

# Lack of a scientific basis for routine discontinuation of oral anticoagulation therapy before dental treatment

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Both physicians and dentists should be educated in how to treat dental patients who are receiving anticoagulation therapy.

Dental practitioners who treat adults most likely will encounter patients who take prescribed or self-administered medications that have anticoagulant effects, which may affect treatment planning. The drugs either affect the production of clotting factors, thereby having a quantitative effect on the amount of clotting factors available in the bloodstream, or they inhibit platelet function in a way that impairs the platelets' ability to clot, thereby having a qualitative effect. Because such use of anticoagulants is common, dentists need to develop a method of assessing patients who receive anticoagulation therapy. Decision making should not be abrogated or delegated to the physician alone. On the contrary, dentists should play an active role in formulating an appropriate treatment plan.

Both physicians and dentists should be educated in how to treat dental patients who are receiving anticoagulation therapy. It is our experience that sometimes a physician's decision to discontinue anticoagulation therapy before oral surgery is not based on sound clinical science, but rather the physician's

**Background.** There is a widespread belief among dental practitioners and physicians that oral anticoagulation therapy in which patients receive drugs such as warfarin sodium must be discontinued before dental treatment to prevent serious hemorrhagic complications, especially during and after surgical procedures.

**Overview.** The authors examine the scientific basis for properly managing the dosage of anticoagulants for dental patients who are receiving anticoagulation therapy. The authors review the appropriate laboratory test values to which dentists should refer when evaluating for dental treatment patients who are receiving anticoagulation therapy. The authors also review clinical studies, published within the past five years, that focus on the frequency and degree of hemorrhagic and related complications among dental patients who are receiving anticoagulation therapy orally to prevent thromboembolic events.

**Conclusions and Clinical Implications.** The scientific literature does not support routine discontinuation of oral anticoagulation therapy for dental patients. Use of warfarin sodium as it relates to dental or oral surgical procedures has been well-studied. Some dental studies of antiplatelet therapy are consistent with the findings in warfarin sodium studies. Dental therapy for patients with medical conditions requiring anticoagulation or antiplatelet therapy must provide for potential excess bleeding. Routine discontinuation of these drugs before dental care, however, can place these patients at unnecessary medical risk. The coagulation status—based on the International Normalized Ratio—of patients who are taking these medications must be evaluated before invasive dental procedures are performed. Any changes in anticoagulant therapy must be undertaken in collaboration with the patient's prescribing physician.



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experiences relative to general surgery, orthopedic surgery and so forth. Wahl<sup>1</sup> described this as one of the factors contributing to the many myths associated with the dental treatment of patients receiving oral anticoagulation therapy. Likewise, dentists may be unfamiliar with the existing literature or may be reluctant to consult with the physician regarding these matters.

Dentists' and physicians' lack of understanding is supported by evidence that many patients undergoing simple oral surgery often are advised by physicians and dentists to discontinue their anticoagulation therapy when, in fact, the literature is replete with excellent studies refuting this practice.<sup>2-6</sup> Some patients even voluntarily suspend oral anticoagulation therapy before any dental procedures, including examinations and radiographs, because of an unfounded fear of experiencing a severe hemorrhage. Another rationale for discontinuing anticoagulation therapy is to improve dentists' ability to see the working field during oral surgery by reducing bleeding in the dental operating field—a practice that disregards the patient's safety.

In this article, we focus on developing a systematic, scientifically based approach for evaluating and subsequently treating dental patients who are receiving anticoagulation therapy by examining the scientific literature in this area. We do not include the subject of congenital bleeding disorders such as hemophilia in this review.

## ORAL ANTICOAGULANT AGENTS

There are two major types of oral anticoagulant agents commonly prescribed for outpatients. The first and most widely used is the warfarin sodium Coumadin (DuPont Pharmaceuticals, Wilmington, Del.), which was ranked 29th among the "Top 200" drugs by prescription in 2001.<sup>7</sup> Warfarin blocks the formation of prothrombin and other clotting factors involved in both the extrinsic and common coagulation pathways,<sup>8</sup> and it prevents the metabolism of vitamin K to its active form in the synthesis of these factors. Warfarin has a characteristically slow onset of action. Therefore, when warfarin therapy is discontinued, it has a prolonged effect; its half-life is 36 hours, which could be the basis for the recommendation to discontinue the therapy for two to three days before dental treatment. Warfarin commonly is prescribed for patients who have prosthetic heart valves or a history of deep venous thrombosis;

myocardial infarction, or MI; stroke; atrial fibrillation; or unstable angina.<sup>8</sup>

The second major group of oral anticoagulant agents is antiplatelet agents. Aspirin is a commonly used drug that falls within this category. It is well-known that today a large portion of the adult population takes aspirin daily without the supervision of a physician. Aspirin inhibits the formation of the prostaglandin thromboxane A<sub>2</sub> within the platelet, thus affecting thrombus formation. Other antiplatelet agents such as clopidogrel act by inhibiting the binding of adenosine diphosphate to a platelet receptor that ordinarily mediates platelet aggregation.

These drugs, especially aspirin, are used widely in the primary prophylaxis of coronary thrombosis, as well as in the secondary prevention of adverse thromboembolic events in patients with a history of coronary thrombosis, stroke and unstable angina.<sup>8</sup> Patients who cannot tolerate aspirin—for example, those who are allergic to aspirin—can be prescribed ticlopidine (Ticlid, Roche Pharmaceuticals, Basel, Switzerland) or clopidogrel bisulfate (Plavix, Bristol-Myers Squibb, New York). Clopidogrel is associated with fewer adverse effects than ticlopidine.<sup>8</sup>

A more recently introduced group of drugs that is being used in the outpatient population includes the agents termed "low-molecular-weight heparins," or LMWHs, such as enoxaparin (Lovenox, Aventis Pharmaceuticals, Boston), ardeparin and dalteparin (Fragmin, Pfizer, New York City). These drugs are potentially valuable to dental patients in three ways. They have a high degree of predictable bioactivity, they can be self-administered, and they eliminate the costly five- to seven-day hospitalization for "heparin windows," which we describe later.

For example, LMWHs can be self-administered by some higher risk patients who receive warfarin therapy and require minor outpatient surgery.<sup>8</sup> Patients receiving LMWHs can sustain adequate anticoagulation, thus reducing risks that exist when warfarin therapy is stopped. In the past, patients who were at higher risk of experiencing a thromboembolism and required surgery such as an oral extraction were admitted to a hospital four days before the minor surgery. In this protocol, termed "heparin windows," warfarin was discontinued and unfractionated heparin was administered in multiple doses, with the prothrombin time, or PT, and the International Normalized Ratio, or INR, being monitored after each

dose. Usually, the patient underwent surgery on the fifth day of hospitalization. Warfarin was readministered immediately postoperatively, and the unfractionated heparin administration was stopped. The patient remained in the hospital until adequate therapeutic levels of warfarin—as determined by PT and INR tests—were re-established. This heparin window technique was costly and consumed a great deal of time and resources.

The benefits of LMWHs are many. Foremost are reduced cost and time. Patients will discontinue warfarin and begin taking an LMWH per their physicians' prescription. Because of the higher bioavailability of LMWHs (95 percent), continuous PT and INR testing is unnecessary. An additional benefit is that patients can self-administer the drug. Patients then may undergo outpatient surgery and reinitiate the warfarin therapy under the guidance of their physicians.

Patients with prosthetic heart valves requiring outpatient oral surgery are the only group of patients for whom LMWHs are not recommended.<sup>9</sup> The more conventional heparin windows using traditional unfractionated heparin with inpatient protocols are advised for these patients.<sup>10</sup>

#### IDENTIFYING AND TREATING AT-RISK PATIENTS

Taking a comprehensive medical history is paramount in ensuring that the dentist is optimizing the patient's treatment while minimizing the risk of morbidity. When patients report that they are receiving a medication that falls into the anticoagulant category, dentists and patients can benefit by using the following guidelines<sup>5</sup>:

- identify the reason the patient is receiving anticoagulation therapy;
- assess the potential risk versus benefit of altering the drug's regimen;
- know the laboratory tests used to assess anticoagulation levels;
- be familiar with local methods of obtaining hemostasis both intraoperatively and postoperatively;
- be familiar with the potential complications associated with prolonged or uncontrolled bleeding;

— consult the patient's prescribing physician to discuss the type of dental care and investigate the need to alter the anticoagulant regimen.

In most cases, patients are receiving anticoagulation therapy because of concerns associated with thromboembolic events. The risk of stroke or ischemic cardiac events is always of great concern in the perioperative period and is magnified when the anticoagulant dosage is lowered or discontinued.

Physicians typically prescribe warfarin for patients who have a history of atrial fibrillation, MI or stroke, deep venous thrombosis or prosthetic heart valve replacement.

Atrial fibrillation is a cardiac dysrhythmia in which the effective contraction of the atria is abolished and the atrioventricular, or AV, node is bombarded with a very rapid and irregular series of impulses. Many of these impulses are blocked at the AV node, but many pass through, so that ventricular contractions in untreated patients are rapid and irregular. The more severe the atrial fibrillation is, the greater the potential there is for cardiac insufficiency or heart failure. Because of stagnation of blood in the atria, there is an increased potential for thromboemboli to occur in the pulmonary and systemic vasculature.

MI and stroke are life-threatening disorders resulting from anomalies in the circulatory system. Most commonly, coronary artery disease and cerebrovascular disease result in the narrowing of the lumens of blood vessels in the heart and brain, increasing the likelihood of clot formation.

Deep venous thrombosis may result from multiple etiologies such as surgery of the lower extremities. Regardless of the cause, the potential for pulmonary embolism is of concern, as clots originating in the lower extremities essentially have unrestricted access through large venous tracts to the smaller lumens of blood vessels of the heart and lungs.

Prosthetic heart valve replacement is performed to replace a heart valve that has become totally dysfunctional. These prostheses have a potential to allow thrombus formation, with subsequent release to the cerebral circulation being the most common, life-threatening sequela.

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Because of a high risk of morbidity associated with deep venous thrombosis and prosthetic heart valve replacement, patients with these disorders typically maintain higher levels of anticoagulation therapy, compared with those who have atrial fibrillation or a history of MI or stroke.

## LABORATORY TESTS FOR ANTICOAGULANT DRUG EFFECTS

The test that traditionally has been used to test for the anticoagulation level produced by warfarin therapy is PT. However, because laboratory values varied considerably depending on the type of thromboplastin used in the assay, the World Health Organization introduced the INR 20 years ago.<sup>10</sup> The INR mathematically corrects the PT test results for the quality of the thromboplastin used in the test against an international standard thromboplastin. Patients who are receiving anticoagulation therapy should have INR values in the range of 2.5-3.5; an INR of 3.0 is equivalent to a PT ratio of 1.6 in the average U.S. hematology lab.<sup>8</sup> A patient with normal coagulation parameters would exhibit an INR of 1.0. Scientifically, one would have to know the patient's INR to make a judgment before safely altering an oral anticoagulant dosage recommendation. The effect of antiplatelet agents is assessed using Ivy's test bleeding time assay (forearm puncture), which has less-than-ideal reliability. Qualitative platelet assays are expensive. Future clinical studies may clarify how we can best assess the effects of this family of drugs.

## RESULTS OF CLINICAL STUDIES

Several clinical studies have addressed the issue of adjusting oral anticoagulant levels before dental procedures. In 1998, Devani and colleagues<sup>11</sup> reported on 65 patients receiving warfarin therapy who had an average INR of 2.7 and an average age of 62.3 years, and who underwent 133 extractions. The control group included 32 patients who stopped receiving warfarin therapy two days before the procedure. After the extractions, subjects were observed at 30 minutes postoperatively, and they self-reported bleeding at three and five days postoperatively. An oxycellulose socket dressing (Surgicel, Johnson & Johnson, New Brunswick, N.J.) was used as a local hemostatic measure. None of the subjects experienced immediate postoperative bleeding at 30 minutes. One patient from the control group with an INR of 1.8 had intermittent oozing on the

second postoperative day, and one patient from the study group with no change in preoperative anticoagulant use had intermittent oozing on the third postoperative day. No other subjects experienced delayed hemorrhage. Significantly, in 43 percent of the patients who stopped receiving anticoagulation therapy two days before surgery, the average INR value fell below 1.5 (normal coagulation). Devani and colleagues concluded that due to the difficulty in predicting the drop in the INR value in any given patient, the risk of experiencing a thromboembolism outweighs the risk of experiencing excessive postoperative bleeding.

Blinder and colleagues<sup>12,13</sup> reported the outcomes of two studies that documented postoperative bleeding in oral surgery patients, who were receiving oral anticoagulation therapy, when various local hemostatic measures (gelatin sponges only, tranexamic acid mouthrinse or fibrin glue with gelatin and sutures) were used without preoperative interruption of their anticoagulation therapy. In the earlier study, 150 patients with INR values that ranged from 1.5 to 4.0 were evaluated for postoperative bleeding after 359 extractions.<sup>12</sup> Of all subjects, only 13 (8.6 percent) had postoperative bleeding, all of which was controlled with local hemostatic measures.

More recently, the same group compared preoperative INR values with postoperative bleeding in 249 patients undergoing 543 extractions.<sup>13</sup> The patients were placed in five groups according to their INR values as measured on the day of the procedure (1.5-1.99, 2-2.49, 2.5-2.99, 3-3.49 and > 3.5). The local hemostatic measures used were gelatin sponges and sutures. Thirty patients (12 percent) exhibited postoperative bleeding, but there was no correlation between preoperative INR values and the incidence of bleeding across groups. The report concluded that local hemostasis with gelatin sponges and suturing was sufficient to prevent postoperative bleeding in patients receiving oral anticoagulation therapy.

Ardekian and colleagues<sup>14</sup> evaluated 39 adult dental patients who were taking 100 milligrams of aspirin daily for a variety of cardiovascular conditions and who underwent oral surgery. The experimental group of 19 patients continued to take aspirin, while the other 20 patients had their aspirin regimen discontinued for seven days before oral surgery. (Aspirin irreversibly alters platelet function, so offset of the anticoagulant



effect requires synthesis of new platelets.) Intraoperative bleeding was assessed quantitatively by the collection of suctioned blood. There was no statistical difference between the two groups across extractions of varying complexity, though procedures that are more complex resulted in significantly more bleeding in both groups. The study concluded that there was no reason to discontinue low-dose aspirin therapy before oral surgery based on the incidence or severity of postoperative bleeding.

Another study quantitatively evaluated bleeding in 35 oral surgery patients who were receiving long-term anticoagulation therapy.<sup>15</sup> Statistically, no greater intraoperative bleeding was observed in patients who continued receiving anticoagulation therapy than in those in whom anticoagulation therapy was discontinued 72 to 96 hours preoperatively.

Similarly, Evans and colleagues<sup>16</sup> performed a randomized, controlled clinical trial in 109 patients who underwent oral surgery. The control group consisted of 52 patients whose warfarin therapy was stopped two days before tooth extraction, and the remaining patients, all of whom had INR values less than 4.0, underwent oral surgery without discontinuation of anticoagulation therapy. While the overall incidence of bleeding complications was higher in the group receiving continuous anticoagulation therapy than in the control group (26 percent versus 14 percent), the difference was not statistically significant, and all bleeding episodes were managed successfully with local measures. Interestingly, this study reported that bleeding did not correlate well with the number of teeth extracted.

In a Spanish study, of 125 patients who underwent 367 extractions while receiving continuous oral anticoagulation therapy, 91.7 percent exhibited mild bleeding, 7.9 percent experienced moderate bleeding, and only 0.4 percent (one patient) experienced serious bleeding.<sup>17</sup>

In 2003, Zanon and colleagues<sup>18</sup> reported the results of a single-blind, prospective study of 250 patients who were receiving anticoagulation therapy and had INR values between 1.8 and 5.0, as well as 265 patients who were not receiving anticoagulation therapy and who underwent both simple and surgical extractions. In all of the procedures in patients receiving anticoagulation therapy, oxidized cellulose was placed in the surgical site and stabilized with silk sutures, a tranexamic acid-saturated gauze square was

placed for 30 to 60 minutes, and an ice pack was placed on the cheek for one hour postoperatively. The total number of bleeding complications in the group of patients receiving anticoagulation therapy (four out of 250) did not differ significantly from the rate of occurrence in the control group (three out of 250).

Wahl<sup>1</sup> reviewed the literature on this subject in 2000, reporting that in an aggregate of 950 patients receiving continuous anticoagulation therapy, only 12 (< 1.3 percent) required more than local measures to control hemorrhage. The author went on to note that while discontinuation of anticoagulation therapy has been a common practice, bleeding after dental surgery rarely is life-threatening, and, more importantly, there have been four case reports of fatal thromboembolisms resulting from this practice. Loeliger and colleagues,<sup>19</sup> however, have shown that INR values greater than 5.0 are accompanied by an unacceptable risk of serious hemorrhage and that patients with INRs greater than 5.0 are not candidates for surgery.

## DISCUSSION

The weight of evidence in the dental clinical literature does not support the long-held belief that an oral anticoagulant regimen must be altered or discontinued before most dental procedures, including oral surgery. Currently, the INR does not require alteration of the therapy regimen unless the INR value is greater than 4.0, provided that local hemostatic measures are used. INR values greater than 5.0, however, contraindicate a patient's undergoing a surgical procedure.<sup>19,20</sup>

Effective local hemostatic measures include gelatin sponges with silk sutures; systemic, irrigant and mouthrinse forms of tranexamic acid; vasoconstrictors in local anesthetic; and atraumatic surgical techniques.<sup>9,20</sup> From a rational scientific perspective, practitioners must question seriously the practice of arbitrarily discontinuing anticoagulation therapy when the INR value is unknown or out of date.

Furthermore, and quite significantly, anticoagulation therapy is a medical therapy that is planned and adjusted carefully by the prescribing physician and is not within the scope of practice of dentists. Failure to recognize this can result in severe patient morbidity and even mortality. Unfortunately, some physicians are unaware of the dental clinical literature we cite in this article, and they make the same "discontinue

anticoagulant two to three days prior" recommendation when asked about the patient's anticoagulant regimen by a dentist.

Lastly, the incidence of patients receiving antiplatelet therapy will continue to rise. Of concern are patients who require emergency dental care who may aggravate cardiac stresses such as pain and anxiety, while awaiting the passage of time needed to overcome the effects of the antiplatelet drugs. The impracticality of discontinuing these drugs for seven to 10 days must be weighed against the severity of potential thromboembolic events. Articles that document oral surgery experiences of patients taking aspirin alone<sup>21,22</sup> or in combination with clopidogrel bisulfate, for example, have not reported any cases of unusual intraoperative or postoperative bleeding problems. This experience, however, is anecdotal. Thus, a study at the University of Texas Health Science Center at San Antonio Dental School is examining the population of patients who are taking aspirin in combination with clopidogrel bisulfate or taking clopidogrel bisulfate alone to establish scientific and evidence-based guidelines for perioperative management.

## CONCLUSIONS

The literature does not support the routine withdrawal of anticoagulation therapy before dental treatment for patients who are taking such medications. Rather, dentists who anticipate treating patients who are receiving anticoagulation therapy should consult with the prescribing physician to determine the patient's INR and discuss whether dental treatment should be delayed until the INR value is within therapeutic levels (INR = 1.0-4.0). In addition, whenever a patient is receiving regular anticoagulation therapy, the dentist should be prepared for bleeding that may exceed that normally encountered and to provide hemostatic measures. Effective hemostatic measures include use of gelatin sponges with silk sutures; systemic, irrigant and mouthrinse forms of tranexamic acid; vasoconstrictors in local anesthetic; and atraumatic surgical technique. ■

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