KeyCME

Periprosthetic Joint Infections

New Generation of Treatment Strategies, Antibiotics, and Outcomes

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Learning Objectives

- Review challenges faced in preventing and treating PJIs
- Assess emerging patient-specific prevention strategies
- Evaluate a case of post-surgical PJI utilizing a multidisciplinary team

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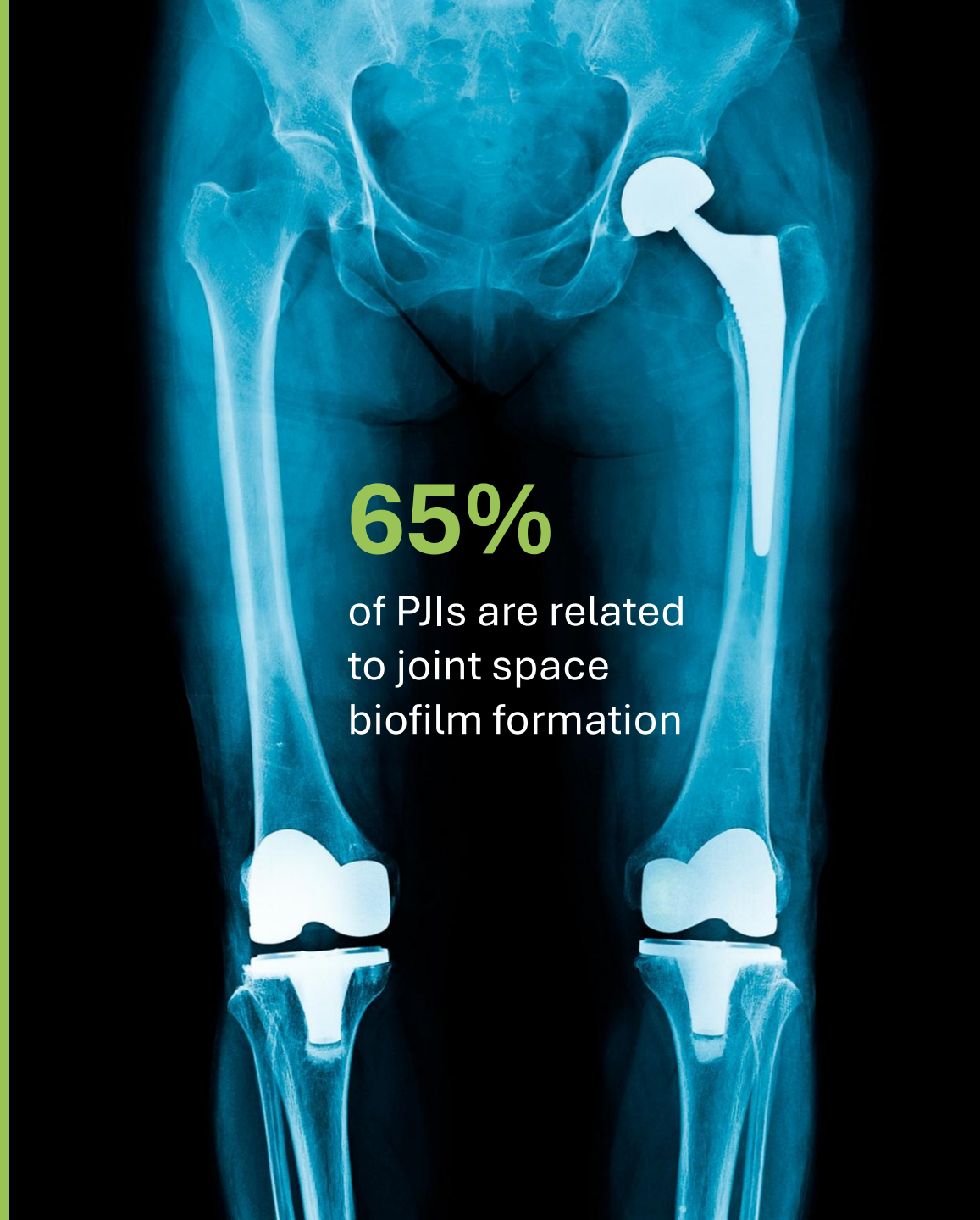
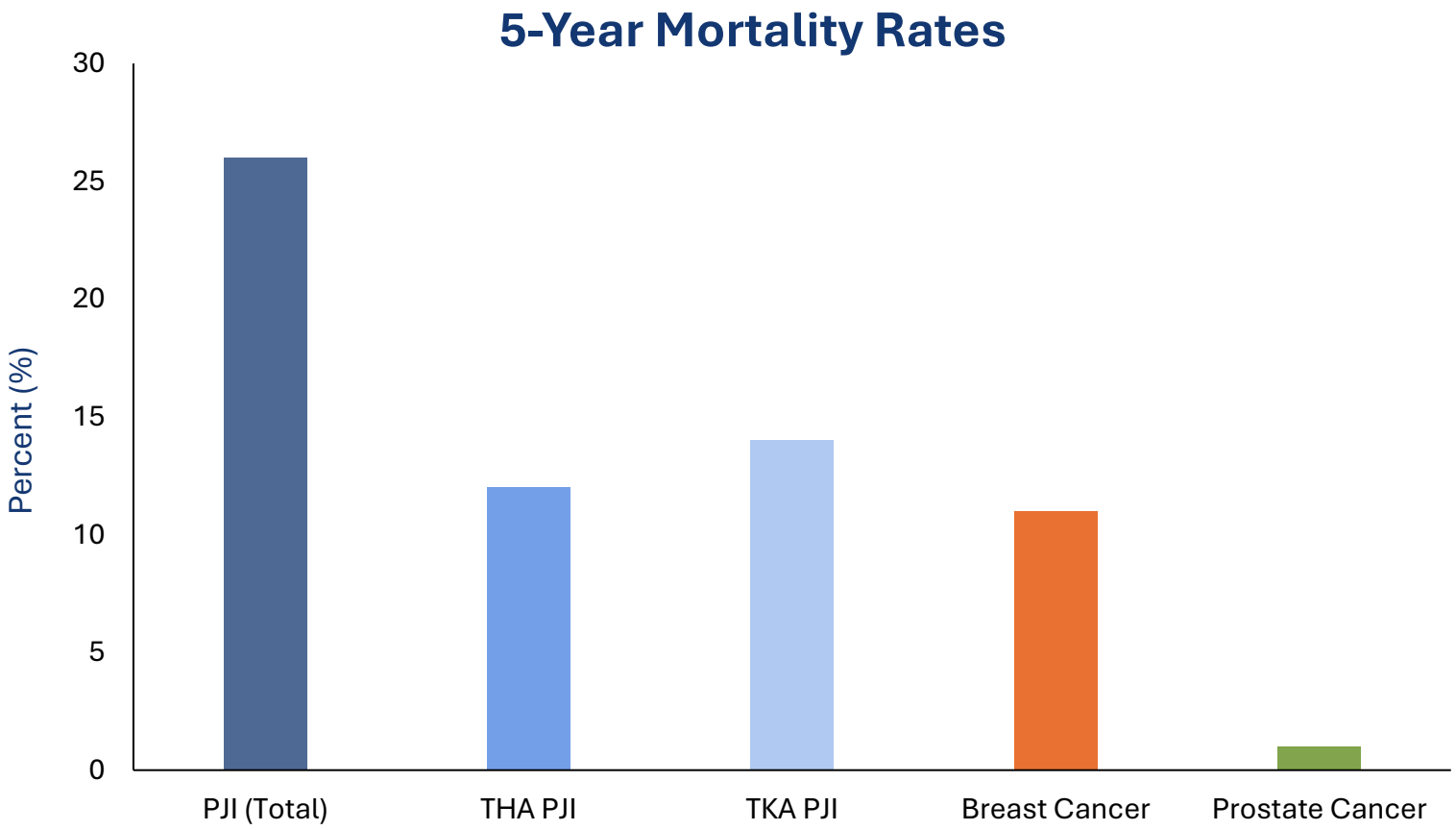
Periprosthetic Joint Infections, Biofilm, and Burden

- Total joint arthroplasty (TJA) is one of the most successful surgical procedures developed in recent decades.
- Periprosthetic joint infection (PJI) is associated with significant morbidity, mortality, and costs.
- Diagnosis is challenging and the majority of PJIs are caused by biofilm.
- Even with resolution, risk of recurrent infection is a significantly increased.
- Treatments are evolving
  - New generations of antimicrobials
  - Greater understanding of pathogenesis
  - Role of prophylaxis and early intervention



Staats A, et al. *Ann Jt*. 2021 Oct;6:43.

PJI Five-Year Mortality Rates Surpass Some Cancers



THA: total hip arthroplasty, TKA: total knee arthroplasty

Zmistowski B, Parvizi J. Orthopedics Today. 2013. https://www.healio.com/news/orthopedics/20130104/a-quarter-of-patients-treated-for-pji-dead-within-5-years. Accessed August 8, 2025.
Ramos MS, et al. *J Arthroplasty*. 2025 Apr 29:S0883-5403(25)00373-0.
Kristensen NK, et al. *J Arthroplasty*. 2025 Jun 4:S0883-5403(25)00650-3.

PJI Risk Factors Differ by Stage and Location

Patient-Associated Risk Factors

- Obesity
- Diabetes mellitus (DM)
- Cardiac disease
- Male sex
- Immunosuppression
- Hypoalbuminemia
- Rheumatoid arthritis
- Liver or renal disease
- American Society of Anesthesiologists score
- Alcohol or tobacco use

Surgery/Hospital-Associated Risk Factors

- Blood transfusion
- Prolonged operative time
- Anticoagulation or thromboprophylaxis
- Prior bariatric surgery
- Previous PJI
- Previous revision

Visperas A, et al. *J Orthop Res*. 2022 Jul;40(7):1477-1491.
Tekin-Taş Z, et al. *Infect Dis Clin Microbiol*. 2024 Jun 28;6(2):93-101.
PJI Clinical Practice Guideline. AAOS. 2019.

PJI Increases Primary and Revision Complications and Costs

- PJI cases are estimated to be over 70,000 per year in the U.S.
  - 0.5% – 1.4% of primary arthroplasty
  - 18%–30% of revisions
- Annual U.S. cost: $1.6 billion
- Revision hip and knee surgeries are expected to increase by 2030.
  - 68% – 176% for revision hip
  - 72% – 170% for revision knees

Visperas A, et al. *J Orthop Res*. 2022 Jul;40(7):1477-1491.

PJIs Are Common Claims for Readmission

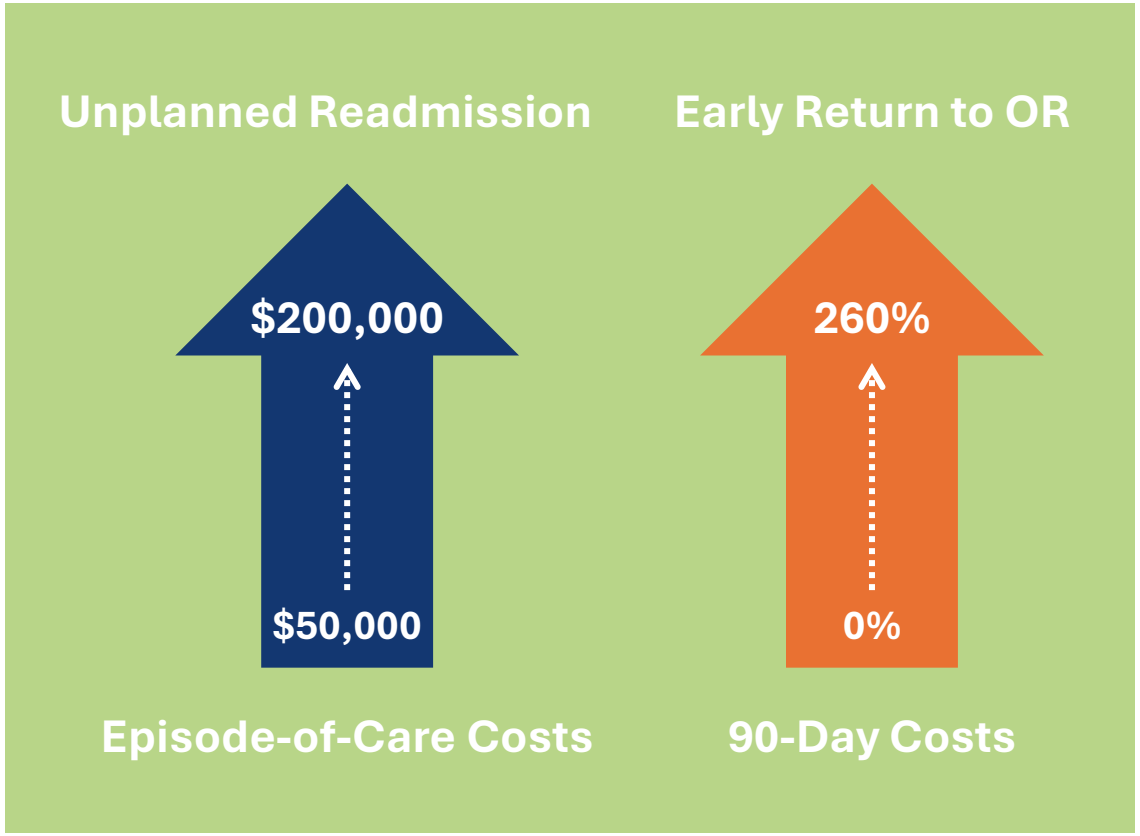
	Average cost per claim (SD)
Most common claims < 90 days of discharge	
1. Dislocation	$53,203 (37,571)
2. PJI	**$132,676 (102,644)**
3. PPFx	$100,845 (61,233)
4. Cellulitis	$28,478 (17,328)
5. Afib	$45,651 (40,215)
Most common THA claims < 90 days of discharge	
1. Dislocation	$52,526 (37,394)
2. PPFx	$103,940 (62,127)
3. PJI	**$123,068 (71,192)**
4. Sepsis	$95,322 (50,905)
5. Cellulitis	$30,599 (11,628)
Most common TKA claims < 90 days of discharge	
1. PJI	**$138 442 (117,779)**
2. Afib	$41,680 (34,797)
3. Cellulitis	$27,418 (19,480)
4. Sepsis	$70,494 (51,860)
5. UTI	$29,075 (13,889)

Afib: atrial fibrillation, PJI: prosthetic joint infection, PPFx: periprosthetic fracture, SD: standard deviation, THA: total hip arthroplasty, TKA: total knee arthroplasty, UTI: urinary tract infection

Bido J, et al. *HSS J*. 2024 May;20(2):187-194.

Bundled Payments Are Affected by Early Revisions

- CMS utilizes bundled payments for TJAs under the mandatory Comprehensive Care for Joint Replacement initiative
  - Fixed reimbursement rate covering all costs during a 90-day episode of care
- Providers instituted strategies to decrease costs
  - Outpatient TJA
  - Shorter inpatient stays
  - Discharge home after inpatient stay
- Does not control for early readmissions and reoperations that affect bundled payments



Bido J, et al. *HSS J*. 2024 May;20(2):187-194.

How Do We Currently Treat PJI?

DAIR

1. **D**ebridement
2. **A**ntibiotics
3. **I**mplant **R**etention

Procedures are not standardized.

Failure Rate

31-63%

Resection

1. One-stage
2. Two-stage
3. 1.5-stage
4. Fusion/Girdlestone

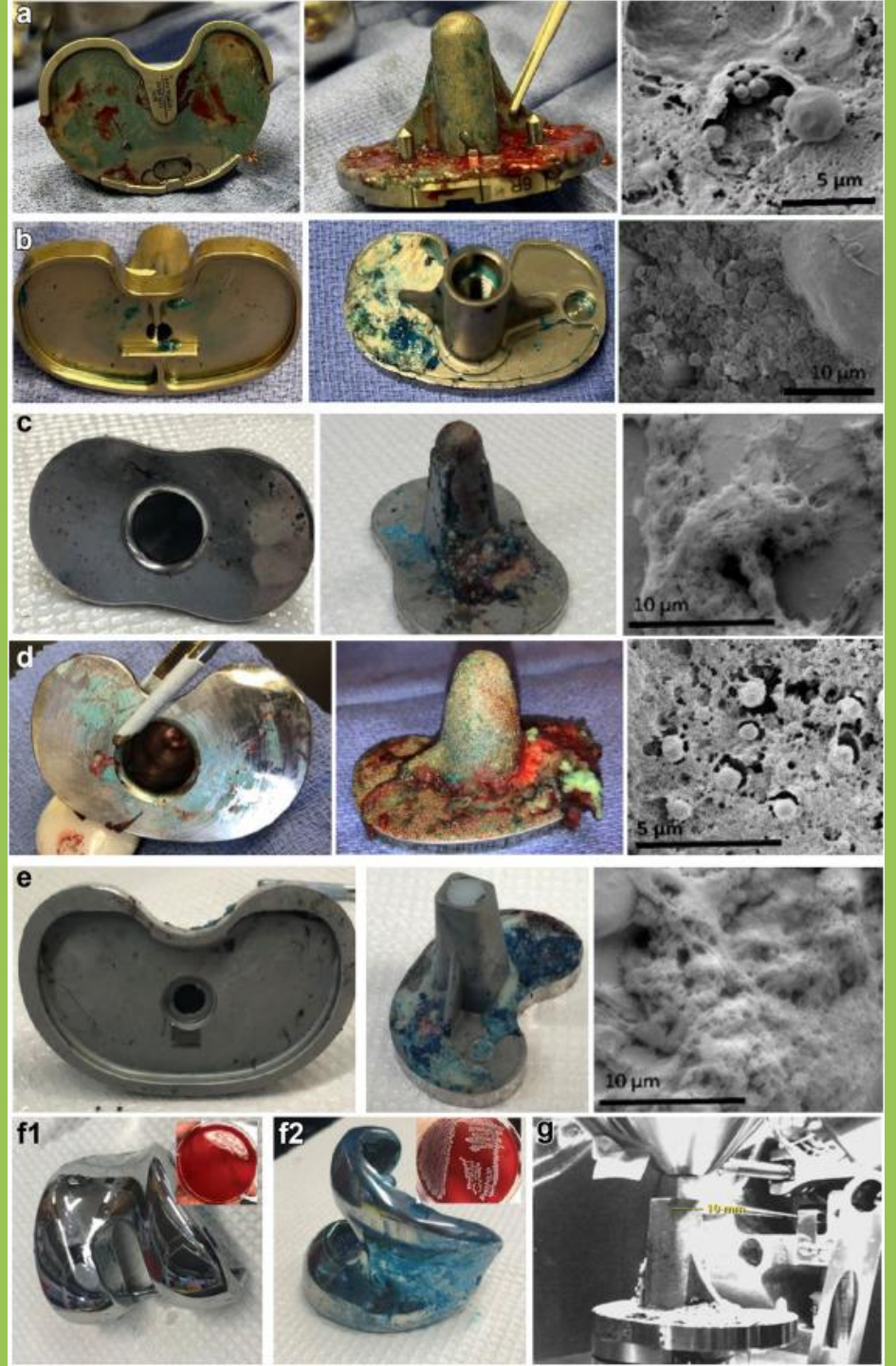
Failure Rate

8-20%

Visperas A, et al. *J Orthop Res*. 2022 Jul;40(7):1477-1491.
Doub JB, et al. *Arthroplast Today*. 2024 Jan 25;25:101314.

Why Does DAIR fail?
Location, location, location….

- Synovial-prosthetic interface is not the only place biofilm can form.
- Many chronic biofilms form on the bone-prosthetic interface that is not accessible during debridement in DAIR surgeries.
- Biofilm on the bone-prosthetic interface, antimicrobial resistance, and biofilm-related antimicrobial tolerance increase risk of DAIR failure.



Doub JB, et al. *Arthroplast Today*. 2024 Jan 25;25:101314.

Success Rates May Differ by Infection Duration or Treatment Course

DAIR Success
(clinical cure with index prosthesis in place)

74% in early infection

49% in late acute infection

44% in chronic infection

Revision Success
(rate of infection eradication after revisions)

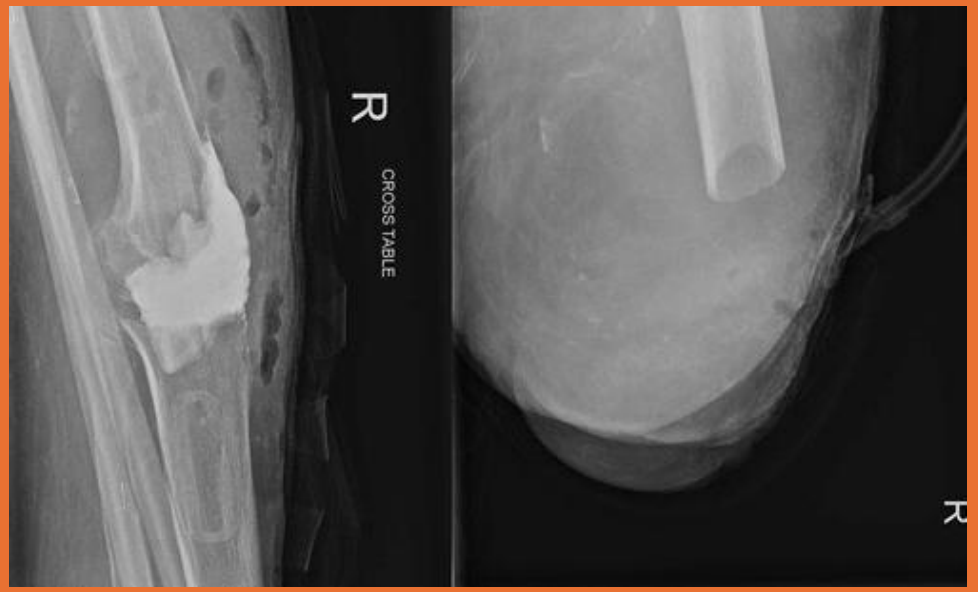
87% in one-stage

83% in two-stage

Patel R. *New Engl J Med*. 2023;388:251-262.

Salvage Options Are Available, but Not Preferable

- **Above knee amputation (AKA)**
  - Initial PJI risk is 0.025% but rises to 5.1% with chronic infection after revision
  - Risks of phantom limb pain and inability of elderly patients to use a prosthetic leg
- **Arthrodesis (KA)**
  - Primary bone-to-bone knee arthrodesis reduces the need for AKA
  - Requires a functioning extensor mechanism
  - Use of KA reduces the risk of subsequent amputations, deaths, or revisions compared to AKA
- **Prolonged suppressive antibiotic therapy (PSAT)**
  - Only alternative to AKA or KA
  - Used in patients who refuse AKA or KA or are not capable of surgery
  - Will not cure infection, but may reduce hospital admissions
  - Survival rate after 2 years is 61%



75-year-old female with PJI from elective TKA and multiple comorbidities. PJI treatment could not control infection and AKA was performed.

Jeys LM, et al. *Ortho Trauma*. 2025;39(1):42-54.
Purcell C, et al. *J Surg Case Reports*. 2025;1.

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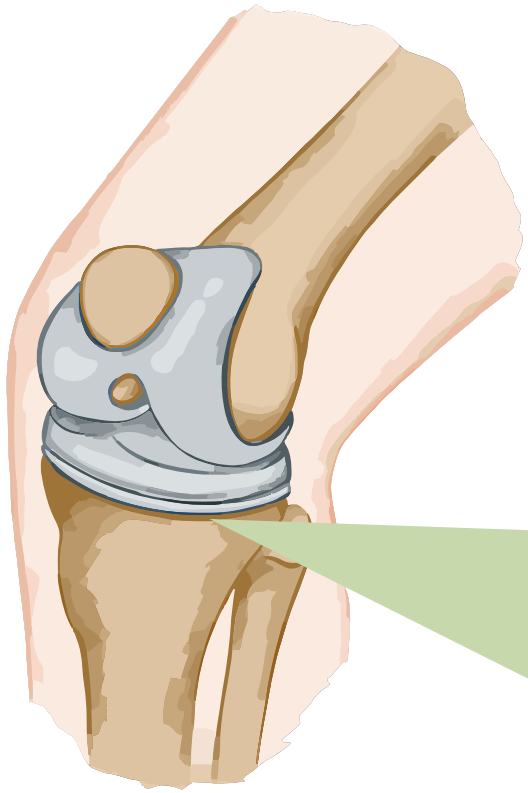
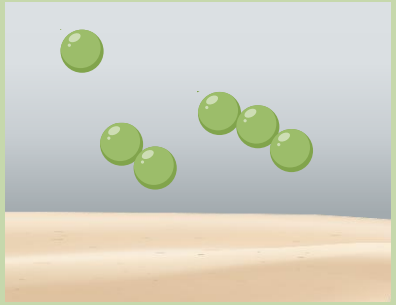
Device-Associated Biofilm Formation Occurs in Stages



1

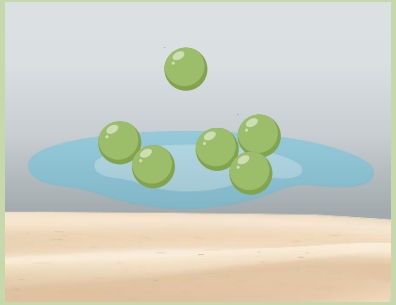
Initial Attachment



Initial surface attachment of planktonic cells onto implant surfaces

2

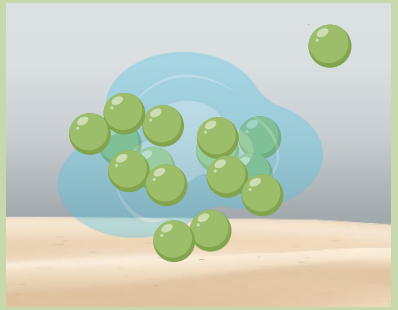
Irreversible Attachment



Transition from planktonic to biofilm phenotype with production of extracellular polymeric substances (EPS)

3

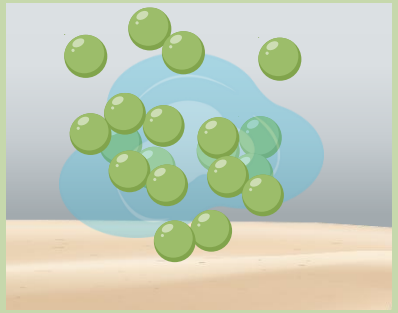
Maturation



Consolidation into distinct microenvironments

4

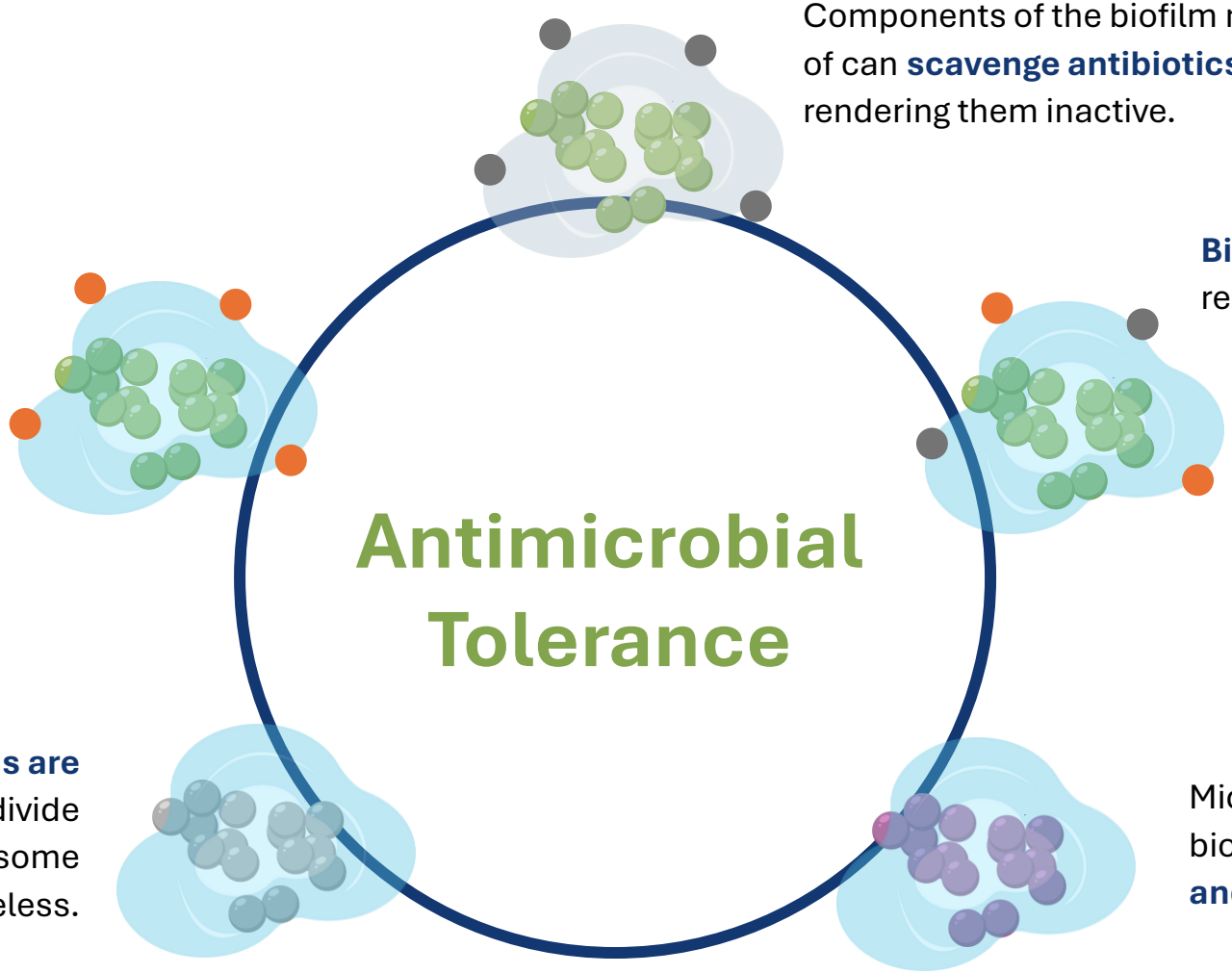
Dispersal



Release of select cells into adjacent environment while the biofilm remains adherent

Staats A, et al. *Ann Jt*. 2021 Oct;6:43.

Biofilm Bacteria Have Factors That Contribute to Antimicrobial Tolerance



Components of the biofilm matrix of can **scavenge antibiotics**, rendering them inactive.

Biochemical conditions reduce antibiotic activity.

Antibiotics may have difficulty diffusing through the matrix of the biofilm and reaching effective concentrations, especially in the inner core.

Microorganisms are dormant and do not divide actively, rendering some antibiotics useless.

Microorganisms in the biofilm may **show adaptive and acquired resistance.**

Rottier W, et al. *Arthroplasty*. 2023 Mar 2;5(1):10.

Some Bacteria Form Biofilm More Readily on Foreign Material

63-75%

Coagulase-negative staphylococcus species, *Staphylococcus aureus* (*S. aureus*), and Pseudomonas *species* account 63-75% of biofilms on medical devices including catheters, shunts, pacemakers, and other orthopedic devices.

37%

Coagulase negative staphylococcus species are some of the most common bacterial strains associated with knee and hip PJI, accounting for upwards of 37% of joint infections.

100,000x

The presence of a foreign body can decrease the inoculation dose of *S. aureus* required for infection by 100,000-fold.

Visperas A, et al. *J Orthop Res*. 2022 Jul;40(7):1477-1491.
Patel R. *New Engl J Med*. 2023;388:251-262.

New PJI Treatment Strategies May Improve PJI Outcomes

Multidisciplinary team approach to consider all factors in choice of treatment

- Duration of infection, stability of prosthesis, condition of tissue, patient's overall health

Culture and susceptibility testing with targeted antibiotic therapy based on antibiogram

- Consider new generation antibiotics, including glycopeptides and lipoglycopeptides

Surgical therapy in parallel to antibiotic therapy

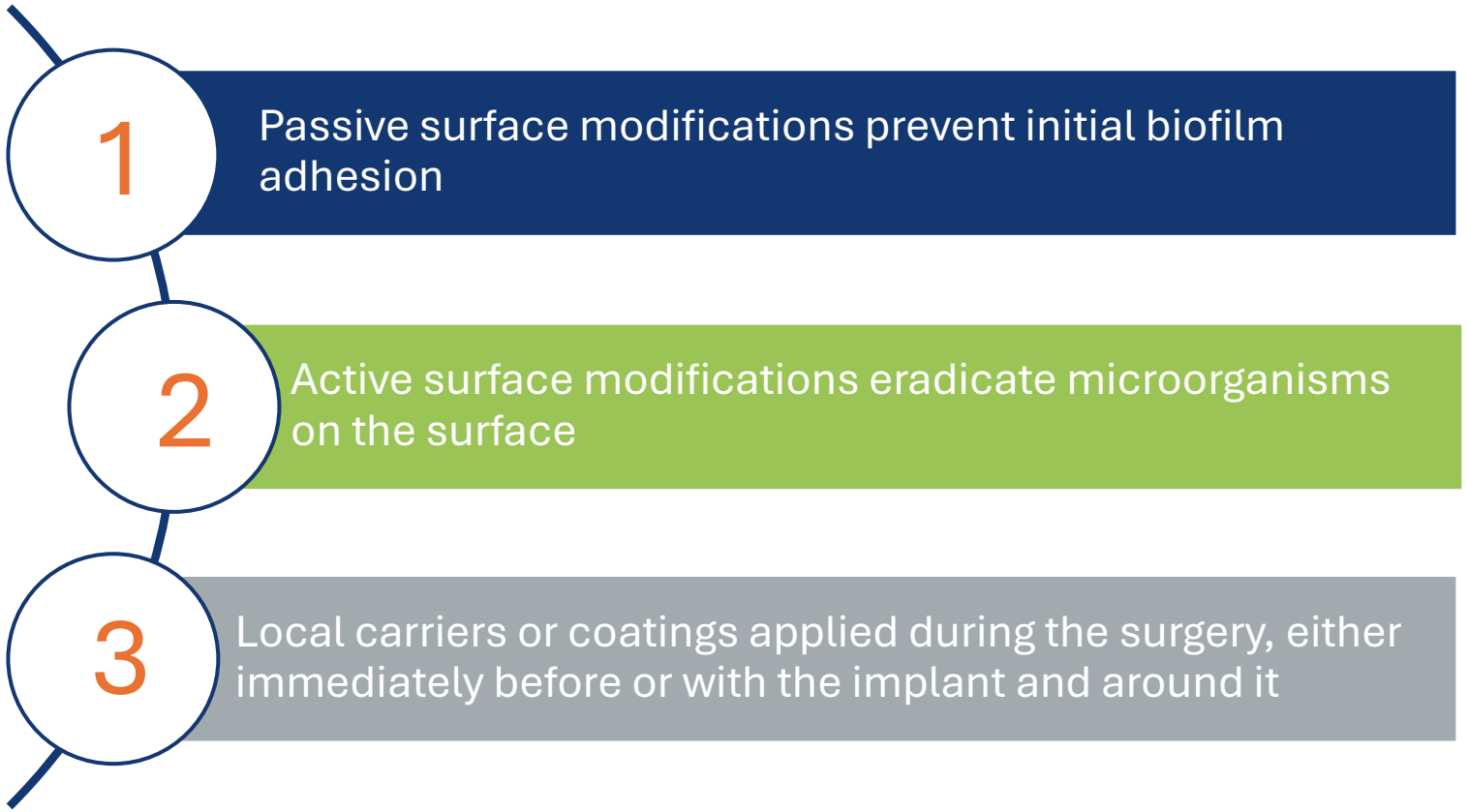
- DAIR only within 4 weeks of initial surgery if prosthesis is stable and soft tissue is good
  - Not recommended for resistant strains
- Two-stage revisions with perioperative targeted antibiotics in both stages for resistant organisms, chronic infections, or when DAIR has failed

Kraus K, et al. *Antibiotics (Basel)*. 2024 Dec 1;13(12):1151.

Modern Prosthetic Material Modifications Can Reduce PJI

All commonly used orthopedic materials are susceptible to colonization by biofilm-forming bacteria.

Strategies for eliminating PJI **before** biofilm can be fully established



Kraus K, et al. *Antibiotics (Basel)*. 2024 Dec 1;13(12):1151.

Universal Decolonization Prior to Surgery May Reduce Surgical Site Infection Rates

20-30% of the **orthopedic population** are carriers of *S. aureus*.

Society for Healthcare Epidemiology of America (SHEA) Decolonization Recommendations for Staphylococcal Surgical Site Infections (SSIs)	Quality of Evidence
Decolonize surgical patients with antistaphylococcal agent in the preoperative setting for orthopedic and cardiothoracic procedures. • Intranasal mupirocin • Chlorhexidine • Povidone iodine	HIGH
Decolonize surgical patients for other procedures at high risk for staphylococcal surgical site infection, such as those involving prosthetic material.	LOW

Kraus K, et al. *Antibiotics (Basel)*. 2024 Dec 1;13(12):1151.
Calderwood MS, et al. *Infect Control Hosp Epidemiol*. 2023 May;44(5):695-720.

Antimicrobial Strategies Involve Targeted Antibiotics Based on Activity, Administration, and Timing

Antimicrobial	Antibiofilm activity	Administration	Caveats
Rifamycins ▪ Rifampicin	▪ Gram + ▪ Staphylococci	Per os and IV	▪ Never use in monotherapy. ▪ When possible, associate with fluoroquinolones. ▪ Preferably not associated with linezolid or cotrimoxazole. ▪ Should not be used empirically. ▪ Start a few days after IV-ATB and only after surgical drains removed and no drainage from the wound.
Fluoroquinolones	▪ Gram + ▪ Gram – ▪ Enterobacter ▪ Pseudomonas	Per os and IV	▪ Preferably do not use in monotherapy. ▪ Against Gram+, when possible, use with rifampicin. ▪ Start a few days after IV ATB and only after surgical drains removed and no drainage from the wound.
Tetracyclines	▪ Gram + ▪ Gram – ▪ Mainly Gram + ▪ Doxycycline and minocycline for Staphylococci	Per os and IV	Preferred antibiotics for suppressive therapy.
Aminoglycosides • Tobramycin	▪ Gram + ▪ Gram – ▪ Pseudomonas		Can be considered in combination with β-lactams and combinations for difficult-to-treat Pseudomonas

Ferreira L, et al. *Front Microbiol*. 2024 Aug 29;15:1435720.

Antimicrobial Strategies Involve Targeted Antibiotics Based on Activity, Administration, and Timing

Antimicrobial	Antibiofilm activity	Administration	Caveats
Glycopeptides ▪ Vancomycin	▪ Gram + ▪ Staphylococci (MRSA) and Enterococci	Per os bioavailability not suitable for PJI infection	Avoid association with rifampicin.
Cyclic lipopeptides ▪ Daptomycin	▪ Gram + ▪ Staphylococci (including MRSA) and Enterococci (including VRE when combined with fosfomycin)	IV only – for PJI use 6–9 mg/kg/day	
Lipoglycopeptides ▪ Oritavancin ▪ Telavancin ▪ Dalbavancin	▪ Gram + ▪ Oritavancin and dalbavancin against Staphylococci (including MRSA)	IV only	
β-lactams	▪ Gram + ▪ Gram – ▪ Pseudomonas	Per os and IV	New β-lactams combined with β-lactamase inhibitors, carbapenems or cephalosporins for difficult-to-treat or multi-drug resistant Pseudomonas
Polymixins ▪ Polymixin B	▪ Gram – ▪ Pseudomonas	IV only	Treatment for multi-drug resistant Pseudomonas when there is no susceptibility to β-lactams or tobramycin.

Ferreira L, et al. *Front Microbiol*. 2024 Aug 29;15:1435720.
Tamma PD, et al. *Clin Infect Dis*. 2024 Aug 7:ciae403.

Considering Antibiotic Mechanism May Offer Improvement in PJI

	Dual MOA	Inhibits Cell-wall Synthesis	Disrupts Cell Membrane	Inhibits Protein Synthesis	Bactericidal
Ceftaroline		X			X
Dalbavancin		X			X
Daptomycin			X		X
Linezolid				X	
Telavancin	X	X	X		X
Vancomycin		X			X

VIBATIV® [Package Insert]. Nashville, TN: Cumberland Pharmaceuticals Inc.; December 2020.
Kahne D, et al. *Chem Rev*. 2005;105(2):425-448.
Steenbergen J, et al. *J Antimicrob Chemother*. 2005;55:283-288.
Bialvaei A, et al. *J Antimicrob Chemother*. 2016;72:354-364.
Mpenge MA and MacGowan AP. *Ther Clin Risk Manag.* 2015;11:565-579.
Sakoulas G, et al. *J Clin Microbiol*. 2004;42(6):2398-2402.
Chen AY, et al. *Int J Clin Pract.* 2007;61(5):853-863.

SHEA Guidelines Suggest Evidence-Based Antimicrobial Prophylaxis to Prevent SSIs

Administer antimicrobial prophylaxis according to evidence-based standards and guidelines. (Quality of Evidence: HIGH)

Antimicrobial administration within one hour prior to incision to maximize tissue concentration. Administering < 1 hour is effective.

- Two hours allowed for vancomycin and fluoroquinolones due to longer infusion times

Select appropriate antimicrobial agents based on the surgical procedure, the most common pathogens known to cause SSI for the specific procedure and published recommendations.

- Although vancomycin is not recommended for routine use, it should be considered for known colonized MRSA, particularly if the surgery involves prosthetic material

Obtain a thorough allergy history.

- Self-reported β-lactam allergy has been linked to a higher risk of SSI due to use of alternative, non–β-lactam and often inferior antibiotics.
- Many patients with a self-reported β-lactam allergy can safely receive a β-lactam antibiotic as prophylaxis.

Discontinue antimicrobial agents after incisional closure in the operating room.

- Antibiotics given after closure contribute to increased resistance, *Clostridioides difficile* infection, and acute kidney injury

Adjust dosing based on patient weight.

Re-dose prophylactic antimicrobial agents for lengthy procedures and in cases with excessive blood loss during the procedure.

Calderwood MS, et al. *Infect Control Hosp Epidemiol*. 2023 May;44(5):695-720.

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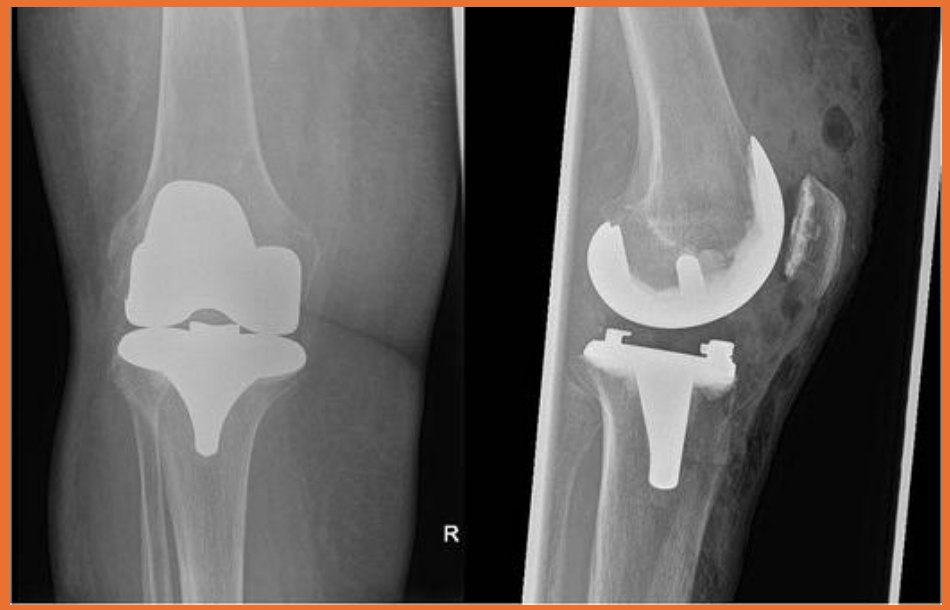
Patient With Multiple Comorbidities

- **Patient:** 75-year-old female patient underwent elective right TKA with patellar resurfacing.
- **Mobilization:** Prior to this procedure patient was able to mobilize using a walker.
- **Comorbidities:** Hypertension, type 2 diabetes, diverticulosis, Parkinson’s disease, obesity.
- **Surgery:** TKA was uneventful, patient was discharged home and requested to continue with rehabilitation.

Purcell C, et al. *J Surg Case Reports*. 2025;1.

Current Standard of Care for Post-op Fracture

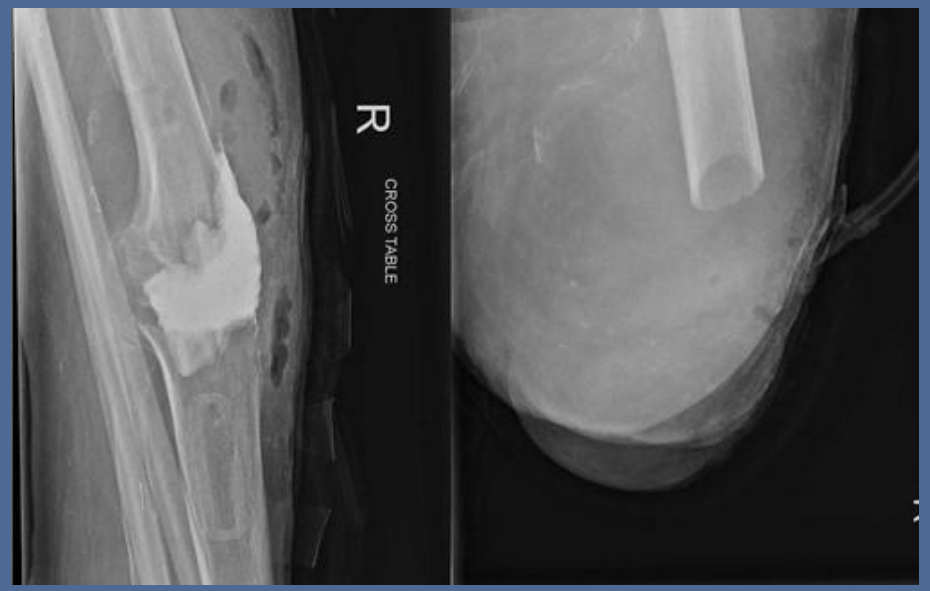
- **Two weeks postop:** Redness and warmth surrounding the knee joint and 2 weeks later felt a “pop” when walking.
- **Mobility:** Presented with a painful, swollen right knee and unable to bear weight.
- **X-rays:** Closed right patellar sleeve fracture.
- **Treatment:** Splint was applied and patient received pain management for fracture.



Purcell C, et al. *J Surg Case Reports*. 2025;1.

PJI Standard of Care Failure

- **Postdischarge:** Over the following month, skin above the fractured patella became necrotic.
- **Treatment:** Patient underwent multiple tissue samplings, patellectomy, removal of implants, and insertion of an antibiotic impregnated cement spacer.
  - Infection was uncontrollable despite appropriate PJI standard of care.
  - AKA was performed and patient was discharged in 4 weeks with mobility limited to hoist transfers.
- **Outcome:** Patient passed away 8 weeks later.



Purcell C, et al. *J Surg Case Reports*. 2025;1.

How Did We Get Here?

Patient had multiple comorbidities and risk factors.

- Hypertension
- Type 2 diabetes
- Parkinson’s disease
- Obesity
- Advanced age
- Limited mobility

What Can We Do Differently?

Consider alternative strategies for approach and treatment.

- Multidisciplinary team
- Perioperative prophylaxis
- New generation antimicrobials

Purcell C, et al. *J Surg Case Reports*. 2025;1.

MRSE and MRSA Can Complicate Standard of Care

- **Patient:** 74-year-old female patient underwent elective left TKA 6 years ago.
- **Comorbidities:** Hypertension, osteoarthritis
- **Surgery:** Over the course of 6 years, the patient has had multiple surgeries, all with positive MRSE cultures.
- **Treatment:** After her last two-stage revision, she was treated with trimethoprim-sulfamethoxazole for 4 months after IV antibiotic treatment.
- **Current presentation:** Six months after her last revision, she presented with pain and tenderness to the knee.

Jose J, Antony SJ. *Int J Ortho Surg*. 2017;25:1.

A New Approach for PJI Treatment

- **Physical:** Significant surgical scars with mild erythema and tenderness of the knee, small effusion, and restricted range of motion.
- **Treatment:** Due to repeated failures of vancomycin and daptomycin, team recommended two doses of IV dalbavancin.
- **Outcome:** No signs of infection at 6-month follow-up.

Jose J, Antony SJ. *Int J Ortho Surg*. 2017;25:1.
Turner NA, et al. *J Am Med Assoc*. 2025 Aug 13:e2512543.