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Antibiotic therapy in pediatric dentistry II. Treatment of oral infection and management of systemic disease

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Abstract

Although there are definitive indications for the prescription of antibiotics in modern dentistry, a survey of the dental literature reveals wide variations in the prescribing practices of dentists. The two main reasons for use of antibiotics in pedodontics are control of oral infection and prevention of subacute bacterial endocarditis (SBE). This is the second part of a two-part review of the literature regarding the use of antibiotics in pediatric dentistry. In this part, the control of frank oral infection and management of patients with systemic conditions complicating dental treatment will be reviewed. The first part deals with the use of antibiotics for prophylaxis against SBE.

Antibiotics are used in dentistry for two major reasons: to control oral infection, and to prevent a bacteremia precipitated by dental manipulations from causing severe systemic sequelae. Antibiotics commonly are prescribed by dentists, and the uses and abuses of these drugs should be familiar to all practicing clinicians.

Proper use of antibiotics depends upon careful diagnosis of the patient's oral disease, adequate knowledge of the patient's systemic condition, and complete understanding of antibiotic therapy. While many articles appear in the dental literature each year concerning one antibiotic or another, there is a paucity of comprehensive information regarding the use of antibiotics in dentistry. Although it long has been accepted that children have different susceptibilities to oral and systemic diseases than adults, and that the metabolism of drugs is often vastly different in the pediatric patient, there are few sources emphasizing the use of antibiotics by dentists treating children.[1–5]

The purpose of this paper is to provide a comprehensive review of literature regarding the proper use of antibiotics in pediatric dental practice for control of oral infection, and in the management of children with systemic conditions which may alter disease resistance and healing response. The use of antibiotics for prophylaxis against subacute bacterial endocarditis is discussed in the first part of this paper. The properties and recommended dosages of specific drugs will not be covered in this paper. A number of pharmacology textbooks give excellent treatment to this subject.

The more serious sequelae of acute orofacial infections of dental origin have been almost completely eliminated in the United States through the development and application of antibiotics. The first antibiotic to be identified was penicillin, still considered to be the drug of choice in the management of most infections of dental origin. Many infections that would have been life-threatening or fatal events a few generations ago have become rarities with the use of this antimicrobial agent.

The goal of antibiotic treatment is to use the smallest amount of the agent most effective against the microorganism causing the infection.[6] It is desirable to choose an agent with a narrow, specific spectrum of activity with as few adverse effects as possible. The surest way to determine which antibiotic will be most effective is to isolate the offending organism with culture and sensitivity tests of the infected area.[7–10] However, it is not always possible to secure an uncontaminated sample from the diseased part, particularly when it is located in the mouth (with its own endemic diverse flora). Moreover, there will be certain instances when it is prudent to begin an immediate course of antimicrobial therapy. In such circumstances, a knowledge of the most likely organism is invaluable.

The most common organisms found in the mouth are gram-positive alpha- and beta-hemolytic streptoccoci, nonhemolytic streptococci, *Staphylococcus aureus*, and *S. albus*.[7, 11, 12] Other common inhabitants are Vincent's spirochetes and fusiform bacilli. According to Burnett, most infections of dental origin are caused by streptococci and staphylococci susceptible to antibiotics with a largely gram-positive spectrum.[13]

The advantages of antibiotic use are obvious, and the disadvantages should be accorded equal attention. With each antibiotic usage there is a possibility of:

1. sensitizing the patient to the drug
2. hypersensitivity reaction
3. toxic reaction
4. the development of stains of microbes resistant to the drug
5. superinfection by other organisms.[7–9, 14, 15]

The dentist must always consider whether using or not using an antibiotic constitutes the greater danger.

Caldwell and Cluff reviewed the hospital records of inpatients to evaluate the risk of adverse reactions to commonly prescribed antimicrobials.[16] The overall risk of adverse reactions for all antimicrobials was 5.4%. Natural penicillin (reputed to be very allergenic) caused adverse reactions in 3.2% of patients receiving it. Tizard also reports a low incidence of adverse reactions with penicillin, especially in pediatric patients.[17]

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In the Caldwell and Cluff study cited above, the penicillinase-resistant penicillins were responsible for adverse reactions in 8% of patients using it, and ampicillin caused 11.4% of patients to suffer ill effects. Cephalosporins and erythromycin were implicated in slightly lower than average adverse-effect occurrence. With all drugs there was a 0.5–1.0% risk of *Candida albicans* overgrowth.

Allergic reactions to antibiotics are divided by types into immediate, accelerated, and delayed reactions. Immediate reactions may be life-threatening: anaphylaxis, angioneurotic edema, and urticaria. Accelerated reactions include laryngeal edema, urticaria, rash, and fever. Delayed responses may include rash, fever, urticaria, and serum sickness syndrome.[18]

The duration of antimicrobial therapy should be determined by the course of the specific infection. Holroyd and Requa-George state that for most infections the drug should be given for 48 hours after all symptoms of infection have been resolved.[8] They also recommend at least 10 days of therapy for all beta-hemolytic streptococcal infections. Immunosuppressed patients and others exhibiting slow healing will require longer than average courses of therapy.

Systemic Disease

Patients with systemic disease are less able to respond physiologically to any infection. Shock, exhaustion, malnutrition, stress, or dehydration lower a patient's resistance to infection. Certain disease states leave the body extremely vulnerable to overwhelming sepsis. Extreme measures may be necessary to support a patient with congenital or acquired immunologic deficiency who has developed orofacial infection or is in need of dental procedures likely to violate tissue integrity.

Patients may develop immunologic deficiencies secondary to medical treatment for a disease. Examples are those who have received therapeutic irradiation, those receiving antimetabolite chemotherapy, and those on long-term systemic corticosteroids. Patients with immunodepression secondary to corticosteroid therapy include some asthmatics, patients with "autoimmune diseases," Crohn's disease sufferers, and graft and organ transplant recipients. Table 1 lists patients with primary or acquired deficiences of the immune system.

Any immunodepressed patient must be evaluated to determine his ability to respond to infectious insult. The more common diseases affecting children will be reviewed here. However, in all cases, if there is doubt that the bodily defenses are adequate to deal with infection, antibiotic therapy effective against the expected infectious organism should be administered.[19, 20] Highly compromised patients should be hospitalized during dental treatment, and a team-approach between dentists and physicians is vital to these patients' well being.

Diabetes

Children with diabetes mellitus are more susceptible to oral infection than children without the disease. The capillary changes associated with diabetes contribute to the finding of impaired healing in these patients.[21] The uncontrolled diabetic has a very low resistance to infection, and no elective dental treatment should be performed until adequate insulin balance has been achieved.[21] Even a diabetic child whose disease is well controlled can become seriously ill from a dental infection.[22] An acute alveolar abscess may precipitate diabetic

Table 1. Immunodepressed patients

A. *Primary Causes*	
active renal disease	nephrotic syndrome
agammaglobulinemia	other blood dyscrasias
agranulocytosis	other malignant disease
diabetes	primary adrenal insufficiency
DiGeorge's syndrome	sarcoid diseases
infectious mononucleosis	tuberculosis
leukemia	
malnutrition	
B. *Secondary causes*	
antimetabolite chemotherapy	
corticosteroid therapy (may include patients with:	
asthma	nephropathy
Crohn's disease	polyarteritis nodosa
dermatomyositis	status/post organ transplant or homograft
juvenile rheumatoid arthritis	systemic lupus erythematosus)
immunosuppressant therapy after organ transplant or homograft	

acidosis even in a controlled diabetic.[21]

There seems to be general agreement that well controlled diabetic patients do not require antibiotic coverage in situations in which a nondiabetic patient would not.[21, 23]

The dentist should evaluate each patient individually, giving consideration to the overall systemic condition, the presence or absence of infection in the oral cavity, and the degree of trauma anticipated from the dental procedures planned.

Any diabetic patient suffering from a severe oral infection should be given antibiotic support intravenously. With severe infection in a compromised patient parenteral medication is indicated. Weinstein has reported poor absorption of drugs given intramuscularly to diabetics.[15]

In juvenile onset diabetes the glomerular filtration rate is elevated. Madacsy et al. found that the serum half-lives of penicillin and carbenicillin are inversely related to the glomerular filtration rate.[24, 25] In order to maintain the same serum levels of these antibiotics, these investigators suggest diabetic patients will need about one and one-half times the usual dose.

Renal Disease

Patients with renal disease present abnormal electrolyte values, abnormal excretion rates, and altered rates of metabolism for some drugs.[26] With elevations of blood urea nitrogen, kidney patients have decreased platelet adhesiveness and prolonged bleeding, and therefore have poorer healing and are more susceptible to infection.[7] Sepsis is a common cause of death in uremic patients, who are debilitated with depressed immunological responses.[27] Bear and Bottomley et al. recommended that patients with active renal disease should be covered with antibiotics for any oral surgical procedure.[7, 27]

Patients on dialysis with arteriovenous shunts or fistulae have a constant nidus where infectious organisms may collect, and are at increased risk for SBE.[27] A shunt infection may prevent dialysis, with life-threatening implications.

Patients who have received kidney transplants have severely compromised resistance to infection.[27] Gold estimates 35% of these patients die of infection.[28] These patients are on immunosuppressant drugs throughout their lives to prevent graft organ rejection. Kidney transplant patients must receive antibiotic prophylaxis against oral infection, and against SBE prior to any breach of the continuity of oral tissues.[27] Bottomley et al. also recommend the use of antimicrobial mouthwash one day before and two days after oral manipulation to reduce the incidence of fungal infections.[27]

The usual dosage of antibiotics, primarily eliminated from the circulation by the kidneys, and drugs with nephrotoxic side effects should not be given to patients with renal disease. Kanamycin, cephaloridine, neomycin, and most tetracyclines are contraindicated.[16, 18, 27, 29] The safest drugs for these patients are those metabolized by the liver.[30] Erythromycin can be given in its usual dosage.[29] Drugs such as penicillin, lincomycin, and cephalothin are retained in the blood much longer than normal. The serum half-life of penicillin in a uremic patient can be 7–10 hours or more.[30] All antibiotic therapy for patients on dialysis and recipients of kidney transplants should be coordinated with the patient's nephrologist, as daily dosages may need to be calculated on the basis of estimated percentage of normal renal function.[30]

Leukemia

Acute lymphoblastic leukemia is the most common leukemia in childhood, with an incidence of about 4/100,000 children.[31, 32] With chemotherapy, antibiotics, and blood component transfusions, a 51% five-year survival rate has been reported.[31] Infection secondary to the immunosuppression of chemotherapy is the most common reason for death during remission.[31, 32] These patients are vulnerable to overwhelming systemic infection, and a dental abscess may be life-threatening. Carey and Chilcote have advised that with granulocyte levels above 1,500/mm^3, prophylactic antibiotic coverage is not necessary for dental treatment, but below this level coverage with penicillin V should be considered.[31] For surgical procedures, prophylactic antibiotics are indicated.[7] Before any dental treatment, platelet levels must be evaluated. All treatment is coordinated with the surpervising hematologist.

Sickle Cell Disease

Patients with sickle cell disease have an increased susceptibility to infections, partially due to decreased splenic function, which is most apparent from age six months until immune system maturation is complete. These children are prone to pneumonia and may be on long-term penicillin therapy as prophylaxis against pneumococcal infection, although pneumovax vaccine is now available. Systolic and diastolic heart murmurs, often accompanied by cardiac enlargement are common. If these patients require SBE prophylaxis, the possibility of penicillin-resistant *S. viridans* strains must be protected against in those on long-term penicillin. Prophylactic antibiotics to cover dental manipulations are not required unless the patient has cardiac disease, but any infection in a child with sickle cell disease should be treated aggressively with adjunctive use of antibiotics.

Other Disease States

All immunosuppressed patients must receive definitive dental treatment when they are in a state of maximum stability. Organ transplant recipients and bone marrow transplant recipients undergo immunosuppression to enhance the prognosis of the transplant. Prophy-

lactic antibiotics should be started shortly before the oral procedures and should be continued until several days afterwards. The dentists may wish to cover the patient with the appropriate antibiotic until oral healing is complete. This treatment must be performed in cooperation with the physician managing the patient's medical problems.[33]

Management of Frank Oral Infections

According to Bear, the infections which most often require antimicrobial therapy in dental practice (in descending order of their occurrence) are:

1. wound contamination
2. abscess formation
3. cellulitis.[7]

Contamination of wounds is frequent in cases of orofacial trauma and also may occur after the trauma of an orosurgical procedure. Extracellular organisms usually are responsible for acute infections, and most oral infections are caused by streptococci and staphylococci or by mixed flora of anaerobic and gram-positive streptococcal microorganisms.[7, 9, 10, 13] Goldberg has reported on increasing incidence of *S. aureus* and *S. albus* infections of odontogenic origin.[34]

In the anaerobic environment of an acute abscess, leukocytic function is impaired with the loss of normal tissue structure—occurring as part of the pathologic process of abscess formation. Direct contact between systemic antibiotics and the pathogens is reduced by the restricted blood flow into the infected area.

When a soft fluctulant mass is detected in the soft tissue overlying the cause of the infection, drainage should be achieved either through an opening of the affected tooth into the pulp chamber, or by incision of the soft tissue fluctulance.[10, 35] Several authors advise the prescription of an antibiotic immediately to combat the attendant bacteremia in cases of acute apical abscesses, whether or not drainage can be accomplished.[10, 36, 37] If drainage is achieved, culture and sensitivity testing should be performed upon the resultant fluid so that in case the infection does not resolve as expected, a change of antibiotic may be made intelligently.[23, 35] In cases of acute periapical infection where drainage cannot be established either by opening the infected tooth or by soft tissue incision, Natkin deems it necessary to prescribe an antibiotic.[35]

In the case of cellulitis, there is usually an increased blood supply so that antibiotic alone may resolve the infection initially. However, in some cases of cellulitis, the soft tissue overlying the infected tooth may be indurated, precluding productive incision and drainage. In these cases Bear recommends removing the cause of the infection prior to discontinuing antibiotic therapy.[7]

Penicillin is the drug of choice for the management of acute oral abscesses and cellulitis, at least until the results of culture and sensitivity testing are available.[23] If the patient is allergic to penicillin, erythromycin should be given. It should be noted that results of culture and sensitivity testing should not be considered more important than clinical findings. If an infection is resolving well, a change of drug should not be made solely because another antibiotic appears more active against the microorganisms in the laboratory.[9, 23, 38]

Despite a wealth of literature regarding appropriate dosages of antibiotics, there is little guidance regarding duration of therapy. Certainly the recommendation by McCallum that antimicrobial therapy continue for at least 24 hours after the patient is afebrile seems reasonable.[23]

Treatment of Orofacial Trauma

Orofacial Lacerations

There is a high incidence of perioral and intraoral lacerations throughout childhood. In most instances, intraoral wounds, although contaminated by the oral flora, will heal well without the developing infection, provided the wound is clean, no foreign bodies are left within the cut surfaces, and sutures are placed to approximate the tissues where needed. However, wounds involving the skin surface, particularly those with skin-to-oral mucosa communication, are most likely to develop infection, and Shira states that patients with these injuries should receive prophylactic antibiotics.[39] Certainly lacerations secondary to dogbites should receive antibiotic therapy directed against the most likely infective flora: beta-hemolytic streptococci and staphylococci.[40] When antibiotics are prescribed after traumatic injury, it must be kept in mind that organisms not endogenous to the oral cavity may have been seeded into the wound, particularly if the wound is "dirty". At the first sign of infection, a culture and sensitivity test should be attempted.

Orofacial Burns

Patients with severe burns on much of their body usually also will have head and neck burns. Children may suffer electrical burns of oral structures from placing live electrical cords in their mouths. Burned tissue is extremely susceptible to infection and prophylactic antibiotics should be instituted immediately.[40]

Reimplantation of Avulsed Teeth

Dentists treating children can expect to treat patients who have suffered traumatic avulsion of one or more permanent teeth. Reimplantation of these teeth in their sockets is accepted treatment—barring contraindications (though the success of this procedure is variable and the prognosis for long-term retention of these teeth is poor). Some suggest the prescription of systemic antibiotics (in addition to the appropriate antitetanus prophylaxis) at the time of reimplantation to prevent complications. Andreasen and Massler feel that the value of antibiotic

prophylaxis is questionable as there is no clinical evidence of a high incidence of infection after reimplantation.[41, 42] The clinician should decide whether or not to use antibiotics on an individual basis, taking into consideration the degree of contamination of teeth and sockets, the extent of related orofacial traumatic injuries, and the systemic condition of the patient. A severely compromised patient is not an appropriate candidate for reimplantation.

Jaw Fractures

The use of antibiotics in the treatment of jaw fractures will not be covered since this therapy probably is not within the province of pedodontics.

Management of Oral Infection

Acute Primary Herpes Infection

This acute infectious disease occurs most often in young children who may become extremely debilitated with high fever and malaise. It is important that fluid intake be continued to avoid dehydration. The etiologic agent in this condition is a virus, and antibiotics have no role in treatment of the primary disease.[1, 43] Penicillin is definitely contraindicated, as it will fix the virus and prolong the disease.[44] McDonald and Avery report that topical application of tetracyclines to ulcerated areas will aid in the control of secondary (bacterial) infection.[19]

Acute Necrotizing Ulcerative Gingivitis (ANUG)

Spirochetal organisms have been isolated from the involved gingivae of patients with ANUG. This disease may occur in young children but the highest incidence is in late adolescence and early adulthood. The patient with severe ANUG will present systemic complications such as fever, malaise, and associated lymphadenopathy. Bear and Benjamin state that only with massive necrosis or systemic effects is systemic antibiotic therapy indicated in addition to the more conservative measures of removing local irritants, improving oral hygiene, and using oxidizing mouthwashes recommended by other authors.[19, 44] The use of metronidazole (a nitroimidazole antimicrobial which is cidal against anaerobic microorganisms) has been reported for treatment of ANUG.[45–47] However, penicillin is the drug of choice, utilizing erythromycin if the patient is allergic to penicillin.[48]

Eruption and Exfoliation of Teeth

Although it is a common belief that children present systemic symptomatology during the "teething" period, studies have not correlated fever or elevated white cell counts with normal tooth eruption.[49] If fever and other systemic disturbances are present at the time of eruption, the source of the infection should be investigated. There is no evidence of a need for antibiotic coverage of tooth eruption or normal exfoliation even in a child susceptible to SBE.[14]

Pericoronitis

In childhood, pericoronitis may develop over any erupting tooth. If incision and drainage can be accomplished in these cases, further treatment usually is unnecessary.[37] Classically, pericoronitis involves the tissues surrounding a mandibular third molar. The degree of infection suffered varies widely and at times this condition will progress to a diffuse cellulitis.[50] Definitive treatment consists of extraction of the tooth, but in the presence of a severe pericoronal infection with associated systemic complications such as local lymphadenopathy, fever, and malaise, many authors advocate systemic antibiotic therapy (in conjunction with drainage if possible) and local irrigation.[1, 18, 51, 52] In a study by Kay, the condition of 56 patients deteriorated rapidly when treated for acute pericoronitis without systemic antibiotics.[53] Penicillin long has been the suggested drug of choice for management of this problem. McGowan et al. reported equally successful results with metronidazole,[a] but in view of the potential problems with this drug, this treatment cannot be recommended.[51] Adverse side effects include gastrointestinal disturbances, urticaria, candida overgrowth, urethral burning, and reversible neutropenia.[54] Of much greater concern is evidence that this agent is carcinogenic in some animals. In view of this fact, it has been advised that this drug be used as seldom as possible until further information is available.[54]

Conclusions

1. All children with systemic disease altering their resistance to infection or their ability to heal should be evaluated individually on the basis of their oral problem and overall systemic condition.
2. All immunodepressed children should be given antibiotic support at the first sign of oral infection. The decision to give antibiotic coverage for traumatic dental procedures should be based on the degree of trauma anticipated, the degree of immunodepression, and the child's general systemic condition.
3. Normal, healthy children should receive antibiotics only when the clinician feels the bacterial assault will overwhelm their natural defenses against infection (or has already done so).

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