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Special Care Dentistry: Part 1. Dental Management of Patients with Inherited Bleeding Disorders

Abstract: The most common cause of excessive bleeding is idiopathic, but bleeding can also be caused by inherited or acquired conditions associated with vascular defects, platelet defects or coagulation disorders. This paper will cover inherited bleeding disorders. Every clinician will encounter a patient who complains of prolonged bleeding following certain procedures; most commonly dental extractions. In the majority of cases the cause is often a local one and can be managed using simple local measures. However, prolonged post-operative bleeding following dental treatment might be one of the first signs of a bleeding disorder in an undiagnosed patient, necessitating referral for further investigations. Some patients may present with an already confirmed diagnosis of a bleeding disorder, requiring appropriate treatment planning and dental management in an appropriate setting with haematological advice. This paper will provide guidance on how to achieve this.

Clinical Relevance: To update clinicians on the dental management of patients with inherited bleeding disorders and how to decide the most appropriate setting for the provision of dental care.

Dent Update 2013; 40: 613–628

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Occasionally, a prolonged case of bleeding in the dental setting may be the first indication that a patient may have an undiagnosed bleeding disorder which requires further investigation. There are also certain inherited connective tissue disorders which predispose to bleeding problems and the clinician will need to be aware of them before commencing certain procedures. Patients who already know that they have a bleeding disorder are able to alert the clinician during the medical history process so that any invasive treatment can be appropriately planned and managed to avoid any complications. Routine dental procedures often cause oral soft tissue trauma, causing local haemorrhage, but in an individual with an inherited bleeding disorder this may be more problematic; for example, fatal haemorrhage has been reported following regional analgesia for dental treatment in haemophiliac patients.[1,2] Therefore, some patients may require prophylactic measures pre-operatively, special precautions peri-operatively and careful management post-operatively.[3] Patients with hereditary bleeding disorders are usually registered with a Haemophilia Reference Centre. For patients with a mild to moderate bleeding disorder, a shared care approach might be appropriate, alternating care between specialist hospital care and primary dental care (including specialists in the salaried dental services), depending on the procedure and the nature and severity of the bleeding disorder. Often, a hospital setting is the most appropriate setting for patients with a severe bleeding condition and associated complications, such as HIV, Hepatitis C or inhibitors, who require invasive dental treatment. There is research evidence that has suggested that known haemophiliacs delay and

avoid dental care for fear of bleeding from dental procedures so that they require more complex treatment and management by the time that they present.[4] Fiske *et al*[5] reported many barriers to accessing dental care, including travelling to specialist centres, waiting times, increased treatment needs and cost. However, there is a dearth of evidence-based guidelines and protocols in managing patients with inherited bleeding disorders[3] and this paper aims to provide some further guidance on this subject.

Haemostasis

Haemostasis depends on interactions between the blood vessel wall, platelets and the clotting pathway. Once a vessel sustains an injury, there is an automatic reflex vasoconstriction to stem the blood flow to the injured area. This process activates platelets as well as the clotting pathway. Activated platelets release more vasoconstrictor agents and also adhere to collagen in the vessel wall, via specific membrane attached receptors. These activated platelets then spread along the vessel wall to where the platelet membrane helps to provide a surface for the interaction of coagulation factors where thrombin formation encourages further platelet fusion. Coagulation is initiated by tissue factor in response to the injury and involves a series of enzymatic reactions (Figure 1). Until recently, it was thought that the intrinsic and extrinsic pathways were separate but it is now recognized that Factor VIIa complex activates both systems as they are linked leading to the activation of prothrombin and conversion of soluble plasma fibrinogen to a stable fibrin clot, which is the endpoint of the clotting cascade.[6] Therefore, a bleeding disorder arises if there is a problem in any part of the haemostatic or clotting pathways, and can be acquired or congenital.

Clinical manifestations of inherited bleeding disorders

Ecchymoses are bruises due to larger extravasations of blood and can measure greater than 1 cm. Inherited coagulation defects, such as haemophilia, usually present as ecchymoses where bleeds occur in muscle (haematoma) or in joints (haemarthrosis – Figure 2). Recurrent bleeds in joints in severe haemophiliacs can cause joint deformity, and some severely affected haemophiliacs may have had joint replacement surgery.[7]

Vascular disorders

As the initial haemostatic response is a vascular one, inherited disorders affecting haemostasis due to vascular disorders will be discussed first. None of the tests mentioned above applies to vascular disorders. It might be helpful to explain certain vascular disorders and how they can cause bleeding problems.

Marfans syndrome

This is an autosomal inherited connective tissue disorder with skeletal, ocular, cardiac and dermatological malformations.[8] Prevalence is 2–3 per 10,000 and affects both sexes equally. It is the most common genetic connective tissue disorder. There is usually great variation in the phenotype within families with the same genetic condition. The diagnosis for Marfans syndrome is usually clinical. The following are affected:

- Skin with striae;
- Heart and blood vessels – thoracic aortic dilation/rupture/dissection, aortic mitral valve/prolapse, mitral regurgitation, abdominal aortic aneurysm, cardiac dysrhythmia;
- Eyes-lens dislocation, glaucoma and myopia;
- Joints – hypermobility, arthralgia;
- Skeleton – misshapen chest;
- Arachnodactyly;

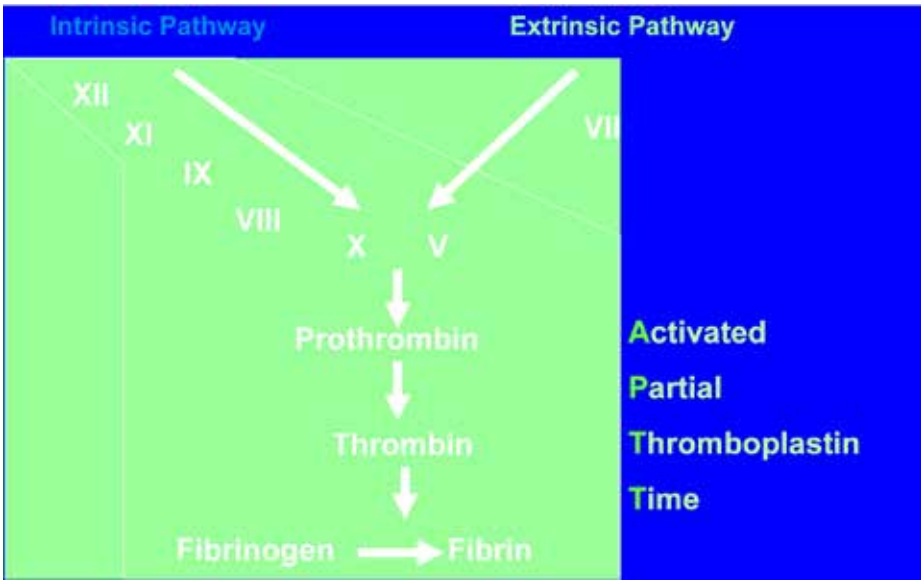

Figure 1. Clotting cascade.

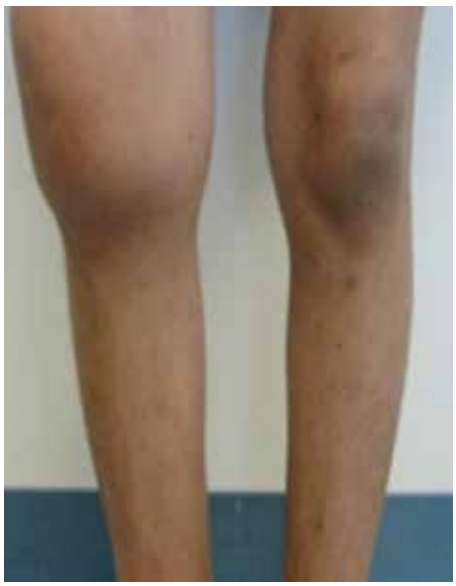

Figure 2. Haemophilia patient with haemarthrosis of the right knee showing a large swelling. (Reproduced with permission from: Giangrande P. *Haemophilia. Best Practice*. London: BMJ Group, 2012. **http://bestpractice.bmj.com** (last accessed 2 April 2012).

■ Maxillary/mandibular retrognathia, long face, high-arched palate.

The condition can be asymptomatic, although patients are usually longer and thinner than average. Fingers and toes are also usually long and thin and patients may not be aware of a bleeding problem.

Osler–Weber–Rendu syndrome

This is also known as Hereditary Haemorrhagic Telangiectasia (HHT/HHT1).

This is a hereditary condition due to a gene mutation. It is inherited as an autosomal dominant trait with a high penetrance, as 97% of people affected exhibit symptoms.[9] The prevalence is between 1 in 5000 and 1 in 8000 of the population. There is vascular dysplasia leading to a telangiectasia (small dilated blood vesssels) and arteriovenous malformations in the skin, mucosa (which can be evident on extra-oral examination) and viscera. Interestingly, the condition usually first presents in adolescence. Most people (62%) are diagnosed by the age of 16, with over 90% of cases presenting with recurrent epistaxis. The nasal mucosa, lips and tongue usually develop mucocutaneous lesions which are sharply demarcated red-papular, macular or spider-like lesions and could help to alert a clinician about problems if invasive procedures were carried out. These lesions can also occur in the conjunctiva, upper respiratory tract, gastrointestinal tract, bronchi, brain and the liver. Cutaneous telangiectasia does not present until adult life. Investigations include capillary microscopy, computerized tomography (CT), magnetic resonance imaging (MRI) and angiography. The differential diagnosis is von Willebrand's disease.

Ehlers-Danlos syndrome

This is a rare autosomal dominant condition which occurs in 1 in 5000 live births. There is disruption of proteins leading to fragile connective tissue and causes laxity of joints or ligaments, as well as fragile skin.[10] It usually presents as ready bruising (due to abnormal bleeding), dissecting aortic aneurysm (at an early age), joint laxity and hyperplasticity of skin. Diagnosis is usually based upon the clinical presentation.

Dental management for vascular disorders

Vascular disorders rarely cause bleeding problems and can be managed in primary care. However, it is important to aid haemostasis by using thorough local measures such as applying pressure, suturing, using haemostatic agents and delivering routine post-operative instructions, both verbally and in writing.

Platelet disorders

Whilst vascular disorders can be managed using local measures, the management of platelet disorders is less straightforward. For people with platelet problems, it is necessary to liaise with the patient's haematologist for certain dental procedures, depending on the severity of the condition and the procedure being carried out.

Platelets originate from the megakaryocyte residing in the bone marrow. The life-span of a platelet is about eight days. The normal platelet level is 150–400 x 10^9/l.[11] Inherited platelet abnormalities tend to affect platelet function rather than platelet number, resulting in a qualitative defect.

Inherited qualitative platelet abnormalities

In inherited qualitative platelet abnormalities, the platelet count, which is taken as part of a Full Blood Count (FBC) test, is normal but the bleeding time is prolonged, as it is platelet function that is impaired (Table 1).

Glanzmann's disease

Glanzmann's disease is also known as Glanzmann's thrombasthenia. It has an autosomal recessive pattern of inheritance and usually presents in infancy or early childhood.[12] Commonly presenting symptoms include petechiae, following minimal or unrecognizable trauma, or epistaxis, which can be severe. Tests will reveal a normal platelet count but an increase in bleeding time, which is associated with a failure of platelet aggregation (Table 1). This is due to deficient or abnormal glycoprotein receptors present on platelet membranes. There are different variants of Glanzmann's disease which vary in severity of presentation. Carriers of the disease usually have no significant bleeding symptom.

Bernard Soulier syndrome

Bernard Soulier syndrome is a congenital thrombocytopenia, although platelets are larger in size.[13] It is a qualitative disorder due to an absence of platelet membrane glycoprotein resulting in defective platelet adhesion. It is an extremely rare disorder of less than one per million and follows an autosomal recessive pattern of inheritance. Its symptoms are similar to those of Glanzmann's disease. Again carriers of the disease present no significant problems.

It is necessary to find out the current platelet activity levels to know how to manage and plan the patient's dental care. As with any bleeding disorder, the following should be discussed with the patient's haematologist:

■ The severity of the reduced level of platelet activity;
■ Planned dental treatment and the bleeding risk;
■ Patient's response to any previous dental treatment.

Management includes avoiding trauma as well as avoiding analgesics, such as aspirin, owing to its antiplatelet effect. Minor bleeding intra-orally can be managed using tranexamic acid, which is an antifibrinolytic agent. It has to be prescribed by a haematologist (as it is not readily available in primary care) to aid haemostasis and any minor surgery should be covered with DDAVP (Table 2).[14] Severe cases might warrant platelet transfusions but carry the risk of patients developing auto-antibodies, known as platelet inhibitors, which inhibit platelet function. All local measures should be carried out to aid haemostasis once the patient has been managed by the haematologist for his/her platelet problem.

Inherited clotting disorders

In the vascular or platelet disorders mentioned so far, post-operative problems following an extraction usually present as prolonged bleeding immediately after the event as part of the initial response to an injury. With clotting disorders, the normal vascular and platelet response will initially mask any problem due to

Test for platelet activity	Test for clotting factors	Procedure	Inherited bleeding disorder
Bleeding time		A tiny cut is made into the skin and the time taken for the bleeding to stop is then measured. It usually takes between 3–8 minutes[8] This test has been superseded by the platelet aggregation test	Bleeding time is prolonged in: von Willebrand's disease Bernard Soulier syndrome (>20 minutes)
Platelet aggregation test		Automated method of measuring the rate and the extent to which platelets aggregate after a chemical is added which stimulates aggregation Tests platelet function where platelet count is normal (150–400x109/l)[8] Helps to determine the cause or potential for excessive bleeding and to facilitate monitoring/evaluation of platelet function in people who bruise easily or have prolonged bleeding or are taking antiplatelet medication	Glanzmann's disease Bernard Soulier syndrome
Blood film (to estimate platelet size)		Blood sample is examined under a microscope	Increased platelet size in Bernard Soulier syndrome
	Activated partial thromboplastin time (APTT)	Performance indicator measuring the efficacy of both the intrinsic pathway and the common coagulation pathway Detects abnormalities in clotting Termed partial thromboplastin time due to the absence of tissue factor which initiates the extrinsic pathway APTT is considered normal if the control APTT and the test APTT are within 10 seconds of each other. Control APTT times are usually 25+/-10 seconds[8,31]	APTT is prolonged in: 1.von Willebrand's disease 2. Haemophilia

Table 1. Blood tests for patients with bleeding disorders.

vasoconstriction and a stable platelet plug will be formed. As the clotting response occurs last, patients will then usually complain of a delayed oozing from the socket some time after the event.

The most commonly inherited clotting disorder is von Willebrand's disease followed by Haemophilia A or Haemophilia B. These disorders are usually due to a deficiency or a lack of a specific haematological factor. For the purpose of this paper, the most commonly occurring inherited disorders will be discussed, although it is important to know that there can be deficiencies in other factors within the clotting pathways.

von Willebrand's disease

Aetiology

This is the most common inherited bleeding disorder and affects about 1% of the population.[14,15,16] Whilst both sexes are equally affected, as it has a dominant inheritance pattern, several studies have reported plasma von Willebrand's Factor to be lowest in blood group O patients, leading to a misdiagnosis of type 1 von Willebrand's disease. Rarely, cases are acquired and associated with hypothyroidism. von Willebrand's Factor is synthesized in the endothelium and megakaryocytes. It has binding sites for collagen and for platelet glycoprotein receptors. von Willebrand's Factor is a carrier protein for Factor VIII and increases its half-life by protecting it from proteolytic degradation. In addition, it also aids platelet adhesion to damaged vascular endothelium and enhances platelet aggregation. Platelet Type von Willebrand's disease is also known as pseudo von Willebrand's disease, which is an autosomal dominant condition and is inherited by gaining functional mutations of the von Willebrand's Factor receptor on platelets. It is similar to Type 2B von Willebrand's disease. Table 2 presents a detailed classification of von Willebrand's disease and its treatment.

Type	Percentage	Type of vWD defect	Factor VIIIc	Desmopressin/DDAVP	Factor VIII replacement
1	80	Partial quantitative Decrease of vWF	May be normal	Nasal spray	-
2A	15	Mainly qualitative Defect of vWF	Reduced	Nasal spray	+ -
2B	Rare	Mainly qualitative Defect of vWF	Reduced	Contra-indicated	+
2C	Rare	Mainly qualitative	Reduced	Nasal spray	+ -
2M	Rare	Mainly qualitative Defect of vWF	Reduced	Contra-indicated	+
2N	Rare	Mainly qualitative Defect of vWF	Reduced	Nasal spray	+ -
3	5	Complete lack of vWF	Reduced	Contra-indicated	+

Table 2. Classification of different types of von Willebrand's disease and its treatment.[14] Factor VIII might be implicated for some types of von Willebrand's disease, depending on the procedure being carried out and the severity of the condition.

Clinical presentation

Bleeding has similar features to those caused by platelet dysfunction, when compared to bleeding as a result of clotting problems, such as haemophilia. The most common presentation is bleeding from the mucous membranes, resulting in menorrhagia, gastrointestinal bleeding, epistaxis, and purpura of the mucous membranes and skin. People with mild forms of the disease may go undetected until there is an episode of prolonged bleeding associated with a dental extraction, severe menstrual bleeding or childbirth.

Diagnosis

von Willebrand's disease is diagnosed by:

- A prolonged bleeding time;
- Usually a prolonged APTT.

As Factor VIII, is a glycoprotein of the following: Factor VIIIR.Ag (also known as von Willebrand's Factor, which binds to platelets and is a carrier for Factor VIIIc); Low Factor VIIIc, which participates in the clotting pathway; and VIIIR:RCO (Ristocetin co-factor) levels, which enhance platelet aggregation, in addition to a prolonged bleeding time and prolonged APTT, there are lower levels of Factor VIIIR.Ag (von Willebrand's Factor) and VIII.RCO in a Factor VIII assay of a patient with von Willebrand's disease.

Treatment

Table 3 presents a summary of systemic therapy to manage bleeding disorders. *Desmopressin* is usually the treatment of choice and is given via a nasal spray (Table 3).[14] However, it is contra-indicated in type 2B von Willebrand's disease as it can stimulate release of dysfunctional von Willebrand's Factor. Type 3 von Willebrand's disease should be managed as severe Haemophilia A, as there is almost a complete lack of von Willebrand's Factor. However, only human plasma contains von Willebrand's Factor, which is effective in treating most people with severe von Willebrand's disease. Recombinant Factor VIII, which has to be genetically engineered, is therefore a non-viable treatment as no recombinant von Willebrand's Factor is available yet, but is being developed.

Oral features

There is usually bleeding from the mucous membranes as well as purpura. Gingival haemorrhage is common. Patients will complain of prolonged bleeding following dental extractions or other invasive dental procedures.

Dental management

A risk assessment must always be carried out prior to any dental treatment due to the increased risk of bleeding. It is mandatory to seek haematologist advice prior to any dental treatment associated with an increased risk of bleeding. Therefore a detailed history and examination must be taken. One should always ask about how any previous dental extractions were managed and if there was prolonged bleeding. The disease severity, procedure versus bleeding risk, previous dental management and response to systemic haematological therapy should all be discussed with the haematologist.[14]

All invasive procedures such as extractions, minor oral/periodontal surgery, implants and deep scaling require haematological cover, depending on the severity of von Willebrand's disease.

Medication	Mode of activity	Route of administration	Dosage	Condition
DDAVP	Synthetic hormone which induces the release of Factor VIIIc, von Willebrand's Factor and tissue plasminogen activator from vascular endothelium	IV infusion one hour before dental treatment 10mg/kg in 20 ml normal saline IV infusion one hour before dental treatment 10mg/kg in 20 ml normal saline over 20 minutes (Multiple DDAVP infusions have been associated with a reduced response) 2–3 fold rise in Factor VIII activity after 90 minutes with a mean half-life of 9.4 hours.[19] More appropriate in mild cases and can only be repeated after 48 hours Factor VIII might be more appropriate to manage post–operative surgical cases Intranasal spray chairside It can also be given subcutaneously	IV infusion over 20 minutes of 0.3–0.5 mcg/kg	
Tranexamic acid	Synthetic derivative of the amino acid lysine Reversible blockade of lysine binding sites on plasminogen Topical alternatives have proved to be a successful alternative to systemic preparations in selected cases[20] although both systemic and topical alternatives have been shown to reduce blood loss[19]	Orally (contra-indicated in patients with residual blood clots) Nausea is a common side-effect Topically	Dose of 1 g (30 mg/kg) four times daily starting one hour before the procedure, or as an infusion 10 mg/kg in 20 ml normal saline over 20 minutes Topical 5% solutions used as a mouthwash 10 ml qds for 1–2 weeks after scaling or dental extractions and placed over socket	
Recombinant Factor VIII	Replaces missing Factor VIII IV infusion	IV infusion Half-life 12 hours	The intranasal spray is delivered as 1.5 mg desmopressin per ml. Each 0.1 ml pump spray delivers 100–150 mcg dosage	

Table 3. Systemic therapy to manage bleeding disorders[14,19,20,32,33] (no bariatric upper doseage limit specified). Haemostatic local measures are essential.

Essentially, management is the same as for Haemophilia A. There is no evidence that having von Willebrand's disease is a contra-indication for having implants. Patients who have poor oral hygiene, florid gingivitis but minimal pockets may also require cover, depending on the severity of their von Willebrand's disease. Following dental treatment, antiplatelet medication for analgesia, such as aspirin or Ibuprofen are contra-indicated. Paracetamol is the usual drug of choice, or combination analgesia such as Co-Codamol™, for further pain relief.

Haemophilia A

Haemophilia A has a prevalence of 1 in 10,000 people and is inherited as a sex–linked recessive trait and therefore affects males.[7,14] However, spontaneous mutations may still occur as 150 point mutations have been characterized. In a third of cases there is no family history. Although females are carriers of the condition, they may still exhibit symptoms of haemophilia and may require haemaotological management through a Haemophilia Reference Centre prior to any invasive dental procedures requiring surgery or extractions, depending on their Factor VIII levels. It is also important to know that haemophilia can also be acquired in later life, but this is extremely rare.

In haemophilia, the diagnostic laboratory findings can be summarized as a prolonged activated partial thromboplastin time (APTT), normal bleeding time and low Factor VIIIc levels (Table 1).

Haemophilia presents as bleeding into muscle or joints (Figure 2). In severe cases, where haemarthrosis is

recurrent, joint deformity may necessitate joint replacement. More seriously, a cerebral bleed after a mild injury can lead to fatal complications. In some cases, post extraction haemorrhage can lead to a diagnosis of haemophilia. Initially, vascular and platelet responses of the haemostatic process operate and bleeding stops, but then there is oozing from the extraction site due to absence of clotting factor. Bleeding into the larynx or pharynx after inferior dental nerve block administration can obstruct the airway with fatal consequences.[7]

Classification

Normal plasma contains 1 unit of Factor VIII per ml. This level is classified as 100%. Haemophilia can be classified as being mild, moderate or severe, depending on the Factor VIII levels in plasma.

Treatment

The main concern is the ability to control any post–operative bleeding related to dental procedures, as local measures alone are insufficient. The severity of bleeding depends on the levels of Factor VIIIc and the degree of trauma. Guidance should always be sought from the patient's haematologist prior to the procedure. The main aim of providing coagulant cover is to raise the existing Factor VIII levels to normal to achieve adequate haemostasis following dental treatment. Normal Factor VIII levels can be achieved by the haematologist administering medication outlined in Table 3.

Most people with mild to moderate levels of Factor VIII can manage their coagulant cover prior to dental treatment through liaison with their Haemophilia Reference Centre. Patients who are most severely affected self-administer Factor VIII prophylactically to prevent joint damage. This necessitates injections three times weekly.

Factor VIII levels of 50–75% are required for minor surgery, such as dental extractions. Patients can be managed post-operatively with tranexamic acid and local measures. For any persistent bleeding, Factor VIII must be administered to manage the problem. For patients having a general anaesthetic, replacement Factor VIII must be administered to prepare the patient for endotracheal intubation, which is likely to cause bleeding due to nasal trauma. Any major surgery should be carried out in a hospital setting and a bed arranged to manage any anticipated complications, where appropriate, in close consultation with the Haemophilia Reference Centre.

Future treatments: gene therapy

Factor VII and IX genes were isolated in the 1980s leading to the development of Recombinant Factor concentrates, although once they enter the circulation these proteins disappear within several hours. Gene therapy makes it possible to deliver the normal missing Factor gene directly into cells by injecting it into a virus which acts as a vector for the Factor VIII gene, which is then injected into the body and invades the host's hepatocytes.[17] Clinical trials indicate that gene therapy may be promising but their discussion is outside the scope of this paper.

Challenges to management of haemophilia patients

These include:

- Hepatitis/HIV;
- Inhibitors;
- Mobility;
- vCJD if blood transfusions have been received.

Hepatitis/HIV

Treatment with contaminated plasma products before 1990 resulted in increased rates of Hepatitis B and C viruses, as well as HIV. The World Federation of Haemophilia[18] conducted a global survey and found that, while 31% of haemophiliacs died from bleeding episodes, a further 20% died from AIDS-related illness and 13% from liver disease. Stigma-associated with blood-borne viruses is a well recognized barrier to care for these patients, despite clinicians being advised to follow universal infection control guidelines.

Problems of Hepatitis C and HIV with regards to dental management include:

- Increased bleeding due to liver damage or thrombocytopenia associated with HIV;
- Delayed healing;
- Impaired drug metabolism associated with hepatitis;
- Dental problems such as caries, periodontal disease, recurrent oral infections, denture problems associated with dry mouth as a result of Hepatitis C/HIV infection;
- Side-effects of any medication including xerostomia.[11]

Therefore, patients who have moderate to severe haemophilia, with complications from co-infection, are best managed in a specialist setting, depending on dental treatment required.

Inhibitors

Inhibitors are auto-antibodies to Factor VIII. Their development remains a major complication in the management of Haemophilia A and has an impact on success as well as the cost of treatment.[19] Inhibitors are more likely to develop in people with severe haemophilia. Both environmental and genetic factors have been implicated in playing a role in inhibitor development.[20,21]

It is vital to ask the patient when taking a history if the patient has inhibitors and, if so, to find out how the patient was dentally managed previously. The haematologist must always be consulted and patients with inhibitors must be treated with caution when carrying out surgical treatment, including administering inferior dental nerve block injections. Traumatic procedures must be avoided unless absolutely necessary.

In patients requiring invasive treatment, Human Factor VIII Inhibitor Bypassing Fractions (FEIBA) can be administered intravenously prior to treatment. These bypassing fractions work by activating Factor X directly, thus bypassing the intrinsic pathway of the clotting cascade altogether. Unfortunately, these products can cause uncontrolled coagulation leading to thromboses. An alternative is to administer 1000,000 units of activated Factor VIIa (Novoseven) which directly acts on the surface of platelets. Using additional haemostatic adjuncts, such as *Tisseel* (a highly concentrated combination of fibrinogen, thrombin and Factor XIII, which crosslinks the clot), together with topical tranexamic acid, helps to stabilize the clot post-operatively. These products are not readily available in primary care and therefore these patients are usually best managed in a hospital setting. Platelets may also be administered to aid

haemostasis. Patients with inhibitors require careful post-operative follow-up care.

Mobility

Access and mobility problems may exist as a result of joint deformity, which is common in severe haemophiliacs. This is due to recurrent bleeds into joints (haemarthrosis – Figure 2) and is a main reason why some haemophiliacs give themselves Factor cover at home prophylactically. It is not uncommon for some haemophiliacs to have prosthetic joint replacements. Joint problems can restrict mobility and therefore clinicians need to be aware of how best to accommodate this group of patients (Figure 2).

vCJD if blood transfusions have been received

It is known that batches of products to treat Haemophilia/von Willebrand's disease have been made from the blood of donors who have been diagnosed later with vCJD.[22] People who have received British blood products between 1980 and 2001 are at risk. There has been a recent identification of CJD in a patient with haemophilia where Factor VII concentrates from human plasma have been implicated as a likely cause. Fortunately, dentistry is classified as a low risk procedure and universal infection control precautions apply.

Dental management

There is research evidence that has suggested that known haemophiliacs delay and avoid dental care for fear of bleeding from dental procedures so that they require more complex treatment and management by the time that they present.[4]Again, it is essential to liaise with the patient's haematologist, to ensure that patients attend for regular dental check-ups and treatment. It is also useful to find out if patients are compliant with medication or advice given by the haematologist. Table 4 outlines medical and dental management in relation to disease severity.

Prevention

Prevention should be started as early as possible in childshood when the teeth begin to erupt. Early prevention will help to reduce the need for dental treatment in the future and hence the need for repeated cover, which is not only uncomfortable for the patient, but is also costly, and repeated cover can lead to the formation of inhibitors, especially in younger patients. It is important to institute the use of fluorides from childhood, fissure sealants/preventive resin restorations and to emphasize the importance of sugar restriction, good oral hygiene and regular check-ups from an early age. An orthodontic assessment should also be carried out at an early stage to predict any future problems, such as overcrowding, which might be avoided. It is vital that patients discharged from paediatric dental services are seamlessly transferred to adult special care services for continuity of care.

Pain and anxiety control

Anxiety and drug dependence have been mentioned as one of the main barriers to managing patients with congenital bleeding disorders. Means of control include:

- Local anaesthesia;
- Conscious sedation;
- General anaesthesia.

Local anaesthesia

Webster *et al*[23] reported an 80% chance of haematomas for haemophiliacs not treated with cover prior to mandibular block injection, whilst infiltrations, intraligamentary, intraosseous and pulpal injections were safer. The World Federation of Haemophilia recommends no Factor cover replacement for buccal infiltrations.[24] Therefore, patients who require restorations in upper teeth can be managed without additional cover in primary care. Local anaesthesia, delivered as an inferior dental nerve block, posterior superior alveolar nerve block, lingual infiltrations or injections in the floor of the mouth must always be appropriately covered by the patient's haematologist prior to dental treatment. Several authors advocate a Factor level of 50% pre-operatively due to reported cases of life-threatening bleeding following inferior dental nerve block or exodontia.[25,26] Failure to achieve this can result in the life-threatening complication of haemorrhage which compromises the airway. Patients with inhibitors must always be monitored post-operatively in spite of cover. Alternative methods of local anaesthesia must be tried, such as infiltrations using Articaine where appropriate. Buccal infiltration of the mandibular first molar with 4% Articaine 1:100,000 epinephrine has resulted in a higher success rate, compared with 2% Lidocaine with 1:100,000 epinephrine in non-haemophiliac patients.[27] It is also more comfortable compared with an inferior dental nerve block injection.[28] However, it is less successful with mandibular second and third molar teeth because of more dense cortical bone. Infiltration anaesthesia and mental block injection is safe in the lower arch without haematological cover and this can be carried out in primary care. Lingual infiltration must be avoided as blood can track down into lingual spaces. Verbal and written post-operative local anaesthetic instructions are essential otherwise additional haematological complications may arise if instructions are not followed.

Conscious sedation

Anxious patients can be treated with inhalation sedation or conscious sedation using Midazolam. In the authors' experience,
there should be no extra problems of haematoma formation at the cannulation site if there is a mild to moderate bleeding disorder, or if the patient has received haematological cover.

General anaesthesia:

A thorough pre-operative assessment in close consultation with the anaesthetist, haemaotologist and the dentist is essential. Nasal intubation should be avoided if possible. 'In-patient' general anaesthesia should be considered for those patients with inhibitors who require complex surgery. Patients who have severe haemophilia may also benefit from staying overnight, depending on the dental procedure being carried out under guidance from the haematologist.[11]

Conservation and fixed prosthodontics

Katz and Terezhalmy[29] stated that certain precautions, such as application of rubber dam and careful placement of the clamp avoiding soft tissue trauma, as well as careful placement of matrix band, can minimize bleeding. High-speed suction should be used with caution to avoid mucosal trauma. Conservative extension of gingival margins and supragingival crown preparations should be considered, where

Severity	Factor VIII levels	Symptoms	Dental treatment	Treatment
Severe	>1% (1 iu/dl)	Spontaneous bleeding usually in childhood Bleeding into muscles/ joints (haemarthrosis) Easy bruising Prolonged bleeding following minor injuries /trauma	Scale and polish Conservation Inferior dental nerve block injection Extractions	DDAVP(Subject to response test) Factor VIII Factor VIII and tranexamic acid
Moderate	1–5% (FVIIIC >5 iu/dl)	Prolonged bleeding following mild to moderate trauma/surgery/extractions	Scale and polish Conservation Inferior dental nerve block injection	DDAVP (Subject to response test) DDAVP and tranexamic acid
Mild	> 5% (FVIIIC >5 iu/dl)	Prolonged bleeding following mild trauma	Scale and polish Conservation Inferior dental nerve block injections Extractions	Nil Nil for buccal infiltrations DDAVP (Subject to a response test) DDAVP and post-operative Tranexamic acid

Table 4. Classification of haemophilia symptoms associated with each category and dental management.

appropriate. Tranexamic acid can be used topically to control any local bleeding. Non-metal impression trays can minimize soft tissue trauma. Fissure sealants should be considered at an early stage as part of the prevention regime. Trauma from a saliva ejector can be avoided by placing gauze beneath it.[28] The authors recommend considering the use of more acceptable pain-free restorative techniques, such as using atraumatic restorative technique (ART) or air abrasion/Carisolv™ gel, where appropriate.[30] Any sharp-edged restorations or dentures must be smoothed.

All patients requiring endodontic treatment should be appropriately covered for their bleeding severity and the proposed procedure. The main concern is to avoid instrumentation through the apex. Using an apex locator can reduce this. Intrapulpal anaesthesia can also help to reduce the risk of bleeding.

Periodontology

In mild haemophiliacs, scaling can usually be carried out without problems using tranexamic acid, depending on their oral hygiene and the extent of pocketing. It is possible to scale tooth by tooth in mild haemophiliacs. If in doubt advice should be sought from the haematologist. In moderate haemophiliacs, DDAVP as well as tranexamic acid might be required, if oral hygiene is poor and pockets are deep (>3 mm). Severe haemophiliacs may require Factor cover and tranexamic acid cover. Any additional treatment, such as conservation, should also be carried out at the same visit to avoid the need for repeat cover. Oraqix non-injectable anaesthetic gel, with a 2.5% Lidocaine and 2.5% prilocaine formulation, for placement with a blunt-ended needle tip into periodontal pockets prior to scaling, is a viable alternative to using local anaesthesia Any periodontal surgery would require appropriate cover, depending on the severity of the condition. A level of Factor VIII at 50–75% is necessary.

Orthodontic treatment

There is no contra-indication to having orthodontic treatment. However, care must be taken with any sharp edges to orthodontic appliances as these can induce bleeding.

Exodontia/dento-alveolar surgery/ maxillofacial surgery

Extractions must be carefully planned, with appropriate special tests and radiographs having been taken at the outset to identify any other problems. When staging extractions, it is important to weigh up the risk of repeated cover and managing bleeding risk. Repeated recombinant cover has been implicated in developing inhibitors. Factor VIII levels should be 50–75%[14,29] for dental extractions or dento-alveolar surgery, which the haematologist will prescribe according to the dental treatment plan. Lingual tissues should be left undisturbed to prevent blood from tracking down the mediastinum. Local measures must be implemented with minimal trauma. Good wound cleaning and placing resorbable sutures, such as Vicryl, help to reduce the risk of further bleeding on removal as they help to stabilize the gum flap. Post-operative bleeding causing blood to track down the mediastinum is usually an indication of inadequate cover. Topical tranexamic acid can be placed into the socket to aid haemostasis. Haemostatic agents, such as Gelfoam and Instat, which

are of bovine origin and contain collagen, can be used. Surgicel is of synthetic origin and mainly consists of cellulose but should be used with caution owing to its acidic pH, which can irritate the socket. Fibrin sealant, which mainly consists of fibrinogen and thrombin, can provide rapid haemostasis, as well as tissue sealing and adhesion. Owing to a concern regarding vCJD, recombinant fibrin glues are becoming more readily available.

Patients should be instructed to have a soft diet for a week following surgery. Antimicrobials are only indicated where there is a risk of infection inducing secondary haemorrhage due to enhanced fibrinolysis. The patient should be warned against any swelling, dysphagia or hoarseness, indicating haematoma formation and risk to the airway. It is important to consider compounding factors such as delayed healing, increased risk of infection and prolonged bleeding due to thrombocytopenia in some patients with HIV disease.

When planning maxillofacial surgery, Factor VIII replacement is necessary for ALL haemophiliacs at a level of 75–100% one hour post-operatively.[14] Tests in addition to Full Blood Count and haemostatic screening include specific antibody tests, fibrinogen estimation, viral screen and liver function tests. Blood is grouped and cross-matched in case of an emergency.

Post-operative pain management should exclude antiplatelet analgesic drugs such as aspirin. Paracetamol or combination drugs with codeine/paracetamol may be a suitable alternative, although care should be taken when prescribing opioids for pain management after conscious sedation owing to the enhanced sedative effects following treatment on the same day.

Treatment in primary care or secondary care

Whilst this largely depends on the patient's bleeding risk, dental procedure and medical management, it is also important to consider clinician confidence or training. Most mild cases can be managed in primary care using local measures for simple procedures such as examination, cleaning and restorations which require infiltration anaesthesia only. More invasive dental procedures in patients with a moderate to severe bleeding disorder should be referred to a specialist setting, depending on the bleeding risk.

Conclusion

Patients with vascular inherited disorders can usually be managed in primary care using local post–operative measures. Some patients with inherited bleeding disorders may not be diagnosed until they have received invasive dental treatment. Therefore, clinicians need to be aware of identifying those people at risk so that their treatment can be better managed. Clinicians may need to make a decision on whether some people can be treated on a shared care basis, alternating between specialist services and primary care, where appropriate.

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Book Review

Nothing But The Tooth: A Dental Odyssey.
By Dr Barry KB Berkovitz. London: Elsevier, 2012 (248pp, £45.99). ISBN: 978-0-12-379190-6

Question: Did you know that?:
- The teeth of sharks and other non-mammalian vertebrates (fish, amphibians and reptiles) have a simple shape and do not have roots?
- The teeth in opposing jaws do not meet so that the function of the teeth is to help grip food and stop it escaping before swallowing it whole?
- In the embryos of many reptiles, rudimentary teeth start to develop but are lost without ever becoming functional?
- The fish of the cichlid family (known as Alluaud's Haplo) possess teeth not only in their jaws but also on bony structures located in the pharynx?

If these are the sort of facts which interest you, then this is the book for you. While it may, at first, look like a textbook, it is much more than this and reads almost like a novel crammed with interesting facts related, more or less, to teeth. The author, Barry Berkovitz, is well known for his career in teaching and researching the structure and function of teeth, and this book illustrates the vast array of interesting material that he amassed during his career, which goes well beyond the comparative anatomy that some of us were taught.

The book starts with a chapter on the jaws of piranhas and explains their extremely specialized teeth, which are put to good effect when these fish hunt in packs. This chapter is followed by one on tusks and ivory. Of note are the facts that, while elephant tusks represent this animal's central incisors in the upper jaw, the tusks of the hippopotamus represent its upper incisors and lower canines and walrus tusks are its upper canines. This chapter then goes on to describe other animals and their tusks. Diverting away from teeth for a chapter, chapter 3 describes how two young dentists (Horace Wells and William Thomas Green Morton) changed the history of surgery by their experiments on anaesthesia. The book returns to teeth for subsequent chapters: teeth in unlikely places; how teeth can reveal where you come from and what you are; and why we cannot have lots of sets of teeth (like a shark!). Believe it or not, there are drawbacks to that. Chapters 14 and 15 cover two notorious people with dental connections and two famous people with dental connections. One of these is Paul Revere, whose exploits are well versed in American history. He was originally a silversmith whose company was struggling, thereupon he decided to enter the dental profession (easy to do in 1768!).

The final chapter of this entertaining, interesting book brings us to a subject in vogue today, *A winning smile*, but these are smiles with a difference since this chapter deals with a variety of different types of dental modification.

There is no question that this book fulfils the original objective of the author when he collected the material, namely, to demonstrate how enjoyable the subject of teeth can be. It comes highly recommended!

FJ Trevor Burke
Editorial Director