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CLINICAL OVERVIEW OF ORTHOPEDIC INFECTIONS AND THE GROWING THREAT OF ANTIMICROBIAL RESISTANCE-A SCHEMATIC REVIEW

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Background :Orthopedic infections are challenging and require effective antimicrobial therapies. New strategies are required due to the emergence of multidrug-resistant strains. Developing innovative medicines, controlling infections, comprehending microbial resistance, and using antibiotics sensibly are all important tactics.

Microbiota in orthopedic infections:

Gram-positive bacteria, particularly Staphylococcus aureus and coagulase-negative staphylococci (CoNS), are the primary causes of orthopedic infections. S.aureus is notorious for its virulence, antibiotic resistance, and biofilm-forming abilities. Orthopedic infections are also caused by other organisms, such as Cutibacterium acnes, Enterococcus, and Streptococcus. PJIs are increasingly being caused by gram-negative bacteria such Pseudomonas aeruginosa and Escherichia coli. Effective therapy is severely hampered by the emergence of antibiotic-resistant strains, such as MRSA, VRSA, and carbapenem-resistant enterobacteria. Developing focused antimicrobial tactics requires an understanding of the range of infections and their resistance patterns.

Tailoring Antimicrobial Therapy for Orthopedic Infections:

Treatment with antibiotics for orthopedic infections should be customized according to patient risk factors, pathogen sensitivity, and culture findings. To lower surgical site infections (SSIs), screening and decontamination procedures for S. aureus are important factors to take into account. In order to avoid SSIs, antibiotic prophylaxis—usually with cefazolin—is essential. Beta-lactam antibiotics, rifampicin, glycopeptides, and fluoroquinolones—which target specific pathogens—are among the available therapy choices. Antibiotics like daptomycin and rifampicin are efficient against bacteria buried in biofilms, thus controlling biofilms is also crucial. Targeted treatment is provided by local antimicrobial administration, such as spacers and bone cements filled with gentamicin. Effective treatment requires an understanding of pharmacokinetics and pharmacodynamics, and combination therapy and targeted delivery can assist treat complicated infections and lower germ resistance.

Conclusions: Antimicrobials are crucial for preventing and treating orthopedic infections. however, resistance poses a significant global challenge. A multifaceted approach is needed, including prudent antibiotic use, stringent infection control measures, and robust stewardship programs. Ongoing research and global collaboration are essential to address this growing threat and preserve the effectiveness of antibiotics.

Key words: Orthopedic infections, Microbiota, Microbial resistance, Antibiotics.

BACKGROUND:

The human body's microbiome is a huge and complex web of bacteria, fungi, and viruses. The epidermis, salivary mucosa, and gastrointestinal tract contain the bulk of the human body's microbiota, which supports a range of physiological functions from metabolism to innate immunity. However, in some circumstances, the growth of these symbiotic bacteria may become uncontrollable, leading to infections that cause biofilms to form. (1) Bacteria have existed in two different states since the beginning of time: sessile (attached to a surface) and planktonic (free-floating).(2) Bacteria exhibit different traits between these two states because bacterial attachment to a surface causes a rapid change in the expression levels of several genes associated with development and synthesis of exopolysaccharide (EPS), sometimes referred to as "slime" or bacterial EPS. This shift begins as soon as bacteria colonize both biotic and abiotic surfaces and results in the production of a protective barrier.(3)

An overview of orthopaedic infections :

Category	Subcategory	Type / Example	Further Classification
Native Tissue	**Hard Tissue**	Bone (Osteomyelitis)	Acute → Hematogenous / Non-hematogenousChronic → Hematogenous / Non-hematogenous
		Vertebral osteo/discitis	Hematogenous / Non-hematogenous
		Cartilage	Bursa (Septic bursitis) → Superficial / Deep
Native Tissue	**Soft Tissue**	Synovium	Tendon Sheath (Infectious tenosynovitis)
		Synovial Joint (Septic arthritis)	Acute → Gonococcal / Non-gonococcalChronic
		Tendons & Ligaments	—
		Muscle	Pyogenic / Non-pyogenic
		Subcutaneous Tissue & Deep Fascia	Necrotizing cellulitis & fasciitisSurgical site infections
Foreign Material	Orthopaedic Hardware	Fracture fixation hardware (pins, screws, plates, etc.)	Early / Delayed-late
		Prosthetic Joint Infection (PJI)	Early / Chronic (delayed-late) / Acute hematogenous seeding
	Retained Foreign Bodies	From penetrating injury	—

Table 1: Types Of Orthopaedic Infections

By connecting clinical insights with scientific breakthroughs, our objective is to illuminate the path forward in the management of orthopedic infections. Orthopedic infections have a wide range of clinical manifestations, and improving diagnostics is essential to ensuring proper diagnosis, effective treatment, and better results.

The phenomenon of multidrug-resistant organisms , Antimicrobial resistance, Treatment failures emergence makes successful antimicrobial treatment even more challenging. We anticipate that this special issue will act as a pivotal force in enriching our understanding of orthopedic infections and fostering discussions aimed at establishing best practices in patient care.

Biofilms and Drug Resistance

The biofilm's structural characteristics and constituent bacteria are responsible for the development of antibiotic resistance. Biofilms may play a major role in the complex phenomena of drug resistance linked to biofilms. Biofilms and related infections can be treated with antibiotics, disinfectants, and germicidal chemicals. When compared to their planktonic stage, bacteria that live in biofilms exhibit a 10–1000-fold increase in drug resistance, particularly antibiotic resistance.(4) For example, it has been noted that all Staphylococcus epidermidis biofilm isolates were vancomycin-sensitive when analyzed planktonically. (5). Nevertheless, over 75% of the microbes that were isolated from a biofilm were resistant to the same drugs.(6)

Targeting Biofilms Therapy:

Controlling biofilms is a challenging issue. If biofilms are not adequately addressed, As a result of the extensive use of antibiotics to treat biofilm-associated illnesses, more aggressive, antibiotic-resistant bacteria have begun to appear, potentially increasing the incidence and severity of infections(7), as well as the mortality and morbidity associated with them.

, requiring the development of innovative methods to remove them. [8].

It is crucial to understand completely how biofilms form, apply efficient communication strategies, and put these strategies into practice in order to effectively regulate them (9) Antibacterial medications, Dietary supplements, surface treatments, and changes to other environmental conditions can all help avoid the formation of biofilms early on. (10)

The pathogen that has been identified determines the choice of antimicrobial drugs. Before beginning oral medicine, initial treatment usually consists of intravenous therapy with a beta-lactam, glycopeptide, or daptomycin to lower bacterial density.

Treatment Duration

- Debridement in addition to retention or one-stage exchange: 12 weeks of treatment
- Two-stage exchange with short interval: 12 weeks of treatment

- Two-stage exchange with interval ≥ 8 weeks: 6 weeks of treatment during implant-free interval

Microorganism / scenario	Antimicrobial agent(s)	Dose (per agent)	Route	Duration / notes
Staphylococcus aureus or coagulase-negative staphylococci — methicillin-susceptible	Rifampin + (flu)cloxacillin	Rifampin 450 mg every 12 h - **450 mg q12h**; Flucloxacillin (or fluclox/fluclox-like) 2 g every 6 h - **2 g q6h**	Rifampin: PO (or IV if used); Flucloxacillin: IV	IV therapy for ~2 weeks, then switch to rifampin + oral fluoroquinolone (e.g., levofloxacin 750 mg q24h or 500 mg q12h depending on drug) for continuation
Staphylococcus aureus or coagulase-negative staphylococci - methicillin-resistant (MRSA / MR CoNS)	Rifampin + vancomycin **or** rifampin + daptomycin	Rifampin 450 mg every 12 h; Vancomycin 1 g every 12 h (adjust per level); Daptomycin 8–10 mg/kg every 24 h	Rifampin: PO; Vancomycin / Daptomycin: IV	IV for ~2 weeks, then rifampin combined with an oral agent (e.g., levofloxacin) **or** continue alternative agents such as daptomycin, teicoplanin,

				fusidic acid, cotrimoxazole, or minocycline per susceptibility and clinical scenario
Streptococcus spp.	Penicillin G **or** ceftriaxone; then follow-on amoxicillin	Penicillin G 5 million U every 6 h; Ceftriaxone 2 g every 24 h; Amoxicillin 750–1000 mg every 8 h (oral)	IV for penicillin/ceftriaxone; Amoxicillin PO for oral follow-on	IV for ~4 weeks, followed by oral amoxicillin as indicated
Enterococcus spp. (penicillin-susceptible)	Penicillin G **or** Ampicillin **or** Amoxicillin **or** (daptomycin + aminoglycoside)	Penicillin G 5 million U every 6 h; Ampicillin 2 g every 4–6 h; Daptomycin 8–10 mg/kg every 24 h (if used)	IV (all)	IV for 2–4 weeks, followed by oral amoxicillin 750–1000 mg every 8 h when appropriate
Enterococcus spp. (penicillin-resistant)	Vancomycin **or** Daptomycin + aminoglycoside	Vancomycin 1 g every 12 h (adjust by levels); Daptomycin 8–12 mg/kg every 24 h (range given)	IV	Duration individualized (typical IV courses); combine with aminoglycoside when indicated by susceptibility and severity
Enterobacteriaceae (quinolone-susceptible)	Ciprofloxacin	750 mg every 12 h	PO	Oral regimen when susceptible (duration per infection severity)
Non-fermenters (e.g., Pseudomonas aeruginosa, Acinetobacter spp.)	Cefepime **or** Ceftazidime + aminoglycoside; then possible oral step-down	Cefepime / Ceftazidime: 2 g every 6 h (dose depends on agent); Aminoglycoside per local dosing	IV (initial)	IV for ~2–4 weeks, followed by oral ciprofloxacin 750 mg every 12 h if appropriate and susceptible
Anaerobes	Clindamycin	IV: 600 mg every 6–8 h; PO step-down: 300 mg every 6 h	IV → PO	IV for ~2–4 weeks, then switch to oral clindamycin 300 mg q6h
Mixed infections (without MR staphylococci)	Amoxicillin/clavulanic acid **or** Piperacillin/tazobacta	Amox/clav: 2.2 g every 8 h (IV formulation); Pip/tazo 4.5 g	IV	IV for ~2–4 weeks, then tailor follow-on regimen to

	m **or** Imipenem **or** Meropenem	every 8 h; Imipenem 500 mg every 6 h; Meropenem 1 g every 8 h		culture and susceptibility

Table 2: target antibiotic Treatment of orthopedic infections

Future directions :

To better understand microbiologic processes, researchers in the domains of food, water, medical, and environmental microbiology need to concentrate on the threat posed by biofilms. The implementation of this approach by the pharmaceutical and healthcare sectors will undoubtedly lead to the development of new biofilm prevention and control techniques. Gaining a deeper understanding of the factors that distinguish the biofilm phenotype from the planktonic phenotype would help future efforts to regulate biofilms.

CONCLUSION:

Orthopedic infections, particularly those involving biofilm formation, pose significant challenges. This study aims to advance our understanding and explore biofilm-targeted therapies to improve treatment outcomes, reduce healthcare costs, and alleviate the psychosocial and financial burden associated with these infections. By developing effective treatment strategies, we can improve patient care and quality of life.

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