Management of Oral ANTICOAGULATION in Patients Undergoing Minor Dental Procedures
As dentists, we are continually updating our knowledge about oral cancer, bacterial endocarditis, diabetes, cardiac disease and all the many ways they intertwine with what we are planning for our patients’ oral health needs. We are also tuned into the signs and symptoms of stroke, heart attacks, high and low blood pressure, and a myriad of other medical conditions that our patients present us with.

Two years ago, we came face to face with signs and symptoms we did not associate with two of the most common and potentially fatal medical conditions: Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE). On May 20, 2010, our daughter, Anna Frutiger, died from a massive pulmonary embolism as a result of an undiagnosed deep vein thrombosis. She was healthy, beautiful, an athlete her whole life, and was living her dream of following us into the dental profession. None of us could have expected that a blood clot would end her life one month after her 23rd birthday, just as she completed her first year of dental school at University of Pittsburgh School of Dental Medicine.

Anna’s story has been shared over the past two years time and time again. The resulting ripple effect has saved lives time and time again. When we approached Dr. Merchant, a former instructor of ours at University of Detroit Mercy, about including something in the MDA Journal about blood clot awareness, she didn’t hesitate. In fact, we quickly were in collaboration with two medical specialists who were enthusiastic to have dentists know more about DVT, PE and blood clots. In addition, they felt it was so important that we also had the latest updates in anticoagulant protocols for our patients. As they pointed out, dentists are in the unique position as health care providers to see generally healthy people at least once or twice annually. While we typically don’t have conversations about blood clots with our patients, we are in a perfect position to educate them and others about potential side effects of medications they may be taking that would contribute to blood clots. We can also make them aware of signs and symptoms that could be life threatening if ignored.

Anna’s story is important because we need to know that blood clots can happen to anyone, at any time, and at any age. Anna was the picture of a happy, healthy young woman who took impeccable care of herself. She exercised daily and was training for a half marathon. Four months before she died, she started complaining of pain behind her knee and in her calf. Initially she thought it was possibly a muscle pull, but kept telling us it felt different than muscle strains she had experienced so many times as a dancer and athlete through high school and college. She also mentioned that she often felt short of breath when she exercised. But it was easy to
attribute both symptoms to the stress and fatigue of being a dental student, which is what she did at first.

When her leg pain persisted, she eventually saw an orthopedic surgeon who found no injury to suggest a muscle pull. After a thorough physical and review of her medical history, her doctor suspected a blood clot in her lower leg. Anna’s only known risk factors were taking a third-generation oral contraceptive. The results of an Ultrasound/Doppler of her leg were negative for a DVT. At a follow-up exam three weeks later, her leg was of normal shape and size, her pain was minimal, and her doctor discharged her.

After her first year of dental school finals Anna traveled with us to Aruba over her spring break, then visited friends on the east coast on two consecutive weekends after that. Between two airplane trips over her break and then an eight-hour bus ride the weekend before she arrested, Anna experienced hours of uninterrupted travel. She called when she got home and was experiencing shortness of breath as she climbed the stairs to her apartment. She was also experiencing an overall fatigue that she could not explain. We talked about the stress of dental school, encouraged her, and urged her to get some rest before classes started the following day.

The next morning, Anna called her best friend to drive her to school because she felt extreme weakness and didn't think she could walk to catch the bus. Anna collapsed on her lawn outside her apartment after walking down the stairs, and blacked out for several seconds. Her roommate and friend called 911 and an ambulance arrived within minutes. Anna was conscious at that point, and asked her friends to call us.

Anna made it to the emergency room, but almost immediately after her arrival suffered a cardiopulmonary arrest. She was immediately taken to surgery to try to dislodge the huge blood clot that caused her massive PE. Over the next two days, a team of doctor and nurses worked round the clock to keep Anna alive. We hoped a miracle might happen; it was something we wished for with all our hearts. Our family was on a roller coaster of emotions, as Anna occasionally would move her arms and we prayed she would awake from her coma. When neurological tests eventually showed that she no longer had brain activity, we were devastated and had to make the decision to take her off life support.

Anna’s doctors immediately consulted with us and encouraged genetic testing for blood clotting disorders. We all tested negative and had no family history of blood clots. Anna’s autopsy determined that she was not predisposed to blood clots, and it seems that the oral contraceptives and her concentrated travel in the month prior to her death were her major clotting risks.

We know that Anna was very tuned into her health and her body. Most people, and especially 23-year-olds, do not suspect that anything fatal is brewing. We know she did not link her birth control pills and shortness of breath to her leg pain or the possibility of a DVT. Although her doctor suspected a blood clot, he saw her as low risk. Moreover, the Ultrasound/Doppler testing is effective for DVT diagnosis only three out of 10 times. This is why we believe strongly that had Anna or ourselves possessed the awareness and knowledge of the risk factors and signs of DVT when she was having symptoms, Anna would be alive today.

We are committed to doing everything possible to support public awareness of blood clots. We know that awareness of signs and symptoms of DVT and PE helps save lives. As we mentioned, Anna’s story has already saved the lives of several individuals who had similar symptoms and sought medical care for blood clots or testing for clotting disorders. We believe our dental practices are a logical place to reach out to people who may potentially be at risk for developing a blood clot and encourage you to find a way to share this information.

We have become very involved in the National Blood Clot Alliance, a non-profit advocacy group whose work is to raise awareness and provide education. We encourage you to learn all you can at www.stoptheclot.org, and to share Anna’s story with those you care about.
So I’m lying on the hospital bed, and the ER doc comes in scratching his head. Not a good sign. It’s pretty much like being in the dental chair and hearing your dentist say “Oops.” Either way, you know something unexpected is happening, has already happened, or is just about to.

What had already happened? I had developed a DVT (deep vein thrombosis; i.e., blood clot on steroids) in my left leg. It was 7.5 cm long and growing in the calf muscle just below my knee. Pieces of the clot had broken off, traveled through my heart chambers and valves and lodged in my lungs, where they are better known as pulmonary emboli (PE).

What hadn’t happened yet? Well, too often the clot isn’t so kind: It grows and when it decides to break off the break can be huge. When that chunk hits home and camps in a major vessel, the first thing you notice is that you are dead.

Obviously, I’m not. What follows is my story. The same thing could happen to anyone reading this. Or, for that matter, to anyone not reading this. In short, if it happened to me, it can happen to anyone.

That’s why the ER doc was puzzled. I don’t fit the profile for people likely to develop a DVT/PE. No family history, on no meds, have regular check-ups. I’m six-foot three, 185 pounds and in decent shape; been drinking protein milkshakes for 20 years, finished the Iceman Cometh Mountain Bike Challenge last fall with a respectable time in the 50-55 age bracket. Guys like me don’t get blood clots, right?

But blood tests coupled with CT scans don’t lie. My D-dimer test, which screens for abnormal clotting activity, came back “off the charts.” And the scan showed multiple emboli in both lobes.

Looking back, there were signs . . . that I could and did explain away.

My aerobic capacity had been subpar for several weeks. I chalked it up to getting older, and never having bonded with my treadmill. Then I took a ski trip to Colorado with some dental school buddies. We flew to Denver first, then on to Telluride, which sits at over 9,000 ft. I’d been there before, and didn’t have any of the travel-related risks for DVT you’ll read about on the stoptheclot.org website.

The flight was uneventful. I got up and moved around a few times, like I always do on planes. Once we landed, I felt fine except for some left knee pain and calf soreness. I also had shortness of breath, but hey, it’s high up there. When we stopped to pick up supplies, I uncharacteristically bought some aspirin, instead of the Motrin I occasionally take for everyday aches and pains. Later, you’ll understand why.

I took the aspirin for altitude sickness and headache, but neither went away after the first few days, like they usually did. What bothered me more was that all week I could not keep up with my ski buddies. After almost every run, they would be at the chair lift waiting for me. I even took a day off from skiing — and I never take a day off on these trips. Again, I factored in the altitude and...
that I was “just getting older.” In the back of my mind that didn’t set, though, because my ski buddies were all getting older, too.

Five days later, I flew home to Michigan. My left leg was still sore, a 7 out of 10 on the pain scale. My ankle looked swollen, which I initially attributed to four days of downhill skiing and ski boot compression that isn’t part of my regular routine.

But like a lot of us, I’m not a complainer; I don’t like to dwell on pain. I just move through it and get things done.

The next day, back at work, I got a lot of things done. Basic routine stuff: a couple crown preps, an endo, quadrant of composites, several emergencies and double hygiene checks. I was dragging, though. Even had to stop and catch my breath while eating a sandwich. I chalked it all up to the time change and airplane ride.

My chalked-up excuses didn’t fly with everyone. Kelly, my wife and business partner, noticed my unusual fatigue. When I propped my leg on my desk for her to inspect, the first thing she noticed was my “cankle.” You know, the body part created when the ankle definition is gone and it just looks like what it is: one big, swollen calf.

She called our doc. One emergency room, blood test and CT scan later, I found myself in the hospital hooked up to IV heparin and irrevocably shell-shocked.

After four days, I was sent home with a six-month prescription for daily Coumadin. I’m one of the lucky ones: Out of the 350,000–600,000 people annually who are diagnosed with DVT/PE, more than 100,000 die. I had competent physicians and a concerned wife, but in some ways I made my own luck. I had already been aware.

My awareness of DVT/PE began almost two years ago, in the most heartbreaking story that can be written. Kelly and I met Rich and Sara in dental school, became friends, and got married two weeks apart. Anna was born to them several years later — a model student, athlete, friend and daughter. She was even becoming one of us! At the time of her death, she was a second-year dental student at the University of Pittsburgh.

Anna wasn’t one of the lucky ones. Her sudden death from a massive DVT/PE was a tragic blow to her family, friends and colleagues. As her story unfolded and we examined the details in perfect hindsight, her death was indeed preventable.

As I grieved for Rich and Sara I could not get over the senselessness of it all. At their suggestion, I joined the National Blood Clot Alliance, and became a frequent visitor on the stop-theclot.org website.

Which is why, in Telluride that day, I bought the aspirin. Did that play a part in me still being here? Maybe. Did memories of Anna convince me to go to the ER that night, even though I would have rather blown it off? Yes, without question.

We never know what things will happen to us, or what things that have happened to other people will affect us enough to take action for ourselves. All I know is, Anna’s death influenced me enough to take action.

What I hope for, and why I wrote this, is that maybe one of you reading this will take a good, hard look at that website, tell your friends and families to do the same, and take action when and if need be. And that maybe, just maybe, that will be enough.

But like a lot of us, I’m not a complainer; I don’t like to dwell on pain. I just move through it and get things done.
When I was a 20-year-old college student, I began to feel a mild pain in my left side. Being an active young person in good physical condition, I did not think anything of it, assuming I caught an elbow on the basketball court or perhaps pulled a muscle. The next day, the pain was worse to the point that I blew off classes, yet being young and naïve, I still was not concerned.

The next morning, I woke up early gasping for breath and in extreme pain, to the point that I could barely stand upright. My roommate rushed me to the hospital, and thus my journey with thrombophilia began. My diagnosis was a pulmonary embolism (PE) in my left lung. By the time my roommate got me to the hospital, my lung had “collapsed” and I was a very sick individual. I was started on Coumadin (generic name warfarin) along with IV heparin to serve as a “bridge” until the Coumadin level reached a therapeutic dose. After being discharged from the hospital, I was forced to drop the summer term and return home to spend the summer at my parents’ house. Recovery took all of the summer, but by the fall semester, I was able to return to school.

A reason for my PE was never found and after a year I was taken off my Coumadin and the doctors told me to live my life as if the PE was nothing but a “freak” occurrence.

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19 years later, I was diagnosed with my second blood clot, a deep vein thrombosis (DVT) in my right calf. The next year, I was taken off my Coumadin and the doctors told me to live my life as if the PE was nothing but a “freak” occurrence. Two years later, I had a DVT in my left calf. Each time, I was placed on Coumadin therapy for six months and then taken off therapy. Truth be told, I fought to get off the Coumadin, as I felt that the risk-to-benefit ratio was not favorable — I’m a fairly active person whose activities include snowmobiling and wilderness fishing. I felt that the risk of a significant bleed due to an accident while out in the woods outweighed the benefit of my Coumadin therapy. My hematologist and I noted a pattern that each DVT happened after air travel, so he had me inject low molecular weight heparin (Lovenox) before each subsequent plane trip. Many plane rides later, everything was fine and we thought we had my case figured out.

Sometimes, hindsight is 20/20, and in my case, this is absolutely true. If I could step back in time and stay on Coumadin after my series of DVTs I surely would. This past Christmas Eve, I began to have a very minor pain in my left tricep area upon waking. I assumed that I “slept funny” and ignored this minor discomfort and we enjoyed a very nice day. That night during church services, I placed my arm around my son and my tricep touched the back of the pew and I felt moderate pain. After returning home, I took off my shirt and saw that my tricep area was red, swollen, and hot. I arrived at the ER 1 a.m. Christmas morning.
knowing that I had a DVT in my arm. I was started on Lovenox and Coumadin and sent home about 6 a.m. Christmas morning just in time to enjoy the beginning of the holiday with my family. The ER doc told me that DVTs in the arm rarely travel, so I wasn’t terribly concerned. Wrong again. December 26th in the evening, I began to have minor pain in my right side. The morning of December 27th the pain was worse, and off to the ER I went. A CT scan revealed two emboli in my right lung. I was admitted to the hospital and continued on the Coumadin and Lovenox. The next morning, I experienced the worse pain of my life. It felt like someone stuck a knife in my back on the right side. Due to infarction caused by the emboli, part of my lung was literally dying. Heavy doses of IV Dilaudid got me through the day. The next morning, the pain was greatly reduced and I felt good enough that the hospital sent me home that evening.

So why do I get these things? I have Factor V Lieden disorder. This disorder was not yet discovered when I had my first PE in my college years. I was diagnosed after the first DVT in my right calf. “Factor V” is the most common inherited cause of thrombophilia. According to the NIH, it affects between 3-8 percent of Americans of European descent. Interestingly, in my case, the disorder has been passed down through my paternal grandmother, who is from the Middle East, where the disorder is very rare. My grandmother did not get her first DVT until she was in her mid-80s and living a sedentary lifestyle. My 70-year-old father and 49-year-old brother also have the disorder and have never had a clot. Ironically, my brother is a business executive and travels more by plane in a month than I do in five years. I hope and pray that he remains asymptomatic. Thankfully, only about 10 percent of people diagnosed with Factor V Leiden disorder ever develop abnormal clots. Women with Factor V are also two to three times more likely to experience multiple miscarriages, and have an increased chance of other pregnancy complications such as preeclampsia and placental abruption. People with Factor V Lieden disorder should think long and hard before they engage in other activities that raise the risk of blood clots — smoking or using birth control pills, for example.

Coagulation factor V is an important steppingstone in the coagulation process. In people like me with a defect in the F5 gene, coagulation factor V does not respond to active protein C, which is intended to shut off the clotting cascade. The result is that what should be a minor thrombus due to a small injury or bruise becomes a major thrombus, which then blocks a deep vein. When a part of the thrombus breaks off and travels in the bloodstream, it becomes an embolis, which moves through the right side of the heart and lodges in the lung, becoming a pulmonary embolism.

The doctors tell me that I can expect the process of recovery to take three to nine months. Depending on what report you read, 10 to 20 percent of PEs are diagnosed at autopsy, so I feel very fortunate to be alive. When people ask what the PE was like, I respond that I got run over by a semi-truck. As time has gone by, the truck that ran me over has reduced to a dump truck, tow truck, pickup truck, and now is about a golf cart.

Needless to say, I am now on anticoagulation therapy for the rest of my life. I am facing reconstructive wrist surgery (2012 is certainly off to a rotten start!) as soon as I recover sufficiently from the PE, so I will be working with my hematologist to go off the Coumadin temporarily and “bridge” with Lovenox before, during, and after my surgery.

We all see people in our practices every day who are taking Coumadin.

If I could step back in time and stay on Coumadin after my series of DVTs I surely would.

As I write this today, it has been 63 days since I suffered my second PE. Recovery has been a slow and arduous process. I continue to improve but still suffer from symptoms of pain in my side, tiredness, and most disconcertingly, pain in my chest similar to angina. The right side of the heart is stressed by a PE as it is pumping blood to the lungs against back-pressure caused by the clot, which causes the heart pain. I would estimate that my ability to exercise in a cardiovascular manner is currently about one-third of what it was before. Do too much, and I suffer from chest pain the rest of the day and usually the next day as well. This is a great improvement from right after the PE when I could only walk about 75 feet.

Routine dentistry up to and including simple extraction does not generally require a patient to be taken off Coumadin. When in doubt, consult with our medical colleagues! After my experiences, I believe that in no situation, ever, should a dentist remove a patient from his or her anticoagulant therapy without the approval and management of their physician. Management of anticoagulation therapy may include going off Coumadin and bridging with Lovenox, or it may be as simple as the patient having an INR test the morning of a scheduled dental procedure to make sure his or her blood is not too “thin.” Personally, I will never again go one single day without managing my disorder. ♦
Facts about the Risk of DVT and PE

Very Simply:
- A Deep Vein Thrombosis (DVT) occurs when a blood clot forms in one of the deep veins of your body, usually in the leg.
- It is most often on one side and can happen in any other part of the body.
- Clots can break off from a DVT and travel to the lung, causing a pulmonary embolism (PE) which can be fatal.

Deep Vein Thrombosis (DVT): Signs and Symptoms:
- Swelling, usually in one leg
- Leg pain and tenderness
- Reddish or bluish skin discoloration
- Leg warm to the touch

Pulmonary Embolism (PE): Signs and Symptoms:
- Sudden shortness of breath
- Chest pain—sharp, stabbing; may get worse with deep breath
- Rapid heart rate
- Unexplained cough, sometimes with blood mucus

Deep Vein Thrombosis and Pulmonary Embolism
- Usually happen because of an acquired trigger or an inherited risk factor

What can you do?
- Keep body weight close to normal for your height
- Stay active
- Avoid inactivity — Move!
- Partner with your doctor/health care professional
- Talk about your risks of blood clots
- Know the side effects/risks with medications you take — share it!

Important Facts and Takeaway Information!
- 350,000 to 600,000 people in the U.S. develop blood clots every year.
- About 100,000 people die in the U.S. annually from a blood clot — in 3 die!
- This is more than those that die from Breast Cancer and AIDS combined!
- In Michigan, blood clots kill as many as 3,300 people of all ages annually.
- In Michigan, as many as 20,000 people suffer from a DVT/PE incident each year.
- As dental professionals, we can make a difference!
CLOTTING RISK: What You Need to Know

**Blood Flows**
- **Go!**
- Stay alert to any change in risk.

**Blood Slows**
- **Caution!**
- Talk with your doctor about risk.

**Blood Clots**
- **Stop!**
- Discuss with your doctor now.

**HIGH RISK**
- Hospital stay
- Major surgery, such as abdominal/pelvic surgery
- Knee or hip replacement
- Major trauma: auto accident or fall
- Nursing home living
- Leg paralysis

**MODERATE RISK**
- Older than age 65
- Trips over 4 hours by plane, car, train or bus
- Active cancer/chemotherapy
- Bone fracture or cast
- Birth control pills, patch, or ring
- Hormone replacement therapy
- Pregnancy or recently gave birth
- Prior blood clot or family history of a clot
- Heart failure
- Bed rest over 3 days
- Obesity
- Genetic/hereditary or acquired blood clotting disorder

**AVERAGE RISK**
- Active
- Younger than age 40
- No history of blood clots in immediate family
- No conditions or illnesses that heighten clotting risk

**DISCLAIMER:** The above chart is a summary and provides estimated risks for blood clots; the information is not intended to be thorough or replace medical advice. NBCA recommends that you speak with your doctor about your clotting risk. ©NBCA 2010
Therapeutic use of oral anticoagulation is common and is indicated for a variety of conditions. The most prevalent indications include prevention of stroke in patients with atrial fibrillation or mechanical heart valves as well as the treatment and prevention of deep vein thrombosis and pulmonary embolism. Atrial fibrillation is the most common cardiac arrhythmia with a prevalence ranging from 0.1% among adults <55 years of age to 9% among those ≥80 years of age. Without prophylaxis, the risk of ischemic stroke in patients with non-rheumatic atrial fibrillation is approximately 5% per year. Like patients with atrial fibrillation, those with prosthetic (mechanical) heart valves require lifelong anticoagulation to prevent thrombosis and stroke. Approximately 45,000 mechanical heart valve replacements are performed yearly in the United States. Deep vein thrombosis is also a common condition affecting between 350,000 and 1 million new patients in the US per year, and according to the National Blood Clot Alliance, the yearly incidence of DVT/PE is estimated to be 11,515 to 19,740 patients in the state of Michigan.

 Interruption of oral anticoagulation can result in life-threatening acute thrombotic events. The risk of cessation varies with the indication for anticoagulation. Recurrent venous thromboembolism carries risk of fatal pulmonary embolism. Consequences of arterial thromboembolism (mostly stroke) from atrial fibrillation or prosthetic heart valves can be quite serious, with a 20% mortality rate and 40% of these strokes will cause permanent disability. In the case of atrial fibrillation, embolic stroke that happens during cessation of anticoagulation is fatal or associated with a severe neurologic deficit in over 60 percent of cases. In patients with a mechanical heart valve and previous thromboembolism, the risk of a thromboembolism when the patient is not taking warfarin is 10% to 20% per year.

Warfarin remains the most widely prescribed anticoagulant for these conditions. Approximately 15% to 20% of all warfarin-treated patients who are assessed for perioperative anticoagulant management require
minor dental procedures. The clinical dilemma of managing oral anticoagulation in patients going for invasive procedures affects an estimated 250,000 patients annually in North America.

The potential for thromboembolic complications with discontinuation of anticoagulation makes management of these patients during dental procedures a challenge. On the other hand, continuation of oral anticoagulation raises the concerns for bleeding. A survey of Dutch dentists revealed that dentists consult with medical colleagues frequently about antithrombotic medication; more than fifty percent of the dentists reported that they were not familiar with the international normalized ratio (INR), and the majority of dentists responded that they felt a need for clinical practice guidelines.

Several groups have published guidelines with recommendations to properly manage patients on oral anticoagulation requiring dental procedures including the American College of Chest Physicians and the American College of Cardiology/American Heart Association.

With the U.S. Food & Drug Administration’s (FDA) recent approval of two novel oral anticoagulants, management of oral anticoagulation by dentists may become more confusing. FDA published data shows that through 2011, approximately 1.1 million prescriptions were dispensed, and approximately 371,000 patients received the factor IIa inhibitor dabigatran (Pradaxa) from U.S. outpatient retail pharmacies.

The mechanism of action, pharmacokinetics and pharmacodynamics of novel oral anticoagulation are different from warfarin. They have rapid onset of action and much shorter half-lives compared to warfarin. Table 1 illustrates pharmacokinetics and properties of the FDA approved or likely to soon be approved medications.

### Guidelines

In an attempt to establish guidance for safe evidence-based management of warfarin during dental procedures, several groups have developed formal guidelines.

The American College of Chest Physicians updated its latest guidelines on the perioperative management of antithrombotic therapy in February 2012. The guidelines risk stratify patients with venous thromboembolism, atrial fibrillation and mechanical heart valves into three groups; high, intermediate and low risk of thrombosis during interruption of anticoagulation for elective non-cardiac surgery. They also stratify patients based on the risk of bleeding during a procedure and continuation of anticoagulation or during heparin/low molecular weight heparin bridging. Minor dental, dermatologic and ophthalmologic procedures are considered very low risk for bleeding if patients remain therapeutically anticoagulated with warfarin. The guidelines specifically suggest that patients who require a minor dental procedure including tooth extractions and endodontic (root canal) procedures continue vitamin K antagonist (warfarin) with co-administration of an oral pro-haemostatic agent or stop warfarin 2 to 3 days (partial interruption) before the procedure are preferred to alternative strategies.

The evidence suggests that guideline-based approaches confer a low risk for bleeding, but minor bleeding (or oozing from gingival mucosa) may be more common than complete interruption of oral anticoagulation and the thromboembolic outcomes with these approaches as rare (0.1%).

The American College of Cardiology/American Heart Association Joint guidelines for valvular heart diseases and atrial fibrillation from 2006 and updated in 2008 and 2011 address the perioperative management of oral anticoagulation differently. The guidelines consider dental care procedures equal to other elective non-cardiac procedures for patients on oral anticoagulation for prosthetic heart valves and suggest risk stratification to decide about the proper approach. They recommend that in patients at low risk of thrombosis, defined as those with a bi-leaflet mechanical AVR with no additional stroke risks, warfarin should be stopped 48 to 72 h before the procedure (so the INR falls to less than 1.5) and restarted within 24 h after the procedure and heparin is usually unnecessary.

Patients, with any mechanical mitral valve replacement or a mechanical aortic valve replacement with other stroke risk factors, are considered at high risk of thrombosis. Therapeutic doses of intravenous unfractionated heparin should be started in these patients when the INR falls below 2.0, stopped 4 to 6 h before the procedure, restarted as early after surgery as possible, and continued until the INR is again therapeutic with warfarin therapy. Subcutaneous unfractionated heparin (15 000 U every 12 h) or low molecular weight heparin (100 U per kg every 12 h) may be considered during the period of a sub-therapeutic INR.

### Table 1

<table>
<thead>
<tr>
<th>New oral anticoagulation</th>
<th>Rivaroxaban</th>
<th>Dabigatran</th>
<th>Apixaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDA approved</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Mechanism of action</td>
<td>Direct factor Xa inhibitor</td>
<td>Direct thrombin inhibitor</td>
<td>Direct factor Xa inhibitor</td>
</tr>
<tr>
<td>Onset of action</td>
<td>2-3 Hours</td>
<td>0.5-3 hours</td>
<td>1-3 hours</td>
</tr>
<tr>
<td>Half life</td>
<td>7-11 Hours</td>
<td>14-17 hours</td>
<td>9-14 hours</td>
</tr>
<tr>
<td>Lab monitoring</td>
<td>Not needed</td>
<td>Not needed</td>
<td>Not needed</td>
</tr>
<tr>
<td>Peak</td>
<td>3 Hours</td>
<td>2 hours</td>
<td>3 hours</td>
</tr>
<tr>
<td>Antidote</td>
<td>None available</td>
<td>None available</td>
<td>None available</td>
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Table 2: Guidelines

<table>
<thead>
<tr>
<th>American Dental Association</th>
<th>American College of Chest Physicians</th>
<th>American Heart Association/American College of Cardiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticoagulant drug regimens should not be altered prior to dental treatment</td>
<td>Continue vitamin K antagonist (warfarin) with co-administration of an oral pro-haemostatic agent or stop warfarin 2 to 3 days (partial interruption) before the minor dental procedures</td>
<td>Continue warfarin for dental cleaning, or simple treatment for dental caries.</td>
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The guidelines however exclude some of the dental procedures from risk stratification and it states that antithrombotic therapy should not be stopped for procedures in which bleeding is unlikely or would be inconsequential if it occurred, such as dental cleaning and simple treatment for dental caries.10

The guidelines for management of atrial fibrillation; however, do not specifically offer recommendations for dental procedures, and it generally states that in patients with atrial fibrillation who do not have mechanical valves, anticoagulation may be interrupted for a period of up to 1 week for surgical or diagnostic procedures that carry a risk of bleeding without heparin. In high-risk patients defined as those with prior stroke, transient ischemic attack, or systemic embolism or when a series of procedures requires interruption of oral anticoagulation for longer periods, un-fractionated or low molecular weight heparin may be administered intravenously or subcutaneously.16 It does not discuss the classification of dental procedures as ones with high or low risk of bleeding. The guidelines do not address these situations in venous thromboembolism, including deep vein thrombosis or pulmonary embolism.

Although the American Dental Association does not have formal guidelines for perioperative management of oral anticoagulation, it offered recommendations for the best approach for dentists. It recommends that for patients on oral anticoagulation like warfarin, anticoagulant drug regimens should not be altered prior to dental treatment.17

Despite the established guidelines and the recommendations of American Dental Association, dental providers’ requests to interrupt warfarin are still often discordant with current guidelines. An anonymous postal survey was sent to all patients on oral anticoagulation followed for more than 1 year by the University of Michigan Anticoagulation service. Patients were asked how many times in the prior year they were requested to interrupt warfarin therapy for a medical or dental procedure or test and the specific indication for the requested interruption in warfarin therapy. A total of 1686 of 2133 (79%) responded. At least one request to interrupt anticoagulation therapy in the prior year was given by 819 of 1648 (50%) respondents. One hundred fifty-six (11.5%) were asked to stop warfarin for dental cleaning.18

Refer to Table 2: Summary of Guidelines and Recommendations for Minor Dental Procedures.

**Oral anticoagulation**

Since its approval for use as a medication in 1954, vitamin K antagonists like warfarin have remained the only available oral anticoagulant until recently making it the most widely prescribed oral anticoagulant drug in North America. Warfarin prevents the liver from manufacturing vitamin K dependent coagulation factors II, VII, IX, and X, and it takes approximately 5 days for these clotting factors to diminish before a patient is fully anticoagulated and their INR is in the therapeutic range.19 Similarly, when warfarin is interrupted, approximately 5 days are required for the clotting factors to reconstitute to physiologic levels.11

Dabigatran, a direct factor II inhibitor, is licensed in the US for stroke prevention in patients with atrial fibrillation. Plasma levels of dabigatran peak two hours after drug administration, and its half-life is 14 to 17 hours, thus its interruption leads to much quicker waning of the anticoagulant effect.15 Dabigatran is 80% renally-eliminated, and the half-life increases with worsening renal function. Accordingly, in case of an anticipated high risk of bleeding procedure, the medication does not need to be interrupted more than one or two days prior to the procedure in patients with normal renal function.

Rivaroxaban, a direct factor Xa inhibitor, is approved by the FDA for venous thromboembolism prophylaxis in patient undergoing elective hip and knee surgery and for stroke prevention in patients with atrial fibrillation.20 It peaks 2 to 3 h after administration, and has a short half-life compared to warfarin of 7 to 11 h.15 Rivaroxaban is also partially eliminated by the kidneys. Due to the rapid offset of rivaroxaban, its discontinuation places patients at an increased risk of thrombotic events. An increased risk of stroke was observed following rivaroxaban discontinuation in a trial of atrial fibrillation.20 An FDA warning states “Xarelto (rivaroxaban) has a boxed warning to make clear that people using the drug should not discontinue it before talking with their health care professional. Discontinuing the drug can increase the risk of stroke.”21
Because both dabigatran and rivaroxaban are at least partially excreted by the kidneys, special consideration is needed for patients with impaired renal function. The offset of these medications is expected to be longer in this group of patients.

Although the American College of Chest Physicians, the American Heart Association, and the American College of Cardiology do not address the perioperative management of these new oral anticoagulants specifically, it seems reasonable, similar to recommendations for warfarin, not to interrupt these medications for minor dental procedures. For major dental and oral surgical procedures where interruption of anticoagulation is required, bridging with low molecular weight heparin (LMWH) has no role when interrupting the new oral anticoagulants because their onset and offset of action and half-lives are similar to LMWH.

A thorough estimate of the risk of bleeding for minor dental procedures while continuing the new oral anticoagulants will require post-approval observational studies. However, data from the randomized trials that lead to FDA approval do offer some opportunity for analysis. Dabigatran was compared to warfarin in 4615 patients who underwent procedures, 13% of which were dental surgeries. There was no significant difference in the risk of perioperative major bleeding or other bleeding outcomes between patients on warfarin and patients on dabigatran.

Local hemostatic measures

The guidelines/recommendations against interruption of oral anticoagulation or altering the dose are based on the fact that clinical trials failed to prove an associated increased risk of clinically significant non-major bleeding when proper local hemostatic measures are applied. In one meta-analysis, minor bleeding occurred in 19.5% of patients who continued their regular dose of warfarin and in 18.9% of patients who discontinued or altered their dose of warfarin before dental extractions. The risk of minor bleeding was not significantly lower for patients who discontinued or altered their warfarin dose (RR = 1.19, 95% CI 0.90–1.50; \( p = 0.22; I^2 = 0\% \)). The subgroup analysis in the same meta-analysis for patients with higher INR for prosthetic heart valves did not show an increased risk of bleeding either.

Different local hemostatic measures have been used by dentists in patients on oral anticoagulation, and several randomized controlled trials have compared these different measures. The most studied local hemostatic agent is tranexamic acid. One

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Table 3: Summary

| Background | • Indications for oral anticoagulation include atrial fibrillation, mechanical heart valves, deep vein thrombosis and pulmonary embolism.  
• Interruption of oral anticoagulation in these patients carry a risk of thromboembolism.  
• Warfarin is the most commonly prescribed oral anticoagulation.  
• Dabigatran and rivaroxaban are the new FDA approved oral anticoagulants. |
| Guidelines | • American Dental Association: Anticoagulant drug regimens should not be altered prior to dental treatment.  
• American College of Chest Physicians: Continue vitamin K antagonist (warfarin) with co-administration of an oral pro-haemostatic agent or stop warfarin 2 to 3 days (partial interruption) before the minor dental procedures.  
• American Heart Association/ American College of Cardiology: Continue warfarin for dental cleaning, or simple treatment for dental caries. |
| Oral anticoagulation | • Warfarin starts working after 2-3 days of administration and takes several days to achieve the desired anticoagulation. INR normalizes after at least 5 days after interruption of warfarin in most patients.  
• Dabigatran’s onset of action is approximately 2 hours and its anticoagulant effect wanes over 1-3 days depending on the patient’s kidney function.  
• Rivaroxaban peaks 2 to 3 hours after administration and has a similar offset time depending on kidney function.  
• Discontinuation of rivaroxaban in patients with atrial fibrillation has been associated with an increase risk of stroke.  
• Both rivaroxaban and dabigatran should not be interrupted prior to minor oral and dental procedures.  
• Dabigatran and rivaroxaban have similar onset and offset of action as low molecular weight heparin, therefore, low molecular weight heparin bridging is not indicated if these anticoagulants require interruption. |
| Local hemostatic measures | • Risk of bleeding after minor dental procedure is minimized by applying local hemostatic measures.  
• Local hemostatic measures include tranexamic acid mouthwash, autologous fibrin glue, histoacryl glue, gelatin sponge, oxycellulose dressing, and fibrin adhesive sockets.  
• Tranexamic acid is an antifibrinolytic agent which inhibits the degradation of fibrin, and when used as a mouthwash is superior to placebo in controlling bleeding after minor dental procedures.  
• Two days of tranexamic acid mouthwash postoperatively is shown to be as effective as 5 days regimen in controlling bleeding after minor dental procedures. |
study compared tranexamic acid mouthwash to placebo used intra-operatively followed by four times a day for a week in 93 patients on oral anticoagulation with a therapeutic INR undergoing single or multiple extractions. Ten of 47 (21.27%) patients in the placebo group developed bleeding that required treatment compared to none in the tranexamic acid group (P<0.01).24

Another randomized trial compared the postoperative use of tranexamic acid mouthwash to intraoperative use of fibrin glue in 49 patients on oral anticoagulation and therapeutic INR. Both groups underwent dental extractions. Two (4%) presented with postoperative bleeding. Both patients were in the autologous fibrin glue group and were found to have grossly elevated INR that was unaccounted for on the day of the bleeding.25 There were no postoperative bleeding complications reported in the tranexamic acid mouthwash group.

A randomized trial attempted to determine the best length of period of tranexamic acid use for patients on oral anticoagulation. A 2-day regimen versus 5-days to prevent postoperative bleeding after dental extraction was studied in 85 patients with a therapeutic INR. Two (2.4%) patients in the group assigned for two days of tranexamic acid and one (1.2%) assigned to 5 days of tranexamic acid had minor postoperative bleeds that required an office intervention to control. This study concluded that a 2-day postoperative course of a 4.8% tranexamic acid mouthwash is equally effective as a 5-day course.26 Other local haemostatic measures have been studied less extensively in the literature. Some of the studied measures included application of hexaacyl chloride, gelatin sponge, oxycelulose dressing, and fibrin adhesive sockets.27, 28

Tranexamic acid is an antifibrinolytic agent. It inhibits the degradation of fibrin, the body’s natural haemostatic factor. Normally, activation of plasminogen results in plasmin, which causes degradation of fibrin. Binding of plasminogen to fibrin makes this process more efficient and occurs through binding sites on plasminogen. In the presence of tranexamic acid, these binding sites are occupied, resulting in an inhibition of fibrin binding to plasminogen and impairment of endogenous fibrinolysis.29

Conclusion

Management of patients on oral anticoagulation who require dental procedures can be challenging. The American Heart Association and the American College of Cardiology joint guidelines recommend continuing warfarin for dental cleaning and simple treatment for dental caries.10 The American College of Chest Physicians guidelines recommend continuing warfarin with co-administration of an oral hemostatic agent or partial interruption of warfarin for two to three days before minor dental procedures.11 The American Dental Association recommends against alteration of oral anticoagulation prior to minor dental procedures.

Tranexamic acid is the most studied local hemostatic agent.17 The risk of major or clinically significant bleeding in patients on warfarin undergoing minor dental procedures is low if tranexamic acid is used perioperatively. Despite the lack of guidelines in the literature, new oral anticoagulants will likely not require interruption for minor dental procedures. If interruption is required for invasive oral surgeries, the cessation period should not exceed one to two days in patients with normal renal function. Because tranexamic acid is an antifibrinolytic agent that inhibits the degradation of fibrin, it should be effective when used perioperatively for patients on the new oral anticoagulation regimens having minor dental procedures. The new oral anticoagulation medications do not need bridging with low molecular weight heparin because they have similar half-lives. ◊

References

About the Authors

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