

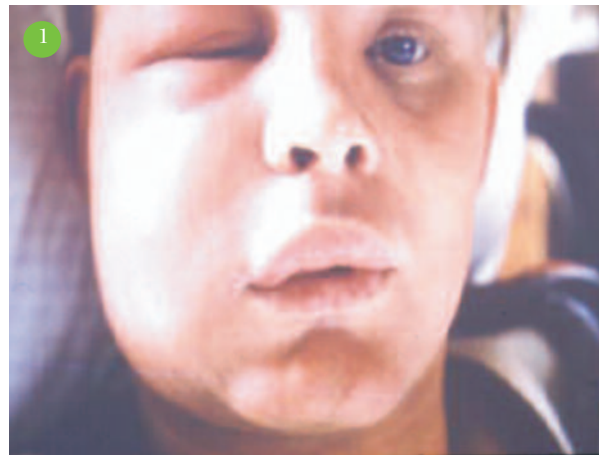
## Antimicrobials and dentistry: a rationale for their use

by Michael V Martin

Antibiotics in general dentistry are grossly overused often with no rationale for their use and little proven benefit for the patient. This paper discusses specific situations where antimicrobials can be used effectively.

**Keywords:** antibiotics, dentistry

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**Fig. 1** A young man with extensive bilateral swelling spreading below the mandible and up to the orbit. This patient requires antibiotic therapy to prevent metastatic spread and to limit the diffuse swelling.

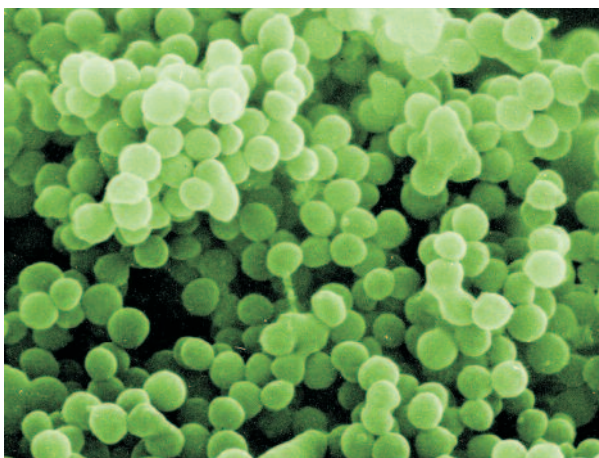
‘...bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA) are not only resistant to all common antibiotics but also to combinations of these agents.’

In 1960, the Editor of *The Lancet* wrote in an introduction to a series on the use of antimicrobials: ‘there are two things to borne in mind when prescribing antibiotics, the microbe and the environment’.<sup>1</sup> The Editor was predicting almost 50 years ago that excessive prescribing of antimicrobials could affect the selection of resistance; his fears have proved correct. The overuse of antimicrobials particularly in medicine, dentistry and agriculture has lead to many agents becoming relatively useless for simple infections due to the emergence of bacterial resistance.<sup>2</sup> What every microbiologist has feared has happened and bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA) are not only resistant to all common antibiotics but also to combinations of these agents.<sup>3</sup> Some people have predicted the end of the ‘antibiotic era’ with predictions of gloom for the future

management of infectious disease. This cataclysm has not quite happened yet, but the situation is so serious that the World Health Organization has designated antibiotic overuse a 'global emergency'.<sup>4</sup>

Antibiotics in general dentistry are grossly overused often with no rationale for their use and little proven benefit for the patient.<sup>5</sup> Surveys of the use of antimicrobials in the UK dentistry have demonstrated clear and consistent overuse.<sup>6</sup> Many dental practitioners prescribe irrationally both prophylactically and therapeutically. This is despite clear and unequivocal guidance based on sound clinical

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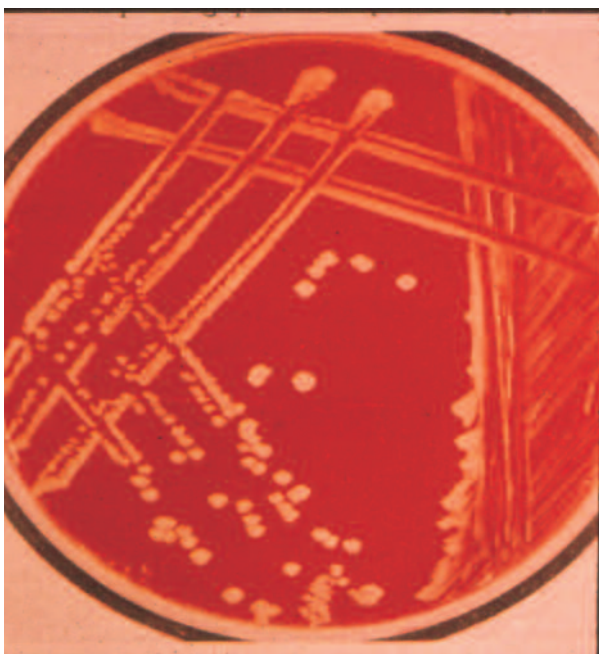


Fig. 2 Methicillin-resistant *Staphylococcus aureus* (MRSA)  $\times 3000$ . Fig. 3 A blood agar plate with haemolytic streptococci.

research.<sup>7</sup> In fact there are very few indications for antimicrobials in dentistry and there should be a decrease in use rather than the observed increase. Much of the pressure to prescribe comes from patient pressure, the fear of medical litigation, or just simply poor clinical decision making.

#### Antimicrobials and the acute dento-alveolar abscess

The most common dental emergency where the use of antimicrobials could be considered is the acute dento-alveolar abscess. This is always preceded by acute or chronic pulpitis where the tooth affected may be tender to percussion and painful. Pulpitis cannot be treated with antimicrobials. The pulp of a tooth is enclosed in a 'closed box' and is becoming necrotic, antimicrobials cannot penetrate or be effective in such a situation; despite this, they are often prescribed without other interventions. Acute or chronic pulpitis can be treated successfully by either endodontic therapy or exodontia, antimicrobials are not required or indicated. When the peri-apical tissues become involved and an abscess is formed the treatment is drainage either by extraction, exodontia or by simple excision; antimicrobials are usually not indicated. If antimicrobials are used, they are an adjunct to the treatment and are used to limit swelling and also prevent metastasis of the infection to such vital organs as the liver, brain or kidney. Antimicrobials will not work, be inhibited or destroyed within an abscess cavity. In an abscess, the low pH will inhibit the adherence of the antimicrobial to the bacteria (pH determines attachment). The proteins present in pus will also attach and block bacterial/antimicrobial attachment sites and microbial enzymes will directly destroy the antibacterial agents. Where antimicrobials are effective is preventing local spread as at the edges of an abscess where there can be effective bacterial/antibiotic interaction. This is evidenced by the presence of an 'antibiotic edge' which forms if there is prolonged use of antimicrobials against large abscesses. Drainage of an abscess and eradication of the cause removes pus and allows the pH to return to normality where antimicrobials can diffuse and kill infecting bacteria. Drainage also removes bacteria and bacterial enzymes and again allows the diffusion into the site of antimicrobials. Antimicrobial treatment alone will never cure dento-alveolar abscesses and should always be accompanied by operative treatment to remove the cause and drain the pus.

The majority of dento-alveolar abscesses can be cured without any antimicrobial treatment, but there are situations where they are indicated. Diffuse spreading infections require antimicrobials particularly if they are invading the fascial spaces below the mandible, or the orbital area. If there is cervical lymphadenopathy and a raised temperature, this is an indication of systemic spread of infection; antibiotics are always indicated in such situations. In all cases, this must be accompanied by removal of the cause and drainage of any pus. Large swellings in afebrile patients which have no associated lymphadenopathy, discrete edges can be managed successfully without antimicrobials. Swelling associated with dento-alveolar abscesses do not always require antimicrobials.

‘Pulpitis cannot be treated with antimicrobials. The pulp of a tooth is enclosed in a ‘closed box’ and is becoming necrotic, antimicrobials cannot penetrate or be effective in such a situation’

### Loading doses

Many clinicians still prescribe high initial doses of antimicrobials and insist that patients finish the course of treatment. With the exception of phenoxymethylpenicillin and erythromycin, increasing the dose of antimicrobial is unnecessary. The absorption of agents such as metronidazole and amoxicillin is so good that increasing the dose has no effect on efficacy or outcome. It is generally accepted that, in order to be effective, the concentration of antimicrobial in the infected area should be at least four times the minimum inhibitory concentration (MIC) of the micro-organisms present. With most agents that are commonly used in the management of acute abscesses, this is easily achieved with standard doses. Increasing the dose of antimicrobial does not increase the speed of absorption, if high tissue concentrations are necessary quickly (*e.g.* in the management of septicaemia) then the intravenous route should be chosen.

### The duration of antimicrobial agents

In the management of acute dento-alveolar infections, it is a common misconception that a course of antimicrobials, for 5 days for example, has to be completed to prevent the emergence of resistance. The converse is true, short courses of antimicrobials prevent selection of resistance and discourage microbial conjugation, which is the transfer of resistance genes between two bacteria. Resistance genes are usually encoded on extra chromosomal elements called plasmids and the process is encouraged by long courses of antimicrobial agents. Since antimicrobial agents are only an adjunct to the treatment of dento-alveolar abscesses, they can be safely stopped when the patient shows signs of recovery. Usually, only 2–3 days of antimicrobials are necessary, and this has been shown to be effective in one extensive study.<sup>8</sup>

### Choice of antimicrobial agent for dento-alveolar abscesses

All dento-alveolar abscesses have been shown to contain a mixture of anaerobic and facultative bacteria. The antimicrobial agents that are best suited as an adjunct to their treatment are agents that are active

against these agents and have cidal activity. Phenoxymethylpenicillin was the antimicrobial agent of choice but its poor absorption when used orally and the fact that many facultative organisms are resistant to it precludes it being a first choice. A combination of metronidazole and amoxicillin is the first choice for dento-alveolar abscesses. Amoxicillin is well absorbed and is cidal against most oral facultative bacteria. Metronidazole still remains the drug of choice for oral anaerobes and, despite it having been used for over 50 years, resistance is virtually unknown. Cephalosporins, such as cefradine and cefalexin, have been used for dento-alveolar abscesses to good effect. For patients who are allergic to penicillins, erythromycin has been used, but this is poorly absorbed and static. Erythromycin has poor activity against anaerobes and is only bacteriostatic in its activity; it should not be used in combination with a cidal agent, such as metronidazole. The second choice which is widely used for penicillin-allergic patients is metronidazole on its own; however, no peer-reviewed clinical trial has been reported.

### Prophylactic antimicrobials in dentistry

Prophylactic antimicrobials are frequently used in dentistry, in fact a third of all agents are used for this purpose. To justify such a high rate of use of prophylactic antimicrobials, the rate of postoperative infection should be high. In fact, in most areas of surgical work in dentistry, the infection rate is very low (often less than 1%) and does not justify prophylactic antimicrobial administration. Consistent high rates of postoperative infection following

oral surgery usually are due to poor aseptic technique.

### The timing and type of prophylactic antimicrobial agents

Definitive work done in the 1940s using experimental animals showed that prophylactic antimicrobials had their maximum effect if given before the operation.<sup>9</sup> This allowed the antimicrobial concentration in the tissue being operated to be maximal at the time of operation. Antimicrobials given after the operation did not have the same effects and for minor operations were unnecessary. This principle can be applied to dentistry with good effect for most oral operations: using one dose of pre-operative prophylactic antimicrobials with no postoperative follow-up doses is all that is necessary. It is also necessary to consider the type of antimicrobial agent to be used and what type of bacteria may usually cause the postoperative infection. The type of agent used must be carefully considered to ensure that high tissue concentrations of antimicrobial can be obtained with the antimicrobial. Amoxicillin is often given before bone surgery in the mandible or maxilla, but this is inappropriate as this agent does not penetrate bone and is not licensed for this purpose. The removal of bone in oral surgery is not necessarily an indication for antimicrobial prophylaxis. In addition, the majority of postoperative oral infections involve anaerobes and metronidazole is usually the more suitable antimicrobial for this purpose. Thus, if soft tissue



**Table 1** Patients who may have reduced defences against infection

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- Patients with laboratory-proven deficiencies in their protection against infectious disease
  - Patients with congenital immune deficiencies
  - Patients in the terminal stages of AIDS
  - Drug-induced immune deficiencies
  - Patients with acute or chronic debilitation
- 

and bone are involved in the oral surgery, a single dose one hour before operation of a combination of metronidazole (200 mg) and amoxicillin (250 mg) should suffice for prophylaxis: no follow doses being necessary. Antimicrobials given after the operation will have little effect.

#### Third molar surgery

It is traditionally recommended that prophylactic antimicrobials are given before third molar surgery, especially if it involves removal of bone. There have now been a large number of placebo-controlled studies which have shown that the routine administration of antimicrobials for third molar surgery has little or no effect on postoperative infection. What matters most in third molar surgery is good operative and aseptic technique. The usual postoperative complications of third molar surgery are pain, swelling trismus and not infection. The swelling, pain and trismus following third molar surgery are often misdiagnosed as infection. Dehiscence of the wound, spreading erythema and pus formation is rare following third molar surgery. Again, good surgical and aseptic technique is more important than antimicrobials for third molar surgery and prophylaxis is usually unnecessary and should not be routine.<sup>9</sup>

#### Implants

Implant surgery is done electively and usually under ideal conditions it should not require prophylactic antimicrobials. There have been numerous placebo-controlled trials that have looked at the effectiveness of prophylactic antimicrobials for implant placement and it has been found to be of little value. One meta-analysis of prophylactic antimicrobials came to the same conclusion.

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*Metronidazole still remains the drug of choice for oral anaerobes and, despite it having been used for over 50 years, resistance is virtually unknown.’*

*‘good surgical and aseptic technique is more important than antimicrobials for third molar surgery and prophylaxis is usually unnecessary and should not be routine.’*

Good surgical and aseptic technique should be all that is necessary.<sup>11</sup>

#### Compromised patients

Compromised patients are those with an increased susceptibility to infection. Many patients, such as diabetics, are often classified as compromised but usually they are not. There are thankfully remarkably few patients who would be unable to cope with oral infection and who require antimicrobial prophylaxis.<sup>12</sup> The list of recognised ‘compromised’ patients is shown in **Table 1**. There are patients who have laboratory-diagnosed deficiencies in their defence mechanisms against infection. These patients principally have deficiencies in their immune system or their white cell function or both; they are rare. Patients born with severe immune deficiencies seldom survive as they have serious intercurrent infections and die early. Patients with the acquired immune deficiency do not require antimicrobial prophylaxis particularly if they are being treated with highly active retroviral therapy (HAART). Only when their CD4 counts get low (circa 100) should prophylaxis be considered. Immune modulating drugs are now used for a variety of conditions from skin conditions to anti-rejection of transplanted organs; the opinion of the supervising physician concerning antimicrobial prophylaxis should be sought. Patients who have had circum-oral radiotherapy or cytotoxic therapy fit into this category and almost always require prophylaxis.

The most difficult group of so-called compromised patients are those who have acute or chronic debilitation. It is difficult to be precise about this group and often the decision to give prophylaxis depends on subjective clinical assessment. Patients who have long-term illness which have left them in a debilitated state often react badly to simple tooth extraction and antimicrobial prophylaxis should be considered for them. Another difficult class of patients is those who are severely ill who require oral surgery; they usually require antimicrobial prophylaxis.

### Antimicrobials and periodontal disease

The use of antimicrobials for the routine treatment of periodontal disease either locally or systemically could have very dangerous consequences for microbial resistance. If antimicrobials were routinely used for the treatment of periodontal disease, then there is no doubt that an enormous amount of microbial resistance would be selected and resistance plasmid-conjugation would occur. The place of antimicrobials is in the treatment of a patient in which all other treatment modalities have failed and compliance with oral hygiene is excellent. This is a minority of patients.

### The teaching of antimicrobial use

There is no doubt that antimicrobials are grossly overused by the dental profession but how can this be prevented? A start must be in the teaching of antimicrobial use in dental schools. Many dental schools in the UK do not have clear policies for antimicrobial use and often there is variation from department to department and between individual clinicians. Many oral surgeons still

routinely give antimicrobial prophylaxis for all in-patient surgery regardless of need. Often, the patients are signed up for antimicrobials as soon as they are clerked on ward admission. Such habits are 'ingrained' into housemen and remain policy in these individuals for life. Perhaps the only way that antimicrobial prescribing will change within the dental profession is by involving litigation. If regulatory bodies such as the GDC took a stand on antimicrobial prescribing both in dental school inspections and their fitness to practice activities things would change. The biggest force for change will be if all practising dentists looked at their prescribing and made it more rational.

### Acknowledgement

The opinions expressed in this paper are those of the author and do not represent any organisation with which he is associated.

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