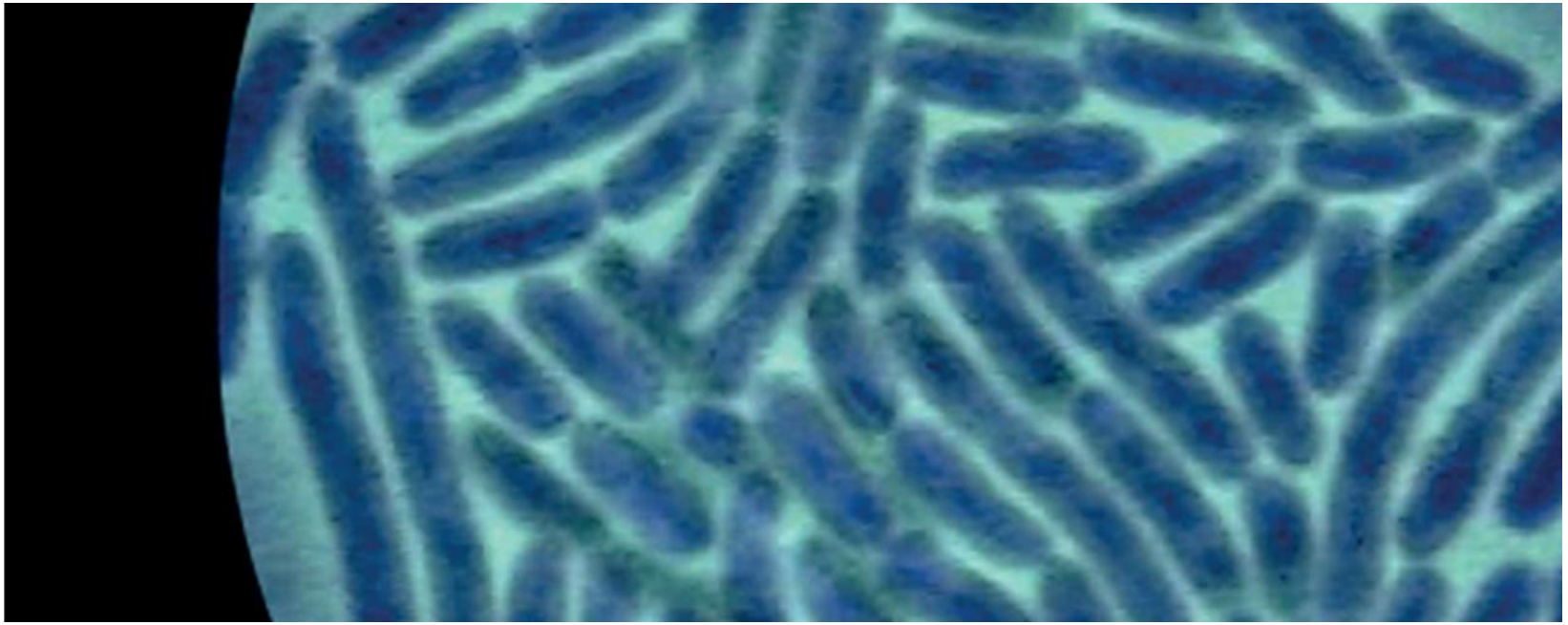

Introduction to Musculoskeletal Infection

In-person training for Distributor Sales Representatives

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Training objectives

At the end of this 30 minute training session you will:

- Understand the fundamentals of musculoskeletal infection; its cause, impact on patients and cost to the healthcare system.
- Be aware of the most common types of musculoskeletal infection and the treatment options available to your surgeons.
- Have gained a working knowledge of the key terms used in discussions about musculoskeletal infection.

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Agenda

- Key terms
- Overview of musculoskeletal infection
- The cause of musculoskeletal infection
- Gram’s method of staining
- Minimum inhibitory concentration (MIC)
- Biofilm
- Periprosthetic joint infection
- Infected non-unions
- Diabetic foot ulcers with osteomyelitis
- Summary of key points

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Key terms

Acute infection: An infection that is present for less than 30 days.

Antibiotic: A drug that kills or inhibits the growth of bacteria but not viruses.

Antimicrobial: An agent that kills microorganisms or inhibits their growth.

Antiphagocytic: Impeding or preventing the action of phagocytes.

Bacteria: A large group of unicellular microorganisms.

Biofilm: A complex community of bacterial cells enclosed in a self-produced extracellular matrix (ECM) that adhere to an inert or living surface.

CDC: Centers for Disease Control and Prevention.

Chronic infection: A prolonged or persistent invasion of the body by pathogens, which indicates that biofilm is present.

Drug-resistant infections: Infections that are resistant to antibiotics commonly used to kill infections caused by resistant strains of bacteria.

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Key terms

ECM: Extracellular matrix is a polysaccharide coating formed by bacteria that contains host proteins acquired by the bacterial network.

Foot ulcer: An open sore or wound that is commonly located on the lower legs or bottom of the feet.

Gram Stain: A method used to differentiate two large groups of bacteria based on their cell wall constituents.

Gram-negative bacteria: Have a cell wall composed of a thin layer of peptidoglycan that is located between an inner cell membrane and a bacterial outer membrane. Gram-negative bacteria take on the color of red/pink counterstain in the Gram's staining method.

Gram-positive bacteria: Have a cell wall composed of a thick layer of peptidoglycan. Stain gram-positive in Gram's method of staining because they retain the color of the crystal violet strain.

HAI: Hospital acquired infection, which is a localized or systemic condition resulting from an adverse reaction to the presence of infectious agents or toxins that occurs in a healthcare setting.

Inoculation: The introduction of an antigenic substance or vaccine into the body to produce immunity to a specific disease.

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Key terms

MIC: Minimum inhibitory concentration is the lowest concentration of an antimicrobial that will inhibit the visible growth of a bacterium.

Musculoskeletal infection: Invasion and multiplication of pathogenic microorganisms in the body.

Non-union: A fracture that will not heal.

OSHA: Occupational Safety and Health Administration.

Osteomyelitis: An infection of bone and bone marrow caused by bacteria.

Phagocytosis: The engulfing and destruction of particulate matter (bacteria) by a cell.

PJI: Periprosthetic Joint Infection is a postoperative complication that can occur following total hip or knee arthroplasty by bacterial inoculation at the time of surgery or through open draining wounds.

Pathogen: Infectious microorganisms such as bacteria, viruses and fungi.

Polymicrobial: Disease state involving multiple species of multiple organisms.

SSI: Surgical Site Infections, which are directly related to an operative procedure.

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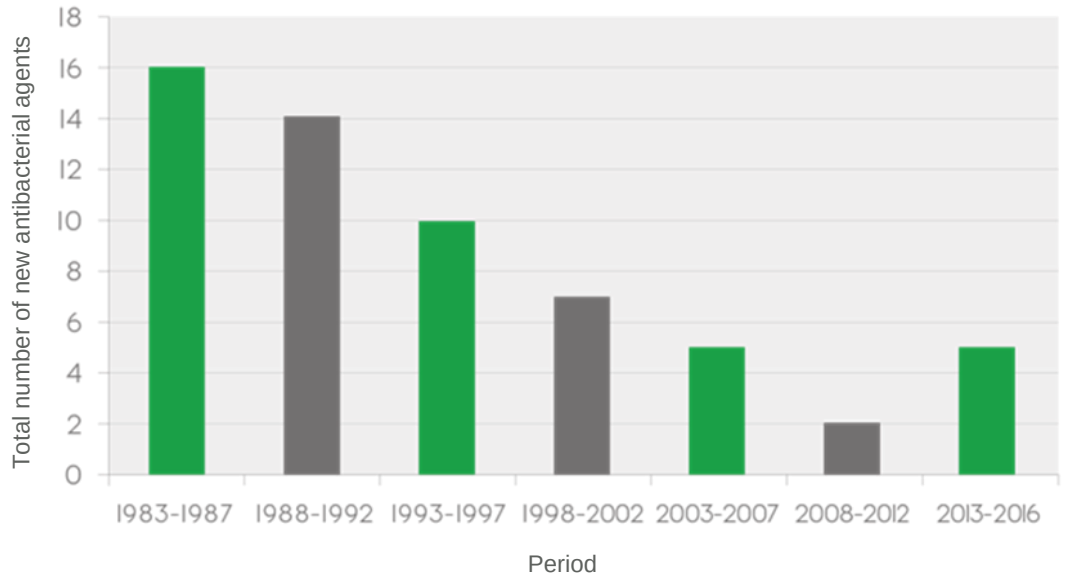
Overview of musculoskeletal infection

Musculoskeletal infections are one of the biggest healthcare challenges of the 21st century

- Caused by invasion and multiplication of pathogenic micro-organisms in the body.
- 50-60% of all hospital acquired infections are caused by antibiotic-resistant bacteria.[1]
- Rapid growth of antibiotic-resistant strains and biofilms continues to outpace the development of new antibiotics and antibiotic strategies.[2,3]

Antibacterial agent development is dwindling [2]



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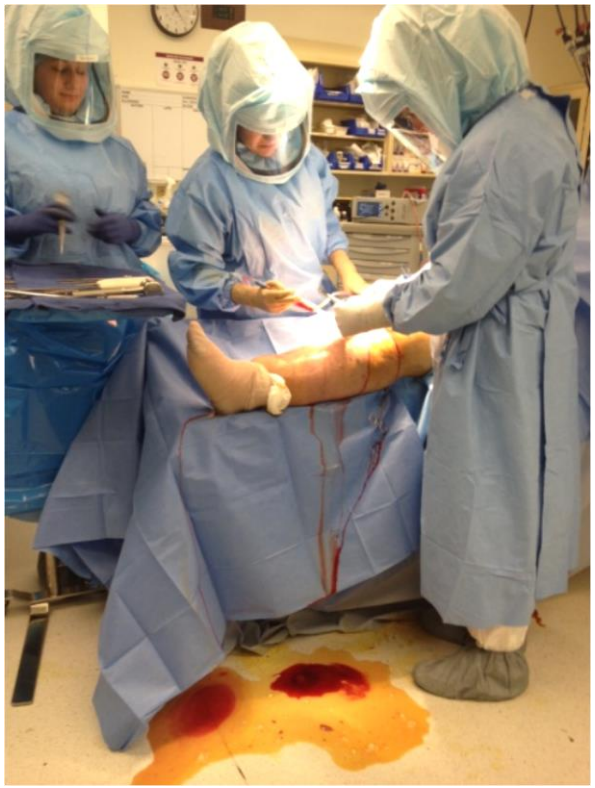
Overview of musculoskeletal infection

Periprosthetic joint infections, infected non-unions & diabetic foot ulcers with osteomyelitis are the most common musculoskeletal infections

- 1.7M patients per year acquire an infection while in the hospital, resulting in 5.8% of deaths.[1]
- Surgical site infections account for approximately 23% of all hospital acquired infections.[4]



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Overview of musculoskeletal infection

Musculoskeletal infections are a huge burden on hospital resources and expenditure

- Musculoskeletal infections can sometimes be treated with antibiotics but often require an additional surgery to treat the infection.
- Hospital acquired infections average $9.8B in the U.S. and $32.5B worldwide.[1]
- Average hospital cost per patient can increase from $32K to $185K when an infection is present.[1]
- The cost of antibiotic-resistant infections is $21B to $34B each year with more than 8 million additional hospital days.[5]

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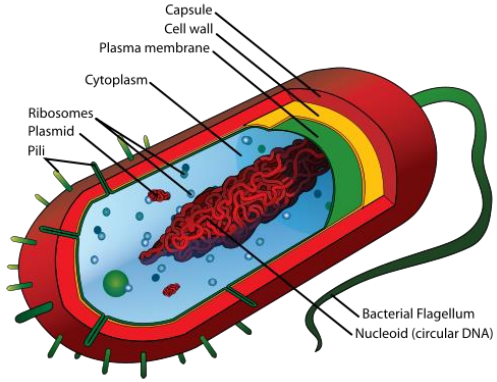
The cause of musculoskeletal infection

Bacteria

- A large group of unicellular microorganisms.
- Differentiated into gram-positive and gram-negative bacteria.



Gram-positive bacteria (77% of bacteria):[6]

- Most commonly found in microscopic skin particles.
- Spread through the air or by direct contact with coated objects.
- Includes *Staphylococci*, *Streptococci*, and *Pneumococci*.
- More receptive to antibiotics than Gram-negative bacteria.

Gram-negative bacteria (23% of bacteria):[7,8]

- Found and transferred through direct contact with wet objects.
- Includes *Eschericia coli*, *Salmonella*, and *Pseudomonas aeruginosa*.
- Resistant to multiple drugs and are increasingly resistant to most available antibiotics.
- Can cause infections of the bloodstream, pneumonia, meningitis, and wound or surgical site infections.

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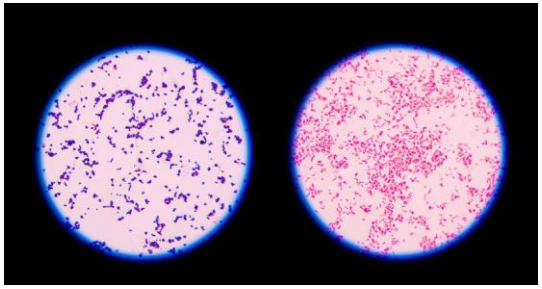
Gram's method of staining

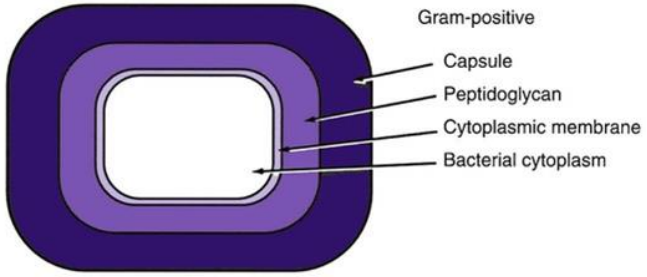
Gram Stain

- A technique used to differentiate bacteria based on the difference in their cell wall properties.
  - Distinguishes between gram-positive and gram-negative bacteria by coloring their cells violet or red.



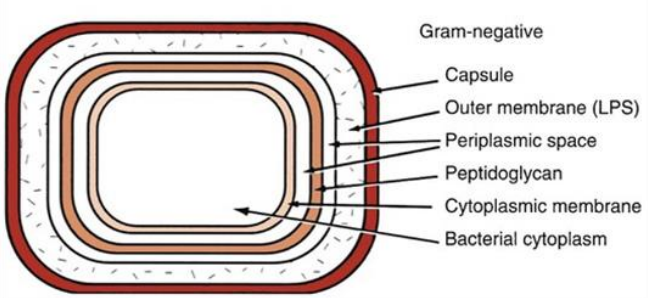
Gram-positive bacteria:

- Cell wall composed of a thick layer of peptidoglycan.
- Stain gram-positive: the cell wall retains the color of the crystal violet stain.



Gram-negative bacteria:

- Cell wall composed of a thin layer of peptidoglycan, located between an inner cell membrane and a bacterial outer membrane.
- Stain gram-negative: the thin cell wall does not retain the crystal violet stain, and takes on the color of the red counterstain.



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Minimum Inhibitory Concentration (MIC)

Overview

- MIC is the lowest concentration of an antimicrobial that will inhibit the visible growth of a bacterium.
- MIC is used by clinicians to choose which antibiotics to administer for specific infections and to identify the clinically effective dose of antibiotic.
  - Different antibiotics are used for gram-positive, gram-negative and polymicrobial infections.
  - Polymicrobial infections often require more than one antibiotic to target all bacterial pathogens.
- This is important because populations of bacteria exposed to an insufficient concentration of a particular drug or to a broad-spectrum antibiotic, can evolve resistance to those drugs.
- MIC scores aid in improving outcomes for patients and preventing drug-resistant microbial strains evolving.

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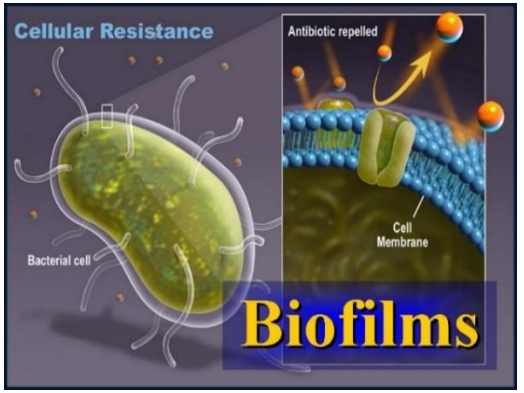
Biofilm

Overview



- Complex community of bacterial cells enclosed in a secreted extracellular matrix (ECM).
- Can adhere to inert or living surfaces.
- Can be the cause of chronic disease.

Properties of biofilm that lead to infection:[9]

- The ECM acts as a mechanical barrier and prevents the inward diffusion of antimicrobials.
- pH differences exist that allow some bacteria to become dormant while others remain active.
- Dormant bacteria are able to withstand antibiotic attack and develop a resistance to antibiotics.
- Biofilm displays antiphagocytic properties that make detection and eradication difficult.
- There are currently no methods or chemicals to dissolve a biofilm.

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Treatment of biofilm

Effective treatment for an established biofilm

- Removal of implant and foreign body material.
- Surgical debridement.
- Local dose of antimicrobial agent(s) at or above MIC.
- Raise pH to a physiological level (infected sites are normally acidic).
- Suppress local inflammation.

Note: The treatment strategy and response to treatment is dependent on the host's (patient) immune system.

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Periprosthetic joint infection (PJI)

Overview

- Post-operative complication following THA and TKA procedures by bacterial inoculation at the time of surgery or through open draining wounds.
  - 1% of primary hip and knee arthroplasties become infected.[10]
  - 16% of hip revisions are carried out due to infection.[11]
  - 23% of knee revisions are carried out due to infection.[11]

- Acute PJI:
  - Present for less than 30 days.
  - Biofilm is not established and treatment is focused on implant preservation.
- Chronic PJI:
  - A prolonged or persistent invasion of the body by pathogens, which indicates that biofilm is present.
  - Two stage procedures are often required for the treatment of the infection and for revision arthroplasty.

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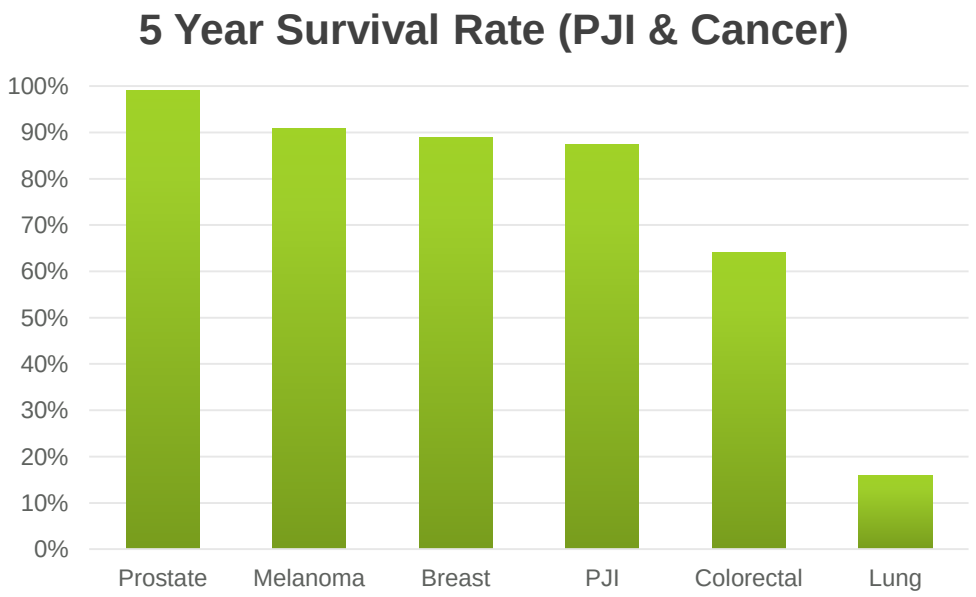
Periprosthetic joint infection (PJI)

Impact

- The current cost of revisions for PJI exceeds $556M in the US and is expected to exceed $1.6B by the year 2020.[12]
- PJI revisions are associated with 5 times the risk of death compared to aseptic revisions.[13]
- Relative 5 year survival rate for patients with PJI is 87.3%, which is lower than the survival rate for the three most common cancers.[13]



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Acute PJI

Treatment example

- Debridement (used when joint components are not loose):
  - Incision and arthrotomy.
  - Irrigation and debridement.
  - Polyethylene insert exchange.
  - Antibiotic therapy.
- One-stage resection arthroplasty:
  - Incision and arthrotomy.
  - Irrigation and debridement.
  - Removal of cement and infected total knee components.
  - Immediate implantation of new total knee components.
  - Lavage and periprosthetic antibiotic therapy.

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Chronic PJI

Treatment example

2 stage resection arthroplasty:

- Stage 1 - Focused on eradicating the infection:
  - Incision and arthrotomy.
  - Resection of implant components.
  - Irrigation and debridement.
  - Use of antibiotic impregnated spacers to maintain space and provide stability.
- Stage 2 - Occurs after infection is eradicated:
  - Incision and arthrotomy.
  - Removal of antibiotic spacers.
  - Irrigation and debridement.
  - Implantation of revision arthroplasty components.
  - Dead space and soft tissue management.

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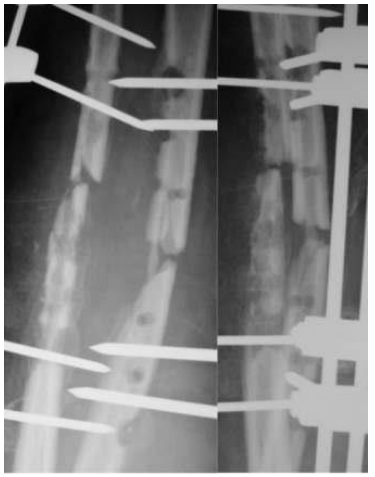
Infected non-unions

Overview

- Post-operative fracture that will not heal.
- Caused by contamination by bacteria and failure of fixation.
- Risk of infection depends on the type of fracture:
  - 0-5% risk with closed fracture.[14]
  - 0-50% risk with open fracture.[14]
- Complications:
  - Bone and soft tissue loss.
  - Internal fixation loosening or breakage.
  - Poor vascularity of the bony fragments.
  - Osteomyelitis.



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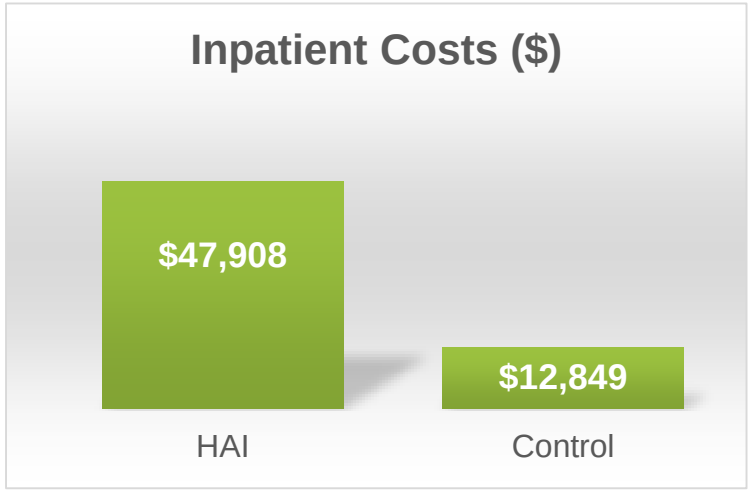
Infected non-unions

A study was conducted to explore the clinical impact and economic burden of hospital acquired infections (HAIs) in trauma patients[15]

- Increased mortality rates for patients with HAIs.
- Longer hospitalization periods for patients with HAIs.
- Higher costs for patients with HAIs.



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Infected non-unions

Treatment example

- Removal of original hardware.
- Debridement.
- Revision stabilization of the fracture.
- Supplemental bone grafting.
    - Unmanaged spaces may contribute to infection.
- Treatment of infection with antibiotics.
- Two stage treatments may also be required to treat the infection and stabilize the non-union.

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Diabetic foot ulcers with osteomyelitis

Overview

- A foot ulcer is an open sore or wound that is commonly located on the lower legs or bottom of the feet.
  - 7.3 million people affected by diabetes in the U.S. have a lifetime risk of developing a foot ulcer.[16,17]
- If untreated, a diabetic foot ulcer can become infected and lead to osteomyelitis.
  - The prevalence of osteomyelitis ranges from 10-20%.[18]
- Osteomyelitis is the leading cause of non-traumatic lower extremity amputations.
  - 60% of lower extremity amputations are caused by osteomyelitis.[18]

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Diabetic foot ulcers with osteomyelitis

Impact

- Diabetic foot ulcers impose a tremendous medical and financial burden on our healthcare system.
  - Patients require frequent emergency room visits, have increased hospital readmissions and require longer lengths of stay.
  - Treatment costs are estimated to be ~$45,000 per patient.[19]
  - Ulcer care adds $9B to $13B to the direct yearly costs associated with diabetes.[20]
- Remission rates for osteomyelitis can range up to 88%.[18]
- Approximately 50% of patients who have foot amputations due to diabetes die within five years.[21]

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Diabetic foot ulcers with osteomyelitis

Treatment example

- Diagnosis of osteomyelitis.
- Remove load from the ulcer site to redistribute force.
- Debridement of infected bone.
- Resection of compromised soft tissue.
- Antimicrobial therapy.
- Wound dressings with regular changes.
- Increased healing rates and decreased length of antibiotic treatment have been reported with early surgical intervention for osteomyelitis.[20]

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Musculoskeletal infection

Key points

- One of the biggest healthcare challenges of the 21st century.
- Present a tremendous medical and economic burden on the healthcare system.
- Represents a major cause of patient morbidity and mortality.
- Care delivery is becoming increasingly challenging and complicated.

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Musculoskeletal infection

Treatment goals

- Provide a novel and innovative solution for high risk patients or infected sites.
- Reduce avoidable complications.
- Improve patient outcomes and decrease hospital readmissions.
- Improve treatments while decreasing overall treatment cost.
- Reduce the potential cost to the hospital of penalties imposed by the Affordable Care Act.

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Musculoskeletal infection

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