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Bleeding Disorders seen in the Dental Practice

Abstract: Dentists may encounter patients with various types of bleeding disorders in their daily practice. Initial recognition of such bleeding disorders and their possible systemic causes, as well as knowing when to refer those cases to secondary care, plays a crucial and important role in reducing potential complications and negative side-effects. This article will give an account of the most common bleeding disorders that dentists might find in their daily dental practice. This will be followed by another article that will cover the management of congenital and acquired disorders found in the dental practice.

Clinical Relevance: Bleeding disorders are occasionally encountered in patients in dental practice. Dentists must be knowledgeable about these disorders and be aware of the impact of such conditions on the management of their patients.

Dent Update 2012; 39: 266–270

In order to control haemostasis following an injury to a blood vessel, a series of events is initiated and these may be summarized as follows:

- Local vasoconstriction;
- Adhesion and aggregation of platelets (this requires platelets to adhere to the exposed collagen in damaged blood vessels [via Von Willebrand's factor with its collagen- and platelet-binding sites] and to

each other by cross-linking with fibrinogen which binds to specific fibrino-binding sites on the platelet surface);

- Activation of the clotting cascade to create a fibrin clot (this has classically been divided into the intrinsic and the extrinsic pathways. Both pathways activate factor V which cleaves prothrombin (II) to release thrombin);
- Activation of coagulation inhibitors to restrict coagulation to the site of the injury;
- Fibrinolysis occurs later to restore vessel potency.

Bleeding disorders could affect any or many of these events and could be acquired or congenital in nature.

Platelet disorders in general could be classified as being *quantitative* or *qualitative* (which could be *inherited*, such as Bernard-Soulier disease and Glanzmann's Thrombasthenia, or *acquired*, like the altered platelet function after Aspirin or NSAIDs intake). They may present clinically with purpura, petechiae, mucosal bleeding, epistaxis and menorrhagia.

Clotting cascade disorders could be divided broadly into *inherited* disorders (like Haemophilia A & B, and Von Willebrand's disease), or *acquired* disorders (like disseminated intravascular coagulation (DIC), liver disease and vitamin

K deficiency).

Bleeding disorders and their systemic causes, if not recognized and dealt with prior to most invasive dental surgery, may have devastating and even life-threatening side-effects. It is, therefore, important that dentists and oral surgeons check their patients' medical and dental histories and give enough time to discuss them with the patients, making sure that these histories are kept up-to-date on a systematic and regular basis.

Signs of a bleeding tendency should be noted when the patient is first seen. The dental surgeon should be looking for general signs such as:^{1,2}

- Bruises (with or without injury), haematomas and ecchymosis: ask for history, causes, ease of getting bruised, frequency, drug and family history;
- Multiple purpurae of the skin, petechiae, swollen joints: ask for history, causes, other bleeding sites, eg gingiva, drug and family history;
- Signs of systemic diseases, such as tachycardia and hypertension in heart disease, jaundice and spider naevi in liver disease, impaired hepatic function and spontaneous 'plaque-free' gingival bleeding, which could be an early sign of leukaemia.

The medical and drug history

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Name of Test	Evaluate	Normal Values	Prolonged in
PT (Prothrombin Time)	The extrinsic pathway (Factors II, V, VII, X and fibrinogen)	12–15 seconds	Warfarin treatment, liver disease, vitamin K deficiency, DIC
INR (International Normalized Ratio)	The extrinsic pathway of blood coagulation	About 1.0 (0.8–1.2)	Warfarin treatment, liver disease, vitamin K deficiency, DIC
APTT (Activated Partial Thromboplastin Time)	The intrinsic pathway of blood coagulation (which includes Factors II, V and X)	25 ± 10 seconds	Heparin treatment, liver disease, haemophilia, DIC, massive transfusion and in some auto-immune treatments, such as in lupus anticoagulant
TT (Thrombin Time)	The abnormality in converting the fibrinogen (a soluble protein) to a fibrin (an insoluble protein)	10–15 seconds	Heparin treatment and DIC
Bleeding Time	To assess the platelet and normal blood vessel functions	2–9 minutes, depending on the method used (ie Ivy vs Duke)	Platelet disorders, vessel-wall disorders, fibrinogen disorders and Von Willebrand's disease

Table 1. Some laboratory-based investigations.

should be studied as patients might have congenital defects that run in families (eg classic Haemophilia A, Haemophilia B (Christmas disease) and Von Willebrand's disease). On the other hand, patients may be taking some anti-coagulant medications that might interfere in haemostasis and prolong bleeding after any surgical intervention, such as warfarin, low-molecular weight heparin and Aspirin. Patients might be alcohol abusers or on recreational drugs such as amphetamines and heroin.³

Previous dental history is also of great importance, especially if the patient reported some issues like:

- Previous bleeding history after dental surgery;
- How many episodes, how long for, how bad was the bleeding, was it prolonged or

excessive, was there a need to transfer the patient to the A&E department or was the bleeding dealt with at the dental practice?;

- Previous side-effects of normal dental procedures.

These could include the development of haematomas, ecchymosis within the soft tissues and early or delayed bleeding.

Such information should direct the dental surgeon's attention towards the underlying cause for such symptoms or the bleeding disorder. Pre-operative communication with the patient's general medical practitioner (or with his/her specialist haematologist, if the patient is under a specialist care) is essential and further laboratory-based investigations may be needed before any invasive procedure can be undertaken. If the disorder is severe

and the patient is at high risk of bleeding, referral of the patient to secondary care would be advisable. Examples of such laboratory-based investigations are presented in Table 1.^{1,2}

The INR (International Normalized Ratio) is the ratio of the patient's PT to a normal control. This evaluates the extrinsic pathway of blood coagulation. The advantage of the INR over the PT is that it uses international standards and thus anti-coagulant control can be compared in different hospitals and clinics across the world.

The normal platelet count is about 150,000–450,000 platelets per micro-litre of blood. In general, changes in platelet count means more bleeding tendency.

Classification of bleeding disorders

A number of classifications are in use for bleeding disorders.^{1,2} Some are based on the main *three* processes of halting bleeding (such as the vasoconstriction, gap-plugging by platelets and the coagulation cascade). Others are based on the bleeding factors that are related to the primary and the secondary haemostasis, or those that are based on the bleeding disorder's origin (such as congenital and acquired).

For the sake of simplicity, bleeding disorders could be classified generally into *four* main categories (Table 2).

The most common disorders among dental patients are platelet-acquired disorders (such as Aspirin and NSAIDs intake), or congenital ones, such as Von Willebrand's disease and, less commonly, congenital deficiency in Factors VIII or IX causing Haemophilia A & B.

Acquired bleeding disorders due to medications

In addition to warfarin and heparin, other common medications, such as low dose Aspirin, clopidogril and dipyridamole may be prescribed to prevent stroke and heart attack. Aspirin and clopidogril irreversibly, while NSAIDs reversibly, inhibit the cyclo-oxygenase-1

Coagulation disorders	<i>Congenital:</i> Haemophilia A, Haemophilia B (Christmas disease) and Von Willebrand's disease. <i>Acquired:</i> Anticoagulants, liver disease, DIC, vit K deficiency.
Vascular defects	<i>Congenital:</i> Connective tissue disease (Ehlers-Danlos syndrome), Osler-Weber-Rendu syndrome. <i>Acquired:</i> Senile purpura, infections, steroids, scurvy.
Platelet defects 1. Platelet number defects 2. Platelet structural defects	Decrease marrow production: Aplastic anaemia, marrow infiltration (leukaemia, myeloma), marrow suppression (cytotoxic drugs, radiotherapy). Excessive destruction: immune thrombocytopenic purpura (ITP), SLE, CLL, heparin treatment, viruses. Thrombotic thrombocytopenic purpura (TTP), sequestration (as in hypersplenism). Myeloproliferative disease, increase urea, Von Willebrand's disease, Bernard-Soulier (giant platelet) syndrome, alcoholism, drug-induced (Aspirin, NSAID).
Fibrinolytic defects	DIC and streptokinase treatments.

Table 2. Classification of bleeding disorders.

(COX-1) enzyme in platelets, preventing thromboxane synthesis and so decreasing platelet aggregation. Patients are at risk of emboli and myocardial infarction if the anti-platelet medication is stopped (stopping Aspirin may increase the risk of thromboembolic events by 0.005%). Studies have shown that patients undergoing simple minor oral surgery experienced minimal bleeding complications when they continued on those medications (these bleeding conditions being controlled with simple local measures). These results indicated that low-dose Aspirin, clopidogril and dipyridamole may be continued if a patient requires minor oral surgery.

For a complicated oral surgery procedure, the anti-platelet medication can be stopped one week before the surgery, after consultation with the patient's physician.

NSAIDs also reversibly bind to the platelet for a limited period of time (approximately 6 hours). Hence, there should be no major complications if a patient is taking a NSAID drugs. Complications may arise if the patient is taking anticoagulant medication and a NSAID together. This combination could increase the risk of bleeding.⁴

Von Willebrand's disease (VWD)^{5,6}

Von Willebrand's factor is an essential co-factor for normal platelet adhesion to damaged sub-endothelium. This factor also serves as a carrier for factor VIII (C) to form the whole VIII complex, protecting VIII (C) from inactivation and clearance.

Von Willebrand's disease is the most common inherited bleeding disorder. It is an autosomal dominant disease that affects both sexes. Expression is variable, with some patients experiencing bleeding only after surgery or major trauma and others suffering from frequent spontaneous bleeding of the mucosal surfaces. In general, the APTT, clotting time and bleeding time are usually prolonged owing to defective platelet adhesion to sub-endothelial tissues. Patients may also present with deep-seated haemorrhages caused by factor VIII deficiency. Prothrombin Time, Thrombin Time and Platelet Count are usually normal. Factor VIII assay is usually reduced, while the Tourniquet test may be positive in most cases.

There are three main types

of VWD, in which VWD is either deficient (partial: type 1, or complete: type 3) or defective (type 2):

Type 1

This is the most common (70%), is autosomal dominant and considered as a quantitative defect. It is usually confirmed with the combination of:

- Abnormal platelet function tests;
- A decrease in Von Willebrand's factor antigen;
- A proportional decrease in factor VIII activity.

Type 2

This has four subtypes (A, B, M, N), all of which are qualitative defects and usually all are autosomal dominants.

Type 3

This is rare but very severe. It is autosomal recessive. The presentation usually resembles that of Classic Haemophilia.

The Von Willebrand's factor circulates as large polymers and serves two main functions:

- The principal function is to form the bridge that allows platelets to adhere to damaged endothelial surfaces;
- The secondary function is to stabilize circulating factor VIII.

Treatment is usually with desmopressin (which raises Von Willebrand's factor levels) in mild disease and a factor VIII/VWF concentrates in more severe diseases.

Haemophilia (hereditary coagulation deficiencies)⁷

Haemophilia is mainly due to a congenital factor VIII deficiency (A - True Haemophilia or Classic Haemophilia) or factor IX deficiency (B - Christmas disease). Both are X-linked recessive disorders. The affected male will not transmit the disorder to his son, because his Y-chromosome cannot carry the haemophilic gene. However, all the daughters will be carriers of haemophilia because they inherit his X-chromosome containing the haemophilic gene. The female carrier will transmit the disorder to half of her sons and a

carrier state to half of her daughters. Of haemophilic patients, 70% have a family history. The other 30% result from new mutation. A small proportion of female carriers may bleed significantly.

Clinical presentation depends on the severity of the deficiency but is generally similar in both types, with easy bruising, muscle and joint haemorrhages and prolonged haemorrhage after surgery or trauma (but no excessive bleeding after minor cuts).

In severe disease (<1% factor VIII), spontaneous bleeding into large joints and muscles occurs, unless regular prophylactic treatment with factor VIII concentrate is given.

Moderate (factor VIII level 1–5%) and mild (factor VIII level 5–40%) disease is usually associated with bleeding on mild or moderate trauma. Factor VIII is given here only in response to trauma or in anticipation of surgery. Previously plasma-derived concentrates resulted in infection with Hepatitis C and HIV. Recombinant factor VIII, uncontaminated with viruses, is now available.

Generally, the Clotting Time is usually prolonged, with the APTT prolonged and corrected by fresh plasma but not serum.

Prothrombin Time, Thrombin Time, Platelet Count and Bleeding Time are usually normal. Factor VIII and factor IX assay will confirm Haemophilia and show that factor VIII is decreased in Haemophilia A, while factor IX is decreased in Haemophilia B.

Haemostatic blood products commonly used in the treatment of patients with coagulation defects

There are many derivatives of blood that are commonly used in the treatment of patients with coagulation defects, such as:⁸⁻¹¹

- Fresh frozen plasma with all its important factors;
- Fresh whole blood platelet concentrates;
- Factor VIII concentrates.

PPSB (factors II, VII, IX X): **PPSB** is the name for the blood product in which the following vitamin K-dependent

coagulating factors are concentrated:

- Factor II - Prothrombin;
- Factor VII - Prokonvertin;
- Factor X - Stuart Prower factor;
- Factor IX - antihæmophilic factor B.
- Prothrombinex (factor II, IX);
- Fibrinogen.

There are a number of procedures that can help minimize the risk of bleeding at the dental surgery, such as:

- Good medical history updates;
- Proper planning and communication with the patient's physician/specialist; and
- Good knowledge of laboratory results (ie INR, PT, APTT, etc).

On the other hand, and in addition to continuous pressure (ie gentle hand pressure, additional stitches), cooling the site (ie Ice Pack), using vasoconstrictors (usually with the local anaesthesia solution) and following an atraumatic approach to surgery, with clever flap designs that decrease the number of blood vessels severed and limit haemorrhage, there are other materials that could be applied to the bleeding site in order to reduce or stop the bleeding. Examples are:

- *Surgicel* (oxidized cellulose): to provide framework for clot formation;
- *Gelfoam* (absorbent gelatine sponge): that stimulates the intrinsic clotting pathway;
- *Thrombostat*: topical thrombin;
- *Kaltostat* (calcium alginate): that releases calcium and aids haemostasis;
- *Ferric/calcium sulphate*: that blocks the vascular channels (in multiple small bony bleeding points);
- *Tranexamic acid* (mainly as mouthwash): given pre- and post-operatively to aid haemostasis by inhibiting fibrinolysis;
- *Collaplug* (collagen): that acts as a mechanical tamponade, stimulates platelet adhesion and aggregation, activates factor VIII and releases serotonin (which in turn causes vasoconstriction);
- *Amicar* (epsilon-amino caproic acid), bone wax, and many others.

The second part of this article will cover, in depth, the management of both congenital and acquired bleeding disorders in the dental practice.

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