# Antibiotics in Dentistry – An Art and Science

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**Abstract**

Antibiotic therapy is an art and a science. There are so many confounding variables, such as suspected pathogen, ability to establish drainage, pharmacokinetic properties of the drug, mechanism of action of the antibiotic, virulence of the infection, the current health status of the host, and host defense mechanisms, that it is not possible to make antibiotic therapy into a mechanistic technologic science. The most important decision for the dental practitioner to make is not only which antibiotic to use but whether to use one at all. This article will discuss important factors to be kept in mind while prescribing antibiotics in dentistry.

**Key Words: -** Antibiotics, SABE, Drug Resistance

## Introduction

The Magic Word "Antibiotic" inevitably springs to mind whenever an infection has to be dealt with. Antimicrobial drugs are the greatest contribution to 20th century of therapeutics. Truly we live in the "Antibiotic era". Beginning with the early work of Sir Alexander Fleming in 1929 when Penicillin became the first "Miracle drug" innumerable lives have been saved from diseases such as pneumonia, wound sepsis and bacteremia's. Dentists were also benefited greatly from discovery of penicillin because most odontogenic infections were believed to be caused by penicillin sensitive organisms. They are most frequently used and misused drugs by dentist themselves.[1-4]

The abuse of antibiotics is not merely that they may be unnecessary, but side effects may be more serious than the original complaints. This is especially true of dentistry, where infections are rarely serious. Despite these problems associated with antibiotic use, antibiotics are essential weapon against infection; hence wise use of antibiotics requires the clinician to take the stance that positive indication must be present before antibiotic drugs are prescribed. The clinician should not assume that antibiotics must be given in all instances of infection.[1-4]

## Principles for Choosing an Appropriate Antibiotic

After ascertaining that the condition is treatable infection, and that it is not likely to resolve by it or by use of local measures (antiseptics, drainage of pus etc.), a suitable drug is to be advised. The choice of drug depends on qualities of *patient, the infecting organism and the drug.*[1-6]

### *Patient Factors*

1. ***Age***

**Age may affect the kinetics of many AMA**

Eg 1: Conjugation & excretion of chloramphenicol is inefficient in new-born, hence larger doses produces –grey baby syndrome

Eg 2: Sulphonamides displace bilirubin from protein binding sites – can causes kernicterus in neonate because their BBB is more permeable.

Eg 3: The t½ of aminoglycosides is prolonged in the elderly and they are more prone to develop VIII nerve toxicity.

Eg 4: Tetracyclines accumulate in the developing teeth & bone, discolour and weaken them and so are contraindicated below the age of 6 years.

2. ***Renal and hepatic functions***

Cautious use and modification of the dose of an AMA (low safety margin) becomes necessary when the organ of its disposal is defective.

**Dose reduction even in mild renal failure**

Aminoglycosides, Cephalosporins, Vancomycin and Amphotericin

| **In moderate renal failure** | **Drugs to be avoided are** |
|---|---|
| Metronidazole | Cephalothin |
| Co-trimoxazole | Tetracyclines(Except doxycycline) |
| Fluroquinolones | Nalidixic acid, Nitrofurantoin |

*Antimicrobials to be avoided or used at lower dose in liver decrease are:-*

| **Drugs to be avoided** | **Drug reduction needed** |
|---|---|
| Erythromycin estolate | Chloramphenicol |
| Pyrazinamide | Metronidazole |
| Tetracyclines | Clindamycin |

3. ***Local factors***

The condition prevailing at the site of infection greatly affects the action of AMA's

Presence of pus and secretion reduces the efficacy of most AMA's especially sulphonamides & aminoglycosides cannot cure peri-apical or periodontal abscess, unless pus is surgically drained.

Presence of necrotic foreign body also makes eradication of infection practically impossible

Haematoma's foster bacterial growth. Tetracycline, penicillins & cephalosporins get bound to degraded Haemoglobin in hematoma

Lowering the pH at site of infection reduces activity of macrolide & aminoglycoside antibiotics

Anaerobic environment in the center of an abscess impairs bacterial transport process, which concentrates aminoglycosides in the bacterial cell rendering them less susceptible.

Penetration barriers may hamper the access of the AMA to the site of infection in sub-acute bacterial endocarditis (SABE), Endopthalmitis prostratitis etc.

**4. *Improved host defense***

Integrity of host defense plays a crucial role in overcoming an infection. Pyogenic infections occur readily in Neutropenic patients, while if cell mediated immunity is impaired, low grade pathogens attack. In an individual with normal host defense, a bacteriostatic AMA may achieve cure, while intensive therapy with cidal drugs is imperative in those with impaired host defense or when organisms are protected with barrier.

**5. *Pregnancy***

All AMA should be avoided in pregnancy that has risk to foetus.

***Penicillin, cephalosporins & erythromycin are reasonably safe***

Tetracyclines carry a risk of acute yellow atrophy of liver, pancreatitis and kidney damage in mother. They also cause tooth discoloration and bone deformities in offspring.

Aminoglycosides can cause foetal ear damage.

Metronidazole though hot teratogenic, its mutagenic potential warrants caution.

**6. *Genetic factors***

Some drugs like sulphonamides & chloramphenicol cause haemolysis in G- 6pd deficient patient.

***Organism Related Considerations***

***A. Empirical Therapy***

Antibiotic therapy is initial / empirical or definitive, depending on whether the organism is identified precisely. Ideally, identification and antimicrobial sensitivity of the infecting bacteria should be determined before instituting systemic antibacterial therapy. However being time consuming (at least 48 hrs), expensive & impractical for dental infections, initial empiric therapy is indicated.

Initial empiric therapy may be instituted with a fair degree of reliability, "When the site and features of infection are well defined, the circumstances leading to infection are well known and the organisms that most common causing such infections are well known". Empirical therapy is especially important in dentistry. Because most dental infections are acute in nature and treatment cannot be delayed. Also it is not always possible to obtain appropriate samples of infected material for bacteriologic testing.

***B. Identification of causative Organism***

Type of bacteria (Aerobic/ anaerobic) and their specific Identification is important for dentist Typical odontogenic infections (alveolar abscess, periodontal abscess, dental pulp infection, chronic periodontitis acute necrotizing gingivitis etc.) are caused by a mixture of aerobic and anaerobic bacteria (70%). Bacteria found in well-circumscribed chronic non-advancing abscesses are mostly anaerobic bacteria, while cellulitis type of infection that do not have abscess formation show exclusively aerobic bacteria, i.e. early infection (cellulitis like) – aerobic bacteria, Severe infection – mixed flora (Aerobic + anaerobic), If infection becomes longer contained & controlled – aerobic environment (only anaerobic flora) Abscess – anaerobic bacteria alone

***C. Antibiotic Sensitivity for causative organism***

Penicillin is excellent for treatment of streptococcal infection and is good to excellent for major anaerobes of odontogenic infections.

Erythromycin is effective against streptococci, peptostreptococci & prevotella but ineffective against fusobacterium.

Clindamycin is both effective against streptococci and five major anaerobes.

Cephalexin is only moderately active against streptococcus (approximately 10% of strain are resistant 70% intermediate sensitive, and 20% are sensitive) and good to very good against all groups of anaerobes.

Metronidazole has no action against streptococcus but has excellent activity against all anaerobic groups.

***Drug Factors***

**1. Use of Specific narrow spectrum antibiotic**

For definitive therapy a narrow spectrum drug which selectively affects the concerned organism is preferred, because it is generally more effective than a broad spectrum. It is less likely to disturb the normal microbial flora (super infections).

Less chances for development of resistant strains.

For empirical therapy often a broad spectrum drug is used to cover all pathogens.

**2. *Use of Bactericidal rather than a bacteriostatic drug***

A bactericidal antibiotic may be preferred over bactoriostatic because it directly reduces number of bacteria at site of infection by killing them while bacteriostatic only prevents increase in number [inhibit growth & reproduction of bacteria]

This is especially important while treating life-threatening infections in patients with impaired host defense. Antibiotic therapy basically reduces the bacterial challenge to allow host defenses to complete treatment and if bactoriostatic drugs are used, they slow growth so that host defense can now eliminate a static population of bacteria & cure the infection but if host defense system is compromised use of bactericidal drug becomes critical. Acute infection generally resolves faster.

Most bactericidal drug exert prolong post antibiotic effect, so that maintenance of drug level continuously above MIC is possible. – While in bacteriostatic drugs if drug level decreases bacteria multiplies & there is relapse of infection. They exert their influence after they are incorporated into the bacterial cell and cell eventually dies, while bacteriostatic drugs exert their influence only when present in patient's tissues.

3. ***Use of least toxic antibiotic***

A less toxic drug is always preferred (because sometimes AMA, along with living bacteria can also kill or injure human cells) Eg: β lactams over aminoglycoside or chloramphenicol.

4. ***Antibiotic with evidence of clinical efficacy / proven history of Success:***

Relative value of different AMA in treating an infection is decided on basis of comparative clinical trials. Reliable clinical data, if available is the final guide for choice of the antibiotic.

Newer antibiotics should be used only when they offer clear advantages over older ones. They may be effective for bacteria against which no other antibiotic is effective.

5. ***Cost***

It is difficult to place a price tag on health but the surgeon should consider the cost of the antibiotic prescribed.

6. ***Patient's drug history and Compliance***

Knowledge of patient drug reaction is critical especially for the patients previous allergic reactions & toxic reactions because

Penicillin is so widely used & allergic rate of penicillin is approximately 5% hence it's important to check for allergy before its administration.

If Patient had a documented anaphylactic reaction to penicillin, a cephalosporin should be avoided unless deemed absolutely essential.

Patients with h/o previous major toxic or minor side effects from an antibiotic are likely to experience the same problem again.

Attempts should be made to identify the drug and an alternative should be used if possible.

7. ***Patient Compliance***

Patient's compliance decreases with increase in number of pills/ day. Hence an antibiotic that would have highest compliance would be the drug that could be given once a day for 4-5 days.

***<u>Principles of Antibiotic Administration</u>***

Once it has been established that patient has an infection and requires antibiotic therapy and kind of antibiotic has been chosen, it must be administrated properly – (dosage, route of administration ,time intervals & concentration of drug) because for optimum action, antibiotic must be present at site of infection in sufficient concentration for an adequate length of time.

***Proper dose***

The goal for any drug therapy should be to prescribe or administer sufficient amounts to achieve desired therapeutic effects but not enough to cause injury to host – This depends on MIC of an antibiotic for a specific bacterium.

***For therapeutic purpose the concentration of an antibiotic at site of infection should be 3-4 times the MIC – dosage – 3-4 times MIC.***

Eg: Aminoglycosides to fluoroquinolones produce concentration dependent inhibition for many organisms i.e. same daily dose of gentamycin produces better action when given as a single dose than divided into 2-3portion.

(But on other hand macrolides to β-lactams produce time dependent inhibition – antimicrobial action depends on length of time , the concentration remains above MIC i.e. division of dose has better effect, but dose should be spaced such that surviving organism again start multiplying and cidal action is exerted)

Therapeutic levels greater then above mentioned criteria (3-4 times the MIC) generally do not improve the therapeutic results i.e. they increases the likelihood of toxicity & is wasteful – critical for antibiotic like gentamycin (effective in conc. of 4 – 6 µg but above 10 µg /ml incidence of nephrotoxicity increases dramatically).

But increased doses may be justified when the site of infection may be isolated from the blood supply, as in abscess formation or in non-vital tissue.

Though not greater than 3-4 times the MIC, sufficient dose must be given to reach therapeutic levels. Sub therapeutics levels may Mask the infection & suppress the clinical manifestation without actually killing the invading microbes.

Further may cause recurrence of infection once the drug is discontinued this under dosage happens – when clinician uses a drug of great potential toxicity & fears a toxic reaction – hence least toxic drug must be used.

***<u>Principles of Antibiotic Dosing for Orofacial Infections</u>***

***Employ high doses for a short duration***

Critical for concentration dependent antibiotic. An oral loading dose is indicated as, without a loading dose, it takes 6-12 hours to achieve most therapeutic blood and tissue levels via oral administration especially important for tetracyclinies.

***Achieve blood levels of antibiotic at 2-8 times the MIC***

Such blood levels are necessary to compensate for the tissue barriers that impede antibiotic penetration to the site of infection.

***Use frequent dosing intervals***

This is important for β –lactam antibiotics such as penicillin –V and first generation cephalosporin (Cephalexin) so as to maintain relatively constant blood levels.

***Determine the duration of therapy by remission of disease***

AMA is terminated when patients host defenses have gained control over infection.

***Proper time intervals***

The frequency of dosage is also important in administration of antibiotics.

The usual dosage intervals for therapeutic use of antibiotic are four times the T½ (plasma half-life – time during which one half of absorbed drug is excreted).
Eg: cefazolin t½-2hrs – intervals 8 hrs

As most antibiotics are eliminated by kidneys, the patient with pre-existing renal diseases & subsequent decreased clearance may require longer intervals b/w doses to avoid overloading.

An alternate, to decrease the dosage & maintain same interval. Doses to maintain same intervals- but therapeutic response depends on increasing peak level – hence most preferred is to increase the time interval (not true for all antibiotics).

***Proper route of administration***

Many AMA can be given orally as well as parentally but aminoglycosides (low absorption) penicillin.G, carbenicillin, vancomycin, many cephalosporins are administered by injections only.

For less severe infections oral antibiotic is preferable, but for more severe infections (spreading cellulites, meningitis, septicaemias) parenteral antibiotic may be chosen. Because: Some bacteria which are not susceptible at oral level are quite susceptible to concentration achieved by parenteral route of administration.

***Oral route – most variable absorption. Hence should be taken in a fasting state (30 mins before or 2 hrs after a meal) for maximum absorption.***

When long-term parental administration is necessary, patients – in such situations I.V route is considered, poorly accept repeated I.M injections.

***Note: Consistency in route of administration is most important i.e. when treating a serious established infection parenteral therapy is method of choice – after initial response –immediate discontinuation of parenteral route to oral administration of drug is tempting. Not to be done-as infections may recur.***
***Penetration of drug***

A drug which penetrates better and attains higher concentration is likely to be most effective.

Penetration of AMA into bone is generally poor but Clindamycin penetrates very well and is a good choice for purulent osteitis and certain other tooth infections.
Fluroquinolones have excellent tissue penetration, attain high concentration in soft tissues, lungs, prostrate joints etc.
Ciprofloxacin and Rifampicin have very good intracellular penetration.

Cefuroxime, ceftriaxone, chloramphenicol and ciprofloxacin attains higher CSF concentration, but on other hand penicillin & Aminoglycosides penetrate poorly into CSF unless meninges are inflamed.

Ampicillin cephalosporin & erythromycin attains higher biliary concentration.

***Need for use of Systemic Antimicrobials in Dentistry***

Antibiotics should not be used as a substitute for needed surgical treatment, nutritional support, or other basic therapies.

Systemic anti-bacterials are used in dentistry for two purposes (table 1 and 2):

Therapeutically
Prophylactically

***Therapeutic Indications:***

- As a definitive treatment in the management of postoperative infections
- As a supportive treatment to the surgical management of infection. (drainage of abscess)
- Fever & chills lasting more than 24 hrs
- Trismus due to infection
- Rapidly spreading cellulitis
- Immunocompromised individuals
- Contaminated maxillofacial infections
- Any procedures with known high risk of infections
- Prophylactic to prevent ***SABE***

**Use of Antibiotics in Periodontics**

- Patients who exhibit continuing loss of periodontal attachment despite diligent conventional mechanical periodontal therapy *(Recurrent or refractory periodontitis).*
- Patients with *aggressive types of periodontitis. Or with medical conditions* predisposing to periodontitis may benefit from antibiotic therapy.
- Patients with *acute or severe periodontal infections* (periodontal abscess, acute necrotizing gingivitis/periodontitis).
- Patients with chronic periodontitis may also benefit from antibiotics with improvement in clinical attachment level, but *many questions regarding the indications for this therapy remain unanswered*.

**Prophylactic Indications:**

Prophylaxis: use of AMA for preventing the setting in of an infection or suppressing contacted infection before it clinically manifests.

***Prophylactic uses of AMA in dental practice:***

- *Prevention of wound infection*
- *Prevention of distant infection*

***Prophylaxis for Dental Wound Infection***

**Criteria for the use of systemic preventive antibiotics in surgical procedures**

- ✓ Systemic preventive antibiotics should be used in the following cases:
  - A high risk of infection is associated with the procedure
  - Consequences of infection are unusually severe
  - The patient has a high NNIS risk index.
- ✓ The antibiotic should be administered preoperatively but as close to the time of the incision as is clinically practical. Antibiotics should be administered before induction of anaesthesia in most situations.
- ✓ The antibiotic selected should have activity against the pathogens likely to be encountered in the procedure.
- ✓ Postoperative administration of preventive systemic antibiotics beyond 24 hours has not been demonstrated to reduce the risk of SSIs.
- ✓ Administration of the antibiotic is by IV; 30 minutes prior to incision is the recommended time (Woods, 1998). Antibiotics should not be administered more than 2 hours prior to surgery.
- ✓ Dose should be double the normal recommended therapeutic dose

***Antimicrobial Combinations***

- Combinations should be used with a specific purpose
- Never use blindly in the hope that ***"if one is good, two is better, & three could cure almost any infections".***
- Every combination is unique; the same drugs may be synergistic for one organism, but antagonistic to another.

***Advantages of combination therapy***

- Broadens the antimicrobial range of a therapeutic regimen beyond that of a single antibiotic.
- Prevents or delays the emergence of bacterial resistance by using agents with overlapping spectra Ex: combination therapy in TB.
- Lowers the required dose of a potentially toxic drug
- Synergistic reactions

***Disadvantages***

May increase adverse effects i.e. toxicity of one agent may enhance the other. Ex: tobramycin + vancomycin

- Potential for antagonistic drug reactions with improperly selected drugs.

***Problems that arise with the use of AMA***

- Drug resistance & its cross resistance.
- Super infections
- Antibioma

***Causes* of *Failure in Antimicrobial Therapy***

- Organism not susceptible to prescribed AMA.
- Resistant pathogen
- Wrong diagnosis & wrong antibiotic
- Incorrect dosage
- Mixed infections with insufficient antibiotic coverage.
- Side effects & drug withdrawal
- Super-infections
- Inadequate host defenses.

***Common Errors***

- Viral infections do not respond to antibiotics
- Ineffective dose of appropriate antibiotic is administered.
- Toxic agents used when less toxic drugs available
- Susceptibility profile of pathogen is unknown
- Patients progress is not monitored

**Conclusion**

Antibiotics should not be used as a substitute for needed surgical treatment, inadequate therapies, or ***fear of unknown***. Remember, 'Infections are cured by the host not by the antibiotics'. Never use combinations blindly in the hope that "if one is good, two is better, and three could cure almost any infections"

Antibiotic therapy is an art and a science. There are so many confounding variables, such as suspected pathogen, ability to establish drainage, pharmacokinetic properties of the drug, mechanism of action of the antibiotic, virulence of the infection, the current health status of the host, and host defense mechanisms, that it is not possible to make antibiotic therapy into a mechanistic technologic science. The most important decision for the dental practitioner to make is not only which antibiotic to use but whether to use one at all.

**Table 1. Indication for antibiotic prophylaxis in oral surgery[7]**

| PROCEDURE | ANTIBIOTIC REGIMEN | EXCEPTIONS |
|---|---|---|
| **Exodontic and dento-alveolar surgery** | None | High risk of infection; communication with sinus or oral cavity |
| **Third molar surgery** | None | High risk of infection |
| **Dental implants** | Preoperative | Also postoperative prophylaxis when high risk of infection |
| **Orthognathic surgery e/o approach** | None | Pre-operative when anticipate oral communication |
| **Orthognathic surgery i/o approach** | Preoperative and 1 day postoperative | None |
| **Mandibular fractures (no oral communication)** | None | None |
| **Mandibular fractures (oral communication)** | Preoperative and 12 hours postoperative | Use prophylactic antibiotics 3—5 days postop when treatment delayed |
| **Facial bone fractures** | Preoperative | None |
| **Soft tissue trauma i/o** | None | High risk of infection |
| **Soft tissue trauma e/o** | None | High risk of infection |
| **Soft tissue trauma with dirty e/o wound** | Preoperative | Use prophylactic antibiotics 3—5 days postop when high risk of infection |
| **Major head and neck surgery** | Preoperative | Use prophylactic antibiotics 3—5 days postop when high risk of infection |

**Table 2. Antibiotics in Endodontics[8]**

| CONDITIONS | ANTIBIOTICS | EXCEPTIONS |
|---|---|---|
| Reversible and irreversible pulpitis | None | None |
| Apical periodontitis | None | Compromised host |
| Peri-apical abscess | I & D followed by antibiotics for 3-5 days | |
| Avulsed tooth | Doxycycline 200 mg loading dose followed by 100 mg for 4 days | None |
| Peri-apical pathology (cyst and granuloma) | None | 1gm pre-operative followed by 500 mg thrice daily for 3 days |

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