



## ANTIBIOTIC PROPHYLAXIS

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**ABSTRACT** Dental infections commonly present with symptoms of pain, fever, and swelling. Surgical and endodontic treatments are the early management of infected teeth, followed by antibiotic therapy. Antibiotics are generally used in dental procedures to treat odontogenic infections, nonodontogenic infections, local infection, focal infection, and prophylaxis. Antibiotic prophylaxis is prescribed for patients with immunosuppressed conditions, infective endocarditis, metabolic disorders, and patients with prosthetic joints. To reduce the complications of unnecessary antibiotic prescriptions especially bacterial resistance, comprehensive guidelines should be established. It has been noted that only about 12% of dentists adequately and correctly prescribe antibiotics, which shows the importance of comprehensive guidelines.

**KEYWORDS** : Prophylactic antibiotics, comprehensive antimicrobial prescribing guidance.

**INTRODUCTION**

Bacteria commonly enter the circulation from the oral cavity. The oral cavity is a portal of entry for many pathogens.

The use of antibiotics prior to an invasive dental procedure has been suggested for a variety of immunocompromised conditions, including neutropenic cancer patients, patients with end stage renal disease treated with hemodialysis, organ transplant patients, and poorly controlled diabetics.<sup>4</sup> The evidence to support the practice of routine antibiotic prophylaxis prior to invasive dental procedures in this populations continues to evolve, however, and decisions to prescribe are often based on medicolegal concerns rather than evidence, which remains poor. For this reasons, dental prescribers need to understand that the negative consequences of repeated antibiotic use, such as increased antibiotic resistance, costs, and potential allergic reactions, must always be weighed against the perceived benefit of infection prevention<sup>4</sup>

Antibiotics prescription may result in some adverse effects such as hypersensitivity reactions and dermatological and allergic disorders. Furthermore, unnecessary prescription of antibiotics could result in several serious complaints, for example, bacterial resistance, gastric and hematological problems, and diversion of bacterial microbiota. Besides, this could lead to oral bacterial resistance which is considered a growing concern in dentistry and medicine as well. To prevent these problems, antibiotics should be prescribed in a narrow spectrum and be limited to acute infections. Moreover, further education and investigation should be conducted to prevent and reduce the problem of antibiotic resistance.<sup>4</sup>

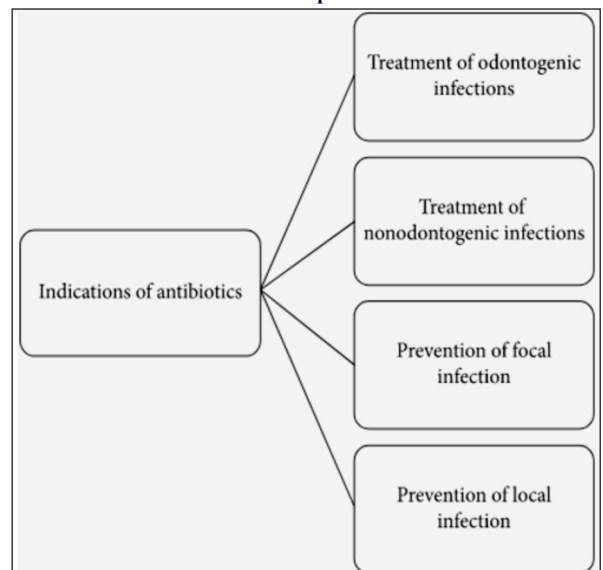
**Different rates of antibiotic prescription by dentists.**<sup>3</sup>

Antibiotic	Prescription rate (%)
Amoxicillin	51.1
Amoxicillin+clavulanic acid	24
Clindamycin	6.6
Azithromycin	5.3
Clarithromycin	4.4
Doxycycline	3.6
Spiramycin	2.2

Erythromycin	1.2
Ciprofloxacin	0.2
Cefadroxil	0.1
Minocycline	0.1
Cefuroxime	0
Others	1.1

**Indications of Antibiotics**

Antibiotics are suggested in the cases of prophylaxis for local and focal infections, besides, for the treatment of odontogenic and nonodontogenic infection. indicated for all Figure summarizes the indications of antibiotics in dental practice.<sup>4</sup>

**Figure****Indications of antibiotics in dental practice.**<sup>3</sup>

### 3. Antibiotic Use in Pediatric Dentistry<sup>3</sup>

Therapeutic antibiotic dose for children.

Agent	Situation	Dose	Maximum dose	Available forms
Amoxicillin	First choice in dental infection	20–40mg/kg/day, e8h	2g/day	Tablet 125mg, capsule 250mg and 500mg and oral suspension 125mg/5ml and 250mg/5ml
Amoxicillin + clavulanic acid	Failure of first choice antibiotic		1000–2800 mg amoxicillin/143–400mg clavulanic acid	Tablet 375mg, 625mg, and 1000mg and oral suspension 228.5mg/5ml
Clindamycin	Penicillin hypersensitivity	10–20mg/kg/day, e6h		Suspension 75mg/5ml
Cephalexin	Necessity of broad-spectrum action	25–100mg/kg/day, e6h		Tablet 125mg, 250mg, and 500mg, capsule 250mg, 500mg, and 750mg, and oral suspension 125mg/5ml and 250mg/5ml
Metronidazole	Anaerobic bacteria	30mg/kg/day, 8h	2g/day	Tablet 200mg, 250mg, 400mg, and 500mg, infusion solution 500mg/5ml, and oral suspension 200mg/5ml

### 4. Antibiotic Therapy during Pregnancy

The drug prescription during the pregnancy should be done more cautiously, as the inappropriate prescription could irrecoverably harm the fetus. In dental practice, the main agents that are commonly used during pregnancy and are considered to be safe during this period are analgesics, anesthetic agents, and antibiotics.<sup>2</sup> Food and Drug Administration (FDA) has classified drugs into 5 groups (A, B, C, D, and X) based on their risk factors during pregnancy and most of the antibiotics are classified to be in class B of FDA arrangement. Furthermore, the pregnant patients should receive a complete adult dose with the usual length of treatment<sup>2</sup>.

Category A- Adequate and well-controlled studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy and no risk in later trimesters. Example drugs -levothyroxine, folic acid, liothyronine<sup>3</sup>.

Category B- Animal reproduction studies have failed demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women. Example drugs metformin, hydrochlorothiazide, amoxicillin.<sup>3</sup>

Category C-Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well controlled studies in humans, but potential benefits warrant use of the drug in pregnant women despite potential risks. Example drugs-gabapentin, amlodipine, trazodone<sup>3</sup>

Category D-There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks. Example drug-losartan<sup>3</sup>.

Category X- Studies in animals or humans have demonstrated fetal abnormalities and there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits. Example drugs- atorvastatin, simvastatin, methotrexate, finasterid<sup>3</sup>.

### 5. The Most Common Prescribed Antibiotics

#### 1. Clindamycin

Clindamycin is an antibiotic used for the treatment of a number of bacterial infections, including bone or joint infections, pelvic inflammatory disease, strep throat, pneumonia, middle ear infections,

and endocarditis. It can also be used to treat acne. In combination with quinine, it can be used to treat malaria. It is available by mouth, by injection into a vein, and as a cream or a gel to be applied to the skin or in the vagina<sup>2</sup>.

Clindamycin could be prescribed in the case of persistent infections, as it has more efficacies in comparison with penicillin and metronidazole. Besides, it has been shown that the bacterial resistance rates against penicillin are higher comparing to clindamycin. Moreover, the agent could be administered IV or IM, besides, oral ingestion<sup>2</sup>.

Clindamycin is also an excellent choice for patients who have an allergy to beta-lactam group antibiotics. The therapeutic dosage of the drug is 600 mg or 300 mg every 8 hours orally or intravenously. The drug is also a proffered alternative for prophylaxis in penicillin-allergic patients for prophylaxis. The usual prophylactic dose is 600 mg before procedure orally or 600 mg intravenously in both penicillin-allergic patients and those who cannot take medication by mouth<sup>2</sup>. Furthermore, more recent studies showed that clindamycin might reduce the risk of dry socket after extraction.

The most common side effects of clindamycin are vomiting, nausea, diarrhea, exanthem, jaundice, hepatitis, neutrophil reduction, eosinophilia, agranulocytosis, blood platelet count change, and pseudomembranous colitis. The agent is contraindicated for cirrhotic patients and for patients with a history of ulcerative and pseudomembranous colitis<sup>2</sup>.

#### 2. Penicillin

Penicillin are a group of antibiotics originally obtained from penicillium moulds. Most penicillin in clinical use are chemically synthesized from naturally-produced penicillin. A number of natural penicillin have been discovered, but only two purified compounds are in clinical use: penicillin G given by IV and penicillin V (given by mouth). penicillin was among the first medications to be effective against many bacterial infections caused by staphylococci and streptococci<sup>1</sup>. They are members of the beta lactam antibiotics. They are still widely used today for different bacterial infections, though many types of bacteria have developed resistance following extensive us<sup>3</sup>.

penicillin is used in the treatment of throat infections, meningitis, syphilis, and various other infections. The chief side effects of penicillin are hypersensitivity reactions, including skin rash, hives, swelling, and anaphylaxis, or allergic shock.<sup>1</sup> The more serious reactions are uncommon. Milder symptoms may be treated with corticosteroids but usually are prevented by switching to alternative antibiotics. Anaphylactic shock, which can occur in previously sensitized individuals within seconds or minutes, may require immediate administration of epinephrine<sup>3</sup>.

#### Semisynthetic penicillins

##### 2.1. Amoxicillin

Amoxicillin is an antibiotic used to treat a number of bacterial infections. It is taken, or less commonly by injection.

Common adverse effects include nausea and rash. Dose may need to be decreased. Its use in pregnancy and breastfeeding does not appear to be harmful. Amoxicillin is in the beta lactam family of antibiotics. The therapeutic dosage for amoxicillin is 500mg every 8 hours or 100mg every 12 hours<sup>1</sup>.

##### 2.2 Penicillin V-acid resistant penicillin

Penicillin V can be taken by mouth because it is relatively resistant to stomach acid. Doses higher than 500 mg are not fully effective because of poor absorption. It is used for the same bacterial infections as those of penicillin G and is the most widely used form of penicillin. However, it is not used for diseases, such as endocarditis, where high blood levels of penicillin are required<sup>1</sup>

##### 2.3. Ampicillin

Ampicillin is used to treat infections by many gram positive and gram negative. Ampicillin is an antibiotic used to prevent and treat a number of bacterial infections, such as respiratory tract infections, UTI, meningitis, and endocarditis.<sup>1</sup> It is used by mouth, by IM, or intravenously. Common side effects include rash, nausea, and diarrhea. It should not be used in people who are allergic to penicillin. Serious side effects may anaphylaxis. While usable in those with kidney problems, the dose may need to be decreased. Its use during

pregnancy and breastfeeding appears to be generally safe<sup>2</sup>.

It is commonly used for patients who cannot orally take drugs, and the prophylaxis dosage is 2mg IV or intramuscular (IM) half an hour before procedure.

#### 2.4. Amoxicillin with Clavulanic Acid (Co-Amoxiclav)

**Amoxicillin/clavulanic acid**, is an antibiotic medication used for the treatment of a number of bacterial infections. It is a combination consisting of amoxicillin, a beta lactam antibiotic, a beta lactamase inhibitor. It is specifically used for otitis media, pneumonia, cellulitis, UTI and It is taken orally or by IV<sup>4</sup>.

Common side effects include diarrhea vomiting, and allergic reactions. It also increases the risk of yeast infections, headaches, and blood clotting disorders. It is not recommended in people with a history of a penicillin allergy. It is relatively safe for use during pregnancy.

The combination of amoxicillin and clavulanic acid is used to treat certain infections caused by bacteria, including infections of the ears, lungs, sinus, skin, and urinary tract. Amoxicillin is in a class of medications called penicillin-like antibiotics. It works by stopping the growth of bacteria<sup>1</sup>.

#### 2.5. Cephalosporin

Cephalosporins are **beta-lactam antimicrobials used to manage** a wide range of infections from gram-positive and gram-negative bacteria. The five generations of cephalosporins are useful against skin infection, resistant bacteria, meningitis, and other infections<sup>2</sup>.

Cephalosporins are indicated for the prophylaxis and treatment of infections caused by bacteria susceptible to this particular form of antibiotic. First-generation cephalosporins are active predominantly against gram positive bacteria, such as and staphylococcus streptococcus. They are therefore used mostly for skin and soft tissue infections and the prevention of hospital-acquired surgical infections. <sup>1</sup>

Successive generations of cephalosporins have increased activity against gram negative bacteria, often with reduced activity against Gram-positive organisms. Cefazolin is suggested for patients who are allergic to penicillin and cannot take the medication by mouth, with the dosage of 1g IV or IM 30 minutes before the procedure<sup>2</sup>.

The antibiotic may be used for patients who are allergic to penicillin due to the different beta lactam antibiotic structure. The drug is able to be excreted in the urine. <sup>1</sup>

Common adverse drug reactions associated with the cephalosporin therapy include: diarrhea, nausea, rash, electrolyte disturbances, and pain and inflammation at injection site. include vomiting, headache, dizziness, oral and vaginal candidiasis, fever<sup>1</sup>.

#### 3. Nitroimidazoles

**5-Nitroimidazole** is an organic compound. The nitro group at position 5 on the imidazole ring is the most common positional isomer. Nitroimidazoles are antibiotics used to treat anaerobic bacterial infections, parasitic infections, and protozoal infections and prevent postoperative infections<sup>2</sup>.

##### 3.1. Metronidazole

Metronidazole has bactericidal activity and acts against anaerobic microorganisms by inhibiting the nucleic acid synthesis; the agent also showed antiprotozoal activity and does not disrupt the protective aerobic microbiota. <sup>1</sup> Combined administration of amoxicillin and metronidazole could cover most of the oral bacteria. Prescription of this combination or metronidazole is also recommended for the treatment of periodontal infections. The drug is commonly prescribed with a dosage of 500–750 mg every 8 hours<sup>3</sup>.

The dental practitioners should bear in mind that metronidazole can interact with some agents such as alcohol (causes nausea, vomiting, and abdominal cramp), disulfiram, warfarin, and hydantoin anticonvulsants. <sup>1</sup> the agent might also result in serious side effects, such as seizures, anesthesia, or paresthesia of the limbs in certain patients. Two cases with metronidazole resistance have been reported in Scotland: one was an infection of the knee joint (with anaerobic streptococci that is found in dental abscess and periodontal disease) and the other was *Bacteroides thetaiotaomicron* bloodstream infection<sup>4</sup>.

#### 4. Macrolides

The macrolides are a class of natural products that consist of a large macro lytic lactone ring. Some macrolides have antibiotic or antifungal activity and are used as. Macrolides are bacteriostatic in that they suppress or inhibit bacterial growth rather than killing bacteria completely<sup>4</sup>.

Antibiotic macrolides are used to treat infections caused by gram positive bacteria (e.g., *Streptococcus pneumoniae*) and limited gram-negative bacteria and some respiratory tract and soft-tissue infections <sup>4</sup>. The antimicrobial spectrum of macrolides is slightly wider than that of penicillin, and, therefore, macrolides are a common substitute for patients with a penicillin allergy. Moreover, macrolides should not be prescribed in patients with progressive cirrhosis, as this could result in liver failure and even death. <sup>1</sup>

##### 4.1. Erythromycin

Erythromycin has bacteriostatic activities and is commonly prescribed for dental caries and dental plaque. The most common microorganism that causes dental caries is *Streptococcus mutans*, which is highly sensitive to erythromycin. Erythromycin can inactivate the caries, and it also can decrease the growth and formation of dental plaque<sup>2</sup>.

Erythromycin should be prescribed with a dosage of 250–500mg every 6 hours. However, the drug is not regularly recommended as it could cause several short-term and long-term adverse effects, such as gastrointestinal problems, hepatotoxicity, and also bacterial resistance. Moreover, the drug is contraindicated in patients taking simvastatin or colchicine and also in patients who suffer from porphyria<sup>2</sup>.

##### 4.2. Clarithromycin

Clarithromycin is a broad-spectrum antibiotic that is considered to be the new generation of erythromycin. the prescription of clarithromycin can be a logical approach for suppressing the pulp and periodontal infections. However, clarithromycin is not usually recommended as the first-line treatment and is used instead of penicillin in patients who cannot tolerate the gold standard treatment of penicillin<sup>1</sup>.

The standard dose for prophylaxis is 500 mg orally 1 hour before the dental procedure. The most common side effects of clarithromycin are gastrointestinal complications, such as nausea and diarrhea. It is indicated that clarithromycin has some new effects such as modulating myocarditis, cardiac rejection, and change of inflammatory signs<sup>1</sup>.

##### 4.3. Azithromycin

**Azithromycin** is an antibiotic medication used for the treatment of a number of bacterial infections. Along with other medications, it may also be used for malaria. It can be taken by mouth or IV with doses once per day. <sup>2</sup> Common side effects include nausea, vomiting, diarrhea and upset stomach. An allergic reaction, such as anaphylaxis, or a type of diarrhea caused by clostridium difficile is possible. No harm has been found with its use during pregnancy Azithromycin is an azalide, a type of macrolide antibiotic. It works by decreasing the production of protein, thereby stopping bacterial growth<sup>2</sup>.

The dosage of the drug is 500mg once a day for three days, in case of therapeutic prescription, and 500mg 1 hour before the oral procedure, in case of prophylactic administration. The common side effects of azithromycin include nausea, diarrhea, and gastrointestinal disorders, and it should not be prescribed in erythromycin-allergic patients. <sup>2</sup>

#### 5. Beta-Lactams

$\beta$ -lactam are antibiotics that contain a beta lactam ring in their chemical structure. This includes penicillin, cephalosporins, monobactams, carbapenems. Most  $\beta$ -lactam antibiotics work by inhibiting cell wall biosynthesis in the bacterial organism and are the most widely used group of antibiotics. Bacteria often develop resistance to  $\beta$ -lactam antibiotics by synthesizing a beta lactamase, an enzyme that attacks the  $\beta$ -lactam ring. To overcome this resistance,  $\beta$ -lactam antibiotics can be given with beta lactamase inhibitor such as clavulanic acid.  $\beta$ -lactam antibiotics are indicated for the prevention and treatment of bacterial infections caused by susceptible organisms. At first,  $\beta$ -lactam antibiotics were mainly active only against gram positive bacteria, yet the recent development of broad-spectrum antibiotics active against various gram-negative organisms has increased their usefulness.

## 6. Fluoroquinolones

Fluoroquinolones are broad-spectrum bactericidal antibiotics that mostly act against Gram-negative bacilli, Gram-positive aerobic cocci, and anaerobic organisms, by preventing the synthesis of DNA. Fluoroquinolones are commonly prescribed for nonodontogenic infections, such as respiratory, genitourinary tract, joint, and bone infections. These agents have a higher capacity of penetration into tissue in comparison with other commonly prescribed antibiotics in dental practice<sup>2</sup>.

The side effects of this class of antibiotics include gastrointestinal reactions and cartilage, joint, tendon, and the central nervous system involvement. Fluoroquinolones must not be prescribed for children because of the possibility of chondrotoxicity in developing cartilage and for patients who use theophylline, as this could result in serious complications, for example, seizure.<sup>2</sup>

### 6.1. Ciprofloxacin

Ciprofloxacin is the second generation of fluoroquinolone antibiotic and is active against Gram-positive and Gram-negative pathogens. Used to treat a number of bacterial infections. This includes bone and joint infections, intra-abdominal infections, certain type of infectious diarrhea, respiratory infections, skin infections, typhoid fever, and UTI, among others<sup>1</sup>. For some infections it is used in addition to other antibiotics. It can be taken by mouth, as eye drops, as ear drops, or intravenously. Common side effects include nausea, vomiting, and diarrhea<sup>2</sup>.

The drug is usually administered orally with a dosage of 500 mg every 12 hours to treat odontogenic infections. The most common side effect of ciprofloxacin is gastrointestinal problems, including, nausea, vomiting, and diarrhea. Dental practitioners should take the patients' history as if they have been using theophylline because the drug interaction could result in severe consequences. The initial signs of theophylline toxicity in these patients are nausea and vomiting, which should not be confused with the side effects of ciprofloxacin<sup>4</sup>.

### 6.2. Moxifloxacin

**Moxifloxacin** is an antibiotic used to treat a number of infections. Moxifloxacin is a broad-spectrum bactericidal agent and a fourth-generation fluoroquinolone.<sup>1</sup>

Moxifloxacin can be considered as a good choice to treat odontogenic and periodontal infections as well, since it has high penetration capacity through periodontal and bone tissues. Moreover, this could be prophylactically prescribed to beta-lactam-allergic patients to prevent bacteremia.<sup>1</sup> However, moxifloxacin is not used as the first-line treatment because of its high price and is usually prescribed when the first-line antibiotics and surgical procedures are failed. The effective dose of the agent to control odontogenic infections is 400 mg once a day. The major concern is that the drug could affect cartilage maturation; hence, it must not be in pregnant and adolescent patients.<sup>2</sup>

## 7. Tetracyclines

Tetracyclines have a broad spectrum of antibiotic action. Originally, they possessed some level of bacteriostatic activity against almost all medically relevant aerobic and anaerobic bacterial genera, both gram positive and gram negative.<sup>1</sup>

The drug could be a reasonable prescription for the treatment of periodontal diseases, as it has anti-inflammatory activity, collagenase inhibition potential, and bone resorption inhibitory capacity; besides, it could help the fibroblasts to attach to the root surface<sup>3</sup>.

Tetracycline is recommended in cases of periodontal diseases, improving marginal attachment and enhancing bone graft. The drug has a long half-life, preserves its antimicrobial activity for a long time, and is released from the tooth surface gradually.<sup>4</sup> However, the agent is not commonly suggested for the treatment of odontogenic infections because of the widespread resistance of pathogens and several side effects, including photosensitivity, nausea, vomiting, diarrhea, loss of appetite, hepatotoxicity, and discoloration of primary and permanent teeth. The prescription of the drug for young children and pregnant women is not recommended because it can cause intrinsic tooth staining during the calcification phase. Besides, tetracycline must not be prescribed for patients with active liver diseases<sup>1</sup>.

## 6. CONCLUSION

Antibiotic therapy is mandatory and essential in medicine and dentistry. Invasive dental procedures if performed in immunocompromised patients should be preceded with an antibiotic prophylaxis<sup>1</sup>.

Consultation with the physicians and specialists is required before any dental treatment is carried out in organ transplant and pregnant patients, the best outcome of dental procedure and to provide the required dose adjustments and thereby preventing complications. Antibiotic therapy is crucial to control dental infections after surgical interventions such as incision, drainage, and pulp debridement<sup>2</sup>. Dentists prefer to prescribe amoxicillin and metronidazole or co-amoxiclav to control dental infections. Moreover, clindamycin is an alternative drug in penicillin-allergic patients<sup>4</sup>.

Accurate use of antibiotics is crucial for the treatment of dental infections; accordingly, comprehensive antimicrobial prescribing guidance should be established for dental professionals.

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