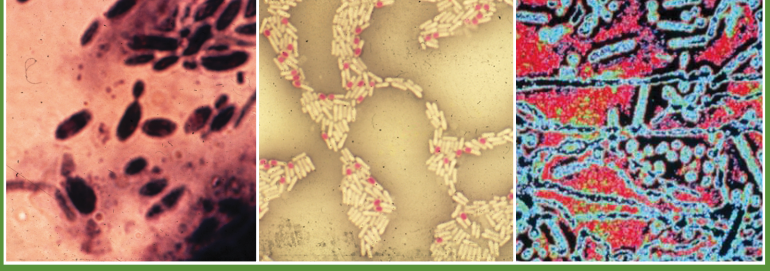

Antimicrobial Prescribing in Dentistry

Good Practice Guidelines

3rd Edition

FGDP (UK)
FACULTY OF GENERAL DENTAL PRACTICE

Faculty of Dental Surgery
ROYAL COLLEGE OF SURGEONS OF ENGLAND

Antimicrobial Prescribing in Dentistry

Good Practice Guidelines

3rd Edition

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FOREWORD

A core function of both the Faculty of General Dental Practice (UK) (FGDP[UK]) and the Faculty of Dental Surgery (FDS) of the Royal College of Surgeons of England is to raise the standards of care delivered to patients, through education of the dental profession and the provision of evidence-based guidance. FGDP(UK) originally published guidance on antimicrobial prescribing for general dental practitioners in 2000. A second edition was published in 2012 which has since been updated to reflect relevant changes in the field. We are delighted that a third edition has been developed as a collaborative project in partnership with FDS, and that the new edition encompasses guidelines for *dentistry* rather than simply *general dental practice*.

As dentists, antimicrobials can be an important adjunctive therapy within our armamentarium for treating oral infection. There are clear benefits for patients when prescribed appropriately, but there are also risks, which is why responsible and judicious prescribing is extremely important. In addition to side effects and adverse reactions, increasing focus has been placed on the potential impact of antimicrobial resistance.

The dental profession has worked assiduously to highlight the importance of antimicrobial stewardship and to promote responsible prescribing. Antimicrobials should only be prescribed when there is a strong clinical indication to do so, and the provision of clear guidance is an important resource to support dentists to prescribe appropriately and responsibly. This third edition of *Antimicrobial Prescribing in Dentistry: Good Practice Guidelines* provides such a resource, and will undoubtedly continue to be a key reference document for the dental team.

We are extremely grateful to the various contributors who have spent considerable time and effort ensuring that this document is informative, accessible and highly relevant to all members of the dental team. In particular, we would like to acknowledge and thank Dr Nikolaus Palmer for his significant contribution as Chair of the Guidance Development Group.

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1 INTRODUCTION

The benefits of prescribing antimicrobials to treat or prevent infections are limited by a number of problems associated with their use, e.g. side effects, toxicity, allergic reactions and importantly, the development of resistant strains of microbes.[1]

Within the last few decades, antimicrobial resistance (AMR) has become a worldwide problem and constitutes a major threat to public health.[2] AMR has increased as a result of widespread use of antimicrobials providing greater opportunity for bacteria to exchange genetic material, allowing resistant genes to spread between bacterial populations and rendering antimicrobials ineffective for their intended use. The inappropriate prescribing of antimicrobials by the healthcare professions is a major concern to be addressed, especially as fewer and fewer new antimicrobials are being developed.[3]

Registered dentists, doctors and non-medical prescribers can legally prescribe from the whole of the British National Formulary (BNF), but dentists treating NHS patients are restricted to prescribing antimicrobials included on the Secretaries of State list published in the BNF.[4] Dentists should not prescribe medicines other than to meet the identified dental needs of patients. They must make an appropriate assessment of the patient's condition, prescribe within their experience and competence, and keep accurate records of the treatment.[5]

It is a legal and regulatory requirement that dentists must involve patients in the decision-making process. This requires acknowledgement of the patients' views about their condition and any proposed treatment.[6,7] In the context of these guidelines, clear information including all the harms and benefits, must be provided to the patient where options may involve antimicrobial prescribing.

Primary care NHS dentists in England prescribe 7.4% of all antimicrobial prescription items in the whole of NHS primary care.[8] The number of prescription items for antimicrobials provided by private dental care practitioners and secondary care dentists is unknown. It is estimated that in total, dentists prescribe 10% of all antimicrobials prescribed in England, and there is evidence of inappropriate use. [9-12]

This guidance has been developed to promote judicious antimicrobial prescribing and antimicrobial stewardship within dentistry. Antimicrobial stewardship has been defined broadly as a coherent set of actions to promote responsible use of antimicrobials.[13] This necessitates organisational or healthcare-wide systems to promote and monitor responsible and appropriate use of antimicrobials to preserve their future effectiveness.[14]

Irresponsible or inappropriate use of antimicrobials include:

- Prescribing in the absence of an infection or where local measures will suffice
- Prescribing prophylactically when not indicated
- An incorrect dose or too long or short duration
- An unnecessarily broad spectrum or narrow spectrum antimicrobial or wrong antimicrobial for the microbiology of a specific infection
- Treatment not adjusted when culture data is available
- Use of IV when oral route can be used
- Choosing an incorrect antimicrobial for a patient with a known allergy

Antimicrobial stewardship is about safe and effective use; prescribing the right antibiotic antimicrobial for the right clinical indication, at the right time, dose and route with minimal toxicity and minimal impact of subsequent resistance to the patient and future patients.[15] Resources to embed antimicrobial stewardship in dentistry are signposted in Appendix 3.

It is generally accepted within dentistry that antimicrobials are indicated:

- As an **adjunct** to the management of acute or chronic infections
- Where definitive treatment has to be delayed, e.g. referral for specialist services for patients requiring a general anaesthetic or sedation, due to inability to establish drainage or if patients have comorbidities requiring hospitalisation.

These patients should, however, be treated as soon as possible to avoid repeat prescribing of antimicrobials

- To prevent infections that may be associated with dental procedures

1.1 SCOPE OF THE GUIDANCE

Registered dentists are the healthcare professionals most likely to manage dental infections, although there is evidence that other healthcare prescribers also prescribe antimicrobials to manage oral and dental infections.[16]

The aim of this guidance is to help healthcare prescribers understand the role of antimicrobial agents in management of oral and dental infections. The guidance also aims to help rationalise and improve standards of antimicrobial prescribing within dentistry and to improve patient care. The guidance is intended to complement, and not replace, the BNF.[4]

This guidance is intended for all healthcare prescribers in primary and secondary dental care, including all general dental practitioners, community dentists, trainees and specialists (including oral and maxillofacial surgery) in the hospital service and those involved in dental education and research. The recommendations are appropriate for all dental patients, including adults, children, the elderly and those with special needs treated in the primary and secondary care setting.

The guidance is not intended to be limiting or restrictive, but to be useful in the decision-making process and to be an aid to effective treatment planning and patient care.

Importantly, it is not the intention of this guidance to provide advice on drug interactions. Dentists should be aware that serious drug reactions can occur between antimicrobial agents and concomitant drugs (e.g. miconazole/fluconazole and warfarin).

Dentists are advised to routinely check the BNF or other authoritative sources, such as the Summary of Product Characteristics via the *Electronic Medicines Compendium*[17] for prescribing information. Information on any aspect of drug prescribing can be obtained from the UK Medicines Information Service (UKMI) (www.sps.nhs.uk). The regional UKMI centre in the North West of England provides a specialist service on drug

use in dentistry (www.sps.nhs.uk/articles/uk-dental-medicines-advice-service-ukdmas/).

This guidance updates the 2012 FGDP(UK) *Antimicrobial Prescribing for General Dental Practitioners* and widens the scope of the title to include management of oral and dental infections by specialists and trainees within the hospital environment.

1.2 DEVELOPMENT AND PRESENTATION OF THE GUIDANCE

In developing the recommendations for this guidance, a guidance development group including general dental practitioners, specialists from the hospital service and patient representatives was formed. The development group reviewed the available evidence, existing guidelines and, when necessary, consensus expert opinion and existing best clinical practice, to formulate its recommendations (see Appendices 1 and 2).

The development group used the GRADE (www.gradeworkinggroup.org) system when making recommendations within this guidance. The recommendations were graded (*strong*, *weak* or *conditional*) based on the quality of the scientific evidence (*high*, *moderate*, *low* or *very low*). It also considered factors such as benefits and harms to patients, specifically side effects, toxicity and AMR, both to the individual patient and the wider population, as well as variability in values and patient preferences. As a result, it was possible to make strong recommendations even where the quality of evidence is weak.[18]

A *strong* recommendation means that most informed patients would choose the recommended management. A *conditional* recommendation is one where there is a finer balance between benefit and harm. In these cases, it is likely that the majority would choose the recommended option.[18]

The **key recommendations** are highlighted in dark green boxes with an indication of the strength of the recommendation and the level of quality of the evidence. Where appropriate, **clinical advice** on assessment and definitive clinical treatment modalities for dental infections based on good clinical practice are included in the text and highlighted in medium green boxes with bullet points or flow charts. **Antimicrobial agents** with the recommended regimens based on the BNF are highlighted in light green boxes.

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2 PRESCRIPTION WRITING

This chapter is adapted from the BNF[1] with kind permission from the Pharmaceutical Press.

Prescriptions should be written or printed legibly in ink or otherwise so as to be indelible. They should be dated and should state the name and address of the patient, the address of the prescriber and an indication of the type of prescriber. In addition, they should be signed by the prescriber (computer-generated facsimile signatures do not meet the legal requirement for paper prescriptions).

The age and the date of birth of the patient should preferably be stated. It is a legal requirement in the case of prescription-only medicines to state the age for children under 12 years.

The following should be noted:

1 The strength or quantity to be contained in capsules, lozenges, tablets etc. should be stated by the prescriber. In particular, the strength of liquid preparations should be clearly stated (e.g. 125mg/5mL).

2 The unnecessary use of decimal points should be avoided, e.g. 3mg, not 3.0mg. Quantities of 1 gram or more should be written as 1g etc. Quantities less than 1 gram should be written in milligrams, e.g. 500mg, not 0.5g. Quantities less than 1mg should be written in micrograms, e.g. 100 micrograms, not 0.1mg. When decimals are unavoidable, a zero should be written in front of the decimal point where there is no other figure, e.g. 0.5mL, not .5mL. Use of the decimal point is acceptable to express a range, e.g. 0.5 to 1g.

3 'Micrograms' and 'nanograms' should **not** be abbreviated. Similarly, 'units' should **not** be abbreviated.

4 The term 'millilitre' (ml or mL) is used in medicine and pharmacy, and cubic centimetre, c.c., or cm^3 should not be used.

5 Dose and dose frequency should be stated; in the case of preparations to be taken 'as required', a **minimum dose interval** should be specified. Care should be taken to ensure children receive the correct dose of the active drug. Therefore, the dose should normally be stated in terms of the mass of the active drug, e.g. '125mg 3 times daily'.

6 The names of drugs and preparations should be written clearly and **not** abbreviated, using approved titles **only**.

7 The quantity to be supplied in primary care may be stated by indicating the number of days of treatment required in the box provided on NHS forms (FP10D in England, GP14 in Scotland and WP10D in Wales). In most cases, the exact amount will be supplied.

In the hospital setting, outpatient prescriptions should note the quantity or duration to be dispensed by the hospital pharmacy. Inpatient medication administration records or drug charts should state duration of treatment and/or a review date.

8 Although directions should preferably be in **English without abbreviation**, it is recognised that some Latin abbreviations are used.

CLINICAL ADVICE

- Never prescribe a drug unless there is a good clinical indication
- Make prescriptions clear
- Use approved names
- Always make the source of the prescription clear
- Always record prescription details in the clinical notes
- Drugs should be prescribed in pregnancy **only** when essential drug treatment is necessary and where the benefit to the mother is greater than risk to the foetus, and all drugs should be avoided if possible during the first trimester[1]
- Avoid abbreviations: give the name of the drug in full

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3 ASSESSMENT OF THE PATIENT

Early recognition and management of dental infections is critical as patients (particularly children and immunocompromised patients) can become systemically ill within a very short space of time. Untreated local infections can spread, causing significant morbidity and even life-threatening sequelae, e.g. Ludwig's angina.[1]

An assessment of the patient and diagnosis should be recorded in the clinical records and include:

- A comprehensive medical and dental history (see FGDP(UK)'s *Clinical Examination & Record-Keeping: Good Practice Guidelines*)[2]
- Assessment of the presence of fever (> 38°C), malaise, fatigue or dizziness (NB: antipyretic effect of patients taking analgesics may temporarily lower the temperature)
- Measurement of the patient's pulse and temperature (normal temperature range is 36.2°C - 37°C[3])
- Definition of the nature, location and extent of the swelling, and any lymphadenopathy
- Identification of the cause of the infection
- Assessment of presence of sepsis using a decision support tool, e.g. NICE Sepsis: Risk stratification tools[4]

Following this assessment in primary care, the clinician should decide whether treatment can be provided or whether referral to a hospital specialist is necessary and urgent, particularly if there is/are:

- Signs of septicaemia, such as grossly elevated temperature (above 39.5°C), lethargy, tachycardia, tachypnoea and hypotension
- Signs of severe sepsis or septic shock (see sepsis decision support tool)[4]
- Spreading cellulitis

- Swellings that may compromise the airway, cause difficulty in swallowing or closure of the eye
- Dehydration characterised by lethargy, dizziness and headache
- Significant trismus associated with a dental infection
- Failure of resolution of infection following previous treatment
- A patient who is unable to cooperate with necessary and appropriate care

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4 ACUTE DENTO-ALVEOLAR INFECTIONS

4.1 ACUTE PERIAPICAL INFECTIONS

Acute periapical infections are infections around the apex of the tooth associated with tooth decay or trauma causing necrosis of the dental pulp. There is associated pain, swelling (localised or spreading), tenderness of the tooth to percussion and mobility, possible raised temperature, malaise, lymphadenopathy and possible dehydration. Appropriate clinical assessment as detailed in chapter 3 is paramount.

It is widely accepted that immediate drainage of infection should be established by extraction of the causative tooth, opening of the root canal and/or incision of the swelling. Failure to do so can lead to spread of the infection and cellulitis.

Matthews et al. systematically reviewed the literature relating to the interventions for management of acute dento-alveolar infections in the permanent dentition.[1] Of the eight eligible trials, six compared antimicrobials as an adjunct to concomitant therapy (incision and drainage, endodontic therapy or extraction) for relief of swelling. Four of these six studies tested alternatives to penicillin. Neither of the two studies comparing antimicrobials with placebo or with no active treatment demonstrated a benefit of antimicrobials.

A Cochrane review, limited to adults with a localised periapical abscess or a symptomatic tooth with a necrotic pulp and with no signs of a spreading infection or systemic involvement, identified two studies which compared the effects of penicillin with placebo as an adjunct to endodontic therapy. The evidence was of very low quality but showed that there was no difference in outcomes (pain, swelling) between patients who received antibiotics and those who received a placebo.[2]

RECOMMENDATIONS

Antimicrobials are only recommended as an adjunct to definitive treatment where there is an elevated temperature, evidence of systemic spread and local lymph node involvement
Strong recommendation, moderate quality evidence

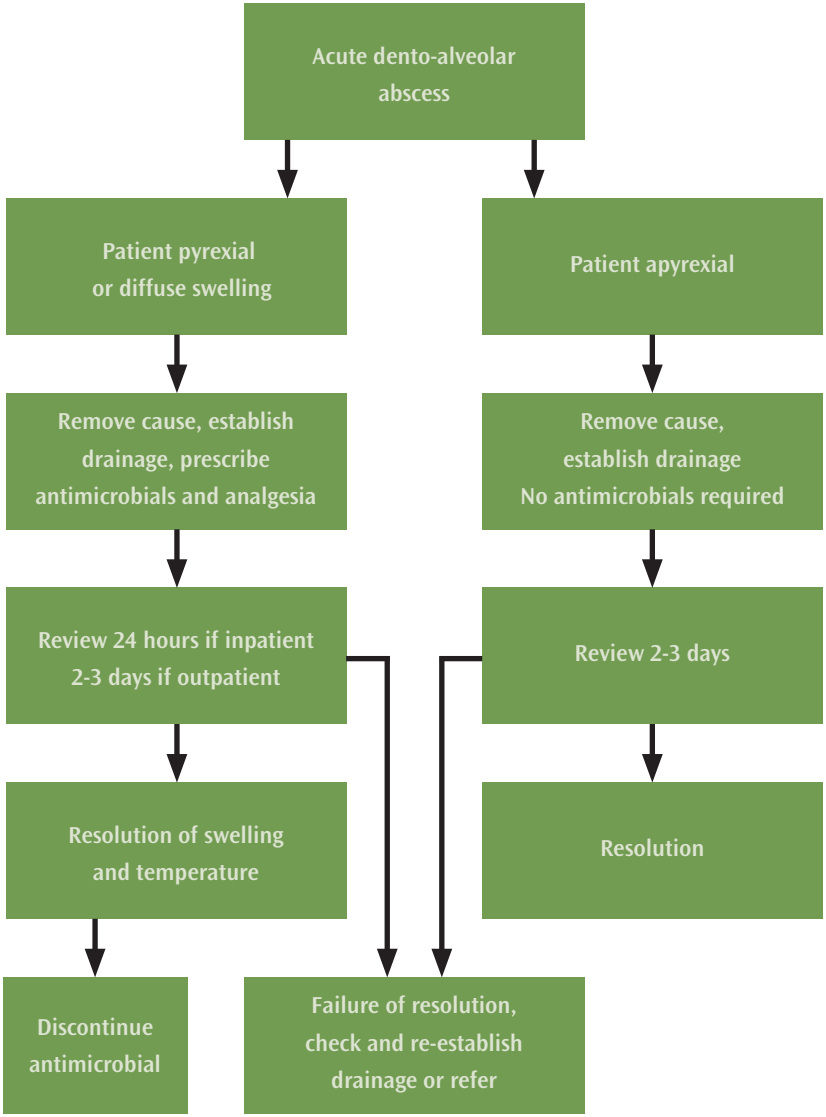
Majority of uncomplicated dental acute infections should be treated by removal of the cause by drainage of the associated abscess, removal of infected pulp contents or by extraction of the tooth
Strong recommendation, low quality evidence

CLINICAL ADVICE

- Remove the source of infection and establish drainage
- Prescribe antimicrobials where there is a clear indication (see recommendation)
- Prescribe or advise analgesics to control pain and fever (see NICE clinical knowledge summary Analgesia – mild-to-moderate pain[3])
- Ensure fluid balance is maintained
- Review the patient 2-3 days after definitive treatment. If resolution of infection and temperature is normal, stop antimicrobials[4,5]
- Review any failure of resolution of temperature and swelling. Failure of resolution is usually caused by failure to establish adequate drainage, poor host response, poor patient compliance or misdiagnosis or infection due to resistant microorganisms
- Where failure of resolution, **re-establish drainage or refer for specialist advice**

An algorithm for clinical management of acute dento-alveolar infections is shown in Figure 4.1.

Figure 4.1 Algorithm for clinical management of acute dento-alveolar infections



4.2 SEVERE RAPIDLY SPREADING DENTO-FACIAL ABSCESSES; CELLULITIS AND LUDWIG'S ANGINA

When an abscess spreads rapidly beyond the dento-alveolar area into the surrounding tissues with systemic signs and symptoms, management usually requires hospital admission (see clinical assessment and indications for referral in chapter 3) due to the possibility of severe complications.

Despite a significant reduction in frequency and mortality, odontogenic infections can still be life-threatening. They may require urgent surgical intervention and intensive care management because of the potential for spread of infection into intracranial and peri-tracheal neck spaces and the risk of airway compromise if appropriate management is not instituted.[6]

Clinical assessment in secondary care:[7]

- Record patient's temperature and clinical signs and symptoms
- Assess extent and nature of swelling, sepsis risk and any trismus, dysphagia, dyspnoea and dysarthria
- Determine source of infection and immediate risk to the airway or infraorbital spread through an OPG radiograph and/or CT scan
- Assess whether cellulitis with oedema or pus is present that requires surgical drainage
- Blood tests (including blood glucose) and blood/pus cultures for sensitivity testing

In an analysis of cases of Ludwig's angina in the paediatric population, it was concluded that successful management includes provision of antimicrobials (usually IV), open surgical drainage of any pus and removal of the cause, usually by extraction of the tooth.[8]

RECOMMENDATION

Antimicrobials (almost always IV) are recommended with incision, drainage and removal of the cause for severe rapidly spreading dento-alveolar infections
Strong recommendation, moderate quality evidence

CLINICAL ADVICE

- Assess airway management. May necessitate an urgent awake surgical airway, such as a tracheostomy or cricothyroidotomy, as conventional endotracheal intubation may be very difficult
- Commence IV antimicrobials + fluids + analgesics
- Keep patient fasted
- Prompt aggressive surgical drainage and removal of cause
- Microbiological aspirate sampling of pus at the time of incision and drainage with sensitivity testing and modification of antimicrobial regimen if necessary
- Review need for IV antimicrobials 24-72 hours post-surgery. Decide whether to stop, switch to oral, change or continue antimicrobials[9]

4.3 ANTIMICROBIAL DRUGS OF CHOICE

Matthews et al. and Martins et al. compared outcomes of β lactam antimicrobials with alternatives in their systematic reviews. They suggested that there was no evidence to recommend one antimicrobial over another in the management of acute dental abscesses with systemic complications when drainage/and or removal of the cause was properly carried out.[1,10]

Antimicrobials are prescribed either empirically based on the microbiology of dental infections and antimicrobial sensitivity established in the literature, or based on the results of microbial susceptibility testing.[11-13]

A penicillin continues to be a highly effective antimicrobial against viridans Streptococci, group C Streptococci and Prevotella, whereas clindamycin was not

shown to be effective as an empirical drug of choice for a large number of odontogenic infections.[14]

A review of systematic reviews of duration of antimicrobial therapy in medical outpatient settings identified that shorter courses are as effective as long courses.[15] Within dentistry, a prospective study showed that when patients with a spreading dental infection were provided with definitive treatment and adjunctive antimicrobials, it was resolved in 2-3 days. In a prospective audit of patients presenting with a spreading infection, provision of drainage and a 3-day course of antimicrobials provided full resolution.[4,5]

Short courses of antimicrobials (up to 5 days) are effective in dental infections and also reduce the pressure to select for antibiotic resistance and reduce side effects.

4.3.1 First choice antimicrobial

A penicillin, such as *phenoxymethylpenicillin* or *amoxicillin*, is effective for dento-alveolar infections. Amoxicillin as a short course high dose has been shown in a randomised control trial to be as efficacious as a conventional phenoxymethylpenicillin regimen in the management of dental infections in children.[16] Amoxicillin may be useful for short course oral regimens for infections when required.

Amoxicillin has a broader spectrum of activity than phenoxymethylpenicillin, which, though as effective, is less reliably absorbed and needs to be taken four times daily on an empty stomach. However, amoxicillin may encourage emergence of resistant organisms. In line with the principles of antimicrobial stewardship, when prescribing antimicrobials to treat an infection that is not life-threatening, a narrow spectrum antibiotic should generally be the first choice.[17]

PHENOXYMETHYLPENICILLIN

Adults

500mg orally four times a day, increased if necessary to 1g every 6 hours for up to 5 days

Children

- 1-5 years: 125mg orally four times a day, increased if necessary up to 12.5mg/kg four times a day for up to 5 days
- 6-11 years: 250mg orally four times a day, increased if necessary up to 12.5mg/kg four times daily for up to 5 days
- 12-17 years: 500mg orally four times a day, increased if necessary up to 1g every 6 hours for up to 5 days

Intravenous injection or infusion for hospital inpatients

BENZYLPENICILLIN SODIUM (PENICILLIN G)

Administered by intramuscular injection, by slow intravenous injection, or by intravenous infusion and maybe combine with IV metronidazole

Adults

0.6-1.2g every 6 hours, dose may be increased if necessary in more serious infections – single doses over 1.2g to be given by intravenous route only

Children

25mg/kg every 6 hours; increased if necessary to 50mg/kg every 4-6 hours (max. per dose 2.4g every 4 hours) in severe infections

Or (see next page)

AMOXICILLIN

Adults

500mg orally three times a day for up to 5 days, increased if necessary to 1g every 8 hours in severe infections

Intravenous injection or infusion for hospital inpatients

500mg every 8 hours, increased to 1g every 6 hours, use increased dose in severe infections

Children

- 1-4 years: 250mg orally three times a day, increased if necessary up to 30mg/kg 3 times a day for up to 5 days
- 5-11 years: 500mg orally three times a day, increased if necessary up to 30mg/kg 3 times a day (max. per dose 1g) for up to 5 days
- 12-17 years: 500mg orally three times a day, increased if necessary up to 1g 3 times a day for up to 5 days. Use increased dose in severe infections

Intravenous injection or infusion for hospital inpatients

20-30mg/kg every 8 hours (max. per dose 500mg), increased if necessary to 40-60mg/kg every 8 hours (max. per dose 1g every 8 hours), increased dose used in severe infection

4.3.2 Second choice antimicrobial[18]

The second choice antimicrobial is either *metronidazole* or a *macrolide*, e.g. clarithromycin, which offers improved pharmacokinetics and toleration compared to erythromycin.

Metronidazole can be used:

- As a first line treatment for patients allergic to a penicillin; or
- As a first line treatment for patients who have had a recent course of a penicillin for another infection; or
- As an **adjunct** to a penicillin in severe spreading infections
- If a predominantly anaerobic infection is suspected or microbiologically proven

Clarithromycin can be used:

- As a first line treatment for patients allergic to a penicillin
- As a first line treatment for patients who have had a recent course of a penicillin

METRONIDAZOLE

Adults

400mg orally three times a day for up to 5 days

Intravenous infusion for hospital inpatients

500mg every 8 hours to be given over 20 minutes

Children

- **1-2 years:** 50mg orally every 8 hours for up to 5 days
- **3-6 years:** 100mg orally every 12 hours for up to 5 days
- **7-9 years:** 100mg orally every 8 hours for up to 5 days
- **10-17 years:** 200-250mg orally every 8 hours for up to 5 days

Intravenous infusion for hospital inpatients

2 months-17 years: 7.5mg/kg every 8 hours (max. per dose 500mg)

CLARITHROMYCIN

Adults

250mg orally twice a day for up to 5 days, increasing to 500mg twice a day in severe infections

Intravenous infusion for hospital inpatients

500mg every 12 hours to be administered in large proximal vein, switch to oral route when appropriate

continued on next page

Children

- **1 month-11 years (body-weight 12-19kg):** 125mg orally twice a day up to 5 days
- **1 month-11 years (body-weight 20-29kg):** 187.5mg orally twice a day up to 5 days
- **1 month-11 years (body-weight 30-40kg):** 250mg orally twice a day up to 5 days
- **12-17 years:** 250mg orally twice a day for up to 5 days, increasing to 500mg twice a day in severe infections

4.3.3 Other antimicrobials available for dento-alveolar infections

Clindamycin has effective antimicrobial activity against oral anaerobes.[12] In prospective randomised controlled trials, it has been shown that the clinical results using clindamycin were similar to those with penicillin for treatment of acute dental abscesses.[19,20]

A higher rate of adverse gastrointestinal effects and diarrhoea has been reported in association with clindamycin treatment[20] and it is well documented that there is an increased risk of *Clostridium difficile* infections with clindamycin. The significant morbidity/mortality associated with *Clostridium difficile* is an important risk that should be included in consent when prescribing clindamycin.

Clindamycin, however, may be the only antimicrobial of choice due to allergy or drug interactions for some individual patients.

Co-amoxiclav (amoxicillin and clavulanic acid) is active against beta-lactamase producing bacteria that are resistant to amoxicillin. The BNF suggests that it may be used for a severe spreading infection with spreading cellulitis and where the infection is not responding to first line antimicrobials.[18] Co-amoxiclav should only be used in patients likely to be managed in secondary care.

A systematic review looked at harms associated with amoxicillin or co-amoxiclav in randomised placebo-controlled trials.[21] Although harms were poorly reported, and

the true incidence was likely to have been higher, diarrhoea was only reported for co-amoxiclav and candidosis for both amoxicillin and co-amoxiclav. The number of courses of co-amoxiclav needed to harm was 10 for diarrhoea. The number of courses of both amoxicillin and co-amoxiclav needed to harm was 27 for candidiasis.[21]

Cephalosporins have been used for oral infections but they offer no advantage over a penicillin in dental infections and are less active against anaerobes.

CLINDAMYCIN

Adults

150-300mg orally four times a day increased if necessary to 450mg every 6 hours in severe infections for up to 5 days

Children

3-6mg/kg orally 4 times a day (max dose 450mg) for up to 5 days

CO-AMOXICLAV

Adults

500/125mg orally every 8 hours for severe infections for 5 days

Children

12-17 years: 500/125mg orally every eight hours for severe infections for 5 days

Intravenous injection or infusion for hospital inpatients

Adults

1.2g every eight hours

Children

3 months-17 years: 30mg/kg every 8 hours (max dose 1.2g every 8 hours)

RECOMMENDATION

The routine prescribing of clindamycin, cephalosporins or co-amoxiclav for dental infections is not recommended and should only be at the direction of a specialist in oral/medical microbiology or infectious diseases

Strong recommendation, moderate quality evidence

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5 CHRONIC DENTAL INFECTIONS

5.1 CHRONIC DENTO-ALVEOLAR INFECTIONS

Chronic dento-alveolar infections occur as a result of decayed or restored teeth, or periodontal-endodontic lesions with a longstanding minor well-localised abscess contained by the host immune system. These infections sometimes spontaneously drain through a sinus tract which can be either intra- or extraoral.

It is generally accepted that definitive dental treatment to remove the cause leads to resolution. Case reports and a review of the literature show that removal of the cause of the infection normally resolves the infection and extraoral cutaneous sinus tracts heal spontaneously.[1,2]

Longstanding chronic infections that fail to respond to treatment are indicative of a more serious problem, e.g. osteomyelitis. These patients should be referred for specialist management.

Antimicrobial therapy is rarely required unless:

- There is an acute flare-up and there is evidence of severe local spread, or
- There is systemic involvement shown by raised temperature and malaise

RECOMMENDATION

Antimicrobials are not recommended for chronic dento-alveolar infections
Strong recommendation, low quality evidence

CLINICAL ADVICE

- Remove the cause by extraction, root canal therapy or surgical endodontics
- If acute flare-up, assess and manage in line with recommendations for acute infections (see chapter 4)
- If there is no resolution, refer for specialist/secondary care management

5.2 OSTEOMYELITIS

Osteomyelitis (OM) is an infection in the bone which usually affects the mandible. It is the result of bacterial infection of odontogenic origin or trauma causing bone death and necrosis.

It may be acute or chronic and two main types of OM are described in the literature. The suppurative variants have the presence of pus and/or fistulas and/or sequestrations, distinguishing them from the non-suppurative variants, which are chronic inflammatory processes of unknown aetiology.[3]

These patients require a comprehensive clinical assessment in secondary care, including blood investigations, microbiological cultures from bone lesions, radiographs, CT/CBCT and MRI scans to rule out differential diagnoses, e.g. bone tumours.

Patients generally present with:

- Deep-seated throbbing pain
- Swelling (initially soft because of oedema, later firm with involvement of the periosteum)
- Non-healing necrotic bone
- Sequestrum formation
- Trismus
- Fever
- Halitosis
- Extraoral draining sinuses
- Lymphadenopathy

The evidence for management of osteomyelitis is based on case reports, cohort studies, reviews and expert consensus.

A literature review of case studies reported management with antimicrobials with a duration varying from 2 weeks to 6 weeks, usually starting with intravenous antimicrobials followed by a variable period of oral antimicrobials.[3] A number of different antimicrobials were used in the studies with successful outcomes, indicating the varying and dynamic nature of the bacterial species in OM.

A multicentre parallel group randomised study showed that in patients who had surgery for bone infections and IV antimicrobials for <7days, there was no clinical advantage of prolonged IV antimicrobials compared to oral antimicrobials.[4]

Antimicrobial treatment should be based on the identification of pathogens from bone cultures at the time of bone biopsy or debridement, and on local guidelines.

RECOMMENDATION

Antimicrobials are recommended for the management of osteomyelitis as an adjunct to surgical debridement

Strong recommendation, very low quality evidence

CLINICAL ADVICE

- Comprehensive clinical assessment
- Radiographs, CT/CBCT and MRI scans
- Microbiological sampling, culturing and antimicrobial sensitivity testing
- Removal of necrotic bone/sequestrum
- Surgical debridement
- Initially prescribe IV antimicrobials followed by oral antimicrobials until resolution

continued on next page

- **Prescribe or advise analgesics to control pain** (see NICE clinical knowledge summary, Analgesia – mild-to-moderate pain[5])
- Review until resolution

5.3 MEDICATION RELATED OSTEONECROSIS OF THE JAW (MRONJ)

MRONJ is where exposed necrotic bone in the maxillofacial region has persisted for more than 8 weeks in a patient who is, or has, undergone treatment with antiresorptive or antiangiogenic agents without current or previous radiotherapy to the area. The exposed necrotic bone may occur spontaneously or following dento-alveolar surgery. Intraoral and extraoral fistulae may develop when the necrotic mandible or maxilla becomes secondarily infected.

The evidence for management is based solely on case series or cohort studies.[6,7] The empiric treatment suggested consists of conservative non-surgical palliative care, control of associated infection and surgical intervention based on staging of the condition.

A Cochrane systematic review found only one RCT on management of MRONJ. This investigated hyperbaric oxygen (HBO) treatment used in addition to antiseptic rinses, antimicrobials and surgery. HBO did not significantly improve healing of MRONJ empiric treatment.[8]

RECOMMENDATION

Antimicrobials are recommended for MRONJ where secondary bacterial infection is present

Conditional recommendation, very low quality evidence

CLINICAL ADVICE

- Remove sources of irritation/trauma
- Ensure good oral hygiene

continued on next page

- Consideration must be given to why the MRONJ has occurred. If it is associated with terminal metastatic cancer, a very conservative approach to management is appropriate
- Microbiological sampling, culture and antimicrobial sensitivity testing
- Prescribe antimicrobial oral rinses
- Prescribe appropriate antimicrobials where infection is evident
- Surgical debridement of sequestra (with care) with non-responsive lesions
- Review

5.4 OSTEORADIONECROSIS (ORN)

Osteoradionecrosis (ORN) is a sequela of radiation therapy in head and neck cancer patients. Currently, there is no gold standard treatment of ORN and no widely accepted guidelines exist due to a lack of good evidence.

A literature review showed that early-stage ORN can be treated conservatively with antimicrobials and meticulous oral hygiene, as for MRONJ. Any sign of progression may require early surgical intervention with debridement and mucosal flaps to cover exposed bone.[9]

The role of HBO treatment and medical management (antifibrotics, antioxidants, steroids) is yet to be defined with robust clinical trials. Extensive surgical resection with microvascular free flap reconstruction may be indicated in some patients with very advanced ORN and persistent symptoms despite conservative treatments.

RECOMMENDATION

Antimicrobials are recommended to control secondary bacterial infections associated with early stage osteoradionecrosis

Strong recommendation, very low quality evidence

CLINICAL ADVICE

- Remove any possible sources of irritation/trauma, e.g. denture
- Perform minor debridement, eliminating sharp bone edges, sharp tooth surfaces
- Advise patient to maintain local hygiene of the area of exposed bone with topical antimicrobial agents
- Microbiological sampling, culture and antimicrobial sensitivity testing
- Prescribe appropriate antimicrobial
- Conservative bone sequestromy may be required in extensive cases
- Surgical removal of large areas of necrotic bone may be required
- Prescribe or advise analgesics to control pain and fever (see NICE clinical knowledge summary, Analgesia – mild-to-moderate pain[5])

5.5 ANTIMICROBIAL DRUG OF CHOICE

Antimicrobials are prescribed either empirically based on the microbiology of the associated dental infection and antimicrobial sensitivity established in the literature, or in the case of osteomyelitis, MRONJ and ONJ, based on the results of microbial susceptibility testing and any local prescribing guidelines. See section 4.3 for antimicrobial regimens.

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6 PERICORONITIS

Pericoronitis is inflammation and infection of the soft tissues around a partially erupted tooth, usually an impacted mandibular third molar. There is no evidence-based guidance for the clinical management of pericoronitis. It is generally accepted, in line with the management of acute dental infections, that local inflammation and infection is managed with local measures, such as removal of the cause (extraction or operculectomy), incision and drainage where necessary.

Where there is evidence of systemic spread, e.g. elevated temperature, severe localised swelling, cellulitis or trismus, antimicrobials should be provided as an adjunct to local measures.[1]

RECOMMENDATION

Antimicrobials are only recommended for pericoronitis as an adjunct to local measures where there is evidence of systemic spread (elevated temperature), severe generalised swelling, cellulitis or severe localised swelling and trismus

Strong recommendation, moderate quality evidence

CLINICAL ADVICE

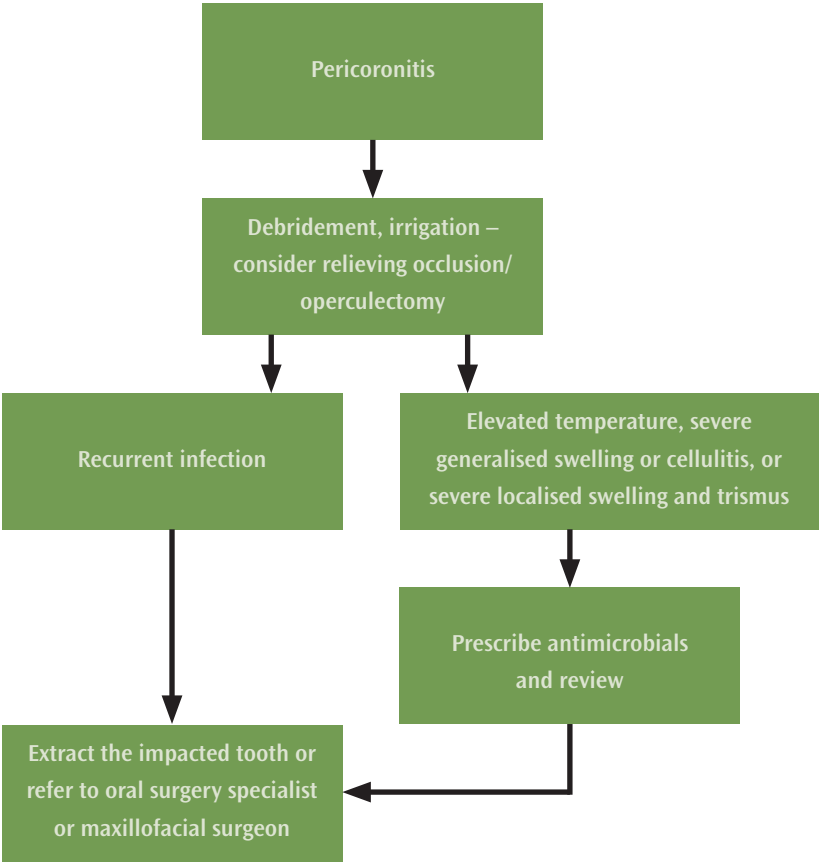
- Debride and irrigate pericoronal space with sterile solution, e.g. saline
- Incision and drainage if localised abscess
- Consider operculectomy

continued on next page

- **Occlusal adjustment to relieve occlusion or extract opposing tooth if traumatising any inflamed pericoronal tissues**
- **Prescribe or advise the use of analgesics** (see NICE clinical knowledge summary, Analgesia – mild-to-moderate pain[2])
- **Advise the use of warm salty mouthwashes**
- **Prescribe appropriate antimicrobials in the presence of severe local disease or if systemic symptoms identified**
- **Extract impacted tooth, if there has been more than one episode, once infection under control** (see NICE Guidance on the Extraction of Wisdom Teeth [TA1])[3]
- **Complex dentofacial infections arising from pericoronitis require urgent surgical management** (see section 4.3)

An algorithm for the clinical management of pericoronitis is shown in Figure 6.1

Figure 6.1 Algorithm for clinical management of pericoronitis



6.1 ANTIMICROBIAL DRUGS OF CHOICE

Two systematic reviews suggested that there is no evidence to recommend one antimicrobial over another in the management of odontogenic infections.[1,4]

Antimicrobials are usually prescribed where indicated, either empirically or based on microbiological studies of pericoronitis infections. Two microbiological studies of pericoronitis infections found that no causative species could be

identified, but most isolates were obligate and facultative anaerobic bacteria.[5,6]

Metronidazole or amoxicillin, both effective against anaerobic bacteria, are recognised as suitable choices of antimicrobial as an adjunct to local measures where indicated.[7]

METRONIDAZOLE

Adults

400mg orally three times a day for up to 5 days[8-9]

Intravenous infusion for hospital inpatients

500mg every 8 hours to be given over 20 minutes

Children

10-17 years: 200-250mg orally every 8 hours for up to 5 days

Intravenous infusion for hospital inpatients

7.5mg/kg every 8 hours (max per dose 500mg)

Or

AMOXICILLIN

Adults

500mg orally three times a day for up to 5 days increased if necessary to 1g every 8 hours in severe infections[8-9]

Intravenous injection or infusion for hospital inpatients

500mg every 8 hours, increased to 1g every 6 hours, use increased dose in severe infections

Children

12-17 years: 500mg 3 times a day, increased if necessary up to 1g 3 times a day, use increased dose in severe infections

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7 DRY SOCKET

Dry socket or localised osteitis is a recognised complication following tooth extraction, with incidence rates of 1-4% with routine extractions, but a reported incidence of 25-30% with impacted lower wisdom teeth.[1]

It occurs 3-4 days post-extraction and is self-limiting, lasting for up to 10 days.[1,2] The aetiology is thought to be associated with surgical trauma, local infection, inadequate oral hygiene and poor aftercare.[3]

There are no RCTs comparing clinical outcomes of prescribing antimicrobials against no antimicrobials in the management of dry socket. In the absence of signs of a spreading infection, it is generally accepted that antimicrobials are contraindicated and management is centred around local measures.[3]

A Cochrane systematic review found there was no evidence to support any interventions for the treatment of dry socket. It also reported that the number of patients needed to treat (NNT) with chlorhexidine to prevent one dry socket was 232. In view of this and reported cases of anaphylaxis, its preventive use for dry sockets is controversial.[4]

RECOMMENDATION

Antimicrobials are not recommended for the management of dry socket in the absence of signs of a spreading infection

Strong recommendation, low quality evidence

CLINICAL ADVICE

- If appropriate, radiograph to exclude a foreign body or retained root
- Irrigate with sterile solution, e.g. saline, to remove debris
- Placing a suitable dressing, e.g. Alvogyl®, in the socket may relieve symptoms but can delay healing[5,6]
- Prescribe or advise analgesics (see NICE clinical knowledge summary, Analgesia – mild-to-moderate pain[7])
- Advise warm salty mouthwashes
- Review the patient for resolution

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8 ACUTE SINUSITIS

Most cases of acute sinusitis (also known as rhinosinusitis) are self-limiting and usually triggered by a viral infection of the upper respiratory tract. In the absence of a dental cause, these cases are best managed by the patient's general medical practitioner.

Acute sinusitis can be diagnosed by:

- Nasal discharge
- Nasal blockage or congestion
- Facial pain localised over the affected sinus that can affect the teeth, upper jaw or eye, side of the face or forehead. Pain in the absence of other symptoms is unlikely to be sinusitis and a dental cause should be ruled out
- Loss or altered sense of smell

In its guideline for antimicrobial prescribing for acute sinusitis, NICE states that most cases of uncomplicated acute sinusitis resolve in 2-3 weeks and respond to watchful waiting and measures to relieve symptoms.[1]

Three systematic reviews and meta-analyses showed that antimicrobials, when compared with placebo, did not significantly increase cure or improve symptoms at 3-5 days follow-up.[2-4] At 7-15 days follow-up, there were statistically significant differences in effectiveness, but the clinical difference was small. Beyond 15 days there was no difference between antimicrobials and placebo in effectiveness.[1]

RECOMMENDATION

Antimicrobials are not recommended for uncomplicated acute sinusitis
Strong recommendation, moderate quality evidence

CLINICAL ADVICE

- Assess whether a dental cause and manage appropriately
- Consider paracetamol or ibuprofen to relieve pain and fever
- Consider suggesting the patient try nasal saline or decongestant, though there is little evidence to recommend their use[1]
- Adequate fluids and rest
- Refer if patient presents with severe symptoms, is systemically unwell, has symptoms and signs of a more serious illness or existing co-morbidities, e.g. immunosuppression, or significant heart, lung, renal, liver or neuromuscular disease

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9 BACTERIAL SIALADENITIS

Sialadenitis is inflammation and swelling of the parotid, submandibular, sublingual or minor salivary glands.

Acute bacterial sialadenitis is characterised by:

- Rapid onset of pain
- Swelling and elevated temperature
- Cellulitis and induration of the adjacent soft tissues may be present, and rarely a cutaneous fistula
- Exudates of pus from salivary gland opening

Chronic sialadenitis is characterised by intermittent, recurrent episodes of tender swelling, usually as a result of obstruction (stricture or calculus) of the duct which can be managed with local measures.

A clinical assessment of the patient (see chapter 3) should include palpation of the gland for the presence of calculi and examination of the ductal opening for purulence. Referral and management to a specialist is required in cases of acute infection, grossly elevated temperature and signs of airway compromise where microbiological culture of pus from the duct and blood cultures can be taken, along with an assessment of fluid and electrolyte balance.

The most common bacterial cause of acute sialadenitis is *Staphylococcus aureus*, which has been cultured in > 50% of cases. Streptococcal species, Gram-negative bacteria and anaerobes are also common causes.[1-3]

There is no good quality evidence on the management of bacterial sialadenitis.

As with acute dento-alveolar infections, accepted practice in the management of acute bacterial sialadentitis with systemic signs and symptoms is drainage of the abscess if present, removal of the cause and prescribing of antimicrobials.[4]

Microbiological studies have shown that acute bacterial sialadenitis is polymicrobial in nature and includes *S. aureus*, oral *streptococci* and Gram-negative anaerobes with aerobic Gram-negative microbes, such as *Klebsiella spp* often recovered in hospital inpatients.[5]

There is no evidence of the efficacy of one antimicrobial or combination over another. Commentators and clinicians have suggested a number of antimicrobials based on the microbiology published in the literature.[5]

A systematic review did find that intravenously administered cephalosporins achieved the highest concentrations in saliva, followed by orally administered cephalosporins and fluoroquinolones. In this study, it was suggested that beta-lactam antimicrobials, especially cephalosporins, are effective as first-line therapy in the conservative treatment of sialadenitis.[6]

RECOMMENDATIONS

Antimicrobials with local measures are recommended for acute bacterial sialadenitis
Strong recommendation, low evidence

Antimicrobials are not recommended for chronic sialadenitis which can be managed with local measures
Strong recommendation, very low evidence evidence

9.1 ANTIMICROBIAL REGIMENS

The BNF makes no recommendations for bacterial sialadenitis. Knowledge of prevalent organisms from microbiological studies and their current sensitivity should guide antimicrobial choice prior to culturing and bacteriological results.

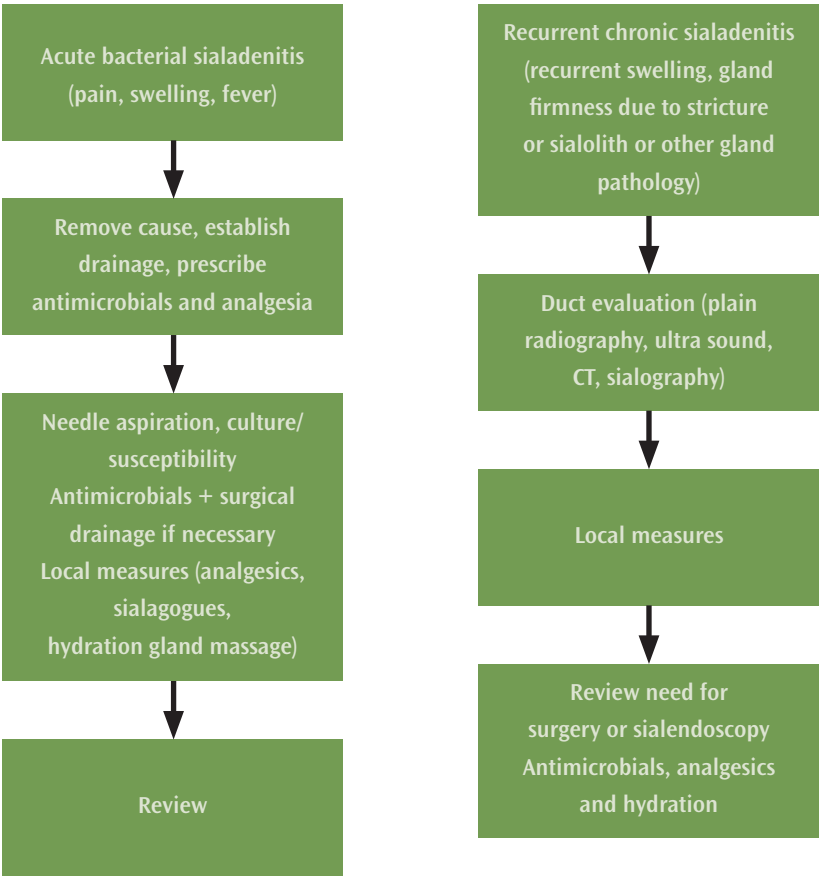
Empirically, antimicrobial therapy in the hospital setting includes flucloxacillin and metronidazole, with addition of gentamycin where necessary, or a third generation cephalosporin for hospital in-patients. Clinicians should be aware of local policies/formularies and seek advice from a clinical microbiologist.

CLINICAL ADVICE

- Institute local measures, e.g. hydration, sialagogues, gland massage, oral hygiene instruction (OHI)
- Prescribe analgesics (see NICE clinical knowledge summary, Analgesia – mild-to-moderate pain[7])
- Refer for specialist management of acute infection with systemic signs and symptoms
- Prescribe antimicrobials empirically based on known microbiology for the acute infection, BUT adjust if necessary following culture and sensitivity testing
- Review acute phase 24-48 hours
- Duct evaluation by radiography, ultra sound scan, sialography, CT scan following control of acute phase. Sialography can also provide symptomatic relief in chronic sialadenitis
- Remove the source of the infection
- Evaluate the need for sialendoscopy or open surgery

An algorithm for clinical management is shown in Figure 9.1.

Fig 9.1 Algorithm for clinical management of sialadenitis



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10 PERIODONTAL DISEASES

10.1 GINGIVITIS

Gingivitis is an inflammatory response of the gingival tissues resulting from bacterial plaque accumulation at and below the gingival margin. A systematic review showed that mechanical plaque control procedures are effective in reducing plaque and gingivitis, and that an antimicrobial rinse has a positive effect on gingivitis.[1]

RECOMMENDATION

Systemic antimicrobials are not recommended for the management of gingivitis

Strong recommendation, moderate quality evidence

CLINICAL ADVICE

- Ensure no underlying medical or nutritional condition, e.g. leukaemia or vitamin C deficiency
- Provide oral hygiene instruction
- Consider antimicrobial rinse
- Review plaque control

10.2 NECROTISING PERIODONTAL DISEASES

These are rare and include necrotising gingivitis, necrotising periodontitis and necrotising stomatitis. They are characterised by gingival necrosis and bleeding, pain and fetid breath. In severe cases, systemic signs and symptoms, such as lymphadenopathy, fever, and malaise may be present.

The possibility of compromised systemic health, smoking and/or stress should be investigated with the patient and managed if necessary, possibly in conjunction with the general medical practitioner.

Spirochetes, fusiforms and bacteroides have all been frequently cultivated from necrotising lesions, but a definitive periodontal pathogen is yet to be implicated.[2]

A literature review showed that it is generally accepted that local therapeutic measures (scaling and polishing, OHI) with adequate pain control provide resolution of the acute phase of necrotising gingivitis.[3]

RECOMMENDATION

Antimicrobials are recommended only as an adjunct to local measures for necrotising periodontal disease where there is evidence of systemic involvement

Strong recommendation, very low quality evidence

10.2.1 Antimicrobial drug choice

The antimicrobial of choice, where there is evidence of systemic involvement, is metronidazole due to the anaerobic nature of the infection. Amoxicillin is an alternative where metronidazole is contraindicated.

METRONIDAZOLE

Adults

400mg orally three times a day for up to 5 days

Children

10-17 years: 200-250mg orally every 8 hours for up to 5 days

Or (see next page)

AMOXICILLIN

Adults

500mg orally three times a day for up to 5 days increased if necessary to 1g every 8 hours in severe infections

Children

12-17 years: 500mg 3 times a day, increased if necessary up to 1g 3 times a day, use increased dose in severe infections

CLINICAL ADVICE

- Provide oral hygiene instruction
- Debridement under local anaesthetic
- Prescribe or advise analgesia (see NICE clinical knowledge summary, Analgesia – mild-to-moderate pain[4])
- Consider recommending an antimicrobial mouthwash
- Only prescribe antimicrobials if evidence of systemic involvement
- Provide or refer for smoking cessation support if indicated
- Review for further treatment and maintenance, consider systemic issues, especially in the presence of a limited response to treatment at review

10.3 PERIODONTITIS

The recent reclassification of periodontitis is based on staging (initial [I], moderate [II], severe [III], very severe [IV]) in terms of interproximal bone loss and grading (slow [A], moderate [B], rapid [C]) progression in terms of percentage bone loss compared to patient age.[5]

Patients with severe/very severe or rapidly progressing forms of periodontitis responding poorly to effective mechanical debridement and excellent patient oral hygiene should be referred for specialist management.

10.3.1 Stage I, II, III; Grade A, B periodontitis or periodontitis in any patient aged >40-45years

It is accepted that it is possible to achieve satisfactory and stable outcomes from root surface debridement (RSD) combined with good patient oral hygiene in this group of patients.

10.3.1.1 Use of systemic antimicrobials

A systematic review and meta-analysis compared non-surgical periodontal therapy with a wide range of systemic antimicrobials against non-surgical periodontal therapy alone in untreated chronic periodontitis.[6] This review (of 43 studies) found that systemic antimicrobials showed a statistically significant additional pocket depth reduction, but the additional benefit was very small and the long-term clinical benefits not proven. Statistically, no specific type of antimicrobial or protocol was superior over another in this meta-analysis. Other studies, including a systematic review of systemic and local antimicrobials in the managment of chronic periodontitis and aggressive periodontitis, showed similar results.[7,8]

Clinicians should weigh up any very small short-term benefits of adjunctive systemic antimicrobial treatment against development of resistance and other unwanted side effects of antimicrobials, such as diarrhoea, nausea, vomiting, thrush, gastrointestinal intolerance and antimicrobial hypersensitivity.[9]

RECOMMENDATION

Systemic antimicrobials are not recommended as an adjunct to thorough and effective mechanical debridement for patients with periodontitis of slow or moderate progression, or in any patient with periodontitis aged >40-45 years

Strong recommendation, moderate quality evidence

10.3.1.2 Use of topical/local antimicrobials

There are a range of local delivery antimicrobial systems available. Indications for their use are limited and should not be considered as a first-line periodontal treatment.

Local delivery antimicrobials are used as an adjunct to conventional subgingival debridement, and their effectiveness is controversial.

A recent Cochrane review showed no statistically significant improvement or long-term benefit with adjunctive use of local antimicrobials in supportive periodontal treatment.[10] A further study showed that these forms of adjunctive therapy are not cost effective.[11]

RECOMMENDATION

Locally delivered antimicrobials are not recommended as an adjunct to effective mechanical debridement in the management of periodontitis
Strong recommendation, low quality evidence

10.3.1.3 Use of low dose (sub-antimicrobial) antimicrobials

Low (sub-antimicrobial) dose doxycycline (SDD) is considered a host modulating agent inhibiting collagenase activity present in periodontitis.

A systematic review and meta-analysis suggested, on the basis of 3 trials that included 46 participants, that use of SDD for 3 months following RSD resulted in a very small extra reduction (~0.9mm) in pocket depth (PD); there was a small extra gain (~0.8mm) in clinical attachment level (CAL) compared to RSD alone after 9 months.[12]

A further systematic review and meta-analysis of 11 trials showed a very small gain in CAL (0.15-0.56mm).[13] The long-term benefit of sub-antimicrobial antimicrobials in the management of periodontal disease is not proven. One study indicated that long-term SDD does not alter or contribute to alterations in the antimicrobial susceptibility of the subgingival microflora compared with a placebo.[14]

Clinicians need to weigh up the extremely limited clinical benefit against the known risks (diarrhoea, nausea, hypersensitivity, vomiting) of prescribing SDD, particularly if used in maintenance programmes.

RECOMMENDATION

Sub-antimicrobial dose antimicrobials (e.g. doxycycline) are not recommended as an adjunct to thorough root surface debridement and excellent home care by periodontal patients

Strong recommendation, low quality evidence

CLINICAL ADVICE

- Consider medical risk factors, e.g. diabetes
- Provide oral hygiene instruction
- Debridement under local anaesthetic
- Consider recommending an antimicrobial mouthwash
- Provide or refer for smoking cessation support if indicated
- Review for further treatment and maintenance
- If isolated site(s) are not responding to RSD despite good plaque control, referral to a specialist should be considered

10.3.2 Stage III, IV periodontitis Grade C in patients aged <40-45years

Following diagnosis in primary care, dentists should consider referral of these patients to a periodontal specialist for management.

In this group of patients (where periodontal disease is advanced and progressing rapidly), the use of systemic antimicrobials as an adjunct to mechanical debridement and oral hygiene instruction has been investigated in a number of RCTs.

Systematic reviews have demonstrated that adjunctive use (to root surface debridement) of systemic antimicrobials can result in greater PD reductions and gains in CAL compared to just root surface debridement alone.[6-9]

In a systematic review and Bayesian network meta-analysis, 9 out of 11 RCT studies showed a statistically significant small gain (~1mm) in CAL and small reduction (~1mm) in PD when systemic antimicrobials (metronidazole or

metronidazole + amoxicillin) were used as an adjunct to RSD compared to RSD alone. This study also showed very limited improvements when systemic doxycycline was used as an adjunct to RSD.[15]

A further placebo-controlled RCT showed that both 3 and 7 day regimens produced similar reductions in PD and CAL gain with adjunctive amoxicillin and metronidazole.[16]

All studies show a variety of regimens (dose/duration/frequency) for the antimicrobials used as an adjunct to RSD. There is no direct evidence to support a specific regimen or protocol for adjunctive systemic antimicrobials with RSD.[7,8,15]

It has been suggested that locally undisrupted biofilm affects the efficacy of systemic antimicrobials, and that they should be commenced at the earliest on the day RSD is started. Current expert consensus is that antimicrobials should be prescribed at the end of a thorough course of RSD, and that such instrumentation therapy should be completed within a week or less.[9]

The benefits of adjunctive systemic antimicrobials at initial therapy were significant compared to those who had antimicrobials at re-treatment in a randomised placebo-controlled, parallel design, double-blind clinical trial.[17]

A systematic review of the effectiveness of systemic antimicrobial therapy noted that nearly all of the studies reported adverse effects (e.g. gastrointestinal discomfort, diarrhoea, nausea) associated with medication.[9]

Clinicians should weigh up the benefits and risks, both at an individual and general population level, when deciding to prescribe systemic antimicrobials as an adjunct to thorough and effective mechanical debridement.

RECOMMENDATION

Systemic antimicrobials are only recommended as an adjunct to effective mechanical debridement, oral hygiene instruction and management of modifiable risk factors in patients aged <40-45 years with rapidly progressing periodontal disease

Conditional recommendation, moderate quality evidence

CLINICAL ADVICE

- Identify and manage risk factors, e.g. smoking
- RSD + OHI
- Consider adjunctive antimicrobials
- Review
- Consider periodontal surgery/regenerative surgery
- Regular reviews and maintenance programme

10.3.3 Antimicrobial drug choice

The choice of antimicrobial in the management of periodontal diseases is empiric, guided by information about the nature of the involved pathogenic microorganism(s) and/or their antimicrobial susceptibility profile. The microbial flora and level of pathogenic species differ for patient and site but is usually associated with anaerobes.

10.3.3.1 First choice antimicrobial

Experts agree that the antimicrobial regimen for treatment of Stage 3,4 Grade C is a combination of amoxicillin with metronidazole.[18] In a placebo-controlled randomised study comparing 3 or 7 day antibiotic regimens with RSD only, both led to a significantly greater clinical improvement.[16] A shorter-duration regimen reduces potential side effects and selective resistance.

AMOXICILLIN

Adults

500mg orally three times a day for up to 5 days

Children

12-17 years: 500mg orally three times a day for up to 5 days

METRONIDAZOLE

Adults

400mg orally three times a day for up to 5 days

Children

12-17 years: 400mg orally three times a day for up to 5 days

10.3.3.2 Second choice antimicrobial

The second choice is a *macrolide*, e.g. azithromycin. This is normally used as an alternative to a penicillin. Azithromycin has been reported to give adjunctive benefits in Grade C cases, particularly at deeper sites.[19] Azithromycin is thought to have some host-modulatory effects.[20]

AZITHROMYCIN

Adults

500mg orally once a day for 3 days

Children

- 12-17 years (body weight 36-45kg): 400mg orally once a day for 3 days
- 12-17 years (body weight 46kg and over): 500mg orally once a day for 3 days

10.3.3.3 Other antimicrobials

Doxycycline has been suggested to have higher availability in the gingival crevice, significantly active against *Aggregatibacter actinomycetemcomitan* and has host-modulating properties. A review by Herrera et al. showed doxycycline had mixed but inferior results compared to other antimicrobials.[8]

DOXYCYLINE

Adults and children 12-17 years
100mg orally twice a day for the first day then once a day for up to 5 days

10.4 PERIODONTAL ABSCESS

The majority of uncomplicated swellings of periodontal origin can be successfully treated by removing the source of the infection. This can be achieved by drainage of the associated abscess (ideally by RSD via the pocket) or by extraction of the tooth.[21]

Antimicrobials are only indicated as an adjunct to definitive treatment where there is an elevated temperature, evidence of systemic spread and local lymph node involvement.[21]

RECOMMENDATION

Antimicrobials are only recommended as an adjunct to definitive treatment for periodontal abscesses where there is an elevated temperature, evidence of systemic spread and local lymph node involvement
Strong recommendation, low quality evidence

For management options see chapter 4.

10.5 PERI-IMPLANT DISEASE

Peri-implant disease is thought to be due to inflammation as a result of biofilm formation following bacterial colonisation of the oral implant and restoration surfaces.

It has been associated with predominantly Gram-negative anaerobic microflora.[22]

10.5.1 Peri-implant mucositis

Peri-implant mucositis is inflammation around the soft tissues of the dental implant, with no signs of bone loss. Generally, peri-implant mucositis if untreated leads to peri-implantitis.

Two RCTs showed no benefit of adjunctive antimicrobial therapy with mechanical therapy.[23,24] A systematic review of 11 RCTs showed that professionally and patient-administrative mechanical plaque control alone reduces bleeding on probing (BOP) and should be considered the standard of care.[25]

RECOMMENDATION

Systemic or local antimicrobials are not recommended for peri-implant mucositis, local measures to improve self-performed oral hygiene are the treatment of choice

Strong recommendation, low quality evidence

CLINICAL ADVICE

- Assess BOP and pocket depth
- Provide appropriate OHI and ensure that prosthesis facilitates this
- Mechanical debridement
- Prescribe antimicrobial mouthwash (very weak evidence)
- Review

10.5.2 Peri-implantitis

Peri-implantitis is an inflammatory disease of the soft tissues surrounding an implant, accompanied by bone loss and multifactorial pathogenesis.

In a Cochrane review, 9 RCTs using different treatment modalities were investigated. One of the RCTs compared metronidazole gel inserted into the pocket against

ultrasonic debridement. There was no significant difference in pocket depth between the groups.[26]

A further review of management of peri-implantitis failed to identify a clear benefit of any particular antimicrobial regimen over others or a control in the management of peri-implantitis.[27]

One RCT study compared azithromycin + RSD with RSD alone. It reported that the use of a 3 day azithromycin course resulted in a very slight statistical improvement in probing depth (~1mm) for 12 months.[28]

RECOMMENDATION

Antimicrobials are not recommended as an adjunct to local management of peri-implantitis

Conditional recommendation, very low evidence

CLINICAL ADVICE

- Assess BOP, pocket depth, bone loss and stability of the implant
- Assess short/long term prognosis of the implant
- Mechanical debridement + OHI
- Stabilise periodontal disease elsewhere
- Consider surgical management in the presence of bone loss
- Review

10.5.3 Apical peri-implantitis, retrograde peri-implantitis

This is a clinically symptomatic periapical lesion that develops shortly after implant insertion, while the coronal portion of the implant achieves a normal bone to implant interface.[29] A number of factors, which may all be related to infection, are believed to predispose to this condition.

No RCT studies have investigated the use of antimicrobials with or without a surgical

approach. A number of case reports have shown that systemic antimicrobials alone can be successful,[30] and that complete resolution cannot be achieved without a surgical approach because of the difficulties in eradicating bacterial colonies from the lesion.[31]

In the absence of clear evidence, and in line with AMS, it would be difficult to justify the prescribing of antimicrobials for this condition.

RECOMMENDATION

Antimicrobials alone, or as an adjunct to surgical management for the treatment of apical peri-implantitis, are not recommended

Conditional recommendation, very low quality evidence

CLINICAL ADVICE

- Attempt to identify the likely cause based on status of the surgical site, placement and technique, and medical history of patient
- Manage conservatively or surgically on a case by case basis

10.5.4 Antimicrobial drug choice

In the extremely rare situation where antimicrobials may be required for peri-implant diseases, see section 10.3.3.

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11 ENDODONTIC THERAPY

11.1 ACUTE PULPITIS

Pulpitis is described as either 'reversible' or 'irreversible'. With reversible pulpitis, the tooth may get better with time or by removal of the cause, or it may progress to irreversible pulpitis and necrosis of the pulp leading to an apical infection.

Topical antimicrobials containing preparations (e.g. ledermix) have been used in the management of pulpitis. There is no good scientific evidence to support the use of topical antimicrobials over other obtundents in the management of pulpitis. The accepted standard of definitive care for irreversible pulpitis is extirpation of the pulp of the affected tooth or extraction.

An RCT compared a placebo group to a group prescribed systemic penicillin for patients presenting with irreversible pulpitis. Antimicrobials did not significantly reduce toothache caused by irreversible pulpitis, and there was no reduction in the number of analgesics taken during the study period.[1] This was a low-powered trial assessed as at low risk of bias in a Cochrane review.[2] Ethical approval for more extensive trials is unlikely.

RECOMMENDATION

Antimicrobials are not recommended for acute pulpitis to prevent pain associated with pulpitis

Strong recommendation, moderate quality evidence

CLINICAL ADVICE

- Provide definitive treatment of the cause
- Prescribe or advise the use of analgesics (see NICE clinical knowledge summary, Analgesia – mild-to-moderate pain[3])

11.2 ACUTE AND CHRONIC PERIAPICAL INFECTIONS

Antimicrobials are not indicated in endodontic therapy (see chapters 4 and 5), unless there are signs of gross local spread of infection or evidence of systemic involvement. They are rarely indicated where drainage cannot be achieved immediately or treatment has to be delayed, e.g. for referral for peri-radicular surgery.

There is no indication for prophylactic antimicrobials before endodontic treatment to prevent endodontic flare-ups as shown with the use of amoxicillin in a prospective, double-blind and placebo-controlled RCT.[4] Administration of penicillin postoperatively in a prospective, double-blind and placebo-controlled RCT did not significantly reduce pain, percussion pain, swelling, or the number of analgesic medications taken for symptomatic necrotic teeth with periapical radiolucencies.[5]

RECOMMENDATION

Antimicrobials are not recommended for most endodontic treatment (see recommendations in chapters 4 and 5)**. Antimicrobials are also not recommended to prevent postoperative pain, swelling or endodontic flare-ups**

Strong recommendation, moderate quality evidence

CLINICAL ADVICE

- See chapters 4 and 5 for management of infections
- Follow existing guidelines on endodontic treatment, e.g. by the European Society of Endodontology[6]

11.3 REGENERATIVE ENDODONTIC PROCEDURES (REP)

Regenerative endodontic procedures (REPs) replace damaged tissues, including dentine, root structures and cells of the pulp-dentine complex.[7] In immature teeth with open apices and necrotic pulps, REPs promote root development and apical closure.[8]

A recent narrative review of the literature suggests high success rates of REP when local antimicrobials (two or three antimicrobial combination) are used as intracanal dressings to achieve disinfection.[9] There are no RCTs on the use and long term success of local antimicrobials against other methods available for REPs.[8]

The risks of using local antimicrobials for disinfection, such as discolouration from minocycline, cytotoxicity, sensitisation, difficulty of removal from the root canal, and more importantly, the development of resistance, should also be compared with using calcium hydroxide when weighing any benefit.

RECOMMENDATION

Local antimicrobials are not recommended for REPs
Conditional recommendation, very low quality evidence

11.4 TOOTH AVULSION

There are guidelines on the management of tooth avulsion which suggest that dentists should consider prescribing antimicrobials when re-implanting an avulsed tooth.[10,11] However, there are no indications for prescribing therapeutic antimicrobials in the absence of systemic infection (see section 4). For prophylactic prescribing of antimicrobials to prevent infection in the management of the avulsed tooth, see section 12.3.1.

RECOMMENDATION

Systemic therapeutic antimicrobials are not recommended when re-implanting avulsed teeth in the absence of systemic infection
Strong recommendation, low quality evidence

CLINICAL ADVICE

See International Association for Dental Traumatology guidelines (https://dentaltraumaguide.org/free-dental-guides/permanent-teeth/)[10]

- Full medical and dental history
- Comprehensive clinical assessment
- Assess the viability and prognosis of re-implantation (extraoral dry time, extra-alveolar time, storage medium, root length, apical status)
- Replant the tooth
- Splint
- OHI, soft diet
- Consider antimicrobial mouth wash
- Prescribe or advise the use of analgesics (see NICE clinical knowledge summary, Analgesia – mild-to-moderate pain[3])
- Assess the need for tetanus
- Review after 7-10 days
- Closed apex: begin RCT 7-10 days post-reimplantation
- Open apex: Monitor vitality and RCT if evidence of pulpal necrosis
- Radiographic review: at 4 weeks, 3 months, 6 months, 1 year, then annually

11.5 PERI-RADICULAR SURGERY

There are clinical situations when non-surgical root canal retreatment is inappropriate and peri-radicular surgery is the treatment of choice. A wide range of success rates for surgical endodontics has been reported (44-95%).[12]

There are no indications for therapeutic antimicrobials in the absence of a systemic infection (see section 4). For prophylactic use of antimicrobials for peri-radicular surgery, see section 12.1.3.

RECOMMENDATION

Therapeutic antimicrobials are not recommended for peri-radicular surgery in the absence of systemic infection

Strong recommendation, moderate evidence

CLINICAL ADVICE

- Good aseptic surgical technique
- Consider antimicrobial mouthwash
- Prescribe or advise the use of analgesics (see NICE clinical knowledge summary, Analgesia – mild-to-moderate pain[3])
- Advise cold compresses with an ice pack 4-6 hours after surgery to reduce postoperative swelling
- Review within 7 days
- Annual radiographic review until healing is observed

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12 ANTIMICROBIAL PROPHYLAXIS – HEALTHY PATIENTS

Antimicrobials have sometimes been prescribed to healthy patients for interventive dental procedures (IDPs) to prevent surgical site infections (SSIs), promote healing and reduce postoperative pain.

Antimicrobial prophylactic use remains a contentious issue in all surgical fields, particularly with the increasing development of antimicrobial resistance. Ideally, antimicrobials should reduce morbidity, but they can also cause adverse effects (e.g. allergy, toxicity) and increase colonisation resistance, resulting in infections with resistant micro-organisms.

12.1 MINOR ORAL SURGERY

12.1.1 Removal of impacted teeth, surgical extractions

A number of systematic reviews have concluded that there is no evidence to support the routine use of prophylactic antimicrobials in reducing the risk of postoperative complications after extraction of wisdom teeth, or teeth requiring surgical extraction.[1-3]

A Cochrane review concluded that 12 people would need to be given antimicrobial prophylaxis, compared to no antimicrobial prophylaxis, to prevent one surgical site infection for extraction of wisdom teeth. Thus, 38 people would need to take antimicrobial prophylaxis to prevent one case of dry socket, and one in 21 people would experience an adverse effect.[1]

Due to increasing antimicrobial resistance, clinicians should carefully consider whether treating twelve healthy patients with antimicrobials to prevent one infection is likely to do more harm than good.[1]

12.1.2 Removal of retained roots

No randomised controlled trials have investigated the effect of an antimicrobial against placebo in reducing the postoperative complications after removing retained roots. Currently, the evidence stems from studies related to wisdom teeth extraction which do not support the routine use of antimicrobial prophylaxis.[1]

12.1.3 Peri-radicular surgery

There are no reported studies demonstrating a high level of surgical site infections with peri-radicular surgery. In a systematic review of antimicrobial prophylaxis for oral procedures, one study specifically showed no differences compared to placebo in preventing infection after endodontic surgery.[4,5] Therefore, antimicrobial prophylaxis is not recommended for peri-radicular surgery.

12.1.4 Surgical removal of soft tissue lesions

No randomised controlled trials have investigated the effect of systemic antimicrobials against placebo in reducing postoperative complications after the removal of non-malignant soft tissue lesions.

An RCT provided some evidence that topical prophylactic oxytetracycline can reduce post-biopsy pain. It was unclear whether this was a result of the anti-inflammatory properties of tetracycline, rather than an antimicrobial effect, as the colonisation levels of microorganisms before and after treatment were not measured.[6]

The use of topical antimicrobials is not recommended as it could lead to antimicrobial resistance which would outweigh the benefit of its use.

RECOMMENDATION

Antimicrobials are not recommended to prevent postoperative complications after peri-radicular surgery, minor surgical removal of soft tissue lesions, extraction of impacted wisdom teeth, surgical extractions of teeth or retained roots

Strong recommendation, high quality evidence

12.1.5 Oral antral communications

Oral antral communications (OAC) may be the result of cysts, trauma, tumours, bisphosphonates or oral surgery. The extraction of maxillary posterior teeth is the most common cause of OAC.

It has been suggested by some authors that an OAC of less than 2mm in diameter tends to close spontaneously. Other authors suggest that sole suturing of the gingiva of less than 5mm allows healing, whereas those larger than 5mm require surgical closure. There is no evidence or consensus. Unless OACs are properly treated, it has been reported that approximately 50% of patients will experience sinusitis 48 hours later, and 90% of patients will develop sinusitis after two weeks of no treatment.[7]

Large acute OACs and cases where root or root fragments have been introduced into the sinus require immediate referral and specialist management within 48 hours.

No RCTs are available, but experts agree that because of the high risk of sinus infection immediately following an OAC, antimicrobials should be prescribed.

RECOMMENDATION

Antimicrobials are recommended to prevent acute sinusitis as a result of an OAC

Strong recommendation, very low evidence

12.1.5.1 Antimicrobial drug choices[8]

12.1.5.1.1 First choice

PHENOXYMETHYLPENICILLIN

Adults

500mg orally four times a day for up to 5 days

Children

12-17yrs: 500mg orally four times a day for up to 5 days

12.1.5.1.2 Second choice (penicillin allergy)

DOXYCYCLINE

Adults

Initially 200mg orally 1 dose for one day, then maintenance 100mg once a day for 4 days

Children

12-17 years: Initially 200mg orally 1 dose for one day, then maintenance 100mg once a day for a further 4 days

Or

CLARITHROMYCIN

Adults

500mg orally twice a day for up to 5 days

Children

12-17yrs: 500mg orally twice a day for up to 5 days

12.1.6 Dental implants

Dental implant procedures are graded as clean-contaminated surgery. Several systematic reviews reported that whilst the risk of implant failure (implant loss) was reduced when prophylactic antimicrobials were used, the incidence of postoperative infection (SSIs) did not significantly reduce.[9-11]

Antimicrobial prophylaxis for implant placement remains controversial. The number of patients needed to treat (NNT) with antimicrobial prophylaxis to prevent one patient having an implant failure in these studies ranged from 25-48. Clinicians should carefully consider any benefit in the context of increasing antimicrobial resistance and stewardship.

There are no RCTs comparing the effect of antimicrobial prophylaxis against no prophylaxis when oral bone augmentation procedures are used in conjunction with dental implant placement.

12.1.6.1 Dental implants without bone augmentation

A number of systematic reviews show that healthy patients undergoing implant surgery for straightforward cases did not benefit from antimicrobial prophylaxis.[12-14] One, a narrative summary of systematic reviews, suggests that the NNT is 50 patients with antimicrobial prophylaxis to prevent one implant failure.[12] A further systematic review and meta-analysis showed that there was a low level of postoperative infections and no significant differences in early, late or total postoperative infections. This study confirmed the findings of previous studies as it showed that antimicrobial prophylaxis is not indicated for prevention of SSIs following implant placement in healthy patients.[15]

However, for complex or compromised patients, a study and expert consensus suggests the results were inconclusive.[12,16]

12.1.6.2 Dental implants with bone augmentation

Cohort studies have suggested that surgical site infections range from about 4-10% in bone augmented implant procedures, even when antimicrobial prophylaxis is used, with contributory factors such as age, oral hygiene and smoking.[17] There also appears to be no difference in SSIs between autologous grafts and allogenic, alloplastic or xenografts.

A small placebo-controlled double blind trial concluded that there was a statistically significant increased risk of having an infectious complication after an intraoral bone graft without antimicrobial prophylaxis.[18] In an RCT comparing preoperative penicillin with clindamycin, there was no difference in infection rates. The infection rates were also found to be low.[19]

Case studies have shown that surgical site infection rates are similar after bone augmented implant placement with preoperative or pre- and postoperative prophylactic antimicrobials. It is, therefore, accepted practice to use a single dose preoperatively.[20-23]

RECOMMENDATIONS

Antimicrobials prophylaxis is not routinely recommended for placing dental implants
Strong recommendation, moderate quality evidence

Antimicrobial prophylaxis is recommended for intraoral bone augmentation when placing dental implants
Strong recommendation, low quality evidence

12.1.6.3 Prophylactic antimicrobial drug regimens

The BNF does not provide advice on prescribing prophylactic antimicrobials for dental treatment. The choice of antimicrobial for prophylaxis should cover the organisms most likely to cause postoperative infections and take the patients' medical and drug history into account.

A systematic review and network meta-analysis on antimicrobial prophylaxis protocols in implant placement concluded that there is insufficient evidence to confidently recommend a specific dosage of amoxicillin, but that the following is effective:[24]

12.1.6.3.1 First choice

AMOXICILLIN

Adults: 3g orally one hour before surgery

12.1.6.3.2 Second choice

In the absence of any published scientific literature for patients allergic to penicillin, clindamycin has been suggested.[13] Clinicians are reminded of the risk of significant morbidity/mortality associated with *Clostridium difficile* when prescribing clindamycin. As this in an important risk to consider, it should be included in consent when prescribing clindamycin.

CLINDAMYCIN

Adults: 600mg orally (4x150mg) one hour before surgery

12.1.7 Regenerative and non-regenerative periodontal surgeries

Surgical site infection rates in regenerative periodontal surgeries is extremely low.[25] In a literature review of RCTs, no statistically significant difference was found in SSI rate (<1%) when using antimicrobial prophylaxis compared to no prophylaxis for periodontal surgery.[26,27]

When enamel matrix derivatives (EMD) were used for the surgical treatment of intrabony periodontal defects, the use of prophylactic antimicrobials did not produce statistically superior pocket depth (PD) reduction and clinical attachment level (CAL) gain when compared to treatment with EMD alone in RCTs.[28-30]

There is no evidence of benefit to support the use of antimicrobial prophylaxis with membranes when used as part of guided tissue regeneration (GTR).[31] Similar outcomes are achieved whether antimicrobial prophylaxis is used or not.

RECOMMENDATION

Antimicrobials are not recommended to prevent postoperative complications for non-regenerative or regenerative periodontal surgeries using EMD or GTR

Strong recommendation, very low quality evidence

12.2 MAXILLOFACIAL SURGERY

12.2.1 Open reduction fractures

Open reduction internal fixation (ORIF) is the treatment of choice for mandible fractures. In a systematic review, 4 RCTs showed no postoperative infections related to maxillary, condylar or zygomatic fractures. There was a decrease in the infection rate of mandibular fractures in the antimicrobial treated groups compared with the control groups.[32]

A further systematic review including RCTs and case series suggested that the overall evidence for the use of prophylactic antimicrobials is poor due to observational studies of poor quality and RCTs of overall low quality.[33]

Evidence from a prospective RCT confirms that there is no benefit from postoperative as well as preoperative antimicrobials.[34] It is generally accepted that a single full therapeutic dose is given no more than 60 minutes prior to surgical incision to prevent SSIs.[35]

An antimicrobial for prophylaxis should cover the organisms most likely to cause infection. It should also take the local resistance patterns and the patient's medical and drug history into account, and be based on local prescribing policies/formularies.

RECOMMENDATION

Antimicrobial prophylaxis is normally only recommended for open reduction of mandibular fractures

Strong recommendation, low quality evidence

12.2.2 Orthognathic surgery

Orthognathic surgery is classed as major clean contaminated maxillofacial surgery. Postoperative infection rates vary between 2% and 33%,[36] therefore, antimicrobial prophylaxis is indicated.

The quality of evidence from RCTs and case series available is very weak and there is still no consensus on the efficacy of antimicrobial prophylaxis, the appropriate drug, and the dose and duration of administration for orthognathic surgery. There is some evidence to support the use of one dose of preoperative antimicrobial prophylaxis to reduce the postoperative infection rate in orthognathic surgery.[36-38]

RECOMMENDATION

Antimicrobial prophylaxis is recommended for orthognathic surgery
Strong recommendation, very low quality evidence

12.2.3 Intraoral bone grafting

There is a paucity of evidence on whether antimicrobial prophylaxis is indicated when block bone grafts are inserted intraorally. One randomised controlled double-blind study showed that there was a statistically significant increased risk of having an infection after an intraoral bone grafting procedure when antimicrobial prophylaxis was not used.[18]

RECOMMENDATION

Antimicrobial prophylaxis is recommended for intraoral bone grafts
Strong recommendation, very low quality evidence

12.2.4 Soft tissue surgery and grafting

Surgical procedures in the maxillofacial region in which the incision and exposure does not extend into the oral cavity, including submandibular and parotid gland surgery and TMJ surgery, are classed as clean surgical procedures.

A prospective RCT showed that there was no benefit of prophylactic antimicrobials in revision clean head and neck surgery.[39] NICE, in its guideline on the prevention and management of surgical site infections, does not support the routine use of antimicrobial prophylaxis for clean surgical procedures.[40]

There are no RCTs investigating placebo vs. antimicrobial prophylaxis in intraoral soft tissue grafting. However, there is evidence that antimicrobial prophylaxis is not required in regenerative periodontal surgeries (see section 12.1.7).

RECOMMENDATION

Antimicrobial prophylaxis is not recommended for soft tissue surgery and grafting

Strong recommendation, very low quality evidence

12.2.5 Major head and neck oncology surgery

In major head and neck oncology surgeries with excision of malignant lesions, RCTs established the need for prophylactic antimicrobials as the wound infection rate with placebo ranged from 20% to 78%, compared with 10% to 25% with those who received prophylaxis.[41,42]

A systematic review provided evidence that there is no difference in the risk of wound infection with 1 day vs. 5 days of systemic antimicrobial prophylaxis in clean-contaminated head and neck surgery, but that no specific antimicrobial could be recommended due to insufficient data.[43]

RECOMMENDATION

Antimicrobial prophylaxis is recommended for head and neck oncology surgery

Strong recommendation, very low quality evidence

12.2.6 Prophylactic antimicrobial drug regimen

The choice of antimicrobial for prophylaxis should cover the organisms most likely to cause infection, take local resistance patterns and patients' medical and drug history into account, and be based on local prescribing policies/formularies. There is strong evidence that a pre-operative single full therapeutic dose one hour before surgery is effective.[35,43]

12.3 REIMPLANTATION OF TEETH

12.3.1 Reimplanting an avulsed tooth

A number of guidelines suggest that antimicrobials should be considered when re-implanting an avulsed tooth.[44-46] Some guidelines suggest that it might be prudent to consider antimicrobial prophylaxis in certain circumstances, e.g. medical history.[46]

In a systematic review and meta-analysis, it was concluded that there was no clinical evidence clearly contradicting or supporting existing guidelines. Also, there was no significant association between prescribing systemic antimicrobials and improved pulp or periodontal outcomes.[47]

It is generally accepted that the evidence for prescribing antimicrobials for reimplantation of an avulsed tooth is very poor. There is also no scientific evidence to recommend one antimicrobial regimen over another.

Dentists should be aware of the risks of adverse effects of antimicrobial resistance to the individual and the population as a whole when considering prescribing antimicrobial prophylaxis for reimplantation of an avulsed tooth.

RECOMMENDATION

Antimicrobial prophylaxis is not routinely recommended for the avulsed tooth in a healthy patient

Strong recommendation, very low quality evidence

CLINICAL ADVICE

- See section 11.4

12.3.2 Auto transplantation

Auto transplantation, or autografts, involve transplantation of a tooth from its alveolus to another site in the same person. A donor tooth (allograft) can be transplanted from another person. The donor teeth commonly used are third molars or premolars.

There are no RCTs comparing the success of using antimicrobial prophylaxis against no antimicrobial prophylaxis in auto transplantation. Some case studies suggest that antimicrobial prophylaxis improves the likelihood of having a good outcome with auto transplantation.[48,49]

A systematic review of outcomes of autotransplanted teeth suggested, following a comparison of observational studies with and without antimicrobial prophylaxis, that the failure rate was 2.5 times higher in studies not using antimicrobial therapy than in those using it.[50] The studies in this review used a variety of antimicrobial regimens (antimicrobial, dose, timing, frequency) and as such, there was no scientific evidence to recommend one antimicrobial regimen over another.

Clinicians should carefully consider any benefit in antimicrobial prophylaxis against increasing AMR and responsibility for AMS before prescribing.

RECOMMENDATION

Antimicrobial prophylaxis may be indicated for auto transplantation
Conditional recommendation, very low quality evidence

CLINICAL ADVICE

- Excellent aseptic surgical technique
- Follow standard procedure for transplantation[51]
- Consider risk/benefit of antimicrobial prophylaxis preoperatively
- Splint for 1-2 months
- RCT when tooth is stable
- Orthodontic/restorative treatment as necessary
- Radiographic review to check root development/resorption

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13 ANTIMICROBIAL PROPHYLAXIS – MEDICALLY COMPROMISED PATIENTS

Antimicrobial prophylaxis (AP) for interventive dental procedures (IDPs) for medically compromised patients remains controversial. In the past, antimicrobials have been prescribed prophylactically to prevent bacteraemias and metastatic infections occurring as a result of IDPs.

The evidence for bacteraemias associated with IDPs has been reviewed, specifically in relation to cardiac patients. It was concluded by the British Society of Antimicrobial Chemotherapy (BSAC) and the National Institute for Health and Care Excellence (NICE) that the magnitude and frequency of bacteraemias resulting from normal oral function (e.g. chewing, toothbrushing) is greater than from IDPs.[1,2]

13.1 CARDIAC DISEASE

The evidence for antimicrobial prophylaxis to prevent infective endocarditis (IE) was not reviewed for this guideline in light of the comprehensive review by NICE and their recent update.[2]

Whilst dental procedures can cause bacteraemia, there is no clear association with the development of IE. Transient bacteraemias from normal function are the likely cause. Prophylaxis may expose patients to the adverse effects of antimicrobials when the evidence of benefit has not been proven.[2]

Dentists should ensure that episodes of infection in people at risk of IE are investigated and treated promptly to reduce the risk of endocarditis developing.

RECOMMENDATION

Antibacterial prophylaxis is not routinely recommended for the prevention of infective endocarditis in patients undergoing dental procedures
(see NICE guideline CG64)[2]
Strong recommendation, moderate quality evidence

Dentists should be aware of the Scottish Dental Clinical Effectiveness Programme's implementation advice for NICE CG64. This re-emphasises the NICE CG64 recommendations, but notes that there are a very small number of dental patients that may require 'special consideration' for antimicrobial prophylaxis.[3]

CLINICAL ADVICE

- Take a comprehensive medical history
- Assess whether the patient is a 'special consideration' for antimicrobial prophylaxis
- Seek advice from patient's cardiologist
- Assess likelihood of interventive dental treatment
- Discuss the risks and benefits of antimicrobial prophylaxis with the patient and explain why antimicrobial prophylaxis is no longer routinely recommended for dental treatment
- Decide on antimicrobial prophylaxis appropriate to the circumstances of the individual and in consultation with them, their cardiologist, their families and carers or guardian
- Stress the importance of maintaining good oral health
- Discuss symptoms with the patient that may indicate infective endocarditis and when to seek expert advice

13.2 TOTAL JOINT REPLACEMENTS

It has been hypothesised that oral bacteria leads to prosthetic joint replacement infections, but the evidence is unproven and relies on anecdotal case reports.[4]

A systematic review including nine studies and additional consulted literature explored the risk of dental interventions and subsequent artificial joint infection. The study concluded that there was no evidence that use of antimicrobial prophylaxis reduces the incidence of joint infection.[5] The BSAC advises that patients with prosthetic joint implants (including total hip replacements) do not require antimicrobial prophylaxis for dental treatment.[6]

RECOMMENDATION

Antimicrobial prophylaxis is not recommended for dental procedures in patients with joint replacements

Strong recommendation, low quality evidence

13.3 MISCELLANEOUS PROSTHETIC IMPLANTS

Patients who have undergone penile, breast, cardiac pacemakers or intraocular implants have never been considered susceptible to infection as a result of IDPs.[6,7] There is no strong evidence to support that these implants are susceptible to dental procedure based infection.[8]

RECOMMENDATION

Antimicrobial prophylaxis is not recommended for dental procedures in patients with cardiac pacemakers, penile, breast or intra-ocular implants

Strong recommendation, very low quality evidence

13.4 RENAL DIALYSIS

Evidence for antimicrobial prophylaxis for patients on dialysis undergoing IDPs is lacking. The risk of infection involves that of vascular access for sites for dialysis (fistula, vascular grafts, and catheters). It has been suggested that there is a theoretical risk that these sites (vascular graft sites of collagen or polyurethane) may be vulnerable to secondary infection as a result of a dental procedure.

There is no clear evidence of metastatic infections resulting from dental procedures in patients receiving renal dialysis, despite patients with end stage renal disease (ESRD) also having complications, including increased cardiovascular risk, cardiogenic pulmonary oedema.[9]

The BSAC recommends that prophylaxis is not required for these patients.[6]

RECOMMENDATION

Antimicrobial prophylaxis for patients undergoing renal dialysis is not normally recommended for dental procedures

Strong recommendation, very low quality evidence

CLINICAL ADVICE

- Consider advice on antimicrobial prophylaxis from renal specialist if there are co-morbidities
- Advise the patient of the need for good oral health
- Provide oral hygiene instruction and dietary advice
- Consider the need for more regular recall examinations

13.5 INTRAVENOUS ACCESS DEVICES

These include central intravenous lines/indwelling catheters used for parenteral nutrition or chemotherapy, and catheters for haemodialysis. There is no scientific evidence of infection of these devices arising from IDPs. The BSAC recommends that antimicrobial prophylaxis is not required for dental treatment.[6]

RECOMMENDATION

Antimicrobial prophylaxis is not required for dental procedures in patients with intravenous access devices

Strong recommendation, very low quality evidence

13.6 IMMUNOCOMPROMISED PATIENTS

Immune function may be impaired by a range of conditions, such as leukaemia, immunosuppressive drugs following organ transplantation, lymphomas, chemotherapy, radiotherapy, poorly controlled diabetes and HIV. As a result, this group of patients are susceptible to opportunistic infections.

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

There is no evidence to support the increased risk of infection from dental procedures or increased risk of surgical site infections (SSIs) arising as a result of dental procedures in these patients.

13.6.1 Diabetes

Diabetes, particularly if poorly controlled, results in increased inflammation and infection risk. Regardless of their diabetic control, dental infections should be treated aggressively and with antimicrobials where indicated, e.g. evidence of systemic spread (see chapter 4).

A review of prophylactic antimicrobial use in diabetic dental patients concluded that well-controlled Type 1 and Type 2 were not a risk for postoperative surgical complications, and that prophylactic antimicrobials should not be prescribed other than in cases where they are indicated in a non-diabetic patient.[10]

A literature review could find no evidence of increased risk of postoperative infections or efficacy of prophylactic antimicrobials in reducing postoperative infections in diabetic patients undergoing surgical dental procedures.[11]

Further, a prospective cohort study showed that in the presence of impaired neutrophil function and poor glycaemic control, there was no increase in post extraction complications.[12]

RECOMMENDATION

Antimicrobial prophylaxis is not recommended routinely for diabetic patients undergoing dental procedures

Strong recommendation, low quality evidence

CLINICAL ADVICE

- Take a comprehensive history including control of diabetes
- Ensure the patient will not undergo hypoglycaemia on the day of treatment
- Prescribe antimicrobials only if indicated for other reasons than diabetes
- Avoid aspirin and corticosteroids as they may have an effect on hypoglycaemic medications
- Refer for specialist advice/management if other significant co-morbidities

13.6.2 HIV

There are no contraindications and few complications associated with comprehensive oral healthcare for these patients. The majority of HIV infected patients are medically stable. For HIV infected individuals, the medical history impacting on the delivery of dental care will not be related to HIV immunosuppression, but to non-HIV associated conditions.

A review of several retrospective and cohort studies shows low infection rates following dental procedures. The rates were comparable with non-HIV patients and none of the studies showed a significant relationship between decrease of infection rate and use of antimicrobial prophylaxis.[13-16]

There is no data to support routine antimicrobial prophylaxis for dental procedures in patients with HIV disease based solely on CD4+ counts before invasive procedures, even when the CD4+ counts are less than 200 cell/mm3.[17]

Less than 1% of HIV infected patients develop severe neutropenia.[18] Although there are no specific recommendations regarding the need for antimicrobial prophylaxis,

patients with severe neutropenia (<500 cells/mm3) should be discussed with the patient's haematologist.

RECOMMENDATION

Antimicrobial prophylaxis is not routinely recommended for HIV patients undergoing dental procedures

Strong recommendation, very low quality evidence

CLINICAL ADVICE

- Take a comprehensive medical history
- Consult with HIV specialist and other medical providers when patients have advanced HIV disease or major comorbidities
- No antimicrobials are indicated unless required for alternative clinical indications
- Provide comprehensive oral healthcare
- Review the need for more frequent recall appointments

13.6.3 Chemotherapy

Many patients undergoing chemotherapy will have significant neutropenia which has led to concerns regarding the risk of developing an infection as a result of dental surgery in the form of SSIs, fever, or sepsis.

It is generally accepted that establishment of good oral health prior to chemotherapy and delay of elective and non-urgent treatment will reduce any likelihood of dentally induced infections.

Infections of dental origin should be aggressively managed by removal of the cause and appropriate use of antimicrobials in consultation with the patient's oncologist. It is most likely that hospital inpatients will be undergoing antimicrobial prophylactic therapy dictated by an oncologist/haematologist.

There is no evidence that dental procedures produce a higher level of SSIs in patients undergoing chemotherapy compared to healthy patients. The BSAC working party has stated that there is also no evidence that dental treatment is followed by a metastatic infection in immunosuppressed or immunodeficient patients.[6] There is no evidence of efficacy of antimicrobial prophylaxis for dental treatment provided to patients undergoing chemotherapy.[9]

RECOMMENDATION

Antimicrobial prophylaxis for dental procedures is not normally recommended for patients undergoing chemotherapy

Strong recommendation, very low quality evidence

CLINICAL ADVICE

- Take a comprehensive medical history
- Stress the importance of good oral health
- Discuss management of dental treatment with the patient's oncologist
- No routine antimicrobials unless indicated for alternative medical reasons
- Treat if possible outside the chemotherapy cycle

13.6.4 Radiotherapy

Radiotherapy carries a risk of osteoradionecrosis (ORN). ORN is an area of exposed devitalised irradiated bone that fails to heal for three months or longer. it can occur spontaneously due to periodontal or apical disease, trauma from dentures, or after surgery or tooth extraction.

A systematic review of ORN suggests that there is an incidence of 7% for extractions reducing to 6% with prophylactic antimicrobials.[19] The risk of developing ORN persists for years after radiotherapy, but evidence of the risk of developing ORN after extraction of teeth outside the field of radiation is almost non-existent.[20]

There are no RCTs or prospective cohort studies to assess the efficacy of prophylactic

antimicrobials in preventing ORN in patients who have undergone radiotherapy to the head and neck. Routine use of prophylactic antimicrobials for dental extractions to prevent ORN is not supported.

Patients who have undergone radiotherapy to the area of the extraction should be referred for specialist management. Access to the radiation records of dosage and radiation field will enable a reliable assessment of the risk of developing ORN post extraction.[21]

RECOMMENDATION

Antimicrobial prophylaxis may be recommended for dental extractions following an assessment of the risk of developing ORN
Conditional recommendation, very low quality evidence

CLINICAL ADVICE

- Ensure good oral health prior to starting any radiotherapy treatment
- Extractions should be done and healing complete prior to radiotherapy
- Referral post radiotherapy to a specialist for risk assessment and management of extractions
- Antimicrobial prophylaxis should be given where clearly indicated
- Long term follow-up after extractions
- Management of ORN if present (see chapter 12)

13.6.5 Solid organ transplants

An increasing number of people are receiving organ transplants and thus living longer, with dental professionals playing an important role in their management.

The transplant patient is at greater risk of infection immediately following transplant because of maximal immunosuppression. As a result of lifetime antirejection medication, they remain immunosuppressed.[22]

There is no evidence that dental treatment is followed by metastatic infections or increased SSIs in immunosuppressed or immunodeficient patients, or that prophylactic antimicrobials are required.[6]

A systematic review showed that the evidence supporting the use of prophylactic antimicrobials for dental procedures in solid organ transplant patients is lacking.[9] There is also a lack of consensus, lack of evidence of efficacy, potential adverse interactions and reported concern that antimicrobial prophylaxis predisposes to the risk of infection by opportunistic organisms in these patients.[22] Oral health providers should discuss the transplant patient's overall health status with their physician and transplant team prior to undertaking dental procedures.

Any dental infections in these patients should be treated aggressively and antimicrobials should be prescribed where there is an indication (e.g. spreading infection) and in consultation with their physician.

RECOMMENDATION

Antimicrobial prophylaxis is not routinely required for patients with solid organ transplants prior to interventive dental procedures
Conditional recommendation, very low quality evidence

CLINICAL ADVICE

- Dental health assessment and treatment prior to transplant surgery
- No dental treatment (stabilisation only for emergencies) for the first 6 months after transplant surgery
- Discuss overall health, dental treatment and the need for antimicrobial prophylaxis on a case by case basis with the medical/surgical team
- Stress the importance of good oral health and regular recalls

13.6.6 Tumours of haemopoietic and lymphoid tissue

Patients with suppressed and/or impaired immune system acquired as a result of these

tumours or management with immunosuppressive drugs may be at risk of septicaemia as a result of dental infections. Various levels of neutropenia have been proposed at certain thresholds for antimicrobial prophylaxis in these patients when undergoing invasive dental interventions.[23]

A systematic review concluded that there is no evidence that these patients succumb to systemic infections or increased SSIs as a result of dental procedures. It is generally accepted that antimicrobial prophylaxis for dental procedures in the afebrile and asymptomatic immunosuppressed patient to prevent infections is not required.[9]

Dental infections should be treated aggressively with antimicrobials where indicated, e.g. spreading infections. Careful evaluation of haematological parameters and consultation with the patient's medical management team during their treatment should be instituted prior to any invasive dental treatments.

RECOMMENDATION

Antimicrobial prophylaxis for dental procedures is not routinely recommended for patients with haemopoietic or lymphoid tumours
Conditional recommendation, very low quality evidence

CLINICAL ADVICE

- Patients are best managed by specialists
- Dental assessment and treatment should be prior to chemotherapy and stem cell treatment
- Consultation and risk assessment of dental procedures during treatment and need for antimicrobial prophylaxis with haematologist/transplant team
- Prescribe antimicrobials where indicated
- Importance of maintaining good oral health during and post treatment

13.6.7 Prevention of medication related osteonecrosis of the jaw

Patients who are prescribed anti-resorptive or anti-angiogenic drugs may have a risk

of medication related osteonecrosis of the jaw (MRONJ) resulting from dental procedures involving the bone, especially extractions. Estimates of risk vary depending on drug treatment regimen, medical diagnosis (e.g. type of cancer or osteoporosis) from 0.1% to 2%.[24,25]

In a review of the literature and existing guidelines, it is strongly recommended that prior to anti-resorptive or anti-angiogenic medication, patients undergo an assessment, remedial treatment and preventive care.[26]

There are no RCTs investigating the efficacy of antimicrobial prophylaxis in preventing MRONJ in dental patients undergoing procedures involving bone. Dentists should balance the very low risk of MRONJ against the side effects and toxicity associated with antimicrobials and the effects of antimicrobial resistance for the individual and the wider population.

RECOMMENDATION

Antimicrobial prophylaxis is not recommended for dental procedures to prevent MRONJ

Strong recommendation, low quality evidence

CLINICAL ADVICE[26]

- Assess, treat and provide preventive advice prior to medical treatment
- Discuss risk of MRONJ with patients taking antiresorptive or antiangiogenic medication
- Refer medically complex patients for specialist advice or treatment
- Provide appropriate treatment including procedures involving bone
- Do not prescribe prophylactic antimicrobials
- Advise patient of clinical signs/symptoms of MRONJ and importance of seeking advice
- Review the patient for healing at approximately 8 weeks
- Refer for specialist management if MRONJ is present (see section 5.3)

13.7 PROPHYLACTIC ANTIMICROBIAL REGIMENS

The BNF does not provide advice on prophylactic antimicrobial regimens for dental treatment to prevent metastatic infections or surgical site infections in patients who are medically compromised.[6] The choice of antimicrobial for prophylaxis should cover the organisms most likely to cause infection, take account of local resistance patterns and patients' medical and drug history.

If antimicrobial prophylaxis is deemed necessary for dental procedures due to the patients' medical history, the antimicrobial choice and regimen should be based on a consultation with the treating medical team and local prescribing policies/formularies.

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14 VIRAL INFECTIONS

Viral infections can manifest themselves in the oral cavity, are initially diagnosed on their clinical presentation and tend to be short lived. These include herpes simplex virus, varicella zoster virus, human immunodeficiency virus, coxsackie virus and paramyxovirus. Infections with herpes simplex are the most common and can usually be managed with supportive therapy.

Caution is necessary in patients who are severely immunocompromised or are unable to take fluids and at risk of dehydration. These patients should be referred to hospital for specialist care. In addition, patients with prolonged infections that fail to resolve should be referred for further investigation.

Management of oral viral infections is symptomatic and usually involves:

- Rest
- Plenty of fluids
- Soft diet
- Antipyretic analgesics
- Antimicrobial mouthwash to reduce secondary infection. Chlorhexidine or hydrogen peroxide are suitable agents. The use of benzydamine mouthwash may provide some pain relief

A small number of patients may require antivirals. Nucleoside analogues, e.g. aciclovir are available for topical application. Aciclovir, valaciclovir or famciclovir can be given orally in suspension or tablet formulations where indicated.

14.1 PRIMARY HERPETIC GINGIVOSTOMATITIS

This is caused by the herpes simplex virus (HSV) and most commonly presents in young children.[1] The incubation period is approximately five days and infection can

be subclinical. Management is primarily with supportive measures as outlined above.

In severe cases, a full case assessment is required (see chapter 3) to assess for raised temperature, swollen lymph nodes, malaise, dehydration or if patients are immunocompromised. These patients may require systemic intravenous antiviral therapy and should be referred for urgent hospital treatment.

In uncomplicated cases, a systematic review suggests that there is some weak evidence of aciclovir being an effective treatment in reducing the number of oral lesions, preventing the development of new extraoral lesions, decreasing the number of individuals with difficulties experienced in eating and drinking, and reducing hospital admission for children under 6 years.[2]

RECOMMENDATION

Antivirals are only recommended for the management of severe cases of primary herpetic stomatitis

Strong recommendation, low quality evidence

CLINICAL ADVICE

- Assess severity, raised temperature, lymphadenopathy
- Assess immunocompetency
- Rapid detection using PCR for immunocompromised patients
- Local measures: soft diet, hydration
- Advise analgesics if necessary (see NICE clinical knowledge summary, Analgesia – mild-to-moderate pain[3])
- Management with antivirals if indicated
- Review patient
- Refer if failure to respond to a specialist to exclude underlying systemic condition

14.1.1 Antiviral drug choice

ACICLOVIR

Adults

Aciclovir 200mg five times a day for five days (longer if new lesions appear during treatment or if healing incomplete)[3,4]

Children

- 1-23 months: 100mg five times a day for five days (longer if new lesions appear during treatment or if healing incomplete)
- 2-17 years: 200mg five times a day for five days (longer if new lesions appear during treatment or if healing incomplete)

14.2 SECONDARY (RECURRENT) HERPES SIMPLEX INFECTIONS (HSV-1)

Synonyms: **herpes labialis, cold sores**

Following a primary herpetic gingivostomatitis infection, herpes simplex remains latent in the trigeminal ganglion. Approximately one third of people develop herpes labialis and a secondary infection from reactivation of the virus.

Patients who are immunocompromised with frequent, persistent or troublesome recurrent HSV, have atypical lesions or an uncertain diagnosis, should be referred to a specialist for management.

A Cochrane systematic review concluded that long-term use of oral antiviral agents can prevent herpes simplex labialis, but the clinical benefit is small. The evidence on topical antiviral agents and other interventions either showed no efficacy or confirmation of efficacy in preventing HSV.[5]

A systematic review of 12 RCTs conducted with healthy patients to compare topical aciclovir or penciclovir with placebo, found that these agents may reduce pain and healing time. However, the results of the studies were inconsistent and of marginal clinical importance.[6]

RECOMMENDATION

Topical antiviral preparations are not routinely recommended for herpes simplex infections

Strong recommendation, moderate evidence

CLINICAL ADVICE

- Assess medical history, particularly immunocompetency
- Assess for any red flags for serious underlying disease
- Refer if concern or uncertainty of diagnosis
- Arrange further investigation if unexplained recurrent, severe or persistent
- Reassure the patient that these are self-limiting and usually heal without scarring
- Provide advice on minimising risk of transmission and avoiding trigger factors
- Over the counter topical preparations may be helpful, e.g. lip barriers or moisturising balm
- Consider prescribing oral antivirals for severe, frequent or persistent lesions

14.2.1 Antiviral drug choice

ACICLOVIR

Adults and children all ages

Apply aciclovir cream 5% to lesions every four hours (five times daily) at first signs of infection

For oral dose for immunocompromised patients, see section 14.1.1

14.3 OROFACIAL VARICELLA ZOSTER INFECTIONS

Synonyms: shingles

Systemic antivirals are advised in patients with herpes zoster infections as they have been found to reduce the incidence of postherpetic neuralgia and viral shedding.[7]

The reduction in viral load is beneficial as it can reduce the risk of corneal infection. Treatment with antivirals should be commenced as soon as possible and within 72 hours of the onset of the rash.

Patients with ophthalmic involvement, who are severely immunocompromised and systemically unwell, or have a severe or widespread rash, multiple dermatomal involvement or symptoms of erythema multiforme, should be referred for specialist treatment.[8] The same applies to immunocompromised children and pregnant or breastfeeding women.[8]

Evidence from a meta-analysis of four randomised trials suggests that aciclovir is more effective than placebo at reducing the duration of pain associated with herpes zoster infection.[8]

A double-blind, randomised trial evaluated the efficacy of oral aciclovir with and without prednisolone for 7 days, or 21 days in acute herpes zoster and postherpetic neuralgia. Aciclovir alone reduced the extent and duration of the pain, the spread of the rash and healing. Prolonged therapy conferred a very slight benefit over the standard 7 day treatment with aciclovir.[9]

RECOMMENDATION

Antivirals are recommended for orofacial varicella zoster infections
Strong recommendation, high quality evidence

CLINICAL ADVICE

- Check that these dental patients are under medical care
- Assessment of clinical signs, symptoms and need for dental treatment
- Avoid elective/routine dental treatment if vesicles are open in the orofacial area

continued on next page

- Provide emergency dental care following standard infection prevention and control procedures
- Antivirals should be started as soon as possible, preferably within 72 hours of the onset of the rash
- Advise patient of infectious nature until vesicles crusted over and importance of self-care
- Refer for urgent specialist management if Hutchinson's sign (vesicles tip or side of the nose), visual symptoms are noted or the patient is immunocompromised child or adult, or pregnant or breast feeding woman
- Refer for specialist management if vesicles fail to heal, new vesicles are forming despite 7 days of antivirals or the patient has had two episodes

14.3.1 Antiviral drug choice[10]

ACICLOVIR

Adults

Aciclovir: 800mg five times a day for 7 days at 4-hourly intervals omitting night time dose

Or

VALACICLOVIR AND FAMCICLOVIR

These are not available within the Dental Practitioner's Formulary. Dental specialists should assess the need to prescribe these as an alternative to aciclovir and consult their local prescribing formulary

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15 FUNGAL INFECTIONS

There are a number of oral fungal infections, some of which are rare, e.g. aspergillosis, histoplasmosis and cryptococcosis. Most oral fungal infections are caused by imperfect yeasts belonging to the genus *Candida*.

15.1 ORAL CANDIDOSIS

Oral candidosis (candidiasis) is most notably associated with *Candida albicans*. Other *Candida* species are found as commensals in the oral mucosa and may be putative pathogens (e.g. *C glabrata*, *C tropicalis*, *C krusei*, *C auris*).

Candida species carriage in the oral cavity, particularly on the dorsum of the tongue, is observed in up to 65% of patients' mouths, with higher colonisation levels in young children and denture wearers. Recurrent infections are problematic in patients where the risk factors or underlying disease cannot be readily eliminated or controlled.

Clinicians should always be mindful that a number of underlying factors predispose to oral candidosis:[1]

- Physiological: elderly, infants, pregnancy
- Local factors: dry mouth, radiotherapy, poor oral hygiene, oral appliance wear, smoking
- Medical: antimicrobial therapy, systemic and inhalation steroid therapy, immunosuppressive medication
- Nutritional: iron, folate, vit B12 deficiencies, anaemia
- Systemic: endocrine disorders including diabetes
- Immune disorders: HIV infection, AIDS
- Malignancy: acute leukaemia, agranulocytosis
- Dry mouth: result of radiation, drug therapy, Sjogren's syndrome

Several classifications of oral fungal infections have been used, but the most frequently adopted divides the infection into primary oral candidosis (localised to oral and perioral tissues) and secondary oral candidosis (generalised candida infections of mucosal membranes and cutaneous surfaces of the body).[2]

Candida infections are superficial or invasive. Superficial infections often affect the mucous membranes and can be treated successfully with topical antifungal drugs. When invasive, they enter the bloodstream causing systemic infections requiring oral or intravenous systemic antifungals.

Clinically, oral candidosis presents as four main variants: pseudomembranous, erythematous, hyperplastic and candida associated lesions.

15.1.1 Pseudomembranous candidosis

Synonyms: thrush, pseudomembranous candidosis

This condition is characterised by creamy white plaques, which diagnostically can be dislodged to leave raw bleeding mucosa. These lesions can appear on any part of the oral mucosa and pharynx. The various factors causing this condition are detailed in section 15.1.[1]

Antifungal therapy is the mainstay of treatment, both therapeutically to treat infections and prophylactically to prevent infections, in medically compromised patients along with local measures, such as:

- Good oral hygiene
- Denture/appliance hygiene
- Rinsing with water following using a corticosteroid inhaler, use of spacer device
- Antimicrobial rinses

In a systematic review, prophylactic antifungals, such as fluconazole, are shown to be more effective than oral nystatin at reducing the proportion of people who develop oral candidosis. This applies to people having chemotherapy or radiotherapy for cancer. It is also shown that it is more effective at preventing candidosis in immunocompromised infants, children and people with AIDS, AIDS-related complex, or CD4+ cell counts of 300 cells/microlitre or less.[3]

Prophylactic use in immunocompromised patients to prevent oral candidosis should be managed by the patient's medical team (haematologist) as part of their treatment.

In a surveillance study of antifungal susceptibility of oral candidal isolates in the UK, oral *Candida* species were shown to have a high level of susceptibilities to a range of antifungal agents.[4] Nevertheless, there is increasing evidence of the development of antifungal resistance.

The recommended therapeutic management of fungal infections is with nystatin suspension, miconazole or fluconazole.[5] Both miconazole and fluconazole seem more effective than nystatin at rates of clinical cure of oral candidosis in immunocompetent and immunocompromised infants and children.[6-8]

Fluconazole is effective for unresponsive infections if a topical antifungal drug cannot be used or if the patient has dry mouth.[5]

RECOMMENDATION

Antifungals are recommended as an adjunct to local measures (where applicable) to manage oral candidosis
Strong recommendation, moderate quality evidence

15.1.1.1 Antifungal drug choices

NYSTATIN

Adults

- 100,000 units oral suspension four times a day after food for seven days, or continued for two days after lesions have healed
- Advise patient to rinse the liquid around their mouth and then hold it against the lesions for five minutes, if possible, before spitting out. Avoid rinsing, eating or drinking immediately after use

continued on next page

Children

1 month-18 years: Use adult dose as above

Or

MICONAZOLE

Adults

Apply 2.5ml of oral gel to the affected area four times a day after food and retain near the lesion before swallowing. Use for at least seven days, after lesions have healed or symptoms have cleared

Children

- 1-23 months: 1.25 mL of oral gel four times a day, treatment should be continued for at least 7 days after lesions have healed or symptoms have cleared, to be smeared around the inside of the mouth after feeds
- 2 -17 years: Apply 2.5ml of oral gel to the affected area four times a day after food and retain near the lesion before swallowing. Use for at least seven days, after lesions have healed or symptoms have cleared

Or

FLUCONAZOLE

Adults

50mg orally once a day for 7-14 days (maximum 14 days unless severely immunocompromised); increased to 100mg a day for unusually difficult infections

Children

- 1 months-11 years: 3-6mg/kg oral suspension (50mg/5ml) swished around the mouth prior to swallowing (increases effectiveness) on first day then 3mg/kg (max 100mg) a day for 7-14 days (maximum 14 days; see note for adults)
- 12-17 years: 50mg once a day for 7-14 days (maximum 14 days; see note for adults)

15.1.2 Erythematous candidosis

Synonyms: antibiotic sore mouth, acute atrophic candidosis

Erythematous candidosis may involve most areas of the oral mucosa and may be painful for the patient. It can be an acute or chronic condition depending upon the duration. Predisposing factors are similar to those seen in pseudomembranous candidosis and may result from loss of the pseudomembrane in pseudomembranous candidosis.

Mainly it is associated with broad-spectrum antimicrobials or the use of steroid inhalers. The treatment of erythematous candidosis is the same as for pseudomembranous candidosis.

Where antimicrobial treatment is the predisposing factor, cessation of treatment leads to spontaneous resolution of the lesions once the bacterial population of the mouth recovers to pre-treatment levels.[9] The use of spacer devices with steroid inhalers can reduce side effects of oral candidosis along with rinsing immediately after use.[10]

Local management of denture-related problems should be undertaken before antifungal treatment is started.

15.1.3 Chronic hyperplastic candidosis

Synonyms: hyperplastic candidiasis, candidal leukoplakia

This chronic form of candidosis presents as a clearly defined, fixed, raised white patch that may be speckled or nodular. It can occur anywhere in the mouth, but has classically been associated with the commissures of the mouth.

Specialist management of this condition is necessary as this is generally considered to be a potential malignant lesion and a diagnostic biopsy is required. The timing of antifungal treatment is a contentious area amongst specialists.

To avoid a second biopsy, many specialists consider use of systemic antifungal treatments prior to the initial biopsy, clearing the candida and its histological effects first, giving a more accurate assessment of the likelihood and degree of dysplasia in the first biopsy. Failure to allow adequate histological resolution time risks over-reporting the degree of dysplasia.

Some specialists prefer to take an initial biopsy, eliminate the candida if present with antifungals, and re-biopsy to assess alteration in tissue behaviour. In this protocol, there is little guidance on sampling intervals, the risk of residual histological effects or recurrence of the infection. This may have an impact on the assessment making, and continued clinical observation of the tissue is even more important in these circumstances.

15.1.4 Candida-associated lesions

15.1.4.1 Chronic erythematous candidosis

Synonyms: denture stomatitis, denture sore mouth

This is usually characterised by inflammation on the denture-bearing maxillary mucosa. Predisposing factors should be eliminated before administering antifungal agents, but they are sometimes required as an adjunct to local measures before constructing new dentures.

Local measures:

- Strict denture hygiene using regular chemical (hypochlorite, not metal dentures, or chlorhexidine) and mechanical cleansing of dentures twice a day
- Leave dentures out at night
- Leave dentures out whenever it is feasible to do so during the day
- Tissue conditioners/soft linings may be used to minimise mucosal trauma in poorly fitting dentures prior to construction of new dentures

In a meta-analysis of RCTs, no statistically significant difference between antifungal treatment and disinfection methods was found for both clinical and microbiological outcomes in denture stomatitis. The meta-analysis did, however, show a statistically significant difference between an antifungal and a placebo for the microbiological outcomes.[11]

A systematic review found that topical fluconazole treatment compared with placebo is more effective than placebo at increasing the proportion of people with a clinical improvement or cure at 2 and 4 weeks. It also found that topical nystatin may be more effective than placebo at increasing clinical cure of denture stomatitis.[3]

Systemic antifungals are indicated only for unresponsive infections to local antifungals, which are usually associated with underlying systemic factors, e.g. immunosuppression or diabetes.

RECOMMENDATION

Antifungals are recommended as an adjunct to local measures for chronic erythematous candidosis

Strong recommendation, moderate quality evidence

15.1.4.1.1 Antifungal drugs of choice[5]

NYSTATIN

Adults

- 100,000 units oral suspension four times a day after food for seven days, or continued for two days after lesions have healed
- Advise patient to rinse the liquid around their mouth and then hold it against the lesions for five minutes, if possible, before spitting out
- Avoid rinsing, eating or drinking immediately after use

Children

1 month-18 years: Use adult dose as above

Or

MICONAZOLE

Adults

Remove dentures and apply 5-10ml of oral gel to the affected area four time a day, until 48 hours after the lesions resolve. The dentures can be reinserted to keep the gel in place

continued on next page

Children

2-17 years old: Apply 2.5ml of oral gel to the affected area four times a day, until 48 hours after the lesions resolve. The dentures can be reinserted to keep the gel in place

FLUCONAZOLE

Adults

50mg once a day for 7-14 days (maximum 14 days unless severely immunocompromised; these patients should be referred for specialist or management); increased to 100mg a day for unusually difficult infections

Children

- 1 months-11 years: 3-6mg/kg oral suspension (50mg/5ml) swished around the mouth prior to swallowing (increases effectiveness) on first day, then 3mg/kg (max 100mg) a day for 7-14 days (maximum 14 days unless severely compromised; these patients should be referred for specialist management)
- 12-18 years: 50mg once a day for 7-14 days (maximum 14 days unless severely immunocompromised; these patients should be referred for specialist management)

CLINICAL ADVICE

- Take a detailed medical history
- Identify and alleviate any predisposing factors, e.g. poorly fitting dentures
- Microbiological sampling and/or blood tests, PCR assay where necessary, e.g. immune depressed patients, differential diagnosis, invasive candidosis
- Biopsy with hyperplastic candidosis to discard the existence of epithelial dysplasia
- Stress importance of good oral hygiene to reduce candidal load and prescribe antimicrobial mouthwash, e.g. chlorhexidine

continued on next page

- Prescribe either topical or systemic antifungal
- Where prolonged courses or higher doses are used, (e.g. immunocompromised), monitoring of liver and renal function is advised
- Review for resolution

15.1.4.2 Angular cheilitis (stomatitis)

This condition presents as cracking and inflammation of the angles of the mouth. It is commonly a *Candida*-associated lesion. The condition is most frequently seen in patients who have denture-related stomatitis.

As with other oral candidal infections, it can be caused by an underlying systemic disease, such as deficiency anaemias, eating disorders, eczema, orofacial granulomatosis, Crohn's disease and immune deficiencies. A reduced/decreased occlusal face height, can also be a possible predisposing condition.

Angular cheilitis has a multifactorial aetiology and may be caused by both yeasts (*Candida* spp.) and bacteria (*Staphylococcus aureus* and beta-haemolytic streptococci) as interacting, infective factors. In patients who do not wear dentures, bacterial infections with staphylococci and/or streptococci are more likely to be cultured from the lesions. Microbiological sampling is useful in determining the therapeutic drugs of choice.

Predisposing factors should be managed (e.g. resolution of intraoral reservoir of candida in patients with chronic erythematous candidosis, provision of new dentures with appropriate occlusal face height after new dentures) and miconazole cream should be the first choice anti-infective agent as it has antifungal activity and some activity against gram-positive cocci. When angular cheilitis is associated with chronic erythematous candidosis, the intraoral infection should be treated concomitantly to eliminate the palatal reservoir.

In cases that are proven to be staphylococci, sodium fusidate ointment is indicated. When the lesions are unresponsive, a combination of miconazole with hydrocortisone maybe effective.

RECOMMENDATION

Topical antimicrobial therapy is recommended as an adjunct to management of underlying and predisposing conditions for angular cheilitis
(Strong recommendation, low quality evidence)

15.1.4.2.1 Antifungal drugs of choice

MICONAZOLE

Adults and children
Apply cream to the angles of the mouth twice a day for 10 days or until lesions have healed

Or

SODIUM FUSIDATE

Adults and children
Apply ointment to angles of the mouth three to four times a day usually for 7 days

Or

MICONAZOLE AND HYDROCORTISONE

Adults and children
Apply cream or ointment to angles of the mouth twice a day for a maximum of seven days

Note that creams are used on wet surfaces and ointments on dry surfaces.

CLINICAL ADVICE

- Take a comprehensive medical and dental history and oral examination
- Assess and manage predisposing factors, e.g. overclosure, denture problems

continued on next page

- Microbiological sampling where necessary
- Blood tests where appropriate
- Manage underlying nutritional and haematological disorders if present
- Stress the importance of good oral/prosthesis hygiene
- Prescribe appropriate ointment/cream
- Review in 2 weeks
- If unresolved, consider systemic antifungal

15.1.4.3 Median rhomboid glossitis (glossal central papillary atrophy)

This condition is uncommon and consists of a well-demarcated area of depapillation on the midline of the dorsum of the tongue (just anterior to the circumvallate papillae). Most cases are symptomless and the condition is currently thought to represent a chronic fungal (candidosis) infection.

In general, no treatment is necessary for median rhomboid glossitis. Predisposing factors include smoking, denture-wearing, corticosteroid sprays and HIV. Management of these can be successful in reducing or resolving the lesion.

For cases with symptoms of persistent pain or a burning sensation where *Candida albicans* infection is shown to be present by microbiological sampling, an antifungal medication may be prescribed to manage the infection and reduce the symptoms. Some cases of median rhomboid glossitis do not respond to antifungal therapy, so blood tests to exclude haematinic deficiencies may be indicated. Very occasionally, a biopsy may also be indicated.

The treatment is essentially the same as for oral candidosis (see section 15.1)

RECOMMENDATION

Antifungals may be of benefit in median rhomboid glossitis as an adjunct to management of predisposing factors in reducing persistent pain and burning sensations in the presence of *Candida* albicans infection
Conditional recommendation, low quality evidence

CLINICAL ADVICE

- As for oral candidosis

15.2 CHRONIC MUCOCUTANEOUS CANDIDOSIS (CMC)

CMC is a rare disease in which individuals have frequent, usually continuous oral thrush which is difficult to treat. Most cases are recognised in childhood. When CMC is found in children it is usually considered genetic with immune defects or endocrinopathies. It is characterised by hyperplastic plaque-like lesions intraorally, with skin lesions and nail defects (candida paronychia) also likely to be present.

Management is with antifungals, such as systemic fluconazole or itraconazole, and it is best managed by specialist collaborative teams.

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A1

GUIDANCE DEVELOPMENT

1.1 BACKGROUND

The Faculty of General Dental Practice (UK) (FGDP[UK]) and the Faculty of Dental Surgery (FDS) at the Royal College of Surgeons of England are committed to improving and maintaining standards of patient care and positively influencing oral health through education and the provision of evidence-based guidelines.

The Faculty of General Dental Practice (UK) is the only academic professional membership body in the UK specifically for general dental practice. Both FGDP(UK) and FDS comprise of members of all branches of the dental profession and many of the specialist societies and organisations within dentistry that support dental teams in providing quality patient care.

This guidance for all dentists was conceived by the editor of the FGDP(UK)'s previous guidance, *Antimicrobial Prescribing in General Dental Practice*, in response to the increasing development of antimicrobial resistance worldwide and a call to provide initiatives to reduce and optimise antimicrobial prescribing for infections.

1.2 METHODOLOGY

The Faculties have sought, where possible, to use a methodology for the guideline development that follows the international standards set out by the AGREE Collaboration.

Comprehensive searches with terms associated with antimicrobials (including types of antimicrobials) and the management of dental infections, prophylactic antimicrobials and dental treatment (with or without medical conditions) to prevent SSIs or metastatic infections, or other relevant areas of antimicrobial use within the scope of the guideline, were completed during 2018/9 using a variety of databases. These included

Medline/PubMed, Embase, Cochrane (CDSR, DARE) CINAHL Plus and NICE Evidence. No limits were placed on the publication dates of the articles.

Articles written in English were retrieved and considered eligible if they were systematic reviews or RCTs. Where systematic reviews and RCTs were not available, cohort studies and case studies were included instead. Microbiological studies of dental infections were also included. All abstracts were screened for relevance, and full text articles retrieved and critically appraised for inclusion.

Systematic reviews that fulfilled five conditions were included: (1) a clear and focused question of relevance to the scope of these guidelines, (2) a comprehensive search strategy, (3) a quality assessed methodology, (4) a clearly presented report of the included RCTs, and (5) a comprehensive and critical discussion of the results.

Where evidence was not available from systematic reviews, RCTs from the last 30 years were included. These answered a focused question within the scope of the guidance and, wherever possible, complied with standards (e.g. CONSORT) for reporting randomised trials.

Cohort and case studies were included where neither systematic reviews, nor RCTs, could provide evidence within the scope of the guideline, and where possible, followed recognised standards (e.g. STROBE) for observational studies.

Other sources of evidence, such as existing guidelines and expert working groups, were also considered and appraised for relevance and quality. GRADE was used to assess and rate the quality of the evidence and to make recommendations.

Some members of the working group drafted sections of the guidelines summarising the evidence available, providing recommendations and clinical advice. This was collated into a draft document and distributed to all members of the guideline development group (GDG). The GDG was asked to review the content and reach consensus on the recommendations. Where there was no evidence or conflicting evidence, the GDG was asked to make consensus recommendations based on current best practice or expert opinion.

Antimicrobial drug regimens and choices for each of the areas within the scope of the guidance were based on the recommendations of the BNF, published literature on microbiological sampling surveys for dental infections, and RCTs where specific antimicrobial regimens were investigated using the aforementioned databases.

1.3 PEER REVIEW

The draft guidelines were peer reviewed, and following assessment of comments received, edited accordingly. The Faculties wish to thank the following peer reviewers for their involvement in developing these guidelines:

Prof Tara Renton
Prof Andrew Smith
Prof Jan Clarkson
Dr Doug Stirling

1.4 CONSULTATION

To evaluate the guidance, a six weeks external consultation was conducted from 10th February 2020 to 22nd March 2020. The consultation draft was sent to a wide range of organisations and individuals within dentistry and in the field of antimicrobial prescribing and stewardship. The consultees were a selection of end users in all sectors of clinical dentistry, and were contacted through the FGDP(UK) and FDS networks.

The Faculty of General Dental Practice UK and the Faculty of Dental Surgery would like to express their thanks to the following organisations and individuals for consulting on the draft guidance:

The Association of Dental Hospitals (ADH)
The British Association for the Study of Community Dentistry (BASCD)
The British Society for Antimicrobial Chemotherapy (BSAC)
The Bristol Dental Hospital and School
The FGDP(UK) Implant Diploma Leads
The National Institute for Health and Care Excellence (NICE)
The Scottish Antimicrobial Prescribing Group – Dental sub-group
The Royal Pharmaceutical Society (RPS)

Adrian Bennett
Igor R. Blum
Tom Cheung
Mark-Steven Howe
Yann Maidment
Tara Renton
Catherine Rutland
Pearse Stinson
Cemal Ucer
Jane Woodington
Simon Wright

Following completion of the consultation period, all comments were reviewed and the guidance amended accordingly.

1.5 REVIEW AND UPDATING

A review of this guidance will take place four years after publication. If in the interim new evidence and working practices become available, this will be assessed and, if appropriate, the guidance updated. This will be completed as soon as possible on the online version available on the Faculties' websites.

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THE GUIDANCE DEVELOPMENT GROUP (GDG)

A Guidance Development Group (GDG) consisting of individuals from a cross section of dentistry was formed to develop and write this guidance. The GDG included representatives from all relevant dental specialities, a pharmacist and a patient representative.

2.1 MEMBERSHIP OF THE GDG

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2.2 CONFLICTS OF INTEREST

All contributors were required to declare any potential conflicts of interest during the development of this guideline. There were no conflicts of interest.

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ANTIMICROBIAL STEWARDSHIP RESOURCES

Antimicrobial stewardship is an organisational or healthcare system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness. It is the use of antimicrobials at the right dose, frequency and duration where clinically indicated that results in the best clinical outcome for treatment or prevention of infection for patients.

The following links provide tools for prescribers of antimicrobials to help put the recommendations in this guidance into clinical practice and to promote judicious use and monitoring of antimicrobial prescribing.

1 **NICE Guidance on Antimicrobial stewardship**
https://www.nice.org.uk/guidance/ng15
2 **Health Education England AMS Training resource guide**
https://www.hee.nhs.uk/sites/default/files/documents/AMR%20Training%20guide%20v16.pdf
3 **Public Health England AMS resource handbook**
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/768999/PHE_AMR_resource_handbook.pdf
4 **Public Health England Dental AMS toolkit**
https://www.gov.uk/guidance/dental-antimicrobial-stewardship-toolkit
5 **British Association of Oral Surgeons Dental AMS e-learning modules**
https://www.baos.org.uk/elearning/
6 **Faculty of General Dental Practice (UK) Antimicrobial self-audit clinical toolkit**
https://www.fgdp.org.uk/antimicrobial-prescribing
7 **Faculty of General Dental Practice (UK) Dental patient information leaflet and poster**
https://www.fgdp.org.uk/sites/fgdp.org.uk/files/docs/in-practice/ab_leaflet.pdf
https://www.fgdp.org.uk/sites/fgdp.org.uk/files/docs/in-practice/ab_poster.pdf

8 **Health and Social Care Act 2008. Code of Practice on the prevention and control of infections and related guidance**
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/449049/Code_of_practice_280715_acc.pdf

Antimicrobial Prescribing in Dentistry

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FACULTY OF GENERAL DENTAL PRACTICE

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