

Antimicrobial stewardship (AMS)

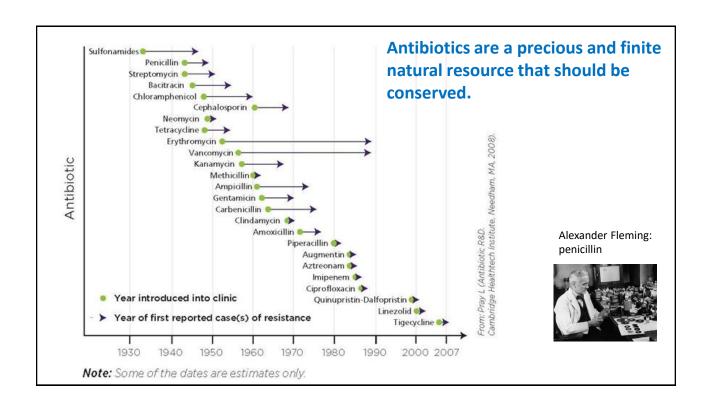
Coordinated interventions designed to improve the appropriate use of antimicrobials. Antimicrobial stewardship promotes the optimal use of antimicrobials through selecting the appropriate agent, dose, therapy duration and administration route.

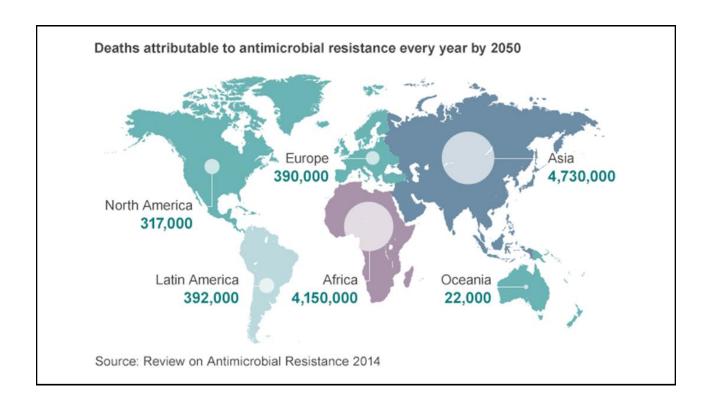


Antimicrobial resistance (AMR)

Resistance of a microorganism to an antimicrobial drug that had previously been effective for treatment of infections by this organism. Resistant microorganisms including bacteria, fungi, viruses







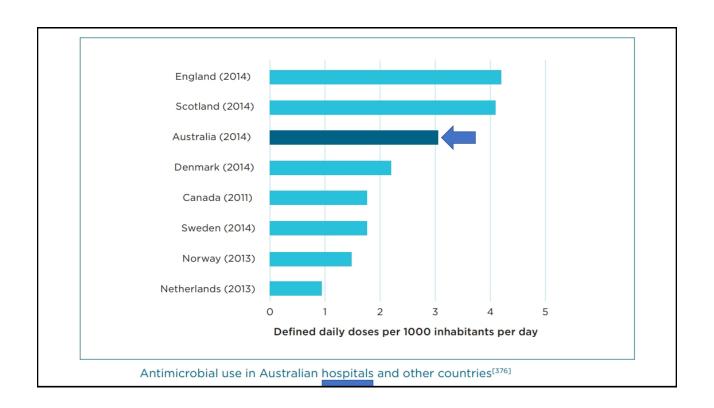


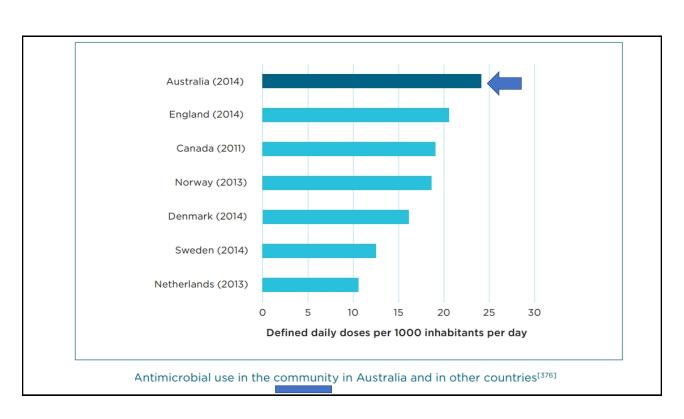
Australian Guidelines for the Prevention and Control of Infection in Healthcare

4.5 Antimicrobial Stewardship

Summary

- Resistance to antimicrobials is commonly found in Australian hospitals and increasingly so in the community. This resistance can have a significant impact on morbidity, mortality and treatment costs.
- A significant driver of antimicrobial resistance is the unnecessary or inappropriate use of antimicrobials. Around one third of all
- antimicrobial use in healthcare is unnecessary or inappropriately prescribed^[376].





Australian Dental Journal



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Trends in Australian dental prescribing of antibiotics: 2005–2016

LJ Walsh,* (6) PJ Ford,* (6) T McGuire,†"; § (6) M vanDriel,¶ (6) SA Hollingworth† (6)

*School of Dentistry, The University of Queensland, Brisbane, Qld, Australia.
†School of Pharmacy, The University of Queensland, Brisbane, Qld, Australia.
‡Faculty of Health Sciences and Medicine, Bond University, Gold Coast, Qld, Australia.
‡Mater Pharmacy, Mater Health, South East Queensland, Brisbane, Qld, Australia.

Primary Care Clinical Unit, Faculty of Medicine, The University of Queensland, Brisbane, Qld, Australia.

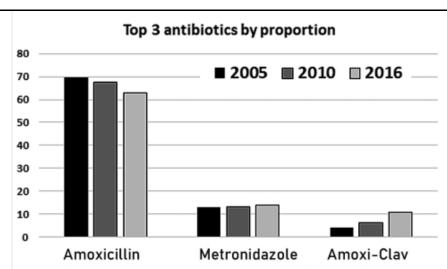


Fig. 4 Dispensed use (proportion of total prescribing for the top three as measured by defined daily doses per 1000 population per day) by Australian dentists for the three most commonly prescribed individual antibiotics (amoxi-clav – amoxicillin plus clavulanic acid) for 2005, 20010 and 2016.

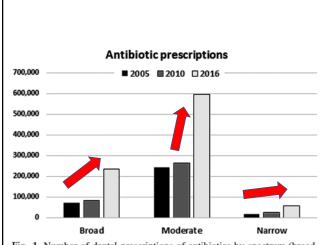


Fig. 1 Number of dental prescriptions of antibiotics by spectrum (broad, moderate and narrow) by year (2005, 2010 and 2016).

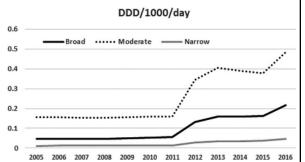


Fig. 2 Dispensed use (defined daily doses per 1000 population per day) of antibiotics by Australian dentists by spectrum (broad, moderate and narrow) between 2005 and 2016.

Acute infection: periapical abscess









Need physical treatments:

<u>drainage</u> of pus by removing the dental pulp (root canal treatment) or by extracting the tooth

ABT are **rarely** needed, and only are used when there has been systemic spread of infection and/or the host is immune compromised.

Key messages 1

- When using antibiotics as an adjunct in managing dental infections, the duration could just be 2 days or 3 days after which time there is a review by the clinician (rather than "take until finished").
 - Taking antibiotics for longer than necessary, increases the risk of resistance. Hence, replace prolonged antibiotic courses by <u>short</u> courses.
 - A shorter course of antibiotics can be as effective as the long course from the past. Hence, replace fixed duration courses with <u>personalized duration</u> of antibiotic therapy.







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Page 1 of 5



ANALYSIS

The antibiotic course has had its day

With little evidence that failing to complete a prescribed antibiotic course contributes to antibiotic resistance, it's time for policy makers, educators, and doctors to drop this message, argue **Martin Liewelyn and colleagues**

Martin J Llewelyn professor of infectious diseases^{1,2}, Jennifer M Fitzpatrick specialist registrar in infection², Elizabeth Darwin project manager³, SarahTonkin-Crine health psychologist⁴, Cliff Gorton retired building surveyor⁵, John Paul consultant in microbiology⁶, Tim E A Peto professor of infectious diseases⁷, Lucy Yardley professor of health psychology⁸, Susan Hopkins consultant in infectious diseases and microbiology⁹, Ann Sarah Walker professor of medical statistics and epidemiology³

¹Department of Global Health and Infection, Brighton and Sussex Medical School, Falmer, BN1 9PS, UK; ²Department of Microbiology and Infection, Brighton and Sussex University Hospitals NHS Trust, Brighton, UK; ³Nuffield Department of Medicine, University of Oxford, UK; ⁴Nuffield Department of Primary Care Health Sciences, Oxford, UK; ⁶Oxford, UK; ⁶Nuflice Health England, Royal Sussex County Hospital, Brighton, UK; ⁷Coxford Biomedical Research Centre, Oxford, UK; ⁶Faculty of Human and Social Sciences, University of Southampton, UK; ⁸Royal Free London NHS Foundation Trust, London, UK; ²Coxrespondence to: M Llewelyn@bsms.ac.uk

The concept of a rigid antibiotic course ignores the fact that patients may respond differently to the same antibiotic, depending on diverse patient and disease factors.

In many situations, stopping antibiotics sooner is a safe and effective way to reduce antibiotic overuse.

Key messages 2

- It is not up to the patient to just decide when to stop taking their antibiotics.
- People must not
 - Use leftover antibiotics at home for self-medication without clinical evaluation.
 - Give their own antibiotics to friends/family without clinical evaluation.
 - Why? Risks of adverse drug reactions, drug interactions, masking of underlying infectious processes, superinfection, and disruption of the microbiome

What should happen

M	INDME
M	Microbiology guides therapy wherever possible
1	Indications should be evidence-based
N	Narrowest spectrum required
D	Dosage appropriate to the site and type of infection
M	Minimise duration of therapy
Е	Ensure monotherapy in most situations

What actually happens!

Factors influencing decisions in primary health care to prescribe antimicrobials

Patient factors	Clinician factors	Contextual factors
Patient demand and expectations Patient unwillingness or inability to receive definitive dental treatment Perceived impact of antimicrobial	Lack of knowledge about antimicrobial prescribing guidelines Diagnostic uncertainty about whether antimicrobials are indicated	Prescribing practices of peers and colleagues Incentives Health care context
refusal on patient satisfaction Patient beliefs about positive impacts of antimicrobials on acute odontogenic pain	Workload contributing to lack of time to provide definitive dental treatment	
Accessibility of dental care	Concerns about medico-legal consequences of failure to prescribe	
	Prescribing habits	
	Pressure from other clinicians (e.g., orthopaedic surgeons) to prescribe prophylactic antimicrobials when not clinically indicated	
	Concern about running late and impacts on patients who are waiting	

Challenge: Biofilms in protected sites within teeth

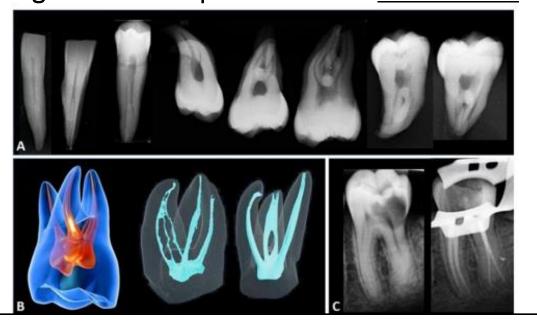


Table 1. The complex composition of endodontic biofilms.

Bacteria-summary

- · Over 400 different bacterial species have been identified in the root canal of teeth
- Endodontic biofilms typically contain around 20 species, but can have many as 30 or more species of bacteria
- The most frequent bacteria in endodontic biofilms belong to the phyla Firmicutes, Proteobacteria, Spirochaetes, Bacteroidetes, and Actinobacteria

Gram-positive bacteria

- Common streptococci include Streptococcus intermedius, S. constellatus and S. mutans, and other facultative or microaerophilic streptococci
- Common enterococci include Enterococcus faecalis
- Gram-positive anaerobes include species belonging to the genera Peptostreptococcus, Eubacterium, and Pseudoramibacter

Gram-negative bacteria

- Gram-negative anaerobic bacteria include species belonging to the genera Fusobacterium, Porphyromonas, Prevotella, and Campylobacter.
- Commonly found Gram-negative bacteria include Tannerella forsythia, Porphyromonas gingivalis, P. endodontalis, Prevotella intermedia, P. nigrescens, Fusobacterium periodonticum, F. nucleatum, and Eikenella corrodens
- Spirochaetes (treponemes) include Treponema denticola, T. socranskii, T. maltophilum, T. lecithinolyticum, T. vincentii, T. pectinovorum, T. amylovorum, and T. medium

Archaea, such as Methanobrevibacter oralis and M. filiformis.

Fungi, including Candida albicans

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B Athanassiadis,* PV Abbott,* LJ Walsh

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Antibiotic	Mechanisms of resistance	Type of resistance
β-Lactams (e.g., penicillins, carbapenems, cephlosporins)	 (a) Overproduction of low-affinity penicillin binding proteins and/or decreased affinity for binding B-Lactams (NB: Intrinsic resistance to almost all cephalosporins) 	Intrinsic
	(b) β-Lactamase production	Acquired
Tetracyclines	(a) Ribosomal protection systems (Tet L,Tet M, Tet O genes)	Acquired
	(b) Efflux pump	Acquired
Lincosamides (e.g., clindamycin)	(a) Low level (b) High level (MLSb phenotype-methylation in 23S ribosomal RNA)	Intrinsic Acquired
Macrolides (e.g., eryhromycin, azithromycin, clarithromycin)	(a) MLSb phenotype (b) Efflux pump	Acquired Acquired
Streptogramin B (e.g., quinupristin) Streptogramin A (e.g., dalfopristin)	MLSb phenotype (NB: Virtually all E. faecalis isolates are resistant)	Acquired Intrinsic
Aminoglycosides (e.g., gentamycin, streptomycin, kanamycin)	(a) Aminoglycoside modifying enzyme (NB: Not effective as monotherapy needs addition of penicillin) (b) Low level (limiting transport of drug across cell membrane)	Acquired Intrinsic
Glycopeptides (e.g., vamcomycin, teicoplanin)	(a) Van A phenotype (b) Van B phenotype (suseptible to teicoplanin)	Acquired Acquired
Fluroquinolones (e.g., moxifloxacin)	(a) DNA gyrase (topoisomerase II,IV) (b) Efflux pump	Acquired Acquired
Chloramphenicol	(a) Chloramphenicol acetyltransferase enzyme (b) Efflux pump (NB: 50% of enterococci are resistant to chloramphenicol)	Acquired Acquired
Trimethoprim and Sulfamethoxazole	Chromosomal mutations in gene encodes dihydrofolate reductase	Acquired

Table 6. COMPAR	ISON OF ANTI	BIOTIC SENSITIV	ITY PROFILE

	Streptococc	us viridans			Staphylococ	ccus Species	
	Antibiotic	Resistance			Antibiotic	Resistance	
2009-2014 (n = 45) 1997-2003 (n = 78) ⁷			2009-2014 (n = 30) 1997-2003 (n = 2		$(n = 24)^7$		
Antibiotic	Species Resistant, %	Antibiotic	Species Resistant, %	Antibiotic	Species Resistant, %	Antibiotic	Species Resistant, %
Penicillin	2	Penicillin	12.9	Penicillin	73	Penicillin	72.7
Clindamycin	32	Clindamycin	13.7	Oxacillin	27	_	_
Erythromycin	29	Erythromycin	16.6	Clindamycin	23	Clindamycin	10.5
Vancomycin	0	Vancomycin	0	Erythromycin	30	Erythromycin	25
				Tetracycline	4	_	_
				Trimethoprim	14	_	_
				Vancomycin	0	Vancomycin	0

Kim, Chuang, and August. Antibiotic Resistance in Orofacial Infections. J Oral Maxillofac Surg 2017.

Antibiotic Resistance in Severe Orofacial Infections



Min Kyoung Kim, *Sung-Kiang Chuang, DMD, MD, † and Meredith August, DMD, MD.

Unnecessary use





Review

Antibiotic Prophylaxis in Dental Implant Procedures in Patients with Orthopaedic Prostheses: A Systematic Review

Angel-Orión Salgado-Peralvo ^{1,2}, Juan-Francisco Peña-Cardelles ^{2,3,4}*, Naresh Kewalramani ^{2,5}, Alvaro Garcia-Sanchez ⁶, María-Victoria Mateos-Moreno ⁷, Eugenio Velasco-Ortega ^{1,2}, Iván Ortiz-García ^{1,2}, Álvaro Jiménez-Guerra ^{1,2}, Dániel Végh ⁸, Ignacio Pedrinaci^{9,10} and Loreto Monsalve-Guil ^{1,2}

Unnecessary use

Australian Dental Journal



Australian Dental Joi

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2018

Is there a consensus on antibiotic usage for dental implant placement in healthy patients?

J Park,* M Tennant,† LJ Walsh,‡ E Kruger† (6)

School of Dentistry, The University of Western Australia, Perth, Western Australia, Australia.

†Department of Anatomy, Physiology and Human Biology, International Research Collaborative, Oral Health and Equity, The University of Western Australia, Perth, Western Australia, Australia, Australia, School of Dentistry, The University of Queensland, Brisbane, Queensland, Australia.

ABSTRACT

This systematic review aimed to determine whether there is consensus for antibiotic prescription in healthy patients undergoing implant placement. A search of PubMed, Embase and Medline databases was conducted in January 2016 to find published journal articles on the use of antibiotics in implant placement, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The inclusion criteria were prospective human clinical trials investigating antibiotic usage during implant placement. Fifteen studies were deemed suitable. In 13 studies, no statistical difference was found between antibiotic use and the incidence of prosthetic failure, implant failure and early postoperative infections. These were rated as having low to high risk bias. Contrary results were reported in two studies, both of which were rated as having a high potential for bias. In conclusion, antibiotic use in healthy patients for the prophylaxis of surgical infection associated with dental implant placement does not appear to improve clinical outcomes. Practitioners should apply principles of antimicrobial stewardship and not use antibiotics as a routine measure in healthy patients.

2019





Review

Antibiotic Prophylaxis on Third Molar Extraction: Systematic Review of Recent Data

Gabriele Cervino 10, Marco Cicciù 1,*0, Antonio Biondi 2, Salvatore Bocchieri 1, Alan Scott Herford 3, Luigi Laino 4 and Luca Fiorillo 1,400





Article

A Systematic Review and Meta-Analysis Evaluating Antibiotic Prophylaxis in Dental Implants and Extraction Procedures

Amrik Singh Gill, Hana Morrissey and Ayesha Rahman *

Results: Seven randomised clinical trials (RCTs)

were included in the final review comprising n = 1368 patients requiring either tooth extraction(s) or dental implant(s). No statistically significant evidence was prophylactic antibiotics in reducing the risk of implant failure $(p = 0.09, RR\ 0.43; 95\%\ CI\ 0.16–1.14)$ or post-operative complications $(p = 0.47, RR:\ 0.74; 95\%\ CI\ 0.34–1.65)$ under normal conditions. Approximately 33 patients undergoing dental implant surgery need to receive antibiotics in order to prevent one implant failure from occurring. *Conclusions:* There is little conclusive evidence to suggest the routine use of antibiotic prophylaxis for third molar extractive surgery in healthy young adults. There was no statistical evidence for adverse events experienced for antibiotics vs. placebo. Based on our analysis, even if financially feasible, clinicians must carefully consider the appropriate use of antibiotics in dental implants and extraction procedures due to the risk of allergic reactions and the development of microbial drug resistance.





Article

Discrepancy in Therapeutic and Prophylactic Antibiotic Prescribing in General Dentists and Maxillofacial Specialists in Australia

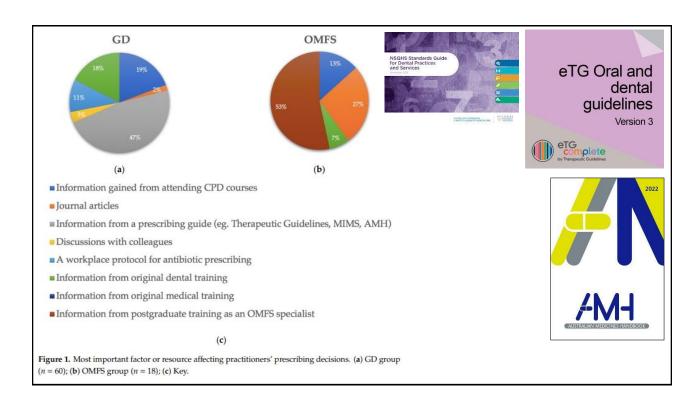
Cheryl Chen *0, Nicole Gilpin and Laurence Walsh

Faculty of Health and Behavioural Sciences, The University of Queensland School of Dentistry, UQ Oral Health Centre, 288 Herston Road, Herston, QLD 4006, Australia; n.v.gilpin@gmail.com (N.G.); l.walsh@uq.edu.au (L.W.)

* Correspondence: cheryl.chen@uq.net.au; Tel.: +61-458-988-627

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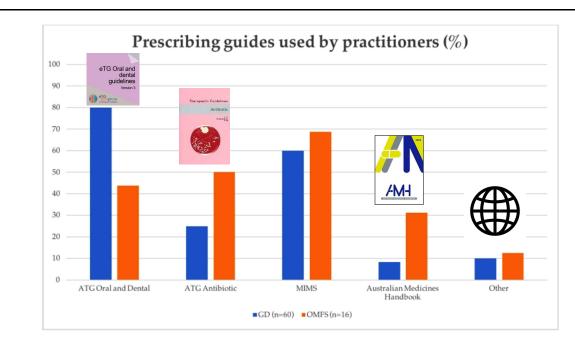


Figure 2. Percentage (%) use of prescribing guides within GD (n = 60) and OMFS (n = 16) groups.

Scenario 1 (Third molar surgical extraction): A healthy 19-year-old patient has been referred to you for extraction of 18, 28, 38, and 48. Imaging and intraoral examination reveals that the 18, 28, and 48 are all completely erupted into the oral cavity. The 38 is mesially impacted and only partially erupted, with a recent (but now resolved) episode of pericoronitis. The patient has no medical conditions and the planned surgical removal will be performed in two appointments under local anesthetic (LA) and sterile surgical conditions, starting with 28/38.

Scenario 2 (Single implant placement): You are going to place an implant to replace the 46 edentulous space in a healthy 45-year-old male patient. The 46 was extracted 6 months ago due to a vertical root fracture. There were no signs of infection at the time of extraction and there are no current signs of infection now. The planned procedure will be a two-stage tissue-level single implant and will involve raising a flap and bone removal. No block or particulate grafting is needed. The procedure will be performed under sterile surgical conditions.



<u>Neither</u> of these common situations warrants the use of antibiotics as surgical prophylaxis.

Table 4. Preferred antibiotic agent/s of practitioners who prescribed antibiotics ¹.

Procedure	Respondent Type		Preferred Antibiotic Agent/s (%)					
			Amoxicillin Only	Phenoxymethylpenicillin Only	Cephalexin Only	Metronidazole Plus Amoxicillin	Amoxicillin/ Clavulanic Acid	
Third molar	Total	n = 23	78.3	8.7	4.3	4.3	0.0	
surgical	GDs 1	n = 12	75	8.3	0.0	8.3	0.0	
extraction	OMFSs	n = 11	81.8	9.1	9.2	0.0	0.0	
Single	Total	n = 31	77.4	0.0	6.5	9.7	6.5	
implant	GDs	n = 18	83.3	0.0	5.6	11.1	0.0	
placement	OMFSs	n = 13	69.2	7.7	7.7	7.7	15.4	

¹ One GD did not specify their preferred antibiotic agent in the third molar surgical extraction case scenario.



Table 5. Medical conditions for which practitioners provide antibiotic prophylaxis.

Medical History	Third Molar Surgical Extraction		Single Implant Placement	
% of practitioners providing antibiotic p				
	GDs	OMFSs	GDs	OMFSs
	(n = 50)	(n = 18)	(n = 27)	(n = 17)
Patients on oral anticoagulants or platelet inhibitors	4.0	5.6	11.1	17.7
HIV positive	24.0 1	55.6 ¹	37.0	47.1
History of injecting drug use	8.0 ²	38.9 ²	14.8	41.2
Chronic hepatitis B or C	14.0	33.3	22.2	41.2
Uncontrolled diabetes mellitus	56.0 ³	100.0 ³	63.0 ²	100.0 ²
Cardiac valve replacement or mitral valve prolapse	92.0	83.3	85.2	88.2
Prosthetic joint in past two years	48.0	72.2	59.3	76.5
History of head and neck cancer and radiotherapy	48.0	55.6	48.2	64.7
Oral bisphosphonate therapy for the past three years	66.0	83.3	63.0	82.4
History of intravenous bisphosphonate therapy	68.0	88.9	55.6 ¹	88.2 1

 $^{^1}$ Significant finding (p < 0.05). Calculated using Fisher's exact test. 2 Very significant finding (p < 0.01). Calculated using Fisher's exact test. 3 Extremely significant finding (p < 0.001). Calculated using Fisher's exact test.

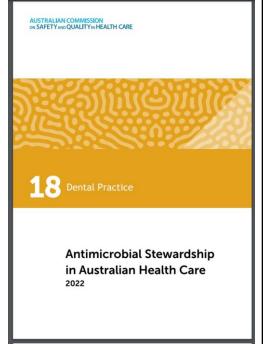
- Antimicrobial resistance (AMR) continues to be one of the greatest threats for our community and the overuse of antimicrobials is a significant contributor to AMR. Overprescribing and inappropriate prescribing of antimicrobials in the management of odontogenic complaints is well documented.
- AMS in dental practice encompasses multiple interventions, including:
 - Professional education for dentists
 - Increased use of prescribing guidelines in dental practice
 - Audit and individual clinician feedback on prescribing practices
- Antimicrobial prescriptions by dentists are a significant contributor to the overall volume of antimicrobials dispensed to the Australian community each year.
- NSQHS Standards Guide
 for Derital Practices
 and Services



 Dental practice has a crucial role to play in AMS to reduce inappropriate antimicrobial use and AMR in the community.

13 April 2022 Chapter 18 published





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Approaches to overcome issues of antimicrobial resistance



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Review

Non-antibiotic antimicrobial agents to combat biofilm-forming bacteria



Yuxue Cao^{a,b}, Mahdi Naseri^c, Yan He^{b,d,**}, Chun Xu^b, Laurence J. Walsh^b, Zyta M. Ziora^{e,*}

- ^a School of Chemistry and Molecular Biosciences, The University of Queensland, QLD 4072, Australia
- ^b School of Dentistry, The University of Queensland, QLD 4006, Australia
- ^c Bioresource Processing Research Institute of Australia (BioPRIA), Department of Chemical Engineering, Monash University, VIC 3800, Australia
- d Department of Oral and Maxillofacial Surgery, Massachusetts General Hospital and Harvard School of Dental Medicine, Boston, MA 02114, USA
- e Institute for Molecular Bioscience, The University of Queensland, QLD 4072, Australia

 Table 1

 Anti-biofilm activities of silver and zinc oxide nanoparticles.

Agent	Bacteria	Anti-biofilm effect
Ag NP-based coating	E. coli	A layer of Ag NPs deposited on glass slides inhibited initial stages of biofilm formation [28]
Ag NPs (size 7-20 nm), colloid	S. aureus	Ag NPs (50 µg/mL) completely killed the bacteria in a 48h biofilm. [29]
Ag NPs (size 20 nm), colloid	E. faecalis	Ag NPs (30 µg/mL) gave a similar anti-biofilm effect as 2% chlorhexidine gluconate when tested against a bacterial biofilm growing on dentine of the root canal walls [30]
Curcumin with Ag NP (size 30 nm), colloid	P. aeruginosa, S. aureus	Nanoparticles (100 µg/mL) disrupted established bacterial biofilms [31]
AgNO ₃ solution	P. aeruginosa, E. coli	AgNO ₃ solution inhibited the growth of P. aeruginosa and E. coli biofilms (MIC of 62.5 μM and 125 μM, respectively) [32]
Ag NPs (35 nm), colloid	Methicillin-resistant coagulase-negative Staphylococci	Ag NPs (55 μ g/mL) inhibited biofilm formation by 91% [33]
Ag NPs (30 nm), colloid	P. aeruginosa	AgNPs (18 µg/mL) completely prevented the biofilm development [34]
ZnO NPs (15 nm), colloid	S. pneumoniae	ZnO NPs (12 µg/mL) decreased biofilm formation by 50% [35].
ZnO NPs (50 nm), colloid	B. subtilis	ZnO NPs (5–10 ppm) inhibited the growth, protein expression and biofilm formation of B. subtilis [36]
ZnO NPs (20-50 nm in width and 20-100 nm in length) coated onto titanium used for a dental implant	Human saliva biofilm	ZnO NPs successfully inhibited the formation of biofilm for 96 h [37]
ZnO NPs (size 65 nm), colloid	P. aeruginosa	ZnO NPs (1 mmol/L) inhibited biofilm formation by 26–100%, elastase production (by 23–100%) and pyocyanin production (by 50–95%) in six clinical sub-strains of <i>P. aeruginosa</i> [38]
TiO ₂ NPs (size 14 nm), colloid	S. mitis	TiO ₂ NPs (100 μ g/ml) killed 40–80% of biofilm bacteria when used as a topical oral hygiene agent (IC50 was 77 μ g/ml. for planktonic bacteria) [39]
TiO ₂ , colloid used to prevent oral diseases	S. mutans	TiO ₂ (0.1 mg/mL) eliminated an S. mutans biofilm in 40 minutes under visible light [40]
TiO2 NP-coated carbon film on medical implants	S. aureus	The coating inhibited biofilm formation [41]
TiO ₂ NP coated titanium implants	Oral multi-species	The coating inhibited 99% of the oral biofilm growth after 16.5 h, compared with the commercially pure titanium [42]
TiO ₂ NPs (size 40–100 nm), colloid	Enterobacter spp.	TiO_2 NPs at 700 μ g/mL caused membrane damage to the outer layer of bacteria in the biofilm. Treatment at 1000 μ g/mL dispersed the biofilm into small clumps [43]

Bacteria listed in this table include Escherichia coli; Enterococcus faecalis; Pseudomonas aeruginosa; Staphylococcus aureus; Methicillin-resistant Staphylococcus aureus (MRSA); Acinetobacter baumannii; Bacillus subtilis; Streptococcus pneumoniae; Streptococcus mitis; and Streptococcus mutans.





Revieu

Novel Approaches to Detect and Treat Biofilms within the Root Canals of Teeth: A Review

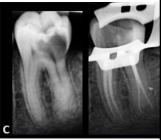
Laurence J. Walsh®

Faculty of Health and Behavioural Sciences, The University of Queensland School of Dentistry, UQ Oral Health Centre, 288 Herston Road, Herston, QLD 4006, Australia; l.walsh@uq.edu.au

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Abstract: Biofilms located within the root canals of teeth are a unique and pressing concern in dentistry and in medical microbiology. These multispecies biofilms, which include fungi as well as bacteria, form in a protected site with low shear stress and low oxygen tension. Systemic antibiotics are of limited value because of the lack of blood flow of the site, and issues with innate and acquired resistance. Physical disruption using hand or rotary powered instruments does not reach all locations in the root canal system where biofilms are present. Alternative strategies including agitated irrigation fluids, continuous chelation, materials with highly alkaline pH, and antimicrobial nanoparticles are being explored to meet the challenge. Detection and quantification of biofilms using fluorescence-based optical methods could provide an indication of successful biofilm removal and an endpoint for physical and chemical treatments.





Broad spectrum antibacterial and antifungal actions, no resistance

Australian Dental Journal Supplement 2007;52:(1 Suppl):S64-S82



The use of <u>calcium hydroxide</u>, antibiotics and biocides as antimicrobial medicaments in endodontics

B Athanassiadis,* PV Abbott,* LJ Walsh†

Abstract

Bacteria have been implicated in the pathogenesis and progression of pulp and periapical diseases. The primary aim of endodontic treatment is to remove as many bacteria as possible from the root canal system and then to create an environment in which any remaining organisms cannot survive. This can only be achieved through the use of a combination of aseptic treatment techniques, chemomechanical preparation of the root canal, antimicrobial irrigating solutions and intracanal medicaments. The choice of which intracanal medicament to use is dependent on having an accurate diagnosis of the condition being treated, as well as a thorough knowledge of the type of organisms likely to be involved and their mechanisms of growth and survival. Since the

development of apical periodontitis associated with root-filled teeth, although studies have shown that the microflora differs in these teeth from that present when there has been pulp necrosis with infection.^{5,6}

Bacteria can exist within the root canal itself, or within other related regions such as the dentinal tubules, accessory canals, canal ramifications, apical deltas, fins, and transverse anastomoses. Apart from the canal itself, all of these other areas are inaccessible to mechanical instrumentation procedures and to the irrigating solutions used during endodontic treatment.

In order to predictably eliminate as many bacteria as possible from the entire root canal system, a combination of mechanical instrumentation and



Better dissolution of Calcium Hydroxide Higher ionisation and pH achieved (Calmix recorded > 14)

High pH> high antimicrobial potential: effective against E.faecalis and C.albicans

Greater diffusion of hydroxyl ions Stimulates hard tissue formation

Contains Ziconium Dioxide Calmix is more radiopaque

Water free and no methyl cellulose will not dry out

Ergonomic syringes, capillary tips and microtips easy to use no manual mixing

