Current perspectives on dental patients receiving coumarin anticoagulant therapy
WW Herman, JL Konzelman, Jr and SH Sutley
J Am Dent Assoc 1997;128;327-335

The following resources related to this article are available online at jada.ada.org (this information is current as of August 25, 2008):

Updated information and services including high-resolution figures, can be found in the online version of this article at:
http://jada.ada.org/cgi/content/abstract/128/3/327

This article appears in the following subject collections:
Pharmacology http://jada.ada.org/cgi/collection/pharmacology

Information about obtaining reprints of this article or about permission to reproduce this article in whole or in part can be found at:
http://www.ada.org/prof/resources/pubs/jada/permissions.asp

© 2008 American Dental Association. The sponsor and its products are not endorsed by the ADA.
CURRENT PERSPECTIVES ON DENTAL PATIENTS RECEIVING COUMARIN ANTICOAGULANT THERAPY

Anticoagulation with coumarin, which is prescribed for more than 1 million people in the United States each year, presents the most common potential bleeding problem that dentists encounter. Dental care for a patient receiving anticoagulant therapy requires balancing the opposing risks of significant hemorrhage from procedures against the potential for thromboembolism from reducing or withdrawing anticoagulant therapy. Despite approximately 40 years of experience with oral anticoagulant drugs, controversy still exists about the safety of dental treatment in a patient receiving this therapy. The authors review the topic in depth and offer detailed recommendations for the dental management of patients receiving coumarin anticoagulant therapy.

ABSTRACT
Despite approximately 40 years of experience with oral anticoagulant drugs, controversy still exists about the safety of dental treatment in a patient receiving this therapy. The authors review the topic in depth and offer detailed recommendations for the dental management of patients receiving coumarin anticoagulant therapy.

Monitoring anticoagulation status and describe current medical practice with respect to the use of coumarin. To assist practitioners who see these patients, we offer detailed recommendations for the dental management of people receiving coumarin anticoagulant therapy.

COUMARIN ANTICOAGULANT THERAPY
Pharmacology of coumarin. The two most widely used coumarin derivatives are warfarin sodium (Coumadin, DuPont Pharma) andbishydroxycoumarin (dicumarol). Both act as vitamin K antagonists and interfere with the γ-carboxylation of factors VII and IX and prothrombin factor as well as the coagulation-inhibitor proteins C and S. The anticoagulant effect depends not only on the reduction in synthesis of vitamin K-dependent proteins but also on the normal clearance of previously synthesized active proteins. Because prothrombin has a half-life of 72 hours, coumarin must be administered for four to five days before adequate anticoagulation is achieved.

Monitoring anticoagulant therapy. Determination and maintenance of coumarin dosage is complicated, and treatment regimens must be highly personalized because of individual differences in absorption, utilization and elimination. Monitoring is essential during the initiation of therapy, whenever any medications are added or withdrawn that might affect anticoagulation, and peri-

JADA, Vol. 128, March 1997 327
The prothrombin time, or PT, is the time required to form a plasma clot after recalcifying citrated plasma in the presence of a crude extract of animal tissue such as rabbit brain or lung in a suspension of phospholipid called thromboplastin.\(^6^7\) Thromboplastins used in medical laboratories vary as to the species source, tissue used and method of preparation, resulting in differing sensitivities to factor deficiencies.\(^9\)

**Why monitoring is changing.** When anticoagulation therapy was first recommended, the target therapeutic range was a prothrombin ratio (PT/control), or PTR, of 2.0 to 2.5.\(^10\) During the 1970s, the sensitivity of the thromboplastins in use decreased but the target range remained the same.\(^11\) The result was that the degree of anticoagulation used by physicians inadvertently became markedly higher than the range originally recommended, with significantly increased hemorrhagic potential.\(^5^1\) Because of this, the World Health Organization introduced the INR to improve the safety and effectiveness of oral anticoagulant therapy.\(^11^1^4\)

**The INR and how it works.**

The INR adjusts for varying sensitivities of the thromboplastins and makes it possible to target the same therapeutic ranges while using different laboratory reagents.\(^11^1^4\) The INR is the patient’s PT divided by the mean normal PT for the laboratory (that is, PTR), with an additional adjustment for the reactivity of the reagents. This adjustment for reagents is termed the international sensitivity index, or ISI, and substantially affects the PTR because it is a power function according to the following formula:

\[
\text{INR} = \text{PTR}^{\text{ISI}}
\]

ISI values for commercial thromboplastins used in the United States range from 1.2 to 2.8.\(^1^4\) The impact of the ISI can be illustrated by a simple example: If a patient has a PT that is 1.5 times the control value, the INR could be as low as 1.6 (if ISI = 1.2) to as high as 3.1 (if ISI = 2.8). The INR is therefore an adjusted PTR, and a higher INR reflects a higher level of anticoagulation with an attendant increased risk of hemorrhage. However, because of the way the INR is derived, it always has a higher value than the PTR.

**Current indications and complications associated with anticoagulant therapy.**

Since the American Heart Association first published guidelines for coumarin therapy in 1954,\(^1^9\) the indications have greatly expanded.\(^1\) Table 1 presents a list of current indications together with the therapeutic target range defined in terms of the INR.\(^1^3^1^4\) Therapeutic ranges are divided into less intense (INR, 2.0 to 3.0) and more intense (INR, 2.5 to 3.5) categories. Therapy may last for relatively short periods, such as three to six months, but often is long-term.\(^1^5\)

Bleeding complications occur frequently with coumarin therapy.\(^6^7\) Approximately 50 percent of these complications occur despite the patient’s INR being in the therapeutic range. Bleeding occurrences may range from mild epistaxis to life-threatening events such as intracranial bleeding.\(^5^7^1^6\) Risk factors for bleeding complications include age of 65 years or older; history of stroke, gastrointestinal bleeding or atrial fibrillation; and other serious comorbid con-
<table>
<thead>
<tr>
<th>DENTAL TREATMENT</th>
<th>SUBOPTIMAL INR RANGE</th>
<th>NORMAL TARGET INR RANGE</th>
<th>OUT OF RANGE</th>
<th>Mechanical Heart Valves</th>
</tr>
</thead>
<tbody>
<tr>
<td>Examination, radiographs, study models</td>
<td>&lt; 1.5</td>
<td>1.5 to &lt; 2.0</td>
<td>2.0 to &lt; 2.5</td>
<td>2.5 to 3.0</td>
</tr>
<tr>
<td>Simple restorative dentistry, supragingival prophylaxis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complex restorative dentistry, scaling and root planing, endodontics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simple extraction, curettage, gingivoplasty</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple extractions, removal of single bony impaction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gingivectomy, apicoectomy, minor periodontal flap surgery, placement of single implant</td>
<td>Probably safe (IR)‡</td>
<td>Probably safe (IR)‡</td>
<td>Probably safe (IR)‡</td>
<td></td>
</tr>
<tr>
<td>Full-mouth/full-arch extractions</td>
<td>Probably safe (IR)‡</td>
<td>Local measures§</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extensive flap surgery, extraction of multiple bony impactions, multiple implant placement</td>
<td>Probably safe (IR)‡</td>
<td>IR§</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Open-fracture reduction, orthognathic surgery</td>
<td>Not advised††</td>
<td>Not advised††</td>
<td>Not advised††</td>
<td>Not advised††</td>
</tr>
</tbody>
</table>

* Green indicates that it is safe to proceed in a routine manner (local factors such as periodontitis/gingival inflammation can increase the severity of bleeding; the clinician should consider all factors when making a risk assessment). Yellow, use caution, but in many instances the procedure can be safely performed with judicious use of local measures. Red, procedure not advised at current INR level; refer to physician for adjustment.
† INR: international normalized ratio.
‡ IR: insufficient research to draw a conclusion.
§ Increased need for use of local measures such as sutures, oxidized cellulose, microfibrillar collagen hemostat, topical thrombin and tranexamic acid.
** IR+: insufficient research, but similar to other procedures for which research data are available.
†† Should not be performed in a dental office on a patient receiving anticoagulant therapy; this is a hospital procedure.
ditions, such as recent myocardial infarction. The risk of bleeding is much higher during the first month of anticoagulant therapy and rises dramatically with increasing anticoagulation intensity. Patients with mechanical heart valve prostheses who are treated with coumarin derivatives experience major bleeding at an incidence of 1.4 events per 100 patient-years.

SAFETY OF DENTAL TREATMENT

Since the introduction of anticoagulant therapy, controversy has existed about whether dental treatment could be safely performed while the patient received anticoagulant therapy or if therapy needed to be reduced or stopped entirely. Additionally, many practitioners were concerned that reduction or elimination of anticoagulant therapy placed the patient at an unacceptable risk of thromboembolism. Subtherapeutic or discontinued anticoagulation in patients with mechanical valve prostheses entails a significant risk of valve thrombosis.

To determine what conclusions could be reached on the basis of reported studies and recommendations concerning the safety of dental treatment for patients receiving anticoagulant therapy, we performed an extensive review of the literature. Our observations are presented below.

The vast majority of reports in the literature indicate that most dental treatment can be safely performed on an outpatient basis for people who are receiving continuous anticoagulant therapy according to accepted guidelines. In some instances, practitioners recommend that treatment be performed at suboptimal levels of anticoagulation. In certain situations, primarily those dealing with complex surgical procedures, there are not sufficient reports to make generalizations about patient treatment. There is a clear need for focused research in this area.

It is inappropriate to group all types of dental treatment into a single category.

The INR should be the basis for determining the patient’s anticoagulation status.

Clearly, a simple restoration with infiltration anesthesia poses much less risk of hemorrhage than multiple extractions requiring a mucoperiosteal flap. The INR should be the basis for determining the patient’s anticoagulation status. While the PT will continue to be reported for some time, the INR is the more accurate index.

In assessing risk, practitioners need to weigh the probability of embolism occurring if anticoagulant therapy is reduced or withdrawn. This risk is highest in patients with mechanical heart valves. Complete withdrawal of anticoagulant therapy is clearly not needed to safely perform the majority of dental procedures.

The probability of hemorrhagic complications increases with increasing levels of anticoagulation. While hemorrhagic complications can occur during surgery and immediately afterward, they commonly arise late (that is, one to five days after surgery).

In an attempt to help dentists determine the safety of dental treatment for patients receiving anticoagulant therapy, we present our conclusions in Table 2. This table lists increasingly invasive dental treatment matched with increasing levels of INR. Dental treatment is divided into detailed categories patterned after those proposed by Sonis and colleagues. This categorization recognizes the increased potential for hemorrhage with increasingly invasive dental treatment.

To assess hemorrhagic risk, we classified the INR into six ranges to recognize the increasing risk of hemorrhage with increasing levels of anticoagulation. Two of the INR ranges are suboptimal (<1.5 and 1.5 to <2.0), which would normally be achieved only after anticoagulant therapy is reduced. Three ranges are considered optimal (2.0 to <2.5, 2.5 to 3.0, >3.0 to 3.5), with the highest range normally recommended only for patients with mechanical heart valves. The last range (>3.5) exceeds the currently recommended target range. When assessing INR values, practitioners need to remember that these values are higher than the PTR from which they are calculated.

DENTAL MANAGEMENT ALGORITHM

We summarize our findings for nonurgent dental care of patients receiving anticoagulant therapy in Figure 1. Dentists should initially pursue two parallel courses of evaluation. A detailed interview of the patient should elicit the name of the attending physician, reason for coumarin therapy, anticipated duration of therapy and moni-
Figure 1. Algorithm for nonurgent dental care of patients receiving anticoagulant therapy. INR: international normalized ratio; PT: prothrombin time.
Figure 2. Partial withdrawal protocol. INR: international normalized ratio.

Consult with physician

Two- (or three-) day cessation of coumarin therapy

Determine INR

Unacceptable INR

Defer for an additional day

Acceptable INR

Repeat INR

Perform dental treatment

Resume coumarin therapy on the evening of the same day

Consultation. Consultation with the patient's physician is an essential step in dental management. During the conversation with the physician, the dentist should verify the information obtained from the patient and obtain the current PT/INR values. The dentist should also describe the anticipated dental treatment. However, in our opinion, it is the responsibility of the dentist to determine if the anticipated care can be accomplished without modifying the patient's anticoagulant therapy and to express this to the physician. Physicians do not have the expertise to evaluate the degree of difficulty, invasiveness, potential morbidity, expected blood loss or other attendant hemorrhagic risks for most dental procedures. While, ultimately, the physician determines whether anticoagulant therapy is to be modified, dentists must be the content experts on dental therapy and its risks.

Testing. Before dental procedures are initiated, it is essential that the patient's anticoagulation status, as measured by a current PT/INR, be known. While hospital-based practitioners may prefer to order these tests, the majority of dentists usually refer patients to the attending physician for testing. For nonurgent procedures, dentists should coordinate their treatment schedule to coincide with normal monitoring of anticoagulation status by the physician (approximately every four to six weeks). Such coordination minimizes the inconvenience and cost to the patient, reinforces the joint management by physician and dentist, and assures the dentist of accurate and timely results. Ideally, testing should be done on the same day as the dental therapy.

Toring schedule and whether frequent dosage modification is necessary. Second, through standard evaluation techniques, the dentist should determine the required types of therapy, with special consideration given to the potential for hemorrhage. Factors affecting risk assessment include the presence of gingival inflammation and periodontitis, need for surgical intervention, need for block anesthesia and number of anticipated treatment visits.

If the duration of anticoagulant therapy is anticipated to be six months or less (common with deep venous thrombosis), the dentist may want to postpone elective care until after the normal cessation of anticoagulant therapy. This is especially true if nonurgent surgery is part of the proposed treatment. However, urgent treatment needs may preclude deferral for any substantial period.

Testing. Before dental procedures are initiated, it is essential that the patient's anticoagulation status, as measured by a current PT/INR, be known. While hospital-based practitioners may prefer to order these tests, the majority of dentists usually refer patients to the attending physician for testing. For nonurgent procedures, dentists should coordinate their treatment schedule to coincide with normal monitoring of anticoagulation status by the physician (approximately every four to six weeks). Such coordination minimizes the inconvenience and cost to the patient, reinforces the joint management by physician and dentist, and assures the dentist of accurate and timely results. Ideally, testing should be done on the same day as the dental therapy.
Alteration of anticoagulation status. There are three general management strategies that can be used if the patient’s INR (or PT) is unacceptable for the anticipated dental procedure. These are to reduce the level of anticoagulation by partially withdrawing the coumarin therapy, discontinuing the coumarin therapy entirely or substituting heparin anticoagulant therapy for coumarin (Figure 1).

Partial reduction or interruption of anticoagulant therapy. If needed to minimize hemorrhagic risk, the patient’s anticoagulation status (INR) may be shifted temporarily to the low end of the therapeutic target range or into a suboptimal range. The most practical way of accomplishing this is by a two- or three-day withdrawal protocol (Figure 2). This results in improved hemostasis and keeps the duration of reduced anticoagulation to a minimum. For most patients, a two-day withdrawal is adequate, but if the patient is aged or has a high INR, the threeday protocol may be necessary.

Cessation of anticoagulant therapy. Another option is to stop coumarin therapy for four or five days before performing dental treatment, which is sufficient time for the effects of the drug to be eliminated. Coumarin therapy is then resumed after dental treatment. However, while this strategy eliminates the risk of hemorrhagic complications, there is an increased risk of thrombotic complications due to underlying disease. In our opinion, complete cessation of coumarin therapy before dental treatment is risky, overused and usually unnecessary.

Substitution therapy. The third alternative is to discontinue coumarin therapy several days before surgery (or other dental treatment) and substitute heparin anticoagulant therapy. With adequate nutrition, vitamin K-dependent factors should return to the normal range, while the heparin preserves adequate anticoagulation. Heparin can be discontinued six to eight hours before surgery, resulting in a minimal period in which the patient is not receiving anticoagulant therapy. Anticoagulant therapy, either with coumarin and heparin or coumarin alone, can then be readministered shortly (12 to 18 hours) after surgery.

Heparinization requires a great deal of medical intervention and usually hospitalization. With the newer low-molecular-weight heparin drugs (enoxaparin, Lovenox, Rhone-Poulenc Rorer Pharmaceuticals; dalteparin, Fragmin, Pharmacia), once-a-day dosing is possible after an initial loading dose, and home treatment is possible. However, substituting heparin for coumarin is a complex and costly medical intervention that should be reserved for patients at greatest risk of thromboembolism (with a mitral valve prosthesis) whose care would normally involve hospitalization.

### ADDITIONAL STRATEGIES AND LOCAL MEASURES TO REDUCE RISK

Additional strategies that lessen the risk to the patient are to subdivide full-arch and full-mouth procedures into two or more smaller procedures; to use infiltration, periodontal ligament or intrasosseous injections in place of block anesthesia when practical; and to use local hemostatic measures.

Multiple local hemostatic measures such as mechanical procedures (sutures, pressure), chemical agents (thrombin) and absorbable hemostatic agents (oxidized cellulose, microfibrillar collagen hemostat) are useful and become increasingly im-
important with more invasive procedures.35,36 Practitioners who treat patients receiving anticoagulant therapy need to have sufficient local hemostatic agents available to treat the anticipated bleeding, and be prepared to deal with any unexpected complications.

As a result of its antifibrinolytic action, tranexamic acid, used as an irrigant intraoperatively and as a mouthwash postoperatively, reduces postoperative hemorrhagic complications.24,38,47,52 In an animal model, the combination of socket packing and oral tranexamic acid completely eliminated excessive blood loss resulting from anticoagulation.52 Topical tranexamic acid was also very effective in eliminating postoperative complications in patients who underwent surgical procedures without alteration of their anticoagulant therapy.24,38,46,47

URGENT DENTAL CARE
Managing urgent dental problems requires that practitioners follow the steps outlined above, but in an expedited manner. Relying on laboratory data from previous monitoring of anticoagulation status is problematic.48 If the patient’s INR has been checked within the previous few days and has been stable for a considerable time, we believe this value is representative of the patient’s current status for non-surgical treatment. However, if the test is more than a few days old, if the patient (at the physician’s direction) has had to adjust the dosage often because of variations in coagulation level, if the patient’s anticoagulation level is relatively high or if a surgical procedure is necessary, it is essential to obtain a current value. If there is any doubt about the patient’s anticoagulation status, a current INR should be obtained.

Vitamin K is well-recognized for its ability to reverse the effect of coumarin anticoagulant.14 Nevertheless, it should be used in only those instances in which very significant hemorrhage has occurred, in as low a dose as possible and always at the direction of a physician.3 Fresh-frozen plasma or factor replacements are used as alternatives for emergency treatment of patients receiving anticoagulant therapy.5 However, local measures are almost always effective for treating dental hemorrhagic complications.

AVOIDANCE OF DRUG INTERACTIONS
A number of medications administered with coumarin can interact to affect anticoagulation markedly.44 While the majority of these drug interactions involve medications prescribed only by physicians, a number of drugs that are used by dentists potentiate or oppose the action of coumarin. The box (“Drugs With the Potential to Affect Anticoagulant Therapy”) provides a selected list of medications with the potential to affect coumarin therapy.

Antibiotic prophylaxis against infective endocarditis is unlikely to affect the patient’s anticoagulation status. However, Wood and Deeble50 recently described three cases in which prophylactic antibiotics were linked to significant increases in the patient’s INR. Salicylates and nonsteroidal anti-inflammatory drugs should be avoided entirely in patients receiving anticoagulant therapy because these agents affect platelet function as well as coagulation.

Practitioners can often find an alternative agent that does not affect coagulation status. However, if any of the medications listed in the box must be prescribed for a course of treatment, the dentist must discuss this with the patient’s physician and monitor anticoagulation status throughout treatment.

CONCLUSION
The introduction of the INR makes planning for and accomplishing dental treatment safer and more predictable. While a risk-benefit assessment must be made for each patient, dentists can perform most dental treatments safely in patients undergoing coumarin therapy without the need for hospitalization or cessation of anticoagulant therapy.