Hypercoagulability syndromes: what the dentist needs to know

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Although many bleeding disorders, such as hemophilia, have been well characterized for many years, the knowledge of hypercoagulability syndromes is significantly less. This is the result of a long-held belief that hypercoagulability disorders were simply related to excessive amounts of the same coagulation factors that patients with bleeding disorders lacked. Now hypercoagulability disorders are better characterized and understood from a pathophysiologic mechanism. In most cases, they are distinct in pathogenesis from bleeding disorders. Patients with clearly identified specific abnormalities of clotting are diagnosed as having primary hypercoagulable states. Almost all presently recognized primary hypercoagulable disorders result from defects in proteins in either the coagulation or fibrinolytic systems. In contrast to the primary disorders, the secondary hypercoagulable disorders result from defects in proteins in either the coagulation or fibrinolytic systems. In contrast to the primary disorders, the secondary hypercoagulable disorders are much more numerous in prevalence and, in most cases, less precisely understood. Fundamental knowledge regarding the basic principles, diagnosis, and treatment of these conditions is very important for the dentist to understand, because a number of these patients may present in the dental office requiring dental care.

Hypercoagulability is a condition in which an alteration of the blood shifts the hemostatic balance toward excessive platelet/fibrin deposition, leading to arterial and/or venous thrombosis.1 Although the concept of hypercoagulability has been recognized clinically for more than a century, in recent years, a number of specific disorders have been better defined as better diagnostic tests have been developed. Moreover, treatment regimens have improved. The currently recognized disorders are generally classified as primary or secondary states, although some of the primary conditions may develop as a result of other disorders (Table I). The primary disorders generally result from abnormalities in proteins of the coagulation system. Although the number of secondary conditions is greater, they are neither well defined nor characterized on a molecular basis. Although the prevalence and clinical significance of hypercoagulability is better understood medically, the dentist needs to be cognizant of the possible impact these diseases have in the practice of dentistry. The purpose of the present review is to describe the diagnosis and treatment of the hypercoagulability syndromes most likely to be encountered by the dentist in practice.

PRIMARY HYPERCOAGULABILITY DISORDERS

In general, primary hypercoagulability disorders are congenital states resulting from defects that manifest by specific coagulation abnormalities that are fixed and persistent, although clinical thrombotic events occur episodically. Moreover, many will become clinically significant in post-adolescence. At present, a list of

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known primary hypercoagulable syndromes is still limited.

**Antithrombin III deficiency (AT III)**

Antithrombin III (also known as heparin cofactor I) is a 65-kD α-globulin made in the liver and endothelial cells whose function is to inhibit the clotting cascade.² It inactivates thrombin directly, but its primary mode of action is to inactivate activated factor X. It also inactivates activated factors VII, IX, and XII and other serine proteases.³

**Epidemiology.** This deficiency is an autosomal dominant disorder and occurs in 1 our of 5,000 healthy blood donors,⁴ making it as common as hemophilia. It is estimated that it occurs in 2%-3% of patients hospitalized with deep vein thrombosis (DVT).⁵ In patients with an AT III disorder the protein may be absent or dysfunctional. Unlike other primary hypercoagulability disorders, AT III deficiency may also develop as an acquired disease. Because the protein is made in the liver and excreted in the urine, it has been identified in patients with liver dysfunction, nephrotic syndrome, and malnutrition, because of the excessive catabolism of proteins.⁶ Some studies showed that the AT III level may be decreased by as much as 15% in women taking estrogen-containing oral contraceptives.⁷ Thrombosis occurs relatively early in life, with 60% of patients presenting by the age of 35 years.⁸ Fifty percent of carriers are asymptomatic.

**Clinical features.** Congenital deficiency of AT III is one of the oldest, best characterized, and most common hypercoagulability disorders and is the prototype of the primary hypercoagulability disorders.

Antithrombin III deficiency is associated almost exclusively with venous thromboembolic complications and venous disease.⁹ Patients with AT III deficiency may present with DVT, pulmonary embolism, or less frequently arterial thrombotic events.¹⁰

**Diagnosis.** The normal concentration of AT III is 150 µg/mL with a range to ±25%. The diagnosis of this disease can be made by immunologic or functional assays. Immunologic (quantitative) assays are easier to perform. However, they do not assess the biologic activity of the AT III that is present and are therefore less accurate than functional assays.¹¹

**Treatment.** Heparin is used for short-term therapy in patients with AT III deficiency that experience thrombotic episodes. The heparin/AT III complex inactivates thrombin factor IIa and factors Xa, IXa, Xla, and XIIa.¹² However, because the activity of heparin is dependent on the interaction with AT III, and the levels of AT III are low, these patients usually require high doses of heparin to obtain the therapeutic anticoagulation. Actually, heparin resistance may provide a clue to the presence of AT III deficiency. Treatment of patients with recurrent thrombotic episodes should use low-molecular-weight heparin. Finally, through recombinant DNA technology, AT III concentrates are becoming available for short-term therapy in high-risk situations, such as pregnancy or surgery.¹³ Prophylactic treatment of asymptomatic individuals is controversial.

**Antiphospholipid syndrome**

Lupus anticoagulant syndrome, or antiphospholipid antibody syndrome, is associated with a group of autoantibodies that demonstrate a wide range of target specificities and affinities, all of which recognize various combinations of phospholipids, phospholipids binding proteins, or both.¹⁴ The term “antiphospholipid syndrome” was first used to indicate the clinical association between antiphospholipid antibodies with a syndrome of hypercoagulability.¹⁵,¹⁶ Antiphospholipid antibodies are mainly associated with thromboembolic events rather than clinical bleeding. However, antiphospholipid antibodies can interfere with both anticoagulant and procoagulant pathways.¹⁷ Although the phospholipid surface used in most in vitro coagulation tests favor inhibition of procoagulant pathways and therefore prolongation of clot formation (i.e., increased bleeding), the microenvironment of cell membranes in vivo may promote inhibition of anticoagulant pathways and therefore favor thrombosis.¹⁷ Antiphospholipid antibodies may refer to the lupus anticoagulant and other antibodies such as anticardiolipin antibodies, that are directed against negatively charged phospholipids. These are associated with a thrombosis tendency in the venous, arterial, and placental circulations as a result of binding of the phospholipids within the platelet membrane.¹⁸,¹⁹ with an increase in platelet aggregation and activation.

Several hypotheses have been proposed to explain the cellular and molecular mechanisms by which antiphospholipid antibodies promote thrombosis. The first implicates activation of endothelial cells. Antiphospholipid antibodies recognize β-2 glycoprotein I bound to
resting endothelial cells, although the basis of the interaction of β-2 glycoprotein I with viable endothelial cells remains unclear. Binding of antiphospholipid antibodies induces activation of endothelial cells, as evidenced by up-regulation of the expression of the adhesion molecules, the secretion of cytokines, and the metabolism of prostacyclins. Activated endothelial cells facilitate binding and aggregation of platelets. A second theory focuses on oxidant-mediated injury of the vascular endothelium. Autoantibodies to oxidized low-density lipoprotein (LDL) occur in association with antiphospholipid antibodies. Oxidized LDL taken up by macrophages leads to macrophage activation and subsequent damage to the endothelial cells.

Epidemiology. Antiphospholipid antibodies have been detected in 30%-60% of patients with systemic lupus erythematosus, and 1%-2% of persons in the general population. Other autoimmune disorders other than lupus also have been reported to have high levels of circulating antiphospholipid antibodies.

Clinical features. Approximately 50% of people with high antibody titers will experience thrombotic complications. Venous thrombosis, especially deep venous thrombosis of the legs, is the most common manifestation of the antiphospholipid syndrome, occurring in 29%-55% of patients with the syndrome during an average follow-up of less than 6 years. Half of these patients had a pulmonary embolism. Arterial thrombosis, however, is less common than venous thrombosis.

Diagnosis. A recent consensus statement provides simplified criteria for the diagnosis of the antiphospholipid syndrome (Table II). A patient with the antiphospholipid syndrome must meet at least 1 of 2 clinical criteria and at least 1 of 2 laboratory criteria. In considering the diagnosis, secondary risk factors that increase the risk to thrombosis should be included. Such factors that can affect venous or arterial beds include stasis, vascular injury, the use of medications such as oral contraceptives, and the other traditional risk factors for atherosclerotic disease. The severity of the clinical presentation is related to the severity and extent of the occlusion.

Treatment. The treatment for patients with antiphospholipid antibodies fall into 2 main areas: prophylaxis with low dose of aspirin in asymptomatic patients and low-molecular-weight heparin for the treatment of an acute thrombotic event and for prevention of further thrombosis of large vessels. A beneficial role for anticoagulation in decreasing the rate of recurrent thrombosis has been shown in multiple studies.

Protein C deficiency

Protein C is a 62-kD glycoprotein with a half-life of 6 hours. Protein C deficiency may develop as an autosomal inherited trait with partial penetration and variable phenotypic expressivity. Because protein C is vitamin K dependent, a deficiency may develop in the absence of vitamin K. Acquired protein C deficiency is seen in liver disease, malignancy, infection, the postoperative state, and disseminated intravascular coagulation. Protein C is activated by thrombin and catalyzed by thrombomodulin released from the endothelial cells. It enhances the activity of recombinant tissue-type plasminogen activator (t-PA), but its primary function in the clotting cascade is to inactivate factors V and VIII with factor S as a cofactor.

Epidemiology. Protein C deficiency occurs in approximately 4%-5% of patients younger than 40 years who present with unexplained deep venous thrombosis. It is usually noted in the late teens.

Clinical features. Since the initial clinical report in 1981, deficiency of protein C has been associated almost exclusively with recurrent superficial and DVT and superficial thrombophlebitis.

Diagnosis. Protein C levels are measured by immunologic or functional laboratory essays. Levels 55%-65% of normal are consistent with deficiency. Because protein C synthesis is vitamin K dependent, patients should not be tested while receiving warfarin.

Treatment. Short-term management of thrombosis is with heparin or low-molecular-weight heparin. For long-term treatment, warfarin may be considered.

Activated protein C resistance (factor V Leiden)

Factor V Leiden is the most common cause of inherited thrombophilia (hypercoagulation). Resistance to activated protein C, which has been linked to a

Table II. International consensus statement on preliminary criteria for the classification of the Antiphospholipid syndrome

<table>
<thead>
<tr>
<th>Clinical criteria</th>
<th>Laboratory criteria</th>
</tr>
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<tbody>
<tr>
<td>Vascular thrombosis</td>
<td>Anticardiolipin antibodies</td>
</tr>
<tr>
<td>One or more clinical episodes of arterial, venous, or small vessel thrombosis, occurring within any tissue or organ</td>
<td>Anticardiolipin IgG or IgM antibodies present at moderate or high levels in the blood on 2 or more occasions at least 6 weeks apart</td>
</tr>
<tr>
<td>Complication of pregnancy</td>
<td>Lupus anticoagulant antibodies</td>
</tr>
<tr>
<td></td>
<td>Lupus anticoagulant antibodies detected in the blood on 2 or more occasions at least 6 weeks apart, according to the guidelines of the International Society on Thrombosis and Hemostasis</td>
</tr>
</tbody>
</table>

Adapted from Wilson et al.
single base-pair mutation in the factor V gene, known as the factor V Leiden mutation, is associated with an increase risk of thrombosis. The resistance of activated protein C promotes the coagulation cascade and clot formation.

**Epidemiology.** The prevalence of heterozygosity for the factor V Leiden mutation in Caucasian, Middle Eastern, and Southeast Asian populations ranges from 1% to 8.5%. The mutation is apparently not present in African Americans, Chinese, Japanese, or Native American populations. The mutation is seen in 11%-29% of patients with venous thromboembolism. Heterozygous carriers of Factor V Leiden have a 3- to 8-fold increased risk for venous thrombosis.

**Clinical features.** Activated protein C resistance is linked with DVT and pulmonary embolism. However, recent studies may suggest that factor V Leiden is less common in patients with pulmonary embolism.

**Diagnosis.** To detect the factor Leiden it is necessary to use multiplex allele-specific polymerase chain reaction amplifications that permit the detection of the mutation.

**Treatment.** Heparin and warfarin are effective anticoagulants agents in the management of this condition. Complications are treated similarly as in patients with protein C deficiency. Long-term therapy is with warfarin or low-molecular-weight heparin.

### Protein S deficiency

Protein S is a vitamin K–dependent plasma protein that functions as a cofactor for activated protein C. Protein S is synthesized by hepatocytes and megakaryocytes. Protein S deficiency is an autosomal dominant disease and can be of quantitative and/or qualitative origin. Fifty percent of protein S circulates free, and 50% circulates bound to C4b binding protein (BP).

Based on the measurement of free and total protein S antigen and functional protein S activity, the deficiency is classified into 3 phenotypes. Type I deficiency is characterized by a decrease in the total protein S antigen and free protein S antigen together (quantitative deficiency). Type II deficiency is characterized by normal total and free antigen levels but reduced protein S activity (functional deficiency). Type III deficiency is characterized by low free protein S levels but normal total plasma concentration of protein S.

**Epidemiology.** The incidence of protein S deficiency is similar to that of protein C deficiency. Protein S deficiency was confirmed in 5% of 141 patients under the age of 45 years who had venous thrombosis. Many patients develop thrombosis before age 25.

**Clinical features.** Patients present with venous thrombosis typically during adolescence and young adulthood. In addition, it has been speculated that protein S deficiency may predispose some persons to premature arteriosclerosis. Phlebitis is a common finding in a patient with protein S, and 74% percent of patients develop DVT.

**Diagnosis.** Protein S deficiency is diagnosed using laboratory tests for the protein S antigen and by using other tests for functional protein S activity (based on clotting assays). Laboratories can test protein S antigen as total antigen (i.e., protein S bound to C4BP plus free protein) or free protein S antigen. Both free and total proteins S are measured by ELISA methods in the laboratory.

**Treatment.** From the treatment viewpoint, heparin and warfarin are effective anticoagulants agents in the management of this condition. Complications are treated similarly as in patients with protein C deficiency. Long-term therapy is with warfarin or low-molecular-weight heparin.

### Homocysteinemia

Elevated levels of homocysteine are risk factors for both arterial and venous thrombosis. Homocysteine is an intermediate of methionine metabolism, and elevated levels may result from a genetic disorder, enzyme deficiency, vitamin B12 deficiency, or folate deficiency. Elevated homocysteine levels cause thrombosis via several mechanisms, including decreased protein C activity, increased factor V activity, induction of endothelial cell tissue factor activity, inhibition of thrombomodulin expression and activation, decreased AT activation activity, and enhanced affinity of lipoprotein and fibrin.

**Epidemiology.** Mild to moderate high levels of homocysteine are present in 5%-10% of the population. The risk of thrombosis is 2-fold greater than in a normal individual.

**Clinical features.** Patients may present with vascular thrombotic events with or without the traditional risk factors for a stroke. If the usual risk factors are not present, a more rigorous search for rarer causes of stroke should be undertaken. It is not a surprise that patients with this condition have histories of strokes and myocardial infarctions early in life (third or fourth decades).

**Diagnosis.** Sensitive assays allow quantification of the total plasma homocysteine concentration. The normal range is 5-15 mmol/L. Acute thrombosis may raise homocysteine levels.

**Treatment.** Dietary supplementation with vitamins B6 and B12 and folic acid can lower homocysteine levels. Reduction of homocysteine levels has not, however, been shown to reduce thrombotic complications. Thrombosis is treated with heparin. Vitamin supplementation may also be helpful.
Dysfibrinolysis

Dysfibrinolysis has been attributed to abnormal amount of plasminogen or low levels of functional plasminogen. It has also been related to defective release of tissue plasminogen activator from the endothelial cells and factor XII (Hageman) deficiency.\(^50\)

Although patients with factor XII deficiency have a significantly prolonged partial thromboplastin time, the clinical manifestation of the disorder is clotting, not bleeding, because factor XII is involved in plasmin generation.\(^51\) All of these conditions have been associated with both venous and arterial thrombotic complications.

Epidemiology. Typically, these disorders are not manifested clinically until the fourth or fifth decade of life, often when some relatively minor vascular procedure, such as arteriogram or arterial blood gas determination, initiates a rapidly progressive thrombotic process.\(^52\)

Clinical features. Patients may present with unexplained venous thrombosis at a young age. It is also a potential hereditary history of venous thrombosis in the family.

Diagnosis. Qualitative and quantitative assays are available to measure the plasminogen activity in vitro.

Treatment. Heparin administration at the time of the arterial interventional procedures, such as catheterization, is vital in reducing the risk of thrombotic complications, and long-term warfarin therapy or low-molecular-weight heparin is also indicated.\(^53\)

OTHER PRIMARY HYPERCOAGULABILITY DISORDERS

There has been renewed attention in elevated plasma factor VIII coagulant activity as an independent marker of increased thrombotic risk. In a population-based case control study performed in the Netherlands, 25% of patients had levels of factor VIII coagulant activity (VIII:C) that were >150% of normal, and they had an adjusted odds ratio of 4.8 for a first episode of venous thrombosis event compared with individuals with levels under 100%.\(^54\) This laboratory abnormality could not be attributed to overt inflammation, because <10% of the patients with factor VIII levels >150% had elevations in acute-phase reactants such as C-reactive protein, fibrinogen, and erythrocyte sedimentation rate. The levels of factor VIII were in relationship with factor VIII antigen concentrations, and it was postulated that the elevations resulted from a constitutive increase in synthesis or an exaggerated response to minimal inflammation.\(^55\) Additional studies are necessary to determine the molecular basis underlying increased factor VIII concentrations and the clinical utility of measuring this parameter in patients with thrombosis.

There have been reports of thrombosis in association with abnormalities in other coagulation or fibrinolytic system proteins. These include heparin cofactor II deficiency;\(^56\) thrombomodulin mutations, and elevations in histidine-rich glycoprotein or plasminogen activator inhibitor 1. However, causal associations between these abnormalities and an increased risk of thrombosis have not been clearly defined.

In the last 5 years, there has been an increase in the number of articles about prothrombin mutation 20210. This mutation was first described in 1996. Prothrombin is the precursor to thrombin in the coagulation cascade. The mutation in the prothrombin gene is at position 20210. The mutation leads to an increased amount of thrombin circulating in the patients’ blood stream. The exact mechanism by which the prothrombin gene mutation results in a thrombophilic state is unclear. The prothrombin gene mutation is seen more commonly in the Caucasian population. About 1%-2% of the general population is heterozygous (1 copy) for the prothrombin gene mutation. The prothrombin gene mutation is relatively uncommon in the aboriginal populations of India, Korea, Africa, and North America. In contrast, rates of 6% have been reported in Spain. Treatment of the prothrombin gene mutation depends upon the individual patient’s risk of recurrent thromboembolic disease, but warfarin is the option for long-term anticoagulation.\(^57\)

SECONDARY HYPERCOAGULABILITY DISORDERS

In contrast to the primary hypercoagulability syndromes, which are limited in number and better described on a molecular basis, the secondary disorders are much more numerous and in most cases less well understood. They are classified into 3 categories: abnormalities of blood vessels, abnormalities of coagulation and fibrinolysis, and abnormalities of the platelets (Table III). A complete discussion of these disorders is beyond the main objective of this review. Two of the more common secondary hypercoagulability syndromes, Trousseau syndrome and heparin-induced thrombocytopenia, have been well characterized and are most likely to be encountered by dentists.

Trousseau syndrome

The relationship between cancer and hypercoagulability was identified by Trousseau more than 100 years ago when he associated recurrent migratory superficial thrombophlebitis and arterial thrombosis with occult malignancies.\(^58\) The presentation of this syndrome is variable and includes 5 overlapping syndromes. In or-
order of decreasing frequency they are: DVT, superficial migratory thrombophlebitis, hemorrhage, arterial thromboemboli, and nonbacterial thrombotic endocarditis.\textsuperscript{59}

Trousseau syndrome seems to represent a form of disseminated intravascular coagulation. It appears that a thromboplastin-like material and endotoxins from necrotic areas are released from the tumor into the circulation; this activates procoagulant proteins or stimulates circulating blood cells such as monocytes to release a protease that activates the coagulation cascade.\textsuperscript{60}

**Epidemiology.** Most of the patients are in the fifth decade, and it occurs more often in men than in women.

**Clinical features.** The syndrome is most frequently associated with malignancies of the pancreas, stomach, lung, colon, ovary, and gallbladder, although it has been seen with tumors of almost all solid organs as well as hematologic malignancies. Thrombotic episodes could be presented months or years before the diagnosis of cancer. Many patients have far-advanced metastatic disease by the time the malignancy is identified.\textsuperscript{59}

**Treatment.** Treatment of these patients is difficult. The drug of choice is heparin, for both short-term and long-term therapy. The dose is critically important and must be monitored frequently.

**Heparin-induced thrombocytopenia**

The use of heparin in hospitals is very common.\textsuperscript{61} One-third of hospitalized patients in the United States, or about 12 million a year, receive heparin. Heparin-induced thrombocytopenia occurs in 3%-30% of patients who receive intravenous heparin for treatment of DVT or pulmonary embolism. In the majority of the cases, thrombocytopenia is the only manifestation of the syndrome and is relatively mild. Platelet count rapidly rises with the discontinuation of the medication. However in 3%-6% of affected patients, this syndrome is severe and is associated with profuse bleeding or, more commonly, arterial and/or venous thrombotic complication. The development of this disease has been associated with bovine- and porcine-derived heparin. It has been observed after intravenous or subcutaneous administration of heparin. Most of the patients develop the thrombocytopenia between the sixth and twelfth days of treatment. It usually occurs in patients with previous exposure to heparin.\textsuperscript{62} Evidence today supports an immunologic-mediated mechanism. It appears that susceptible individuals develop a heparin-dependent antiplatelet antibody that promotes platelet aggregation in the presence of heparin.\textsuperscript{63} Low-molecular-weight heparin causes of thrombocytopenia (incidence about 0.5%) are less common than unfractionated heparin.

**Epidemiology.** The prevalence of thrombocytopenia secondary to heparin administration varies widely, from near 3% to 30%.\textsuperscript{64}

**Clinical features.** Despite thrombocytopenia that can occasionally be severe, bleeding complications are infrequent in heparin-induced thrombocytopenia. On the other hand, patients with heparin-induced thrombocytopenia are at high risk of thrombosis rather than bleeding. The majority of the thrombotic events are venous, although arterial events can also occur. Other clinical manifestations less frequently observed are skin lesions, adrenal hemorrhagic infarction, and acute systemic reactions (e.g., chills, dyspnea, and cardiac or respiratory arrest).

**Diagnosis.** The diagnosis should be suspected in any patient receiving heparin whose platelet count falls, especially if the patient develops a resistance to anticoagulation with heparin that requires progressively higher doses.

**Treatment.** Treatment of these patients must be with warfarin. In some patients, the pathophysiologic process will be reversed by substituting an antigenically different heparin compound.

**DENTAL IMPLICATIONS**

A complete medical history is mandatory in evaluating patients with a recent or remote history of hypercoagulability/thrombosis (reports of DVT or recent thrombotic events must be considered in detail and discussed with the patient’s hematologist). Details should be obtained regarding the age of onset, location of prior thromboses, and results of objective diagnostic studies documenting the thrombotic episode(s). Also, the type of hypercoagulability disorder, if known, must be included in the past medical history.

As with all patients, questions about medications are
extremely important. In many situations the patient remembers the medications they are taking rather than the medical condition for which it was prescribed. For patients with hypercoagulability disorders under treatment with anticoagulants, it is important to ask about the dosage of the anticoagulant, when the therapy was started, and the latest laboratory evaluations used to monitor the condition, including prothrombin time international normalized ratio and partial thromboplastin time.

A family history is particularly important, because a well documented history of hypercoagulability disorder or venous thrombosis in 1 or more first-degree relatives strongly suggests the presence of a hereditary defect in a patient with unknown disease. Patients with hypercoagulability syndromes should be questioned regarding their ethnic background; e.g., factor V Leiden is rarely, if ever, found in aboriginal African, Native American, or Asian populations.

Furthermore, inquiry should be made regarding the presence of constitutional symptoms (diminished appetite, weight loss, and fatigue), pain, hematochezia (fresh blood in the stool), melena (black tarry stools), hemoptysis, and hematuria, because the initial manifestation of a malignancy can be a thrombotic event.

Once the hypercoagulability disorder is established, the dentist may need to modify his/her dental management of the patient. Because each disorder poses unique challenges and these disorders have variable manifestations across patients, only broad recommendations are presented. Individual management must be based upon an expert hematologist opinion with the consideration of the planned dental procedure and the likelihood of bleeding. Although the focus of the present discussion is on hypercoagulability disorders, the greatest challenge is often bleeding associated with the medications used to treat or prevent thrombosis. The risk of bleeding should be considered in terms of the anticipated amount and area of tissue involved in the bleeding. Larger areas involved in bleeding, e.g., quadrant scaling and root planning in a patient with severe periodontal disease, may be more difficult to control than a single tooth extraction in which local measures could be more effective. Local measures to decrease bleeding should be carefully used to achieve maximum local hemostasis.

Comorbid diseases (and the medications being taken for those diseases) that could also result in excessive bleeding must also be considered. Knowledge of the laboratory test used to measure either quantitative or qualitative factors associated with hypercoagulation is important. Likewise, a working knowledge of the laboratory test measuring anticoagulation is essential.

The hematologist should be able to determine if the patient will require lifelong anticoagulation or if the patient will discontinue or decrease the medication in the near future, thus allowing dental care to be deferred to a more hematologically favorable time. Occasionally, hospitalization is required to treat emergent dental issues, such as infection, jaw fractures, etc. During this time, anticoagulation may need to be lowered to perform the oral surgical procedure. The time for anticoagulation diminution should be minimized so as not to favor a thrombotic event. Furthermore, the hematologist may recommend a vena cava filter placement in certain high-risk patients before decreasing anticoagulation.

Finally, the dentist must not further compromise the patient’s coagulation by prescribing medications that directly or indirectly modify a patient’s ability to stop bleeding. This list of medications would include both those that interfere with hemostasis and those that interfere with the metabolism of the patient anticoagulation medications.

### Treatment planning modifications

1. Consult with the hematologist.
2. Consider type of dental procedure and the risk of bleeding.
3. Often, anticoagulation cannot be eliminated but may be attenuated.
4. Careful treatment planning may occasionally require hospital admission for heparinization and close monitoring after treatment.

### Table IV. Summary of primary hypercoagulability syndrome

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Epidemiology</th>
<th>Arterial vs. venous thrombosis</th>
<th>Lab finding</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antithrombin III</td>
<td>Common</td>
<td>Venous</td>
<td>Low AT III</td>
<td>LMW heparin</td>
</tr>
<tr>
<td>Antiphospholipid</td>
<td>Common</td>
<td>Venous 70%, arterial 30%</td>
<td>Several</td>
<td>LMW heparin and warfarin</td>
</tr>
<tr>
<td>Protein C</td>
<td>Rare</td>
<td>Venous</td>
<td>Low protein C</td>
<td>LMW heparin and warfarin</td>
</tr>
<tr>
<td>Protein S</td>
<td>Rare</td>
<td>Venous</td>
<td>Low protein S</td>
<td>Heparin and warfarin</td>
</tr>
<tr>
<td>Homocysteinemia</td>
<td>Common</td>
<td>Venous and arterial</td>
<td>Low homocysteine</td>
<td>LMW heparin and vitamins</td>
</tr>
<tr>
<td>Dysfibrinolysis</td>
<td>Rare</td>
<td>Venous and arterial</td>
<td>Low factor XII</td>
<td>Heparin and warfarin</td>
</tr>
</tbody>
</table>

LMW, low-molecular-weight.
5. Local measures, including absorbable gelatins (e.g., Gelfoam from Pharmacia & Upjohn), absorbable hemostats (e.g., Surgicel from Johnson & Johnson), and topical thrombin, should be implemented when appropriate. 

6. Postoperative dental medications should not interfere with the anticoagulation medication. 

7. For patients with a history of DVT, the Trendelenburg or subsupine position (where the legs are higher that the heart) is contraindicated owing to the risk of gravity-dependent embolization.

SUMMARY

Although hypercoagulability disorders are not common, they occur with sufficient frequency that the dentist may encounter patients with these diseases (Table IV). The key to minimizing possible complications, such as bleeding, is to perform an adequate history and develop a close working relationship with the treating physician/hematologist.

REFERENCES


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