

## IN BRIEF

- The use and benefits of antimicrobial prophylaxis in third molar surgery is controversial and there are no definite recommendations on the role of prophylactic antibiotics.
- Medically compromised patients are a group which may benefit from antimicrobial use.
- Antibiotic administration is not without risks including anaphylaxis, development of resistant bacteria and unjustified medical costs.

# Antibiotic prophylaxis and third molar surgery

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The issue of prophylactic antibiotic therapy in third molar surgery is highly controversial. The current evidence questions the benefits of routine prophylactic antibiotic therapy which does not appear to overcome the risk of undesirable outcomes after third molar removal. In our opinion there is no justification for routine antibiotic prophylaxis for third molar surgery.

## INTRODUCTION

Third molar surgery is one of the most commonly performed procedures in oral and maxillofacial units and in general practice.<sup>1</sup> Prophylactic antibiotic therapy is defined as 'the administration of any antimicrobial agent that prevents the development of disease';<sup>2</sup> the antibiotic must be present in the systemic circulation at a high level at the time of surgery and is usually given as one dose. Peterson<sup>3</sup> set the following five principles (Table 1) of antibiotic prophylaxis:

- 1) The surgical procedure should have a significant risk of infection.
- 2) The correct antibiotic for the surgical procedure should be selected.
- 3) The antibiotic level must be high.
- 4) The timing of the antibiotic administration must be correct.
- 5) The shortest antibiotic exposure must be employed.

For best possible practice and patient care, all of the above criteria must be fulfilled. The use and benefits of antimicrobial prophylaxis in third molar surgery is controversial and there are still no definite recommendations on the role of prophylactic antibiotics.

Controversies surround the role of antibiotics in relation to removal of soft tissue, full or partial bony impacted third molar, optimal timing, dose, duration and route of administration. Here, we aim to present the current evidence and critically review the literature regarding the routine use of antibiotic therapy in the removal of third molars.

## Complications after third molar surgery

Pain, swelling, and trismus are common, non-infection related complications of third molar surgery. Other complications may be associated with infection and include exposed necrotic bone, ulceration, soft tissue swelling and erythema, intraoral/extraoral sinus, localised / generalised lymphadenopathy (Table 2). Post-operative infection usually presents with dry socket and less commonly may manifest with severe fascial space involvement.<sup>4</sup> Factors which appear to be associated with post-operative infection include full or partial bony impaction, rather than the routine extraction of teeth,<sup>5</sup> and the presence of preoperative infection.<sup>6</sup> The reported incidence of postoperative infection varies between 1–12.60%<sup>7–18</sup> (Table 3) There was also variation in the reported rate of alveolar osteitis ranging from 1% to 6.3%.<sup>16,19–20</sup>

## Post-operative complications and prophylactic antibiotics

There is a considerable volume of evidence that advocates antibiotics for the prevention of infection following third molar surgery.<sup>13,21–26</sup> Other articles do not specifically comment on infection rates but support the use of antibiotics on the basis

of reduced postoperative complications.<sup>27</sup> Improvement from trismus, reduction of pain and swelling with improved healing are outcomes that have been used to assess the success of antibiotics.<sup>28–30</sup> Many workers recommend the use of prophylactic antibiotics for extractions, including third molar surgery, only when active infection is present at the time of surgery.<sup>31,32</sup> But Barclay<sup>33</sup> compared the use of metronidazole versus a placebo involving non-acute pericoronitis patients in a randomised controlled study.

Development of pain and alveolar osteitis postoperatively were examined. No significant difference between the two groups was found. In a randomised, double-blind, placebo controlled clinical trial examining the prophylactic use of penicillin and tinidazole in third molar surgery Happonen *et al.*<sup>14</sup> reported no advantages over the placebo after third molar surgery. Kazino *et al.*<sup>34</sup> compared the administration of metronidazole with a placebo and a homeopathic remedy. Parameters such as pain, swelling, trismus and wound healing were evaluated. Between these groups there was no significant difference up to the eighth day postoperatively. After the eighth day the patients receiving metronidazole demonstrated better wound healing and less pain and swelling compared with the other groups.

Many authors do not support the indiscriminate administration of antibiotics prophylactically since the incidence of postoperative infections is too low to justify such action.<sup>11,20</sup> Goldberg *et al.*<sup>10</sup> in a series of 500 patients reported that antibiotic prophylaxis was not useful in preventing postoperative infection. Curran *et*

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**Table 1 Criteria for antibiotic prophylaxis**

- A strong link between surgical procedure and infection
- The appropriate antibiotic for the surgical procedure must be selected
- The antibiotic level must be high at the time of surgery
- The shortest effective antibiotic exposure must be employed

**Table 2 Complications following third molar surgery that may be associated with infection**

- Exposed necrotic bone
- Wound breakdown
- Soft tissue swelling and erythema
- Trismus
- Pain
- Intraoral and/or extraoral sinus
- Localised/generalised lymphadenopathy

*al.*<sup>9</sup> also concluded that antibiotic prophylaxis was not useful for the prevention of postoperative infection. Mitchell<sup>13</sup> also reported no significant difference between the incidence of infection in the study and placebo groups, although methodological discrepancies made the data difficult to interpret. Some laboratory markers of infection have been used to evaluate antibiotic prophylaxis for impacted third molars. Recently, Bulut *et al.*<sup>35</sup> measured the levels of C-reactive protein and alpha-1 antitrypsin pre-operatively and post-operatively in patients who received either prophylactic antibiotics or placebos. They concluded that antibiotic prophylaxis is not always indicated in patients who undergo surgery for the removal of third molars. Capuzzi *et al.*<sup>36</sup> compared postoperative amoxicillin for four days with no antibiotics in 146 patients and found no statistical difference when postoperative swelling and pain were evaluated. Monaco *et al.*<sup>37</sup> examined the incidence of dry socket and antibiotics; they reported no significant difference between the group receiving amoxicillin and the group with no administration of antibiotics. Prophylactic antibiotics given beyond the perioperative period in other forms of 'clean-contaminated' surgery provided no additional benefit.<sup>34</sup>

In the most recent prospective, double blind, randomised, placebo-controlled clinical study Sekhar *et al.*<sup>38</sup> reported results from three patient groups. One hundred and fifty one patients who were to have lower wisdom teeth removed under local anaesthesia were included in that study. One group was given 1 g oral metronidazole one hour preoperatively; the second group was given 400 mg of oral metronidazole eight-hourly for five days

postoperatively and the third group was the placebo. Parameters such as pain, swelling, trismus between days 1 and 6 postoperatively, and state of the wound were evaluated. They reported no significant differences in the outcome between the three groups and concluded that antimicrobial prophylaxis did not seem to reduce morbidity after removal of third molars. The results in a study by Yoshii *et al.*<sup>39</sup> suggested that 1-day therapy with lenampicillin may at least be recommended as a prophylaxis for mandibular third molar surgery in medically healthy patients. However this study was unable to detect post-operative complications in patients with no antibiotic prophylaxis since such group was not included in the comparison.

Poeschl *et al.*<sup>40</sup> designed a prospective study involving three groups of patients requiring the removal of third molars. The patients in the first group received antibiotic treatment with amoxicillin/clavulanic acid as an oral medication carried out for five days postoperatively. In the second group clindamycin was used. In the third group, the patients received no antibiotic treatment. They concluded that the specific postoperative oral prophylactic antibiotic treatment after the removal of lower third molars did not contribute to a better wound healing, less pain, or increased mouth opening and could not prevent the cases of inflammatory problems after surgery, and therefore was not recommended for routine use.

**Parenteral antibiotics, support for their use and timing**

Parenteral therapy is indicated if the oral route is impractical and particularly for the urgent treatment of severe infections (fig 1). Considering the value of preoperative parenteral antibiotics, a body of evidence favours their use<sup>21-23,41</sup> in third molar surgery. Extensive studies of third molar removal in patients with fully or partial bony infection of third molars favour the use of prophylactic parenteral antibiotics, since lower postoperative infection rates have been reported.<sup>5</sup> Piecuch *et al.*<sup>5</sup> in their study involving bony impacted third molars the use of preoperative parenteral antibiotics resulted in a significantly reduced post-operative infection rate. However, no advantage has been shown in soft tissue impaction alone.<sup>37</sup>

The timing of parenteral antibiotic prophylactic administration appears to be important.<sup>17,37</sup> When considering the analogy of surgical removal of third molars to 'clean-contaminated surgery' it is reasonable to assume that the optimal time for the administration of antibiotics is up to two hours preoperatively.<sup>36,42</sup>

Thomas *et al.*<sup>43</sup> after an audit of antibiotic prescribing practises suggested that preoperative parenteral antibiotics are unwarranted for routine third molar surgery in medically fit patients. Support however was given to conclusions by others<sup>29</sup> about the use of parenteral and broad spectrum antibiotics in the management of medically compromised patients. In that study, however, the timing of parenteral antibiotic administration was not clear and this may explain their findings.

**Antibiotic choice and dose and parenteral prophylaxis**

Considering infections after the removal of third molars, the organisms most commonly isolated included streptococci, anaerobic gram-positive cocci and anaerobic gram-negative rods. For optimal prophylaxis the antibiotic agent used must have good bone penetrance, be active against the required micro-organisms and should be widely distributed in body fluids. Clindamycin has proven efficacy for treatment of bone / joint infections.<sup>44</sup> Clindamycin is a lincosamide antibiotic with a primarily bacteriostatic action against Gram-positive aerobes and a wide range of anaerobic bacteria. High concentrations may be weakly bacteriocidal against sensitive strains. Following parenteral administration clindamycin is widely distributed in body fluids and tissues including bone. When 600 mg are infused intravenously, peak concentrations of 10 µg ml<sup>-1</sup> are achieved by the end of the infusion.<sup>45</sup>

**Prophylactic antibiotics and systemic complications**

Systemic antibiotic administration is the most common form of antibacterial prophylaxis in clinical practice.<sup>45</sup> Antibiotic administration is not without risks including anaphylaxis, development of resistant bacteria and unjustified medical costs.<sup>37,46</sup> Other undesirable consequences include

**Table 3 Infection rates for mandibular third molars reported in the literature**

Investigator	Infections (%)
Hochwald <i>et al.</i> <sup>7</sup>	1.0
Rud <sup>8</sup>	4.0
Curran <i>et al.</i> <sup>9</sup>	8.2
Goldberg <i>et al.</i> <sup>10</sup>	4.2
Osborne <i>et al.</i> <sup>11</sup>	3.4
Sisk <i>et al.</i> <sup>12</sup>	1.2
Mitchell <i>et al.</i> <sup>13</sup>	11.0
Happonen <i>et al.</i> <sup>14</sup>	11.8
Loucota <sup>15</sup>	1-5.0
Chiapasco <i>et al.</i> <sup>16</sup>	1.5
Piecuch <i>et al.</i> <sup>17</sup>	3.5
Nordenram <i>et al.</i> <sup>18</sup>	12.6

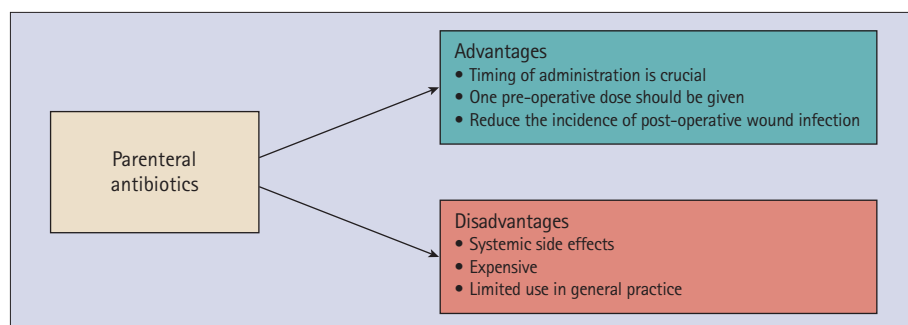


Fig. 1 Parenteral antibiotic prophylaxis

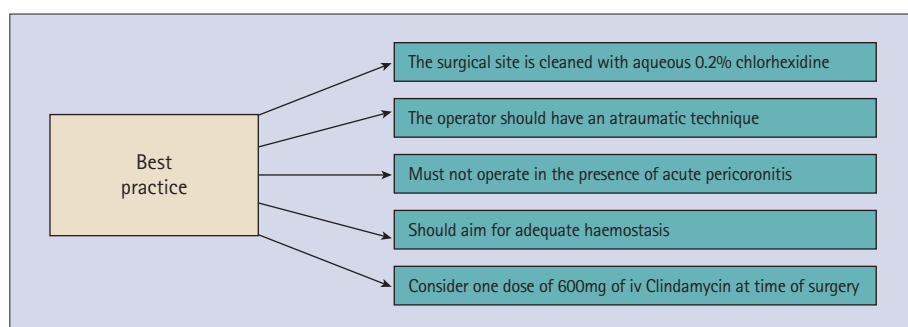


Fig. 2 Practical approach for the prevention of infection following third molar surgery

patients allergic to penicillin, 600 mg of oral clindamycin 1h pre-operatively should be used.

**Practical approach for the prevention of postoperative infection for third molar surgery**

Many reports in the literature have explored the efficacy of antibiotics in reducing post-operative pain, trismus and oedema. The results favour aspects such as an aseptic surgical site and an established technique aiming to minimise trauma.<sup>20</sup> In the oral cavity, patient and operation characteristics may influence the risk of a post-operative infection. Factors that increase the possibility of post-operative infection include age, nutritional status, diabetes, smoking, obesity, coexisting infections elsewhere in the body, colonisation with pathogens and a compromised immune response.<sup>52-54</sup> Operational factors that may contribute to a post-operative infection include poor operative site preparation, duration of operation, foreign body in the surgical site, poor haemostasis, failure to obliterate dead space, extensive tissue trauma.<sup>54</sup> For best practice therefore we suggest that the surgical site is cleaned with aqueous 0.2% chlorhexidine. The operator should have an established technique, must not operate in the presence of acute pericoronitis and aim for minimal trauma and adequate haemostasis (Fig. 2). In the literature rare but serious complications of exodontias, such as a submasseteric abscess following the uneventful extraction of a non-infected maxillary third molar<sup>55</sup> may provide a case for prophylaxis. However we feel that such complications are so rare and may be prevented as suggested by the authors by careful injection of local anaesthetic with aspiration. It is important to emphasise that surgical antibiotic prophylaxis can be an adjunct to and not a substitute for a good surgical technique.

**In our opinion**

There is a plethora of studies that advocate or disapprove of the use of antibiotics in the removal of third molar surgery. Many have been criticised for methodological shortcomings, fuelling an ongoing controversy in antimicrobial use. Most of the studies focus on a potential relationship between antibiotics and post-operative complications and avoiding issues such as use of aseptic technique, and surgical procedure to minimise trauma. By evaluating the literature it appears that antibiotics may provide benefits in some instances and little or no benefit in others. Medically compromised patients are a group which may benefit from antimicrobial use. There

the interaction with other medical products and therefore an indirect effect in the management of other medical conditions. Direct toxicity may affect the gastrointestinal tract with nausea, vomiting, diarrhoea and abdominal pain. Haematological complications include neutropenia, thrombocytopenia and haemolysis. Alteration in the normal flora may result in candidiasis and pseudomembranous colitis. Antibiotic administration may result in nephrotoxicity with proteinuria and renal failure. The hepatobiliary tract may be affected with jaundice hepatitis and alteration in the liver function tests. Neuropathy -VIII<sup>TH</sup> nerve dysfunction and peripheral neuropathy may complicate antibiotic administration.

For best patient care the benefits and risks of antibiotic prophylaxis must be considered closely. The final decision regarding the administration of prophylactic antibiotics for an individual patient must depend on:<sup>47</sup> 1) the patient's risk of surgical site infection 2) the severity of complications of surgical site infection 3) the effectiveness of prophylaxis in that operation 4) the consequences of prophylaxis for the patient such as the increased risk of colitis.

**Prophylactic antibiotics and the patient with a history of radiotherapy**

Patients with a history of previous radiotherapy for head and neck cancer are at risk of developing osteoradionecrosis (ORN) following even 'simple' extractions

or biopsies that overlie bone.<sup>48</sup> Although the role of infection in the development of ORN has been brought into question in recent years most publications concerning exodontia following radiotherapy favour their use. The most appropriate antimicrobial regime is controversial and in a recent survey of oral and maxillofacial consultants in this country<sup>49</sup> there was a wide variation in practice. Most supported pre-operative antimicrobial use for the surgical removal of lower posterior teeth and 89% included a post-operative course. A wide range of bacteria may be isolated in the oral cavity and may be involved in infection under suitable conditions. The microbial involvement in the pathogenesis of ORN has not been fully elucidated. Scanning electromicroscopy of the bacterial colonisation in specimens obtained during head and neck resections<sup>50</sup> implicated oral streptococci including *Strep. intermedius*, *Strep. constellatus*, *Strep. oralis*, *Strep. mitis*, *Strep. sanguis*, *Strep. salivarius*. Facultative enteric bacteria including *Enterococcus*, *Escherichia*, and *Klebsiella* were also isolated. Others included *Staphylococcus epidermidis*, *Neisseria species*, *Capnocytophaga*, *Peptostreptococcus species*, *Gemella morbillorum* as well as *Fusobacterium nucleatum*. Taking into account the above a broad spectrum antibiotic should provide adequate prophylaxis in the patient at risk of ORN. Recent recommendations<sup>51</sup> suggested that a single dose of either 3 g oral amoxicillin or in those

appears to be very little clinical gain by the administration of a postoperative oral antibiotic alone. When contemplating the surgical removal of bone-impacted third molars, one dose of parenteral prophylactic antibiotics at induction may be considered. However there is no advantage in patients where bone removal is not required. Taking into account the above finding, there is no justification for the routine use of prophylactic antimicrobials in third molar surgery and therefore it cannot be recommended.

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