INTRODUCTION

Joint replacement (arthroplasty) significantly improved the quality of life in a large number of patients with degenerative joint disease. In the increasingly elderly population, the number of arthroplasties performed rises continuously. It is one of the most successful surgeries and less than 10% of recipients develop a complication during their lifetime. Although prosthetic joint infection (PJI) is a rare event (usually occurring in <1-2% of primary arthroplasties), it represents a significant complication that is associated with high morbidity, need for complex treatment, and substantial healthcare costs. In addition to prolonged hospitalization, PJI can lead to unsatisfactory functional results or even permanent disability, including arthrodesis or leg amputation [(1)].

After primary joint replacement, the infection rate during the first two postoperative years is usually <1% in hip and shoulder prostheses, <2% in knee prostheses, and <9% in elbow prostheses. However, the reported infection rates are probably largely underestimated, since many cases of presumed aseptic failure are caused by an unrecognized infection, particularly low-grade infections caused by low-virulent skin bacteria.[(2)] After revision surgery for any reason, the infection rates are usually considerably higher (up to 40%). Importantly, prosthetic joints remain susceptible to hematogenous seeding

during their entire lifetime. Therefore, the frequency of infection should be reported as incidence rate (per prosthesis-year) rather than as risk (without specified denominator). In addition, the incidence of PJI will most likely continue to rise due to increasing numbers of implanted prostheses in the aging population, longer prosthesis indwelling times exposed to a higher cumulative risk for infection during the implant lifetime, and better detection methods for microbial biofilms or unusual bacteria involved in PJI. [3]

Aim Of The Essay

To evaluate patient with Peri-prosthetic joint Infections and to illustrate the recent trends of diagnosis and management.

PATHOGENESIS

Pathophysiology:

It is considered that the minimum forming dose of bacterial pustule is reduced by log^{10} in case of presence of a foreign body. This reduction of the minimum infection forming dose has also been observed in terms of avital bone and soft tissue. The so-called race for the surface between human cells and planktonic bacteria, which is crucial for the further fate of the implant, begins directly with the implantation of the biomaterial. The fundamental first step of biomaterial-associated infection is bacterial adhesion, triggered by a pathogenetic sequence. (4)

The adhesive colonisation of the biomaterial after the implantation process results in a bacterial resistance against host defense mechanisms and the systemic antibiotic therapy. This can lead to a transformation of non-pathogenic to pathogenic bacteria resulting in an infection that cannot be cured in numerous cases without the removal of the implant.To a certain extent, adhesion of bacteria depends on the surface characteristics of the biomaterials.(4) In general, the implant surface exposed to a biological environment is surrounded by a conditioning film.(5) Initially, the surface repels the bacteria as both are anionic. During this phase of bacterial adhesion,

physical London-van der Waal's forces and hydrophobic molecules of bacteria and biomaterial enable an adequate contact time in order to form an irreversible bond. This initial bond is followed by the proliferation of a biofilm containing bacteria, polysaccharides and ions, which is considered the final stage of infection.[6] By the time of biofilm formation, the bacteria have created a protective environment against host defence mechanisms and antibiotic agents. The biofilm acts as a buffer against the ever changing influences of the direct environment and simplifies the exchange of nutrients and elimination of waste products. The ability of biofilm formation and adherence to implant surfaces has been described as an important factor of pathogenicity of bacteria and especially applies to the species of staphylococci. [6] Evidence suggested intracellular internalization of staphylococci as a mechanism contributing to pathogenesis of PJI and resistance to treatment. According to this concept, staphylococci can invade and live inside the host cells, facilitating long term persistence of the microorganism in bone via evasion of antibiotics and immune system responses. "Small colony variant" strains are particularly skilled in invading and living inside the host cells. These strains have mutations that impair the electron transport pathway. [7]

Risk factors:

Risk factors can divided into three categories: host, operating room environment, and surgical variables.

It is important to determine the risks within each category in order to develop adequate, successful preventative approaches.[8]

Host:

The first category involves risk factors related to the host, such as aging, increase body weight, alcohol abuse, and comorbidities that may increase the risk of subsequent complications as hypertension, hyperlipidemia, diabetes mellitus, rheumatoid arthritis, cardiac diseases (coronary heart disease, peripheral vascular disease, congestive heart failure, ….), cerebrovascular disease (stroke, paralysis, dyskinesia,….), renal insufficiency, renal failure and dialysis, anemia (aplastic, autoimmune, iron deficiency), coagulopathy, urinary tract infection, liver disease (hepatitis B, hepatitis C, hepatic insufficiency), malignancy (all visceral, metastatic and melanoma), tuberculosis, venous thromboembolic disease rheumatologic disease, obesity, coagulopathy. [9,10,11]

Other factors as wound healing complications, Prior surgery or infection of the joint or adjacent bone or perioperative non articular infection also can affecting the periprosthetic infection. [9]

Operating room environment:

Second category includes risk factors related to operating room environment as the frequency of traffic into and out of an operating room during surgery, quality of air in the operating room, risk factors associated with healthcare personnel and risk factors related to the patient undergoing the operation. [12]

Surgical variables:

Last category is surgical variables which began by skin preparation and include surgical procedures and postoperative care. [13]

Infecting organisms:

A variety of different bacterial species can cause deep periprosthetic infection Staphyloccus aureus and coagulase negative staphylococci, especially S. epidermidis, account for the majority of implant infections, [14,15] although a wide range of gram-positive and gram- negative organisms as well as anaerobic organisms have also been identified. Peri-prosthetic infection may also be caused by numerous micro-organisms, e.g.Haemophilus spp., Acinetobacter spp., Mycobacterium tuberculosis, Clostridiumdifficile,[16] Aspergillus spp., Candida spp.[17] have been reported to cause peri-prosthetic infections. In a study by **Marculescu and Cantey (2008)**, 19% of PJI episodes were polymicrobial. [18] (see Table 1)

Table (1): Percentage of Different Pathogens Causing Peri-prosthetic Infections. [19]

Pathogen	Incidence (%)
Staphylococci Coagulase-negative staphylococci Staphyolococcus aureus	**50–60** **25–30** **25**
Gram-negative, aerobic rod-shaped bacteri including enterobacteriaceae, e.g. Escherichia coli, Proteus spp., Morganella morganii, Serratia marcescens, Citrobacter freundii, Salmonella enterica and non-fermenting pathogens such as Pseudomanas spp., Stenotrophomonas maltophilia, Alcaligenes spp.	**20**
Streptococci (S. agalacticae, rarely others)	**10–15**
Poly-microbial	**10-15**
Anaerobic bacteria (among others Probionibacterium spp., Prevotella spp., Peptostreptoccci, Bacteroides spp., Veilonellaparvula	**7–10**
Other pathogens	**2**
Without a positive culture	**10**

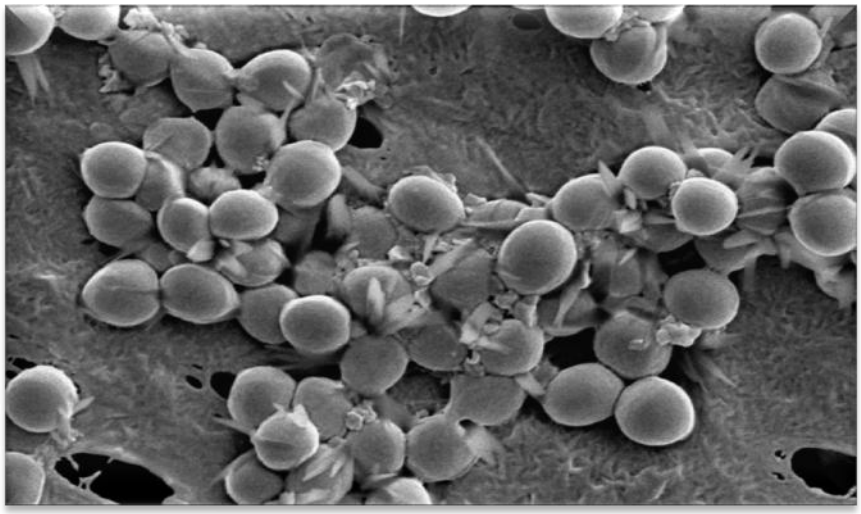

Fig (1): Staphylococcus Aureus Biofilm[20]

The time of infection varies by species: S. aureus predominate in early infections, and S. epidermidis, Prppionbacterium acnes and peptostreptococci present later in delayed infections. [19] (see table 2)

Table (2): Most Frequent Pathogens of Peri-prosthetic Infections Classified In Terms of the Onset of Infection. [19]

Classification	Pathogen(s)
Early infection (up to two months after implantation)	Staphylococcus aureus Aerobic, Gram-negative rod-shaped bacteria Coagulase-negative staphylococci
Delayed infection (2 to 12 months after implantation)	Coagulase-negative staphylococci Staphylococcus aureus Micro-organisms of the skin flora Aerobic, Gram-negative rod-shaped bacteria
Late infection (>12 months after implantation)	Coagulase-negative staphylococci Micro-organisms of the skin flora Staphylococcus aureus Aerobic, Gram-negative rod-shaped bacteria Anaerobic bacteria (especially Peptococcus, Peptostreptococcus)

Routes of infection:

Bacteria may come into contact with the biomaterial via direct contamination at the time of surgery, contiguous spread or haematogenous and lymphogenous dissemination. Furthermore, it is considered that bacteria causing a peri-prosthetic infection within the first two years after implantation must have reached the host during the operation. If the infection occurs later, a haematogenous or lymphogenous dissemination has to be assumed.[19]

CLASSIFICATION

The major aim of a system for periprosthetic infections is to help the orthopedic surgeon to identify the acuteness or chronicity of the infection, predict the complexity of the treatment procedure and ensure that all necessary devices are available at the time of the first revision surgery as well as of further surgical interventions if necessary. Moreover, a classification system should also permit a valid and reliable comparison of results from similar case mixes.[21]

1) **McPherson et al (2002)** developed a staging system for periprosthetic hip infections taking into consideration the acuteness of the infection, the overall medical and immune health status of the patient, and the local wound condition (see Table 3). This system has been used in clinical practise especially in the United States and the United Kingdom.[22]

Table (3): Staging system for periprosthetic infections according to McPherson [22]

Infection Type	Systemic Host Grade	Local extremity grade
I: early postoperative infection	A: uncompromised	1: uncompromised
(< 4 postoperative weeks)	B: compromised	2: compromised
II:hematogenous infection	(1-2 compromising factors)	(1-2compromising factors)
(< 4 weeks duration)	C: significant compromise	3:significant compromise
III: late chronic infection	(> 2 compromising factors) or one of	(>2compromising factors)
(> 4 weeks duration)	- absolute neutrophil count < 1000	
	- CD4 T cell count < 100	
	- intravenous drug abuse	
	- chronic active infection at another site.	
	- dysplasia or neoplasm of the immune system.	

The systemic compromising factors includes: age > 80, immunosuppressive drugs, alcoholism, malignancy, chronic active dermatitis or cellulitis, pulmonary insufficiency, chronic indwelling catheter, renal failure requiring dialysis, chronic malnutrition, systemic inflammatory disease, current nicotin use, systemic immune compromise, diabetes, hepatic insufficiency. [22]

The local compromising factors includes: active infection present > 3-4 months, multiple incision with skin bridges, soft tissue loss from prior trauma, subcutaneous abscess, synovial cutaneous fistula, prior periarticular fracture or trauma about a joint, prior local irradiation, vascular insufficiency to extremity. [22]

2) **Tsukayama et al (2003).** proposed a 4-stage system consisting of early postoperative-, late chronic-, and acute hematogenous infections, and positive intraoperative cultures of specimens obtained during revision of a presumed aseptically loose total hip prosthesis. [23] **Type I:** Positive intraoperative culture during revision surgery initially performed for aseptic loosening. **Type II:** Acute infection, initiating within 4 weeks after implantation, associated with intraoperative contamination and presenting with classic symptoms of fever, inflammation, and fluid/pus. **Type IIA:** Superficial to joint capsule. **Type IIB:** Deep to joint capsule. **Type III:** Acute hematogenous infection in a previously normal joint, with onset usually later than 4 weeks and extension through the joint capsule. **Type IV:** Late chronic infections more than 4 weeks after primary implantation with sinus, indurations, and joint involvement. [23]
3) **Cierny and DiPasquale (2003)** tried to adjust the Cierny classification system for osteomyelitis in adult patients. also

for the classification of periprosthetic total joint infections.[24,25] In this system, prosthetic joint infections are entered as anatomic types of the disease: early and superficial osteomyelitis (Type II) or late and refractory osteomyelitis (Type IV of the initial osteomyelitis staging system). Besides this anatomic differentiation, the authors added local and systemic host factors that may affect treatment and prognosis. In this system, patients are categorized as A-, B-, or C-hosts. A-hosts are healthy and without healing deficiencies. B-hosts are compromised by one or more local and/or systemic parameters, C-hosts are patients for whom the morbidity of cure far exceeds that of their illness or surpasses their capacity to withstand curative treatment. C-hosts are not considered candidates for aggressive surgical intervention but rather for conservative treatment. [21,24]

- ***$B^{(L)}$ – Host*** *(local compromise): chronic lymphedema, venous stasis, major vessel disease, Arteritis, extensive scarring, radiation fibrosis, retained foreign bodies (suture, buckshot).*[21,24]

- ***$B^{(S)}$ - Host*** *(systemic compromise): malnutrition, immune deficiencies, chronic hypoxia, malignancies, diabetes mellitus, extremes of age (-2 years, + 70 years), current nicotine abuse, chronic nicotine abuse, major organ failure.*[21,24]

Diagnosis

The diagnosis of TKA and THA sepsis can be challenging for both musculoskeletal and nonmusculoskeletal care providers. Despite a thorough patient history, physical examination, multiple diagnostic tests, and complex algorithms, differentiating periprosthetic joint infection from aseptic loosening of TKA and THA can be difficult in some cases. [26]

History and Physical Examination

Evaluation of medical and surgical history as well as physical examination is an excellent screening tool for periprosthetic joint infection and helps guide subsequent diagnostic evaluation. A tentative diagnosis may often be based solely on information given during the patient interview. Although the history focuses on the chief complaint, it is important to consider the entire person and other possible medical complaints. A detailed comprehensive history provides insight into additional factors that may influence the best course of treatment. [26]

The classic presentation is that of a painful joint with swelling, hotness, and redness. The location and character of pain can provide important insights into the possible etiology. Constant pain present with activity, at rest and at night often indicates deep infection. This can be supported by a history of