amoxicillin and macrolides. Usually erythromycin was a poor choice because many organisms are resistant to it. Study results showed that resistance to clindamycin is increasing, so drugs such as azithromycin and moxifloxacin may be appropriate alternatives.

The length of time patients were to take their antibiotics was usually 5 to 7 days, but dentists in several studies exceeded these durations. Little evidence exists to support a specific duration of treatment, but therapeutic antibiotics typically are used for 7 days or until 3-day symptom resolution. Seven- to 10-day therapeutic durations were used for patients who are immunosuppressed or have severe infections (Table).

Factors Influencing Prescribing Patterns

Most dentists acquired their prescribing knowledge from reputable sources, although some cited personal communication delivered verbally in an informal manner as their primary source of information. Prescribing behaviors changed throughout dentists' careers based on a number of factors. Included in these influencing factors were audits, education, and training. Because of the highly diverse and inconsistent characteristics of the dentists and their practices, no conclusions regarding specific practitioner characteristics in relation to prescription habits and knowledge could be drawn.

DISCUSSION

Dentists vary in their antibiotic prescribing behaviors, whether for prophylactic or therapeutic purposes. Often their patterns contradict the evidence currently available and the recommendations of professional organizations. Dentists are prone to influences such as patient pressure or medical provider pressure, as well as their own past prescribing behaviors.

Clinical Significance

Changes in dentists' inappropriate prescribing behaviors will require patience and perseverance. In addition to recognizing and implementing professional organizations' recommendations, dentists must use their clinical judgment and consider the type and site of any surgery done, the potential morbidity associated with infection, and the patient's general and systemic health. For patients who are immunocompromised, the dentist should consult the patients' medical care providers.

Stein K, Farmer J, Singhal S, et al: The use and misuse of antibiotics in dentistry: A scoping review. *J Am Dent Assoc* 149:869-884, 2018

Reprints available from K Stein, Dental Public Health, 124 Edwards St, Toronto, ON, Canada, M5G 1G6; e-mail: kelli.stein@utoronto.ca

Guidelines for dental antibiotic prescriptions

BACKGROUND

The emergence of resistant strains of bacteria to penicillins and other antibiotics has become a global public health problem. Dentists are part of the problem because they write between 3% and 11% of all antibiotics prescribed by health care professionals. Unfortunately, the awareness of both antibiotic resistance and its relationship to antibiotic prescribing by dentists remains low. Dentists need to become informed about the scope of the problem as well as factors that contribute to antibiotic resistance and are relevant to dentistry.

DENTAL ANTIBIOTIC USE

Infections of odontogenic origin usually require dental treatment, with the removal of the source of infection proving to be the most efficacious approach. Antibiotics are often added to this local treatment approach, often on an empirical basis rather than based on clinical indications. Penicillins are used more commonly than other antibiotics, but between 5% and 20% of bacteria commonly isolated from endodontic abscesses have demonstrated resistance to penicillins, and this number is increasing.

The bacteria found in orofacial odontogenic infections are mixed and can include both commensal and opportunistic organisms. These bacteria not only find safe harbor in the biofilm but can also develop internal mechanisms to resist antibiotic actions.

RESISTANCE

Resistance to antibiotics can be either intrinsic or acquired. Intrinsic resistance is a characteristic property of the microorganisms, making the entire species of bacteria resistant. Acquired resistance doesn't affect the entire species but just certain strains. It can be the result of chromosomal mutation or horizontal acquisition through gene transfer. This second mechanism allows resistant genes to be spread in different strains of the same species and between different bacterial species. Gene transfer can be achieved through transformation, transduction, or conjugation. In transformation, bacteria containing antibiotic-resistant genes

excrete segments of their DNA into the environment when they die, allowing nearby competent bacteria to acquire them. Transduction is similar but the DNA segment is incorporated into a phage particle before reaching the recipient organism. Conjugation is where a plasmid is transferred from the donor to the recipient bacteria; physical contact between the 2 bacterial cells is required.

The rate of spread of resistant bacteria through horizontal acquisition of genes is faster than that seen with chromosomal mutation. Conjugation can produce a wide promulgation of antibiotic-resistant genes and the development of multidrug-resistant bacteria. It's likely the most common method by which bacteria transfer genetic elements in human and ecosystem situations.

The types of resistance fall into 4 broad categories. The bacteria's active binding site for the antibiotic may be conformationally altered, the bacterial genome may be altered to restrict antibiotics from the cell, antibiotics may be actively extruded out of a bacterial cell through the efflux pump, or enzymatic inactivation may cause antibiotic destruction. The last method is commonly seen with beta-lactam antibiotics in the presence of bacteria that produce beta-lactamase enzymes. The presence of beta-lactamase producing bacteria was first identified in 1986 and also demonstrated a greater recovery of beta-lactamase producing bacteria in persons who recently took penicillin.

The main reason bacteria become resistant is selective pressure. When the bacteria susceptible to the given antibiotic are inhibited, the environment then allows resistant bacteria to multiply, causing selective pressure on the emergence of resistant strains. The density of antibiotic usage and the total consumption of antibiotics determine the degree of selection pressure and the magnitude of the formation of resistant bacteria. With greater ingestion of antimicrobial agents, bacteria are more frequently exposed to the medicine, giving them more chances to develop or acquire resistance.

Resistant commensals form after the individual takes an antibiotic. If the same antibiotic is rarely used, the resistant strains can eventually be diluted out and replaced by susceptible bacteria. With increased use and more widespread use of the antibiotic, the balance between resistant and susceptible bacteria tips in favor of the resistant bacteria.

STRATEGIES FOR REDUCING BACTERIAL RESISTANCE

The strategies usually adopted to manage resistance include preventing the infections and spread of resistance through immunization, safe food preparation, and appropriate infection control protocols. At a national level, the consumption of antibiotics and spread of antibiotic-resistant infections are monitored. The development of new antibiotics is another method, but has slowed for various socioeconomic and nonmedical factors.

Table 3. The Antimicrobial Creed

M microbiology guides therapy wherever possible
I indications should be evidence-based
N narrowest spectrum required
D dosage appropriate to the site and type of infection
M minimise duration of therapy
E ensure monotherapy in most situations

(Courtesy of Teoh L, Stewart K, Marino R, et al: Antibiotic resistance and relevance to general dental practice in Australia. *Austral Dent J* 63:414-421, 2018.)

PROPER DENTAL PRESCRIBING

Current data indicate that the numbers of dental prescribed antibiotics is increasing worldwide. A significant proportion of dentists prescribe antibiotics when they aren't needed or for incorrect clinical indications. It should be noted that dentists' prescribing decisions are multifactorial and complex, with nonclinical factors also providing guidance.

The recommended guideline for prescribing in Australia is the Therapeutic Guidelines: Oral and Dental, expressed by the mnemonic MINDME (Table 3). The MINDME protocol in dental practice recommends selecting antibiotics that have the narrowest spectrum required, at the appropriate dose, and for the length of time needed to target the bacteria most often found in odontogenic infections. The preferred first choice for odontogenic infections is phenoxymethylpenicillin. Moderate to broad-spectrum antibiotic prescriptions for dental infections are inappropriate because these agents are more likely to contribute to the development of antibiotic resistance than narrow-spectrum agents.

Another problem is the packaging of medications. The pack size doesn't always correlate with the specified length of time an antibiotic should be given. Rather than instructing the patient to "finish the course," dentists should specify exactly how many days the patient should take the antibiotic. Shorter courses are effective for dentoalveolar infections as long as the source of the infection has been drained. It is suggested that pathologic testing of unresolved infections be considered to minimize the inappropriate use of antibiotics.

Clinical Significance

High antibiotic usage is correlated to a higher level of antibiotic resistance worldwide. Dental practitioners have a responsibility to address the problems of unnecessary prescribing; inappropriate prescribing choices, including the preference for moderate to broad-spectrum antibacterial agents rather than narrow-spectrum agents; and considering evidence-based indications and guidelines to minimize the misuse of antibiotics.

Appropriate dental prescribing should also use antibiotics only in an adjunctive role to the use of active local treatment that addresses the source of the infection. Patients should receive counseling on how to take the antibiotic so that errors in administration can be avoided. Patient education can also address problems related to individuals expecting or requesting antibiotics that are incorrect and persons who are unwilling to accept local treatment.

Teoh L, Stewart K, Marino R, et al: Antibiotic resistance and relevance to general dental practice in Australia. *Austral Dent J* 63:414-421, 2018

Reprints available from M McCullough, Melbourne Dental School, The Univ of Melbourne, 720 Swanston St, Carlton, Vic 3010, Australia; e-mail: m.mccullough@unimelb.edu.au

BURNING MOUTH

Advances in the causation and treatment of burning mouth syndrome

BACKGROUND

Burning mouth syndrome (BMS) is poorly understood in terms of its etiology, making management challenging. Generally, BMS is characterized by oral pain and discomfort in a patient with normal-appearing mucosa and no local or systemic condition typically associated with stomatodynia. This rare condition is likely caused by multiple factors, which makes it more difficult to diagnose. The current state of knowledge regarding the causes and treatment of BMS was detailed.

PUTATIVE CAUSES

Pain Perception

Recent studies suggest that about 30% to 60% of patients with BMS suffer from neuropathic pain, along with reduced sensitivity to cold and warmth and diminished thermal pain thresholds compared to healthy control subjects. BMS patients can be grouped into those who experience peripheral small fiber neuropathy, those with major subclinical central trigeminal neuropathy, and those who have inhibitory dopaminergic deficiency.

Patients with BMS have structural and functional deficits in key brain regions related to pain perception, specifically the medial prefrontal cortex and the hippocampus. Changes in the gray matter of the pain matrix are also described. Low cerebral blood flow may be present in patients with BMS and depression. Dopamine levels in the putamen may also be diminished in BMS patients.

Activity in the postcentral gyrus is stronger in those with BMS in response to angry facial expressions, which may link psychological disorders with brain function in BMS. The peripheral nervous system is also implicated and includes specific defects in pain sensory pathways. Some study indicates that blockade of the artemin/GFRα3/TRPV1 axis may prove therapeutically efficacious.

Dysgeusia

Although the finding is poorly understood, several studies report abnormal taste sensation among BMS patients. Electrogustometry (EGMt) is a technique that estimates taste detection thresholds and assesses the integrity of the taste pathways. One study found that patients with BMS had diminished taste sensitivity in the fungiform and foliate taste buds. The EGMt values at the tongue's lateral borders and tips correlated with visual analog scale scores for these patients. Alterations in salivary composition could affect the salivary pH and alter EGMt results, but the results so far indicate that pain perception and dysgeusia may be interrelated among BMS patients.

Neuroendocrine and Hormonal Problems

Patients with BMS have neuroendocrine and endocrine system dysfunction. Compared to control patients, their plasma adrenaline levels are significantly lower and cortisol levels are slightly increased. Significant decreases are seen in dehydroepiandrosterone (DHEA), the precursor of testosterone and estradiol. Salivary 17β-estradiol levels correlate with disease severity, whereas cortisol levels and cortisol/DHEA ratios in whole saliva have demonstrated an inverse relationship to the severity of oral burning. It has been hypothesized that these alterations may be caused by abnormal oscillations in the hypothalamic-pituitary-adrenal (HPA) axis, which controls the secretion of adrenal hormones. Decreased DHEA levels are indicative of HPA dysfunction, so dysregulation of these systems likely contributes to chronic pain conditions, including BMS.

Psychological Factors

Patients with BMS tend to experience higher levels of psychogenic disturbances compared to the general population. Nearly all studies performed since 2000 report an association between psychological factors and BMS. Anxiety and depression are more common among BMS patients, with women experiencing psychological factors more often than men. The specific factors seen in women are somatization, obsessive compulsive disorder, and paranoid ideation. The depression in those with BMS correlates with plasma noradrenaline and cortisol levels as well.