Infectious complications after open fractures

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CLINICAL PRACTICE GUIDELINE: Open Fracture Guideline

UPSTATE UNIVERSITY HOSPITAL | Trauma Center

5/1/2020

- Open Fracture Is one in which the fracture fragments communicate with the environment through a break in the skin.
- The skin wound may lie at a site distant to the fracture and not directly over it. Therefore, any fracture that has a concomitant wound should be considered open until proven otherwise
- The presence of an open fracture either isolated or as part of a multiple injury complex increases the risk of infection and soft tissue complications.

Open Fracture Management

Jessica L. Sop; Aaron Sop.

Last Update: August 14, 2021.

- Infection is the most obvious complication from open fracture.
- The risk of infection is related to the severity of the injury ,as follows：
  - **Gustilo-Anderson type I, 0-2%**
  - **Gustilo-Anderson type II, 2-10%**
  - **Gustilo-Anderson type III, 10-50%**

Summary of the Gustilo and Anderson classification

	I	II	III-A	III-B	III-C
Energy of mechanism	Low	Moderate	High	High	High
Wound size	<1 cm	>1 cm	Usually >10 cm	Usually >10 cm	Usually >10 cm
Soft tissue injury	Low	Moderate	Extensive	Extensive	Extensive
Contamination	NO	Low	Severe	Variable	Variable
Conminution/ Fracture pattern	No/ Simple	Some/ Simple	Severe/ Complex	Severe/ Complex	Severe/ Complex
Soft tissue coverage	Yes	Yes	Yes	No, requires reconstructive procedure	Variable
Vacular injury injury	No	No	No	No	Yes, require reparation

What are the pathogenic characteristics of infection after open fracture?

- Two different pathogenic mechanisms can lead to SSI, which can be differentiated based on time of occurrence and pathogenesis.
- In both cases, SSI can be viewed as indicating **failure of prophylactic antibiotic therapy.**

- 1. **Direct inoculation of bacteria**, during either the traumatic skin injury or the internal fixation, and persisting despite initial debridement.

- 2. Although uncommon, The other is **nosocomial hematogenous contamination by bacteria released from another site** (e.g., catheter, urine, or lungs).
- Chiefly in patients with severe **comorbidities** and multiple fractures who are managed in the **ICU**.
- The risk for developing an infection in this setting is quite low, usually **less than 1%** in healthy individuals, although this varies depending on the injury and the operation performed.

Risk Factors

- **Chronic diseases** that lower the immune system may put you at greater risk for infection after fracture. These include:
- Diabetes mellitus
- Immune deficiencies (such as HIV)
- Rheumatoid arthritis
- the lifestyle , included: first and foremost, smoking and using nicotine products, having morbid obesity, poor nutrition, or poor hygiene.

- With the increase of surgical duration, exposure time of surgical incision and deep tissues to the airborne pathogenic bacteria will increase. correspondingly, and immunity of human body to microorganism will be compromised.
- It has been reported that **the risk of SSI increased approximately 78% with every extra hour of surgical duration in tibial plateau fractures**.

- Body temperature is vital in maintaining normal human activities.
- In one study the **incidence of SSI** increased **3-fold** when a patient's body temperature **is 2°C lower** than the normal temperature.
- Hypothermia can lead to dysfunction of coagulation and contraction of vasculature around surgical site, this circumstance will compromise the immunity of tissue to pathogenic microorganism.

- Patients with a low level of blood platelet were prone to forming haematoma and impairs wound healing.
- patients that were critically injured were prone to having **severe stress** reactions, and this condition would result in a higher level of preoperative leukocyte.
- Therefore, the high level of leukocyte may be a sign of severe injury and suspicious infection for open fracture patients.

- General anaesthesia may significantly inhibit leukocyte chemotactic migration, phagocytosis, lymphocyte function.
- moreover, the tissue oxygenation might reduce with the prolongation of anaesthesia time.
- This result suggested that **nerve block and spinal anaesthesia should be the first choice in the procedure** of fracture fixation and soft tissue reconstruction in open fracture.

JOT JOURNAL OF ORTHOPAEDIC TRAUMA

Surgical Site Infection After Open Upper Extremity Fracture and the Effect of Urgent Operative Intervention

Devon J Ryan et al. J Orthop Trauma. 2020 May.

- A total of 22,578 patients from **New York**, including 1298 patients with open injuries.
- **The overall wound infection rate was 0.79%.** Patients with open injuries were found to have a higher incidence of infection compared with those with closed injuries.
- **Conclusions:** **The overall risk** of surgical site infection following intervention for open or closed upper extremity fractures **remains low**. Risk factors for infection include open injury, obesity, and cigarette smoking. **There was no difference in the infection rate based on the urgency of operative debridement**.

Incidence of surgical-site infection following open reduction and internal fixation of a distal femur fracture

Medicine: February 2019 - Volume 98 - Issue 7 - p e14547

- Totally, of 665 patients from China who underwent ORIF of distal femur fractures were reviewed and **24 SSIs** were found, indicating the **overall incidence of SSI was 3.6%**.
- The rate of **deep SSI was 1.2%** and **superficial SSI was 2.4%**.
- *Staphylococcus aureus* was the most common causative pathogen, followed by mixed bacterial and *S. epidermidis* and others.
- Open fracture, temporary use of external fixation, obesity, smoking, DM, and preoperative reduced albumin level were identified as independent risk factors associated with SSI.

IWJ International Wound Journal Open Access

Surgical site infection following operative treatment of open fracture: Incidence and prognostic risk factors

February 2020

- A total of 2692 patients from **China**, The **overall incidence of SSI was 18.6%,** with **17.0%** and **1.6%** for **superficial** and **deep infection**, respectively.
- The earliest and latest occurrence of SSI was, respectively, 3 and 71 days postoperatively.
- Microorganism examination results showed that **Enterococcus faecalis** was the most common pathogenic bacteria, followed by **Pseudomonas**, **S.A**, **Acinetobacter** *baumannii*, and **S. epider*midis***.

Multivariate analysis of prognostic risk factors of SSI following open fracture

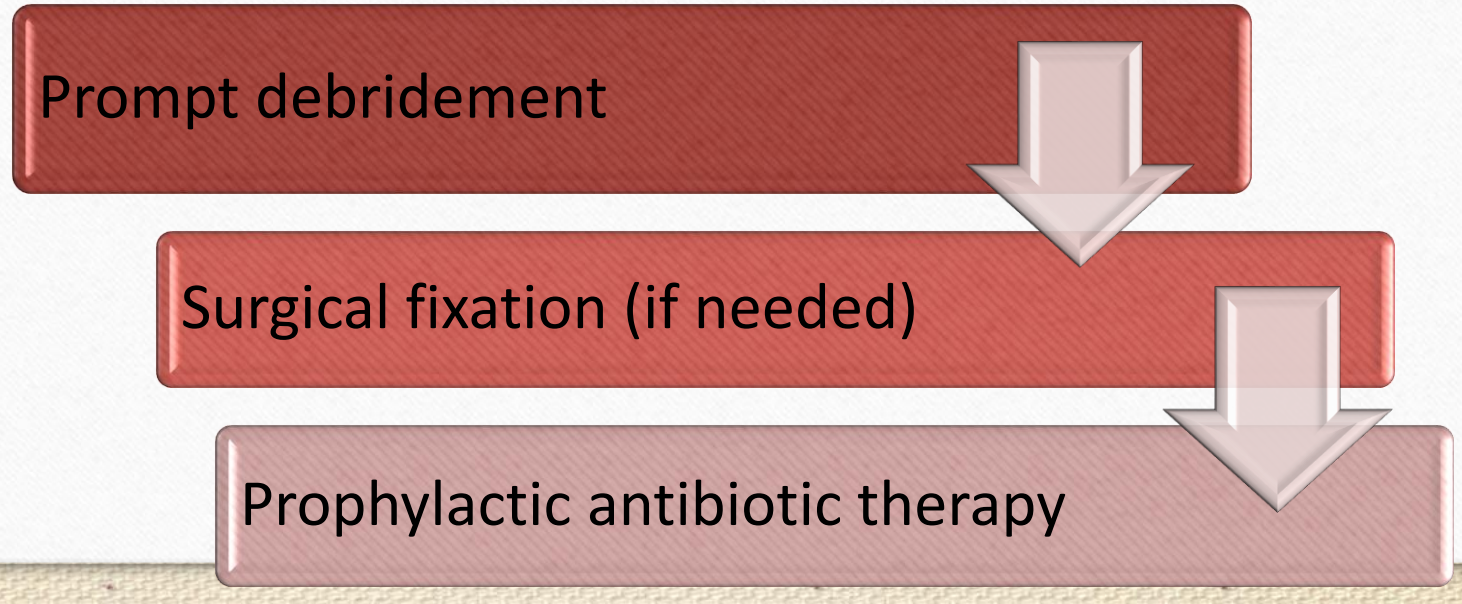
Variable	Odds ratio	95% CI	*P* value
Fracture type	3.18	2.67-5.39	.000
Surgical duration > 122 minutes	2.52	2.03-4.23	.006
Anaesthesia time > 130 minutes	1.43	1.13-1.81	.003
Body temperature < 36.4°C	1.98	1.42-2.76	.000
GLU > 100 mg/dL	2.06	1.20-3.21	.002
PLT < 288×10^9	1.51	1.13-1.67	.005
WBC > $.4 \times 10^9$	1.36	1.08-1.72	.010

Open Fractures Treatment & Management

Updated: May 06, 2020 | Author: Erin Pichiotino, MD; Chief Editor: Murali Poduval, MBBS, MS, DNB

Prevention

- **Measures for prevention of infections following open fracture include:**



Time to surgical debridement

- Historically, it was widely accepted that **emergent debridement of open fractures was essential for improving outcomes**.
- The 6-hour rule had been frequently utilized as it was believed to reduce infection and nonunion rates. Despite questionable initial evidence, the rule recommended that open fractures be operatively debrided within 6 hours from the time of the injury.

✓Bednar DA, Parikh J. Effect of time delay from injury to primary management on the incidence of deep infection after open fractures of the lower extremities caused by blunt trauma in adults. J Orthop Trauma.1993;7:532–535.

- One study of **315 patients with lower extremity** open fractures evaluated the relationship between time to surgical debridement and incidence of infection. They found **that time from injury to initial operative debridement was not associated with infection risk.**
- A systematic review subsequently assessed **the 6-hour rule** in relation to infection and nonunion rates. It was determined that judicious delays greater than 6 hours to operative debridement **do not result in a statistically significant difference in infection, nonunion, and perioperative morbidity rates.**
- Another study identified no significant difference in incidence of infection whether initial debridement occurred **prior to or after 12hours post-time of injury.**

✓Prodromidis AD, Charalambous CP. The 6-hour rule for surgical debridement of open tibial fractures: a systematic review and meta-analysis of infection and nonunion rates. J Orthop Trauma. 2016;30:397–402.
✓Hendrickson SA, et al. Time to Initial Debridement and wound Excision (TIDE) in severe open tibial fractures and related clinical outcome: a multi-centre study. Injury. 2018;49:1922–1926.

- A **prospective cohort study** of 736 patients with open fractures found that infection was actually associated with increasing Gustilo grade and not time to surgery or antibiotics.
- A **retrospective study** assessing 459 open fractures, found that among **Grade II and III** open fractures, there was a statistically **significant increase in the rate of deep** infection for each hour of delay. The relationship demonstrated **an increase in infection rate of 3% per hour of delay**. Meanwhile, the Grade I open fractures in their study did not develop deep infections.

✓Weber D, et al. Time to initial operative treatment following open fracture does not impact development of deep infection: a prospective cohort study of 736 subjects. J Orthop Trauma. 2014;28:613–619.
✓. Westgeest J, et al. Factors associated with development of nonunion or delayed healing after an open long bone fracture: a prospective cohort study of 736 subjects. J Orthop Trauma. 2016;30:149–155.

- **Finally, the British Association for Plastic Surgeons along with the British Orthopaedic Association created their current standards for the management of open fractures.**

- They only recommend immediate surgical exploration of open fractures in the presence of: **gross contamination, compartment syndrome, a dysvascular limb, and a multiply injured** patient within 8 hours.
- In the absence of these findings, their standards recommend surgical debridement to be completed **within 24hours of the injury**.
- **In essence, their standards refute the previously recommended debridement of all open fractures within 6hours of the injury.**

Effective Date: 3/2021

✓Conclusion:

Whenever possible **skin defects** overlying open fractures should be closed **at the time of initial debridement**.

Whenever possible, **soft tissue coverage** should be completed within **7days** of injury for open fractures associated with wounds requiring skin grafting or soft tissue transfers.

March 2020

Antibiotic utilization in open fractures

Yousif Atwan, MD[a,*], Theodore Miclau, MD[b], Emil H. Schemitsch, MD, FRCSC[a], David Teague, MD[c]

OTA INTERNATIONAL

Time to antibiotic administration

- In the setting of open fractures, it has long been understood that **antibiotic prophylaxis is an important factor for decreasing the incidence of deep infections**.
- Nonetheless, timing of antibiotic prophylaxis in the setting of open fractures was not always well understood and has historically been administered "as soon as possible."

✓Harper KD, Quinn C, Eccles J, et al. Administration of intravenous antibiotics in patients with open fractures is dependent on emergency room triaging. PLoS One. 2018;13:e0202013.

- One study suggested that antibiotic administration **within 3 hours** of injury **decreases infection rates six-fold**.
- A more recent retrospective study indicated that if antibiotics were given within 66 minutes of injury, the infection rate was 0%, but increased to 17% if antibiotics were delayed beyond this time frame.

✓Lack WD, Karunakar MA, Angerame MR, et al. Type III open tibia fractures: immediate antibiotic prophylaxis minimizes infection. J Trauma. 2015;29:1–6.

- Some studies demonstrated **clear benefits of early antibiotic** administration of antibiotics within **3hours** of injury rather than those administered greater than 3hours.
- A study of 237 consecutive open long bone fractures **did not reveal a statistically significant difference** in terms of the effect of antibiotic administration timing on incidence of infection.

❑Most studies recommended recommendation of appropriate prophylactic antibiotics within 1 hour of admission in all open fractures.

Duration of antibiotic coverage

- **After antibiotics have been initiated in the setting of open fractures, controversy still surrounds appropriate duration of dosing.**
- Earlier studies had suggested an adequate duration for antibiotic administration to be **3 to 5 days.**
- Another studies recommended further antibiotic coverage for **only 24hours** after wound closure.
- A **randomized, double-blind, prospective** study of 264 open fractures who receive **24hours or 5 days** of postsurgical antibiotics showed a short course of AB is as effective as a long course in terms of incidence of infection.

✓Mundi R, et al. Open tibial fractures: updatedvguidelines for management. JBJS Rev. 2015;3:
✓ Isaac SM, et al. Antibiotic prophylaxis in adults with open tibial fractures: what is the evidence for duration of administration? A systematic review. J Foot Ankle Surg.2016;55:146–150.

- Recent reviews recommend **24hours** of antibiotic coverage for **Gustilo type I and II** open fractures.
- For Gustilo type III open fractures, it is suggested antibiotic coverage for 72hours after injury but no longer than 24 hours after wound closure.

- Prolonged administration of prophylactic antibiotics does not reduce the risk of infection and can lead to the development of resistant organisms.

- Some of the literature strongly questions this practice, and concern has been raised regarding the development of resistant systemic nosocomial infections in the polytrauma patient because of overuse of perioperative antibiotics.
- Nonetheless, **there remains the need for a rigorous multicenter** randomized control trial to assess the optimal duration of antibiotic coverage **to reduce risk of infection**, **yet not increase risk of antibiotic resistance.**

uchealth University of Colorado Hospital

Antibiotic selection

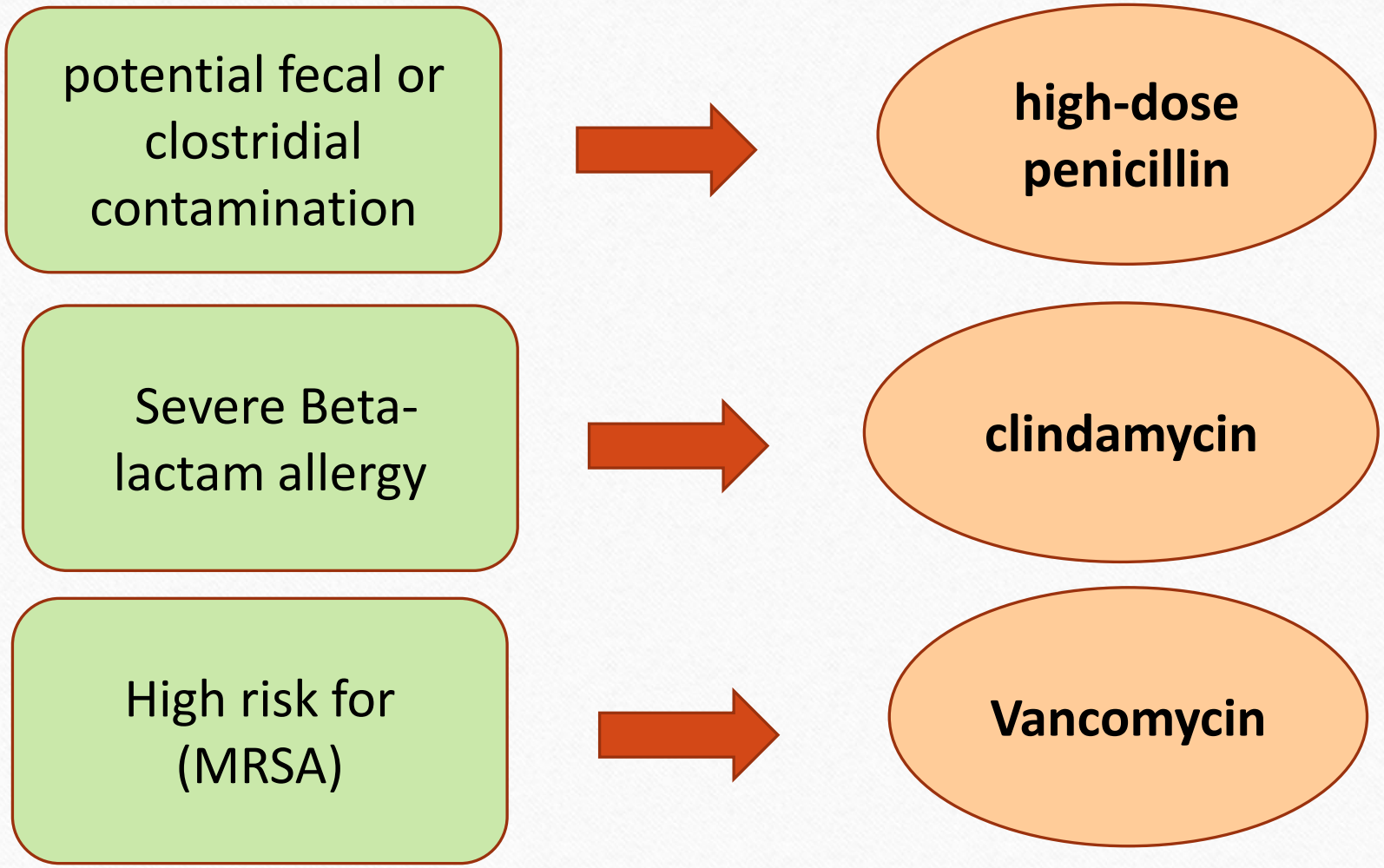
- There is also controversy about the perfect antibiotic prophylaxis in the treatment of open fractures.

- The most common organisms include Staphylococcus aureus, coagulase-negative staphylococci, and aerobic gram negative bacilli. Other less commonly include enterococci, anaerobes, fungi, and mycobacteria .
- but depending on the geographic situation, the resistances of these bacteria may change, and orthopedic surgeons should identify **the local resistances of the bacteria in their respective area**.

Antibiotic selection

Type I & II	**AB against gr+ organism**	Cephalosporins such as cefazolin Cefuroxime
Type III	**AB against gr+ & gr - organism**	Aminoglycosides such as gentamicin ampicillin-sulbactam .
Type III & water exposure	**AB against *Pseudomonas***	ceftazidime, cefepime, piperacillin/tazobactam

Antibiotic selection



Utilization of local antibiotics

- Although systemic IV ABs have improved outcomes, local prophylaxis has historically been utilized in a variety of forms as well.
- **Disrupted vascular anatomy** in the setting of complex open fractures may result in **decreased local tissue concentration** of intravenously delivered antibiotics.
- With local antibiotics delivered directly to the traumatic site, local tissue concentrations may be higher than could be achieved with IV ABs .
- Furthermore, in the setting of internal fixation, local antibiotics may reduce the formation of biofilm and colonization of bacteria.

✓Morgenstern M, et al. The effect of local antibiotic prophylaxis when treating open limb fractures: a systematic review and meta-analysis. Bone Joint Res. 2018;7:447–456.

- A **meta-analysis** including 2738 patients from 8 studies assessed

the effect of local antibiotic prophylaxis in the setting of open limb fracture.

- Six studies utilized antibiotic loaded **poly methyl methacrylate** beads and 2 studies utilized local antibiotics without a carrier substance.

❖ Their analysis suggested a risk reduction of 11.9% in fracture-related infection if additional local prophylactic antibiotics were also given. Nonetheless, heterogeneity, potential bias, and low-quality studies limit this finding.

✓O'Toole RV, et al. Local antibiotic therapy to reduce infection after operative treatment of fractures at high risk of infection: a multicenter, randomized, controlled trial. J Orthop Trauma. 2017;31:S18–S24.

- The METRC group completed the first-large **multicenter, randomized, controlled trial** assessing the efficacy of locally administered vancomycin powder in the setting of an open fracture.
- Analysis of the deep infections demonstrated less gram-positive bacteria but more gram-negative infections in the treatment group rather than the control group.
- These findings are consistent with known vancomycin activity against gram-positive pathogens.

Vancomycin Powder Use in Fractures at High Risk of Surgical Site Infection

(*J Orthop Trauma* 2021;35:23–28)

- A recent publication suggests **Vancomycin powder may play a role in lowering surgical-site infection** rates after fracture fixation.
- **A larger randomized controlled trial is needed** to validate these findings a benefit in the use of early vancomycin powder in the wound (locally) to **prevent biofilm formation**.
- Other strategies for antibiotic elution in the fracture site are being studied, for example, gentamicin-coated nails are promising, with low infection rates , or the use of gentamicin sponges.

The tetanus status of all patients with open fractures should be assessed and updated as necessary

- If the wound is high risk for Clostridium contamination and the patient has not had a booster in the **last five years**, tetanus toxoid should be given.
- If the patient **has not completed** the tetanus series, both tetanus toxoid and tetanus immune globulin should be administered.

Diagnosis

- **The diagnosis is challenging and based on a combination of various diagnostic criteria**:

✓ past medical history, host physiology, clinical presentation, laboratory tests, imaging modalities and culturing of intraoperative tissue samples.

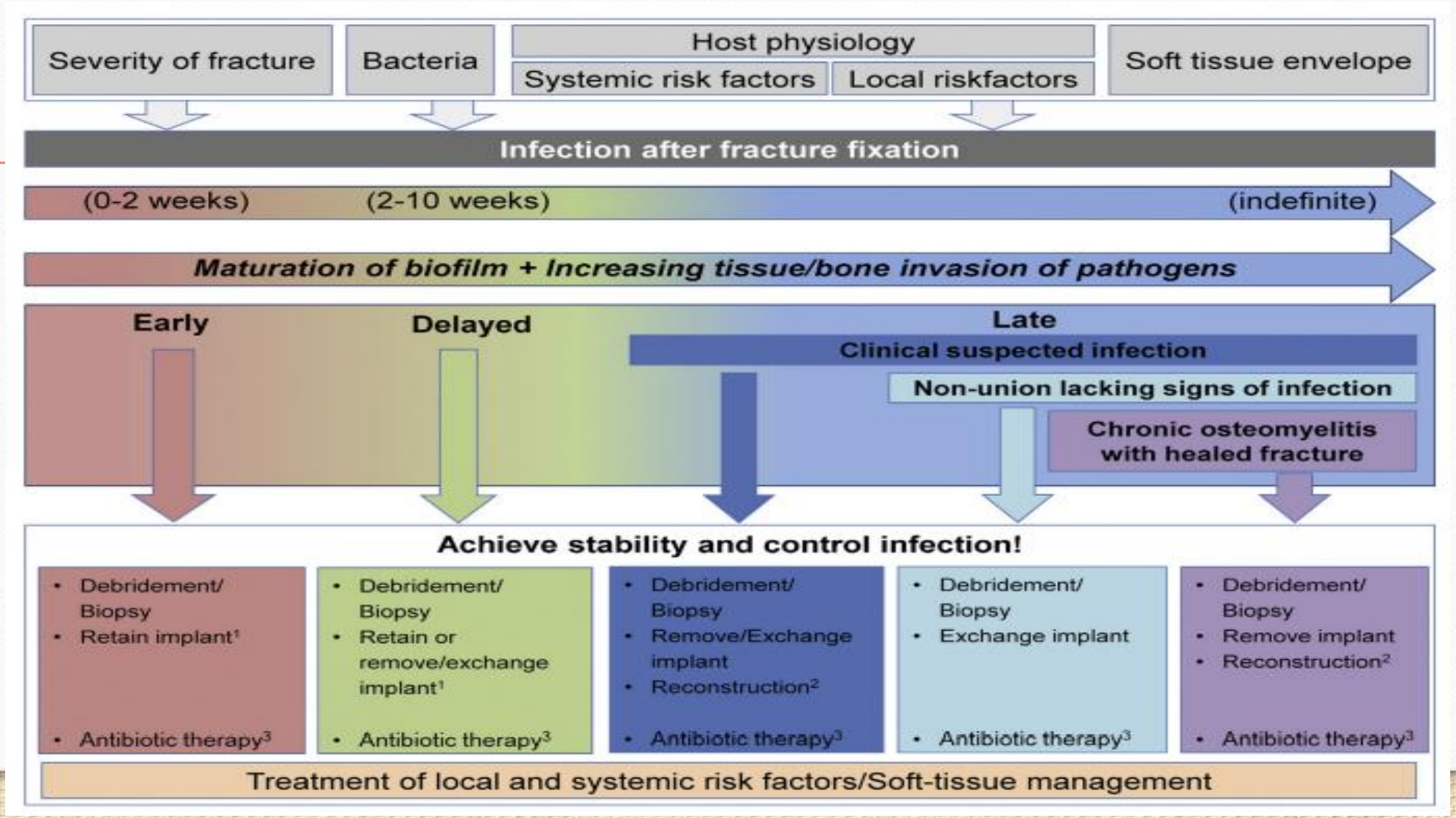
- Local signs of infection should be considered an infection until proven otherwise.

- Signs such as a **draining fistula** from the implant or **pus drain**age are considered **definitive signs** of infection.

Symptoms

- An infection after fracture will usually cause increased **pain, warmth, redness, and swelling** around the affected area—more than what is considered normal.
- Clinical manifestations of **osteomyelitis** following fracture include poor wound healing and fracture nonunion.
- In addition, **pus will drain** from the injury, **fever, chills, and night sweats** may exist.
- If the infection is near a joint, the **joint** may be painful and difficult to move

classification and treatment algorithm



Please cite this article in press as: W.J. Metsemakers, et al., Infection after fracture fixation: Current surgical and microbiological concepts, Injury (2016), http://dx.doi.org/10.1016/j.injury.2016.09.019

Early infection (<2 weeks)

- Early IAFFs are often a **clinical diagnosis** since the patient generally presents with **classic signs** of infection.
- Highly virulent organisms, like S.A, are frequent causative agents.
- At **one-week** post-inoculation, the bone **does not show signs of osteomyelitis** despite the presence of bacteria.
- Furthermore, bone healing is in the '**inflammatory or soft callus stage**' and so there will be **no fracture stability** at this early stage

Delayed infection (2–10 weeks)

- **Patients can present with symptoms consistent with either early or late infections**.
- For example, **hematomas**, which may be expected in **earlier** stages, or alternatively, a **fistula** can also present itself after 9 weeks, which may be more often associated with **late** infections.
- Delayed infections are typically due to less virulent bacteria, such as Staphylococcus epidermidis and as the **duration** of infection extends, **biofilms** mature and become **more resistant** to antibiotic therapy.

- Normal **bone healing** takes **up to 10 weeks**, with a ‘hard callus stage’ that is situated between 3 and 16 weeks.
- Experimental studies have shown that S. epidermidis inoculation into a fracture gap can lead to non-union rates of 83–100% at 8 week and **osteomyelitis** often occur **within 2–10 weeks**, so, treatment choices are often different compared to early onset infections.

Late infection (>10 weeks)

- Many patients can present with subtle symptoms, mostly lacking systemic manifestation .
  - In patients presenting with **compromised functionality** and **stress dependent pain**, infection with low-virulence microorganisms should always be considered a possible cause.
- Although bone healing may have taken place in some cases, severe inflammation with osteomyelitis lead to instability of the osteosynthesis. **Periosteal new bone formation** around the periphery of the infected area often necessitate extensive and repeated debridements, resulting in bone defects.

OSTEOMYELITIS AFTER A CONTAMINATED OPEN FRACTURE

- Contaminated open fractures can lead to the development of osteomyelitis of the fractured bone, typically at the fracture site in 3% to 25% of cases, depending on the type of fracture, the level of contamination, the degree of soft tissue injury, and whether systemic and local antimicrobial therapies have been administered.
- The bones of the **lower extremity** are typically involved, most often the tibia or fibula.
- Untreated, infection ultimately may lead to **nonunion** of the infected site, **chronic osteomyelitis**, or **amputation**.

Laboratory examination

- Blood tests: WBC,ESR,CRP ((low sensitivity and specificity)
- the **change over time** is more helpful than the absolute value. Persistent elevation or a secondary rise in CRP can be an indicator.

- Because a healing fracture may show the same positive test results as an infection, it is often **hard to firmly diagnose an infection after a fracture.**

Imaging

- Imaging studies are of limited usefulness during the first few weeks, as they may fail to show changes over time and are not suitable to differentiate between septic and aseptic changes in active infections.
- **CT** : provides more details
- **MRI** is the method of choice to evaluate soft-tissue involvement , However in cases of IAFF, metal artefacts impair correct evaluation.
- **bone scintigraphy** has limited value in the diagnosis of IAFF
- **WBC imaging** : not routinely available.
- **FDG-PET** : Its role in IAFF still remains inconclusive.

Microbiology

- The microbiologic diagnosis is established via cultures obtained at the time of debridement for possible infection, rather than at the time of initial debridement following fracture.
- Not all microbes colonizing the wound at the time of injury cause sustained infection in the bone, and pathogens not present at the initial injury may colonize and infect wounds subsequently.

Microbiology

- Cultures from an open wound at the time of initial fracture fixation should be avoided .

- Similarly, **swab cultures** at the time of revision surgery do not reliably represent the pathogens in the bone and are therefore **not recommended.**
- Whenever possible, **antibiotics** should be **avoided for at least 2 weeks** before microbiological culturing.

Microbiology

- In case of suspected infection, at least three bone biopsies should be taken close to the implant and in regions of macroscopically perceived infection such as necrotic bone tissue or non-unions .
- Identification of a virulent species such as S.A or E. coli in a superficial sample or a single positive biopsy can be considered definitive proof of SSI-ORIF.

- Presence of a commensal micro-organism in the surgical site is far **more challenging** to interpret and If the same microorganism is cultured in at least two separate biopsies, it is believed to be relevant.
- If involvement of an **adjacent joint** is suspected, joint fluid for analysis should be aspirated.

- If implanted hardware is removed during surgery, these should be sent to the microbiological laboratory.
- Although culturing is still believed to be the gold standard for microbiologic assessment, **molecular methods (PCR)** are increasingly being added to identify difficult to culture pathogens, Especially after antibiotic pre-treatment
- (risk of false-positive results from contaminants , cannot distinguish between live or dead bacteria and does not provide broad information about susceptibility to antibiotic).

Orthopaedics & Traumatology: Surgery & Research 103 (2017) S67–S73

Operative treatment of early infection after internal fixation of limb fractures (exclusive of severe open fractures)

What general principles guide the management IAOF?

- Surgical **debridement** with irrigation (all necrotic tissue or bone)
- Take **samples** of the infected tissue During surgery,
- Fracture **fixation** (if needed),
- Antimicrobial therapy tailored to culture and susceptibility data

✓ A bone infection can be hard to eliminate. It may require long-term antibiotic treatment, as well as several surgeries.

Clinical Microbiology and Infection 26 (2020) 572–578

Empirical antibiotic therapy

- After surgical debridement and sampling, empirical antibiotic therapy should be started in case of high suspicion of infection.
- The choice of empiric therapy depends on the **local epidemiology** of microorganisms and **risk factors** of the patient (i.e. previous antibiotics, comorbidities, previous hospitalisations, previously recovered pathogens).
- As a rule, initial empiric therapy should include a lipoglycopeptide and an agent against GNB, thereafter it should be adapted according to culturing results as soon as possible.

Targeted treatment strategies

- In general, antibiotic therapy can either be **curative or suppressive** (for control the infection until the fracture is healed and the implant can be removed) **The duration of targeted antibiotic therapy** :

The duration of targeted antibiotic therapy :

Implant retention	Implant removal
• Duration of **12 weeks**	• Duration of **6 weeks**

✓The current recommendation is that IV therapy should be limited to 1-2 weeks, until the patient is stable and culture results are known, then switch to oral therapy.

✓**To achieve optimal union**, it may be necessary to administer **parenteral antibiotic therapy for as long as fixation hardware remains in place**.

✓Once fracture union is achieved, fixation hardware should be removed (if possible), with additional debridement.

Antibiotic treatment according to the pathogen

Pathogen	Antibiotic therapy	Dose (normal renal function)
Staphylococcus spp.	**2 weeks**	
Methicillin-susceptible	Flucloxacillin ***plus***	2 g every 6 h. iv.
	Rifampicin	450 mg every 12 h iv./po.
Methicillin-resistant	**2 weeks**	
	Vancomycin *or*	15 mg/kg every 12 h iv.
	Daptomycin ***plus***	6–8 mg/kg every 24 h iv.
	Rifampicin	450 mg every 12 h iv./po.
all *Staphylococcus* spp.	**followed by**	
	Rifampicin ***plus***	450 mg every 12 h po.
	1st choice	
	Ciprofloxacin *or*	750 mg every 12 h po.
	Levofloxaxin or	500 mg every 12 h po.
	2nd choice	
	Cotrimoxazole *or*	1 double strength tablet every 8 h po.
	Fusidic acid or	500 mg every 8 h po.
	3rd choice	
	Clindamycin or	600 mg every 8 h po.
	Minocyclin or	100 mg every 12 h po.
	Linezolid	600 mg every 12 h po.
***Streptococcus* spp.**[a]	**4 weeks**	
	Penicillin G *or*	5 Mio IU every 6 h iv.
	Ceftriaxon	2 g every 24 h iv.
	followed by	
	Amoxicillin *or*	1000 mg every 8 h po.
	Clindamycin	600 mg every 8 h po.
***Enterococcus* spp.**	**whole therapy**[b]	
Penicillin-susceptible	Amoxicillin *or*	2 g iv. every 6 h iv.
	Penicillin G	5 Mio IU every 6 h iv.
Penicillin-resistant	**whole therapy**	
	Vancomycin *or*	15 mg/kg every 12 h iv.
	Daptomycin or	6–8 mg/kg every 24 h iv.
	Linezolid	600 mg every 12 h iv./po.

Pathogen	Antibiotic therapy	Dose (normal renal function)
***Enterococcus* spp.**	**whole therapy**[b]	
Penicillin-susceptible	Amoxicillin *or*	2 g iv. every 6 h iv.
	Penicillin G	5 Mio IU every 6 h iv.
Penicillin-resistant	**whole therapy**	
	Vancomycin *or*	15 mg/kg every 12 h iv.
	Daptomycin or	6–8 mg/kg every 24 h iv.
	Linezolid	600 mg every 12 h iv./po.
Enterobacteriaceae	**2 weeks**	
	β-lactam antibiotic according to susceptibility	iv.
	followed by	
	Ciprofloxacin	750 mg every 12 h po.
***Enterobacter* spp. and Nonfermenters**	**2–4 weeks**	
(e.g. *P. aeruginosa*)		
	Cefepime *or*	prolonged infusion (3 h):
	Ceftazidim[c] *or*	1–2 g every 8 h iv.[d]
	Meropenem	2 g every 8 h iv.
	followed by	1–2 g every 8 h iv.[d]
	Ciprofloxacin	750 mg every 12 h po.
***Propionibacterium* spp.**	**2–4 weeks**	
	Penicillin G *or*	5 Mio IU every 6 h iv.
	Ceftriaxon[e]	2 g every 24 h iv.
	followed by	
	Amoxicillin *or*	1000 mg every 8 h po.
	Clindamycin	600 mg every 8 h po.
Gram-negative Anaerobes	**whole therapy**	
(e.g. *Bacteroides*)		
	Metronidazol	500 mg every 8 h iv./po.
Mixed infections	Individualized therapy according	
(without methicillin-resistant *S. aureus*)	to susceptibility	

Local antibiotic therapy

- Local application of antimicrobials at the site of infection through different carriers has gained increasing attraction.
- Especially in the light of impaired blood flow to the site of infection and necrotic bone tissue, the advantage of achieving very high local concentration of antimicrobials with low systemic exposure is compelling .
- Nowadays, the mostly used antimicrobials are gentamicin, tobramycin, vancomycin and cephalosporins.

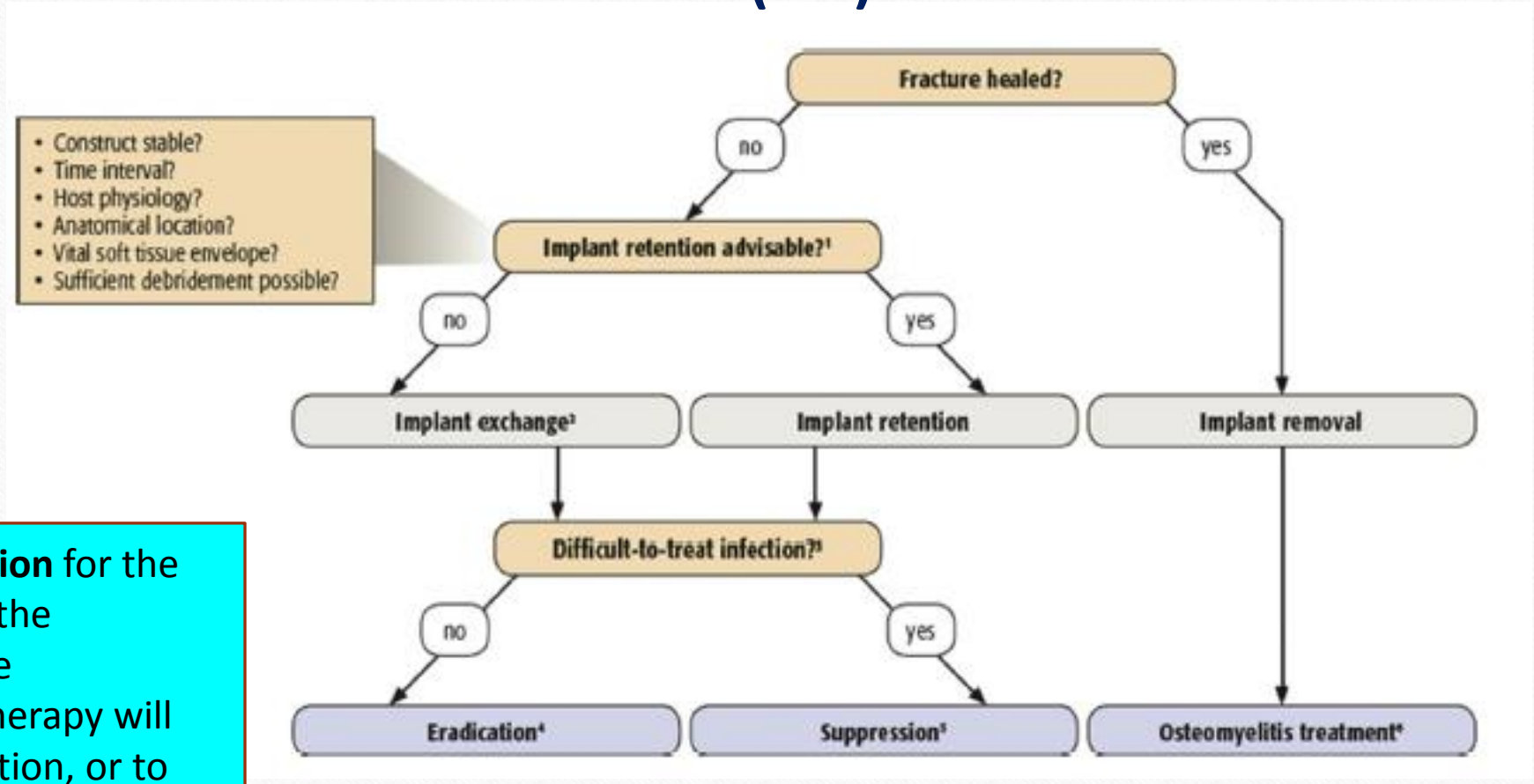
Continuous Local Antibiotics Perfusion Therapy for Acute Deep Infections after Open Fractures

January 2022

- In a case series, **acute deep infections after open fractures** managed using the continuous local antibiotic perfusion (CLAP) therapy.
- After sufficient debridement, gentamicin solution was continuously infused (2 mL/h) for **7–12** days by syringe pump through an inlet tube placed on the infected area
- After an average of 9.5 days of CLAP therapy, symptoms of infection disappeared and the bacterial culture was negative. There were no cases of recurrence during the follow-up period and no complications.

✓To date, **there is no** clear evidence of advantage of the addition of local antibiotic to systemic therapy in **randomized clinical trials**. Despite this, local antibiotics seem to lower infection rates in open fractures

Algorithm describing the basic treatment principles for fracture-related infection (FRI).



✓An often **challenging decision** for the surgeon is whether to leave the **hardware in place**, under the assumption that antibiotic therapy will suffice to eradicate the infection, or to **remove the hardware** while administering appropriate antibiotics.

How can fracture healing be obtained once the infection seems to be eradicated?

- The first step is to confirm the eradication of the infection, based on a converging set of findings from the **clinical evaluation**, **laboratory tests** and **imaging** studies, together with the knowledge that a full course of antibiotic treatment was given.
- In SSI-ORIF, eradication of the infection can be confirmed only after discontinuation of the antibiotics, i.e., after 2–3 months.
- Infection may delay the healing of the fracture.careful clinical and radiological evaluations should be performed once a month, to assess the extent and durability of the bone formation.
- A follow-up of a minimum of 12 months after cessation of therapy is required.

Thanks for your attention!