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- Objectives** To review the latest evidence on antibiotic prophylaxis for patients with total joint replacements to prevent prosthesis infections.
- Data sources** Literature search of Medline and PubMed until June 2009.
- Study selection** Studies of patients with total joint replacements from around the world, studies concerning antibiotic prophylaxis, as well as chemoprophylaxis guidelines from orthopaedic associations were searched.
- Data extraction** Literature review, original articles, case reports, best practice guidelines.
- Data synthesis** With the rising incidence of patients with total joint replacements, subsequent deep infection of the implants is a rare but dreaded complication which has immense physiological, psychological, nancial, and social implications. Guidelines from urologists, gastroenterologists, and dental surgeons attempt to identify high-risk patients who may be more susceptible to prosthetic joint infections. These patients are provided with prophylactic antibiotics before any invasive procedure that may cause bacterial seeding to prosthetic joints. Most orthopaedic associations around the world adopt a similar policy to provide prophylaxis to cover any anticipated chance of bacteraemia. The American Association of Orthopaedic Surgeons adopts the most cautious approach in which all patients with total joint replacements who undergo any procedure that breaches a mucosal surface receive prophylactic antibiotics.
- Conclusion** The guidelines from the American Association of Orthopaedic Surgeons seem to have an all-encompassing policy when it comes to providing prophylactic antibiotics. Nonetheless, physicians must still exercise their judgement and customise the treatment to each patient. The benefits of prophylactic antibiotics must be balanced against the risks of drug side-effects and the emergence of antibiotic resistance.

Key words
Antibiotic prophylaxis; Endoscopy;
Infection; Replacement, arthroplasty;
Surgical procedure, operative

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Introduction

With an ageing population, total joint replacements are becoming more common. In the United States, at least 400 000 total hip and knee replacements are performed every year; in Hong Kong the number approaches 2000 per year. One uncommon but devastating complication after joint replacement surgery is late infection of the prosthesis, which has extremely high cost implications. The guidelines on prophylactic antibiotics prior to joint replacement surgery to prevent postoperative infections are very clear. However, there are no clear guidelines on providing future chemoprophylaxis to cover subsequent invasive procedures to prevent late haematogenous infection in these patients. While the prescription of prophylactic antibiotics to prevent endocarditis in high-risk cardiac patients is quite clear, orthopaedic surgeons from around the world have differing opinions on prophylactic antibiotics for patients with prosthetic joints. In this review, the current evidence and data concerning this issue are discussed.

Bacteriology of infected joint replacements

Infection of the prosthetic joint can be classified as 'early', 'delayed', or 'late' according to the time of its onset. Early infections are defined as those that occur within 3 months of

surgery and delayed infections are those occurring 3 to 24 months after surgery.^{1,2} It is commonly assumed that these are due to the operation itself for which preoperative prophylactic antibiotics are given. Late infections are largely attributed to haematogenous spread of bacteria from other sites of the body. Fortunately, they are uncommon and are quoted to ensue in less than 1% of patients with hip replacements, and less than 2% of patients with knee replacements.³ However, the cost of treating a 'late-infected' prosthesis is prohibitive and it is for this condition that we investigate whether or not prophylactic antibiotics are of any use. Of 578 patients with late-infected joint replacements at the Mayo Clinic, 53% were due to staphylococci, 9% to streptococci, 6% to Gram-negative organisms, and 4% to anaerobes.⁴ From this, it can be deduced that the sources of bacteria are from the skin, respiratory, gastro-intestinal, and urogenital tracts. The life-time risk of haematogenous infection of prosthetic joints due to *Staphylococcus* bacteraemia has been estimated to be as high as 34%.⁵

Dental treatment

Reviews in the literature revealed that 6 to 11% of all cases of infected prosthetic joints can be attributable to dental procedures.^{6,7} The bacteria isolated from blood cultures following dental work are mainly viridans streptococci, *Gemella* spp, *Peptostreptococcus* spp, *Neisseria* spp, *Actinomyces* spp, *Prevotella* spp, and other anaerobes. However, routine daily activities such as tooth-brushing and even chewing produce even greater degrees of bacteraemia than dental procedures.⁸ It is reasoned that the risks of spontaneous bacteraemia from poor oral hygiene and periodontitis pose a greater risk than routine dental operations. Therefore, the American Dental Association has stated that antibiotic prophylaxis is not mandatory for routine dental procedures in patients with prosthetic joints. Antibiotics should only be given for patients who are considered at increased risk for infection. These include joint replacement surgery done within the past 2 years, previous infection of a prosthetic joint, inflammatory arthritis, type 1 diabetes mellitus, haemophilia, immunosuppression, a history of previous or current malignancy, dental extraction, periodontal procedures, dental implantation, root canal work, descaling if bleeding is anticipated, specialised injections of local anaesthetic, or placement of orthodontic bands.⁹ For these patients, amoxicillin or ampicillin 2 g, a first- or second-generation cephalosporin, or clindamycin 600 mg given orally 1 hour before the dental procedure is adequate. A second dose is seldom needed. The Australian Orthopaedic Association, British Orthopaedic Association, Swiss Society for Infectious Diseases,¹⁰ and New Zealand

關節置換術後抗生素的預防性應用

目的 對接受關節置換術的病者，可施用抗生素以防假體感染。本研究回顧相關的最新資料。

資料來源 搜索至2009年6月於Medline及PubMed發表的文獻。

研究選取 檢索全球對關節置換術病例的研究，及骨科醫學會對預防性抗生素應用的研究以及化學藥物預防的應用指引。

資料選取 文獻、原創論文、病例報告、常規應用指引。

資料綜合 需要接受關節置換術的病人不斷增加，儘管隨後發生植入體深層感染的情況並不多見，但卻是嚴重的併發症，對患者身心健康、財政，以至對社會都有所影響。泌尿外科、胃腸病學、牙科均設有指引，用以識別可能較易出現人工關節術後感染的高危病人。對這類患者，醫院在進行創傷性手術前，會先施用抗生素，以防術中可能在人工關節處造成細菌繁殖。全球大部分骨科醫學會採納類似的預防措施，以導絕菌血症發生的機會，當中以美國骨科醫學會所採納的措施最為謹慎，該會指引申明，對接受關節置換術的病人，如手術會傷及黏膜表面的，都會採取預防性抗生素應用的措施。

結論 美國骨科醫學會的指引，對預防性抗生素應用採取「包圍式」的策略，但應用時，醫生必須加以判斷，因應患者的個別情況來醫治，要衡量應用預防性抗生素所帶來的好處，以及藥物的副作用和抗生素抗藥性的弊端之間的平衡。

Orthopaedic Association¹¹ have all made very similar suggestions for prescribing prophylactic antibiotics only for patients at an increased risk of infection. For their respective risk factor lists, the corresponding guideline of each association should be referred to.

Joint replacement surgery performed within 2 years seems to be an often-quoted risk for deep infection based on the theoretical reason that the postoperative period confers a degree of inflammation which increases the blood flow to the prosthetic joint. This is assumed to carry an increased risk of haematogenous spread of infection. This was apparently so in the series reported by LaPorte et al⁷ in which 50% of dentistry-associated prosthetic joint infections occurred within 2 years of the index joint replacement surgery. However, this is not always the case as illustrated in a study done by Waldman et al in 1997 in which late joint infections after dental procedures were also analysed.⁶ In this study, 'late' infections were defined as deep infections which developed more than 6 months after the index joint replacement surgery; onset of infections after joint replacement ranged from 26 to 95 months, with a mean of 72 months. Thus, none of these infections ensued within the presumed high-risk period of

TABLE 1. Risk factors for patients with prosthetic joints undergoing urological procedures (adapted from Best Practice Policy from American Urological Association, 2008¹³)

Increased risk of haematogenous total joint infection	Increased risk of bacteraemia associated with urological procedures
Patients during the first 2 years after prosthetic joint replacement	Any stone manipulation (includes shock-wave lithotripsy)
Immunocompromised patients with prosthetic joint replacements <ul style="list-style-type: none"> • Inflammatory arthropathies (eg rheumatoid arthritis, systemic lupus erythematosus) • Drug-induced immunosuppression • Radiation-induced immunosuppression 	Any procedure with transmural incision into urinary tract (does not include simple ligation with excision or percutaneous drainage procedure)
Patients with prosthetic joint replacements and co-morbidities <ul style="list-style-type: none"> • Previous prosthetic joint infections • Malnourishment • Haemophilia • HIV infection • Diabetes • Malignancy 	Any endoscopic procedures of upper tract (kidney and ureter)
	Any procedure that includes bowel segments
	Transrectal prostate biopsy
	Any procedure with entry into the urinary tract (except for urethral catheterization) in individuals with higher risk of bacterial colonisation: <ul style="list-style-type: none"> • Indwelling catheter or intermittent catheterization • Indwelling ureteral stent • Urinary retention • History of recent/recurrent urinary tract infection or prostatitis • Urinary diversion

2 years. We would therefore question whether or not an increased infection risk in the immediate postoperative period is a valid assumption.

While dental associations attempt to identify high-risk patients for the prescription of prophylactic antibiotics, the American Academy of Orthopaedic Surgeons published a more inclusive guideline in 2009. Further details can be accessed via their “latest recommendations” section.¹²

Urological interventions

Any procedure that involves breaching the urological tract is considered clean-contaminated surgery. The likelihood of bacteraemia increases if bacteriuria is present.¹³ In a prospective study by Girou et al¹⁴ of 284 patients who underwent prostatectomies, transurethral resection, and open urological surgery, 22% who had sterile urine cultures preoperatively developed bacteriuria postoperatively. Bacteraemia subsequently developed in one patient. Dabasia et al¹⁵ reported the case of a patient who developed an *Enterococcus faecalis* infection of his total hip replacement after undergoing a transurethral resection of the prostate without prophylactic

antibiotics. According to the American Urological Association (AUA), patients fulfilling two criteria—namely (1) increased risk of haematogenous total joint infection, and (2) increased risk of bacteraemia associated with urologic procedures—should be given prophylactic antibiotics (Table 1). The antibiotic that should be given is a single dose of quinolone orally 1 to 2 hours preoperatively, or intravenous (IV) ampicillin 2 g plus gentamicin 1.5 mg/kg 30 to 60 minutes preoperatively. For those who do not meet both sets of criteria, the AUA recommends that the surgeon uses his or her discretion for each patient.¹³

While urological associations attempt to identify patients with high risk of joint infections before prescribing prophylactic antibiotics, the American Academy of Orthopaedic Surgeons recently issued more inclusive guidelines in 2009. These can be accessed via their “latest recommendations” section.¹²

Gastro-intestinal endoscopic procedures

There are case reports of patients who developed infections of their knee replacements after a colonoscopy.^{16,17} It has been estimated that 1.9% of patients with late infection of prosthetic joints are due to endoscopic procedures.¹⁸ Any procedure that breeches the alimentary tract under controlled conditions and without unusual contamination is considered clean-contaminated surgery. Gross spillage from the gastro-intestinal tract would render it to be contaminated surgery. Previous studies have found bacteraemia in up to 5% of upper endoscopies, 5% of sigmoidoscopies, and 8% of colonoscopies.^{19,20} However, these numbers have recently been challenged as they are similar to rates of contamination of blood cultures (4-12%).²¹ Understandably, the rates of bacteraemia increase as endoscopies are accompanied by procedures such as biopsy or polypectomy. The highest rate of bacteraemias (approaching 45%) was encountered in dilatation of oesophageal strictures and sclerotherapy of oesophageal varices.¹⁹ According to the guidelines set by the American Society for Gastrointestinal Endoscopy in 2008,²² there are still no clear data to support the use of prophylactic antibiotics in patients with prosthetic joints. Therefore, prophylactic antibiotics are not recommended in these patients prior to gastro-intestinal endoscopic procedures.²² As for formal gastro-intestinal surgeries, the usual prophylactic antibiotics are given as for any other patients.

From the literature, prophylactic antibiotics are not recommended for patients with prosthetic joints undergoing endoscopic procedures. In 2009 however, the American Academy of Orthopaedic Surgeons issued guidelines which are far more inclusive. These

are detailed in the next section.

Latest recommendations

The prevention of haematogenous spread of bacterial infection to prosthetic joints has often been likened to antibiotic prophylaxis for endocarditis in high-risk cardiac patients. However, the differences between these two conditions in terms of anatomy, blood supply, microorganisms, and mechanisms of infection are so great that this analogy should not be made.²³ Given the huge costs associated with treating an infected joint replacement, the latest recommendation from the American Association of Orthopaedic Surgeons in 2009 suggests antibiotic prophylaxis for all total joint replacement patients prior to any invasive procedure that may cause bacteraemia.¹² A single pre-procedure dose is usually sufficient and the antibiotic should be discontinued 24 hours thereafter. Extra attention must be paid to patients with the following risk factors: immunocompromised/immunosuppressed state (drug- or radiation-induced), inflammatory arthropathy (eg rheumatoid arthritis, systemic lupus erythematosus), co-morbidities (eg obesity, smoking), previous prosthetic joint infections, malnourishment, haemophilia, HIV infection, type 1 diabetes, malignancy, and megaprosthesis.¹² Table 2 lists the recommended antibiotics to be used. The website of the American Academy of Orthopaedic Surgeons¹² can be referred for more details about suggested antibiotic cover for invasive procedures in subspecialties such as obstetrics and gynaecology, ophthalmology, head and neck, and vascular surgery.

In addition to the myriad of guidelines, clinicians must evaluate each patient individually and balance the benefits of antibiotic prophylaxis with the risks of increasing bacterial resistance, adverse side-effects, and drug interactions. Antibiotic-associated infections such as *Clostridium difficile* colitis have also been quoted as a caveat to consider before prescribing prophylactic antibiotics,²⁴ though this risk appears unrealistic as typically only a single dose of a narrow-spectrum agent is prescribed.

TABLE 2. Antibiotic prophylaxis recommendations for different procedures (adapted from Information Statement from the American Association of Orthopaedic Surgeons, February 2009¹²)

Procedure	Antimicrobial agent	Dose*
Dental	Cephalexin, cephadrine, amoxicillin	2 g PO
Urological	Ciprofloxacin	500 mg PO 400 mg IV
Upper endoscopies	Cefazolin	1-2 g IV
Sigmoidoscopies, colonoscopies	Metronidazole	1 g PO

* PO denotes orally and IV intravenously

Our practice

Our guidelines are quite similar to those of the American Academy of Orthopaedic Surgeons. We advise that patients with prosthetic joints should receive a single dose of oral amoxicillin 2 g 2 to 3 hours prior to any dental procedure. For those undergoing urological procedures, a single dose of oral ciprofloxacin 500 mg or IV ciprofloxacin 400 mg should be given 1 hour prior to the procedure. For patients undergoing urological procedures via the transrectal approach, the prophylaxis should cover bowel flora. Patients undergoing upper endoscopies should be given a single IV dose of cefazolin 1 g 1 hour prior to the endoscopy. For patients undergoing sigmoidoscopies or colonoscopies, overseas literature supports the use of a single dose of oral metronidazole 1 g given 1 hour prior to the endoscopy. Although there are no local guidelines for endoscopic procedures, the guidelines from IMPACT (Interhospital Multi-disciplinary Programme on Antimicrobial ChemoTherapy²⁵) advise a dose of IV cefuroxime 1.5 g and a dose of IV metronidazole 500 mg to be given to all patients prior to elective colorectal surgeries. For patients with allergies to the aforementioned antibiotics, consultation with microbiologists may be advisable for advice on appropriate alternatives. Individual considerations must be made for each patient. In circumstances where the use of antibiotics is unclear, discussion with the local microbiologist is advised.

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