

CLINICAL PRACTICE GUIDELINES

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ANTIBIOTIC PROPHYLAXIS AGAINST WOUND INFECTION FOR ORAL SURGICAL PROCEDURES



MINISTRY OF HEALTH MALAYSIA

Statement of Intent

These guidelines are meant to be a guide for clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not necessarily ensure the best outcome in every case. Every health care provider is responsible for the management of his/her unique patient based on the clinical picture presented by the patient and the management options available locally.

Review of the Guidelines

These guidelines were issued in 2003 and will be reviewed in 2005 or sooner if new evidence becomes available

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**CLINICAL PRACTICE GUIDELINES
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RATIONALE AND PROCESS OF GUIDELINE DEVELOPMENT

Rationale

A multidisciplinary meeting in Scotland in November 1997 which involved clinicians, pharmacists, microbiologists, nurses and medical managers identified surgical antibiotic prophylaxis as representing one of the areas where there was a great variation in practice across Scotland.¹ The evidence from a study on prophylactic antibiotic prescribing in the National Health Service General Dental Practice in England, suggests that a significant number of the practitioners surveyed prescribe prophylactic antibiotics inappropriately, both for surgical procedures and for patients at risk from endocarditis. There is also evidence that practitioners prescribe antibiotic prophylaxis for clinical procedures and medical conditions for which there is little evidence to indicate its use. The results suggest that there is a need for the development of guidelines for practitioners on the appropriate prophylactic use of antibiotics.²

Such variation in the practice of surgical antibiotic prophylaxis may similarly be found in this country. A survey among the Ministry of Health Oral Surgery units in this country showed that for surgical prophylaxis there was a wide variation in the choice of antibiotics used. There was also a widespread use of metronidazole and a number of broad spectrum antibiotics (Ampicillin, Amoxycillin, 2nd and 3rd generation Cephalosporins etc).³ A survey done among Dental Officers in Pahang and Malacca revealed that a significant number of Dental Officers did not understand the meaning of antibiotic prophylaxis and which drugs and regime to use.⁴

Lastly, a number of the commonly used textbooks in Dentistry as well as the guidelines recommended by the Expert Committee on Rational Use of Antibiotics and the National Clinical Practice Guidelines by SIGN do not address the use of prophylactic antibiotics in oral surgical procedures adequately (Appendix 1).

Process

These clinical practice guidelines on ‘Antibiotic Prophylaxis against Wound Infection for Oral Surgical Procedures’ was prepared by a committee of Oral Surgeons from the Ministry of Health Malaysia, University Malaya and the Private Sector and a Microbiologist and a Pharmacist from the Ministry of Health following the process of CPG development formulated by the Ministry of Health Malaysia. A standard methodology based on a systematic review of evidence was used to look at the literature. These guidelines were presented at an open forum in the Academy of Medicine meeting and the Ministry of Health Malaysia and Academy of Medicine websites for comments from interested individuals before the final document was completed.

OBJECTIVES, QUESTION AND TARGETS

Objectives

These guidelines are intended to provide evidence in

- identifying which oral surgical procedures require prophylactic antibiotic cover against wound infection.
- assisting the surgeon to decide which antibiotics to use and what regime to follow.

These guidelines however do not cover

- antibiotics prophylaxis to prevent blood borne infection (e.g. prophylaxis against infective endocarditis)
- the use of antibiotics to treat established infections

Clinical Question

The clinical questions attempted to be answered by these guidelines include:

- i) Could the incidence of surgical wound infection be reduced when the use of antibiotic prophylaxis is indicated?
- ii) Could inappropriate use of antibiotics be eliminated?

Target Population

These guidelines are to be applied to adults as well as children undergoing both elective oro-maxillofacial (OMF) operations as well as procedures involved in the management of trauma to the OMF region.

Target Group

These guidelines are developed for the use of all Oral Surgeons and Dentists involved in the management of oral surgical patients.

KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

The definitions of the types of evidence and the grading of recommendations used in this guideline originate from the US Agency for Health Care Policy and Research and are set out in the following tables.

STATEMENTS OF EVIDENCE

Ia	Evidence obtained from meta-analysis of randomised controlled trials
Ib	Evidence obtained from at least one randomised controlled trial
IIa	Evidence obtained from at least one well-designed controlled study without randomisation
IIb	Evidence obtained from well-designed quasi-experimental study
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies
IV	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities

GRADES OF RECOMMENDATIONS

A	Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation (Evidence levels Ia, Ib)
B	Requires the availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation (Evidence levels IIa, IIb, III)
C	Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality (Evidence level IV)

GOOD PRACTICE POINTS

- ⊗ Recommended best practice based on the clinical experience of the guideline development group

SUMMARY OF RECOMMENDATIONS

1. Antibiotic prophylaxis is indicated irrespective of the class and duration of surgery for patients
 - with an ASA score > 2
 - with medical conditions resulting in decreased host defenses
 - whose preoperative stay exceeds 3 days
 - in whom an implant or graft is inserted.

2. In relation to class of surgery
 - antibiotic prophylaxis is not indicated in minor oral surgery
 - antibiotic prophylaxis is not indicated in extraoral major oral surgery if the duration is < 2 hours but is indicated if the surgery extends > 2 hours
 - antibiotic prophylaxis is indicated in intraoral or combined intraoral and extraoral major oral surgery

3. In relation to trauma
 - ❖ Soft tissue injury
 - Antibiotic prophylaxis is not indicated when the patient is first seen in the Emergency Department, for laceration wounds which are
 - * not extensive
 - * visibly clean
 - * treated early
 - Antibiotic prophylaxis is indicated when the patient is first seen in the Emergency Department, for laceration wounds which are extensive
 - For extensive laceration wounds seen early, in which a delay in treatment is expected, prophylactic antibiotics should be started immediately and continued until definitive treatment
 - Laceration wounds seen late or wounds which are visibly contaminated should be assumed to be infected
 - ❖ Open fractures of the facial bones
 - Antibiotic prophylaxis is indicated and should be administered when the patient is first seen in the Emergency Department
 - When a delay in treatment for open fractures is expected antibiotics should be started on admission and continued until temporary or definitive fixation of the fractures
 - Open fractures that are seen late should be assumed to be infected
 - Antibiotic prophylaxis is indicated in the surgical management of open fractures of the facial bones

- ❖ Closed fractures of the facial bones
 - Antibiotic prophylaxis is not indicated when the patient is first seen in the Emergency Department
 - Antibiotic prophylaxis is indicated in the surgical management of closed fractures of the facial bones in most instances.

4. Drugs used, route, dose, timing, frequency

❖ Drugs

- Penicillin is the drug of choice for intraoral surgery while clindamycin is the drug of choice for patients in whom penicillin is contraindicated
- A combination of penicillin and cloxacillin are the drugs of choice for extraoral or extraoral combined with intraoral surgery while clindamycin alone would be the drug of choice for patients in whom penicillin is contraindicated
- The alternative to clindamycin would be either vancomycin (IV) or erythromycin ethyl succinate (oral)

❖ Route

- For procedures under LA, antibiotics should be given orally provided this route is not contraindicated but for procedures under GA antibiotics should be given IV.

❖ Dose

- The first dose of the prophylactic antibiotic should be given at twice the usual therapeutic dose
- When surgery is prolonged, subsequent intraoperative doses are required and are given at the therapeutic dose.

❖ Timing

- The 1st dose of the prophylactic antibiotic should be given just before surgery - 1 to 2 hours before surgery for oral antibiotics or at induction of GA for IV antibiotics

❖ Frequency / Duration

- A single preoperative dose is required in most situations
- When surgery is prolonged, subsequent intraoperative doses are required with the dosage interval approximately one half the therapeutic interval
- No further doses should be given after completion of the operation.

ABBREVIATIONS

AHA	American Heart Association – Writing Group for Recommendations on Prevention of Bacterial Endocarditis
ASA	American Society of Anesthesiologists
BSAC	British Society for Antimicrobial Chemotherapy – Endocarditis Working Party
CDC	Centre for Disease Control
CPG	Clinical Practice Guidelines
GA	General Anaesthesia
G +ve	Gram Positive
G-ve	Gram Negative
IV	Intravenous
IM	Intramuscular
LA	Local Anaesthesia
MOS	Minor Oral Surgery
MRSA	Methicillin Resistant S. Aureus.
OMF	Oral & Maxillofacial
SWI	Surgical Wound Infection
ST	Soft Tissue
#	Fracture

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1. INTRODUCTION

1.1 Background

The landmark animal study by Burke⁵ first defined the scientific basis for the peri-operative use of antimicrobial agents in the prophylaxis against surgical wound infection. From this study Burke established several important principles for the prevention of infection in surgery. First, the effectiveness of defence against bacteria depends largely on natural resistance, which is by far the most important factor in preventing infection. Second, this resistance is reduced by the abnormal physiology induced by anaesthesia and operation. Third, the risk of infection can be decreased and, in specific cases, infection prevented by supplementing the host's antibacterial resistance, but only if the supplement is delivered before bacterial contamination of the tissue so that it is available to supplement the patient's intrinsic efforts during the early decisive period. Fourth, supplements to host resistance serves no purpose if they are delivered for periods longer than 4 hours following the end of the period of active bacterial contamination.

As postoperative wound infection is the most common nosocomial infection in patients undergoing surgery⁶ these guidelines were formulated to help optimise the use of antibiotics. Indiscriminate prescribing of antibiotics may adversely affect the patient, cause the emergence of antibiotic resistant strains of bacteria and increase the cost of health care.

1.2 Goals of antibiotic prophylaxis

The goals of prophylactic administration of antibiotics to surgical patients are to

- reduce the incidence of surgical wound infection (SWI).
- use antibiotics in a manner that is supported by evidence of effectiveness.
- minimise the adverse effects of antibiotics.

2. BENEFITS OF ANTIBIOTIC PROPHYLAXIS AND RISKS ASSOCIATED WITH ANTIBIOTIC USE

2.1 Benefits of antibiotic prophylaxis

- Antibiotic prophylaxis where indicated would reduce the incidence of surgical wound infection and hence reduce the incidence of morbidity to the patient - if the consequence of surgical wound infection is severe, prophylactic antibiotics will be of obvious value e.g. in patients with compromised host defences.
- Prophylactic antibiotics when used appropriately have the potential to reduce incidence of adverse reactions of antibiotics as well as costs well below the level encountered when antibiotics are used to treat established infections.⁷
- Surgical wound infections would almost always increase the length of hospital stay for inpatients. Prophylaxis therefore has the potential to shorten hospital stay but there is little direct evidence.

2.2 Risks associated with antibiotic use⁸

- When an antibiotic is administered, strains of organisms sensitive to the antibiotic are killed which will allow proliferation of resistant strains of these organisms. This therefore renders the antibiotic ineffective in prophylaxis or treatment of infection associated with these resistant strains.
- An antibiotic administered to a patient can act as an antigenic stimulus and hence produce an allergic reaction. Allergic reactions manifest either locally or systemically at varying degrees of severity ranging from minor skin lesions to anaphylactic shock and death.
- An antibiotic kills or arrests the proliferation of bacteria sensitive to it. This may include normal gut flora, some of which are responsible for reabsorption of water, electrolytes and synthetic oestrogens (as found in oral contraceptives) and the production of vitamin K. Thus, the administration of an

antibiotic may cause diarrhoea, increased risk of pregnancy in women taking contraceptive pills and increased risk of bleeding especially in patients taking warfarin.

- As susceptible organisms are destroyed, they may be replaced by other organisms not affected by the antibiotic such as *Candida albicans* and *Clostridium difficile* (which might result in candidiasis and pseudomembranous colitis respectively).

The final decision on whether to use prophylactic antibiotics should take into consideration both the benefits of antibiotic prophylaxis and the risks associated with antibiotic use for each individual patient ⊗

3. INDICATIONS FOR SURGICAL ANTIBIOTIC PROPHYLAXIS

There are multiple risk factors involved, independent of each other which are predictive for subsequent wound infection.

These factors include

- ASA score.
- length of preoperative stay in the hospital.
- compromised host defenses.
- insertion of implants and grafts.
- surgical wound class and duration of surgery.

In OMF trauma however, there may be additional factors predisposing to infection (See Sec. 3.4.3).

3.1 ASA score (appendix 2) and length of preoperative stay in hospital

Garibaldi et al ⁹ collected prospective epidemiological data and their analysis of that data revealed that postoperative wound infection rate was related to the ASA status of the patient, and the length of preoperative stay in the hospital.

Culver et al ¹⁰ looked at data collected under the National Nosocomial Infection Surveillance System and their analysis of that data revealed that postoperative wound infection rate was related to the ASA status.

ASA scores > 2 are associated with increased risk of wound infection ^{9,10} (Table 2).

III

Preoperative stay > 3 days is associated with an increased risk of wound infection ⁹ (Table 2).

III

Guidelines for prevention of wound infection by the CDC in Atlanta ¹¹ advises that preoperative hospital stay should be as short as possible and therefore tests and therapeutic measures that will prolong the stay beyond one day should be performed as outpatient services if possible.

3.2 Compromised host defences

Patients with certain medical conditions resulting in decreased host defenses have a reduced resistance to infection and hence a high probability of developing postoperative infection.⁷ More importantly, in these patients the risk of SWI far outweighs the risks associated with antibiotics.⁸ It would therefore be appropriate to prescribe prophylactic antibiotics for these patients when they undergo any form of surgery.^{8,12,13}

IV

Conditions in which there are compromised host defences would include among others, patients

- with diseases that compromise their immunity (e.g. poorly controlled diabetes, AIDS, leukemia etc).
- who have had radiotherapy at the operative site.
- who are on immunosuppressive / cytotoxic drugs.
- with a history of recurrent wound infection but without a specific immunodeficiency.

It has also been shown that malnutrition is associated with an increased incidence of wound infection¹⁴ and correction of the nutritional deficiencies may reduce the chances of infection.¹¹

3.3 Insertion of implants and grafts

Gristina¹⁵ showed that the surface of implants facilitate bacterial adherence and also that the presence of an implant can compromise the host's defence to the extent that normal flora with little or no virulence potential, can cause infections at the implant-host interface. **IIb**

Infection related to implants is relatively resistant to antibiotic therapy and most often requires removal of the prosthesis or infected tissue.¹⁶ **IV**

As part of the comprehensive Dental Implant Clinical Research Group (DICRG) clinical implant study, the data for 2,973 implants were recorded and correlated.¹⁷ The results showed a significantly higher implant survival rate in patients who had received preoperative antibiotics. **III**

Trieger¹⁸ in his position paper reviewed the literature and came to the conclusion that antibiotic prophylaxis is indicated in the surgical placement of endosseous implants. **IV**

Failure of the implants could also have significant cost implications to the patient. **⊗**

One large retrospective study¹⁹ however, showed that antibiotic prophylaxis for routine dental implant surgery offers no advantage to the patient.

Until proper controlled and randomised trials are done, the available evidence shows that there may be an increased incidence of infection associated with the insertion of dental implants and hence prophylactic antibiotics are indicated.

The use of grafts as in reconstructive surgery can be associated with significant morbidity (both at the recipient site, and at the donor site in autogenous grafts) together with significant time and cost implications. Management of infection if it does occur can be difficult and the outcome is often disappointing. Infections associated with the graft (recipient or donor site) should be prevented and prophylactic antibiotics are therefore indicated. In most cases however, the class and duration of the surgery would be such that prophylactic antibiotics are indicated anyway.



Antibiotic prophylaxis be indicated irrespective of the class and duration of surgery for patients

- with an ASA score > 2 **B**
- whose preoperative stay exceeds 3 days **B**
- with medical conditions resulting in decreased host defences **C**
- in which an implant is inserted **B**
- in which a graft is inserted **⊗**

3.4 Surgical wound class and duration of surgery

3.4.1 Minor oral surgery

Properly designed and well controlled clinical studies to evaluate the necessity of antibiotic prophylaxis in minor oral surgery (MOS) are difficult to perform because the postoperative risk of surgical wound infection is generally low and extensive observations are required to demonstrate a significant difference.

Three randomised, controlled trials,^{20,21,22} two audits^{8,23} and a number of authors^{13,24,25} have recommended that antibiotic prophylaxis is not necessary in MOS.

IB

It has also been reported that the use of antibiotics confers no advantage even when impacted teeth are removed in the presence of acute infection.²⁶

III

The risk of infection in MOS has been estimated to be < 1%.^{24,25} By normal surgical standards therefore antibiotic prophylaxis is not necessary.

IV

It may also be argued that postoperative infection in MOS is rarely serious and is readily amenable to treatment.

Antibiotic prophylaxis is not indicated in minor oral surgery

A

3.4.2 Major oral surgery

Garibaldi⁹ and Culver¹⁰ (refer section 3.1) showed that postoperative wound infection rate was related to the class of surgery. Referring also to Tables 1^{9,10,24} and 2⁹ it is seen that the infection rate associated with Class 1 surgery may be sufficiently low as not to warrant the use of prophylactic antibiotics. The infection rate associated with Class 2 surgery however, may be high enough to warrant the use of prophylactic antibiotics.

III

Garibaldi⁹ and Culver¹⁰ (refer section 3.1) also showed that postoperative wound infection rate was related to the duration of the surgery. Duration of surgery > 2 hours was associated with a significant infection rate (refer Table 2⁹).

III

Table 1: Impact of surgical wound class alone on the probability of wound infection

Category / Class		Definition	Probability of infection		
			Ref-10	Ref-9	Ref-24
Minor oral surgery		<ul style="list-style-type: none"> This category includes simple soft tissue and dentoalveolar surgery and examples of procedures in this category would include surgical removal of impacted teeth, excision of small benign soft tissue and bony lesions, etc. 	1-2%	2.2%	<1 % 2 %
Major oral surgery	Class 1 surgery (clean surgery)	<ul style="list-style-type: none"> No transection of the respiratory, GI, or urinary tract (extraoral only approaches), no inflammation encountered and no break in aseptic technique. Examples of Oral Surgical procedures in this category would include submandibular and parotid gland surgery, TMJ surgery etc. 			
	Class 2 surgery (clean-contaminated surgery)	<ul style="list-style-type: none"> Respiratory, GI tract entered (transoral or combined transoral and extraoral approaches) but no inflammation or significant bacterial contamination occurs. Examples of Oral Surgical procedures in this category would include orthognathic surgery, major preprosthetic surgery, major tumour surgery etc. 	10-20%	8.5%	10-15%

Category / Class		Definition	Probability of infection		
			Ref-10	Ref-9	Ref-24
	Class 3 surgery (contaminated surgery)	<ul style="list-style-type: none"> • Operations where acute inflammation (without pus) is encountered or where there is major breakdown in aseptic technique or fresh traumatic wounds. • Examples of Oral Surgical procedures in this category would include the management of compound facial bone fractures. 	20-35%	28%	20-30%
	Class 4 surgery (dirty infected surgery)	<ul style="list-style-type: none"> • Operations in which there is established clinical infection (with pus) or old traumatic wounds. • Examples of Oral Surgical procedures in this category would include the management of visibly contaminated oro-facial lacerations or compound facial bone fractures and oro-facial lacerations seen and treated late. 	25-50%		50%

Table 2 : Impact of surgical wound class and other important risk factors on the predicted probabilities for wound infection (Garibaldi et al ⁹)

Variables	Surgical wound class		
	Class 1	Class 2	Class 3
None	2.2%	8.5%	28%
ASA > 2	4.2%	13%	35%
ASA > 2 and duration > 120 min	8.3%	20%	41%
ASA > 2 and duration > 120 min, intraoperative contamination	17%	37%	61%
ASA > 2 and duration > 120 min, intraoperative contamination, preoperative stay > 3 days	27%	45%	65%

i) *Extraoral surgery (Class 1 surgery)*

Examples of Oral Surgical procedures in this category would include submandibular and parotid gland surgery, TMJ surgery etc.

In Class 1 surgery with no other risk factors, the expected infection rate is around 2% (refer also Table 1).^{9, 10, 24}

IV

A prospective, randomized, controlled trial²⁷ showed no difference in infection rates for patients undergoing clean (Class 1) surgery whether they received prophylactic antibiotics or not.

IIb

The clinical practice guidelines for antibiotic prophylaxis in surgery produced by the SIGN³ do not recommend the use of antibiotic prophylaxis for this class of surgery.

IV

Antibiotic prophylaxis is therefore not indicated in Class 1 surgery.

However, if the duration of the surgery is > 2 hours, this is associated with a significant infection rate⁹ (ref Table²⁹) and antibiotic prophylaxis is indicated.

III

Antibiotic prophylaxis is not indicated in major extraoral surgery in which the duration of the procedure is < 2 hours

A

Antibiotic prophylaxis is indicated in major extraoral surgery in which the duration of the procedure is > 2 hours

B

ii) *Intraoral surgery (Class 2 surgery)*

Examples of Oral Surgical procedures in this category would include orthognathic surgery, major preprosthetic surgery, major tumour surgery, etc.

In Class 2 surgery the expected infection rate is around 10%.^{9, 10, 24}

Theoretically, one would expect a greater rate of infection in intraoral surgery as the mucosa cannot be antiseptically treated as well as before skin surgery.²⁶ Also after 6-12 hours of fasting in preparation of the surgery there would be an increased bacterial count in the mouth.²⁸

The clinical practice guidelines for antibiotic prophylaxis in surgery produced by the SIGN¹ recommend the use of antibiotic prophylaxis for this class of surgery.

IV

A survey of clinical trials of antibiotic prophylaxis in colon surgery²⁹ and a meta-analysis of randomised, controlled clinical trials of antibiotic prophylaxis in biliary tract surgery³⁰ (both Class 2 surgeries) showed that antibiotic prophylaxis is obviously beneficial.

Ia

A survey of 84 hospitals³¹ showed that all of them used antibiotic prophylaxis for intraoral orthognathic procedures.

IV

One randomized, controlled, and double blind study showed that there was a statistically significant increased risk of an infectious complication after bimaxillary orthognathic surgery without antibiotic prophylaxis.³² Another randomized controlled and double blind study also showed an increased incidence of infection in patients not receiving antibiotic prophylaxis but the results were not statistically significant.³³

Ib

A number of authors recommend that prophylactic antibiotics be used.^{24, 28, 33, 34, 35}

IV

A number of studies have however, shown that there is no difference in the infection rates in surgery carried out with or

without prophylactic antibiotics^{36, 37, 38} but these were not controlled studies.

The face and oral cavity may have a greater inherent natural immunity than other areas of the body because of its excellent blood supply and other factors. However, from the evidence shown it would seem appropriate to use prophylactic antibiotics for major intraoral surgery until properly designed studies prove otherwise.

Antibiotic prophylaxis would also obviously be indicated for combined intraoral and extraoral surgery.

Antibiotic prophylaxis is indicated in major intraoral or combined major intraoral and extraoral surgery

A

3.4.3 Oral & maxillofacial (OMF) trauma management

In OMF trauma there may be additional factors predisposing to infection. The skin and mucosa of the head and neck are frequently traumatised. Fractures may be open to the oral cavity or skin. There may be disruption of blood supply, significant blood loss and possibly tissue anoxia. Dead spaces are created and loss of tissue occurs. Foreign body material may be present. Contamination and devitalisation of tissues may occur. The general condition of the patient may be altered by shock. All or some of these factors may be present in a single patient.

i) Management of oro-facial soft tissue injuries in which suturing is required

In the management of visibly contaminated soft tissue injury early surgical debridement is considered to be the single most important step.

A number of studies have shown that the incidence of infection in patients with minor laceration wounds treated with prophylactic antibiotics is similar to or greater than the control groups not receiving antibiotics.³⁹⁻⁴² **IIa**

Hence, prophylactic antibiotics are not indicated for minor laceration wounds. More extensive laceration wounds would require prophylactic antibiotics.^{39, 40} **IV**

When a delay in treatment is expected antibiotics should be started on admission to the Emergency Department and continued until definitive treatment is carried out usually within 24 hours. Once this has been accomplished antibiotic administration is no longer necessary.^{43, 44} **IV**

If there has been a delay of 3 hours or more in treatment of lacerations, bacteria may have proliferated to a level that will result in infection. Therefore the prophylactic use of antibiotics within 3 hours after injury might be effective in preventing infection.^{40, 45} **IV**

Laceration wounds, which are seen more than 3 hours after the injury or wounds that are visibly contaminated, should be assumed to be infected^{40, 45, 70} and antibiotics should be prescribed as for an established infection.

- Antibiotic prophylaxis is not indicated for laceration wounds which are not extensive, visibly clean, and treated within 3 hours of injury** **A**
- Antibiotic prophylaxis is indicated for laceration wounds that are extensive, visibly clean, and treated within 3 hours of injury** **C**

- Laceration wounds that are seen within 3 hours of the injury and when a delay in treatment is expected, prophylactic antibiotics should be started immediately and continued until definitive treatment. Antibiotics should not be continued after the procedure** **C**
- Laceration wounds that are more than 3 hours old or wounds which are visibly contaminated at the time the patient is first seen should be assumed to be infected.** **C**

ii) *Management of compound fractures of the facial bones*

In the management of compound fractures of the facial bones early surgical debridement and adequate fracture stabilization are the most important aspects of treatment.

Two randomized, controlled trials^{46,47} have shown that early antibiotic administration is necessary to prevent infection in the fracture site and that without antibiotics infection rates of around 45% could be expected.

Ib

A number of authors have advocated the use of prophylactic antibiotics.^{24, 43, 45}

IV

When a delay in treatment is expected antibiotics should be started on admission to the Emergency Department and continued until temporary or definitive fixation of fractures is done usually within 24 hours. Once this has been accomplished antibiotic administration is no longer necessary.^{43, 44}

IV

If there has been a delay of 3 hours or more in treatment of the fractures, bacteria may have proliferated to a level that will result in infection. Therefore the prophylactic use of antibiotics within 3 hours of the injury might be effective in preventing infection.^{40, 45, 70} Compound facial bone fractures first seen after 3 hours of the injury should be assumed to be infected^{40, 45, 70} and antibiotics should be prescribed as for an established infection.

IV

The evidence has shown that antibiotic prophylaxis is indicated in the surgical management of closed fractures⁴⁸ (Refer 3.4.3.3) hence the surgical management of open fractures would almost certainly require prophylactic antibiotics.

Ia

Antibiotic prophylaxis is indicated in the management of open fractures of the facial bones and should be administered when the patient is first seen in the Emergency Department **A**

When a delay in treatment is expected antibiotics are continued until temporary or definitive fixation of the fractures is done **C**

Open fractures that are more than 3 hours old at the time the patient is first seen should be assumed to be infected **C**

Antibiotic prophylaxis is indicated in the surgical management of open fractures of the facial bones

iii) Management of closed fractures of the facial bones

In the management of closed fractures of the facial bones prophylactic antibiotics are not indicated when the patient is first seen. **⊗**

A Cochrane Review of controlled trials came to the conclusion that antibiotic prophylaxis should be offered to those undergoing surgery for closed fractures (long bones). ⁴⁸ **Ia**

The surgical procedures involved in the management of closed fractures would fall under Class 1 and Class 2 surgeries and the indications would be as discussed previously.

Antibiotic prophylaxis is not indicated in the management of closed fractures of the facial bones when the patient is first seen **⊗**

Antibiotic prophylaxis is indicated in the surgical management of closed fractures of the facial bones **A**

The only exception would be an extraoral only approach less than 2 hours in duration

4 ADMINISTRATION OF PROPHYLACTIC ANTIBIOTICS

The basic principles of antibiotic prophylaxis is to choose the right antibiotic, provide adequate concentrations of the antibiotic in the tissues at the onset and throughout the operative procedure and to discontinue the antibiotic at the end of the period of increased risk which is the end of the operation.⁷

4.1 Choice of antibiotic

i) Principles

Important principles to be followed in the selection of antibiotics are

- the antibiotic selected should be effective against the pathogens most frequently responsible for SWI after the that particular operation.
- the spectrum of the antibiotic chosen should be as narrow as possible to reduce the incidence of resistant bacteria.
- the antibiotic selected should be of low toxicity.
- the antibiotic selected should be bactericidal.

ii) Use of an alternative antibiotic

The results of a study done by Leviner et al⁴⁹ showed that in order to minimize the development of resistant bacterial strains, procedures in which prophylactic antibiotics are administered should be scheduled in intervals of not less than 10 days.

IIb

The British Society for Antimicrobial Chemotherapy (BSAC) Endocarditis Working Party recommends that any given antibiotic should not be used more than twice in a month for prophylaxis. If more than 2 procedures are to be done in a month, an alternative antibiotic is recommended.⁵⁰

IV

The Writing Group for Recommendations on Prevention of Bacterial Endocarditis of the American Heart Association (AHA)⁵¹ referring to the study by Leviner⁴⁹ and the BSAC recommends that if the same antibiotic is to be used for prophylaxis, a time interval between procedures should be observed to reduce the potential for emergence of resistant organisms.

IV

iii) Allergy to first choice antibiotic

An alternative antibiotic is required in patients who have a history of allergy to the recommended antibiotic.^{50, 51}

When the first choice antibiotic is contraindicated, an alternative antibiotic should be used if

- a second procedure needs to be carried out on the same patient in less than 10 days
- more than 2 procedures need to be carried out on the same patient within the same month
- the patient is allergic to the first choice antibiotic

B

C

C

4.1.1 For intraoral surgery

The bacteria that cause oral infection are among the numerous species of bacteria that constitute the normal flora of the oral cavity. They are primarily⁵²

- aerobic G +ve cocci (*Streptococcus viridans* gp.).
- anaerobic G +ve cocci (peptococci and peptostreptococci).
- anaerobic G -ve rods (*Prevotella melaninogenica* [old name *Bacteroides melaninogenicus*] and *Fusobacterium nucleatum*).

Oral infection is a mixed infection (pathogenic complex) in which anaerobes outnumber aerobes by 2:1, but anaerobes are thought to need aerobes to provide an environment in which to grow^{53, 54}. It has been shown that a pure strain of anaerobes introduced to a site does not cause infections.⁵⁵ Aderhold et al⁵⁶ suggested that the early phase of an infection involves streptococci which prepare the environment for subsequent anaerobic invasion. The results of a study done by Lewis et al⁵⁷ supported this concept. The aerobic streptococci therefore most likely initiate infections following intraoral surgery.

IV

IIb

IIb

For antibiotic prophylaxis, effective antibiotics against the aerobic streptococci are therefore thought to be sufficient and total effectiveness against anaerobes may not be necessary.⁴³

IV

i) Patients in whom Penicillin is not contraindicated

For most patients who have intraoral procedures, Penicillin would be the drug of choice because ^{24, 26, 33, 34, 35, 43, 53, 54} **IV**

- it has a relatively narrow spectrum of activity.
- it has a very low toxicity.
- it is very effective against the streptococci involved in the initiation of oral infection.
- there are no known resistance to penicillin for the aerobic streptococci (Table 3). **IIb**
- it is also reasonably effective against the oral anaerobes.

Table 3: Percentage of antibiotic resistance for Group A Streptococcus isolates in Hospital Kuala Lumpur for 1997, 1998, 1999 and 2000

	1997	1998	1999	2000
Ampicillin	5.1 (152)	1.2 (117)	0 (139)	0 (109)
Cefuroxime	3.6 (76)	2.3 (72)	0 (135)	0 (110)
Erythromycin	13.1 (160)	2.7 (107)	0 (10)	15.5 (110)
Penicillin	0 (156)	0 (117)	0 (139)	0 (119)

() Number of isolates

Hunt et al ⁵⁸ tested antibiotic susceptibility of bacteria cultured from exudates taken from oral infections and showed that all the pure and mixed streptococcal cultures he tested were sensitive to Penicillin. **IIb**

Ampicillin, Amoxycillin and the 2nd and 3rd generation Cephalosporins are extended spectrum antibiotics developed to give coverage against aerobic gram negative organisms which are not involved in oral infections (eg H influenza and E coli etc). These broad spectrum antibiotics are more importantly not as effective as Penicillin against aerobic gram positive streptococci. ^{43, 54} **IV**

ii) Patients in whom Penicillin is contraindicated

Clindamycin is a very reliable antibiotic against oral infections as it has excellent activity against G +ve streptococci as well as against the G-ve anaerobes.^{53, 54, 59} It is bactericidal in the high doses used in prophylaxis.⁵⁴ IV

Mueller et al⁶⁰ demonstrated that Clindamycin concentrations above the MIC₉₀ of those organisms most likely to cause oral infection were reached in all the kinds of OMF tissues investigated. He therefore came to the conclusion that from the pharmacokinetic point of view, Clindamycin is suitable for perioperative prophylaxis during OMF procedures. IIb

Clindamycin is the latest recommendation by both the BSAC⁵⁰ and AHA⁵¹ as an alternative for patients in whom penicillin is contraindicated for prophylaxis against infective endocarditis. IV

It has been reported that Clindamycin has a propensity to cause pseudomembranous colitis. It may be that these reports are exaggerated and that the risk is no greater than that with many of the other more frequently prescribed antibiotics.⁶¹ IV

The BSAC⁵⁰ stated that as far as they could determine, in more than 20 years there has been only one reported case of pseudomembranous colitis after a single injection of Clindamycin. This prompted the BSAC to follow the AHA⁵¹ in recommending the use of IV Clindamycin (oral Clindamycin was already recommended). IV

Clindamycin is therefore a suitable alternative for patients in whom Penicillin is contraindicated.

4.1.2 For extraoral surgery

i) Patients in whom Penicillin is not contraindicated

In surgery that is extraoral (transcutaneous) an antibiotic must be chosen that is effective against both *Staphylococcus aureus*, and the aerobic skin streptococci^{24, 53, 62, 63}. Penicillin as has been mentioned previously is the drug of choice against streptococci, but most staphylococci are now resistant to Penicillin. IV

Cloxacillin is still effective in infections caused by *Staphylococci aureus*.^{59, 62, 63} (ref Table 4 – Oxacillin is a drug used to represent cloxacillin in laboratory testing). **IIb**

Table 4: Percentage of antibiotic resistance for Methicillin sensitive *Staph aureus* isolates in Hospital Kuala Lumpur for 1999 and 2000

	1999		2000	
Ampicillin	35.3	(51)	60.9	(92)
Erythromycin	62	(2243)	10.8	(2203)
Oxacillin (Methicillin)	0	(2278)	0	(2274)
Penicillin G	89.7	(78)	88	(2253)
Vancomycin	0	(1435) (for MRSA)	0	(1535) (for MRSA)


() Number of isolates

Oxacillin has been shown in a number of studies to be effective in transcuteaneous procedures.⁶⁴⁻⁶⁶ **Ia**

A combination of Cloxacillin and Penicillin would hence be effective against both streptococci and staphylococci and is therefore indicated for use in extraoral surgery. **Ia**

A Cephalosporin alone is also effective against both the streptococci and staphylococci.^{59, 67} The combination of Penicillin and Cloxacillin is however preferred because its spectrum of antimicrobial activity is narrower than that of the broad-spectrum Cephalosporins and as mentioned previously Penicillin is more effective against streptococci than the Cephalosporins.

ii) Patients in whom Penicillin is contraindicated

Clindamycin is effective against both streptococci and staphylococci.^{53, 54, 59} Refer also to evidence in section 4.1.1.2. Clindamycin alone is a suitable alternative to the Penicillin / Cloxacillin combination if Penicillin is contraindicated. **IV** 

4.1.3 Third-line antibiotics

i) Vancomycin

Vancomycin is an attractive antibiotic to consider in transcuteaneous and intraoral surgery. Vancomycin is bactericidal and is effective against G +ve streptococci and especially against *Staphylococcus aureus*^{50,59} (also ref Table 5). However its cost and leading place in the treatment of MRSA (Methicillin resistant *S Aureus*) have led most clinicians to reserve this antibiotic for the management of MRSA. It can be used as an alternative to Clindamycin in patients in whom Penicillin is contraindicated.^{50,59}

IV

Table 5 : Percentage of antibiotic resistance for MRSA isolates in Hospital Kuala Lumpur from 1998 to 2000

	1998	1999	2000
Vancomycin	0 (1072)	0 (1435)	0 (1505)
Fusidic Acid	5.5 (1072)	11.8 (1435)	21.9 (1478)
Rifampicin	4.1 (1072)	11.0 (1435)	21.3 (1505)

() Number of isolates

ii) Erythromycin

As Vancomycin is not effective by mouth for systemic use⁵⁹, the alternative to Clindamycin if an oral antibiotic is indicated would be Erythromycin Ethyl Succinate. Erythromycin was the previously recommended antibiotic for patients in whom Penicillin was contraindicated by both the BSAC and AHA.

⊗

For intraoral surgery

- **Penicillin is the drug of choice** **B**
- **Clindamycin is the drug of choice if penicillin is contraindicated** **B**
- **The alternative to Clindamycin would be either Vancomycin (IV) or Erythromycin Ethyl Succinate (oral)** **C**

For extraoral or extraoral combined with intraoral surgery

- **A combination of Penicillin and Cloxacillin are the drugs of choice** **B**
- **Clindamycin alone is the drug of choice if Penicillin is contraindicated** **B**
- **The alternative to Clindamycin would be either Vancomycin (IV) or Erythromycin Ethyl Succinate (oral)** **C**

4.2 Choice of route of administration

It has been shown that peak plasma concentrations of an antibiotic are reached more quickly after rapid IV administration than continuous IV infusion or IM injections.⁶⁸ Intravenous administration of antibiotics as a bolus dose is therefore the optimal method to ensure adequate levels in the tissues during a surgical procedure. However, all the drugs recommended in this guidelines should not be given as a bolus but by slow IV injection or infusion (see *note below)

IV administration is the route of choice for procedures under GA.^{50, 53, 69}

For procedures under LA, oral administration is the route of choice⁵⁰ and will ensure adequate levels of the antibiotics in the tissues during the procedure. It is less invasive than IV and more acceptable to the patients.

*** Note:**

- IV Benzyl Penicillin should be given by slow intravenous injection or by infusion.⁵⁹
- IV Cloxacillin should be given by slow intravenous injection or by infusion.⁵⁹
- IV Clindamycin should be given in 50ml of diluent over 10 minutes (because rapid injection may cause a precipitate drop in BP, nausea, vomiting and arrhythmias).⁵⁹
- IV Vancomycin should be given as an infusion over 100 min. (because of its toxicity).⁵⁹

For procedures under LA – antibiotics should be given orally provided this route not contraindicated **C**

For procedures under GA – antibiotics should be given IV **B**

4.3 Dose selection

For the antibiotic to be maximally effective the concentration of antibiotic in the plasma must be high so as to allow diffusion into the tissues that will be contaminated by the bacteria. Normal therapeutic levels are ineffective.^{24, 43} The peak therapeutic concentration of an antibiotic at the site of potential infection should be three or four times the minimum inhibitory concentration.²⁶ **IV**

The prophylactic antibiotic dose is therefore at least twice the therapeutic dose.^{24, 43, 50} Subsequent doses, which are given if the surgery is prolonged, should be at the usual therapeutic dose as recommended by the BSAC in antibiotic prophylaxis against infective endocarditis.⁵⁰ **IV**

The recommended doses are for adults and for patients with normal hepatic and renal functions are as follows:

Antibiotic	Therapeutic dose	Prophylactic dose
Oral Penicillin (Phenoxymethyl Penicillin) (Pen V)	500mg	1g
IV Penicillin (Benzyl Penicillin) (Pen G)	1 mega unit	2 mega units
Oral Clindamycin	300mg	600mg
IV Clindamycin	300mg	600mg
Oral Cloxacillin	500mg	1g
IV Cloxacillin	500mg	1g
Oral Erythromycin (E. Ethyl Succinate)	400mg	800mg
IV Vancomycin	500mg	1g

The first dose of prophylactic antibiotic should be given at twice the usual therapeutic dose. Subsequent doses should be given at the therapeutic dose. C

4.4 Timing of administration and duration of prophylaxis

In a large prospective trial ⁷⁰ done to study the occurrence of SWI in relation to timing of antibiotic prophylaxis a number of important conclusions were derived: IV

- Use of antibiotics within the 2 hour period before an operation was associated with the lowest rate of SWI.
- Patients who had antibiotic prophylaxis from 2 to 24 hrs before the initial incision had a wound infection rate of 6 times more.
- Patients who received antibiotic prophylaxis more than 3 hrs after the initial incision had more than 5 times the rate of wound infection.

It has also been shown that antibiotic therapy beyond the day of operation fails to reduce further the incidence of wound infection.^{1,71} IV

A selective environment for the overgrowth of resistant bacteria begins only when susceptible organisms in the host are killed. Short-term use of prophylactic antibiotics has therefore probably little or no influence on the growth of resistant bacteria.^{24,33} IV

A meta-analysis of randomised, controlled clinical trials of antibiotic prophylaxis showed no difference in infection rates between single dose and multiple dose regimes.³⁰ **Ia**

A full course of antibiotics is only necessary when treating established infection.

For effective antimicrobial prophylaxis adequate concentrations of the antibiotic must be present in the tissues at the onset and throughout the operative procedure.^{7, 11, 13, 24, 53, 72} **IV**

The antibiotic should be discontinued at the end of the period of increased risk, which is the end of the operation and therefore antibiotics should not be prescribed after completion of the operation.^{7, 24, 31, 34, 53, 72} **IV**

Burke⁷ proposed that prophylactic antibiotics should be repeated every 3 hours during the operation. As a general rule the prophylactic dosage interval is approximately one half the usual therapeutic interval.^{24, 33} **IV**

Antibiotic	Therapeutic interval	Prophylactic interval
Oral Penicillin (Phenoxymethyl Penicillin)	6 hr	3 hr
IV Penicillin (Benzyl Penicillin)	6 hr	3 hr
Oral Clindamycin	6 hr	3 hr
IV Clindamycin	6 hr	3 hr
Oral Cloxacillin	6 hr	3 hr
IV Cloxacillin	6 hr	3 hr
Oral Erythromycin (E. Ethyl Succinate)	12 hr	6 hr
IV Vancomycin	6 hr	3 hr

A single dose of antibiotic is required for surgery less than 3 hours **A**

- 1 to 2 hours before surgery for oral antibiotics
- at induction of GA for IV antibiotics

When surgery is prolonged, subsequent intraoperative doses are required **C**

- the prophylactic dosage interval is approximately half the therapeutic interval

No further doses should be given after completion of the operation **C**

5. CONCLUSION

It is important to emphasise that surgical antibiotic prophylaxis is an adjunct to and not a substitute for good surgical technique. Antibiotic prophylaxis should be regarded as one component of an effective policy for control of hospital-acquired infection.

These guidelines are the current recommendations of the committee towards good practice and good management of patients requiring Oral Surgery. We accept that there may be individual preferences but all decisions to adopt any recommendation must be made by the practitioner in the light of available evidence, resources and the circumstances presented by individual patients.

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APPENDIX 1

Inadequacy of some existing guidelines and textbooks on antibiotic prophylaxis

Document / Book	Indication	Recommended Regime
Guidelines on the use of antibiotics. Ministry of Health 1994 ⁷³	For prophylaxis in major head and neck surgery	2 nd or 3 rd generation cephalosporins and metronidazole
Scottish Intercollegiate Guidelines Network. Antibiotic Prophylaxis in Surgery ³	Prophylaxis recommended for contaminated and clean/contaminated head and neck surgery	No mention of which antibiotics and regimes to use – there is a mention that beta -haemolytic streptococci are susceptible to penicillins, macrolides and clindamycin while the oral anaerobes are susceptible to metronidazole and coamoxiclav
Rowe. A Comprehensive Guide to Clinical Dentistry. 1989	Minor oral surgery - antibiotic cover for those procedures involving bone removal Major oral surgery - antibiotic cover recommended	Regime not mentioned Penicillin V 250mg qid for 5 days or Erythromycin 250mg qid for 5 days
Howe GL. Minor Oral Surgery. 2nd Edition 1971.	No mention of perioperative antibiotic prophylaxis	
Wright Seward, Harris and McGowan. Outline of Oral Surgery Part One. 2 nd Edition Revised Reprint 1992. Wright	3 rd molar surgery Major resections Prevention against loss of bone graft	Metronidazole 3-5 days postoperatively Metronidazole 3-5 days postoperatively Metronidazole and Flucloxacillin or a Cephalosporin postoperatively for at least 72 hrs (no mention of doses)

APPENDIX 2**ASA Score**

The American Society of Anaesthesiologists (ASA) has devised a preoperative risk score based on the presence of co-morbidities at the time of surgery

ASA score	Physical Status
1	A normal healthy patient
2	A patient with a mild systemic disease
3	A patient with a severe systemic disease that limits activity, but is not incapacitating
4	A patient with an incapacitating disease that is a constant threat to life
5	A moribund patient not expected to survive 24 hours with or without operation