in veterinary medicine today (*Figure 3*) and classifications have been shown to determine the risk of infection in humans, ranging from 0–2% for type I open fractures, 2–10% for type II and 10–50% for type III (Gustilo et al, 1984; Patzakis and Wilkins, 1989). Multiple newer classification schemes have been proposed more recently, which may be advantageous for patient management, particularly in communicating accurate expectations to pet owners. A comprehensive review of all classification systems would require a separate article, but two particularly promising schemes warrant brief discussion.

In 2010, the Orthopaedic Trauma Association (OTA) open fracture study group published their classification system for open fractures in humans (OTA, 2010). This system takes into account five characteristic aspects of the pathoanatomy of an open fracture, irrespective of the anatomical site. These five aspects refer to the condition of the skin, muscle, vasculature, bone and degree of contamination. Again, there is some subjectivity and there remains some margin for error or misinterpretation (Agel et al, 2013; Trompeter et al, 2020). Again, there is some subjectivity: 'extensive degloving', 'muscle loss' and 'muscle function' are seen as descriptors and there remains some margin for error
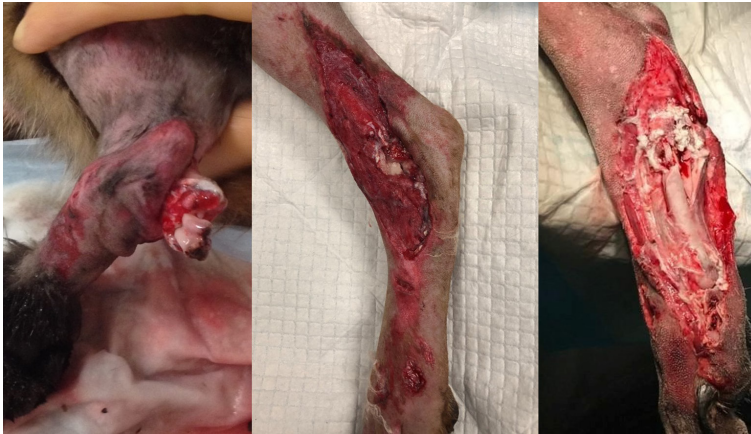
Figure 3. Open fractures affecting the tarsus in one cat (left panel) and two dogs (central and right panels) all of which were graded as Type III open fractures on the Gustilo-Anderson scale. The fracture in the cat (left) was graded as a Type IIIa as, although there was substantial soft tissue trauma and contamination, there was adequate soft tissue to close the wound primarily. The two fractures in dogs (central and right) were both graded as Type IIIb because of the extensive soft tissue loss that precluded primary closure and additional periosteal stripping. The extensive variation that can still exist within one classification using the Gustilo–Anderson classification scheme is evidenced by the two canine cases.

or misinterpretation (Trompeter et al, 2020). Nonetheless, this system was shown to be superior to the Gustilo-Anderson system in relation to the detail of description of open fractures (Ghoshal et al, 2018) and its prognostic value (Hao et al, 2016) and it has been reported to have moderate to excellent interobserver reliability.

The Ganga Hospital Open Injury Severity Score (GHOISS) was proposed in 2006 (Rajasekaran et al, 2006). Many of the shortcomings of the Gustilo-Anderson classification are addressed in this system. With these improvements, the GHOISS can provide a clear prediction of outcome in human patients with the most severe trauma to the lower leg. However, the primary focus of this score has been that of a decision making tool in limb salvage versus amputation, more than a true classification system aiming to offer guidance for reconstruction (Rajasekaran and Sabapathy, 2007). Good specificity and sensitivity (Madhuchandra et al, 2015) and ease of use have been reported, showing it to be simple to use in a clinical context (Rajasekaran et al, 2009). A framework such as this, which draws direct parallels between the type of injury and surgical treatment is, in theory, ideal. While the clear advantage of the GHOISS lies in its help in decision-making, therein also lies its downfall. The system does not function as a generalised classification system for open fractures, nor was it designed to. It was designed to address the poor sensitivity and specificity to predict salvage or outcome in Gustilo-Anderson type IIIa and IIIb fractures in people (Rajasekaran et al 2006). It cannot provide guidelines for surgical management or rehabilitation for less severe injuries (Rajasekaran and Giannoudis, 2012).

A major problem with all the classification systems to date is that they define groups of patients based on complication rates rather than functional outcomes. At present, there are extremely limited data, beyond anecdotal and personal experience, on which

to base long-term patient prognoses. A full return to function represents a far greater measure of success than the presence or absence of infection and this should be considered in the development of future classification schemes (Trompeter et al, 2020). Additionally, while initial classification in the emergency room remains one of the best available ways to guide prognosis, it is important to remember that the true extent and severity of the injury cannot be fully assessed in the emergency room. The degree of contamination and soft tissue crushing injury are important factors for classifying an open fracture, which may be mistakenly overlooked in a wound of small size. Therefore, classification of the open fracture, and the impact on prognosis, should be finalised in the operating room following wound exploration and debridement (Zalavras, 2017).

Systemic antibiotic therapy

Early antibiotic administration is a key principle of open fracture management, because most patients with open fractures have contaminated wounds (Patzakis et al, 1974; Gustilo and Anderson, 1976). Systemic antibiotics should be administered in all patients with open fractures and local antibiotics in select cases. The role of antibiotics in reducing the infection rate in human patients with open fractures was demonstrated by Patzakis et al (1974) in a prospective randomised study. The infection rate when cephalothin was administered before debridement was 2.3% compared with 13.9% when no antibiotics were used.

Early antibiotic administration is very important as delayed administration of the first dose of antibiotic prophylaxis increases the risk of infection markedly (Wilkins and Patzakis, 1991). Patzakis and Wilkins (1989) initially reported that a delay longer than 3 hours post-injury was associated with increased risk of infection and subsequent animal and clinical studies have corroborated these findings. Penn-Barwell et al (2012a) used a rat femur model with a defect contaminated with *Staphylococcus aureus* and found that delaying antibiotics to 6 or 24 hours had a detrimental effect on the infection rate regardless of the timing of surgery. Lack et al (2015), in a retrospective study of 137 type III open tibial fractures in people, demonstrated that administration of antibiotics beyond 66 minutes from injury was an independent risk factor for infection with an odds ratio of almost four.

The optimal length of antibiotic therapy remains controversial. Evidence in the human field suggests that antimicrobial cover should commence within 3 hours of injury and should continue at least until first debridement. Antibiotics should continue to be administered until primary closure of the wound, or for a total of 72 hours, whichever is sooner (Lenarz et al, 2010; Venkatadass et al, 2017). A recent meta-analysis of comparative studies on antibiotic protocols demonstrated insignificant differences in the incidence of infection-associated complications with prolonged therapy (>72 hours), or a short course (<72 hours), irrespective of fracture severity. Comparable results were achieved when comparing even shorter courses (24–48 hours) to prolonged therapy (Messner et al, 2017). The recommendation in people is that antibiotic cover should not be extended beyond 72 hours unless there is an indicated need, such as the development of sepsis. An additional 2-day administration of antibiotics is
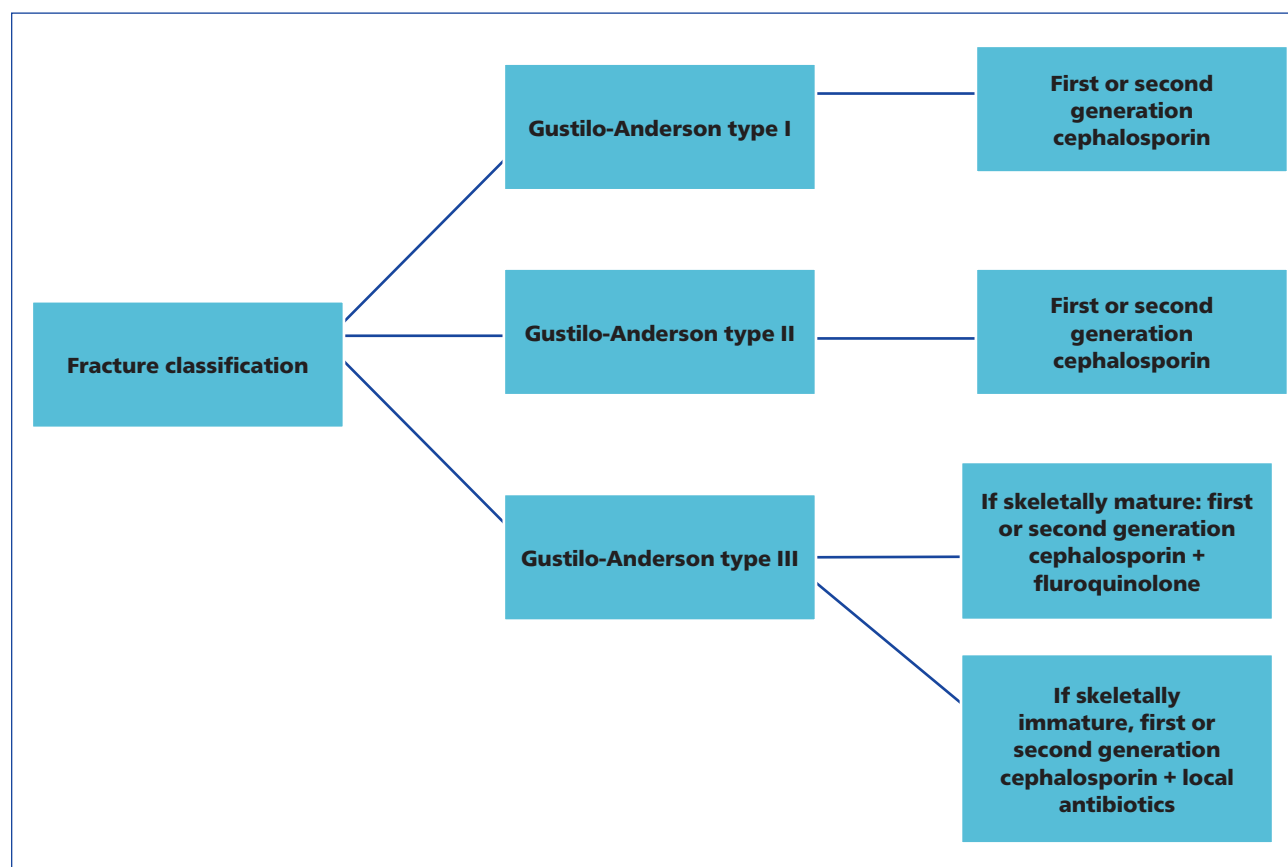
Figure 4. Summary flow chart demonstrating the decision-making process regarding antibiosis in open fracture patients.

recommended for subsequent surgical procedures, such as repeat debridement and wound closure (Patzakis and Wilkins, 1989; Templeman et al, 1998).

Although the necessity of antibiotics has been definitively established, there is no firm consensus on the optimal choice of agents and specifically, on the necessity of gram-negative coverage, especially for less severe injuries (Zalavras, 2017). In severe, type III fractures, there is wide agreement that gram-positive and gram-negative coverage is needed, and this is usually provided by a first-generation cephalosporin and historically, an aminoglycoside in people (Patzakis and Wilkins, 1989; Hoff et al, 2011; Luchette et al, 2000; Templeman et al, 1998; Zalavras et al, 2007). For less severe, type I and II open fractures, the necessity for gram-negative coverage remains controversial, with some authors recommending administration of a cephalosporin only (Hoff et al, 2011; Luchette et al, 2000; Templeman et al, 1998), and others maintaining that combination therapy is warranted (Patzakis and Wilkins, 1989; Zalavras et al, 2007). Some of the variation in these study findings may result from misclassification of the open fracture wound. As noted earlier, the severity of injury will be better appreciated in the operating room following wound exploration and debridement and when classified in the emergency room, it is possible that type IIIa fractures with a small open wound may be misclassified as a type I or II open fracture. As a result, a type IIIa fracture may

be treated inappropriately with cephalosporin only, leading to a higher risk for infection.

Aminoglycosides for gram-negative coverage have fallen out of favour because of associated dose-dependent nephrotoxicity and irreversible ototoxicity. While these present less of a concern now that shorter courses of antibiotics are being recommended, alternatives have been considered and their use has become more widespread. Fluoroquinolones have been proposed as an alternative to aminoglycosides based on their broad-spectrum antimicrobial coverage, bactericidal properties, oral administration and good tolerance. A randomised prospective study in people showed that ciprofloxacin as a single agent in type I and II open fractures resulted in a similar infection rate (6%) compared with combination therapy with a cephalosporin and an aminoglycoside (Patzakis et al, 2000). However, in type III fractures, ciprofloxacin was associated with a higher infection rate of 31%, compared with 7.7% in the combination therapy group. While fluoroquinolones are commonly used as an alternative to aminoglycosides for open fracture management in companion animals, they do have a dose-dependent cytotoxic effect on bone healing in in vivo studies in rats (Huddleston et al, 2000), with histology indicating inhibition of endochondral ossification. Therefore, the use of fluoroquinolones may be contraindicated in juvenile open fracture patients (Garner et al, 2020).

Based on the aforementioned data or type I and II open fractures, either first- or second-generation cephalosporin is used
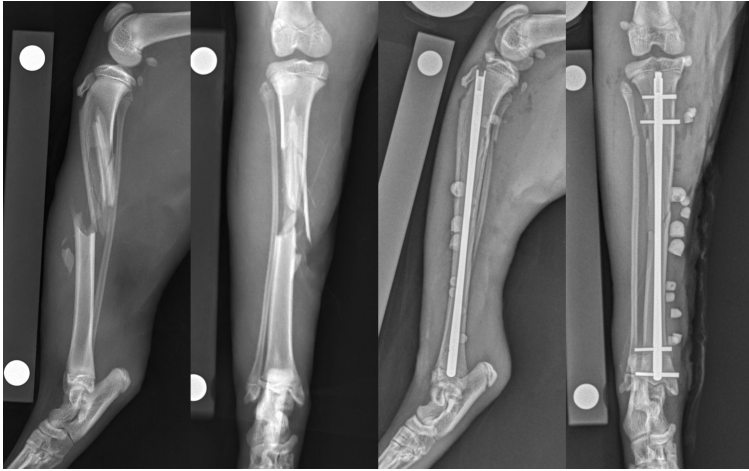
Figure 5. Mediolateral and craniocaudal radiographs of the left tibia, preoperatively (left) and postoperatively (right) following stabilisation of a Gustilo-Anderson Type III open fracture in a 7-month-old cat including primary wound closure. Vancomycin-impregnated calcium-sulphate beads can be seen on the immediate postoperative views. These were used in this case, in conjunction with a cephalosporin, to provide broad-spectrum coverage without affecting bone development in this skeletally immature patient. The use of local antibiotic therapy in conjunction with systemic antibiotic therapy in this case was elected to allow high concentrations of antibiotic to be delivered rapidly to the bone and surrounding tissues with limited risk of systemic absorption and consequent side effects.

by the authors. For type III open fractures in skeletally mature animals, a combination of cephalosporin and fluoroquinolone is used to provide both gram-positive and gram-negative coverage. In the face of a type III open fracture in a juvenile animal, where the use of fluoroquinolone prompts concern, a first- or second-generation cephalosporin in conjunction with local antibiotic administration is used to provide broad-spectrum coverage. This decision-making process is detailed in *Figure 4*.

Wound cultures obtained at patient presentation or intraoperatively do not help select the optimal antibiotic regimen, because they fail to identify the organism causing a subsequent infection in most cases (Fischer et al, 1991; Lee, 1997). Depending on the study, only 18–26.9% of infections that develop in people following open fractures are caused by an organism identified by perioperative cultures (Patzakis et al, 2000; Bosse et al, 2017). Studies have also investigated the effect of timing of culture and one such study reported that pre-debridement cultures identified the infecting organism only 22% of the time, with post-debridement cultures identifying the causative organism 42% of the time (Lee 1997). Based on this study by Lee et al (1997), post-debridement cultures would be preferable to pre-debridement cultures, but their accuracy remains suboptimal. In most cases, infections are not caused by the organisms initially present in the wound, but by nosocomial organisms that subsequently contaminate it (Zalavras, 2017). Indeed, one study reported that 92% of open fracture-associated infections were caused by bacteria acquired while the patient was hospitalised (Carsenti-Etesse et al, 1999). As such, routine cultures at the time of injury are not recommended (Garner et al, 2020). However, there is consistent agreement that

cultures should be performed if active infection is noted during the healing process, in order to guide antibiotic use.

Local antibiotics

Local delivery of antibiotic therapy is commonly used as an adjunct to systemic antibiotics in people with open fractures and is becoming more common in veterinary patients also. A commonly used delivery vehicle is polymethylmethacrylate (PMMA) cement, which can be manually moulded by the surgeon into beads with diameters ranging from 5–10mm. Several antibiotics including aminoglycosides, vancomycin and cephalosporins can be successfully incorporated into PMMA cement for local delivery.

Morgenstern et al (2018) performed a systemic literature review with a pooled data analysis investigating local antibiotic prophylaxis in people. They compared standard systemic antibiotic treatment with standard antibiotic prophylaxis plus additional local antibiotic prophylaxis. In 2738 patients, an overall infection rate of 7.9% was determined. Patients treated with additional local antibiotics suffered infection in 4.6% of cases, while infection occurred in 16.5% of all patients with only systemic antibiotic prophylaxis. Owing to heterogeneity within the groups, a low level of evidence in the primary studies and a potential risk of bias, it was advised to interpret these results with caution (Morgenstern et al, 2018).

Since PMMA bead chains are not resorbable, removal of the beads requires a second surgery. Bioabsorbable delivery vehicles such as calcium sulphate, collagen fleeces and phospholipid gels appear to be promising alternatives (Sørensen et al, 1990; McKee et al, 2002; Penn-Barwell et al, 2014), although there is a limited evidence-base for their use in open fractures. Only two case series in humans have been published, using calcium sulphate pellets as antibiotic carriers in open fracture treatment (Cai et al, 2010; Helgeson et al, 2009), and to the authors' knowledge, there is only one small case series in dogs and cats that evaluates the use of antibiotic-impregnated calcium sulphate beads (Peterson et al, 2021). In this study 16 cases were included, 10 of which were treated therapeutically and six of which were treated prophylactically. Infections did not occur in any of the six cases treated prophylactically, while infection resolved in 6 out of the 10 cases treated therapeutically. Major complications associated with bead implantation were not encountered (Peterson et al, 2021). Further studies are certainly required before definitive recommendations can be made in humans or in companion animals, but implantation does appear to be well tolerated. The authors have used antibiotic-impregnated calcium sulphate beads during stabilisation of open fractures in a small number of cases (*Figure 5*), none of which have developed infection to date and as such, the preliminary findings appear to mirror those of the small case series mentioned above.

Modern bioabsorbable carriers are able to elute therapeutic concentrations of antibiotic for over seven days, based on pharmacokinetic studies (Stockley et al, 2008, Howlin et al, 2015; Stravinskas et al, 2016; Van Moojen et al, 2008). Hence, local antibiotic therapy may allow for shorter courses of systemic antibiotics to be used for orthopaedic infection (Buchholz et al, 1981; Calhoun et al, 1993; Stockley et al, 2008; Klemm,

2001; Taggart et al, 2002; Hoad-Reddick et al, 2004), limiting the frequency of side effects, cost and selection pressure for antimicrobial resistance. Shorter courses of systemic medications are also likely to improve client compliance, which in veterinary medicine is often suboptimal (Adams et al, 2005; Papich, 2013). A randomised, controlled open-label non-inferiority trial evaluating the duration of systemic antibiotics in adults with orthopaedic infection treated operatively and with local antibiotic therapy is ongoing in humans, comparing short or long systemic antibiotic regimes (Dudareva et al, 2019). If a strategy using local antibiotics in combination with a short systemic antibiotic regime is shown to be non-inferior, this will be advantageous for the patient, as well as contributing to antimicrobial stewardship.

Irrigation or lavage

Irrigation or lavage serves to decrease bacterial load and remove foreign material from the wound, another pivotal component of open fracture wound management. While most protocols recommend copious volumes of irrigation fluid, despite intensive preclinical and clinical research, no reliable data for the appropriate volume of lavage solution exists (Rupp et al, 2020).

Historically, there has been substantial debate regarding exactly which solution should be used for irrigation and at what pressure. The fluid lavage of open wounds trial (FLOW) was initiated to answer these questions, in a multicentre prospective randomised controlled trial, including 2447 patients at 41 sites (Bhandari et al, 2015). Three different wound irrigation pressures, as well as saline versus castile soap for irrigation solution, were compared. The primary endpoint was reoperation for the promotion of wound or bone healing and treatment of wound infection within a follow-up period of 12 months. Reoperation rates were not found to depend on irrigation pressures, but reoperation was more frequent after the use of a soap irrigant (14.8%) compared to saline (11.6%) (Bhandari et al, 2015). Patient-reported outcomes during 12-month follow-up did not depend on irrigation solutions or irrigation pressure (Sprague et al, 2018). Thus, the potential drawbacks of high pressure irrigation with bacterial seeding into the intramedullary canal (Bhandari et al, 1998) and myonecrosis of soft tissue (Chiaramonti et al, 2017) evidenced in animal experiments could not be proven to be clinically relevant and low pressure irrigation seems to be a viable and economical treatment option. This research indicates that the lavage pressures commonly adopted in veterinary medicine, of 7-8 pounds per square inch (psi), appear to be appropriate; this pressure can be reliably achieved using a 1-litre fluid bag with an external pressure sleeve at 300mmHg. While the use of large syringes and needles likely produces pressures substantially higher than 8psi, given the lack of significance of irrigation pressure in the FLOW trial mentioned above, this is not considered to be contraindicated.

Other authors have proposed the use of antibacterial or antiseptic solutions for wound irrigation, but this is no longer recommended as antiseptic solutions may be toxic to host cells and are better avoided (Bhandari et al, 2001). In a rat model of open fracture, when saline and the antiseptics iodophor and hydrogen peroxide were compared for irrigation, saline was found to be comparably effective and superior in minimising

wound inflammation compared to both antiseptics (Cheng et al, 2015). Toxic effects against host tissue have been reported for chlorhexidine as well, in addition to a rebound effect of bacterial growth caused by chlorhexidine-induced tissue damage (Penn-Barwell et al, 2012b). When considering the use of antibiotics in irrigation solutions, clinical data comparing human patient outcomes such as fracture union, development of infection and healing of soft tissue wounds did not demonstrate an advantage of bacitracin solution. Indeed, significantly more wound healing disturbances were noted in the antibiotic additive group (Anglen et al, 2005).

Reasonable alternatives to saline appear to be distilled water, and even tap water. Comparing saline with distilled water in a clinical prospective trial (Olufemi et al, 2017) and with tap water in a preclinical porcine open fracture model (Penn-Barwell et al, 2012b), demonstrated comparable outcomes for both compared to saline solution. For open fracture cases with limited contamination, the authors use sterile isotonic saline in large volumes for wound irrigation. For severely contaminated cases, initial irrigation is carried out with tap water, in order to limit cost to the client, followed by large quantities of sterile saline for the final stages.

Debridement

Thorough surgical debridement plays a critical role in the management of open fractures (Swiontkowski, 1989; Tetsworth and Cierny, 1999). Devitalised tissue and foreign material promote the growth of microorganisms and constitute a barrier for the host's defense mechanisms and therefore should be removed. Debridement should be performed in the operating room. Surgical extension of the wound allows assessment of the degree of soft tissue damage and contamination. Skin and subcutaneous tissue are sharply debrided back to bleeding edges. Muscle is debrided until viable tissue is identified by its bleeding, colour and contractility. A repeat debridement can be performed after 24–48 hours based on the degree of contamination and soft tissue damage. The goal is a clean wound with viable tissues and no infection. In injuries requiring flap coverage, debridement should also be repeated at the time of the soft tissue procedure (Zalavras, 2017).

Traditionally, debridement has been recommended within 6 hours of presentation. The rationale behind this figure is believed to date back to early studies on microorganism load following contamination (Friedrich, 1898; Werner et al, 2008). In more recent literature, the 6-hour window does not show a clear evidence base. Many human studies do not show a significant difference in the incidence of infection, regardless of whether debridement is performed early or is delayed, as long as antibiosis is attended to appropriately (Halawi and Morwood, 2015; Ali et al, 2013; Werner et al, 2008; Schenker et al, 2012). Patzakis and Wilkins (1989) reported that the infection rate was similar in open fracture wounds debrided within (6.8%) and after (7.1%) 12 hours of injury and concluded that elapsed time from injury to debridement is not a critical factor for development of infection in patients receiving antibiotic therapy. Schenker et al (2012) performed a meta-analysis on the effect of timing on the overall risks of infection in open long

bone fractures in people and again, found no difference in the rate of infection following delayed debridement irrespective of injury severity or anatomical location. Although bacterial populations in an untreated contaminated wound do increase over time, it appears early antibiotic administration and thorough surgical debridement can effectively reduce contamination. As a result, small delays in surgical management do not appear to translate to increased infection rates and may allow for stabilisation of the patient, as well as for treatment of the patient by experienced surgical teams with all the necessary equipment available (Zalavras, 2017).

Wound closure

The optimal timing of wound closure also remains controversial. Historically, concerns about deep infection by anaerobic organisms led to the practice of not closing wounds in open fractures (Trueta, 1976). Delayed wound closure prevents anaerobic conditions in the wound, permits drainage, allows for repeat debridement at 24–48 hours and gives time for tissues of questionable viability to declare themselves.

However, in recent years, primary wound closure has been proven to be beneficial in people, resulting in lower deep infection and nonunion rates. Scharfenberger et al (2017) demonstrated fewer deep infections (4% vs 9%) and nonunions (13% vs. 29%) in Gustilo-Anderson type I-IIIa fractures when comparing immediate wound closure to delayed soft tissue coverage. Jenkinson et al (2014) described similar results, with an infection rate of 4.1% in fractures treated with immediate closure, compared to 17.8% in cases treated with primary delayed closure. For fractures requiring soft tissue reconstruction by flap coverage, low infection rates of 1.5% were reported after flap reconstruction within 72 hours (Godina, 1986), compared to an infection rate of 60% in similar injuries treated via flap coverage after 7 days (Olesen et al, 2015).

Based on the literature, primary closure of open fracture wounds is recommended in select cases, provided there is no severe tissue damage or contamination, early administration of antibiotics has taken place, meticulous debridement has been executed and the wound edges can be approximated without tension (Zalavras, 2017). In such cases, where necessary, the use of muscle flaps appears to be superior to the use of fasciocutaneous flaps (Harry et al, 2008). Delayed closure remains recommended in cases with extensive soft tissue damage and gross contamination, in patients presenting with a considerable delay, in wounds with tissues of questionable viability and in wounds that cannot be approximated without tension (Zalavras, 2017). In cases where delayed wound closure is elected, the wound should not be left open to the outside environment, to prevent contamination with nosocomial pathogens. One option to seal the wound is a technique that involves the insertion of antibiotic-impregnated PMMA beads into the open fracture wound, which is then sealed by a semipermeable barrier; the so-called 'bead-pouch technique'. Negative pressure wound therapy can also be used (Okike and Bhattacharyya, 2007).

Fracture stabilisation

As the focus of this article is on the emergency management of open fractures, significant discussion of stabilisation is beyond the scope, although stabilising an open fracture remains an important component of management. Stability at the fracture site prevents further injury to the soft tissues and enhances the host response to contaminating organisms (Worlock et al, 1994). Fracture stability facilitates wound and patient care and allows early motion and functional rehabilitation of the extremity. Fracture stabilisation can be accomplished with interlocking nails, plate and screw fixation or external fixation. Selection among these methods depends upon careful evaluation of the fracture, soft tissue and patient characteristics. More than one method may be applicable to a specific injury.

Future directions

While standards on antibiotic cover and management of soft-tissue injuries have helped to reduce the incidence of infection and consequent complications following open fracture, the risk remains higher than for closed injuries. Injuries complicated by infection are more likely to require further operative management (Zelle and Boni, 2015) and experience complications with bony union. As such, investigation of adjunctive therapies with the potential to further reduce complication rates and enhance functional outcomes are ongoing.

One promising area is in the use of recombinant human bone morphogenetic proteins (rhBMP) 2 and 7, which have shown promise in the treatment of open fractures in people. The use of rhBMP-2 enclosed in an absorbable collagen sponge has been shown to be safe and efficacious in the management of open fractures, with a lower need for secondary surgical intervention, faster fracture healing and fewer infections seen (Govender et al, 2002; Swiontkowski et al, 2006). This may hold promise in the future, pending further research for both people and companion animals.

Another area of ongoing research is that of antimicrobial functionalising of the implant surface, with a view to avoiding the formation of biofilm on metallic implants. Different antimicrobial coatings such as poly(d, l-lactide), silver and povidone-iodine have been tested in clinical studies (Schmidmaier et al, 2006, 2017; Hardes et al, 2010; Fuchs et al, 2011; ; Tsuchiya et al, 2012; Shirai et al, 2014; Metsemakers et al, 2015). Except implants functionalised with gentamicin coatings, none of the clinically tested coatings have been used for open fractures. Two case series in people reported favourable outcomes in 8 and 19 patients treated for open tibial shaft fractures, respectively (Schmidmaier et al, 2006; Fuchs et al, 2011). Lower infection rates for silver coated megaprostheses in tumoral prosthesis surgery (Hardes et al, 2010) and salvage revision arthroplasty (Zajonz et al, 2017) suggest a clinical application of silver coated implants in fracture care. However, no clinical studies of silver coated implants in fracture care exist, yet. Additional research is required in this area but it may present a promising route to lowering complication rates for open fracture management.

Conclusions

Open fractures are associated with an increased risk of complications, such as infection and nonunion, and appropriate emergency management is critical to reducing these risks. The

early instigation of broad-spectrum antibiosis is essential, as delays in administration directly correlate with increased infection rates. While debate persists regarding the optimal agent choice, for grade I and II fractures coverage with first- or second-generation cephalosporins appears to be appropriate, while fluoroquinolone should be added for type III fractures. Local antibiotics may play a valuable role in select cases based on the limited evidence presented and the ready availability of resorbable delivery vehicles renders their use inherently more attractive. Wound irrigation represents a pivotal component of emergency management and high-quality research indicates that sterile saline, at any pressure between 2 and 20 psi, leads to the lowest infection and reoperation rates, although distilled water or even tap water may represent reasonable alternatives. Provided appropriate systemic antibiosis has been administered, small delays in wound debridement do not translate to increased complication rates, so delaying this until an experienced surgical team is available is recommended. As the majority of open fracture infections appear to be caused by nosocomial bacteria that contaminate the wound, rather than bacteria present at the time of injury, wound cultures are generally not indicated to guide antibiotic choice and primary wound closure should be performed where appropriate. In cases with extensive soft tissue damage, gross contamination, tissues of questionable viability, or where wounds cannot be closed without tension, delayed closure remains the prudent approach, but every effort should be made to seal the wound from the external environment to limit contamination with nosocomial pathogens.

Conflict of interest:

The authors declare that there are no conflicts of interest.

References

Adams VJ, Campbell JR, Waldner CL, Dowling PM, Shmon CL Evaluation of client compliance with short-term administration of antimicrobials to dogs. J Am Vet Med Assoc. 2005;226:567–574. https://doi.org/10.2460/javma.2005.226.567

Agel J, Evans AR, Marsh JL et al. The OTA open fracture classification: a study of reliability and agreement. J Orthop Trauma. 2013;27(7):379–385. https://doi.org/10.1097/BOT.0b013e3182820d31

Ali AM, Noyes D, Cogswell LK. Management of open fractures of the lower limb. Br J Hosp Med (Lond). 2013;74:577–580. https://doi.org/10.12968/hmed.2013.74.10.577

Anderson JT, Gustilo RB. Immediate internal fixation in open fractures. Orthop Clin North Am. 1980;11:569–578. https://doi.org/10.1016/S0030-5898(20)31458-9

Anglen JO. Comparison of soap and antibiotic solutions for irrigation of lower-limb open fracture wounds. A prospective, randomized study. J Bone Joint Surg [Am]. 2005;87(A):1415–1422.

Bhandari M, Adili A, Lachowski RJ. High pressure pulsatile lavage of contaminated human tibiae: an in vitro study. J Orthop Trauma. 1998;12(7):479–484 https://doi.org/10.1097/00005131-199809000-00009

Bhandari M, Adili A, Schemitsch EH. The efficacy of low-pressure lavage with different irrigating solutions to remove adherent bacteria from bone. J Bone Joint Surg Am. 2001;83(3):412–419. https://doi.org/10.2106/00004623-200103000-00014

Bhandari M, Jeray KJ, Petrisor BA et al. FLOW Investigators. A trial of wound irrigation in the initial management of open fracture wounds. N Engl J Med. 2015;373:2629–2641. https://doi.org/10.1056/nejmoa1508502

Bosse MJ, Murray CK, Carlini AR et al. METRC: Assessment of severe extremity wound bioburden at the time of definitive wound closure or coverage: Correlation with subsequent postclosure deep wound infection (METRC bioburden study. J Orthop Trauma. 2017;31(Suppl 1):S3–S9. https://doi.org/10.1097/BOT.0000000000000805

Brumback RJ, Jones AL. Interobserver agreement in the classification of open fractures of the tibia. The results of a survey of two hundred and forty-five orthopaedic surgeons. J Bone Joint Surg Am. 1994;76(8):1162–1166 https://doi.org/10.2106/00004623-199408000-00006

Buchholz HW, Elson RA, Engelbrecht E, Roettger LH et al. Management of deep infection of total hip replacement. J Bone Joint Surg Br. 1981;63:342–353. https://doi.org/10.1302/0301-620X.63B3.7021561

Cai X, Han K, Cong X et al. The use of calcium sulfate impregnated with vancomycin in the treatment of open fractures of long bones: a preliminary study. Orthopedics. 2010;33(3). https://doi.org/10.3928/01477447-20100129-17

Calhoun JH, Henry SL, Anger DM, Cobos JA, Mader JT. The treatment of infected nonunions with gentamicin-polymethylmetacrylate antibiotic beads. Clin Orthop Relat Res. 1993;295:23–27

Carsenti-Etesse H, Doyon F, Desplaces N et al. Epidemiology of bacterial infection during management of open leg fractures. Eur J Clin Microbiol Infect Dis. 1999;18:315–323. https://doi.org/10.1007/PL00015012

Cheng Q, Zhang XF, Di DH, Zhao GY, Cui XW. Efficacy of different irrigation solutions on the early debridement of open fracture in rats. Exp Ther Med. 2015;9:1589–1592. https://doi.org/10.3892/etm.2015.2325

Chiaramonti AM, Robertson AD, Nguyen TP et al. Pulsatile lavage of musculoskeletal wounds causes muscle necrosis and dystrophic calcification in a rat model. J Bone Joint Surg Am. 2017;99:1851–1858. https://doi.org/10.2106/JBJS.17.00330

Dudareva M, Kumin M, Vach W et al. Short or long antibiotic regimes in orthopaedics (SOLARIO): a randomised controlled open-label non-inferiority trial of duration of systemic antibiotics in adults with orthopaedic infection treated operatively with local antibiotic therapy. Trials. 2019;20:693. https://doi.org/10.1186/s13063-019-3832-3

Fischer MD, Gustilo RB, Varecka TF. The timing of flap coverage, bone-grafting, and intramedullary nailing in patients who have a fracture of the tibial shaft with extensive soft-tissue injury. J Bone Joint Surg Am. 1991;73(9):1316–1322

Friedrich P. Die aseptische Versorgung frischer wunden, unter mittheilung von their-versuchen uber die Auskeimungszeit von infectionserregem in frischen wunden. Arch Clin Chir. 1898;57

Fuchs T, Stange R, Schmidmaier G, Raschke MJ. The use of gentamicin-coated nails in the tibia: preliminary results of a prospective study. Arch Orthop Trauma Surg. 2011;131:1419–1425. https://doi.org/10.1007/s00402-011-1321-6

Garner MR, Sethuraman SA, Schade MA, Boateng H. Antibiotic prophylaxis in open fractures: evidence, evolving issues and recommendations. J Am Acad Orthop Surg. 2020;28(8):309–315. https://doi.org/10.5435/JAAOS-D-18-00193

Ghoshal A, Enninghorst N, Sisak K, Balogh ZJ. An interobserver reliability comparison between the Orthopaedic Trauma Association's open fracture classification and the Gustilo and Anderson classification. Bone Joint J. 2018; 100B(2):242–246. https://doi.org/10.1302/0301-620X.100B2.BJJ-2017-0367.R1

Godina M. Early microsurgical reconstruction of complex trauma of the extremities. Plast Reconstr Surg. 1986;78:285–292. https://doi.org/10.1097/00006534-198609000-00001

Govender S, Csimma C, Genant HK, Valentin-Opran A. B-EiSfTTS Group. Recombinant human bone morphogenetic protein-2 for treatment of open tibial fractures: a prospective, controlled, randomized study of four hundred and fifty patients. J Bone Joint Surg Am. 2002;84:2123–2134. https://doi.org/10.2106/00004623-200212000-00001

Gustilo RB, Anderson JT. Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: retrospective and prospective analyses. J Bone Joint Surg Am. 1976;58(4):453–458. https://doi.org/10.2106/00004623-197658040-00004

Gustilo RB, Mendoza RM, Williams DN. Problems in the management of type III (severe) open fractures: a new classification of type III open fractures. J Trauma. 1984;24(8):742–746. https://doi.org/10.1097/00005373-198408000-00009

<div class="key-points">

KEY POINTS:

- Open fractures are associated with an increased risk of complications, such as infection and non-union, and appropriate emergency management can significantly reduce these risks
- The most commonly used classification scheme for open fractures in veterinary medicine remains the Gustilo-Anderson classification. While limitations of this scheme are recognised, classification does determine the risk of infection and as such, can be used as a basis to discuss prognosis with owners
- Early instigation of broad-spectrum antibiosis is essential in animals with open fractures as delays in administration directly correlate with increased infection rates
- Neither pre- nor post-debridement wound cultures are recommended to guide antibiotic choice as the majority of open fracture infections appear to be caused by nosocomial bacteria that contaminate the wound, rather than bacteria present at the time of injury
- Wound irrigation is a critical component of emergency open fracture management with sterile saline representing the ideal irrigation agent at any pressure being 2–20 pounds per square inch.

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Gustilo RB, Merkow RL, Templeman D. The management of open fractures. J Bone Joint Surg Am. 1990;72(2):299–304

Halawi MJ, Morwood MP. Acute management of open fractures: an evidence-based review. Orthopedics. 2015;38(11):E1025-33. https://doi.org/10.3928/01477447-20151020-12

Hao J, Cuellar DO, Herbert B et al. Does the OTA open fracture classification predict the need for limb amputation? A retrospective observational cohort study on 512 patients. J Orthop Trauma. 2016;30(4):194–198. https://doi.org/10.1097/BOT.0000000000000479

Hardes J, Von EC, Streitbuerger A et al. Reduction of periprosthetic infection with silver-coated megaprostheses in patients with bone sarcoma. J Surg Oncol. 2010;1 01:389–395. https://doi.org/10.1002/jso.21498

Harry LE, Sandison A, Paleolog EM et al. Comparison of the healing of open tibial fractures covered with either muscle or fasciocutaneous tissue in a murine model. J Orthop Res. 2008;26:1238–1244. https://doi.org/10.1002/jor.20649

Helgeson CMD, Potter MBK, Tucker CCJ, Frisch LHM, Shawen LSB. Antibiotic-impregnated calcium sulfate use in combat-related open fractures. Orthopedics. 2009;32(5):323. https://doi.org/10.3928/01477447-20090501-03

Hoad-Reddick DA, Evans CR, Norman P, Stockley I. Is there a role for extended antibiotic therapy in a two-stage revision of the infected knee arthroplasty? J Bone Joint Surg Br. 2004;87:171–174. https://doi.org/10.1302/0301-620X.87B2.15640

Hoff WS, Bonadies JA, Cachecho R et al. East practice management guidelines work group: update to practice management guidelines for prophylactic antibiotic use in open fractures. J Trauma. 2011;70(3):751–754. https://doi.org/10.1097/TA.0b013e31820930e5

Horn BD, Rettig ME. Interobserver reliability in the Gustilo and Anderson classification of open fractures. J Orthop Trauma. 1993;7(4):357–360

Howlin RP, Brayford MJ, Webb JS et al. Antibiotic-loaded synthetic calcium sulfate beads for prevention of bacterial colonization and biofilm formation in periprosthetic infections. Antimicrob Agents Chemother. 2015;59:111–120. https://doi.org/10.1128/AAC.03676-14

Huddleston PM, Steckelberg JM, Hanssen AD, Rouse MS et al. Ciprofloxacin inhibition of experimental fracture healing. J Bone Joint Surg Am. 2000;82:161–173

Jenkinson RJ, Kiss A, Johnson S et al. Delayed wound closure increases deep infection rate associated with lower-grade open fractures: a propensity-matched cohort study. J Bone Joint Surg Am. 2014;96(5):380–386. https://doi.org/10.2106/JBJS.L.00545

Klemm K. The use of antibiotic-containing bead chains in the treatment of chronic bone infections. Clin Microbiol Infect. 2001;7:23–31 https://doi.org/10.1046/j.1469-0691.2001.00186.x

Lack WD, Karunakar MA, Angerame MR et al Type III open tibia fractures: immediate antibiotic prophylaxis minimizes infection. J Orthop Trauma. 2015;29(1):1–6. https://doi.org/10.1097/BOT.0000000000000262

Lee J. Efficacy of cultures in the management of open fractures. Clin Orthop Relat Res. 1997;339:71–75 https://doi.org/10.1097/00003086-199706000-00010

Lenarz CJ, Watson JT, Moed BR et al. Timing of wound closure in open fractures based on cultures obtained after debridement. J Bone Joint Surg [Am]. 2010;92-A:1921–1926. https://doi.org/10.2106/jbjs.i.00547

Luchette FA, Bone LB, Born CT et al. Practice management guidelines for prophylactic antibiotic use in open fractures. 2000. http://www.east.org/education/practice-management-guidelines/open-fractures-prophylacticantibiotic-use-in-update (accessed 17 September 2021)

Madhuchandra P, Rafi M, Devadoss S, Devadoss A. Predictability of salvage and outcome of Gustilo and Anderson type-IIIA and type-IIIB open tibial fractures using Ganga Hospital scoring system. Injury. 2015; 46(2):282–287. https://doi.org/10.1016/j.injury.2014.11.003

McKee MD, Wild LM, Schemitsch EH et al. The use of an antibiotic-impregnated, osteoconductive, bioabsorbable bone substitute in the treatment of infected long bone defects: early results of a prospective trial. J Orthop Trauma. 2002;16(9):622–627. https://doi.org/10.1097/00005131-200210000-00002

Messner J, Papakostidis C, Giannoudis PV, Kanakaris NK. Duration of administration of antibiotic agents for open fractures: meta-analysis of the existing evidence. Surg Infect (Larchmt). 2017;18:854–867. https://doi.org/10.1089/sur.2017.108

Metsemakers W, Reul M, Nijs S. The use of gentamicin-coated nails in complex open tibia fracture and revision cases: a retrospective analysis of a single centre case series and review of the literature. Injury. 2015;46(12):2433–2437. https://doi.org/10.1016/j.injury.2015.09.028

Morgenstern M, Vallejo A, McNally M et al. The effect of local antibiotic prophylaxis when treating open limb fractures: a systematic review and meta-analysis. Bone Joint Res. 2018;7(7):447–456. https://doi.org/10.1302/2046-3758.77.BJR-2018-0043.R1

Okike K, Bhattacharyya T. Trends in the management of open fractures. A critical analysis. J Bone Joint Surg (Am). 2007;88:2739–2748. https://doi.org/10.2106/00004623-200612000-00025

Olesen UK, Juul R, Bonde CT et al. A review of forty-five open tibial fractures covered with free flaps. Analysis of complications, microbiology and prognostic factors. Int Orthop. 2015;39(6):1159–1166. https://doi.org/10.1007/s00264-015-2712-z

Olufemi OT, Adeyeye AI. Irrigation solutions in open fractures of the lower extremities: evaluation of isotonic saline and distilled water. SICOT-J. 2017;3:7. https://doi.org/10.1051/sicotj/2016031

Orthopaedic Trauma Association. Open fracture study group: a new classification scheme for open fractures. J Orthop Trauma. 2010; 24:457–464

Papich MG. Antibiotic treatment of resistant infections in small animals. Vet Clin North Am Small Anim Pract. 2013;43:1091–1097. https://doi.org/10.1016/j.cvsm.2013.04.006

Patzakis MJ, Harvey JP Jr, Ivler D. The role of antibiotics in the management of open fractures. J Bone Joint Surg Am. 1974;56(3):532–541

Patzakis MJ, Wilkins J. Factors influencing infection rate in open fracture wounds. Clin Orthop Relat Res. 1989;(243):36–40

Patzakis MJ, Bains RS, Lee J et al. Prospective, randomized, double-blind study comparing single-agent antibiotic therapy, ciprofloxacin, to combination antibiotic therapy in open fracture wounds. J Orthop Trauma. 2000;14(8):529–533. https://doi.org/10.1097/00005131-200011000-00002

Penn-Barwell JG, Murray CK, Wenke JC. Early antibiotics and debridement independently reduce infection in an open fracture model. J Bone Joint Surg Br. 2012a;94(1):107–112. https://doi.org/10.1302/0301-620X.94B1.27026

Penn-Barwell JG, Murray CK, Wenke JC. Comparison of the antimicrobial effect of chlorhexidine and saline for irrigating a contaminated open fracture model. J Orthop Trauma. 2012b;26(12):728–732. https://doi.org/10.1097/BOT.0b013e31826c19c4

Penn-Barwell JG, Murray CK, Wenke JC. Local antibiotic delivery by a bioabsorbable gel is superior to PMMA bead depot in reducing infection in an open fracture model. J Orthop Trauma. 2014;28(6):370–375. https://doi.org/10.1097/BOT.0b013e3182a7739e

Peterson LC, Kim SE, Lewis DD et al. Calcium sulfate antibiotic-impregnated bead implantation for deep surgical site infection with orthopedic surgery in small animals. Vet Surg. 2021;50(4):748–757. https://doi.org/10.1111/vsu.13570

Rajasekaran S, Babu JN, Dheenadhayalan J et al. A score for predicting salvage and outcome in Gustilo type-IIIA and type-IIIB open tibial fractures. J Bone Joint Surg Br. 2006;88(10):1351–1360. https://doi.org/10.1302/0301-620X.88B10.17631

Rajasekaran S, Dheenadhayalan J, Babu JN et al. Immediate primary skin closure in type-III A and B open fractures: results after a minimum of five years. J Bone Joint Surg Br. 2009;91(2):217–224. https://doi.org/10.1302/0301-620X.91B2.21228

Rajasekaran S, Giannoudis PV. Open injuries of the lower extremity: issues and unknown frontiers. Injury. 2012;43(11):1783–1784. https://doi.org/10.1016/j.injury.2012.08.039

Rajasekaran S, Sabapathy SR. A philosophy of care of open injuries based on the Ganga hospital score. Injury. 2007;38(2):137–146. https://doi.org/10.1016/j.injury.2006.04.135

Rupp M, Popp D, Alt V. Prevention of infection in open fractures: Where are the pendulums now? Injury. 2020; 51(S2):S57–S63. https://doi.org/10.1016/j.injury.2019.10.074

Scharfenberger AV, Alabassi K, Smith S et al. Primary wound closure after open fracture: a prospective cohort study examining nonunion and deep infection. J Orthop Trauma. 2017;31:121–126. https://doi.org/10.1097/BOT.0000000000000751

Schenker ML, Yannascoli S, Baldwin KD, Ahn J, Mehta S. Does timing to operative debridement affect infectious complications in open long-bone fractures? A systematic review. J Bone Joint Surg Am. 2012;94-A:1057-64. https://doi.org/10.2106/JBJS.K.00582

Schmidmaier G, Lucke M, Wildemann B, Haas NP, Raschke M. Prophylaxis and treatment of implant-related infections by antibiotic-coated implants: a review. Injury. 2006;37(2):S105–12. https://doi.org/10.1016/j.injury.2006.04.016

Schmidmaier G, Kerstan M, Schwabe P, Südkamp N, Raschke M. Clinical experiences in the use of a gentamicin-coated titanium nail in tibia fractures. Injury. 2017;48(1):2235–2241. https://doi.org/10.1016/j.injury.2017.07.008

Shirai T, Tsuchiya H, Nishida H et al. Antimicrobial megaprostheses supported with iodine. J Biomater Appl. 2014;29:617–623. https://doi.org/10.1177/0885328214539365

Sørensen TS, Sørensen II, Merser S. Rapid release of gentamicin from collagen sponge: in vitro comparison with plastic beads. Acta Orthop. 1990;61(4):353–356. https://doi.org/10.3109/17453679008993535

Sprague S, Petrisor B, Jeray K et al. Wound irrigation does not affect health-related quality of life after open fractures: results of a randomized controlled trial. Bone Joint J. 2018;100-B(1):88–94. https://doi.org/10.1302/0301-620X.100B1.BJJ-2017-0955.R1

Stockley I, Mockford BJ, Hoad-Reddick A, Norman P. The use of two-stage exchange arthroplasty with depot antibiotics in the absence of long-term antibiotic therapy in infected total hip replacement. J Bone Joint Surg Br. 2008;90B(2):145–148. https://doi.org/10.1302/0301-620X.90B2.19855

Stravinskas M, Horstmann P, Ferguson J et al. Pharmacokinetics of gentamicin eluted from a regenerating bone graft substitute. In vitro and clinical release studies. Bone Joint Res. 2016;5(9):427–435. https://doi.org/10.1302/2046-3758.59.BJR-2016-0108.R1

Swiontkowski MF. Criteria for bone debridement in massive lower limb trauma. Clin Orthop Relat Res. 1989;(243):41–47

Swiontkowski MF, Aro HT, Donell S et al. Recombinant human bone morphogenetic protein-2 in open tibial fractures: a subgroup analysis of data combined from two prospective randomized studies. J Bone Joint Surg Am. 2006;88(6):1258–1265. https://doi.org/10.2106/00004623-200606000-00013

Taggart T, Kerry RM, Norman P, Stockley I. The use of vancomycin-impregnated cement beads in the management of infection of prosthetic joints. J Bone Joint Surg Br. 2002;84:70–72. https://doi.org/10.1302/0301-620X.84B1.0840070

Templeman DC, Gulli B, Tsukayama DT et al. Update on the management of open fractures of the tibial shaft. Clin Orthop Relat Res. 1998;350:18–25

Tetsworth K, Cierny G III. Osteomyelitis debridement techniques. Clin Orthop Relat Res. 1999;360:87–96. https://doi.org/10.1097/00003086-199903000-00011

Trompeter AJ, Furness H, Kanakaris NK, Costa ML. Classification of open fractures: the need to modernize. Bone Joint J. 2020;102-B(11):1431–1434. https://doi.org/10.1302/0301-620X.102B11.BJJ-2020-0947

Trueta J. Reflections on the past and present treatment of war wounds and fractures. Mil Med. 1976;141(4):255–258. https://doi.org/10.1093/milmed/141.4.255

Tsuchiya H, Shirai T, Nishida H et al. Innovative antimicrobial coating of titanium implants with iodine. J Orthop Sci. 2012;17(5):595–604. https://doi.org/10.1007/s00776-012-0247-3

Van Moojen DJ, Hentenaar B, Vogely CH et al. In vitro release of antibiotics from commercial PMMA beads and articulating hip spacers. J Arthroplast. 2008;23(8):1152–1156. https://doi.org/10.1016/j.arth.2007.08.020

Venkatadass K, Grandhi TSP, Rajasekaran S. Use of Ganga Hospital open injury severity scoring for determination of salvage versus amputation in open type IIIB injuries of lower limbs in children - an analysis of 52 type IIIB open fractures. Injury. 2017;48(11):2509–2514. https://doi.org/10.1016/j.injury.2017.09.010

Werner CML, Pierpont Y, Pollak AN. The urgency of surgical débridement in the management of open fractures. J Am Acad Orthop Surg. 2008;16(7):369–375. https://doi.org/10.5435/00124635-200807000-00002

Wilkins J, Patzakis M. Choice and duration of antibiotics in open fractures. Orthop Clin North Am. 1991;22(3):433–437. https://doi.org/10.1016/S0030-5898(20)31673-4

Worlock P, Slack R, Harvey L et al. The prevention of infection in open fractures: an experimental study of the effect of fracture stability. Injury. 1994;25(1):31–38. https://doi.org/10.1016/0020-1383(94)90181-3

Zajonz D, Birke U, Ghanem M et al. Silver-coated modular Megaendoprostheses in salvage revision arthroplasty after periimplant infection with extensive bone loss–a pilot study of 34 patients. BMC Musculoskelet Disord. 2017;18:383. https://doi.org/10.1186/s12891-017-1742-7

Zalavras CG, Patzakis MJ. Open fractures: evaluation and management. J Am Acad Orthop Surg. 2003;11(3):212–219. https://doi.org/10.5435/00124635-200305000-00008

Zalavras CG, Marcus RE, Levin LS et al. Management of open fractures and subsequent complications. J Bone Joint Surg Am. 2007;89(4):884–895. https://doi.org/10.2106/00004623-200704000-00027

Zalavras CG. Prevention of infection in fractures. Infect Dis Clin N Am. 2017;31:339–352. https://doi.org/10.1016/j.idc.2017.01.005

Zelle BA, Boni G. Safe surgical technique: intramedullary nail fixation of tibial shaft fractures. Patient Saf Surg. 2015;9:40. https://doi.org/10.1186/s13037-015-0086-1