Bleeding Disorders of Importance in Dental Care

Literature Review by Sina Moshiri

History Taking

- The initial recognition of a bleeding disorder may occur in a dental practice. Proper dental and medical evaluation of a patient is necessary before treatment. The patient should be asked for a history of significant or prolonged bleeding after dental extraction
- Any clinically significant bleeding episodes must be noted during history-taking:
  - bleeding continuing past 12 hours
  - bleeding for which patient calls or returns to dental clinic or seeks medical care
  - bleeding causing a hematoma or ecchymosis within soft tissue
  - requires blood product support
  - history of nasal or oral bleeding
- Majority of dental bleeding episodes are minor and do not require special precautions or treatment
- Many bleeding disorders run in families so a careful family history for bleeding disorders is needed
- Medications:
  - Complete list of current and past medications and recreational drugs is required
  - Consultation with the patient's physician is recommended for those receiving anticoagulants or antiplatelet drugs
  - Patients with previous or active drug abuse may suffer from liver dysfunction or damage and are at risk of excessive bleeding due to altered production of coagulation factors
  - Intravenous drug use carries risk of transmission of infection diseases such as HCV or HIV and can lead to altered liver function
  - Some potential signs for bleeding disorder may include: multiple purpura of skin, bleeding wounds, hematomas or swollen joints. Also signs of underlying systemic disease may be evident. Liver disease may manifest as jaundice, Spider nevi, and ascites.
  - If a bleeding disorder is suspected, the patients primary care physician will order laboratory testing, including blood counts and coagulation studies

Table 1 Systemic diseases causing coagulopathies

Disease	Common causes	Resulting coagulation defect
Renal failure and uremia	Diabetes mellitus Hypertension Glomerulonephritis Pyelonephritis	Inhibition of platelet adhesion and primary aggregation from glycoprotein IIb-IIIa deficit
Hepatic failure	Alcohol abuse Hepatitis B and C Cancer (hepatocellular carcinoma)	Loss of liver tissue and clotting factors including vitamin K-dependent factor II, VII, IX, X except VII and von Willebrand's factor Obstructive jaundice
Bone marrow failure	Alcohol abuse Cancer (leukemia) Myelosuppressive medications (chemotherapy agents) Uremia (renal failure)	Reduced number of functional platelets Anemia from bone marrow suppression

Table 2 Laboratory tests for the hemostatic system include

Variable	Function	Norm
Bleeding time	assess platelet function	norm: 2-7 mins
Activated partial thromboplastin time (aPTT)	evaluate intrinsic coagulation	norm: 25 ± 10 sec
International normalized ratio (INR)	measure extrinsic pathway	norm: 1.0
Platelet count	quantify platelet function	norm: 150,000-450,000/uL

Types of Bleeding Disorders

- May be categorized as coagulation factor deficiencies, platelet disorders, vascular disorders or fibrinolytic defects (Table 1)

1. Coagulation disorders

   Congenital

   - **Hemophilia A**
     - Deficiency in factor VIII or anti-hemophilic factor
     - Inherited X-linked recessive trait occurring in males
     - Symptoms: delayed bleeding, ecchymosis, deep hematomas, epistaxis, spontaneous gingival bleeding, hemarthrosis
     - Mild hemophilia A: 6-50% of normal factor VIII activity, associated with bleeding during surgery or trauma
     - Moderate hemophilia A: 1-5%, bleeding after mild injury
     - Severe hemophilia A: <1%, spontaneous bleeding
     - Management for the dental patient consists of:
       - Increasing factor VIII levels
       - Replacing factor III and inhibiting fibrinolysis
       - DDAVP (desmopressin) to increase endogenous factor III levels
       - Hemostasis is achievable in mild hemophilia. DDAVP may be used with anti-fibrinolytics to improve hemostasis.
       - Anti-fibrinolytic therapy may be used post-operatively to protect formed blood clots. Tranexamic acid is most commonly used.
     - Factor VIII replacement options:
       - factor VIII concentrates
       - fresh frozen plasma (FFP)
       - cryoprecipitate
     - Highly purified factor VIII concentrates, made using recombinant or monoclonal antibody purification are preferred due to greater viral safety
     - Patients who develop antibodies to factor VIII require a higher dose of factor VIII
   - **Hemophilia B**
     - Factor IX deficiency
     - Managed using replacement therapy with highly purified virally inactive fator IX concentrates
     - Prothrombin complex concentrates may also be used
   - **von Willebrand's disease**
     - Most common hereditary coagulation disorder - incidence of 1/10,000
     - Not sex linked
     - Type I to Type IV and may vary in severity
     - Mild conditions managed with DDAVP, severe disease requires factor VIII replacement

Table 3 Pre-surgical treatment for hemophilia A

Condition		
Mild bleeding	Dose: 15 U/kg **factor VIII** q8-12h, 1-2 days Target: 30% of normal level	Dental bleeding, oropharyngeal bleeding, hematuria, epistaxis, hemarthrosis
Major bleeding	Dose: 50 U/kg factor VIII q8-12h, 7-14 days	Same as mild including CNS hemorrhage, retroperitoneal hemorrhage, gastrointestinal bleeding
Adjunctive therapy	Desmopressin (DDAVP), tranexamic acid, epsilon-aminocaproic acid (for mild disease)	

Acquired

- Coagulation defects may be acquired
- **Liver disease**
  - Synthesis of clotting factors may be reduced which may result in a variety of bleeding disorders depending on the extent of liver damage
  - For prolonged prothrombin time and partial thromboplastin time management includes vitamin K and fresh frozen plasma infusion for an immediate but temporary effect
  - Or cryoprecipitate for replacement of factor VIII deficiency and replacement therapy for disseminated intravascular coagulation
- **Drug induced**
  - Warfarin, low-molecular-weight heparin and dicumarol are commonly used anticoagulant drugs

2. Platelet disorders
   - May be hereditary or acquired.
   - Due to decreased platelet production, excess consumption or altered function
   - Common clinical features are bleeding from superficial cuts and lesions, spontaneous gingival bleeding, petechiae, ecchymosis and epistaxis
   - Minimum blood platelet level suitable for minor dental surgery is 50,000/uL and >100,000/uL for extensive surgery. If the count is below these levels, platelet transfusion is carried out 30 minutes before surgery. Local measures are usually sufficient to control bleeding in platelet levels below 100,000/uL.
   - Idiopathic thrombocytopenic purpura - an acquired platelet disorder which may require oral systemic steroids 7-10 days
   - Glanzmann thrombasthenia is an autosomal recessive disorder causing defect in platelet aggregation, which requires platelet infusion before surgery.
   - Drugs interfering with platelet function include acetylsalicylic acid (ASA) and dipyridamole. Discontinuation of these drugs is not required for routine procedures.
3. Vascular defects
   - Rare and usually associated with mild bleeding confused to the skin or mucosa
   - Scurvy, hereditary hemorrhagic telangiectasia (HHT) and other vascular defects may be treated with laser ablation, embolization, sclerosing therapy
4. Fibrinolytic defects
   - May occur in patients on medical anticoagulant therapy or those with coagulation syndromes where fibrin is consumed such as disseminated intravascular coagulation (DIC)
   - Care must be managed in consultation with a hematologist

Table 4 Common bleeding disorders

Coagulation actors deficiencies	**Congenital**
	Hemophilia A and B
	von Willebrand's disease
	other factor defiencies (rare)
	Acquired
	Liver disease
	Vitamin K deficiency, warfarin therapy
	Disseminated intravascular coagulation
Platelet disorders	**Quantitative disorder (thrombocytopenia)**
	Immune-mediated
	Idiopathic
	Drug-induced
	Collagen vascular disease
	Sarcoidosis
	Non-immune mediated
	Disseminated intravascular coagulation
	Microangiopathic hemolytic anemia
	Leukemia
	Myelofibrosis
	Qualitative disorder
	Congenital
	Glanzmann thrombasthenia
	Von Willebrand's disease
	Acquired
	Drug-induced
	Liver-disease
	Alcoholism
Vascular disorders	Scurvy
	Purpura
	Hereditary hemorrhagic telangiectasia
	Cushing syndrome
	Ehlers-Danlos syndrome
Fibrinolytic defects	Streptokinase therapy
	Disseminated intravascular coagulation

Oral Findings

- Platelet deficiencies may cause petechiae or ecchymosis in oral mucosa and spontaneous gingival bleeding. In cases of leukemia, platelet disorders may present alone or in conjunction with gingival hyperplasia. Hemosiderin (iron deposits) and other blood degradation products may cause brown deposits on surface of teeth due to chronic bleeding
- Patients with hemophilia may experience multiple oral bleeding events in their life time. However hemarthrosis of the temporomandibular joint is uncommon.
- Dental caries and periodontal disease has a higher incidence in bleeding disorder patients. This may be due to a fear of bleeding resulting in a lack of effective oral hygiene and professional care.

Dental Management

- Dental management depends on the severity of the conditions and the planned procedure.
- For minor surgical procedures for a patient with mild bleeding disorder, slight or no modifications are required.
- Patients with severe bleeding disorders will require restoration of the hemostatic system to acceptable levels combined with local and adjunctive hemostatic measures.

- Patients with drug-induced coagulopathies may require discontinuation of the drug or dose modification prior to procedure.
- In instance of irreversible coagulopathies (liver failure), replacement of missing factors may be necessary.

Table 5 Local hemostatic agents

Brand name	Generic name
Gelfoam (Pfizer, Markham ON)	Absorbant gelatin sponge
Bleed-X (QAS, Orlando, Florida)	Microporous polysaccharide hemispheres
Surgicel (Ethicon, Markham, ON)	Oxidized cellulose
Tisseel, Evicel (Baxter, Mississauga ON)	Fibrin sealant
Thrombostat (Pfizer)	Topical thrombin
Cyklokapron (Pfizer)	Tranexamic acid
Amicar (Wyeth, Markham ON)	Aminocaproic acid

Pain Control

- Nerve-block anesthetic injections should be avoided in patients with coagulopathies. The area of injection is highly vascularized, which carries a risk of hematoma formation. An inferior alveolar nerve block may result in extravasation of blood into the oropharynx, which can produce gross swelling, pain, dysphagia, respiratory obstruction and death from asphyxia. Commonly used dental blocks require minimum clotting factor levels of 20-30%.
- When appropriate, anesthesia should be limited to infiltration and intraligamentary injections. Vasoconstrictor should be used to minimize bleeding.
- Alternative techniques such as sedation with benzodiazepine or nitrous oxide may be employed to minimize the need for regional anesthesia
- Patients with severe disorders or those requiring extensive treatment with factor replacement may be treated in a hospital under general anesthesia

Oral Surgery

- Surgery carries the highest risk of bleeding
- For coagulopathies, transfusion of appropriate factor to 50-100% of normal levels is recommended for single bolus infusion in an outpatient setting. Patients with hemophilia may require post-operative factors to help maintain hemostasis. This may be done with factor infusion, DDAVP, cryoprecipitate or fresh frozen plasma. Consultation with hematologist should be done before surgery.
- Local hemostatic agents and techniques (Table 5) may be used to assist in hemostasis. Caution as the use of vasoconstrictors may cause rebound vasodilation and increase risk of late bleeding. Absorbable hemostatic materials assist in clot formation and stability but may increase the risk of infection and delayed healing and should be avoided in immunosuppressed patients. Topical thrombin is applied directly to bleeding areas and converts fibrinogen to fibrin and facilitates rapid hemostasis. Topical fibrin glue can reduce the amount of factor replacement needed when used along with anti-fibrinolytic agents.
- Use of anticlotting medications does not usually pose a significant problem for dental treatment. ASA therapy is typically unaltered and bleeding is managed with local hemostatic measures; however, if it is to

be withdrawn ASA should be stopped at least 10 days prior to surgery. Similarly, other antiplatelet drugs (clopidogrel and dipyridamole) do not require discontinuation. Consult with patient's physician before any decision is made. Patients receiving warfarin require blood work to determine their INR (international normalized ratio). Normal therapeutic range is 2.0-3.0 and most oral surgical procedures can be performed if INR is <3.0. For INR values greater than 3.0 a physician referral for adjustment is suggested. One must consider the risk of reducing level of anticoagulation in patients on warfarin for risk of thromboembolic event. Patients taking heparin are often on hemodialysis due to end-stage kidney disease. Heparin has a short half-life (5 hours) and patients may be treated safely on non-dialysis days.

Periodontal Procedures

- Periodontal health is essential in patients with bleeding disorders, as inflamed and hyperemic periodontal tissues carry risk of increase bleeding. Further, periodontal disease may warrant tooth extraction, which may be complicated in these patients. Patients with coagulopathies may neglect their oral health from fear of bleeding during tooth brushing. This neglect leads to increase gingivitis, periodontitis and caries.
- Routine periodontal probing, supra-gingival scaling and polishing can be done without risk of significant bleeding. Factor replacement is usually not required for sub-gingival scaling for mild coagulopathies. Ultrasonic instrumentation may produce less tissue trauma. However, for severely inflamed tissues, initial treatment with chlorhexidine rinse and gross debridement is helpful to reduce tissue inflammation before deep scaling. Factor replacement may be required before extensive periodontal surgery and for nerve blocks. Periodontal packings and stents can be used to aid hemostasis and protect the surgical sites; however, these adjuncts can be dislodged by severe hemorrhage or sub-periosteal hematomas. Anti-fibrinolytic agents may be introduced into periodontal dressings to enhance hemostasis. Post-treatment anti-fibrinolytic mouthwashes (tranexamic acid) can also be used to control protracted bleeding.

Restorative & Endodontic Procedures

- General restorative procedures do not pose significant risk of bleeding. Rubber dam should be used to prevent damage to soft tissues, but care should be taken to avoid lacerating the gingiva during placement. Saliva ejectors and high-speed suction should be used carefully since they can injure the floor of mouth and cause hematoma or ecchymosis.
- Endodontic therapy is preferred over extraction when possible. Root canal therapy does not usually pose a significant risk of bleeding but surgical endodontic treatment may require factor replacement.

Prosthodontic Procedures

- Usually do not carry a significant risk of bleeding. Adjustments should be made to removable prosthesis to prevent tissue trauma. Oral tissue should be handled carefully to prevent ecchymosis.

Orthodontic Procedures

- Poses minimal risk of bleeding. The appliance should not impinge on soft tissues and oral hygiene must be atraumatic.

Drug Interactions

- Many medications prescribed by dentists may interfere with hemostasis and increase risk of bleeding. ASA and nonsteroidal anti-inflammatory drugs (NSAIDs) can increase the effect of warfarin. Penicillin, erythromycin, metronidazole, tetracycline and miconazole can also potentiate effect of warfarin. Care should be taken when prescribing these drugs to patients with bleeding disorders or on anticoagulant

therapy. As always, consultation with the patients' physician before planning invasive treatment or dose adjustments.

Table 4 Principal agents for systemic management of patients with bleeding disorders

Agent	Description	Common indications
Platelets	1 unit = 50 mL raises count approximately by 6000	Platelet count: <10E3 in non-bleeding individuals <50E3 pre-surgical level <50E3 actively bleeding patient Non-destructive thrombocytopenia
Fresh frozen plasma	1 unit = 150-250 mL 1 hour to thaw Contains factors II, VII, IX, X, XI, XII, XIII and heat labile V and VII	Undiagnosed bleeding disorder with active bleeding Severe liver disease Transfusing >10 units of blood Immunoglobulin deficiency
Cryoprecipitate	1 unit = 10-15 mL	Hemophilia A, von Willebrand's disease (when factor concentrate and DDAVP not available) Fibrinogen deficiency
Factor VIII concentrate	1 unit = ↑ 2% factor VIIII Heat-treated variant contains VWF Recombinant and monoclonal = pure factor VIII	Hemophilia A with active bleeding, pre-surgery Some cases of von Willebrand's disease
Factor IX concentrate	1 unit = ↑ 1-1.5% factor IX Contains factor II, VII, IX and X Monoclonal formulation = pure IX	Hemophilia B with active bleeding or pre-surgery Prothrombin complex concentres used for hemophilia A with inhibitor
Desmopressin	Synthetic antidiuretic hormone analog 0.3 ug/kg IV or SC Intranasal application	Active bleeding or pre-surgery for some patients with von Willebrand's disease, uremic bleeding 2° to liver disease, bleeding esophageal varices
Epsilon-aminocaproic acid	Anti-fibrinolytic: 25% oral solution (250 mg/mL) Systemic: 75 mg/kg q6h	Adjunct to support clot formation
Tranexamic acid	Anti-fibrinolytic: 4.8% mouth rinse Systemic: 25 mg/kg q8h	Adjunct to support clot formation

Summary

- Bleeding disorders may impact planned dental treatment, depending on the severity of the disorder and the type of procedure planned
- Consultation with the patients physician and hematologist is recommended prior to treatment or drug dose adjustments
- Bleeding disorders may be categorized as platelet disorders, coagulation factor deficiencies, vascular disorders or fibrinolytic defects
- Oral findings may include petechiae or ecchymosis, and may be related to systemic diseases (renal failure, hepatic failure, bone marrow failure)
- Majority of mild to moderate coagulopathies and platelet disorders may be managed with local measures including gelfoam, surgical, topical thrombin.

- Severe bleeding disorders may require prior platelet or factor transfusion and require close planning with the patients hematologist

Reference

- Gupta, Anurag, Joel B. Epstein, and Robert J. Cabay. "Bleeding disorders of importance in dental care and related patient management." *Journal of the Canadian Dental Association* 73.1 (2007)

Appendix A Drugs that may interfere with hemostasis

ASA and ASA-containing compounds

Alka-Seltzer (ASA)
Alka-Seltzer XS (ASA, caff eine, acetaminophen)
Anadin, Anadin Maximum Strength (ASA, caffeine)
Anadin Extra, Anadin Extra Soluble (ASA, caff eine, acetaminophen)
Asasantin Retard (ASA, dipyridamole)
Askit (ASA, aloxiprin, caff eine)
Aspav (ASA, papaveretum)
Aspro Clear, Maximum Strength Aspro Clear (ASA)
Carpin (ASA)
Co-codaprin (ASA, codeine phosphate)
Codis 500 (ASA, codeine)
Disprin, Disprin CV, Disprin Direct (ASA)
Disprin Extra (ASA, acetaminophen)
Disprin tablets (ASA, caff eine, chlorphenarmine, phenylephrine)
Imazin XL (ASA, isosorbide mononitrate)
Migramax (ASA, metoclopramide hydrochloride)
Nurse Sayles' Powders (ASA, caff eine, acetaminophen)
Phensic (ASA, caffeine)
Veganin (ASA, acetaminophen, codeine)

Other nonsteroidal anti-inflammatory drugs

Acelofenac
Azapropazone
Celecoxib
Diclofenac
Difl unisal
Etodolac
Fenbufen
Fenoprofen
Flubriprofen
Ibuprofen
Indomethacin
Ketoprofen
Ketorolac
Mefenamic acid
Meloxicam
Nabumetone
Naproxen
Phenylbutazone
Piroxicam
Rofecoxib
Sulindac
Tenoxicam
Tiaprofenic acid
Tolfenamic acid

Antibiotics/antifungals

Aztreonam
Cephalosporins (2nd and 3rd generation)
Erythromycin
Fluconazole
Imipenem
Isoniazid
Ketoconazole
Meropenem
Metronidazole
Miconazole
Penicillins
Piperacillin
Rifampicin
Sulfonamides
Tetracyclines
Ticarcillin
Trimethoprim

Other medications

Ateplase
Amiodarone
Anabolic steroids
Barbiturates
Carbamazepine
Chloral hydrate
Cholestyramine
Chronic alcohol use
Cimetidine
Corticosteroids
Dipyridamole
Disulfi ram
Heparin
Omeprazole
Acetaminophen
Phenytoin
Quidine
Sucalfate
Tamoxifen
Vitamin E (megadose)
Warfarin