Quality Resource Guide

Fifth Edition

Dental Care for Patients with Bleeding Disorders

Author Acknowledgements

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Educational Objectives

Following this unit of instruction, the practitioner should be able to:

1. Understand basic physiologic elements of normal hemostasis and common hematologic impairments.
2. Recognize the importance of the medical history in identifying the patient at risk for a bleeding disorder.
3. Recognize clinical signs suggestive of a hematologic impairment.
4. Develop a protocol to manage commonly encountered bleeding risk scenarios in dental practice.

MetLife designates this activity for **1.0 continuing education credits** for the review of this Quality Resource Guide and successful completion of the post test.

The following commentary highlights fundamental and commonly accepted practices on the subject matter. The information is intended as a general overview and is for educational purposes only. This information does not constitute legal advice, which can only be provided by an attorney.

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The content of this Guide is subject to change as new scientific information becomes available.

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Introduction

Numerous routine dental therapies often cause some level of bleeding, which may be quickly and effectively controlled for most patients. However, for the patient with an underlying hematologic impairment, bleeding associated with dental therapy may lead to serious and potentially grave consequences.

Fortunately, the majority of these patients are easily identified with a thorough medical history and clinical examination.[1] The purpose of this guide is to review: 1) the physiology of hemostasis, 2) types of hemostatic impairment, and 3) a suggested protocol to identify and manage the dental patient with an increased bleeding risk.

Review of Physiology

Normal hemostasis is defined as the physiologic balance of procoagulant and anticoagulant factors that maintain the fluid flow of blood and the structural integrity of the vasculature. A simplified view is that either extrinsic or intrinsic vascular injury initiates a series of physiologic responses (platelet activation, coagulation cascade) that ultimately lead to the formation of a platelet-fibrin thrombus (clot) that arrests bleeding. Subsequent tissue repair results in the degradation and ultimate destruction of the no longer necessary clot. A simplified illustration of the coagulation cascade is presented in **Figure 1**. [Figure 1 is for illustrative purposes only and the inferred linear flow to hemostasis does not represent the complexity that occurs in vivo][2]

Impairment of any component or components of the hemostatic process may result in a bleeding disorder. Underlying causes may be acquired or inherited and are summarized in **Table 1**. Acquired coagulation disorders due to prescribed medical therapy (iatrogenic) are the most frequently encountered hematologic impairments in clinical dental practice.[1]

Identifying the Patient with a Hematologic Impairment

The majority of patients with a hematologic impairment are identified through the completion of a thorough medical history and clinical examination.[1] Historical considerations that are useful to identify an "at-risk" patient include:

1) current or past bleeding problems (prolonged bleeding) affecting the patient or blood relatives;
2) bleeding problems related to past surgical or traumatic events;
3) exposure to agents (drugs, chemicals, supplements) associated with increased bleeding risk, and;
4) the presence of diseases associated with increased bleeding risk.

Affirmative responses must be pursued for further explanation and detail. For example, if the patient answers "yes" to an inquiry about easy bleeding or bruising, the clinician should inquire further to determine the clinical pattern. This allows the practitioner to separate the less concerning ("I got these bruises after I bumped into the coffee table") from the more concerning ("These bruises appeared without hitting anything" or "I just started noticing them"). Episodes of prolonged bleeding that resulted in a visit to the doctor's office or hospital are also important historical findings.

A dentist's clinical examination should not be limited to the oral cavity. It should include inspection of exposed skin to determine the presence of ecchymoses (**Figure 2**), purpura, petechiae, spider angiomas, jaundice, cyanosis, or pallor. Ecchymoses, purpura, and petechiae are bruises with dimensions of >1 cm, 2 mm to 1 cm, and ≤ 2mm, respectively. Oral cavity findings suggestive of a potential bleeding problem include petechiae (**Figure 3**), purpura, ecchymoses, jaundice, pallor, enlarged gingival tissues, ulceration, and hemorrhage.

Figure 1 - Simplified Coagulation Cascade

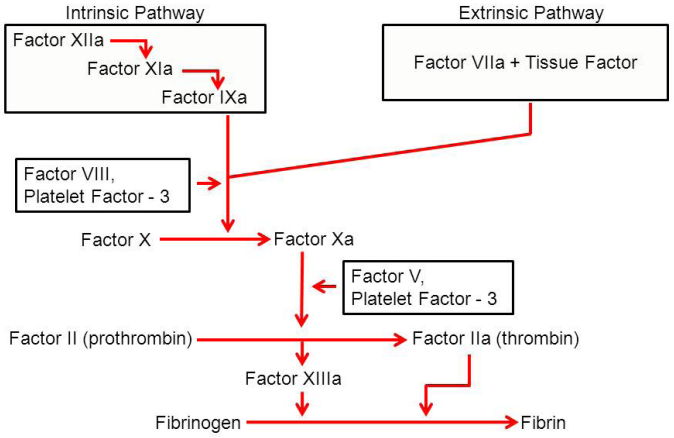

Figure 2

Ecchymoses observable on elderly individual taking warfarin.

Figure 3

Intraoral petechiae and purpura in individual undergoing cancer chemotherapy.

Any patient presenting with an equivocal history or clinical signs and symptoms suggestive of an undiagnosed or poorly controlled bleeding disorder requires further medical evaluation to establish a diagnosis.[1] While an experienced dental practitioner may order basic laboratory testing (**Table 2**) to assess bleeding risk status, most dentists will refer the patient to their physician for further evaluation and diagnosis. Once the specific hematologic impairment is identified, it must be documented in the patient's chart.

Despite obtaining a noncontributory medical history and noting no abnormalities on clinical examination, direct observation of excessive bleeding during or after a dental procedure may represent the first and only clue of a patient's underlying hematologic impairment.

Suggested Management Guidelines

Establishing the diagnosis allows the dentist to develop a plan tailored to address the dental needs of the individual patient. Such a plan must consider not only the extent of surgical therapy needed, but also the patient's overall medical status and the dentist's clinical experience.[1,3-5] For infrequently encountered scenarios such as an inherited disorder, a medical consultation is warranted to determine the patient's current status and his/her ability to tolerate the anticipated dental care in either a general practice or specialist setting. The dentist should clearly describe in the consult the anticipated bleeding associated with necessary dental care ("restore tooth #2 with no anticipated mucosal incisions or tearing – no, or minimal, bleeding anticipated", "simple extraction of two (2) teeth with primary soft tissue closure following the procedure – moderate, locally controllable bleeding anticipated"). In general, a patient determined to have extensive surgical needs, a labile hemostatic profile, significant contributory co-morbidities (*e.g.*, liver disease, renal disease), or the need for treatment modifications not routinely available in the dental office setting warrants referral to a practitioner with expertise in managing such cases (Oral and Maxillofacial Surgeon, Hospital Dentist, or Oral Medicine clinician).

Table 1 - Summary of Conditions of Impaired Hemostasis

Acquired Conditions

- **Acquired disorders of the vasculature**
  - Infection: Typhoid or meningococcal septicemia, measles
  - Nutritional: Scurvy
  - Allergic: Henoch-Schönlein purpura, serum sickness
- **Acquired disorders of platelets**
  - Increased destruction or inhibited production
    - Drugs (chemotherapy, thiazide diuretics, alcohol, others)
    - Infection (Human Immunodeficiency Virus)
    - Vitamin deficiency (Folate, B12)
    - Irradiation
    - Marrow infiltration (tumor, leukemia)
    - ITP – immune thrombocytopenic purpura
    - Hypersplenism
    - Others
  - Qualitative platelet impairment
    - Drugs (aspirin, non-steroidal anti-inflammatory drugs, ethanol)
    - Herbal supplements (Garlic, Ginko biloba, Ginger, Green tea)
    - Uremia
    - Liver disease
    - Acquired von Willebrand disease (often observed in autoimmune disease, lymphoproliferative disorders)
- **Acquired disorders of coagulation**
  - Liver disease
  - Vitamin deficiency (biliary tract obstruction, malabsorption, antibiotics)
  - Anticoagulant drugs (heparin, coumarin, dabigatran, rivaroxaban, edoxaban)

Inherited Conditions

- **Inherited disorders of the vasculature**
  - Hereditary hemorrhagic telangiectasia
  - Hereditary hemorrhagic thrombasthenia
- **Inherited disorders of platelets**
  - von Willebrand disease
  - Glanzman's thrombasthenia
  - Bernard-Soulier disease
- **Inherited disorders of coagulation**
  - Hemophilia A (Factor VIII deficiency)
  - Hemophilia B (Factor IX deficiency)
  - Other factor deficiencies

General therapeutic principles recommended when treating any patient with a hematologic impairment include:

1. judiciously administer local anesthesia;
2. employ meticulous surgical technique;
3. remove granulation tissue that could promote continued bleeding;
4. accomplish primary soft tissue closure when possible;
5. use adjunctive hemostatic agents when appropriate (see **Table 3**), and;
6. follow-up with the patient to ensure no complications.

Postoperative instructions should be clearly explained and given in written form to the patient and/or their caregiver to ensure that activities that may increase the risk of clot disruption (sucking through a straw, sucking candy, smoking, rinsing, strenuous activity) are avoided. The use of any medication that may adversely affect the underlying hematologic condition, such as aspirin and NSAIDs, is to be avoided.[1,5,6] Patients with a hematologic impairment should be scheduled early in the day, and early in the week, since immediate complications occur within hours following a procedure and delayed complications usually occur within a couple days following a procedure.[1] The dental practitioner should never independently adjust the dosage of any medically prescribed medication (*e.g.*, aspirin, NSAID, warfarin) intended to affect the patient's hemostatic profile. Such adjustments are under the purview of the managing physician.

The most likely bleeding-risk scenario the general dentist will encounter is the patient being medically managed to reduce thromboembolic risk. Contemporary guidance generally recommends against the routine interruption or reduction of antithrombotic medication when such a patient requires a minor surgical procedure in the dental setting. The preponderance of evidence reveals that the bleeding risk associated with minor dental surgery can be effectively managed. In contrast, reducing the antithrombotic medication to accommodate minor dental surgery leads to an increased risk for a potentially fatal thromboembolic event.[3-7] While the definition of a "minor dental surgery " is debatable, it may be defined as the simple extraction of ≤3 teeth; crown and bridge procedures; implant placement, and scaling or periodontal surgery initially restricted to a limited area to allow assessment of bleeding.[3,6]

Table 2 - Common Laboratory Tests to Assess Hemostasis[1]

Test	Purpose	Normal Range
aPTT	Evaluate intrinsic and common pathways of coagulation	25 - 30 seconds
PT	Evaluate extrinsic and common pathways of coagulation	11 - 15 seconds
TT	Evaluate the level and function of fibrinogen	9 - 13 seconds
Platelet count	Measure of number of platelets	140,000-400,000/uL

Table 3 - Adjunctive Hemostatic Agents*

Agent	Features
Gauze	For direct pressure.
Absorbable gelatin sponge (Gelfoam® - Pfizer, Inc.)	Serves as a scaffolding to help stabilize the clot; recommend stabilization with suture or splint.
Chitosan (Patch® Pro -Tricol Biomedical, Inc.)	Provides a physical barrier to protect the wound bed; recommended to be gently removed after 48 hrs.
Absorbable collagen (creos™ - Nobel Biocare)	Mild to moderate bleeding is usually controlled in 2-5 minutes.
Microfibrillar collagen hemostat (Helistat™ - Integra LifeSciences Corp.)	Attracts platelets and triggers aggregation to promote platelet plug formation.
Absorbable collagen dressing (CollaTape®, CollaPlug® CollaCote® - ZimVie, Inc)	Sutured in or over the wound or placed under a stent; fully resorbed in 30 days.
Resorbable oxidized cellulose (Surgicel® - Johnson and Johnson)	Swells on contact with blood to increase pressure in socket to enhance hemostasis.
Topical thrombin (Thrombostat™, Thrombin-JMI®, others)	Topical thrombin should not be used with collagen and cellulose products due to inactivation from pH alterations.
Tissue glue (Histoacryl® - H. B. Fuller Medical Adhesive Technologies, LLC.)	Tissue glue.

* Partial listing. Practitioners should check with their supplier for comparable products.

The Patient on Antiplatelet Medication (Aspirin, or Aspirin & $P2Y_{12}$ Inhibitor)

Aspirin (81-325 mg/day) is commonly prescribed for a patient as a first-line agent to reduce the risk of stroke or heart attack. Aspirin acts to irreversibly reduce platelet aggregation. Another antiplatelet drug, such as a $P2Y_{12}$ inhibitor, may be prescribed to reduce platelet activity further (**Table 4**).[8] This is called dual antiplatelet therapy (DAPT).

Available research indicates the increased bleeding risk associated with a minor surgical intervention in patients taking low-dose aspirin or aspirin plus a $P2Y_{12}$ inhibitor is effectively managed using good surgical technique, appropriate gelatin or collagen hemostatic agents, primary soft tissue closure, and direct pressure for 15-30 minutes.[9-13]

The Patient on Warfarin

Warfarin (Coumadin®) is a vitamin K antagonist prescribed for the prophylaxis and treatment of venous thrombosis, pulmonary embolism, thromboembolic complications related to atrial fibrillation, and/or cardiac valve replacement. It may also be prescribed post myocardial infarction (MI) to reduce the risk of death, recurrent MI, and thromboembolic events such as stroke or systemic embolization.[14,15] Warfarin interferes with the production of coagulation Factors II, VII, IX, and X in the liver. It has a narrow therapeutic index, individual patient response is highly variable, and it is affected by numerous food and drug interactions (**Table 5**). As a consequence, both patient compliance and drug efficacy is often compromised, resulting in the need for frequent laboratory monitoring.[16,17] The laboratory test used to monitor warfarin efficacy is the international normalized ratio (INR) and targeted therapeutic values typically run between 2.0 and 3.5.

While increased bleeding is to be anticipated in the patient taking warfarin, limited dental surgery may be safely accomplished by verifying the patient's INR and using the adjunctive measures listed in **Table 3**. It is essential to verify and document that the INR is within the therapeutic range and was obtained within 72 hours before the procedure.[1,6] The use of appropriate gelatin with thrombin or collagen hemostatic agents, primary tissue closure, and direct pressure for 15-30 minutes is usually sufficient to establish hemostasis. A plasminogen inhibitor oral rinse for 2 days post-surgery may also be beneficial (see **Table 6**).[1,6,20-22] If the INR exceeds the therapeutic range, the surgery should be deferred, and the patient should be evaluated by his/her physician. This is for the benefit of the patient.

Table 4 - $P2Y_{12}$ Inhibitors

Ticagrelor (Brilinta®)	Clopidogrel (Plavix)	Prasugrel (Effient®)	Cangrelor (Kengreal®)

Table 5 - Common Warfarin Drug Interactions†

Drugs That Potentiate Warfarin (CYP2C9, 1A2, and/or 3A4 inhibitors)		**Drugs That Antagonize Warfarin (CYP2C9, 1A2, and/or 3A4 inducers)**
Alprazolam	Amiodarone	Barbiturates
Cimetidine	Ciprofloxacin	Carbamazepine
Clarithromycin	Fluconazole	Nafcillin
Ketoconazole	Metronidazole	Omeprazole
Miconazole	Oral contraceptives	Phenytoin*
Phenytoin*	Propranolol	Prednisone
		Pioglitazone
		Rifampin
Drugs That Augment Bleeding Risk		
Anticoagulants	Antiplatelets	NSAIDs
Serotonin Reuptake Inhibitors		Acetaminophen**
Foods & Herbal Supplements That Affect Bleeding Risk		
Foods and Herbal Supplements That Potentiate Warfarin		**Foods and Herbal Supplements That Antagonize Warfarin**
Alfalfa	Garlic	St. John's wort
Anise	Ginko biloba	Ginseng
Bilberry	Green tea,	foods high in Vitamin K
Cranberry juice		(green leafy vegetables, cruciferous vegetables)

† Drug interaction checker available at Drugs.com: https://www.drugs.com/drug_interactions.html

* Phenytoin administration initially augments warfarin effect, but after time may act to antagonize warfarin effect. The mechanism is unknown.[18]

** Acetaminophen may potentiate warfarin and other oral anticoagulants. The interaction has generally been associated with prolonged ingestion of relatively high acetaminophen dosages (2 g/day for at least 3 consecutive days), not with brief, intermittent exposures of average doses.[19]

Table 6 - Available Formulations of Plasminogen Inhibitors[22]

Agent	Instructions for Use
Aminocaproic acid 5gm/20mL IV solution compounded to 5% mouth rinse. Disp: 100mL	Following dental procedure, hold 10mL (2 tsp) in the mouth for 1-2 minutes, then spit out. May repeat every 2 hours.
Tranexamic acid IV solution compounded to 5% mouth rinse. Disp: 100mL	

The Patient on a Combined Antiplatelet/Anticoagulant Regimen

In select scenarios, such as for a patient with a mechanical heart valve and a history of vascular disease, or a patient with additional risk factors for thromboembolism, a combined warfarin and low dose aspirin regimen may be in place. In this scenario, minor surgical care may be safely accomplished with verification of the patient's INR and use of appropriate adjunctive hemostatic measures.[23]

The Patient on a Direct Oral Anticoagulant (DOAC)

DOACs include the reversible direct thrombin inhibitor Dabigatran etexilate (Pradaxa®)[24] and the reversible Factor Xa inhibitors apixaban (Eliquis®)[25], edoxaban (Savaysa®)[26], and rivaroxaban (Xarelto®).[27] The medical indications for these agents are extensive (see **Table 7**).

When compared to warfarin, DOACs exhibit more predictable bioavailability, have fewer drug interactions (see **Table 8**), are prescribed on a fixed dose schedule, and since they produce a more stable anticoagulant effect, do not require routine anticoagulation monitoring.[16,17,28]

Based on improved patient convenience and compliance compared to warfarin, the number of patients prescribed these medications in the United States has grown to an estimated 4 million.[28] Recent studies and reviews support the premise that for the patient on a DOAC, minor surgical procedures (as previously defined) performed in the dental office are manageable using the same protocol previously discussed for warfarin.[6,29-33]

Table 7 - Available DOACs

Agent	Indications for Use
Dabigatran etexilate (Pradaxa®)[24]	• To reduce the risk of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation. • For the treatment of deep venous thrombosis (DVT) and pulmonary embolism (PE) in adult patients who have been treated with a parenteral anticoagulant for 5-10 days. • To reduce the risk of recurrence of DVT and PE in adult patients who have been previously treated. • For the prophylaxis of DVT and PE in adult patients who have undergone hip replacement surgery. • For the treatment of venous thromboembolic events (VTE) in pediatric patients 8 to less than 18 years of age who have been treated with a parenteral anticoagulant for at least 5 days. • To reduce the risk of recurrence of VTE in pediatric patients 8 to less than 18 years of age who have been previously treated.
Apixaban (Eliquis®)[25]	• To reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation. • For the prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE), in adult patients who have undergone hip or knee replacement surgery. • For the treatment of DVT and PE, and for the reduction in the risk of recurrent DVT and PE following initial therapy. • Treatment of venous thromboembolism (VTE) and reduction in the risk of recurrent VTE in pediatric patients from birth and older after at least 5 days of initial anticoagulant treatment.
Edoxaban (Savaysa®)[26]	• To reduce the risk of stroke and systemic embolism (SE) in patients with nonvalvular atrial fibrillation (NVAF). • For the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) following 5 to 10 days of initial therapy with a parenteral anticoagulant.
Rivaroxaban (Xarelto®)[27]	• To reduce risk of stroke and systemic embolism in nonvalvular atrial fibrillation. • For treatment of deep vein thrombosis (DVT). • For treatment of pulmonary embolism (PE). • For reduction in the risk of recurrence of DVT or PE. • For the prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery. • For prophylaxis of venous thromboembolism (VTE) in acutely ill medical patients. • To reduce the risk of major cardiovascular events in patients with coronary artery disease (CAD). • To reduce the risk of major thrombotic vascular events in patients with peripheral artery disease (PAD), including patients after recent lower extremity revascularization due to symptomatic PAD. • For treatment of VTE and reduction in the risk of recurrent VTE in pediatric patients from birth to less than 18 years. • For thromboprophylaxis in pediatric patients 2 years and older with congenital heart disease after the Fontan procedure.

Summary

Dental treatments may cause bleeding, which is quickly and effectively physiologically controlled for most patients. However, the patient with an underlying hematologic impairment may incur serious and potentially grave consequences from dental therapy. Fortunately, the majority of these patients are easily identified through the medical history and clinical examination. The general dentist will most frequently encounter "patients at risk for bleeding" who are taking medication(s) to reduce thromboembolic risk. Contemporary guidance generally recommends there be no interruption or reduction of antithrombotic medication when the patient requires a minor dental surgical procedure.

Table 7 - Potential NOAC Drug Interactions

Dabigatran	Apixaban, Rivaroxaban, & Edoxaban
P-Glycoprotein inducers *reduce* dabigatran activity (*e.g.,* rifampin, carbamazepine, dexamethasone)	Strong inducers of both CYP34A and P-Glycoprotein (*e.g.,* rifampin, carbamazepine, phenytoin, St. John's wort) reduce activity
P-Glycoprotein inhibitors *increase* dabigatran activity (*e.g.,* ketoconazole, itraconazole, clarithromycin)	Strong inhibitors of both CYP34A and P-Glycoprotein (*e.g.,* itraconazole, ketoconazole, posaconazole, voriconazole) increase activity

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POST-TEST

Internet Users: This page is intended to assist you in fast and accurate testing when completing the "Online Exam." We suggest reviewing the questions and then circling your answers on this page prior to completing the online exam.

(1.0 CE Credit Contact Hour) Please circle the correct answer. 70% equals passing grade.

1. **Which of the following intraoral findings should raise suspicion of an underlying bleeding problem?**
   a. varicosity
   b. gingivitis
   c. hemangioma
   d. petechiae
   e. a & b
   f. b & d

2. **Which of the following statements is not true?**
   a. Any patient presenting with an equivocal history or clinical signs and symptoms suggestive of an undiagnosed or poorly controlled bleeding disorder requires further medical evaluation to obtain a diagnosis.
   b. Affirmative responses to a question concerning easy bruising or bleeding must be pursued for further explanation and detail.
   c. Accomplishing a careful history will identify all patients at risk for excessive bleeding when undergoing a simple dental extraction.
   d. Oral cavity findings suggestive of a potential bleeding problem include petechiae, jaundice, pallor, hyperplastic gingival tissues, and hemorrhage.

3. **A basic laboratory test used to screen for a bleeding disorder include:**
   a. complete blood count.
   b. hematocrit.
   c. platelet count.
   d. white blood cell count.

4. **Bob has been instructed by his physician to take 81mg of aspirin a day. His tooth #2 is non-restorable and indicated for extraction. It is acceptable practice to advise him to stop taking his aspirin for 4 days before his appointment to have tooth #2 extracted.**
   a. True
   b. False

5. **Which of the following statements about warfarin is true?**
   a. Drug interactions may cause major changes in the efficacy of warfarin.
   b. Dietary influences on warfarin activity are rare.
   c. The laboratory test to monitor the efficacy of warfarin is the activated partial thromboplastin time (aPTT).
   d. All the above statements are true.

6. **Mr. Jones is taking warfarin for his atrial fibrillation, and he needs teeth #14 and #15 extracted. Which of the following co-morbidities is likely to raise his risk for excessive bleeding?**
   a. Liver disease
   b. Osteoarthritis
   c. Renal disease
   d. a & c
   e. a, b, & c

7. **Mr. Jones is taking warfarin for his atrial fibrillation, and he needs ten teeth extracted due to severe periodontal bone loss. Which of the following options is not an acceptable therapy approach?**
   a. Plan to extract 2-3 teeth at a time using meticulous technique and primary soft tissue closure following the procedure, and verify that the INR is within the therapeutic range within 72 hours of each appointment.
   b. Advise the patient to half his warfarin dose and return to the clinic in 3 days for the surgery.
   c. Refer the patient to an Oral and Maxillofacial Surgeon, Hospital Dentist, Oral Medicine clinician.

8. **Drugs which may potentiate warfarin activity include:**
   a. Carbamazepine
   b. Clarithromycin
   c. Prednisone
   d. Pioglitazone
   e. All the above

9. **Mr. Jones is taking rivaroxaban for his atrial fibrillation and needs teeth #s 14 & 15 extracted due to severe periodontal bone loss. Your best option is to:**
   a. Extract the teeth using meticulous technique and establish primary soft tissue closure.
   b. Advise the patient to half his rivaroxaban dose and return to the clinic in 3 days for the surgery.
   c. The day before his appointment verify that his INR is in the therapeutic range and proceed with therapy.
   d. Consult with his managing physician for guidance.

10. **When compared to warfarin, the new anticoagulant drugs (dabigatran etexilate and apixaban) exhibit more predictable pharmacokinetics and pharmacodynamics. The best measure to monitor their efficacy is the INR.**
    a. Both statements are true.
    b. Both statements are false.
    c. The first statement is true and the second statement is false.
    d. The first statement is false and the second statement is true.

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Evaluation - Dental Care for Patients with Bleeding Disorders 5th Edition

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4. Please rate the written materials and visual aids used.	☐	☐	☐	☐	☐	
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10 **9** **8** **7** **6** **5** **4** **3** **2** **1** **0**

extremely likely — neutral — not likely at all

What is the primary reason for your 0-10 recommendation rating above?

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