

PRACTICE GUIDELINES



Use of Antibiotics in Dentistry



**ACADEMY OF MEDICINE
SINGAPORE**



**COLLEGE OF DENTAL SURGEONS
SINGAPORE**

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College of Dental Surgeons, Singapore
Academy of Medicine, Singapore
81 Kim Keat Road
#11-00 NKF Centre
Singapore 328836

MESSAGE BY THE PRESIDENT OF THE COLLEGE OF DENTAL SURGEONS, ACADEMY OF MEDICINE SINGAPORE

Dear Friends and Colleagues,

The College of Dental Surgeons Singapore (CDSS) is pleased to present the Clinical Practice Guidelines on the Use of Antibiotics in Dentistry. This is a comprehensive, current, and evidence-based document that details the use of Antibiotics in the Practice of Dentistry. Insightful and relevant, this is a must have reference for every dental practitioner, so that prudence can be exercised to avoid the dangers of incorrect, unnecessary and over-prescription of antibiotics.

The College and its small army of researchers and writers have over the years collated the necessary information to present this in an easily referenced Dental Discipline Specific format and it was an initiative that had started pre-Covid.

Many thanks to the Workgroup Chairs Dr Myra Elliot (Pre-Covid) and Dr Chang Kok Meng (Post-Covid) and their research and editorial teams for all their hard work. Many thanks too to the Academy of Medicine Singapore (AMS) for the many rounds of reviews by the AMS Specialists and the Education, Training and Editorial Teams for piecing everything together, and to the Ministry of Health (MOH) and their Team of Specialists for additional reviews to verify the accuracy and currency of the information.

We all aim to do right by our patients.

We hope that you will find this Guideline useful.

DR POH YU-JIN

President

College of Dental Surgeons Singapore (CDSS)

FOREWORD

Dentists in Singapore frequently encounter situations where use of antibiotics may be considered. Prescription of antibiotics could be in association with the management of odontogenic infections, other clinical situations and dental treatments. They can also vary depending on patient profile - young to old, healthy to medically compromised or prophylactically in consideration of pre-existing medical conditions.

While use of antibiotics remain irreplaceable in dental practice, traditional life-saving antibiotics are at risk of being rendered ineffective as the overuse and misuse of such medications accelerate the development of resistance in microbes. Antimicrobial resistance (AMR) has been named by the World Health Organization as amongst the top ten threats to global public health.

Recognizing the above, the College of Dental Surgeons, Academy of Medicine Singapore convened a workgroup, helmed by Dr Myra Elliott, to create practice guidelines for the use of antibiotics in dentistry. Unfortunately, the good work by the original workgroup was put on hiatus largely due to the COVID pandemic. As uncertainties from the pandemic eased, the project was picked up again by a re-energized workgroup. We worked hard to revamp and update the manuscript. The delay, though regrettable, has fortuitously allowed us to include the latest updates which were made available more recently.

I am honoured to have been given the opportunity to work on the Guidelines with Dr Elliott and members of the workgroup pre- and post-pandemic. I hope that our dental colleagues in Singapore will find the Guidelines useful for their daily practice and embrace antimicrobial stewardship as a norm moving forward.

DR CHANG KOK MENG

Chairperson of Workgroup (Post-COVID)

Levels of evidence and grades of recommendation

Levels of evidence

Level	Type of Evidence
1 ⁺⁺	High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias
1 ⁺	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2 ⁺⁺	High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2 ⁺	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2 ⁻	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

Grades of recommendation

Grade	Recommendation
A	At least one meta-analysis, systematic review of RCTs, or RCT rated as 1 ⁺⁺ and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1 ⁺ , directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2 ⁺⁺ , directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated 1 ⁺⁺ or 1 ⁺
C	A body of evidence including studies rated as 2 ⁺ , directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated 2 ⁺⁺
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated 2 ⁺
GPP (good practice points)	Recommended best practice based on the clinical experience of the guideline development group

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1. EXECUTIVE SUMMARY OF RECOMMENDATIONS

Details of recommendations can be found in the main text at the pages indicated.

Clinical Overview

GPP General guidelines for antibiotic prescription

1. An accurate diagnosis for any clinical condition is necessary. There is no justification for prescribing antibiotics without medical indication.
 2. Check on medical history, concurrent medication and allergy status of the patient.
 3. Use a narrow spectrum antibiotic of the correct dose in preference to a broad spectrum one.
 4. If treating empirically, revise the treatment regime based on the patient's progress and bacteriology results.
 5. Be knowledgeable on the side effects of the drug being prescribed.
- (pg. 24)

GPP

Therapeutic use of antibiotics in dentistry

B Antibiotic treatment alone may initially slow down or stop a mild odontogenic infection. However, without definitive operative treatment to address the source of infection, infection will recur after antibiotic therapy ends (pg. 25).

Grade B, Level 2++

C Antibiotics are normally indicated when there is systemic involvement like fever, general malaise, spreading infection leading to cellulitis, trismus, dysphagia and local lymph node involvement (pg. 25).

Grade C, Level 2++

A Once drainage or removal of cause of infection has been performed, all antibiotics tested were equally effective. Antibiotics play a secondary role, provided that the antibiotic fits in with the action spectrum that has been proved to be effective in dental infections (pg. 25).

Grade A, Level 1+

GPP In the immunocompromised host, there is lack of evidence to support or object to the use of antibiotic prophylaxis for invasive dental procedures. Dental hygiene has to be emphasized. Where appropriate/ possible, dental treatment prior to administration of immunosuppressive therapy should be considered. In addition, care has to be taken into the consideration of the depth of immunosuppression and type of dental treatment recommended prior to offering antibiotic prophylaxis, and this should be done in consultation with the treating specialist (pg. 25).

GPP

Use of Antibiotics in Oral & Maxillofacial Surgery

Tooth extractions

A There is no evidence to support prescribing antibiotics for routine dental extractions of non-infected teeth (e.g. recently fractured, lone standing or non-periodontally involved teeth) in healthy patients (pg. 26).

Grade A, Level 1

Surgical extractions

A For impacted third molar surgery, there is evidence that pre-operative prophylactic antibiotics does reduce the risk of infection, dry socket and post-operative pain. However, use of antibiotics has also been found to result in increased mild and transient adverse effects. There is no evidence that antibiotics prevent fever, swelling or restrictions in mouth opening after third molar surgery (pg. 26).

Grade A, Level 1

Prevention of Medication-Related Osteonecrosis of the Jaw (MRONJ)

D Antibiotics with good bone penetration may be considered for dentoalveolar surgical procedures for patients at higher risk of developing MRONJ, even though its effectiveness is unknown (pg. 29).

Grade D, Level 4

Established MRONJ

GPP It appears that a more prudent approach to treating patients with established MRONJ would be to consider operative therapies (i.e. surgical intervention) when non-operative strategies (i.e. medical therapy in the form of antibiotics, etc) have failed (pg. 30).

GPP

Dental extractions for patients with history of irradiation to the head and neck region

D Pre-procedural and post-procedural antibiotics with good bone penetration may be considered in at risks patients for osteoradionecrosis, undergoing dentoalveolar surgical procedures, even though its effectiveness is uncertain (pg. 31).

Grade D, Level 4

Alveolar osteitis (dry socket)

A There is no evidence for the routine use of systemic antibiotics for management and prevention of dry socket (pg. 31).

Grade A, Level 1+

Odontogenic and non-odontogenic infections of bacterial origin

A There is no role for the indiscriminate use of antibiotics to treat infections without first removing the source of infection or performing surgical debridement to reduce the microbial load (pg. 32).

Grade A, Level 1+

GPP Consideration should be given for microbiological swabs of purulent discharge collected during incision and drainage. These can be sent for culture and sensitivity tests, which will help guide antibiotic treatment. Empirical antibiotics of choice in odontogenic infections are penicillins in combination with metronidazole (pg. 32).

GPP

GPP For non-odontogenic bacterial infections, the mainstay of treatment is still removal of the source of infection (e.g. cellulitis secondary to an infected acne vulgaris or folliculitis) and empiric antibiotics targeting the organisms specific to the infected area (e.g. cloxacillin for skin organisms) while waiting for the results of culture and sensitivity tests (pg. 32).

GPP

Dental and cranio-maxillofacial trauma

B The use of perioperative prophylactic antibiotics is recommended for fractures of the dentate mandible and dentoalveolar portions of the maxilla (pg. 32).

Grade B, Level 2+

B There is some evidence of benefit for middle third fractures of the face that are compounded into the paranasal sinuses and or oral cavity (pg. 32).

Grade B, Level 2

A Short term preoperative and perioperative antibiotics are adequate as prophylaxis. There is no evidence of any benefit for postoperative antibiotics going beyond 24 hours in the healthy patient (pg. 33).

Grade A, Level 1

Facial deformity, cleft, craniofacial and orthognathic surgery

B Consistent with surgery in clean contaminated wounds in the healthy patient, there is some evidence that antibiotics given for prophylaxis preoperatively and perioperatively is effective in reducing surgical site infection in facial deformity correction, cleft lip and palate, craniofacial and orthognathic surgery patients (pg. 33).

Grade B, Level 2+

A There is some evidence that a longer course of antibiotics for 5 days reduces the incidence of surgical site infection somewhat for orthognathic surgical patients, the benefit of which needs to be weighed against the risks of longer administration (pg. 33).

Grade A, Level 1+

Temporomandibular joint procedures

A For procedures not involving a transoral approach or minimally invasive like arthrocentesis, there is no need for any antibiotic prophylaxis. If any oral mucosal incisions are involved, there is evidence that surgical site infection is reduced if prophylactic antibiotics for 24 hours are given (pg. 33).

Grade A, Level 1+

Surgical pathology

A For procedures not involving a transoral approach (e.g. parotidectomy, excision of skin lesions), there is no need for any antibiotic prophylaxis. If any oral mucosal incisions are involved, there is evidence that surgical site infection is reduced if prophylactic antibiotics for 24 hours are given (pg. 34).

Grade A, Level 1+

Aesthetic facial procedures

A For procedures not involving a transoral approach (e.g. rhytidectomy, blepharoplasty) or minimally invasive (e.g. injection of botulinum toxin and dermal fillers) there is no need for any antibiotic prophylaxis. If any oral mucosal incisions are involved, there is evidence that surgical site infection is reduced if prophylactic antibiotics for 24 hours are given (pg. 34).

Grade A, Level 1+

Use of Antibiotics in Dental Implantology

Antibiotics at the time of implant placement

A Antibiotic prophylaxis is not indicated in straightforward implant surgery. The routine use of systemic antibiotics to accompany dental implant placement in healthy patients is not supported in the literature (pg. 35).

Grade A, Level 1 to 1+

D Antibiotics may be considered in patients undergoing dental implant placement procedures who are immunocompromised and who show signs of systemic infection (pg. 35).

Grade D, Level 4

Antibiotics for bone grafting, sinus lift procedures

D Systemic antibiotics may be considered in specific complex dental implant cases involving bone grafting and sinus lift procedures (pg. 36).

Grade D, level 4

Antibiotics for stage 2 implant surgery

A Prescription of antibiotics preoperative and postoperative is not indicated in stage 2 implant surgery (pg. 36).

Grade A, Level 1+

Antibiotics during the prosthetic phase

A There is no evidence of benefit in giving antibiotics during the prosthetic phase of dental implant treatment (pg. 36).

Grade A, Level 1+

Management of peri-implantitis with antibiotics as an adjunct to surgical and mechanical treatment

B Peri-implantitis should be treated mechanically and surgically. Antibiotics cannot replace surgical intervention. There are no controlled studies to demonstrate the efficacy of adjunctive use of systemically delivered antibiotics (pg. 37).

Grade B, Level 2+

Use of Antibiotics in Periodontology

Use of antibiotics in non-surgical periodontal treatment

B Adjunctive systemic antibiotics should only be considered if severity and extent of the disease as well as history of medication are considered. Adjunctive systemic antibiotics should only be taken simultaneously with mechanical removal of supra- and especially subgingival bacterial biofilms. There is indirect evidence that adjunctive systemic antibiotics should be initiated in direct context with mechanical debridement (full-mouth scaling) (pg. 39).

Grade B, Level 2++ to 1

B In periodontitis patients younger than 56 years of age exhibiting probing pocket depths (PPD) ≥ 5 mm in at least 35% of sites, systemic antibiotics can be administered parallel to non-surgical periodontal therapy. Patients with periodontitis aged ≥ 56 years should not take systemic antibiotics, a priori. In patients showing no PPD > 4 mm or PPD > 4 mm in less than 35% of sites, systemic antibiotics should not be considered as part of periodontal treatment (pg. 39).

Grade B, Level 1 to 1+

B In patients younger than 36 years of age or patients formerly diagnosed with aggressive periodontitis, systemic antibiotics in the context of mechanical sub-gingival plaque removal can be performed (pg. 39).

Grade B, Level 1 to 1+

A Administration of systemic adjunctive antibiotics in the context of full-mouth scaling is not to be based on bleeding on probing (BOP) incidence alone (pg. 40).

Grade A, Level 1

A Due to concerns to patient's health and the impact of systemic antibiotic use to public health, its routine use as an adjunct to subgingival debridement in patients with periodontitis is not recommended. Based on the available evidence, however, its adjunctive use may be considered for special patient categories (e.g. generalized periodontitis Stage III in young adults) (pg. 41).

Grade A, Level 1+

GPP There is no direct evidence to recommend a specific protocol for the use of adjunctive systemic antimicrobials with non-surgical mechanical debridement. However, indirect evidence suggests that antibiotic intake should start on the day of debridement completion; debridement should be completed within a short time (preferably <1 week) and debridement should be done to an adequate quality, because these may help to improve the results (pg. 41).

GPP

Use of antibiotics in periodontal surgery

B It is important to ensure that antibiotic use in periodontal surgery is based on a careful assessment of the individual's patient's needs. Systemic antibiotics may be considered in specific cases where there is a risk of infection (e.g. patients with immunocompromising medical conditions such as diabetes) or when performing extensive periodontal surgeries (e.g. large areas of hard tissue augmentation) (pg. 41).

Grade B, Level 2++ to 1

Use of Antibiotics in Endodontics

Use of systemic antibiotics in conventional root canal treatment

A Systemic antibiotics are not recommended in treating irreversible pulpitis, symptomatic apical periodontitis and localised acute apical abscess in healthy adults with no systemic signs and symptoms (pg. 42).

Grade A, Level 1

A Current evidence does not support the use of systemic antibiotics in preventing endodontic flare-ups (pg. 43).

Grade A, Level 1

C Current evidence suggests systemic antibiotics are not recommended in promoting periapical healing of the apical pathosis (pg. 43).

Grade C, Level 2+

Use of systemic antibiotics in endodontic surgery

A Current evidence suggests prophylactic systemic antibiotics are not necessary for preventing postoperative infection in routine endodontic microsurgery in healthy adults (pg. 44).

Grade A, Level 1

Use of Antibiotics in Dental Traumatology

GPP At present, dental practitioners are advised to follow existing International Association for Dental Traumatology (IADT) guidelines for the management of luxation, fractures and avulsion injuries, including the use of antibiotics (pg. 48).

GPP

Use of Antibiotics in Paediatric Dentistry

A Prevention of disease, regular dental care and maintenance of good oral health, not the use of antibiotics, should be the foundation of paediatric dental practice in Singapore (pg. 49).

Grade A, Level 1

A Amoxicillin is the empirical choice for odontogenic infections and paediatric endocarditis prophylaxis in non-allergic children (pg. 49).

Grade A, Level 1

B For paediatric patients allergic to penicillin, cephalosporins such as cephalexin can be considered as an alternative for odontogenic infections (pg. 50).

Grade B, Level 2

B Beta-lactam antibiotics may be indicated where both staphylococcal and streptococcal infections are present. Use of such antibiotics in paediatric patients might result in gastrointestinal disturbances (pg. 50).

Grade B, Level 2

A Clindamycin should be avoided due to frequent and severe reactions related to the gastrointestinal tract. Macrolide antibiotics (clarithromycin and azithromycin) should be used with caution for paediatric patients due to the potential for cardiotoxicity. Where there is allergy to penicillin and cephalosporins, azithromycin is still considered an acceptable drug of choice (pg. 50).

Grade A, Level 1

D The use of tetracyclines should be prescribed with caution in paediatric dental patients (pg. 51).

Grade D, Level 3

A Metronidazole may be indicated for the paediatric patient as additional adjunctive therapy in combination with amoxicillin if anaerobic bacteria involvement is present (pg. 51).

Grade A, Level 1

Use of Antibiotics in Geriatric Dentistry

GPP In general, no specific modifications in the pharmacotherapy of antibiotics are needed for the healthy geriatric patient (pg. 52).

GPP

D Dose reduction of antibiotics is advisable in elderly patients diagnosed with renal disease (pg. 52).

Grade D, Level 4

Use of Antibiotics in the Immunologically Compromised

Diabetes Mellitus

C There is no evidence of increased risk of postoperative infections or efficacy of antibiotic prophylaxis in reducing postoperative infections in patients with diabetes mellitus undergoing surgical dental procedures (pg. 55).

Grade C, Level 2

C Antibiotic prophylaxis should only be considered in situations where it would be used for systemically healthy patients (pg. 56).

Grade C, Level 2

Human Immunodeficiency Virus (HIV)

C Pre-operative antibiotics should not be routinely administered to HIV patients (pg. 56).

Grade C, Level 2

D Antibiotic cover is recommended for HIV patients with severe neutropenia (<500 cells/mm³) (pg. 56).

Grade D, Level 4

Pre-cancer therapy

D Antibiotic prophylaxis is indicated for invasive dental procedures (e.g. subgingival scaling, endodontics, extractions) in patients with neutropenia (<1000 cells/mm³), and should be done in liaison with the oncologist (pg. 58).

Grade D, Level 4

During cancer therapy

GPP Patients undergoing cancer therapy with dental emergencies (e.g. acute pain or swelling) should be treated in a hospital setting in close consultation with the oncologist, and with the institution of measures to increase the haematological indices, which may include antibiotic prophylaxis (pg. 58).

GPP

Chemotherapy patients

GPP Antibiotic prophylaxis should not be routinely administered to patients who have completed chemotherapy (pg. 59).

GPP

Haemopoietic stem cell transplant (HSCT) patients

GPP Antibiotic prophylaxis may be indicated for invasive dental treatment up to 12 months after completion of HSCT, and the HSCT team should be consulted prior to the provision of dental care (pg. 59).

GPP

Post-organ transplant

GPP Given the current state of knowledge, it may be reasonable to administer antibiotic prophylaxis to post single-organ transplant patients for invasive dental procedures (pg. 60).

GPP

Use of Antibiotics in Patients with Renal Disease

GPP Inpatients with chronic kidney disease, doses of antibiotics prescribed should be adjusted according to renal function. Knowledge of the patient's creatinine clearance (CrCl) or glomerular filtration rate (GFR) is essential. Practitioners should refer to local drug references (i.e. National Drug Formulary - <https://www.ndf.gov.sg/>) for the most updated dose adjustment recommendations (pg. 61).

GPP

Renal dialysis

D Antimicrobial prophylaxis for patients undergoing renal dialysis is not routinely recommended for dental procedures (pg. 62).

Grade D, Level 4

Antibiotic Prophylaxis in Dentistry

Infective Endocarditis (IE)

C It is reasonable to shift the disproportionately large focus on antibiotic prophylaxis to an emphasis on oral hygiene and prevention of oral disease (pg. 63).

Grade C, Level 2+

D Maintenance of optimal oral health and hygiene may reduce the incidence of bacteraemia from daily activities and is more important than prophylactic antibiotics for a dental procedure to reduce the risk of IE (pg. 64).

Grade D, Level 3

GPP The committee recommends that dental practitioners follow the 2021 American Heart Association (AHA) Scientific Statement update on the “Prevention of Viridans Group Streptococcal Infective Endocarditis” (pg. 65).

GPP

D Prophylaxis against infective endocarditis is reasonable before dental procedures that involve manipulation of gingival tissue, manipulation of the periapical region of teeth, or perforation of the oral mucosa in patients with underlying cardiac conditions associated with the highest risk of adverse outcomes from IE (pg. 65).

Grade D, Level 3

Nonvalvular cardiovascular devices and vascular grafts

D There is no convincing evidence suggesting that microorganisms associated with dental procedures cause infection of nonvalvular vascular devices at any time after implantation (pg. 66).

Grade D, Level 3

D Antimicrobial prophylaxis is not recommended for dental or other invasive procedures not directly related to device manipulation to prevent infection of cardiovascular implantable electronic devices (CIED), which include pacemakers and similar devices (pg. 66).

Grade D, Level 4

D Antibiotic prophylaxis for dental procedures is not recommended for patients with coronary artery stents or other vascular stents (pg. 66).

Grade D, Level 4

D Antimicrobial prophylaxis is not recommended for prevention of IE in patients with vascular grafts (e.g. coronary artery bypass graft surgery) or peripheral vascular grafts and patches (including those used for haemodialysis) who undergo a dental procedure (pg. 66).

Grade D, Level 4

Prosthetic joints

D In general, patients with prosthetic joints are not recommended to receive prophylactic antibiotics before dental treatment (pg. 70).

Grade D, Level 3

GPP For patients potentially at higher risk of experiencing prosthetic joint infections, the need for prophylactic antibiotics should be considered after discussion with the orthopaedic surgeon and the patient. If antibiotics are deemed necessary, the orthopaedic surgeon should recommend the appropriate antibiotic regimen (pg. 70).

GPP

GPP Consideration may be given to consider pre-procedure prophylactic antibiotics in some of these scenarios which include, but are not limited to the following:

1. Patients with previous late artificial joint infection.
 2. Patients with increased morbidity associated with joint surgery (wound drainage/haematoma).
 3. Patients undergoing treatment of severe and spreading oral infections (cellulitis).
 4. Patients with increased susceptibility for systemic infection.
 5. Patients with congenital or acquired immunodeficiency.
 6. Patients on immunosuppressive medications.
 7. Patients who are diabetics and have poor glycaemic control.
 8. Patients with systemic immunocompromising disorders (e.g. rheumatoid arthritis, systemic lupus erythematosus).
 9. Patients in whom extensive and invasive procedures are planned.
 10. Patients who are at significant risk of medication-related osteonecrosis of the jaws.
- (pg. 71)

GPP

Pins, plates and screws

D Antibiotic prophylaxis is not indicated for patients with pins, plates and screws or other “orthopaedic hardware” that is not within a synovial joint (pg. 71).

Grade D, Level 4

2. INTRODUCTION

2.1 Objectives and scope of guidelines

- To review the use of antibiotics in the practice of all branches of dentistry.
- To review the necessity of use of antibiotics in immunologically compromised patients and those who have been on various immunosuppressive drug therapies.
- To update the guidelines on antibiotic prophylaxis for infective endocarditis and orthopaedic prosthetic devices.

2.2 Target group

These guidelines are intended for use by all dental practitioners.

2.3 Guideline development

These guidelines have been produced by a committee comprising general dental practitioners, oral and maxillofacial surgeons, periodontists, endodontists, paediatric dentists, special needs dentists, oral medicine clinicians and infectious disease specialists. They were developed using the best available current evidence and expert opinion. The workgroup formulated this clinical practice guideline by reviewing published international guidelines and current evidence available in the research and clinical practice literature. The grading system used in the guidelines is described on the inside cover of this booklet.

2.4 Assessing the evidence

In assessing the evidence, different study designs were considered including randomised controlled trials, cohort studies, case control studies, uncontrolled clinical trials and expert opinions.

2.5 Scope of guideline

This clinical practice guideline is not intended as a protocol but aims to assist dental practitioners in making evidence-based clinical decisions in their management of patients. The dental practitioner managing the patient is ultimately responsible for clinical decisions made after evaluating the patient's individual medical history, clinical presentation and available treatment options. In the management of such patients, consultation with the physician concerned is prudent.

2.6 Review of guidelines

Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence could supersede recommendations in these guidelines. The workgroup advises that these guidelines be scheduled for review 5 years after publication, or if new evidence appears that requires substantive changes to the recommendations.

3. CLINICAL OVERVIEW

3.1 Rise of antibiotic resistance

The benefits of antibiotics are undisputable. However, because of the overuse and misuse of antibiotics, there is also a rise of antibiotic resistance globally. In Singapore, the high rates of prescription of broad-spectrum antibiotics have contributed to significant rates of antimicrobial resistance.^{1,2} Infections from methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococci* (VRE) and extended beta-lactamase producing gram negative bacteria have become commonplace. In recent years, we have seen the rise of carbapenem-resistant Enterobacteriaceae colonization and infections in Singaporean hospital inpatients².

Under antibiotic pressure, subsets of bacteria may undergo genetic mutations that confer resistance to antibiotics, thus giving these mutants a survival advantage. Examples of such mutational resistance include genes that encode for specific enzymes that hydrolyse and inactivate certain antibiotics, or genetic mutations that promote expression of membrane efflux pumps that can actively remove the active antibiotic before it has a chance to exert its effect on the bacteria. Such mutational resistance is compounded by the ability for bacteria to share and propagate these resistance genes via various horizontal gene transfer methods among different strains and species of bacteria that share the same ecological niche.

A single dose of amoxicillin can cause an ecological imbalance and induce resistant strains in the oral microflora.³ Even short courses of antibiotic treatment will reduce the impact of antibiotics on the commensal oral flora, thus reducing antibiotic susceptibility.⁴ It is known that there is a transference of resistance genes from oral *Streptococci* to *Streptococcus pneumoniae*.^{5,6,7,8}

Odontogenic infections leading to deep neck abscesses causing severe airway obstruction were found in about 28% of patients from a Singapore hospital.⁹ There are increasing reports of difficulties in managing severe orofacial infections, attributed mainly to antibiotic resistance.^{10,11} In this latter study, penicillin resistance was found in 32% of isolates, clindamycin resistance in 29.3 % of isolates in patients who all had previous doses of antibiotics.

3.2 Use of antibiotics in dentistry

Prescription of antibiotics by dentists is widespread for odontogenic infections. Published data about antibiotic prescribing practices of dentists are generally lacking. In the UK and the USA dentists prescribe between 7% to 18% of all the prescriptions written for beta-lactams, macrolides clindamycin and metronidazole.^{12,13} Amongst all the health professions, dentists are the third highest prescribers of antibiotics after family medicine and internal medicine physicians.

Inappropriate prescribing is relatively common in dentistry - whether it is the necessity of the prescription or frequency of administration or the number of days the patient is given the drug.¹⁴

3.3 Commonly used antibiotics in dentistry

Antibiotics prescribed by dentists are generally amoxicillin, co-amoxiclav, metronidazole, clindamycin, cephalosporins, azithromycin, clarithromycin, erythromycin and ciprofloxacin.

In practice, courses of antibiotics are usually given orally for a period of 3 to 10 days.¹² Antibiotics are mostly used empirically without the identification of the causative microorganism. Treatment is often decided on a presumptive basis, fundamental on probabilistic reasoning.¹⁴

3.4 Adverse drug reactions in the use of antibiotics

Antibiotics may be associated with unfavourable side effects^{15,16} ranging from:

- Gastro-intestinal disturbances, (vomiting, abdominal cramps, watery diarrhoea).
- Fatal anaphylaxis (shortness of breath, hives, swelling of lips/face or tongue, collapse).
- Other milder allergic reactions (dermatitis, rash, erythema, flushing, localised oedema, pruritus and urticaria).
- Vaginal itching /discharge.
- Coated tongue, taste disturbances, oral candidiasis.
- Antibiotic resistance.

3.5 Improved antibiotic stewardship is necessary

Antibiotic stewardship is a coordinated program that promotes the appropriate use of antibiotics, improves patient outcomes, reduces microbial resistance, and decreases the spread of infections caused by multidrug-resistant organisms.

3.6 **GPP** General guidelines for antibiotic prescription

1. An accurate diagnosis for any clinical condition is necessary. There is no justification for prescribing antibiotics without medical indication.
2. Check on medical history, concurrent medication and allergy status of the patient.
3. Use a narrow spectrum antibiotic of the correct dose in preference to a broad spectrum one.
4. If treating empirically, revise the treatment regime based on the patient's progress and bacteriology results.
5. Be knowledgeable on the side effects of the drug being prescribed.

GPP

3.7 Duration of antibiotic therapy

The duration of antibiotic therapy depends on the severity of the infection and the antibiotic used.

The standard recommendation for odontogenic infections is for a period between 3 to 7 days. Patients should be reviewed after two to three days to monitor the response. Once there is clinical improvement, antibiotic therapy should be curtailed.

A study compared amoxicillin treatment for 3 or 7 days and found no statistically significant differences between the groups, suggesting that the antibiotics should be reduced. After removal of cause, the duration of antibiotic therapy can be reduced to 3 days.¹⁷⁻¹⁹

Biomarker tests like C-reactive protein, procalcitonin and white cell count are blood tests that can monitor the progression of infection. These results often indicate that the infection is controlled and thus the use of the antibiotic can be stopped.

3.8 Therapeutic and prophylactic use of antibiotics in dentistry²⁴

For acute dentoalveolar infections, treatment should be:

1. Removal of source of infection (e.g. extractions).
2. Surgical drainage.
3. Drainage through the root canal.

Operative treatment is the cornerstone of successful management. Adjunctive systemic antibiotics are not necessary in most cases of localised uncomplicated apical abscesses.²⁰

B Antibiotic treatment alone may initially slow down or stop a mild odontogenic infection. However, without definitive operative treatment to address the source of infection, infection will recur after antibiotic therapy ends.^{20,21}

Grade B, Level 2++

C Antibiotics are normally indicated when there is systemic involvement like fever, general malaise, spreading infection leading to cellulitis, trismus, dysphagia and local lymph node involvement.^{20,22-24}

Grade C, Level 2++

A Once drainage or removal of cause of infection has been performed, all antibiotics tested were equally effective. Antibiotics play a secondary role, provided that the antibiotic fits in with the action spectrum that has been proved to be effective in dental infections.²⁴

Grade A, Level 1+

GPP In the immunocompromised hosts, there is lack of evidence to support or object to the use of antibiotic prophylaxis for invasive dental procedures. Dental hygiene has to be emphasized. Where appropriate/ possible, dental treatment prior to administration of immunosuppressive therapy should be considered. In addition, care has to be taken into the consideration of the depth of immunosuppression and type of dental treatment recommended prior to offering antibiotic prophylaxis, and this should be done in consultation with the treating specialist.

GPP

4. USE OF ANTIBIOTICS IN ORAL AND MAXILLOFACIAL SURGERY

Oral and Maxillofacial Surgery (OMS) entails the surgical management of disorders and diseases of the mouth, jaw, face and surrounding regions. Intraoral mucosal incisions are frequently involved. Incisions made in this area are considered clean-contaminated wounds even in the most favourable of circumstances (i.e. pre-operative cleansing with antiseptic swabs and the use of sterile drapes and instruments).^{25,26} The incidence of infection is 5.5% in clean-contaminated wounds compared to 4.8% for clean wounds. In general, for routine dentoalveolar surgery, the use of antibiotics is not recommended (strict aseptic surgical techniques is preferred) except in at-risk cases. These may include those with established infections (e.g. abscesses from odontogenic origin), poor local conditions (e.g. traumatised tissues, previous radiotherapy or antiresorptive therapy, operative difficulties) or poor host conditions (e.g. compromised immune system, poor nutrition), where there is a significant increased risk of infection.²⁷ Amoxicillin is the antibiotic of choice for most dentoalveolar infections/ surgery (broad oral bacteria coverage, minimum adverse effects); alternatives include amoxicillin-clavulanic acid or metronidazole.

4.1 Tooth extractions

A There is no evidence to support prescribing antibiotics for routine dental extractions of non-infected teeth (e.g. recently fractured, lone standing or non-periodontally involved teeth) in healthy patients.²⁸⁻³¹

Grade A, Level 1

4.2 Surgical extractions

A For impacted third molar surgery, there is evidence that pre-operative prophylactic antibiotics does reduce the risk of infection, dry socket and post-operative pain. However, use of antibiotics has also been found to result in increased mild and transient adverse effects. There is no evidence that antibiotics prevent fever, swelling or restrictions in mouth opening after third molar surgery.³¹

Grade A, Level 1

4.3 Antibiotic prophylaxis pre-procedure and for prevention of infection in special situations

Antibiotic prophylaxis use in OMS and dentistry is commonly understood to be pre-procedural to prevent infective complications in distant sites like infective endocarditis or prosthetic joint infection. Antibiotic prophylaxis is also given to prevent surgical site infections and the term antibiotic prophylaxis is used and understood for both reasons.

In the last decade, there have been significant changes to the guidelines for antibiotic prophylaxis. These changes have been driven by global concerns regarding antimicrobial resistance and subsequent recommendations that any prescription of antibiotics should be appropriate and judicious. The incidence of transient, cumulative bacteraemia caused by routine oral hygiene procedures (i.e. tooth brushing, flossing, pulsating water irrigators, interdental brushes, etc) is often the same as the incidence caused by many dental treatments.^{32,33}

Refer to Chapter 13 for more details on antibiotic prophylaxis for prevention of infective endocarditis and prosthetic joints infections.

4.3.1 Use of antibiotics for patients on antiresorptive and antiangiogenic medications

Medication-related osteonecrosis of the jaw (MRONJ) is a clinical condition characterised by mandibular or maxillary bone necrosis and exposure, associated with the use of anti-resorptive or anti-angiogenic agents. The pharmacological agents associated with MRONJ are:

1. Antiresorptive agents, including bisphosphonates (e.g. alendronate, pamidronate, zoledronate) and receptor activator of nuclear factor kappa-B-ligand inhibitors, RANKL inhibitors (e.g. denosumab).
2. Antiangiogenic agents (e.g. bevacizumab, sorafenib, sunitinib).
3. Sclerostin Inhibitor (romosozumab)

Bisphosphonates are a class of antiresorptive medications used primarily for the treatment and prevention of conditions related to bone loss, such as:

1. Cancer-related conditions, including hypercalcaemia of malignancy, skeletal related events associated with bone metastases and multiple myeloma.
2. Osteoporosis.
3. Osteopenia.
4. Other metabolic bone diseases, including Paget's disease of bone and osteogenesis imperfecta.

Bisphosphonates may be administered orally or intravenously.

RANKL inhibitors inhibit osteoclastic function, decrease bone resorption, and increase bone density. They are also used for osteoporosis and metastatic bone diseases.

Romosozumab is a monoclonal antibody that binds to and inhibits sclerostin resulting in increased bone formation.

Risk factors for MRONJ include:

1. Dental extractions and other dentoalveolar surgery (e.g. periodontal surgery, implant surgery).
2. Presence of periapical disease, periodontitis.
3. Use of removable prosthesis (causing mucosal trauma).
4. Longer duration of antiresorptive therapy.
5. Antiresorptive therapy used in cancer patients and in conjunction with antiangiogenic drugs (e.g. multiple myeloma, breast cancer, prostate cancer, lung cancer).
6. Smoking.
7. Patients on chemotherapy, disease-modifying antirheumatic drugs (DMARDs) and corticosteroid therapies as well as other immunocompromised states (e.g. diabetes mellitus).³⁴

Current estimates for the risk of developing MRONJ after extractions in osteoporotic patients range from 0 to 0.15% for those on bisphosphonates, while the risk is higher for those on denosumab at 1%. For cancer patients exposed to bisphosphonates, the risk for MRONJ after extractions ranges from 1.6% to 14.8%, with an average risk of about 1 to 5% not dissimilar to the risk of developing osteoradionecrosis (ORN) after extractions in irradiated head and neck patients.³⁴

MRONJ is considered present if there has been treatment with anti-resorptive or anti-angiogenic agents, presence of exposed bone or bone probed through a fistula persisting for more than 8 weeks, and no history of radiotherapy and no metastatic disease to the jaws.³⁴

4.3.1.1 Prevention of MRONJ

There is evidence that the risk of developing MRONJ can be minimised if patients to be prescribed medications associated with MRONJ undergo dental evaluation and have their oral health stabilised prior to the commencement of the drug therapy. This would include completion of all necessary dental treatment such as extraction of teeth with poor prognosis, restoration of teeth, periodontal therapy, endodontic therapy, adjustment and correction of dental prosthesis, implementation of good oral hygiene

practices and other preventive dentistry measures including regular dental recalls/examinations.³⁴⁻³⁷

Patients at risk of developing MRONJ should undergo comprehensive dental evaluation to achieve good oral health before commencement of antiresorptive/antiangiogenic drug therapy.³⁴⁻³⁷

During antiresorptive therapy, routine non-invasive dentistry (restorative procedures, scaling and root planning, endodontic therapy) should proceed, with emphasis on preventive dentistry and non-invasive treatment protocols (e.g. endodontics vs extractions).

When indicated, atraumatic surgeries should be performed, with primary mucosal closure of sites, and if multiple surgical procedures are indicated, quadrant (segmental) procedures are advised, observing for healing before proceeding to other areas of the oral cavity.

Although lacking robust data and good clinical evidence, several groups in recent years have advocated the use of antimicrobial mouthwashes and systemic antibiotics before and after oral surgical procedures to minimise the risk of MRONJ.^{34-36, 38-41}

The use, type and duration of antibiotics would depend on the degree of invasiveness of the procedure, the presence of odontogenic infection and the health status of the patient. An antibiotic with good bone penetration has been advised e.g. penicillin, amoxicillin (+/- clavulanic acid) or metronidazole.^{34, 38, 41} Antibiotic regimes/protocols that have been used by several groups for patients at risk for MRONJ have been summarised by Bermudez-Bejarano EB et al.⁴¹

D Antibiotics with good bone penetration may be considered for dentoalveolar surgical procedures for patients at higher risk of developing MRONJ^{34-36, 38, 39, 41}, even though its effectiveness is unknown.

Grade D, Level 4

4.3.1.2 Established MRONJ

Treatment goals for patients with established MRONJ are as follows:

1. Eliminate pain.
2. Control infection of the hard and soft tissues.
3. Minimize progression and occurrence of bone necrosis.

GPP It appears that a more prudent approach to treating patients with established MRONJ would be to consider operative therapies (i.e. surgical intervention) when non-operative strategies (i.e. medical therapy in the form of antibiotics etc.) have failed.³⁷

GPP

4.3.2 Dental extractions for patients with history of irradiation to the head and neck region

Patients who had radiotherapy to the head and neck region are at lifelong risk of developing progressive radiation-induced hypoxia, hypocellularity and hypovascularity of the jaws, leading to diminished reparative ability of the bone.⁴²

Osteoradionecrosis (ORN) is defined as non-healing necrotic bone in a previously irradiated site that has been present for three months in the absence of any neoplastic disease. ORN can develop spontaneously, can be secondary to odontogenic disease or denture trauma but most cases develop following dental extractions. Thus, it is the standard of care in many cancer centres for patients to undergo dental evaluations prior to radiotherapy (RT) to the head and neck to remove sources of oral infections. This includes extraction of teeth with poor prognosis that may require removal in the future following RT. Preventive oral care programmes should be instituted as the risk of oral disease (i.e. dental caries) post RT is high.⁴³

Patients undergoing head and neck radiotherapy should have a comprehensive dental evaluation, including removal of sources of oral infection, extraction of teeth with poor prognosis, at least 2 to 3 weeks before the planned treatment.

Nevertheless, patients can still require extractions post-radiation because of the increased risk of tooth loss due to caries in these patients. In such situations, endodontics and restorative options should be explored first.

If extractions are required post RT, it has been recommended that atraumatic extractions with primary tension-free closure of sites, be carried out within 6 months of the RT to reduce the risk of ORN. After radiation, there is a 5-6 month window period of tissue healing and repair before progressive fibrosis and loss of vascularity (hypovascularity) occurs.^{42, 44}

Antibiotic prophylaxis has been recommended for extractions and surgical procedures in post-RT patients.⁴⁵⁻⁴⁷ However, the use of antibiotics, pre-extraction and post-extraction, for prevention of ORN is not supported by good, high-level evidence.⁴⁵ An uncontrolled study with the following regime has produced no case of ORN after extractions:⁴⁶

- Amoxicillin 500mg taken orally every 8 hourly starting from 10 days before the extraction and continued for 7 days after the extraction. In patients allergic to beta-lactam antibiotics, clindamycin 300mg was taken orally every 8 hourly starting from 10 days before the extraction and continued for 7 days after the extraction.
- Antibacterial mouthwashes with 10 ml of undiluted chlorhexidine gluconate 0.2% solution were used for 1 min every 12 hourly starting from 10 days before the extraction and continued for 7 days after the extraction.

D Pre-procedural and post-procedural antibiotics with good bone penetration may be considered in at risks patients for osteoradionecrosis, undergoing dentoalveolar surgical procedures, even though its effectiveness is uncertain.

Grade D, Level 4

4.4 Alveolar osteitis (Dry socket)

Alveolar osteitis or alveolar osteitis sicca dolorosa is more commonly known as dry socket. It is a painful condition that commonly occurs after a tooth extraction. There are disagreements over the role of bacterial infection in the pathogenesis of dry socket.⁴⁸

There is evidence that alveolar osteitis is self-limiting and resolves even without treatment.^{48,56}

A There is no evidence for the routine use of systemic antibiotics for management and prevention of dry socket.^{31,48-56}

Grade A, Level 1+

A 0.12% chlorhexidine oral rinse before treatment may be a relevant clinical option with little iatrogenic risk for prevention of dry socket.^{48, 56}

4.5 Odontogenic and non-odontogenic infections of bacterial origin

A There is no role for the indiscriminate use of antibiotics to treat infections without first removing the source of infection or performing surgical debridement to reduce the microbial load.⁵⁷⁻⁶¹

Grade A, Level 1+

The mainstay of treatment includes the following:

1. Removal of offending tooth/teeth.
2. Incision and drainage (I&D) if clinically applicable.
3. Provision of appropriate antibiotics and analgesics.

GPP Consideration should be given for microbiological swabs of purulent discharge collected during incision and drainage (I&D). These can be sent for culture and sensitivity (C&S) tests, which will help guide antibiotic treatment. Empirical antibiotics of choice in odontogenic infections are penicillins in combination with metronidazole.⁵⁹

GPP

GPP For non-odontogenic bacterial infections, the mainstay of treatment is still removal of the source of infection (e.g. cellulitis secondary to an infected acne vulgaris or folliculitis) and empiric antibiotics targeting the organisms specific to the infected area (e.g. cloxacillin for skin organisms) while waiting for the results of C&S tests.⁵⁹⁻⁶¹

GPP

4.6 Dental implant placement

Please refer to Chapter 5 – Use of antibiotics in Dental Implantology.

4.7 Dental and cranio-maxillofacial trauma

Fractures of parts of the oral cavity, specifically the mandibular body/symphysis and maxillofacial skeleton that are covered by mucoperiosteum are by definition compound fractures and are at increased risk of infection.^{62,63}

B The use of perioperative prophylactic antibiotics is recommended for fractures of the dentate mandible and dentoalveolar portions of the maxilla.^{62,63}

Grade B, Level 2+

There is no consensus on whether antibiotics are beneficial for orbital, zygomatic and condylar fractures.

B There is some evidence of benefit for antibiotics for middle third fractures of the face that are compounded into the paranasal sinuses and or oral cavity.⁶³

Grade B, Level 2

A Short term preoperative and perioperative antibiotics are adequate as prophylaxis. There is no evidence of any benefit for postoperative antibiotics going beyond 24 hours in the healthy patient.⁶⁴⁻⁶⁸

Grade A, Level 1

4.8 Facial deformity, cleft, craniofacial and orthognathic surgery

B Consistent with surgery in clean contaminated wounds in the healthy patient, there is some evidence that antibiotics given for prophylaxis preoperatively and perioperatively is effective in reducing surgical site infection in facial deformity correction, cleft lip and palate, craniofacial and orthognathic surgery patients.⁶⁸⁻⁷⁰

Grade B, Level 2+

A There is some evidence that a longer course of antibiotics for 5 days reduces the incidence of surgical site infection for orthognathic surgical patients, the benefit of which needs to be weighed against the risks of longer administration.⁶⁹⁻⁷¹

Grade A, Level 1+

4.9 Temporomandibular joint procedures

A For procedures not involving a transoral approach or minimally invasive like arthrocentesis, there is no need for any antibiotic prophylaxis. If any oral mucosal incisions are involved, there is evidence that surgical site infection is reduced if prophylactic antibiotics for 24 hours are given.⁶⁴⁻⁶⁸

Grade A, Level 1+

4.10 Surgical pathology

This term covers surgical management of cysts, benign and malignant tumours of the maxillofacial area and salivary gland diseases.

A For procedures not involving a transoral approach (e.g. parotidectomy, excision of skin lesions), there is no need for any antibiotic prophylaxis. If any oral mucosal incisions are involved, there is evidence that surgical site infection is reduced if prophylactic antibiotics for 24 hours are given.⁶⁴⁻⁶⁸

Grade A, Level 1+

4.11 Aesthetic facial procedures

A For procedures not involving a transoral approach (e.g. rhytidectomy, blepharoplasty) or minimally invasive (e.g. injection of botulinum toxin and dermal fillers) there is no need for any antibiotic prophylaxis. If any oral mucosal incisions are involved, there is evidence that surgical site infection is reduced if prophylactic antibiotics for 24 hours are given.^{72,73}

Grade A, Level 1+

5. USE OF ANTIBIOTICS IN DENTAL IMPLANTOLOGY

Osseointegrated dental implant treatment entails insertion of a fixture, mostly from titanium alloy or commercially pure titanium, into the alveolar bone of the maxilla and mandible, almost exclusively by an intraoral procedure. There are implants placed in the maxillofacial regions for retention of maxillofacial prostheses of the nasal, orbital and auricular regions, primarily in the skin and mucosa of the adjacent region. These will not be considered further here.

Incisions made in the oral mucosa are classified as clean-contaminated wounds.^{25,26} The incidence of surgical site infection in clean-contaminated wounds have been quoted as slightly higher (5.5 %) than those placed in clean wounds (4.8 %).²⁷

5.1 Antibiotics at the time of implant placement

Antibiotics are no substitute for strict aseptic techniques in implant surgery.

The role of antibiotic prophylaxis in surgical placement of dental implants been suggested in the past. Esposito et al, in a Cochrane systematic review series⁷⁴, suggested that 2 g of amoxicillin given orally 1h preoperatively significantly reduced failures of dental implants placed in ordinary conditions, while no significant benefits were achieved with postoperative antibiotics. Subsequent clinical studies and systematic reviews have not found any significant benefits with the use of pre- and postoperative antibiotics regimes, in particular for healthy patients undergoing uncomplicated implant surgeries.⁷⁵⁻⁷⁸

A Antibiotic prophylaxis is not indicated in straightforward implant surgery. The routine use of systemic antibiotics to accompany dental implant placement in healthy patients is not supported in the literature.⁷⁴⁻⁷⁸

Grade A, Level 1 to 1+

D Antibiotics may be considered in patients undergoing dental implant placement procedures who are immunocompromised and who show signs of systemic infection.^{78,79}

Grade D, Level 4

5.2 Antibiotics for bone grafting, sinus lift procedures

There is minimal data on the benefits of antibiotics use for these procedures.

The European Association for Osseointegration Consensus Conference⁷⁹ concluded that the beneficial effects of antibiotics prophylaxis cannot be excluded in “complex cases” such as patients requiring bone grafting procedures.

A recent systematic review concluded that there is insufficient evidence to support either the use or non-use of preventive antibiotic therapy for sinus elevation therapies.⁸⁰

D Systematic antibiotics may be considered in specific complex dental implant cases involving bone grafting and sinus lift procedures. ^{79,80}

Grade D, level 4

5.3 Antibiotics for stage 2 implant surgery

A Prescription of antibiotics preoperative and postoperative is not indicated in stage 2 implant surgery. ⁷⁵⁻⁷⁹

Grade A, Level 1+

5.4 Antibiotics during the prosthetic phase

A There is no evidence of benefit in giving antibiotics during the prosthetic phase of dental implant treatment. ⁸¹

Grade A, Level 1+

5.5 Management of peri-implantitis with antibiotics as an adjunct to surgical and mechanical treatment

B Peri-implantitis should be treated mechanically and surgically. Antibiotics cannot replace surgical intervention. There are no controlled studies to demonstrate the efficacy of adjunctive use of systemically delivered antibiotics.⁸²⁻⁸⁵

Grade B, Level 2+

Use of topical antibiotics delivered locally in various forms like gel, fibres seem to show statistically significant improvements in the levels of bleeding on probing and probing depth in comparison to mechanical debridement alone, chlorhexidine rinses and photodynamic therapy.⁸³

Locally delivered or topical antibiotics developed for oral use vary greatly due to heterogeneity in delivery agents and active ingredients. Hence, unlike systemic antibiotics, the effectiveness and efficacy for each locally delivered antibiotic studied cannot be generalized across the entire class. Caution should be taken when interpreting all types of studies relating to locally delivered antibiotics.

6. USE OF ANTIBIOTICS IN PERIODONTOLOGY

Periodontal diseases are inflammatory conditions affecting the periodontium and inextricably linked to dysbiotic oral microbiome. Despite this, the use of antibiotics in the management of periodontitis is seldom within the first line of treatment, and never used as a standalone modality of treatment. Health professionals should always be aware of the possibility of antibiotic resistance and potential negative effects of antibiotics on the human microbiome. Thus, a sensible and restricted use of antibiotics is needed. Compared to planktonic cells, the effectiveness of antibiotics is significantly reduced in biofilms. An essential prerequisite for the use of adjunctive systemic antibiotics during periodontal therapy is the mechanical disruption of the integrity of the subgingival biofilm and its reduction during full-mouth scaling. In addition, the necessary effect concentration in periodontal pockets can hardly be reached without disaggregating subgingival plaque mechanically.

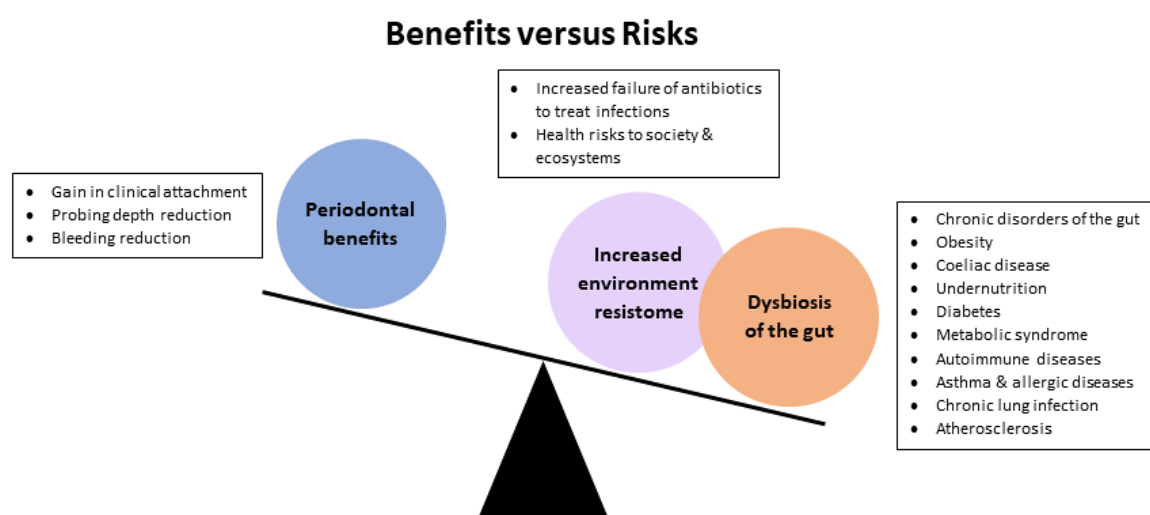


Figure 1. Diagram adapted from Jepsen K & Jepsen S. *Antibiotics/antimicrobials: systemic and local administration in the therapy of mild to moderately advanced periodontitis. Periodontology 2000, Vol. 71, 2016, 82–112.*

6.1 Use of antibiotics in non-surgical periodontal treatment

A recent review paper⁸⁶ evaluated whether there was a meaningful clinical benefit regarding the use of systemic adjunctive antibiotics in the treatment of patients with periodontitis. The paper concluded that most systematic reviews and randomised controlled trials showed a significant positive effect of adjunctive systemic antibiotics compared to controls. These positive effects gain clinical relevance in patients with severe periodontal disease aged 55 years and younger.

Systemic antibiotics as an adjunct to non-surgical periodontal therapy should be sensibly administered and restrictively used. Only certain groups of periodontitis patients showed a significant and clinically relevant benefit after intake of systemic antibiotics during periodontal therapy. Avoiding antibiotic resistance and possible side effects on the human microbiome should be a focus of dentists and physicians. Hence, a sensible administration of antibiotics is mandatory. In addition, taking reference from the latest European Federation of Periodontology S3 level clinical practice guideline for the treatment of Stage I-III periodontitis⁸⁷, the following guidelines are provided:

To diagnose periodontal disease, an adequate anamnesis as well as periodontal status including probing pocket depths (PPD), clinical attachment levels (CAL), and bleeding on probing (BOP) needs to be performed.

B Adjunctive systemic antibiotics should only be considered if severity and extent of the disease as well as history of medication are considered. Adjunctive systemic antibiotics should only be taken simultaneously with mechanical removal of supra- and especially subgingival bacterial biofilms. There is indirect evidence that adjunctive systemic antibiotics should be initiated in direct context with mechanical debridement (full-mouth scaling).^{88,89}

Grade B, Level 2++ to 1

B In periodontitis patients younger than 56 years of age exhibiting probing pocket depth (PPD) \geq 5 mm in at least 35% of sites, systemic antibiotics can be administered parallel to non-surgical periodontal therapy. Patients with periodontitis aged \geq 56 years should not take systemic antibiotics, a priori. In patients showing no PPD $>$ 4 mm or PPD $>$ 4 mm in less than 35% of sites, systemic antibiotics should not be considered as part of periodontal treatment.⁹⁰⁻⁹³

Grade B, Level 1 to 1+

B In patients younger than 36 years of age or patients formerly diagnosed with aggressive periodontitis, systemic antibiotics in the context of mechanical sub-gingival plaque removal can be prescribed.⁹⁴⁻¹⁰⁰

Grade B, Level 1 to 1+

It must be borne in mind that all included systematic reviews and RCTs used the classification of 1999 or older. Thus, patients diagnosed with aggressive periodontitis had to have attachment or radiographic bone loss at more than two non-adjacent sites. Using the new classification of 2017¹⁰¹, patients 36 years or younger should at least exhibit Stage II periodontitis.

A Administration of systemic adjunctive antibiotics in the context of full-mouth scaling is not to be based on bleeding on probing (BOP) incidence alone.^{88, 90, 91, 99, 102-105}

Grade A, Level 1

No specific recommendations can be given for patients with diabetes regarding adjunctive systemic antibiotics during non-surgical anti-infective therapy. The above-mentioned recommendations should be applied.^{103, 104}

For periodontitis patients regularly consuming tobacco (smoking, chewing), no specific recommendations can be given. In these patients, the guidelines mentioned above can be followed.^{103, 106}

A recent systematic review and meta-analysis looked at the efficacy of adjunctive locally delivered antimicrobials in periodontal therapy. This includes antibiotics and antiseptics (e.g. chlorhexidine) delivered in the form of fibres, gels, chips or microspheres. Statistically significant differences were observed in 6- to 9-month studies for PPD reduction and CAL gain, while significant differences were only observed for PPD and not for CAL in long-term studies.¹⁰⁷

Specific locally administered sustained-release antibiotics as an adjunct to subgingival instrumentation in patients with periodontitis may be considered.¹⁰⁷

Locally delivered or topical antibiotics developed for oral use vary greatly due to heterogeneity in delivery agents and active ingredients. Hence, unlike systemic antibiotics, the effectiveness and efficacy for each locally delivered antibiotic studied cannot be generalized across the entire class. Caution should be taken when interpreting all types of studies relating to locally delivered antibiotics.

A Due to concerns to patient's health and the impact of systemic antibiotic use to public health, its routine use as an adjunct to subgingival debridement in patients with periodontitis is not recommended. Based on the available evidence, however, its adjunctive use may be considered for special patient categories (e.g. generalized periodontitis Stage III in young adults).¹⁰⁸

Grade A, Level 1+

GPP There is no direct evidence to recommend a specific protocol for the use of adjunctive systemic antimicrobials with non-surgical mechanical debridement. However, indirect evidence suggests that antibiotic intake should start on the day of debridement completion; debridement should be completed within a short time (preferably <1 week) and debridement should be done to an adequate quality, because these may help to improve the results.

GPP

6.2 Use of antibiotics in periodontal surgery

The prevalence of post-surgical infection in various periodontal surgical procedures has been reported to be low in the literature.

Current literature¹⁰⁹⁻¹¹² suggest that there may be no benefit in using antibiotics for the sole purpose of preventing post-surgical infections even though perioperative antibiotics are commonly used when performing periodontal surgeries.

There is only weak indirect evidence that antibiotics may provide additional benefits in terms of clinical improvements in the regenerative/reconstructive periodontal surgery of intrabony defects and no evidence for a benefit in furcations. Until new data are gained and in the context of antibiotic stewardship, it may be questionable to justify the adjunctive use of systemic antibiotics. Additional large-scale, controlled clinical studies are needed to determine the role of perioperative antibiotics in the prevention of periodontal post-surgical infections.

B It is important to ensure that antibiotic use in periodontal surgery is based on a careful assessment of the individual's patient's needs. Systemic antibiotics may be considered in specific cases where there is a risk of infection (e.g. patients with immunocompromising medical conditions such as diabetes) or when performing extensive periodontal surgeries (e.g. large areas of hard tissue augmentation).

Grade B, Level 2++ to 1

7. USE OF ANTIBIOTICS IN ENDODONTICS

The primary aim of the endodontic treatment is the elimination and prevention of microbial infection within the root canal systems. It is well established that apical periodontitis is caused by microbes, much of which are obligatory anaerobes existing in the form of biofilms.^{113 - 116} Biofilm confers up to 1000-fold resistance against the antimicrobial agents with its extracellular polymeric matrix as a physical barrier.^{117,118} Within the matrix, close proximity of the bacteria consortium allows for quorum sensing and horizontal gene transfer to take place, contributing to the altered phenotypic expression and virulence.¹¹⁹ Hence, aseptic chemo-mechanical instrumentation plays a crucial role in endodontic treatment.^{120 - 122}

Antibiotics are used only as an adjunct and may be used as systemic or topical applications, depending on the clinical scenarios.

7.1 Use of systemic antibiotics in conventional root canal treatment

Systemic antibiotics are used as an adjunct in the following situations:

1. Systemic signs and symptoms (e.g. malaise, lymphadenopathy and pyrexia).^{123,124}
2. Associated with spreading odontogenic infection.¹²⁵
3. Immunocompromised patients presenting with acute apical abscess/odontogenic infection.¹²³

Numerous meta-analyses and randomised controlled trials have shown that antibiotics are not recommended in cases of:

1. Irreversible pulpitis.^{126, 127}
2. Symptomatic apical periodontitis and acute apical abscess in the absence of systemic signs and symptoms.^{123, 128 - 132}

A Systemic antibiotics are not recommended in treating irreversible pulpitis, symptomatic apical periodontitis and localised acute apical abscess in healthy adults with no systemic signs and symptoms.

Grade A, Level 1

Based on randomised controlled trials and cohort studies, the use of antibiotics is also not recommended in preventing post-operative flare-ups.¹³¹⁻¹³⁵ Flare-up is defined as “an acute exacerbation of an asymptomatic pulpal and/or periradicular pathosis after the initiation or continuation of root canal treatment”,¹³⁶ and such incidents result in unscheduled visits to the dentists.^{131,132}

A Current evidence does not support the use of systemic antibiotics in preventing endodontic flare-ups.

Grade A, Level 1

No randomised controlled study looked at the effect of antibiotics on periapical healing of the teeth with periapical pathosis. Cohort studies have shown no difference in radiographic and clinical healing among patients with or without antibiotics in both primary root canal treatment and retreatment.^{137, 138}

C Current evidence suggests systemic antibiotics are not recommended in promoting periapical healing of the apical pathosis.

Grade C, Level 2+

7.2 Use of systemic antibiotics in endodontic surgery

Prospective cohort studies conducted by von Arx and co-workers reported no statistical difference in the use of systemic antibiotics on the outcome of healing rate.^{139, 140} The antibiotics were given for cases with the history of acute infection, with the presence of clinical signs and symptoms and in cases where the surgical duration is expected to be longer than one hour.

One systematic review¹⁴¹ examined the effects of surgical and non-surgical retreatment of teeth with persisting apical pathosis, in which it examined the effect of antibiotic prophylaxis on the incidence of post-operative infection. One randomised controlled trial¹⁴² showed no evidence in the use of antibiotics reducing the occurrence of postoperative infection. However, the surgical duration of this study was short at 30 minutes, and the benefit of antibiotics is not known in cases with extended surgical periods.¹⁴³

A Current evidence suggests prophylactic systemic antibiotics are not necessary for preventing postoperative infection in routine endodontic microsurgery in healthy adults.

Grade A, Level 1

Intentional replantation, a method by which a tooth is purposefully extracted and repaired before placing it back into the original socket¹⁴⁴, has been used as an alternative approach to accessing persisting apical pathosis. To date, no studies seem to have examined the factors affecting the outcome of the intentional replantation due to heterogeneity in replantation techniques.¹⁴⁵ The advocated techniques vary from study to study and currently, there is no consensus on the use of preoperative systemic antibiotics.¹⁴⁶ The majority of the studies do not recommend the use of preoperative antibiotics unless indicated for prophylactic reasons such as prevention of infective endocarditis. Further studies are necessary for establishing the protocol.

7.3 Use of topical antibiotics as an intracanal medicament and an irrigant

Antibiotics are also available in the market as an intracanal medicament for inter-appointment temporalisation or as an irrigant. It may be combined with a corticosteroid, or another antibiotic for this purpose.

7.3.1 Antibiotic/corticosteroid formulation

Various antibiotics are combined with 1% triamcinolone acetonide as an anti-inflammatory agent. Some of the examples are Ledermix[®] (3% demeclocycline hydrochloride), DoxyPaste (3% doxycycline hydrate), and Odontopaste[®] (5% clindamycin hydrochloride). Such intracanal medicament is found to be effective in controlling postoperative pain, attributed to the incorporation of the corticosteroid.^{147,148} Ledermix[®] is also studied extensively for its possible role in arresting infection-related (inflammatory) external root resorption (Refer to Chapter 8 – Use of antibiotics in Dental Traumatology).

One major limitation of the use of tetracycline is the resistance of the endodontic microbiota against tetracycline.^{149, 150} Likewise, clindamycin is not as efficacious as β -lactam antibiotics such as amoxicillin/clavulanate potassium.^{149, 151}

Another major side effect of using tetracycline is the light-induced discolouration of the tooth structure due to photo-oxidation¹⁵² which is evident when used as an intracanal medicament.^{153, 154} One case report on the hypersensitivity due to tetracycline within Ledermix® was reported, which resolved immediately after washing the medicament out of the canals.¹⁵⁵

An attempt was made to add calcium hydroxide, a commonly used antimicrobial medicament, to Ledermix® and Odontopaste® mixtures to reap the benefit of both medicaments. However, the combination resulted in a rapid reduction in the efficacy of steroids and antibiotic components.^{156, 157}

Currently, a position statement issued by the European Society of Endodontology does not recommend the use of topical antibiotics in routine endodontic treatment.¹²⁴

7.3.2 Triple antibiotic combination

Endodontic infection is polymicrobial, and it is unlikely that a single antibiotic would be able to eliminate microbes within the root canal systems completely. Introduced by Hoshino and colleagues, a triple antibiotic combination consisting of ciprofloxacin, metronidazole and minocycline is increasingly used in disinfection of the root canal systems.^{158, 159} Its use has gained traction, especially in the field of regenerative endodontic therapy of the necrotic immature permanent tooth.¹⁶⁰⁻¹⁶²

The American Association of Endodontists (AAE) regularly updates the current considerations for regenerative procedures on its website. In the current consideration as of May 2021, disinfection of the canal is advised with either calcium hydroxide or a low concentration of 1-5mg/ml of triple antibiotic pastes (TAP).¹⁶³ Dental practitioners are reminded to check the case selection criteria such as the allergy status of the patients. Due to the inherent risk of discolouration by minocycline, alternative combinations such as double antibiotic pastes without minocycline^{164, 165} or modified TAP with clindamycin, amoxicillin or cefaclor could be considered.¹⁶⁶

In terms of disinfection and clinical outcome, the efficacy of TAP seems comparable to calcium hydroxide/chlorhexidine gel.¹⁶⁷⁻¹⁶⁹ So far, no results from randomised controlled trials are available on the efficacy of a combined antibiotic mixture compared to calcium hydroxide on the clinical outcomes of the regenerative procedure.

7.3.3 Endodontic irrigant

Doxycycline is used as one of the constituents of the endodontic irrigant known as MTAD, which also contains citric acid and a detergent (polysorbate 80). A randomised controlled study using MTAD and chlorhexidine after initial irrigation of sodium hypochlorite showed no further bacterial reduction compared to sodium hypochlorite alone.¹⁷⁰ Another clinical trial showed no statistically significant difference in terms of post-operative pain comparing the use of MTAD with ethylenediaminetetraacetic acid (EDTA).¹⁷¹

8. USE OF ANTIBIOTICS IN DENTAL TRAUMATOLOGY

Both systemic and topical antibiotics are used in the field of dental traumatology. The International Association for Dental Traumatology (IADT) established the clinical guidelines based on findings from the clinical observations and experimental studies.¹⁷²⁻¹⁷⁵ Due to ethical reasons, it is difficult to conduct studies with a higher level of evidence (e.g. randomised controlled trials) in dental traumatology. Despite this, the result of a retrospective case-control study showed compliance with the IADT guidelines significantly reduced the occurrence of post-injury complications.¹⁷⁶

8.1 Luxation and fractures

At present, IADT guidelines do not recommend the use of antibiotics for the management of luxation and fracture injuries of permanent and primary dentition, unless concomitant soft tissue injuries or the medical condition warrants antibiotic coverage.^{172, 173, 175} Prospective cohort studies showed that antibiotics had limited effects on both pulpal and periodontal healing for both root fractures and intrusive luxation injuries.^{177, 178} A systematic review and meta-analysis of the management of intrusive luxation reflected a large disparity in antibiotic administration among the selected papers and the authors were unable to conclude the impact of the antibiotic on the healing outcome.¹⁷⁹

In another retrospective cohort study examining complications in the dentition due to alveolar process fracture, no significant differences were noted with the use of penicillin on the occurrence of pulp necrosis.¹⁸⁰

8.2 Replantation of the avulsed permanent teeth

Evidence for use of antibiotics (tetracycline group) comes from experimental studies for the replantation of the avulsed permanent teeth¹⁸¹⁻¹⁸⁵, showing more favourable results in controlling infection-related external root resorption and pulp revascularisation. However, the results of prospective cohort studies did not show the effectiveness of systemic antibiotics in both pulpal and periodontal healing.^{186,187} This finding corroborated with the other retrospective clinical studies.^{188,189} When a meta-analysis was conducted on the studies mentioned above, the evidence was inconclusive and the authors advised continued reference to the current IADT guidelines.¹⁹⁰ From the findings of another retrospective study, systemic antibiotics did not reduce the occurrence and severity of infection-related root resorption in mature teeth.¹⁹¹

At present, the IADT guideline recommends the use of systemic antibiotics for the replantation of an avulsed tooth. Doxycycline is not recommended for patients under the age of 12 due to the risk of tooth discolouration. The use of topical antibiotics is no longer recommended.¹⁷⁴ Soaking the avulsed tooth in doxycycline suspension did not seem to improve pulpal and periodontal outcomes compared to saline in a retrospective case-control study.¹⁹²

8.3 Antibiotics as an intracanal medicament

The use of Ledermix® as an intracanal medicament in the prevention of infection-related resorption has been extensively studied in experimental animal models, showing a more favourable result in reducing the occurrence of infection-related root resorption.¹⁹³⁻¹⁹⁶ However, the use of triamcinolone alone also proved to be as effective as Ledermix® in periodontal healing in a dog study.¹⁹⁷ In a randomised clinical trial comparing the use of Ledermix® and calcium hydroxide, no significant difference in periodontal healing was noted.¹⁹⁸ If used, the current IADT guidelines advise immediate placement of corticosteroid or corticosteroid/antibiotic formulation as an intracanal medicament for at least six weeks.¹⁷⁴

8.4 Autotransplantation

Autotransplantation is a surgical procedure of transferring a donor tooth to another extraction site or surgically created socket on the edentulous site within the same individual.¹⁹⁹ While many cohort studies examined the prognostic factors associated with this procedure, a large majority of studies prescribed antibiotics empirically and there is large heterogeneity in the pattern of prescription.^{200,201} In one systematic review and meta-analysis of the clinical outcome of mature transplanted teeth, prescription of systemic antibiotics resulted in lower root resorption and failure rate.²⁰¹ This was not corroborated in the other two systematic reviews where the information was insufficient to conduct meta-analyses.^{200,202} Further studies are necessary for establishing the protocol.

GPP At present, dental practitioners are advised to follow existing International Association for Dental Traumatology (IADT) guidelines for the management of luxation, fracture and avulsion injuries, including the use of antibiotics.

GPP

9. USE OF ANTIBIOTICS IN PAEDIATRIC DENTISTRY

The over-arching goal of the use of antibiotics for dental infections in the paediatric patient is prudent and judicious prescription.²⁰³ Up to 80% of prescriptions of antibiotics before dental procedures were shown to be unnecessary as risk factors were not present.²⁰⁴ Antibiotics must thus be prescribed conservatively to minimize the risk of developing both resistance and adverse effects in children.²⁰⁵⁻²⁰⁷ Antibiotics should only be used as adjuncts, and not alternatives to dental treatment indicated to control the infection source.²⁰⁸

A Prevention of disease, regular dental care and maintenance of good oral health, not the use of antibiotics, should be the foundation of paediatric dental practice in Singapore.

Grade A, Level 1

9.1 Amoxicillin

Amoxicillin (a penicillin derivative) is still considered the empirical choice for odontogenic infections in non-allergic children²⁰⁹, mainly due to its wide gram-positive bacterial coverage and effectiveness against oral flora^{174,210}, good absorption with sustained serum effects,²⁰⁷ and low incidence of adverse reactions.¹⁷⁴ Amoxicillin also remains the drug of choice for paediatric endocarditis prophylaxis.²¹¹

While antibiotic therapy is not indicated for bacterial infection confined within pulpal or periradicular tissue, oral suspension of amoxicillin is most commonly indicated in acute facial swelling or facial cellulitis of odontogenic origin. This should be administered in conjunction with surgical intervention. Parenteral infusion should be considered if signs of systemic progression such as fever or breathing difficulties develop.²¹²⁻²¹⁵

Intraoral puncture wounds and lacerations that appear to have been contaminated by extrinsic bacteria, debris, foreign bodies, open fractures and joint injury have an increased risk of infection and should be managed as soon as possible by systemic antibiotics²⁰⁵, with amoxicillin being the drug of choice.²¹⁶

A Amoxicillin is the empirical choice for odontogenic infections and paediatric endocarditis prophylaxis in non-allergic children.²⁰⁷

Grade A, Level 1

B For paediatric patients allergic to penicillin, cephalosporins* such as cephalexin can be considered as an alternative for odontogenic infections. ^{211,217}

Grade B, Level 2

**Cephalosporins should not be used in patients with a history of anaphylaxis, angioedema or urticaria with penicillins.*

9.2 Amoxicillin clavulanate potassium

Beta-lactam antibiotics may be indicated where both staphylococcal and streptococcal infections are present²¹⁸, such as in acute salivary gland swellings of bacterial nature. In children, this includes conditions such as juvenile recurrent parotitis and submandibular sialadenitis. ^{219,220} However, its use in the paediatric population may be associated with gastrointestinal disturbances.

B Beta-lactam antibiotics may be indicated where both staphylococcal and streptococcal infections are present. Use of such antibiotics in paediatric patients might result in gastrointestinal disturbances.

Grade B, Level 2

9.3 Clindamycin, clarithromycin and azithromycin

Clindamycin was the alternative to penicillin allergy in particular for use in endocarditis prophylaxis. However, clindamycin has been associated with significant adverse reactions related to *Clostridiodes difficile* reactions, and is no longer indicated.²⁰⁷ Clarithromycin and azithromycin, while relatively safe in paediatric patients, may be associated with cardiac complications such as cardiotoxicity²²¹ and should be considered with care as an alternative to penicillin when allergy is present.

A Clindamycin should be avoided due to frequent and severe reactions related to the gastrointestinal tract. Macrolide antibiotics (clarithromycin and azithromycin) should be used with caution for paediatric patients due to the potential for cardiotoxicity. Where there is allergy to penicillin and cephalosporins, azithromycin is still considered an acceptable drug of choice.

Grade A, Level 1

9.4 Doxycycline

Due to the well-documented risk of tooth discolouration,²¹¹ the tetracycline class of antibiotics must be prescribed with caution in paediatric dental patients. However, doxycycline may be indicated where there is penicillin, cephalosporin and macrolide allergy²⁰⁷ as short-term use (less than 21 days) of doxycycline has not been associated with internal tooth discolouration in children under age 8.²²²⁻²²⁴

Additionally, due to its anti-inflammatory and anti-resorptive effects, doxycycline is appropriate for dental trauma such as in the avulsion of immature or mature permanent incisors.^{101,174} It is important to note that amoxicillin or penicillin should still be the drug of choice in avulsions.¹⁷⁴

D The use of tetracyclines should be prescribed with caution in paediatric dental patients.

Grade D, Level 3

9.5 Metronidazole

Metronidazole may be indicated as additional adjunctive therapy in combination with amoxicillin if anaerobic bacterial involvement is present,^{217,225} but this is advisable after culture and susceptibility testing of isolates from the involved sites.^{205,226} The use of this drug may be necessary to control pathogenic growth in acute facial swellings, skin and bone infections,²¹¹ and paediatric periodontal conditions such as necrotizing periodontitis or periodontal disease associated with systemic conditions in children.⁹⁶

A Metronidazole may be indicated for the paediatric patient as additional adjunctive therapy in combination with amoxicillin if anaerobic bacteria involvement is present.

Grade A, Level 1

10. USE OF ANTIBIOTICS IN GERIATRIC DENTISTRY

The judicious use of antibiotics in the geriatric patient is recommended as this population group may be at increased risk of the adverse effects of inappropriate antibiotic use, such as drug reactions and interactions, antimicrobial resistance and *Clostridioides difficile* infections.

10.1 Pharmacokinetic changes in the elderly

Absorption – While aging is associated with a decrease in gastrointestinal function, most studies of drug absorption have demonstrated minimal effects. However, other underlying conditions in elderly patients (e.g. swallowing difficulties, poor nutrition, multiple gastrointestinal conditions) may affect absorption of many drugs.

Distribution – Aging is associated with a decrease in total body water and lean body mass, and an increase in adipose tissue stores. As a result, the volume available for distribution of water-soluble drugs is decreased, leading to a higher plasma concentration for a given dose and an increased likelihood of a more profound effect or possible toxicity.

Metabolism – The main organ involved is the liver, and the metabolic process is significantly reduced with physiological aging of the organ. Slower metabolism and decreased clearance rate can lead to the accumulation of antibiotics in the plasma, increasing its concentration and predisposing to toxicity.

Elimination – Although drugs are eliminated from the body by different routes, the kidney is a major organ involved. Kidney function decreases with age due to a decrease in kidney mass and reduction in functional nephrons and mean glomerular filtration rate and renal plasma flow are reduced by 30% when compared with the young.

Renal excretion of penicillin and cephalosporins decrease with the physiological aging of kidneys, and reduction of doses of antibiotics may be required to reduce the likelihood of adverse effects.²²⁷

GPP In general, no specific modifications in the pharmacotherapy of antibiotics are needed for the healthy geriatric patient.

GPP

D Dose reduction of antibiotics is advisable in elderly patients diagnosed with renal disease.²²⁸

Grade D, Level 4

10.2 Polypharmacy in the elderly

There is a high prevalence of polypharmacy in elderly patients as they often suffer from a multitude of chronic diseases (e.g. diabetes, hypertension, congestive heart failure). Additionally, the use of over-the-counter medication and traditional Chinese medication (TCM) is prevalent in the elderly. Elderly patients are thus more susceptible to drug interactions and adverse drug reactions associated with antibiotic therapy.
227,229-231

It is necessary to regularly review the patient's medication list for potential drug interactions.

Table 1: Antibiotic-induced adverse drug reactions in elderly patients as summarized by Ouanounou et al 2015 and Soraci et al 2023.^{227,231}

Antibiotic	Commonly Associated Adverse Drug Reactions
Beta lactam antibiotics (Including Penicillins and Cephalosporins)	Diarrhoea, drug fever, interstitial nephritis, thrombocytopenia, <i>Clostridioides difficile</i> -associated colitis, rash, anaemia, neutropenia
Clindamycin	Diarrhoea, <i>Clostridioides difficile</i> -associated colitis
Clarithromycin	Cholestatic hepatitis and drug interactions
Azithromycin	Gastrointestinal intolerance, QT prolongation, ototoxicity
Fluoroquinolone	Nausea, vomiting, QT prolongation, <i>Clostridioides difficile</i> -associated colitis, CNS effects, decreased seizure threshold
Tetracyclines (including Doxycycline)	Oesophageal ulcers, oesophagitis, photosensitivity

Table 2: Antimicrobial-induced drug interactions in elderly patients as summarized by Ouanounou et al 2015 and Soraci et al 2023.^{227,231}

Antibiotic	Interacting Drug(s)	Effect
Amoxicillin	Allopurinol	Rash
Fluoroquinolones	Pharmaceuticals containing aluminium, magnesium, iron or zinc	↓ absorption of fluoroquinolones
	Antiarrhythmic	Ventricular arrhythmia
Metronidazole	Warfarin	↑ effect of warfarin
	Alcohol	Disulfiram-like reaction*
	Phenytoin	↑ phenytoin levels
Azithromycin	Pharmaceuticals containing aluminium or magnesium	↓ absorption of azithromycin
Clarithromycin	HMG-CoA reductase inhibitors, cyclosporine, digoxin, warfarin, theophylline	↑ effect of interacting drug

*Flushing, fast heartbeats, nausea, thirst, chest pain, vertigo, drop in blood pressure

11. USE OF ANTIBIOTICS IN THE IMMUNOLOGICALLY COMPROMISED

Immune function may be impaired by a range of conditions, such as poorly controlled diabetes, HIV, immunosuppression secondary to cancer and cancer therapy, immunosuppressive drugs following organ transplantation. As a result, these patients are susceptible to opportunistic infections.

It is recognised that prompt, aggressive management of dental infections in immunocompromised patients is imperative and should be carried out in consultation with the patient's medical specialist.

However, there is no evidence to support an increased risk of infection or surgical site infections arising as a result of dental procedures in these patients.²³²

11.1 Diabetes mellitus

Diabetes, particularly if poorly controlled, results in increased inflammation and infection risk. Regardless of their diabetic control, dental infections should be treated aggressively and with antimicrobials where indicated (e.g. evidence of systemic spread).²³²

There is currently no evidence to support the use of prophylactic antibiotics for well-controlled diabetics; they are at no greater risk of post-operative infection than healthy individuals.²³³

Wound healing is unlikely to be of concern in the oral cavity unless the patient has undergone invasive oral surgery. Type II diabetes mellitus patients undergoing extraction of erupted teeth with no acute odontogenic infection should not receive antibiotic prophylaxis.^{234,235}

Poorly controlled diabetics should be referred to their medical practitioners for correction of their glycaemic control before further invasive dental work.²³³

C There is no evidence of increased risk of postoperative infections or efficacy of antibiotic prophylaxis in reducing postoperative infections in patients with diabetes mellitus undergoing surgical dental procedures.²³⁶

Grade C, Level 2

C Antibiotic prophylaxis should only be considered in situations where it would be used for systemically healthy patients.

Grade C, Level 2

However, until there is more data supported by well-conducted clinical studies, the clinician should consider other factors that might further compromise the diabetic patient's systemic and local immune response (e.g. infections, other co-morbidities and smoking habits) when deciding if antibiotic prophylaxis should be administered prior to invasive procedures.

11.2 Human Immunodeficiency Virus (HIV)

Whether HIV infected patients have a greater propensity for experiencing complications from dental treatment has been controversial.

Expert consensus suggests that routine antibiotic cover to prevent septicaemia from bacteraemia arising from dental procedures is not indicated based solely on the patient's HIV status.²³⁷

There is no data to support routine antibiotic prophylaxis for patients with HIV solely based on CD4+ counts – even when CD4+ counts are less than 200 cells/mm³.²³⁸

C Pre-operative antibiotics should not be routinely administered to HIV patients.^{232,239,240}

Grade C, Level 2

D Antibiotic cover is recommended for HIV patients with severe neutropenia (<500 cells/mm³).²³⁷

Grade D, Level 4

11.3 Immunosuppression secondary to cancer and cancer therapy

There are no formal, evidence-based guidelines for use of prophylactic antibiotics in this group of immunologically compromised patients. Many of these patients will receive some form of cancer chemotherapy, and may present with clinically significant neutropenia, raising concerns of the possibility of systemic bacteraemia and disseminated infection resulting from invasive dental procedures.

In addition, some of these patients are immunocompromised by virtue of their disease (e.g. leukaemia).²⁴¹

11.3.1 Cancer therapy

The major modalities of cancer therapy include surgical resection, radiotherapy, chemotherapy, haematopoietic stem cell transplantation (HSCT) and bisphosphonate therapy. Immunosuppression may result secondary to chemotherapy and HSCT.

Chemotherapy involves the use of drugs (cytotoxic or cytostatic agents) that avoid proliferation of the neoplastic cells and/or cause their destruction. The main problem with this treatment is the lack of selectivity of the chemotherapy drugs, which also affect normal cells with a similarly accelerated cell cycle (e.g. bone marrow cells, hair follicle cells).²⁴²

HSCT is performed, in general, in acute forms of leukaemia and some cases of chronic myeloid leukaemia. Treatment with HSCT aims to repopulate the bone marrow, previously destroyed with high doses of chemotherapy (with or without radiation), with normal healthy cells. The patient will be subject to long term immunosuppression, and is susceptible to infections.²⁴³

11.3.2 Risk assessment

The risk of performing dental treatment in patients with cancer is dependent on their state of health, phase of cancer therapy and invasiveness of the dental treatment required.

In assessing patients for dental procedures, two haematological indices are particularly important: neutrophil and platelet counts. When neutrophil count is low and the procedure cannot be delayed, prophylactic antibiotic therapy protocols should be considered, depending on the degree of neutropenia. While there is no consensus in the literature, most authors recommend antibiotic prophylaxis with values less than 1,000 cells/mm³.²⁴³

11.3.3 Pre-cancer therapy

Dental treatment at this stage is based on priorities and should focus on acute dental needs. Elective dental treatment can be postponed to a later time when haematological indices of the patient stabilise.

Dental evaluation should ideally occur immediately after diagnosis and before initiation of chemotherapy to allow the removal of potential or existing sources of dental disease and infection.²⁴²⁻²⁴⁴

Patients with haematological malignancies may be immunocompromised at this stage, and present with clinically significant neutropenia. These patients may require antibiotic prophylaxis before dental procedures, and the haematologist or oncologist should be consulted prior to commencing dental treatment.

D Antibiotic prophylaxis is indicated for invasive dental procedures (e.g. subgingival scaling, endodontics, extractions) in patients with neutropenia (<1000 cells/mm³), and should be done in liaison with the oncologist.²⁴⁵⁻²⁴⁷

Grade D, Level 4

11.3.4 During cancer therapy

Patients undergoing chemotherapy are immunosuppressed and hence are susceptible to systemic infections. All elective dental treatments should be avoided during cancer therapy. If emergency treatment is required (e.g. to relieve acute pain or infection), close consultation with the haematologist or oncologist is mandatory.²⁴²

Some of these patients may also have indwelling vascular catheters or ports that are at risk of infections. While there is no evidence of catheter-related infection associated with dental procedures, this remains a controversial topic and some continue to endorse antibiotic prophylaxis for this group of patients.^{248, 249}

GPP Patients undergoing cancer therapy with dental emergencies (e.g. acute pain or swelling) should be treated in a hospital setting in close consultation with the oncologist, and with the institution of measures to increase the haematological indices, which may include antibiotic prophylaxis.²⁴¹

GPP

11.3.5 Post-cancer therapy

11.3.5.1 Chemotherapy patients

After immune competence has been restored post-chemotherapy, elective dental treatment may be provided. Clinicians should check and confirm that blood counts have normalised.^{242, 243}

Patients on maintenance chemotherapy or those with persistent haemato-oncology disease may require pre-operative blood tests before invasive dental treatment. Due to potential bleeding and infection risks, close liaison with the oncologist is required.²⁴⁵

GPP Antibiotic prophylaxis should not be routinely administered to patients who have completed chemotherapy.

GPP

11.3.5.2 Haemopoietic stem cell transplant (HSCT) patients

Immune reconstitution may take months after the HSCT, even if haematological status appears normal.^{244, 250}

Elective dental treatment should be avoided during the immediate post-transplant period (up to a year). These patients are under long term immunosuppression and may be prone to infections. The patient's oncologist should be consulted regarding the need for antibiotic prophylaxis before providing urgent dental care involving invasive dental procedures.^{243, 250}

GPP Antibiotic prophylaxis may be indicated for invasive dental treatment up to 12 months after completion of HSCT, and the HSCT team should be consulted prior to the provision of dental care.

GPP

11.4 Organ Transplant Patients

The solid organ transplant patient is at greater risk of infection immediately following transplant because of maximal immunosuppression. As a result of lifetime antirejection medication, they remain immunosuppressed.²³²

Consistent recommendations regarding dental care and the need for antibiotic prophylaxis in transplant patients are lacking.

Patients scheduled for organ transplantation should undergo a comprehensive dental evaluation and undergo any necessary dental treatment to eliminate potential source of oral infections, prior to the transplantation process.

11.4.1 Pre-transplant

If antibiotics are deemed necessary, the practitioner should be cautious when prescribing erythromycin and clarithromycin as they can alter the level of cyclosporine rendering greater immunosuppression than is required. Consultation with the physician is prudent.²⁵¹

11.4.2 Post-transplant

Post-transplantation guidelines for recipients of solid-organ transplants frequently advise antibiotic prophylaxis before dental procedures, but there is no evidence-based data from controlled clinical trials to support this recommendation, nor is a consensus evident.

Table 3: Dental management after transplant^{251,253}

Period of Time	Dental Treatment
Immediate <i>First 3 months after surgery</i>	Only emergency treatment carried out in hospital. Antibiotic prophylaxis.
Stable <i>>3/12, with no signs of rejection</i>	Elective dental care can be carried out, preferably 6 months after transplant. Antibiotic prophylaxis for invasive dental treatment.
Transplant rejection <i>Acute or chronic</i>	Only emergency treatment. Antibiotic prophylaxis.

GPP Given the current state of knowledge, it may be reasonable to administer antibiotic prophylaxis to post single-organ transplant patients for invasive dental procedures.²⁵²⁻²⁵³

GPP

12. USE OF ANTIBIOTICS FOR PATIENTS WITH RENAL DISEASE

The kidneys play a key role in the elimination of waste products of metabolism and are also a major route of elimination for many drugs. Chronic kidney disease leads to a progressive loss of excretory and endocrine function of the kidneys, thereby affecting drug metabolism and clearance. This may lead to an accumulation of drugs and their by-products in the body, potentially causing toxic effects. Some drugs may require dose adjustments to account for reduced kidney function.

While blood levels of urea and creatinine can be used to assess the excretory functions of the kidneys, a better index of kidney function is the estimated glomerular filtration rate (eGFR).

GPP In patients with chronic kidney disease, doses of antibiotics prescribed should be adjusted according to renal function. Knowledge of the patient's creatinine clearance (CrCl) or glomerular filtration rate (GFR) is essential.^{254,256} Practitioners should refer to local drug references (i.e. National Drug Formulary - <https://www.ndf.gov.sg/>) for the most updated dose adjustment recommendations.

GPP

12.1 Renal dialysis

In end-stage renal disease, renal replacement can be by transplantation, haemodialysis and peritoneal dialysis. In haemodialysis, blood flows from an arterio-venous access into a dialysis machine and through a filter that removes excess fluid and uraemic solutes. In peritoneal dialysis, a catheter is placed in the peritoneal cavity and a dialysis fluid is exchanged at regular intervals.²⁵⁴

There is a lack of evidence that bacteraemia from invasive dental procedures could cause infection of prosthetic vascular grafts used for haemodialysis.

While endocarditis in renal patients carries a higher mortality rate, it is recommended that antibiotic prophylaxis is only given to patients undergoing haemodialysis who have known cardiac risk factors.²⁵⁵

Although data is limited, there are some recommendations for the use of preprocedural antibiotics in patients undergoing peritoneal dialysis before invasive dental procedures to prevent bacterial peritonitis.²⁵⁷ Scientific data supporting this is weak. Current dental literature and dental societal guidelines do not mention any specific recommendations. The renal physician should be consulted if in doubt.

D Antimicrobial prophylaxis for patients undergoing renal dialysis is not routinely recommended for dental procedures.^{232,241}

Grade D, Level 4

13. ANTIBIOTIC PROPHYLAXIS IN DENTISTRY

Antibiotic prophylaxis prior to dental procedures were intended to prevent distant site infections of cardiac valves and prosthetic joints. However, the effectiveness of such measures is uncertain and there are no published evidence-based studies, to date, to support secondary prophylaxis for patients undergoing dental procedures.

Current guidelines recommend pre-procedural antibiotic prophylaxis less often than in the past. This is because of concerns about antimicrobial resistance, adverse drug reactions, drug costs, lack of evidence of efficacy and increased understanding about the importance of daily (cumulative) incidence of bacteraemia compared to bacteraemia from episodic (infrequent) dental procedures.²⁵⁸⁻²⁶¹

13.1 Infective endocarditis (IE)

Sporadic high-grade bacteraemia caused by invasive dental procedures were thought to be the main risk factor for IE of oral origin, hence the widespread recommendations for the use of pre-procedural antibiotic prophylaxis, to prevent IE. However, it is now believed that cumulative, low-grade bacteraemia, triggered by normal daily activities such as tooth brushing, flossing and chewing, are of greater significance. Data from bacteraemia studies strongly suggest that the incidence of bacteraemia annually from toothbrushing and other daily activities far exceeds that of dental office procedures, perhaps by hundreds of times per year.^{262,263}

Furthermore, there is evidence that increased levels of dental plaque/calculus and gingival disease increased the frequency (and likelihood) of IE-related bacteraemia after toothbrushing.²⁶⁴

For the above reasons, the current emphasis is on the maintenance of good oral health and prevention of oral disease rather than antibiotic prophylaxis in patients at risk for IE.

C It is reasonable to shift the disproportionately large focus on antibiotic prophylaxis to an emphasis on oral hygiene and prevention of oral disease.^{258,260}

Grade C, Level 2+

D Maintenance of optimal oral health and hygiene may reduce the incidence of bacteraemia from daily activities and is more important than prophylactic antibiotics for a dental procedure to reduce the risk of IE.^{207,260}

Grade D, Level 3

Persons at risk of developing bacterial IE should establish and maintain the best possible oral health to reduce potential sources of bacterial seeding. Optimal oral health is maintained through regular professional dental care and the use of appropriate dental products, such as manual, powered and ultrasonic toothbrushes, dental floss, and other plaque-removal devices.²⁵⁸

Evidence for the efficacy of antibiotic prophylaxis in preventing IE is weak. To date there is no prospective, randomised, placebo-controlled study on the efficacy of antibiotic prophylaxis to prevent IE in dental patients at risk. The few published retrospective epidemiological studies related to this question have had varied outcomes with regards to benefit from antibiotic prophylaxis.²⁵⁸⁻²⁶⁰

A recent Cochrane Database systematic review in 2022 of antibiotic prophylaxis of IE in dentistry²⁶⁵ concluded that there was no evidence to determine whether antibiotic prophylaxis before dental procedures was effective or ineffective. An extensive systematic review and meta-analysis of all studies available from 1960 to 2016 on antibiotic prophylaxis for infective endocarditis, published by Cahill TJ et.al.³², found limited evidence for benefit or harm and could not come to any definite conclusion on the effectiveness of antibiotic prophylaxis. This meta-analysis did indicate that antibiotic prophylaxis reduced the incidence of bacteraemia, but this may not translate to a statistically significant protective effect against IE.

However, in a recent US study of almost 8 million patients, Thornhill et al.²⁶⁶ showed for the first time that antibiotic prophylaxis before invasive dental procedures (in particular extractions and surgical procedures) in high-risk cardiac patients did indeed reduce the incidence of IE.

Major revisions to guidelines were issued from 2007 onwards by the American Heart Association (AHA)^{258,267}, the European Society of Cardiology (ESC)²⁵⁹ and the National Institute for Health and Care Excellence (NICE) in UK²⁶⁰, significantly limiting the indications for use of antibiotic prophylaxis. The 2007 AHA guideline on “Prevention of Infective Endocarditis” has become a widespread standard and is similar to the European Society of Cardiology statement, both of which restrict the use of antibiotic prophylaxis to the highest risk cardiac patient (AHA 2007 guidelines specifically restrict prophylaxis to those at greatest risk of adverse outcomes from IE).²⁵⁸

NICE²⁶⁰ states that antibiotics prophylaxis against IE is not recommended routinely for patients undergoing dental procedures. Notably, in an update by the Scottish Dental Clinical Effectiveness Programme (SDCEP) in August 2018²⁶⁸ and endorsed by NICE, the following recommendations were issued: “The vast majority of patients at increased risk of infective endocarditis will not be prescribed prophylaxis. However, for a very small number of cardiac patients at increased risk (similar to those identified by AHA and ESC guidelines) it may be prudent to consider antibiotic prophylaxis (non-routine management), in consultation with the patient and their cardiologist or cardiac surgeon”.

The AHA Scientific Statement update on the prevention of IE was published in May 2021²⁰⁷ and it recommended no changes to the 2007 IE prevention guidelines. The writing group undertook a review of studies (epidemiological, microbiological studies) and found no convincing evidence of an increase in viridans group Streptococcal (VGS) IE among patients with low, moderate or high risk of IE or adverse outcomes from VGS IE since publication of the 2007 guidelines.

GPP The committee recommends that dental practitioners follow the 2021 AHA Scientific Statement update on the “Prevention of Viridans Group Streptococcal Infective Endocarditis”²⁰⁷.

GPP

D Prophylaxis against infective endocarditis is reasonable before dental procedures that involve manipulation of gingival tissue, manipulation or the periapical region of teeth, or perforation of the oral mucosa in patients with underlying cardiac conditions associated with the highest risk of adverse outcomes from IE. ^{207,258,267} (Table 4, 5)

Grade D, Level 3

Dental practitioners should have a low threshold to refer patients for medical assessment if any at risk cardiac patient develops signs and symptoms suggestive of IE after invasive dental procedures or even in the course of routine treatment for oral disease. ^{207,261}

Refer to Tables 4, 5 for antibiotic regimes and cardiac conditions for which antibiotic prophylaxis is recommended for various dental procedures.²⁰⁷

13.2 Nonvalvular cardiovascular devices and vascular grafts

These include coronary artery stents, coronary artery bypass grafts, cardiovascular implantable electronic device (CIED) [pacemakers, implantable cardioverter-defibrillator (ICD)], peripheral vascular stents, haemodialysis grafts, intra-abdominal/intra-thoracic vascular grafts, and intravascular catheters [e.g. peripheral venous/arterial catheters, central venous catheters, pulmonary artery catheters, peripherally inserted central venous catheters (PICC)].

A review of the literature from 1950 to 2007 for publications on cardiac electrophysiological device infections reported no hematologic infection from dental, gastrointestinal, genitourinary, dermatologic, or other procedures.²⁶⁹

AHA in 2003²⁷⁰ and updates in 2010²⁶⁹, 2021²⁰⁷ conclude:

D There is no convincing evidence suggesting that microorganisms associated with dental procedures cause infection of nonvalvular vascular devices at any time after implantation.

Grade D, Level 3

D Antimicrobial prophylaxis is not recommended for dental or other invasive procedures not directly related to device manipulation to prevent infection of cardiovascular implantable electronic devices, which include pacemakers and similar devices.

Grade D, Level 4

D Antibiotic prophylaxis for dental procedures is not recommended for patients with coronary artery stents or other vascular stents.

Grade D, Level 4

For vascular grafts:^{269,271}

D Antimicrobial prophylaxis is not recommended for prevention of IE in patients with vascular grafts (e.g. coronary artery bypass graft surgery) or peripheral vascular grafts and patches (including those used for haemodialysis) who undergo a dental procedure.

Grade D, Level 4

Table 4: Conditions for which antibiotic prophylaxis (AP) is suggested for prevention of infective endocarditis (IE) ^{207,258,259,267}

AP Recommended	AP Not Recommended
<p>Prophylaxis against IE is reasonable before dental procedures that involve manipulation of gingival tissue, manipulation of the periapical region of teeth, or perforation of the oral mucosa in patients with the following:</p> <ol style="list-style-type: none"> 1. Prosthetic cardiac valve or material: <ol style="list-style-type: none"> a) Presence of cardiac prosthetic valve. b) Transcatheter implanted prosthetic valves. c) Cardiac valve repair with devices, including annuloplasty rings, chords/clips. d) Left ventricular assist devices or implantable heart. 2. Previous, relapse or recurrent IE. 3. Congenital heart disease (CHD): <ol style="list-style-type: none"> a) Unrepaired cyanotic CHD, including palliative shunts and conduits. b) Completely repaired CHD with prosthetic material or device, whether placed by surgery or transcatheter during the first 6 months after the procedure. c) Repaired CHD with residual defects at the site of or adjacent to the site of a prosthetic patch or prosthetic device. d) Surgical or transcatheter pulmonary artery valve or conduit placement such as Melody valve and Contegra conduit. 4. Cardiac transplant recipients who develop cardiac valvulopathy. 	<p>Dental procedures for which AP is NOT recommended:</p> <ol style="list-style-type: none"> 1. Anaesthetic injections through noninfected tissue 2. Taking dental radiographs 3. Placement of removable prosthodontic or orthodontic appliances 4. Adjustment of orthodontic appliances 5. Placement of orthodontic brackets 6. Shedding of primary teeth 7. Bleeding from trauma to the lips or oral mucosa <p>Prophylaxis is no longer recommended for the following patients:</p> <ol style="list-style-type: none"> 1. Mitral valve prolapse 2. Rheumatic heart disease 3. Congenital heart conditions (atrial septal defect, ventral septal defect, hypertrophic cardiomyopathy) 4. Septal defect closure devices when complete closure is achieved 5. Calcific aortic stenosis 6. Bicuspid aortic valve 7. Implantable electronic devices such as pacemakers or similar devices 8. Peripheral vascular grafts and patches, including those for haemodialysis 9. Coronary artery stents or other vascular stents 10. CNS ventriculoatrial shunts 11. Vena cava filters 12. Pledgets

AP – Antibiotic prophylaxis; IE – Infective endocarditis; CHD – Congenital heart disease

Table 5: Antibiotic prophylaxis regimens for prevention of BACTERIAL ENDOCARDITIS for dental procedures^{207, 259}

Situation	Medication	Regimen: Single dose 30 to 60min before procedure
Oral	Amoxicillin	Adults: 2g Children: 50mg/kg
Unable to Take Oral Medication	Ampicillin OR Cefazolin or ceftriaxone	Adults: 2g IM or IV Children: 50mg/kg IM or IV Adults: 1g IM or IV Children: 50mg/kg IM or IV
Allergic to Penicillin – Oral	Cephalexin*§ OR Azithromycin or clarithromycin OR Doxycycline	Adults: 2g Children: 50mg/kg Adults: 500mg Children: 15mg/kg Adults: 100mg Children: <45 kg, 2.2mg/kg : >45 kg, 100mg
Allergic to Penicillin and unable to take oral medication	Cefazolin or ceftriaxone §	Adults: 1g IM or IV Children: 50mg/kg IM or IV

NOTE: Clindamycin is NO longer recommended for antibiotic prophylaxis for a dental procedure

*Or other first- or second-generation oral cephalosporin in equivalent adult or paediatric dosage.

§ Cephalosporins should not be used in a person with a history of anaphylaxis, angioedema or urticaria with penicillins or ampicillin.

13.3 Prosthetic joints

Differing protocols/guidelines have been published over the years regarding antibiotic prophylaxis for patients with prosthetic joints undergoing dental procedures. This was despite a lack of evidence for oral *Streptococcus* species being involved in prosthetic joint infection, the predominant microbe in late prosthetic joint infections (PJI) normally being *Staphylococci* species.²⁷²

In 2012 a panel of experts from the American Academy of Orthopaedic Surgeons (AAOS) and the American Dental Association (ADA) reviewed the available evidence on dental treatment and prosthetic joint infection.²⁷³ The expert panel concluded that the available evidence failed to demonstrate an association between dental procedures and prosthetic joint infections or any effectiveness for antibiotic prophylaxis. The committee recommended: “The practitioner *might* consider discontinuing the practice of routinely prescribing prophylactic antibiotics for hip and knee prosthetic joints undergoing dental procedures”.

In 2014, a panel of experts convened by the ADA Council on scientific affairs updated the findings and recommendations of the 2012 panel.²⁷⁴ The 2014 panel judged that the current best evidence failed to demonstrate an association between dental procedures and PJI. Recently, the Second International Meeting on Musculoskeletal Infection in their proceedings report, “International consensus on orthopaedic infections (prevention, postoperative factors) came to the same conclusions that “there is no role for routine prophylactic antibiotics administration prior to dental procedures”. The consensus meeting also brought up the issue of the need for a patient to postpone having an invasive dental procedure after total joint arthroplasty. The committee speculated, in absence of evidence, that the seeding of an implant is more likely to occur if the implant had not osseointegrated and recommended delaying nonurgent dental procedures until osseointegration of uncemented components were complete.²⁷⁵

In the most recent study in a US health care population, on the link between late prosthetic joint infections, invasive dental procedures and the use of preprocedural prophylaxis, Thornhill and co-workers²⁷⁶ concluded there was no significant association between invasive dental procedures and late prosthetic joint infections. Further the authors found no effect of antibiotic prophylaxis cover for dental procedures in reducing the risk of late prosthetic joint infections. The authors advised that “dental antibiotic prophylaxis use to prevent prosthetic joint infections should, therefore, cease”.

A similar large study in England also concluded that there was no association between invasive dental procedures and late prosthetic joint infections.²⁷⁷

The current best evidence failed to demonstrate an association between dental procedures and prosthetic joint infections.

D In general, patients with prosthetic joints are not recommended to receive prophylactic antibiotics before dental treatment.

Grade D, Level 3

Practitioners may consider delaying non-urgent invasive dental procedures, if possible, in patients after total joint arthroplasty, until osseointegration of uncemented components are complete.

The ADA report²⁷⁴ also noted, in their review of a case-control study²⁷², several peri- and postoperative factors associated with an increased risk for prosthetic joint infections, independent of dental factors. This included a history of complications associated with joint replacement surgery (e.g. wound infection, haematoma) and being immunocompromised (rheumatoid arthritis, current use of systemic corticosteroids/immunosuppressive drugs, presence of malignancy, history of chronic kidney disease) or having diabetes mellitus²⁷² (see section 13.5).

Due to weak evidence that some patients with certain medical conditions or with a history of joint complications, may develop PJI, a further recommendation was made for practitioners to consult the orthopaedic surgeon when planning to perform invasive dental procedures in such situations and discuss the need for prophylactic antibiotics.²⁷⁴ Of note the AAOS has developed an ‘Appropriate Use Criteria (AUC)’ tool to assist the orthopaedic surgeon and the dental practitioner in identifying clinically situations and “potentially at-risk patients for which antibiotic prophylaxis may reduce the “theoretical” risk of experiencing post procedural PJI.²⁷⁸ The Appropriate Use Criteria Decision making tool can be accessed at the AAOS website at www.orthoguidelines.org/go/auc/.²⁷⁹

GPP For patients potentially at higher risk of experiencing prosthetic joint infections, the need for prophylactic antibiotics should be considered after discussion with the orthopaedic surgeon and the patient. If antibiotics are deemed necessary, the orthopaedic surgeon in consultation with infectious disease physician should recommend the appropriate antibiotic regimen.

GPP

GPP Consideration may be given to consider pre-procedure prophylactic antibiotics in some of these scenarios which include, but are not limited to the following:

1. Patients with previous late artificial joint infection.
2. Patients with increased morbidity associated with joint surgery (wound drainage/haematoma).
3. Patients undergoing treatment of severe and spreading oral infections (cellulitis).
4. Patients with increased susceptibility for systemic infection.
5. Patients with congenital or acquired immunodeficiency.
6. Patients on immunosuppressive medications.
7. Patients who are diabetics and have poor glycaemic control.
8. Patients with systemic immunocompromising disorders (e.g. rheumatoid arthritis, systemic lupus erythematosus).
9. Patients in whom extensive and invasive procedures are planned.
10. Patients who are at significant risk of medication-related osteonecrosis of the jaws.

GPP

Currently antibiotics prophylaxis is not indicated for all dental patients with prosthetic joint replacements in United Kingdom²⁷⁹, Canada²⁸¹ and Netherlands²⁸². In Australia²⁸³ and New Zealand²⁸⁴ antibiotics is not routinely recommended unless the patient is significantly immunocompromised or has an infected prosthetic joint.

13.4 Pins, plates and screws

D Antibiotic prophylaxis is not indicated for patients with pins, plates and screws or other “orthopaedic hardware” that is not within a synovial joint.^{285,286}

Grade D, Level 4

14. GLOSSARY

AAOS	American Academy of Orthopaedic Surgeons
ADA	American Dental Association
AHA	American Heart Association
BOP	Bleeding on Probing
C&S	Culture & Sensitivity
CAL	Clinical Attachment Loss
CHD	Congenital Heart Disease
ESC	European Society of Cardiology
HIV	Human Immunodeficiency Virus
HSCT	Haematopoietic Stem Cell Transplantation
I&D	Incision & Drainage
IADT	International Association for Dental Traumatology
IE	Infective Endocarditis
MRONJ	Medication Related Osteonecrosis of the Jaw
NICE	National Institute for Health and Care Excellence
OMS	Oral and Maxillofacial Surgery
ORN	Osteoradionecrosis
PJI	Prosthetic Joint Infections
PPD	Probing Pocket Depths
RT	Radiotherapy
TAP	Triple Antibiotic Pastes
VGS	Viridans Group Streptococci

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16. WORKGROUP MEMBERS

The members of the workgroup, who were appointed in their personal professional capacity, are:

Chairpersons

Adj. A/P Elliott Myra Nee Lin Wen Jui
Discipline of Oral and Maxillofacial Surgery
Faculty of Dentistry National University Centre for
Oral Health, Singapore
Oral & Maxillofacial Surgeon, Aesthetic
Reconstructive Jaw Surgery
Mount Elizabeth Medical Centre

Dr Chang Kok Meng
Specialist in Periodontology
Private Practice

Editorial & Writing Group Members

Dr Chang Kok Meng
Specialist in Periodontology
Private Practice

Dr Guay Peiru, Melissa
Senior Dental Surgeon
National Healthcare Group Polyclinics

Dr Robinson Narendran Andrew
Adjunct Associate Professor
Discipline of Oral and Maxillofacial Surgery
Faculty of Dentistry, National University Centre for Oral Health, Singapore

Members (in alphabetical order)

Dr Chergng Pei Zhi Benjamin
(College of Physicians, Singapore)
Senior Consultant
Department of Infectious Diseases
Singapore General Hospital

A/P Raymond Wong Chung Wen
Discipline Director
Oral & Maxillofacial Surgery
Faculty of Dentistry
National University Centre for Oral Health,
Singapore

Dr Ode Wataru
Consultant, Clinical Lead
Endodontics
National University Centre for Oral Health,
Singapore

CI A/P Tay Ban Guan Andrew
Senior Consultant
Department of Oral and Maxillofacial
Surgery
National Dental Centre Singapore

CI A/P Ong Meng Ann Marianne
Senior Consultant
Periodontics, Department of Restorative
Dentistry
National Dental Centre Singapore

Dr Teo Kuo-Yih, Terry
Specialist in Paediatric Dentistry
Private Practice