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Executive summary of recommendations from the American Dental Association Council on Scientific Affairs

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This executive summary is based on a report developed by an advisory committee of the American Dental Association Council on Scientific Affairs following an appraisal of the literature identified by means of a systematic search.[1]

The purpose of this report is to help dentists make treatment decisions based on the current best evidence when available, and on expert opinion when necessary, for patients being treated with antiresorptive agents (Table 1[2]). In an effort to improve the quality and efficiency of oral health care, the advisory committee compiled this report as an educational tool to assist dentists when discussing oral health with patients receiving antiresorptive therapy, as well as when treating these patients. This executive summary focuses on patients receiving antiresorptive therapy for low bone mass rather than on patients receiving antiresorptive therapy for cancer treatment. The committee chose this focus because patients with low bone mass are seen routinely by

ABSTRACT

JADA CE CONTINUING EDUCATION ARTICLE 1

Background. This narrative review of osteonecrosis of the jaw in patients with low bone mass receiving treatment with antiresorptive agents is based on an appraisal of the literature by an advisory committee of the American Dental Association Council on Scientific Affairs. It updates the committee's 2008 advisory statement.

Methods. The authors searched MEDLINE for literature published between May 2008 (the end date of the last search) and February 2011.

Results. This report contains recommendations based on the findings of the literature search and on expert opinion that relate to general dentistry; periodontal disease management; implant placement and maintenance; oral and maxillofacial surgery; endodontics; restorative dentistry and prosthodontics; orthodontics; and C-terminal telopeptide testing and drug holidays.

Conclusions. The highest reliable estimate of antiresorptive agent–induced osteonecrosis of the jaw (ARONJ) prevalence is approximately 0.10 percent. Osteoporosis is responsible for considerable morbidity and mortality. Therefore, the benefit provided by antiresorptive therapy outweighs the low risk of developing osteonecrosis of the jaw.

Clinical Implications. An oral health program consisting of sound hygiene practices and regular dental care may be the optimal approach for lowering ARONJ risk. No validated diagnostic technique exists to determine which patients are at increased risk of developing ARONJ. Discontinuing bisphosphonate therapy may not lower the risk but may have a negative effect on low-bone-mass–treatment outcomes.

Key Words. Oral and maxillofacial pathology; alveolar bone; antiresorptive agent–induced ostenecrosis of the jaw; bisphosphonate-associated osteonecrosis; jaw; oral and mandibular diseases; oral pathology.

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TABLE 1

Antiresorptive agents.

BRAND NAME	GENERIC NAME	DOSAGE	MANUFACTURER	APPROVED (DATE)	INDICATIONS*†
Oral Formulations					
Actonel	Risedronate sodium	5-, 35-, 75- and 150-milligram tablets	Warner Chilcott, Dublin	Worldwide (1998)	To prevent and treat osteoporosis in postmenopausal women; to increase bone mass in men with osteoporosis; to prevent and treat osteoporosis in men and women that is caused by treatment with steroid medicines such as prednisone; to treat Paget disease of bone in men and women
Atelvia	Risedronate sodium	35-mg tablet (once weekly)	Warner Chilcott	Worldwide (2010)	To treat osteoporosis in post-menopausal women
Bonefos	Clodronate disodium (not commercially available in United States)	400-mg capsules (Canada), 800-mg tablets (Europe)	Bayer, Toronto; Bayer Schering, Berlin	Canada (1992), Europe (1985)	To treat and prevent osteoporosis in women after menopause; to treat hypercalcemia and osteolysis due to malignancy; to reduce occurrence of bone metastases in primary breast cancer
Boniva	Ibandronate sodium	2.5-mg tablet once daily, 150-mg tablet once monthly	Genentech (a member of the Roche Group), South San Francisco, Calif.	United States (2003)	To treat and prevent osteoporosis in women after menopause
Bonviva	Ibandronate sodium	150-mg tablet once monthly	Genentech	Europe (2004)	To treat and prevent osteoporosis in women after menopause
Didronel	Etidronate disodium	400-mg tablet	Warner Chilcott	United States (1983), Europe	To treat Paget disease of bone; to prevent and treat heterotopic ossification in people who have undergone total hip replacement surgery or in people who have had an injury to the spinal cord **Note:** off-label use to treat and prevent osteoporosis caused by corticosteroid therapy; in addition, this medication may be used to treat a high calcium level in the blood that may occur with some cancers
Etidronate (generic)	Etidronate	200-, 400-mg tablet	Mylan Pharmaceuticals, Morgantown, W.V.	United States (2003), Europe	
Fosamax	Alendronate sodium	5-, 10-, 35-, 40- and 70-mg tablets	Merck & Co., Whitehouse Station, N.J.	United States (1995), Europe (1995)	To treat or prevent osteoporosis in women after menopause; to increase bone mass in men with osteoporosis; to treat osteoporosis in men or women being treated with corticosteroid medicines; to treat Paget disease of bone
Fosamax Plus D	Alendronate sodium/ cholecalciferol	70-mg tablet or 70-mg oral solution	Merck & Co.	United States (2005), Europe (2005)	To treat osteoporosis in post-menopausal women; to increase bone mass in men with osteoporosis
Generic alendronate	Alendronate sodium	5-, 10-, 35-, 40- and 70-mg tablets	Various	Worldwide (2008)	To treat or prevent osteoporosis in women after menopause; to increase bone mass in men with osteoporosis; to treat osteoporosis in men or women being treated with corticosteroid medicines; to treat Paget disease of bone
Skelid	Tiludronate disodium	240-mg tablets (equivalent to 200-mg base)	Sanofi-Aventis, Bridgewater, N.J.	United States (1997)	To treat Paget disease of bone
Aredia	Pamidronate disodium	30-, 90-mg vials	Novartis Pharmaceuticals, East Hanover, N.J.	Worldwide (2001)	To treat moderate or severe hypercalcemia with malignancy, with or without bone metastases; to treat osteolytic bone metastases of breast cancer and osteolytic lesions of multiple myeloma in conjunction with standard antineoplastic therapy; to treat Paget disease of bone

* According to manufacturers' product information.

† Because of the effect that therapeutics such as bisphosphonates have on bone remodeling, antiresorptive drugs now are being used off-label to treat patients with several pathological bone processes other than osteoporosis, such as giant cell lesions, giant cell tumor of bone, osteogenesis imperfecta, fibrous dysplasia, Gaucher disease and osteomyelitis. Source: Landesberg and colleagues.[2]

TABLE 1 (CONTINUED)

BRAND NAME	GENERIC NAME	DOSAGE	MANUFACTURER	APPROVED (DATE)	INDICATIONS*†
Parenteral Formulations					
Bonefos	Clodronate disodium	60 mg/ 1 milliliter, 1,500-mg single dose	Bayer, Bayer Schering	Canada (1992), Europe (1985)	To treat Paget disease of bone; to treat hypercalcemia due to metastatic bone disease, multiple myeloma and parathyroid carcinoma
Boniva IV	Ibandronate sodium	3 mg/3 mL single use	Genentech	United States (2006), Europe (2006)	To treat osteoporosis in postmenopausal women
Prolia	Denosumab	60-mg subcutaneous injection every six months	Amgen, Thousand Oaks, Calif.	United States (2010), Europe (2010)	To treat postmenopausal women who have osteoporosis and are at high risk of experiencing fracture
XGEVA	Denosumab	120 mg in 1.7-mL subcutaneous injection every four weeks	Amgen	United States (2010)	To prevent skeletally related events in patients with bone metastases from solid tumors
Reclast (United States), Aclasta (Europe)	Zoledronic acid	5 mg in a 100-mL ready-to-infuse solution	Novartis Pharmaceuticals	United States (Reclast) (2007), worldwide (Aclasta) (2005)	To treat osteoporosis in postmenopausal women; to prevent osteoporosis in postmenopausal women; to increase bone mass in men with osteoporosis; to treat and prevent glucocorticoid-induced osteoporosis in patients expected to receive glucocorticoid therapy for at least 12 months; to treat Paget disease of bone in men and women
Zometa	Zoledronic acid	4 mg/5 mL single-dose vials	Novartis Pharmaceuticals	Worldwide (2001)	To treat hypercalcemia of malignancy; to reduce and delay bone complications due to multiple myeloma and bone metastases from solid tumors, in conjunction with anticancer medications

general dentists, and dosing, apparent risk and patient care are different for patients receiving antiresorptive therapy for cancer treatment. This report updates the 2008 advisory statement from the American Dental Association Council on Scientific Affairs.[3]

NOMENCLATURE

The 2008 advisory statement[3] included use of the term "bisphosphonate-associated osteonecrosis of the jaw," or BON. A nonbisphosphonate antiresorptive agent—denosumab (Prolia, Amgen, Thousand Oaks, Calif.)—now is available for treatment of women with postmenopausal osteoporosis. Aghaloo and colleagues[4] reported a case of ONJ in a patient with cancer who received denosumab therapy. Other antiresorptive agents, including cathepsin K inhibitors, also could prove to be associated with ONJ. Therefore, the panel proposes that all cases of ONJ related to the administration of antiresorptive therapeutic agents be termed "antiresorptive agent–induced ONJ" (ARONJ). This term encompasses cases associated with bisphosphonates, as well as cases associated with the use of other antiresorptive agents. We use ARONJ throughout this report unless it is important to denote ONJ associated with a specific antiresorptive agent.

METHODS

We searched MEDLINE for literature published between May 2008 (the end date of the last search) and February 2011 by using this search strategy: ("Osteonecrosis"[Medical Subject Headings (MeSH) terms] OR osteonecrosis) AND ("Diphosphonates"[MeSH] OR "bisphosphonate*" OR "denosumab") AND ("Jaw"[MeSH] OR "jaw") NOT "Addresses"[Publication Type] NOT "News"[Publication Type] NOT "Newspaper Article"[Publication Type] AND (English[lang]). The authors also searched the Cochrane Central Register of Controlled Trials by using the following strategy: (Osteonecrosis OR "avascular necrosis" OR chemonecrosis) AND (Diphosphonate* OR bisphosphonate* OR denosumab) AND (jaw).

ABBREVIATION KEY. ARONJ: Antiresorptive agent–induced osteonecrosis of the jaw. **BON:** Bisphosphonate-associated osteonecrosis of the jaw. **CTX:** C-terminal telopeptide. **MeSH:** Medical Subject Headings.

PANEL CONCLUSIONS

On the basis of a review of the available scientific literature and expert opinion, the panel reached the following conclusions.

The risk of developing ARONJ in a patient who does not have cancer appears to be low, with the highest prevalence estimate in a large sample of patients about 0.10 percent.[5] At present, there are no published studies that adequately address incidence. The few studies published to date involved the use of a wide range of methods, all with potential shortcomings, and the incidence estimates reported varied. Without good information about the incidence of ARONJ, it is difficult to predict risk in general, and it is impossible to predict a specific patient's risk.

ARONJ can occur spontaneously but more commonly is associated with specific medical and dental conditions and procedures, including dental procedures and conditions that increase the risk of experiencing bone trauma. Most commonly, ARONJ is associated with invasive bone procedures such as tooth extractions.[6-8] Age older than 65 years, periodontitis, prolonged use of bisphosphonates (for more than two years), smoking, denture wearing and diabetes have been associated with an increased risk of developing ARONJ.[6-10] The results of several studies do not show consistently that corticosteroid use is a risk factor.[11-14] Investigators in one study (which they controlled for the effects of several known or potential confounders) found that smoking and obesity were risk factors for ARONJ in patients with cancer who were receiving intravenous zoledronic acid.[15]

If a physician prescribes or is planning to prescribe an antiresorptive agent, it is important for the patient and the patient's dentist to be informed. The panel advises that clinicians ask questions during the health history interview process about osteoporosis, osteopenia and the use of one of the various antiresorptive agents. Both medical and dental communities continue to study ways to prevent and treat ARONJ to ensure the safest possible result for dental patients being treated with antiresorptive agents.

The physician serves as the best source of information regarding the need for antiresorptive therapeutic agents. Given the significant benefits of these medications and the significant skeletal and psychosocial complications of osteoporosis, a physician likely will recommend continued antiresorptive treatment during dental treatment despite the slight risk of the patient's developing ARONJ. Although neither the physician nor the dentist can eliminate the possibility of ARONJ's developing, regular dental visits and maintaining excellent oral hygiene are essential components of risk management for the patient. Open communication regarding treatment options is a fundamental requirement for all members of the health care team, but it is particularly important for those whose patients have significant dental problems or active ARONJ.

PANEL RECOMMENDATIONS FOR DENTAL CARE OF PATIENTS WITHOUT CANCER RECEIVING ANTIRESORPTIVE THERAPY

These recommendations focus on conservative surgical procedures, proper infection control technique, appropriate use of oral antimicrobials and the principle of effective antibiotic therapy when indicated. Because of a paucity of clinical data regarding the dental care of patients receiving antiresorptive therapy, these recommendations are based primarily on expert opinion. They are intended to help dentists make clinical decisions and should be considered along with the practitioner's professional judgment and the patient's preferences. Dentists are encouraged to review the full report[1] before treating patients receiving antiresorptive therapy. As new information becomes available, these recommendations will be updated, as appropriate.

GENERAL TREATMENT RECOMMENDATIONS

Practitioners generally should not modify routine dental treatment solely because of the use of antiresorptive agents. All patients should receive routine dental examinations. Patients for whom antiresorptive agents have been prescribed and who are not receiving regular dental care likely would benefit from a comprehensive oral examination before or early in their treatment.

Informing patients before they undergo dental care. A discussion of the risks and benefits of dental care with patients receiving antiresorptive therapy is appropriate. When informing a patient about the risk of developing ARONJ, the dental care provider must keep in mind that the patient may not be aware of this risk.[16] This may raise the patient's concerns about the continuation of dental treatment.

Points that dental care providers can discuss with patients when informing them about the risks of bisphosphonate therapy include the following.

- Antiresorptive therapy for low bone mass places them at low risk of developing ARONJ

(the highest prevalence estimate in a large sample is about 0.10 percent[5]).
- The low risk of developing ARONJ can be minimized but not eliminated.
- An oral health program consisting of sound oral hygiene practices and regular dental care may be the optimal approach for lowering the risk of developing ARONJ.
- No validated diagnostic technique currently is available to determine which patients are at increased risk of developing ARONJ.
- Discontinuing bisphosphonate therapy may not eliminate the risk of developing ARONJ. However, discontinuation of bisphosphonate therapy may have a negative impact on the outcomes of low-bone-mass treatment. Therefore, significant dental risks need to be present for clinicians to consider cessation of antiresorptive therapy for low bone mass, cancer or other off-label purposes. The advisory committee recommends that all members of the health care team discuss this before discontinuing bisphosphonate therapy.

The dental care provider should inform the patient of the dental treatment needed, alternative treatments, the way in which any treatment relates to the risk of ARONJ, other risks associated with various treatment options and the risk of forgoing dental treatment even temporarily. The clinician should encourage the patient to consult with his or her physician about health risks associated with discontinuation of antiresorptive therapy. All decisions with respect to use of drugs prescribed for medical conditions should be discussed with the prescribing physician. Misinformation and misunderstandings can lead to severe and preventable adverse events. Therefore, clinicians should present to the patient a balanced assessment of the current information.[17] The dental office staff should instruct patients who receive treatment with antiresorptive agents to contact their dentist if any problem develops in the oral cavity.

Making treatment decisions. The dental care provider may have to decide whether to treat a patient who has been exposed to antiresorptive agents. As discussed earlier, the risk of developing ARONJ is lower for a patient who is not being treated with these drugs for cancer. The panel recommends that a patient with active dental or periodontal disease should be treated despite the risk of developing ARONJ, because the risks and consequences of no treatment likely outweigh the risks of developing ARONJ. Leaving active dental disease (caries, periodontal disease, extensive periapical abscesses or granulomas) untreated can lead to complications that may require more extensive and risky treatments.

Before starting therapy, the dentist should inform the patient to the fullest extent possible. He or she should consider documenting the discussion of risks, benefits and treatment options with the patient (see earlier discussion) and obtaining the patient's written acknowledgment of that discussion and consent for the chosen course of treatment. The dentist should retain in the patient's dental record the acknowledgment of the discussion and consent for treatment.

Prevention and treatment planning. Table 2[4,8,18] describes strategies for managing the oral health of patients receiving antiresorptive therapy in an effort to prevent ARONJ. A major goal in the prevention of ARONJ is to limit the possibility of extensive or multifocal involvement. Despite the absence of supporting evidence, a localized clinical approach to dentoalveolar surgery in patients receiving antiresorptive therapy for low bone density may help the practitioner assess the risks on an individual basis and before putting multiple quadrants at risk. Common scenarios include, but are not limited to, a patient's needing full-mouth tooth extractions for dentures or a patient's needing full-mouth periodontal surgery. For example, the dentist could extract a single tooth or perform alveolar surgery in one sextant initially while treating the patient with chlorhexidine or another topical antiseptic.[19] The dentist may assume that the patient's healing response is adequate once he or she observes normal healing of the surgical site or sites. Antiseptic agents may be used for a longer period if the area remains inflamed, irritated or erythematous. After establishing the patient's apparently adequate healing response, the clinician could consider a more accelerated surgical treatment plan involving multiple (or all) sextants at a single appointment.

Because periapical pathoses, sinus tracts, purulent periodontal pockets, severe periodontitis and active abscesses that already involve the medullary bone may exacerbate osteonecrosis and are themselves risk factors for ARONJ, the dentist should treat them expeditiously. When dental pathoses are not evident, the trial sextant approach may be applicable. The sextant-by-sextant approach does not apply to emergency cases, even if multiple quadrants are involved.

TREATMENT RECOMMENDATIONS FOR SPECIFIC CONDITIONS

Management of periodontal diseases. Patients receiving antiresorptive therapy who have active chronic periodontal diseases gener-

TABLE 2

Prevention strategies for patients receiving antiresorptive therapy* (absent evidence of ARONJ†).

VARIABLE	CONSIDERATIONS FOR MANAGING PATIENTS' ORAL HEALTH
Duration of Antiresorptive Therapy	
Before therapy	▬ Optimal time to establish lifetime oral health awareness, as the long-term nature of antiresorptive therapy is associated with ever-increasing ARONJ risk ▬ Optimal period to remove unsalvageable teeth and perform invasive dentoalveolar procedures, although a less stringent requirement than that for patients being treated with these drugs as part of cancer therapy ▬ On assessment of the overall caries risk, periodontal disease risk and "dental intelligence quotient" of the patient, the dentist is best qualified to establish an appropriate treatment plan in coordination with the patient and the patient's physician
< 2 years	▬ Above discussions and assessments often are not performed or even possible before start of antiresorptive therapy, but all remain applicable after treatment has begun ▬ Risk during this period is very low; however, a few cases of ARONJ have been reported‡ ▬ Dentoalveolar procedures involving periosteal penetration or intramedullary bone exposure (for example, extractions, apicoectomies, periodontal surgeries, implants or biopsies) seem to carry a minimal risk of the patient's developing ARONJ ▬ Chlorhexidine rinses are advised whenever periosteal or medullary bone exposure is anticipated or observed ▬ In patients with multiple surgical needs, a trial segmental approach may be helpful in assessing a specific patient's risk of developing osteonecrosis and in reducing the likelihood of developing multifocal ARONJ
≥ 2 years	▬ Continue as above while advising the patient and physician who prescribes antiresorptive drugs that the risk of developing ARONJ continues to increase with extended drug use
Any length of therapy	▬ The dentist should discuss antiresorptive therapy with the patient's physician as it relates to the patient's oral health ▬ Discontinuation of antiresorptive therapy should be a medical decision based primarily on the risk of experiencing skeletally related events (for example, fractures) secondary to low bone density, not the potential risk of developing ARONJ ▬ No oral or maxillofacial surgical procedures are strictly contraindicated, although it is the opinion of the expert committee that treatment plans that minimize periosteal and/or intrabony exposure or disruption are preferred
Risk Assessment	▬ Serum C-terminal telopeptide levels have not shown reliability or accuracy in predicting risk of developing ARONJ; therefore, serum testing is not recommended to predict risk ▬ Although the trial segmental or sextant approach to surgical procedures has not been studied in a prospective fashion, this approach should help limit the extent of ARONJ in a given patient
Emergency Dental Therapy	▬ All extractions or dentoalveolar surgeries required on the basis of dental or medical emergencies are appropriate, regardless of the number of extractions or surgeries and multifocality
Routine Dental Care	▬ Good oral health and routine dental care always are recommended

* Limited data suggest similar levels of risk for patients treated with oral bisphosphonates, intravenous bisphosphonates and subcutaneous denosumab in the treatment of low bone density. Similar prevention strategies appear appropriate for each of these modalities, with comparable modification according to duration of drug therapy. This does not mean that no differences exist between these treatment modalities, and further studies are needed. Sources: Aghaloo and colleagues[4]; Grbic and colleagues.[18]

† ARONJ: Antiresorptive agent–induced ostenecrosis of the jaw.

‡ Source: Mavrokokki and colleagues.[8]

ally should receive appropriate forms of nonsurgical therapy, which should be combined with the commonly recommended reevaluation at four to six weeks. However, this is not to say that surgical procedures are contraindicated in these patients. Because tooth extractions constitute a risk factor for ARONJ, practitioners should monitor patients regularly and treat them with the goal of preventing progression of periodontal disease to the point at which tooth extractions are necessary. The goal of surgical periodontal treatment should be to obtain access to root surfaces, and, when possible, practitioners should use atraumatic techniques that minimize dentoalveolar manipulation.

There are no published studies, to our knowledge, in which investigators evaluated the risk of ARONJ or the success of implant treatment after periodontal procedures such as guided tissue regeneration or bone grafting. Use of such techniques should be considered judiciously on the basis of a patient's need. Primary soft-tissue closure after periodontal surgical procedures is desirable, when feasible, although extended periosteal bone exposure for the sake of primary closure may increase, rather than decrease, the risk of developing ARONJ. Patients who do not have periodontal disease should receive preventive therapy or instruction in prevention of periodontal disease.

Implant placement and maintenance. Investigators in several relatively small, short-term studies examined the risk of ARONJ, implant failure or both in women with a history of bisphosphonate use.[20-23] Although there are case reports of ARONJ at implant osteotomy sites, the relative scarcity of ARONJ and dental implant failure in patients treated with bisphosphonates, despite the large number of such patients receiving dental implants, is reassuring. Indeed, Fugazzotto and colleagues[20] noted no postoperative cases of ARONJ in 61 patients in whom the average duration of bisphosphonate use was 3.3 years. None of the implants failed in this population. In a population of 42 patients treated with bisphosphonates (range, six months to 11 years) who received 101 implants, Bell and Bell[21] observed no ARONJ and a 95 percent implant success rate. Using telephone and e-mail surveys, Grant and colleagues[22] noted no ARONJ associated with 468 implants placed in 115 patients receiving bisphosphonate treatment and a 99.6 percent success rate. Koka and colleagues[23] compared 121 implants placed in 55 patients treated with bisphosphonates (approximately one-third of whom had been treated for more than five years) with 166 implants placed in 82 patients who had not received bisphosphonate treatment. They did not observe ARONJ in either group, and the implants in the two groups exhibited similar profiles, with a 99.2 percent success rate in bisphosphonate users and a 98.2 percent success rate in nonusers.

Taken together, these data are encouraging. Dentists can inform patients that the risk of developing ARONJ as a result of antiresorptive therapy is low, and that the success rates for implants placed in patients receiving bisphosphonate treatment appear to be no different in the short term (that is, less than 10 years) from the success rates for implants placed in patients without a history of bisphosphonate treatment. Presently, antiresorptive therapy does not appear to be a contraindication for dental implant placement. However, larger and longer-term studies are needed to determine if implants placed in patients exposed to antiresorptive agents perform as well as those placed in patients who have not been exposed to these agents.

Oral and maxillofacial surgery. When treatment of dental diseases, periodontal diseases or both has failed, surgical intervention may be the best alternative. Practitioners should inform patients receiving antiresorptive therapy who are to undergo invasive surgical procedures that there is the risk, albeit small, of developing ARONJ. Although surgical procedures are not necessarily contraindicated, the practitioner, as part of the informed consent process, should discuss alternative treatment plans with the patient; these include endodontics (including endodontic treatment followed by removal of the clinical crown), allowing the roots to exfoliate (instead of extraction) and use of fixed and removable partial dentures.

If extractions or bone surgery is necessary, dentists should consider a conservative surgical technique with primary tissue closure, when feasible. Placement of semipermeable membranes over extraction sites also may be appropriate if primary closure is not possible. In addition, before and after any surgical procedures involving bone, the patient should rinse gently with a chlorhexidine-containing rinse until the extraction site has healed. The chlorhexidine regimen may be extended depending on the patient's healing progress, but twice-daily use for four to eight weeks is a common regimen. Some evidence exists that antibiotic prophylaxis starting one day before and extending three to seven days after dental procedures may be effective in preventing ARONJ.[24] In addition, Lodi and colleagues[25] reported that the use of chlorhexidine and systemic antibiotics before and after tooth extraction appeared to reduce the risk of ARONJ in a small study of 23 patients.

In patients who already have ARONJ, researchers have reported limited evidence that teriparatide, a recombinant form of parathyroid hormone, may be helpful in treatment of the disease.[26-28]

Endodontics. In patients with an elevated risk of developing ARONJ, endodontic treatment is preferable to surgical manipulation if a tooth is salvageable. Practitioners should use a routine endodontic technique; however, the panel does not recommend manipulation beyond the apex. Limited evidence shows that periapical healing after endodontic therapy is similar regardless of whether or not a patient has a history of bisphosphonate use.[29] Endodontic surgical procedures should be guided by the same recommendation as that given for any oral or maxillofacial surgical procedure described earlier.

Restorative dentistry and prosthodontics. No evidence exists that malocclusion or masticatory forces increase the risk of developing ARONJ. Practitioners should perform all routine restorative procedures with the goal of minimizing the impact on bone, so as not to increase the risk of infection. To avoid ulceration and possible bone exposure, practitioners should adjust prosthodontic appliances promptly for fit.

Orthodontics. There are no large published

studies in which investigators examined the effect of bisphosphonates on orthodontic treatment. Case reports have recounted inhibited tooth movement in patients receiving bisphosphonate therapy.[30,31] Dentists should advise patients of this potential complication. However, clinicians also have performed orthodontic procedures successfully in patients receiving antiresorptive therapy, and it is not necessarily contraindicated.[31,32]

Orthodontics is unique in the dental specialties in that its existence is based on the delicate balance between osteoclast function and osteoblast function. While orthodontic treatment occurs predominantly in children and in patients in early adolescence, one in five orthodontic patients in the United States is an adult.[33] The orthodontic literature concerning bisphosphonates concentrates primarily on the ability of these drugs to stabilize teeth after treatment or on topical application to a localized area during orthodontic therapy.[34] However, with the advent of antiresorptive bone agents, there potentially are 44 million Americans in whom orthodontic movement may be compromised by the medication. Orthodontists need to recognize the potential problem of ARONJ and the alteration in bone physiology caused by antiresorptive therapy.[31,32,35] The duration of orthodontic treatment may be longer, and predictable, uniform tooth movement may be compromised with use of antiresorptive agents. Orthognathic surgery and tooth extractions result in more extensive bone healing and remodeling. The orthodontic considerations related to such cases should include the potential risks of surgery, as well as the potential postsurgical delayed tooth movement. Treatment planning in these cases may require increased vigilance.

C-TERMINAL TELOPEPTIDE TESTING AND DRUG HOLIDAYS

Serum-based bone turnover markers are biochemical markers of bone remodeling. Two such markers are C-terminal telopeptide (CTX) and N-terminal telopeptide. These markers together represent each end of the three strands of type 1 collagen, and each is used in tests that monitor bone turnover. Investigators in some studies have advocated the use of serum CTX to predict the risk of developing ARONJ,[36-41] while others have questioned its utility.[42-46]

Although a few studies have been conducted regarding the suspension of antiresorptive drug therapy during treatment of ARONJ, no study results to date have confirmed that drug holidays are effective in prevention of ARONJ without increasing the skeletally related risks of low bone mass. At present, there is insufficient evidence to recommend the use of serum tests, such as serum CTX, as a predictor of ARONJ risk. In addition, there is insufficient evidence to recommend a holiday from antiresorptive drug therapy or waiting periods before performing dental treatment for prevention of ARONJ. For a complete discussion of the rationale behind this recommendation regarding use of serum CTX and drug holidays, refer to the full report.[1]

CONCLUSIONS

The clinical recommendations in this report, which are based on a critical evaluation of the relevant scientific evidence, do not represent a standard of care. The clinical recommendations should be integrated with the practitioner's professional judgment and the patient's needs and preferences. Treatments and procedures appropriate to a specific patient rely on communication between the patient, the dentist and other health care practitioners. This report focuses on prevention of ARONJ in patients being treated with antiresorptive agents for osteoporosis. The significant therapeutic benefit of antiresorptive agents in these patients far outweighs the small risk of developing ARONJ. ■

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