Guidance on the dental management of patients with haemophilia and congenital bleeding disorders

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IN BRIEF

- Aims to increase understanding of bleeding disorders for all dental practitioners, including community dental practitioners, hospital dentists and oral surgeons.
- Aims to improve this patient group's access to dental care in the community and within the hospital setting.

PRACTICE

VERIFIABLE CPD PAPER

Recommendations for dental preventive strategies and treatment planning were originally developed through consensus meetings by the Scottish Oral Health Group for Medically Compromised Patients and published in 2003 as a Guideline. The United Kingdom Haemophilia Centre Doctors' Organisation (UKHCDO) Dental Working Party has updated these recommendations following the AGREE II approach (www.agreetrust.org), involving a literature search, a review of national and international guidelines and after seeking the opinions of haemophilia treaters in the United Kingdom by an online survey. Where possible, evidence from the literature is graded according to the 'GRADE' system (www.bcshguidelines.com/bsch_process/evidence_levels_and_grades_of_recommendations/43_grade.html); however, overall there is a lack of robust data and most studies have methodological limitations. The objective of this guidance, which is largely consensus-based, is to assist dental practitioners in primary and secondary care to provide routine dental care for patients of all ages with congenital bleeding diatheses in order to improve overall access to dental care. The guidance may not be appropriate in all cases and individual patient circumstances may dictate an alternative approach. Date for guideline review: May 2016.

INTRODUCTION

This advisory document aims to dispel a number of myths concerning the management of patients with congenital bleeding disorders. Although patients with congenital bleeding disorders have an increased risk of significant bleeding from invasive dental and oral surgery procedures[1,2] the majority of routine non-surgical dental treatment can be provided in a general dental practice or within the community and salaried dental service.[3,4] Successful management involves close collaboration between haemophilia treaters and dentists,[1,3,5-7] and dental treatment should be organised, especially in patients on prophylaxis regimens, to minimise exposure to factor replacement therapy.

The provision of dental treatment in patients with congenital bleeding disorders has often been neglected.[1] In the 1960s most treatments were performed under general anaesthesia and extraction followed by provision of dentures was often the only treatment plan. Since the introduction of coagulation factor concentrates and antifibrinolytic agents this is no longer the case.[8-10] The advent of new materials, attention to meticulous operative technique, use of local haemostatic agents, and an increasing interest in the prevention of dental problems along with the development of minimally invasive techniques heralds a new era in dental care for patients with congenital bleeding disorders.

A major anxiety of patients with congenital bleeding disorders is the risk of bleeding either during or after treatment, as well as concerns about dentists' understanding of their bleeding condition and its management.[3,6] Many patients also worry when their gingivae bleed on brushing and so avoid brushing, which exacerbates the problem, especially if preventive dentistry is difficult to access in a primary care setting. A significant number of patients have also experienced the refusal of treatment by general dental practices. As a result, individuals may avoid the dentist until extensive treatment needs arise. This group of patients requires the same level of routine dental care as any other patient and good preventive practice is essential. A retrospective audit of the dental health status of 31 consecutively referred haematology patients attending a Scottish dental hospital demonstrated that untreated decay and numbers of missing teeth increase significantly with age, and delays in intervention result in extractions becoming the chosen treatment.[11] With a few exceptions (for example, exfoliation of deciduous teeth, orthodontic extractions, removal of impacted wisdom teeth) a dental extraction should be viewed as a treatment failure.

This guidance aims to provide:

a) An overview of the commonest congenital bleeding disorders
b) An outline of haemostatic agents, including local haemostatic measures
c) An emphasis on the importance of preventive strategies
d) Strategies for elective and emergency treatment planning.

1.0 INHERITED BLEEDING DISORDERS

Individuals with haemophilia do not bleed more profusely than an individual with

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Table 1 The severity of haemophilia, clinical manifestations and recommendations for dental treatments

Degree of haemophilia	Factor percentage (Normal range 50–100%)	Clinical features	Dental treatment
Severe	<1%	Frequent spontaneous bleeds	Enhanced preventive advice and treatment with general dental practitioner or community dentist. Should have all dental treatments except for prosthetics carried out in a hospital setting with specialist dental unit, unless prior arrangements made with the haemophilia centre and general dental practice or community dental practice.
Moderate	2-5%	May have spontaneous bleeds	Enhanced preventive advice and treatment with general dental practitioner or community dentist. Manage as for severe haemophilia.
Mild	6-40%	Bleed after trauma or surgery	Enhanced preventive advice and treatment with general dental practitioner or community dentist. Do not require all treatments carried out at the hospital; should be seen every two years by the specialist dental team at the haemophilia centre. Close liaison between dentist and the haemophilia centre is necessary; some procedures may require prophylactic cover and this will be arranged and provided by the haemophilia unit.
Carrier	Factor level may vary		If the factor level is <50% carriers should be treated as mild haemophilia.

Table 2 Basic classification of von Willebrand disease: clinical features and treatment

Type	Inheritance	Clinical features	Treatment
Type 1	Autosomal dominant	Commonest form of vWD accounting for up to 80% of cases; quantitative deficiency of a normal vWF molecule.	A trial of DDAVP should be given to establish the response, or factor concentrate if response to DDAVP is unsatisfactory.
Type 2	Autosomal dominant	Accounts for approximately 15% of cases; reflects qualitative defects in the vWF molecule.	Factor concentrate
Type 3	Autosomal recessive	Symptoms tend to be severe; reflects a severe deficiency of the vWF molecule.	Factor concentrate

normal coagulation, but may bleed for a longer period of time,[12] and may experience delayed bleeding due to clot instability.

1.1 HAEMOPHILIA A AND B

There are two main types of haemophilia: haemophilia A is the commonest, accounting for approximately 85% of all cases of haemophilia (incidence 1:5,000 live male births), and characterised by a deficiency of factor VIII (FVIII). Haemophilia B is characterised by a deficiency of factor IX (FIX) (incidence 1:30,000 live male births).[13] Both types of haemophilia are inherited as X-linked recessive conditions and share identical clinical manifestations.[14] Coagulation factor assays performed in a specialist haemostasis laboratory enable differentiation between the types of haemophilia.

There is a spectrum of severity of haemophilia, defined as 'mild', 'moderate' or 'severe' according to the plasma levels of FVIII or FIX activity (Table 1). Patients with 'severe' haemophilia have frequent spontaneous bleeds into muscles and weight bearing joints; those with 'moderate' haemophilia have few spontaneous bleeds but bleed after minor trauma, and those with 'mild' haemophilia bleed only after surgery, dental extractions, or trauma. Mild haemophilia may not be diagnosed until a procedure, such as a dental extraction, causes prolonged bleeding.[3] Female carriers of haemophilia may have low factor levels and may be at risk of bleeding.

Patients may be on prophylactic factor regimens. This involves the administration of factor replacement therapy prescribed on an individual basis, usually on alternate days or three times weekly, to minimise spontaneous bleeding. It is important that dental treatment should be scheduled to take place at times of factor administration to minimise the risks of therapies and reduce overall treatment costs.

1.2 VON WILLEBRAND DISEASE (VWD)

von Willebrand disease is the commonest congenital bleeding disorder and is characterised by a deficient or abnormal plasma protein known as von Willebrand factor (vWF). It is an autosomal dominant condition, and affects both males and females. The vWF protein stabilises FVIII and enables platelet interaction with the blood vessel wall. Bleeding after dental extractions may be a presenting feature of this condition.[15,16] Clinical manifestations include mucocutaneous haemorrhage and gingival bleeding, features that are secondary to platelet dysfunction. There are three subtypes of vWD (Table 2) and patients in each subtype may be categorised into mild, moderate and severe at the time of diagnosis. Dental management is the same for the equivalent categories of patients with haemophilia, as outlined in Table 1. In the majority of patients with type 1 vWD, treatment with desmopressin is used (Section 2.2) and type II and type III vWD usually require the administration of coagulation factor replacement therapy with a FVIII concentrate rich in vWF. Currently this is derived from human plasma as no recombinant vWF concentrate is yet available.

1.3 FACTOR XI DEFICIENCY

Factor XI deficiency differs from haemophilia A and B by the lack of bleeding into joints and muscles. The inheritance is autosomal and may occur in either sex. There is typically an unpredictable mild

bleeding tendency that may be provoked by surgery in areas with high fibrinolytic activity such as tonsillectomy and dental procedures. The bleeding risk is difficult to assess from the level of severity of factor deficiency[17] making this congenital bleeding disorder a challenge to treat. Therapeutic options include incrementing factor XI levels by administration of fresh frozen plasma or the administration of factor XI concentrates and through use of antifibrinolytic agents.

1.4 INHIBITORS TO FVIII OR FIX

Patients with haemophilia may develop antibodies to factor therapy and require concentrates known as 'by-passing therapies' to enable haemostasis to be achieved.[18]

Recombinant factor VIIa (rfVIIa, NovoSeven®) is administered as a bolus injection and a treatment consists of 90 µg/kg every two hours for three doses. The half-life of rfVIIa is two hours so it is imperative that the rfVIIa is given on time. The concurrent administration of tranexamic acid enhances clot stability. An alternative therapy is an activated prothrombin complex concentrate, FEIBA®. This is a plasma-derived product, and is given at a dose of 50-100 units/kg, maximum daily dose of 200 units/kg. The use of tranexamic acid should be avoided with FEIBA as it may increase the risk of thromboembolism.

These treatments are highly costly. Patients with inhibitors to FVIII or FIX therapy should be managed by optimal prevention and early diagnosis along the philosophy of a 'Minimum Intervention in Dentistry approach'.[19] This may include atraumatic restorative treatment in which the administration of local anaesthesia is almost never required.

1.5 RARE BLEEDING DISORDERS

There are many other inherited bleeding disorders; the same first principles apply to the dental management of these disorders in primary care. Patients with inherited bleeding disorders are provided with a haemorrhagic states card that outlines the nature of their factor deficiency and main treatment strategies, in addition to the contact details of the local haemophilia centre.

2.0 MANAGEMENT STRATEGIES

An overall treatment plan must take account of the patient's bleeding risk; this is assessed by considering: the type and severity of the congenital bleeding disorder; the location and extent of dental surgery; and the experience of the treating dentist.[1]

A number of dental procedures do not require augmentation of coagulation factor levels including examinations, fissure sealants, small occlusal restorations without the need for local anaesthesia and supragingival scaling. For procedures that do require increment in the factor levels, there may be four therapeutic management options depending on the type of haemophilia and vWD, namely:

1. Coagulation factor replacement therapy
2. Release of endogenous factor stores using desmopressin (DDAVP)
3. Improving clot stability by antifibrinolytic drugs, for example, tranexamic acid
4. Local haemostatic measures.

2.1 COAGULATION FACTOR REPLACEMENT THERAPY

For patients with moderate and severe haemophilia A and B, coagulation factor replacement therapy is the main form of therapy. Factor concentrate is administered by intravenous infusion, either by the individual or by parents and family, or by a haemophilia treater at the haemophilia centre. The timing of administration is important as factor levels will decline, therefore dental procedures should be performed as close to the time of administration of factor concentrate as possible, normally within 30 minutes to an hour. Factor replacement therapy may be prescribed on a prophylactic basis to prevent bleeds, or may be administered 'on-demand' when a bleed occurs. In the past, factor concentrates were plasma-derived and held the possible complication of transfusion-transmitted infections. However, the development of recombinant factor replacement therapy has reduced the risk of blood borne infection.[20] Factor concentrates are expensive so it is important that as much dental work as possible is performed on any one occasion to avoid the need for further factor concentrate administration. One of the most feared complications following the administration of factor concentrate is the development of inhibitors or antibodies which immediately negate the effect of the infused factor concentrate.

2.2 DESMOPRESSIN (DESAMINO-8-D-ARGININE VASOPRESSIN [DDAVP])

The synthetic antidiuretic hormone, desmopressin, stimulates release of endogenous FVIII and vWF from stores in patients with mild haemophilia and vWD[21,22] and is an established therapy for the control of bleeding associated with injury and minor general and oral surgical procedures. Patients with haemophilia B do not respond to DDAVP.

DDAVP can be administered one hour pre-procedure subcutaneously (0.3 µg/kg using the 15 µg/ml concentration). Alternatively, DDAVP (0.3 µg/kg in 50 ml of normal saline) can be administered intravenously (4 µg/ml concentration) one hour pre-procedure as a slow intravenous infusion over 20–30 minutes. The intranasal dose is 150 µg to one nostril for patients weighing <50 kg and to both nostrils for those weighing ≥50 kg.

Patients usually undergo an elective trial of DDAVP at the haemophilia centre to assess their responsiveness. Repeated treatments may cause a diminished response, most likely due to exhaustion of the endothelial stores, in addition to fluid retention and symptomatic hyponatraemia.[21] Fluid intake should be restricted for around 24 hours after DDAVP is given. Adverse reactions to DDAVP given intravenously include mild tachycardia, hypotension and facial flushing. Headache, nausea and abdominal cramps may also be reported.[22] DDAVP should be avoided in patients with ischaemic heart disease. DDAVP should be avoided in young children due to risks of hyponatraemia and is contraindicated in children under two years of age.

2.3 ANTIFIBRINOLYTIC AGENTS

Tranexamic acid (Cyklokapron®) competitively inhibits the activation of plasminogen to plasmin thereby inhibiting fibrin clot lysis. It is available in intravenous and oral preparations as well as in the form of a mouthwash. Until recently the mouthwash preparation was commercially unavailable and an unlicensed preparation could only be obtained from a 'special-order' manufacturer, creating practical issues for prescribing in primary care.

Orally, tranexamic acid is given at a dose of 15–25 mg/kg which approximates to 1 g

for the majority of adults every 6-8 hours. Ideally this should be given two hours pre-operatively, and continued for up to 7-10 days post-procedure. There is no evidence to support a 10-day over a 7-day course. The distribution of orally administered *versus* tranexamic acid mouthwash has been compared in plasma and saliva samples of 30 healthy volunteers in a study by Sindet-Paedersen.[23] Following oral tablet administration, peak plasma levels occurred after two hours but with no detectable levels in saliva. Conversely, after using mouthwash, salivary levels peaked after 30 minutes and remained therapeutic for at least two hours; plasma levels were very low, indicating that fibrinolysis within the mouth could only be effectively inhibited by using the mouthwash preparation.

When used alone in anticoagulated patients, with no local haemostatic dressing, tranexamic acid mouthwash reduces postoperative bleeding compared to placebo mouthwash.[24,25] Pooling the results of five studies involving tranexamic acid mouthwash as the sole antifibrinolytic agent, delayed post-procedural bleeding occurred in 3.6% of patients compared to a post-procedural bleeding rate of 5.4% when results were compared with studies involving local haemostatic measures and suturing without antifibrinolytic agents.[24–28] The British Committee for Standards in Haematology Guidelines recommend tranexamic acid (route non-specified) for use in the control of oral bleeding in acquired coagulation disorders such as patients on vitamin K antagonists, for example, warfarin.[29]

In patients with congenital bleeding disorders, the use of systemic tranexamic acid and epsilon aminocaproic acid have been demonstrated in two small randomised controlled studies in the early 1970s to control haemorrhage following dental extraction (GRADE 1B).[30,31] A combination of systemic plus local tranexamic acid has been demonstrated to be associated with a reduced amount of bleeding compared to monotherapy in retrospective single-centre observational and case-control studies of dental extraction in patients with haemophilia (GRADE 2C).[32,33] In a small double blind randomised controlled trial of 13 patients with all severities of haemophilia A and B conducted by Lee and colleagues,[34] the use of tranexamic acid mouthwash after dental scaling was found to be as effective as factor replacement therapy in the control of gingival haemorrhage (GRADE 1 B).

Tranexamic acid mouthwash (10 ml of a 5% solution) should be commenced just before the dental procedure to increase salivary levels, and continued 6-hourly for 7-10 days. For adults the mouthwash should be gently swilled inside the mouth for 2-3 minutes and then swallowed or gently expelled. For children the use of tranexamic mouthwash poses practical challenges as the recommended dose as per the British National Formulary can be exceeded if the mouthwash is swallowed. There may be practical issues involved in procuring tranexamic acid mouthwash in the community.[35] In the hospital setting, tranexamic acid mouthwash can be prepared from the solution used for intravenous injection as a 'special-order' or can be bought as a ready-made solution from the manufacturer. Special-order formulations of tranexamic acid mouthwash hold a limited short shelf life of 5-14 days and are costly (cost varying from £65 to over £200 depending on the pharmacy for a 7-day course).[35] If a special-order formulation of tranexamic mouthwash is supplied directly from the dentist to the patient, then the Medicines Act 1968 dictates compliance with the labelling of dispensed medicinal products.[35]

Tranexamic acid is freely soluble in water and it has been suggested that a 500 mg tablet could be crushed and dissolved in 10 ml water to make up a 5% mouthwash solution.[36] There are no safety or efficacy data to support this unlicensed approach. The mouthwash is also reported to be unpalatable.

Table 3 Dental anaesthetic procedures and factor replacement therapy[44]

Procedures that do not require factor cover (specifically applies to adult patients only; paediatric patients may receive factor replacement therapy before local anaesthetic infiltration as directed by the haemophilia unit)	Procedures that require factor cover (applies to both adult and paediatric patients)
Buccal infiltration	Inferior dental block
Intra-papillary injection	Lingual infiltration
Intra-ligamentary injections	

2.4 SUTURING AND LOCAL HAEMOSTATIC MEASURES

In adult patients suturing and local haemostatic measures provide a useful adjunctive therapy to the augmentation of factor levels for dental extractions and invasive dental procedures.[1] Both resorbable and non-resorbable sutures are acceptable.

In children, practice and opinion varies in the use of sutures. Suturing is avoided in some centres due to concern about the higher number of puncture holes and a view that suturing is not necessary in small sockets; there is also a view that delayed bleeding may occur upon cessation of factor cover and removal of sutures. Other centres advocate use of sutures and local haemostatic measures if dental extractions or oral surgical procedures are carried out under general anaesthetic in order to prevent the requirement of a second general anaesthetic to suture and pack if bleeding should occur. Local haemostatic measures include oxidised cellulose, Surgicel®, resorbable gelatine sponge, Gelfoam®, cyanoacrylate tissue adhesives and surgical splints.[37] A number of novel haemostatic agents Lyostpt® and Ankaferd Blood Stopper[38] may also be of use.

3.0 PREVENTION

The delivery of dentistry has moved away from a treatment-focused approach to a preventive model of care. To support primary care teams and dental teams in the delivery of a preventive approach, evidence-based simplified prevention guides have been designed by the Department of Health[39] and the Scottish Dental Clinical Effectiveness Programme (SDCEP),[40,41] and are available online. Based on SDCEP prevention and management of caries in children guidance, all children should have a caries risk assessment. Standard prevention is suitable for children who are low caries risk and enhanced prevention for children at increased risk of caries or allocated to a high caries risk category due to other factors (for example, a medical condition). All children with congenital bleeding disorders would be allocated as

high caries risk due to the complexity and morbidity of treatment when caries does occur in this group of patients. Emphasis is placed on the importance of regular dental follow-up, with fluoride varnish (5%) placed three to four times per year, and the principles of toothbrushing to prevent dental caries and periodontal disease by removal of the biofilm of dental plaque. A 30-year study of work performed in a single private dental surgery[42] established an association between patients who maintain a high level of oral hygiene with a reduced incidence of caries and periodontal disease. Toothbrushing technique, duration (two minutes twice daily is advisable) and the regular replacement of toothbrushes and use of disclosing tablets to locate inadequately brushed areas are promoted.[43] Use of fluoride-containing toothpastes have been shown to reduce the incidence of dental caries in children, and children who are three and over should be advised on toothpastes containing 1350–1500 ppm fluoride. Children over the age of ten should be prescribed 2800 ppm fluoride toothpaste. Dietary advice should routinely be given to patients to promote good oral health using four day food diaries, including advice regarding reduction in the frequency and amount of sugars, restriction of foods and drinks with a high sugar content at meal times only, and an outline of cariogenic foods and drinks such as carbonated beverages, fruit juices and cereals.[43] Smoking should be strongly discouraged and NHS Stop Smoking Services are available to assist dental patients who wish to stop smoking.

4.0 TREATMENT PLANNING

Patients with congenital bleeding disorders require formulation of a comprehensive treatment plan with an overall goal of achieving satisfactory haemostasis. The patient should hold an understanding of the treatment aims and the process followed to reach this goal. This will involve detailed liaison with the haemophilia centre. General measures to reduce accidental trauma and minimise damage to oral mucosa should be employed at all times including careful use of saliva ejectors, careful removal of impressions and care in the placement of radiographic films.[1,43]

Factor concentrate replacement therapy should be administered as close to the time of the dental procedure as possible. Patients with severe haemophilia, or with inhibitors, may require assessment by the haemophilia team post-procedurally and may require admission for 24-hour monitoring to ensure no late bleeding complications arise.

The use of post-procedural advice sheets should be encouraged and enables written instruction to be given after the patient leaves the surgery. This sheet should include contact telephone numbers for advice during and outwith working hours for emergencies, and should include the telephone number for the haemophilia centre.

Should the haemophilia centre and the dental department be located at different sites, practical issues surrounding administration of therapies before dental procedures, and monitoring at the haemophilia centre following dental procedures should be audited through the United Kingdom Haemophilia Centre Doctors' Organisation (UKHCDO) Triennial Audit Scheme.

4.0.1 LOCAL ANAESTHESIA

In adults, local anaesthetic infiltration using a slow injection technique and modern fine gauge single-use needles can usually be used without the need for factor replacement therapy.[1,43-45] In children there are differing views and advice should be sought from the paediatric haemophilia centre; for children on regular prophylaxis a dose of factor replacement therapy may be administered before infiltration.

Augmentation of factor levels with or without tranexamic acid is required in all age groups when inferior alveolar and posterior superior alveolar dental nerve-blocks are given; there is a risk of muscle haematoma, in addition to potential airway compromise due to haematoma formation in the retromolar or ptyerygoid space.[2,3,45] Factor replacement therapy is also necessary for lingual infiltration and floor-of-mouth injections in all age groups as there may be a significant risk of haematoma (Table 3). Specifically in adults the consensus view is that intraligamentous or intrapapillary injections do not require haemostatic cover; however, it would be advised to give buccal infiltration at the time of the injection to avoid pain.[1,43,44]

There are no restrictions regarding the type of local anaesthetic used, and 2% lidocaine with 1 in 80,000 epinephrine is routinely used in restorative dentistry; the use of a vasoconstrictor improves local haemostasis.[1] Recently there have been reports that the use of articaine with 1:100,000 epinephrine may achieve more optimal bone penetration. This local anaesthetic has been described for infiltration as an alternative to inferior dental block in the restoration of mandibular molars, removing the need for pre-operative factor cover.[46,47]

4.1 ELECTIVE TREATMENT

4.1.1 Scaling and periodontal disease

Routine periodontal probing, supragingival scaling, and polish (including ultrasonic scaling) is unlikely to cause prolonged bleeding for patients, especially those with mild conditions.[43,44] If the gingival health is poor, prevention of further damage to periodontal tissues is necessary by instituting an immediate treatment plan that may require several visits to prevent excessive bleeding.[1,43] The use of tranexamic acid (oral or mouthwash) (Section 2.3)[34] and/or factor replacement therapy may be required to control bleeding and the haemophilia centre should be consulted.[9] The use of antibacterial mouthwashes and antibiotics may be necessary.

4.1.2 Orthodontic treatment

Fixed and removable orthodontic appliances may be used as long as enhanced preventive advice including oral hygiene instruction and demonstrations are carried out.[41,44] The appliance should be designed so that the gingival and buccal mucosa cannot be damaged by sharp edges or wires. Discussion with the haemophilia centre is necessary if any surgical procedures are required.[1]

4.1.3 Prosthodontic (construction of dentures) treatment

The provision of any removable prosthesis and the use of full or partial dentures should not pose any additional problems in this group of patients.[43]

4.1.4 Restorative treatment (fillings, crowns, bridges)

Restorative dentistry, including the provision of crowns and bridges, is associated

with low bleeding risk and can be carried out safely in general dental practice. If an inferior dental block or lingual infiltration is required, coagulation factor concentrate will be necessary (Table 3). A survey of all United Kingdom haemophilia centres conducted in 2010 by the UKHCDO indicated that the majority of survey responders aim for a single pre-procedural factor level of 50-80% (unpublished data). The use of minimal invasive techniques are advancing and may be highly relevant in patients with congenital bleeding disorders.[19,41]

4.1.5 Endodontic (root canal) treatment

Endodontic treatment should not cause problems.[1] However, if vital pulp tissue is present at the apical foramen this may bleed for some time and cause pain.[43] The use of 4% sodium hypochlorite for irrigation and calcium hydroxide paste appears to minimise this problem.[43]

4.1.6 Implants

Evidence-based protocols have not been established for the use of implants in patients with inherited bleeding disorders. Treatment should be individually planned in discussion with the haemophilia centre.[1]

4.1.7 Dental extractions and oral surgical procedures

Dental extractions and minor surgical procedures under local anaesthesia should be planned after discussion with the local haemophilia centre. This is especially relevant in patients with mild forms of congenital bleeding disorders, or those who live geographically a long distance from the haemophilia centre.

At present there is insufficient evidence to support the administration of topical antiseptics and antibiotics before extraction. Cautery may be required following the removal of granulation tissue from areas of chronic inflammation and should be considered on an individual basis.[1,48]

4.1.7.a Recommendations for factor replacement therapy

The European Haemophilia Standardisation Board note that most studies in the literature are based on replacement with a single dose of factor concentrate to a minimum pre-operative factor level of 30-50% for individuals undergoing dental extraction. However, a survey of 26 European Haemophilia Comprehensive Care Centres, representing 15 different countries, recommended the administration of concentrate to raise factor levels to 60-80%, with one third of centres administering repeat doses.[49] It should be noted that the level of evidence in the majority of studies are GRADE 2C based on retrospective, single centre and observational or case-control study design.

The UKHCDO Dental Working Party Survey noted a similar variation in practice, with the majority of UK haemophilia centres aiming for a minimum single factor level of 50%, but with a range of pre-operative factor levels from 30–60%, and with some centres giving repeat doses on a second day. All UK centres responding to the UKHCDO Dental Working Party Survey used a combination of factor therapy with some form of antifibrinolytic therapy (unpublished data).

It is important that factor concentrate is administered as near to the time of the extraction as possible. In children, the routine exfoliation of primary teeth does not routinely require factor replacement therapy. If prolonged bleeding is encountered discuss with a consultant in paediatric dentistry who can liaise with a consultant paediatric haematologist. Children with severe haemophilia requiring dental extraction will usually require a general anaesthetic and factor replacement therapy will be required to cover intubation.

4.1.7.b Recommendations for antifibrinolytic therapy

There is evidence from the literature that antifibrinolytic therapy plus factor replacement therapy is more effective than factor replacement therapy alone (GRADE 1B),[30,31] and that antifibrinolytics and attention to local haemostasis are also of benefit[49–53](GRADE 2C). The European Haemophilia Standardisation Board Survey indicated that antifibrinolytic therapy is normally administered for a period ranging from 5-10 days.[49] The UKHCDO Dental Working Party Survey indicated either oral tranexamic acid or tranexamic mouthwash is administered for 3-7 days following dental extraction in 100% of survey responders, with variable practice regarding pre-operative administration of antifibrinolytic therapy. There is a small body of evidence (GRADE 2C) to support the combined use of oral tranexamic acid and tranexamic mouthwash together.[32,33,49,53]

4.1.7.c Dental extractions in patients with inhibitors to FVIII and FIX

For patients with inhibitors to FVIII and FIX, it may be advisable to extract only one tooth at a time and to observe the patient for a 24-hour period after the extraction. The haemophilia centre will arrange bypassing factor replacement therapy to be given before and after the extraction. A soft vacuum-formed splint may be constructed in advance of the extraction to cover the socket completely. Following extraction, packing with Gelfoam® rolled in thrombin powder (Thrombostat®) or use of Surgicel® may aid haemostasis. A splint can then be fitted and left *in situ* for 48 hours.

Use of tranexamic acid, either as a mouthwash or in oral form, must be discussed with the haemophilia centre. Tranexamic acid mouthwash may be safely used as an adjunct but systemic treatment is best avoided when patients are treated with FEIBA® due to increased risks of thromboembolic complications.

4.2 EMERGENCY TREATMENT

4.2.1 Acute pulpitis

The pain in adults can usually be controlled by removing pulp from the tooth. In paediatric patients local anaesthesia is used as for any other patient who presents with acute pulpitis. If patients cannot tolerate this treatment an urgent referral to a specialist paediatric unit is required as use of sedation or general anaesthesia may be indicated. A temporary dressing should be used if the tooth is not restorable and the haemophilia centre contacted for planning of the extraction.

4.2.2 Dental abscess with facial swelling

Antibiotics should only be prescribed if there is local spread or signs of systemic infection. Advice regarding appropriate antibiotic cover can be obtained from the document *Drug prescribing for dentistry: dental clinical guidance*.[54] Advice should be sought from the haemophilia centre for factor concentrate cover.

4.2.3 Fractured teeth

This usually occurs following direct trauma to the teeth. The soft tissues are often damaged and should be treated appropriately. The damaged teeth should be managed in a similar manner to any traumatised teeth remembering that factor cover may be required if there is significant bleeding.

5.0 OTHER ISSUES

5.1 Analgesia

Analgesia may be necessary for the management of dental pain or abscess, or for alleviation of pain post procedure. Aspirin, and aspirin-containing medications, should be avoided in patients with bleeding disorders as the haemorrhagic tendency may worsen as a result of the inhibitory effect on platelet function.[54] The use of non-steroidal anti-inflammatory drugs may be beneficial to control dental pain but their prescription should be discussed with the haemophilia centre as they may increase the risk of bleeding if taken pre-procedure.[55] Paracetamol and codeine-based preparations are safe alternatives.

5.2 Antibiotics

There are no contra-indications to any antibiotics from the dental section of the British National Formulary for patients with congenital bleeding disorders.[43]

5.3 Transfusion-transmitted infections

In the past, patients may have received plasma-derived concentrates and contracted hepatitis or HIV viruses. The presence of HIV has been demonstrated to have no influence on the treatment outcome for dental procedures.[56]

No special precautions are required for individuals with bleeding disorders and the same level of cross-infection prevention should be implemented for all patients.[57] Individuals who have been treated with UK-sourced plasma products between 1980 and 2001 are viewed as 'at risk' of Creutzfeldt-Jakob disease (CJD) including variant CJD (vCJD). The dental care of these patients should not be compromised, and this group of patients can be treated in the same way as any member of the general public. Satisfactory decontamination procedures are required. Special precautionary measures may require to be taken should referral for head and neck surgery be necessary; it is important that information of a patient's 'at risk' status is provided to the patient's dentist by the haemophilia centre and recorded in the dental records and included in any referrals for surgery.[58]

SUMMARY OF KEY RECOMMENDATIONS

Access to dental care

1. Every haemophilia centre should have ready access to a hospital dental service. Access to hospital and community dental services should be audited through the United Kingdom Haemophilia Centre Doctors' Organisation (UKHCDO) Triennial Audit Scheme
2. There should be clear documentation of liaison between the haemophilia centre, the hospital dentist and general dental practice regarding the nature of the patient's congenital bleeding disorder, treatment plans and the risk of transfusion-transmitted infection
3. For patients with mild congenital bleeding disorders the majority of routine non-surgical dental treatment can be provided in general dental practice; close liaison with the hospital dental service and the haemophilia centre are necessary.

PREVENTIVE CARE

1. At each routine haemophilia follow-up visit there should be written documentation about the patient's oral health status and advice should be provided on preventive care. The use of patient leaflets should be encouraged. This may be recorded as an outcome measure, and may be audited through the UKHCDO Triennial Audit Scheme.

PROCEDURES

1. Treatment planning is essential for good outcome and should involve liaison between the dentist and the haemophilia centre. Consideration should be given to careful scheduling of invasive dental procedures to minimise re-exposure to factor concentrate. Written post-procedural instructions should be provided and must include emergency contact numbers for the haemophilia centre
2. Prior to inferior dental block and lingual infiltration, augmentation of coagulation factor levels is essential in all age groups. In adults the consensus opinion is that this is not necessary for buccal infiltration, intra-papillary injections and intra-ligamentary injections. In children augmentation of coagulation factor levels is preferred for buccal infiltration, intra-papillary injections and intra-ligamentary injections (consensus opinion)
3. For invasive dental procedures, coagulation factor concentrate is required to a minimum level of 50% (single dose) although an individual treatment plan is necessary for each patient and a repeat dose may be required (consensus opinion)
4. In adults peri-operative anti-fibrinolytic agents including oral tranexamic acid and/or 5% tranexamic mouthwash should be prescribed solely or in combination before and post dental extraction for up to seven days. In children oral tranexamic may be used in all ages but mouthwash should be restricted to older children to avoid exceeding the recommended dose if the mouthwash is inadvertently swallowed. (Level of evidence for oral tranexamic acid: GRADE 1B; for tranexamic acid mouthwash: GRADE 2C; for combination systemic and local antifibrinolytic therapy: GRADE 2C; for duration of antifibrinolytic therapy: consensus opinion.)
5. In adult patients undergoing dental extractions, bleeding may be minimised by the use of either resorbable or non-resorbable sutures and additional local measures such as Surgicel®, Gelfoam®, cyanoacrylate tissue adhesives and surgical splints (consensus opinion). In paediatric patients practice and opinion varies regarding the use of sutures. In general sutures are used less but there is no contra-indication to their use (consensus opinion)
6. There are no restrictions regarding the type of local anaesthesia used
7. There are no contra-indications to any of the antibiotics from the dental formulary of the British National

Formulary for patients with congenital bleeding disorders

8. Aspirin and aspirin-containing medications should be avoided. Paracetamol and codeine-based preparations are safe alternatives for patients with congenital bleeding disorders
9. The use of non-steroidal anti-inflammatory medications may be useful to alleviate dental pain, but should be discussed with the haemophilia centre (consensus opinion).

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1. Hewson I D, Daly J, Hallett K B *et al.* Consensus statement by hospital based dentists providing dental treatment for patients with inherited bleeding disorders. *Aust Dent J* 2011; **56:** 221–226.
2. Heiland M, Weber M, Schmelzle R. Life-threatening bleeding after dental extraction in a haemophilia A patient with inhibitors to factor VIII: a case report. *J Oral Maxillofac Surg* 2003; **61:** 1350–1353.
3. Dougall A, Fiske J. Access to special care dentistry, part 5. Safety. *Br Dent J* 2008; **205:** 177–190.
4. Dougall A, O'Mahoney B. Evaluation of a collaborative model of shared care designed to increase access to preventive and restorative dentistry for patients with haemophilia. *Haemophilia* 2010; **16 (Suppl 4):** 50 (Abs no 11FP04).
5. Harrington B. Primary dental care of patients with haemophilia. *Haemophilia* 2000; **6 (Suppl 1):** 7–12.
6. Fiske J, McGeoch R J, Savidge G, Smith M P. The treatment needs of adults with inherited bleeding disorders. *J Disabil Oral Health* 2002; **3:** 59–61.
7. Stubbs M, Lloyd J. A protocol for the dental management of von Willebrand's disease, haemophilia A and haemophilia B. *Aust Dent J* 2001; **46:** 37–40.
8. Vinckier F, Vermylen J. Dental extractions in haemophilia: reflection on 10 years' experience. *Oral Surg Oral Med Oral Pathol* 1985; **59:** 6–9.
9. Kats J O, Terezhalmy G T. Dental management of the patients with haemophilia. *Oral Surg Oral Med Oral Pathol* 1988; **66:** 139–144.
10. Gupta A, Epstein J B, Cabay R J. Bleeding disorders of importance in dental care and related patient management. *J Can Dent Assoc* 2007; **73:** 77–83.
11. Manton S, Martin A, Bhuta B. A retrospective audit of the dental health status and treatment needs of referred haematology patients attending a UK dental hospital. *Haemophilia* 2010; **16 (Suppl 4):** 51 (Abs no 11FP09).
12. Berry E, Hilgartner M, Mariani G, Sultan Y, Members of the Medical Advisory Board, World Federation of Haemophilia; Jones P (ed). *Haemophilia: facts for health care professionals.* Geneva: World Health Organization, 1996.
13. Mannucci P M, Tuddenham E G. The haemophilias – from royal genes to gene therapy. *N Engl J Med* 2001; **344:** 1773–1779. Erratum in: *N Engl J Med* 2001; **345:** 384.
14. Bolton-Maggs P H, Pasi K J. Haemophilias A and B. *Lancet* 2003; **361:** 1801–1809.
15. Keila S. Uncontrolled bleeding during endodontic treatment as the first symptoms for diagnosing von Willebrand's disease. *Oral Surg Oral Med Oral Pathol* 1990; **69:** 243–261.
16. Wilde J T, Cook R J. von Willebrand disease and its management in oral and maxillofacial surgery. *Br J Oral Maxillofac Surg* 1998; **36:** 112–118.
17. Bolton-Maggs P H B. *Factor XI deficiency and its management,* 3rd ed. Montréal: World Federation of Haemophilia, 2008. (Treatment of Haemophilia monograph, no 16).
18. Brewer A. *Dental management of patients with inhibitors to Factor VIII or Factor IX.* Montréal: World Federation of Haemophilia, 2008. (Treatment of Haemophilia monograph, no 45).
19. Leal S C. Minimum intervention in dentistry: applicability for dental care of patients with inherited bleeding disorders. *Haemophilia* 2010; **16 (Suppl 4):** 50 (Abs no 11S02).
20. United Kingdom Haemophilia Centre Directors Organization Executive Committee. Guidelines on therapeutic products to treat haemophilia and other hereditary coagulation disorders. *Haemophilia* 1997; **3:** 63–77.
21. Mannucci P M. Desmopressin (DDAVP) in the treatment of bleeding disorders: the first twenty years. *Haemophilia* 2000; **6 (Suppl 1):** 60–67. Erratum in: *Haemophilia* 2000; **6:** 595.
22. Mannucci P M, Ruggeri Z M, Pareti F I, Capitanio A. 1-Deamino-8-d-arginine vasopressin: a new pharmacological approach to the management of haemophilia and von Willebrand's disease. *Lancet* 1977; **309:** 869–872.
23. Sindet-Paedersen S. Distribution of tranexamic acid to plasma and saliva after oral administration and mouth rinsing: a pharmacokinetic study. *J Clin Pharmacol* 1987; **27:** 1005–1008.
24. Ramström G, Sindet-Paedersen G, Hall G, Blombäck M, Alander U. Prevention of postsurgical bleeding in oral surgery using tranexamic acid without dose modification of oral anticoagulants. *J Oral Maxillofac Surg* 1993; **51:** 1211–1216.
25. Sindet-Paedersen S, Ramström G, Bernvil S, Blombäck M. Haemostatic effect of tranexamic acid mouthwash in anticoagulant-treated patients undergoing oral surgery. *N Engl J Med* 1989; **320:** 840–843.
26. Carter G, Goss A. Tranexamic acid mouthwash – a prospective randomized study of a 2-day regimen vs 5 day regimen to prevent postoperative bleeding in anticoagulated patients requiring dental extractions. *Int J Oral Maxillofac Surg* 2003; **32:** 504–507.
27. Carter G, Goss A, Lloyd J, Tocchetti R. Tranexamic acid mouthwash *versus* autologous fibrin gluein patients taking warfarin undergoing dental extractions: a randomized prospective clinical study. *J Oral Maxillofacial Surg* 2003; **61:** 1432–1435.
28. Blinder D, Manor Y, Martinowitz U, Taicher S, Hashomer T. Dental extractions in patients maintained on continued oral anticoagulant, comparison of local haemostatic modalities. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1999; **88:** 137–140.
29. Perry D J, Noakes T J, Helliwell P S. Guidelines for the management of patients on oral anticoagulants requiring dental surgery. *Br Dent J* 2007; **203:** 389–393.
30. Forbes C D, Barr R D, Reid G *et al.* Tranexamic acid in control of haemorrhage after dental extraction in haemophilia and Christmas disease. *Br Med J* 1972; **2:** 311–313.
31. Walsh P N, Rizza C R, Matthews J M *et al.* Epsilon-Aminocaproic acid therapy for dental extractions in haemophilia and Christmas disease: a double blind controlled trial. *Br J Haemol* 1971; **20:** 463–475.
32. Stajčić Z. The combined local/systemic use of antifibrinolytics in haemophiliacs undergoing dental extractions. *Int J Oral Surg* 1985; **14:** 339–345.
33. Sindet-Paedersen, Stenbjerg S. Effect of local antifibrinolytic treatment with tranexamic acid in haemophiliacs undergoing oral surgery. *J Oral Maxillofac Surg* 1986; **44:** 703–707.
34. Lee A, Boyle C A, Savidge G F, Fiske J. Effectiveness in controlling haemorrhage after dental scaling in people with haemophilia by using tranexamic acid mouthwash. *Br Dent J* 2005; **198:** 33-38
35. Randall C (ed). Surgical management of the primary care dental patient on warfarin [updated March 2007]. North West Medicines Information Centre, 2007. Available at: www.app.dundee.ac.uk/tuith/Static/info/warfarin.pdf (accessed 20 August 2013).
36. Ambados F. Preparing tranexamic acid 4.8% mouthwash. *Aust Prescr* 2003; **26:** 75.
37. Adornato M C, Penna K J. Haemostatic technique. Using a splint in oral bleeding. *N Y State Dent J* 2001; **67:** 24–25.
38. Ak G, Çakır O, Kazancıoğlu H O, Zulfikar B. The use of a new haemostatic agent: Ankaferd Blood Stopper in haemophiliacs. *Haemophilia* 2010; **16 (Suppl 4):** 51 (Abs no 11P12).
39. Department of Health and British Association for the Study of Community Dentistry. *Delivering better oral health: an evidence based toolkit for prevention,* 2nd ed. London: Department of Health, 2009.
40. Scottish Dental Clinical Effectiveness Programme. *Prevention and management of dental caries in children: dental clinical guidance.* Dundee: Scottish Dental Clinical Effectiveness Programme, 2010.
41. Scottish Dental Clinical Effectiveness Programme. *Oral health assessment and review: guidance in brief.* Dundee: Scottish Dental Clinical Effectiveness Programme, 2011.
42. Axelsson P, Nyström B, Lindhe J. The long-term effect of a plaque control programme on tooth mortality, caries and periodontal disease in adults. Results after 30 years of maintenance. *J Clin Periodontol* 2004; **31:** 749–757.
43. Brewer A, Correa M E. *Guidelines for dental treatment of patients with inherited bleeding disorders.* Montréal: World Federation of Haemophilia, 2006. (Treatment of Haemophilia monograph, no 40).
44. Brewer A K, Roebuck E M, Donachie M *et al.* The dental management of adult patients with haemophilia and other congenital bleeding disorders. *Haemophilia* 2003; **9:** 673–677.
45. Freedman M, Dougall A, White B. An audit of a protocol for the management of patients with hereditary bleeding disorders undergoing dental treatment. *J Disabil Oral Health* 2009; **10:** 151–155.
46. Smith G, Dougall A. To audit the success rate using 4% articaine as buccal infiltration in order to anaesthetise mandibular molars for restorative dental treatment in patients with a hereditary coagulation disorder. *Haemophilia* 2010; **16 (Suppl 4):** 51 (Abs no 11FP11).
47. Robertson D, Nusstein J, Reader A, Beck M, McCartney M. The anaesthetic efficacy of articaine in buccal infiltration of mandibular posterior teeth. *J Am Dent Assoc* 2007; **138:** 1104–1112.
48. Israels S, Schwetz N, Boyar R, McNicol A. Bleeding disorders: characterization, dental considerations and management. *J Can Dent Assoc* 2006; **72:** 827.
49. Hermans C, Altisent C, Batorova A *et al.* Replacement therapy for invasive procedures in patients with haemophilia: literature review, European survey and recommendations. *Haemophilia* 2009; **15:** 639–658.
50. Ramström G, Blombäck M. Tooth extractions in haemophiliacs. *Int J Oral Surg* 1975; **4:** 1–17.
51. Baudo F, de Cataldo F, Landonio G, Muti G. Management of oral bleeding in haemophilic patients. *Lancet* 1988; **2:** 1082.
52. Rakocz M, Mazar A, Varon D, Spierer S, Blinder D, Martinowitz U. Dental extractions in patients with bleeding disorders. The use of fibrin glue. *Oral Surg Oral Med Oral Pathol* 1993; **75:** 280–282.
53. Waly N G. Local antifibrinolytic treatment with tranexamic acid in haemophilic children undergoing dental extractions. *Egypt Dent J* 1995; **41:** 961–968.
54. Scottish Dental Clinical Effectiveness Programme. *Drug prescribing for dentistry: dental clinical guidance,* 2nd ed. Dundee: Scottish Dental Clinical Effectiveness Programme, 2011.
55. Lockhart P B, Gibson J, Pond S H, Leitch J. Dental management considerations for the patient with an acquired coagulopathy. Part 2: Coagulopathies from drugs. *Br Dent J* 2003; **195:** 495–501.
56. Scully C, Watt-Smith P, Dios R D, Giangrande P L. Complications in HIV-infected and non HIV infected haemophiliacs and other patients after oral surgery. *Int J Oral Maxillofac Surg* 2002; **31:** 634–640.
57. British Dental Association. Infection control. www.bda.org/dentists/advice/ba/ie.aspx (accessed 13 November 2013).
58. Department of Health. Guidance on minimising transmission risk of CJD and vCJD. Available at: www.gov.uk/government/publications/guidance-from-the-acdp-tse-risk-management-subgroup-formerly-tse-working-group (accessed 20 August 2013).