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Abstract

Usually dentists in Australia give patients oral antibiotics after dentoalveolar surgery as a prophylaxis against wound infection. When this practice is compared to the principle of antibiotic prophylaxis in major surgery it is found to be at variance in a number of ways. In major surgery, the risk of infection should be high, and the consequences of infection severe or catastrophic, before antibiotic prophylaxis is ordered. If it is provided then a high dose of an appropriate spectrum antibiotic must be present in the blood prior to the first incision. Other factors which need to be considered are the degree of tissue trauma, the extent of host compromise, other medical comorbidities and length of hospitalization. Standardized protocols of administration have been determined and evaluated for most major surgical procedures. Dentoalveolar surgery is undoubtedly a skilled and technically challenging procedure. However, in contrast to major surgical procedures, it has a less than five per cent infection rate and rarely has severe adverse consequences. Dentoalveolar surgery should be of short duration with minimal tissue damage and performed in the dental chair under local anaesthesia. Controlled studies for both mandibular third molar surgery and placement of dental implants show little or no evidence of benefit from antibiotic prophylaxis and there is an adverse risk from the antibiotic. This review concludes that there is no case for antibiotic prophylaxis for most dentoalveolar surgery in fit patients. In the few cases where it can be considered, a single high preoperative dose should be given.

Key words: Antibiotic prophylaxis, dentoalveolar surgery, infection.

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# INTRODUCTION

Antibiotic prophylaxis for surgery is the prescription of antibiotics to prevent the development of infection at a surgical site.<sup>1</sup> It is different to the prescription of antibiotics to prevent infection occurring at a distant site, such as the heart<sup>2</sup> or around implanted foreign bodies.<sup>3</sup> It is also different to the therapeutic use of antibiotics to treat established bacterial infections.<sup>4</sup> It requires a high rate of post-operative bacterial infection at the wound site; evidence that appropriate use of

S54

antibiotics will reduce the incidence of wound infection: and that there is a lower risk of adverse reactions to the antibiotics.

In dentoalveolar surgery, particularly the removal of antibiotics third molars, are prescribed prophylactically.5,6 In an Australian study of the prescribing habits of general dental practitioners, antibiotics were prescribed prophylactically for the removal of 19 per cent of asymptomatic partially erupted third molars and for 75 per cent of third molars with recurrent pericoronitis. Most (78-90 per cent) prescribed a five day course of amoxycillin, commenced post-operatively, with a negligible use of concurrent local measures. Only 22 per cent knew the correct incidence of allergy for penicillin with most under estimating the incidence of adverse events.<sup>7</sup>

Recently the use of antibiotic prophylaxis for third molars has become controversial with reviews based on clinical studies,<sup>8,9</sup> rather than opinion,<sup>10</sup> challenging the value of antibiotic prophylaxis.

The use of antibiotics in both medicine and agriculture has been the subject of scrutiny in the last decade. It is widely agreed by health authorities that it is necessary to reduce the total use of antibiotics.<sup>11</sup> This is to conserve antibiotics for use in life-threatening infections, to reduce the development of bacterial resistance and to minimize the chance of serious adverse reactions. The strategies to achieve this involve the careful evaluation of clinical practice by evidencebased analysis, by improved education of prescribers and by community education.<sup>12</sup>

This review analyses the evidence for the use of prophylaxis in dentoalveolar surgery. To achieve this, it examines the principle of antibiotic prophylaxis in surgery in general; the nature and range of dentoalveolar surgery; the nature and incidence of bacterial wound infections and other complications; the evidence for and against prophylaxis decreasing wound infection; the risks of antibiotic prophylaxis; and the important modifiers which need to be considered. From the evidence, some recommendations are made.

# The principles of antibiotic prophylaxis in surgery

The principles of antibiotic prophylaxis in general surgery, including its sub-specialities, are well established.<sup>1,13,14</sup> Most surgical specialities and institutions have well developed prophylaxis guidelines.<sup>15</sup> These relate to the procedure, the type of antibiotic and the dosage regimen to be used. With the procedure, the risk of infection needs to be significant,

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for example in bowel resection where, in the absence of proper bowel preparation and antibiotic prophylaxis, the risk of infection is high and potentially fatal. If the risk of infection is low but the consequences are serious then antibiotic prophylaxis is also indicated. An example is orthopaedic hip replacement, where the incidence of post-operative infection is low of the order of 0.39 per cent.<sup>16</sup> However, if a hip replacement becomes infected, the consequences are devastating. Of those hips that become infected, four per cent will need amputation at the level of the hip and the mortality rate is reported as high as five per cent.<sup>17</sup> The individual patient having the procedure needs to be carefully considered. Increasing age, medical comorbidities, immunosuppression and the possible increased length of the procedure and length of hospitalization will also increase the risk of wound infection.

The antibiotic to be chosen needs to have the narrowest spectrum to cover the most likely pathogens involved in wound infection. The patient's history of adverse reactions and hypersensitivity to the chosen antibiotic needs to be known.<sup>15</sup>

The administration of prophylactic antibiotics needs to have been completed before the commencement of the procedure. A high level of the antibiotic needs to be in the patient's bloodstream at the time of the first incision. Planning is required if oral administration is used as it should be given one hour prior to the procedure. In general surgery the intravenous route is most commonly used and the penicillins and cephalosporins can be given as a push dose at induction. Some antibiotics require a longer infusion, for example metronidazole which requires 15 minutes per gram and vancomycin which requires 100 minutes per gram. This requires pre-operative planning.<sup>15</sup>

A single dose prior to commencement of the procedure is all that is required. If a procedure is longer or delayed after the induction dose of the antibiotic has been given or there is greater tissue damage than expected, a second dose can be given. This usually follows the half the normal time dosage regimen. For example, penicillin will be repeated at three hours, not the usual six hours and four hours for a cephalosporin which is usually given eight hourly.<sup>15</sup>

# Dentoalveolar surgery

Dentoalveolar surgery is a term that covers the full range of procedures performed by general dentists and most dental specialists including periodontists. Dentoalveolar procedures comprise approximately 60 per cent of procedures performed by oral and maxillofacial surgeons.<sup>18</sup> It ranges from soft tissue surgery, such as biopsy and removal of hyperplasias and extractions ranging from the removal of mobile periodontally involved teeth to the removal of deeply bone-impacted teeth and the placement of implants. Successful completion requires good judgement, considerable dexterity and high technical skills and training. However, its procedural magnitude is not comparable to major maxillofacial surgery or the examples of bowel resection or orthopaedic hip replacement surgery discussed in the preceding section of this paper. Dentoalveolar surgery should not involve extensive tissue damage and rarely takes a long operative time. Individual, difficult bone-impacted mandibular third molars can usually be removed in less than 30 minutes if the operator has the appropriate skill and instrumentation.

The most commonly studied aspect of dentoalveolar surgery relates to the removal of bone-impacted third molars by oral and maxillofacial surgeons. To a lesser extent dental implant placement by oral and maxillofacial surgeons and periodontists has been studied. There are a few studies on the performance of these procedures by general practitioners. Generally, it could be expected that general practitioners would have longer operating times and more tissue damage as they perform these procedures less frequently. Removal of impacted third molars and placement of dental implants are the procedures at most risk from infection or serious adverse consequences. The remainder of this paper will concentrate on these procedures.

# The nature and incidence of bacterial wound infection in dentoalveolar surgery – third molars

The key issue is the accurate diagnosis of the nature of complications following dentoalveolar surgery. The most common problem is confusing the acute inflammation of traumatic origin with wound infection. The normal process of removing an impacted third molar is incision, muco-periosteal flap elevation, bone removal, tooth sectioning and then the trauma of retraction and elevation of the tooth. This will always result in post-traumatic inflammation, the exception being in an immunosuppressed patient. The patient should be expected to have some degree of pain, swelling, heat, redness and limitation of jaw opening following dentoalveolar surgery. This is normal and is not diagnostic of infection although this error has been made in previous Australian dental guidelines.<sup>19</sup>

The other area of misdiagnosis relates to alveolar osteitis or dry socket. This is a problem of wound healing and is not a bacterial infection. Clinical and laboratory studies have shown that increased fibrinolytic activity occurs with the early phase healthy socket. This condition has recently been reviewed critically and will not be further discussed in this paper.<sup>20</sup>

The definition of third molar wound infection should include the following: the presence of cellulitis, which is a hot tense swelling; the presence of fluctuation; purulent discharge from the extraction site for more than 72 hours after surgery; pain and swelling that either worsens or fails to improve 48 hours after surgery; and persistent hyperpyrexia, more that 39°C at 48 hours or more after surgery.

This is a broad, all-inclusive classification of bacterial wound infections.<sup>6,21</sup> Laboratory markers have also been used to identify evidence of infection.<sup>22</sup>

Australian Dental Journal Medications Supplement 2005;50:4.

Table 1. Infection rates for mandibular third molar removal

Investigators	Infection Rate
Hochwald <i>et al</i> <sup>23</sup>	1.0%
Sisk <i>et al</i> <sup>24</sup>	1.2%
Chiapasco <i>et al</i> <sup>25</sup>	1.5%
Piecuch <i>et al</i> <sup>6</sup>	3.4%
Rud <sup>26</sup>	4.0%
Goldberg et al <sup>27</sup>	4.2%
Curran <i>et al</i> <sup>28</sup>	8.2%
Mitchell <sup>29</sup>	27.0%
Nordenram <i>et al</i> <sup>30</sup>	12.6%
Mitchel and Morris <sup>31</sup>	11.0%

Using these criteria, in whole or in part, the incidence of reported wound infection, whether using antibiotic prophylaxis or not, is reported in the range of 1-27 per cent (Table 1).<sup>23-31</sup> However, the reported incidence is around 3-5 per cent.

# Antibiotic prophylaxis - third molars

A review of some recent well designed studies is presented in Table  $2.^{\scriptscriptstyle 6,32\text{-}34}$ 

There are very few well designed studies investigating antibiotic prophylaxis as compared to the number of third molar removals performed worldwide.18,35 The paper by Piecuch et al.<sup>6</sup> could easily be dismissed. It is retrospective with patients not randomly assigned by the surgeon, and the 'no antibiotic group' is very small. However, its sheer size coupled with the scientific reputation of the senior author means it must be considered. The finding that placing antibiotic cones in the socket give the best results is not relevant to prophylactic antibiotics and was a surprise finding to the authors. The main finding was that when the types of surgery were further stratified there was no benefit for maxillary third molars, erupted or soft tissue impacted mandibular molars but a significant benefit for deep bone impactions. This finding was not supported by the prospective randomized studies,<sup>32,33</sup> or the study using post-operative antibiotics.<sup>34</sup>

A Cochrane Review of the use of antibiotic prophylaxis in the removal of third molars is currently in progress but has not been published yet.<sup>36</sup> There are no

prospective randomized Australian studies on antibiotic prophylaxis for the removal of third molars. The authors' institution ceased using antibiotic prophylaxis for routine third molar removal approximately a decade ago. There has been no change in the infection rate with or without prophylactic antibiotics. A large specialist oral and maxillofacial surgery practice in Victoria, Australia, has made a similar change with a similar outcome. Likewise a large multi-surgeon private practice in South Australia has no reported difference in postoperative infection rates where one of the surgeons uses prophylactic antibiotics for all cases. The other surgeons only use antibiotics therapeutically when there is evidence of current infection.

### **Dental implant considerations**

Dental implants are an interesting subset in dentoalveolar surgery. They involve the elective placement of a large foreign body through a microbiologically infested field into the bone. If a dental implant becomes bacterially infected the chance of failure is high. For this reason antibiotic prophylaxis is universally applied. As with dentoalveolar surgery, much of the current practice is not based on scientific evidence but on anecdotal statements of individual practitioners. There are many reasons that implants fail including poor surgical technique, factors leading to early loading, lack of bone quality and patient factors including habits such as tobacco smoking. As stated in the section on the principles of prophylaxis, the reason to use prophylactic antibiotics is if there is a demonstrated high rate of postoperative infection or the results of a post-operative infection are severe deleterious effects. Neither of these conditions apply with dental implants. If dental implants become infected the worst that can happen is the implant is lost. The only deleterious effect is to the surgeon's ego and the patient's physical, psychological and financial status and all of these are modest, not catastrophic. Many practitioners are failing to follow sound surgical principles and expecting antibiotics to overcome these deficiencies. An example of unsound surgical principles is when a practitioner removes an infected tooth and then immediately places an implant. It again must be stated that antibiotics are not a cover for inappropriate techniques.

Investigator	Type of study	Groups	Size	Findings
Piecuch <i>et al</i> <sup>6</sup>	<ul><li> Retrospective</li><li> Non random</li><li> Surgeon assignment</li></ul>	<ul><li>No antibiotic</li><li>Pre-op systemic</li><li>Intrasocket antibiotics</li></ul>	6713 extractions	<ul> <li>Significant difference between no antibiotic and full bone impactions (p&lt;0.002)</li> <li>Significant difference for intrasocket antibiotics (p&lt;0.001)</li> </ul>
Happonen <i>et al</i> <sup>32</sup>	<ul><li> Prospective</li><li> Randomized</li><li> Placebo</li></ul>	<ul><li> Pre-op Penicillin</li><li> Pre-op Tinidazole</li><li> Placebo</li></ul>	136 extractions	No significant difference
Sekhar <sup>33</sup>	<ul> <li>Prospective</li> <li>Randomized</li> <li>Double blind</li> <li>Placebo controlled</li> </ul>	<ul><li> Pre-op Metronidazole</li><li> Post-op Metronidazole</li><li> Placebo</li></ul>	151 patients	No significant difference
Poeschl <i>et al</i> <sup>34</sup>	<ul><li> Prospective</li><li> Randomized</li></ul>	<ul><li>Post-op Amoxycillin/ Clavulanic acid</li><li>Clindamycin</li><li>No antibiotic</li></ul>	288 patients	No significant difference

Table 2. Clinical studies of antibiotic prophylaxis for third molars

Of the several causes of dental implant failure one may be due to bacterial contamination at implant insertion.<sup>37</sup> This has lead to the empirical use of antibiotic prophylaxis. The controlled clinical trials showed conflicting results.<sup>38:40</sup>

The Cochrane Review on antibiotics to prevent complications following dental implant treatment found no randomized controlled studies which met its criteria. It concluded that there is no appropriate systematic evidence to recommend or discourage the use of antibiotic prophylaxis to prevent complication and failure of dental implants.<sup>41</sup>

# Antibiotic regimens for mandibular third molar removal and dental implants

Most antibiotic regimens used in dentoalveolar surgery fail to meet the key criteria of surgical prophylaxis, namely that the antibiotics must be in the blood stream prior to the commencement of the procedure.<sup>13,14</sup> They also tend to involve a relatively low dose over a long period.<sup>7</sup>

The early antibiotic prophylactic regimens for dental implants did start with a pre-treatment dose of 2g of penicillin, orally one hour prior to the procedure but were continued for up to 10 days.<sup>42</sup> Subsequently, they have been progressively shortened to one to three day regimens.<sup>43</sup> A recent Swedish study did not use any antibiotic prophylaxis with no difference in infection rate as compared to the short antibiotic regimens.<sup>39</sup>

### Adverse reactions to antibiotics

All drugs carry risks, although in the past, for antibiotics, this has not been highly considered by medical and dental practitioners. The risks associated with antibiotics are gastro-intestinal tract upset, colonization of resistant or fungal strains, cross reactions with other drugs and allergies, including anaphylaxis and death. Mild reactions, including urticaria, occur in 0.7-10 per cent of penicillin courses, with a usual range of 1-3 per cent.<sup>44</sup> This rate has and will increase over time as exposure increases. Anaphylactic reactions occur in 0.04-0.011 per cent of patients receiving penicillin for prophylaxis and 10 per cent of cases of anaphylaxis are fatal.<sup>45</sup> The most common antibiotic recommended for prophylaxis will cause harm for some patients.

#### Other considerations - host compromise

The material presented in this paper thus far relates to medically fit and well patients. In patients with a significant reduction in host defences the risk of infection increases. This has been quantified for patients with HIV/AIDS for dentoalveolar surgery where there is a 10-fold increase in the infection rate.<sup>46</sup> Similarly, patients on immunosuppressants for organ tissue transplants or malignancy will have an increased infection rate. Patients with poorly controlled diabetes mellitus may have increased problems. This may be due to many factors including reduced neutrophil

Australian Dental Journal Medications Supplement 2005;50:4.

chemotaxis and high levels of circulating glucose. The need for prophylaxis antibiotics in this group has not been quantified in any controlled studies. Well controlled diet or non-insulin dependent diabetes patients are probably no different to fit patients.

There is another subgroup of patients where the prime problem is reduced bone healing capacity. This includes irradiated bone where there is a risk of osteoradionecrosis. This is most commonly triggered by extraction. This may be prophylactically or therapeutically treated with hyperbaric oxygen.47 Patients with bone diseases, treated with bisphosphonates, have recently been shown to be prone to a small risk of developing osteonecrosis.48 This is initiated by extraction which should be avoided if possible. To date there is no simple effective treatment for patients with non-healthy wounds who are taking bisphosphonates.<sup>48,49</sup> On an anecdotal basis, extractions in these patients are performed with the minimum amount of trauma and with an antibiotic prophylaxis. There are no controlled studies supporting or discouraging this practice.

In patients with depressed host responses or abnormal bone healing, the dental treatment plan needs to be modified. Treatment to get the patient dentally fit would involve extractions. Conservation with endodontics should be considered. Asymptomatic impacted teeth are best left alone and dental implants are best avoided.

#### Other considerations – community issues

Currently, the community remains convinced of the power of antibiotics. Patients will demand antibiotics and feel inappropriately treated if these are not offered or prescribed. They may even be supported in their demand by medical and dental practitioners who have not kept up-to-date with current trends. However, acceding to a patient's request for antibiotics without medical indication is not a justifiable action. Currently, there are extensive public and professional educational programs in progress and they need to be continued.<sup>12,50</sup>

Legal issues increasingly intrude into health practice. However, our research has not found an Australian judgement dealing with the use or failure to use prophylactic antibiotics in dentistry, although this has been an issue in a matter which was settled out of court.<sup>51</sup> The present test for negligence in Australia with respect to diagnosis or treatment is whether the dental practitioner acted in a manner that was widely accepted in Australia by other members of the dental profession as competent professional practice.52 The practice must be rational but it does not have to be universally accepted - in fact, differing opinions can each be widely accepted. When it comes to providing advice, the dental practitioner needs to give the patient the information that a reasonable person in the patient's position would attach significance to as well as any information that the practitioner is, or reasonably should be, aware that the particular patient would be likely to attach significance to.53

Since in some circumstances the majority of dental practitioners frequently prescribe prophylactic antibiotics, one could argue that this is 'competent professional practice'. However, the law does have a clear understanding of risk versus benefit for the patient as it is also skilled in assessing and balancing expert evidence-based arguments.

The practitioner will have exhibited competent professional practice when he/she recognizes the circumstances where prophylactic antibiotics may be indicated and provides the option of prophylactic antibiotics where they are not therapeutically indicated. The practitioner who bases a careful review and application of current evidence-based medical treatment should not be concerned about legal issues.

### Other considerations - local measures

A key issue in preparation for surgery is local measures. In all general surgical procedures the operative site skin or mucosa is prepared with antibacterial agents. In bowel surgery the bowel is preoperatively prepared. In dentoalveolar surgery performed under general anaesthesia or sedation, many oral and maxillofacial surgeons will surgically prepare the skin but not the intra-oral wound site. There have been a small number of controlled studies on pre- and post-operative rinsing of the mouth with antiseptic solutions. Chlorhexidine gluconate 0.12 per cent mouth rinse has been reported to reduce the incidence of dry socket but not wound infection from third molar surgery. It reduces the bacterial load by pre- and postoperative rinsing.<sup>54</sup> However, a similar study comparing normal saline, chloramine T, povidone iodine or sodium bicarbonate as a rinsing agent showed no statistically significant differences.<sup>55</sup> Attempts at using a chlorhexidene mouth rinse whilst waiting for the local anaesthetic to work in the authors' institution extraction clinic were discontinued on the grounds of patient objection to the taste. This is an area of further study as it is simple, rationally based, and has no adverse sequelae.

### Summary

In principle antibiotic prophylaxis is only indicated if the risk of infection and/or its consequences clearly outweigh the risk of adverse reactions to the antibiotic.

In principle and practice antibiotic prophylaxis must be completed with an appropriate narrow spectrum antibiotic in high doses prior to the commencement of the procedure. There is a known adverse risk from antibiotics.

Most dentoalveolar surgery and the most commonly used antibiotic regimes in dental practice fail one or both of the above principles.

There are no randomized controlled clinical studies of antibiotic prophylaxis for dentoalveolar surgery, including third molar removal and dental implantation, which meet the strict criteria of the Cochrane Research Group. Other less rigorous studies show conflicting and commonly equivocal results.

# Table 3. Recommendations – Indications for antibiotic prophylaxis

For most dentoalveolar procedures in fit, non-host compromised patients antibiotic prophylaxis is NOT required or recommended Consider antibiotic prophylaxis for:

- difficult bone impactions with previous history of recurrent infections\*
- dental implants

- patients whose immune system is significantly compromised Balance the low risk of wound infection against the adverse risk from the antibiotic

\*Patients with evidence of active infection in the area of planned surgery do not have a prophylactic indication but may have a therapeutic indication.

#### Table 4. Antibiotic regimens

2g Penicillin oral, one hour prior to the procedure 1g Penicillin I/V, immediately prior to the commencement of the procedure 1g Amoxycillin I/V, just before commencement of the procedure If hypersensitive to Penicillin Clindamycin 600mg oral, 1 hour prior to the procedure Clindamycin 600mg I/V, just prior to the procedure Local Measures Consider disinfection of the wound site with a 1% chlorhexidine rinse pre-operatively

Antibiotic prophylaxis for dentoalveolar surgery thus should only be considered in a limited number of circumstances. These relate to a few extensive dentoalveolar procedures in patients with significant host compromise. These findings are presented in Table 3 and Table 4.

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