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Significance of 'Clotting Factors' in Prosthodontic Treatment Procedures -A Review.

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ABSTRACT

Bleeding disorders and a lack of clotting factors, like hemophilia A (factor VIII deficiency), hemophilia B (factor IX deficiency), von Willebrand disease (VWD), and factor XIII deficiency, make it much harder to do prosthodontic procedures like fixed partial dentures (FPDs) and dental implants because of the risk of too much bleeding, hematoma formation, and delayed healing. These operations entail invasive measures (e.g., tooth preparation, implant osteotomy, or soft tissue manipulation), requiring customized protocols to guarantee hemostasis. Effective management necessitates multidisciplinary collaboration with hematologists, preoperative evaluation (e.g., HEMSTOP questionnaire, factor level testing), and targeted interventions, including factor replacement (to 50–100 IU/dL), desmopressin for mild VWD, antifibrinolytics (e.g., tranexamic acid), and local hemostatic agents (e.g., fibrin glue, gelatin sponges). Recent improvements, such factors with longer half-lives, non-factor therapy (like emicizumab), and flapless implant procedures, make things safer and allow for outpatient care. To reduce difficulties and improve prosthodontic results in these patients, it is important to use atraumatic procedures, preventative dental initiatives, and standardized protocols.

Keywords: Bleeding disorders, Clotting factors, Hemophilia, von Willebrand disease, Prosthodontics, dental implants, Fixed partial dentures, Antifibrinolytics.

Introduction

Bleeding and clotting factors are important parts of the hemostatic system, which controls blood clotting to stop too much bleeding or blood clots.

Clotting Factors

Clotting Factors: Clotting factors are proteins in the blood that work together in the coagulation cascade to make a blood clot, which stops bleeding. The liver makes most of these, and some of them need vitamin K to be made. There are 13 clotting factors, and several of them have common names: [1-4]

1. **Factor I (Fibrinogen)**: Converted to fibrin, forming the mesh of a clot.
2. **Factor II (Thrombin)**: Converts fibrinogen to fibrin and activates other clotting factors.
3. **Factor III (Tissue Factor/Thromboplastin)**: Initiates the extrinsic pathway of coagulation.
4. **Factor IV (Calcium)**: Facilitates interactions between clotting factors.
5. **Factor V (Proaccelerin)**: Enhances thrombin production.
6. **Factor VI**: Not used (previously thought to be a distinct factor).
7. **Factor VII (Proconvertin)**: Activates the extrinsic pathway.
8. **Factor VIII (Antihemophilic Factor)**: Supports the intrinsic pathway; deficiency causes hemophilia A.
9. **Factor IX (Christmas Factor)**: Activates in the intrinsic pathway; deficiency causes hemophilia B.
10. **Factor X (Stuart-Prower Factor)**: Central to both intrinsic and extrinsic pathways.
11. **Factor XI (Plasma Thromboplastin Antecedent)**: Supports intrinsic pathway activation.
12. **Factor XII (Hageman Factor)**: Initiates the intrinsic pathway.

13. **Factor XIII (Fibrin-Stabilizing Factor)**: Stabilizes the fibrin clot.

Bleeding Disorders and Clotting Factors: Deficiencies or dysfunctions in clotting factors can lead to bleeding disorders: **[5,6]**

- **Hemophilia A**: Deficiency in factor VIII.
- **Hemophilia B**: Deficiency in factor IX.
- **Von Willebrand Disease**: Involves von Willebrand factor (vWF), which aids platelet adhesion and carries factor VIII.
- **Fibrinogen Disorders**: Deficiency or abnormal fibrinogen can cause bleeding or clotting issues.

Other Factors in Hemostasis:

- Platelets: Small pieces of cells that stick to broken blood arteries and release substances to help blood clot.
- Von Willebrand Factor (vWF): Connects platelets to collagen at the site of an injury and keeps factor VIII stable.
- Anticoagulant Proteins: Proteins such as Protein C, Protein S, and antithrombin control clotting to stop too many thrombus from forming.
- Fibrinolytic System: This system stops thrombosis by breaking down clots with plasminogen and tissue plasminogen activator (tPA).
- Clinical Importance:
- Too little of some clotting factors (like hemophilia) might cause too much bleeding.
- Too much clotting can lead to thrombosis, such as deep vein thrombosis or pulmonary embolism.
- Treatments include of factor replacement therapy, anticoagulants (such as heparin or warfarin), or antifibrinolytics (such as tranexamic acid). **[5,6]**

Key Clotting Factors for Dental Practitioners

Factor VIII (Antihemophilic Factor):

Importance: Not having enough of it might cause hemophilia A, which makes you bleed a lot. For these people, dental extractions or other invasive operations can cause bleeding that lasts longer than normal.

Dental Relevance: Individuals with hemophilia A necessitate pre-procedural factor VIII replacement medication or desmopressin (DDAVP) to elevate factor VIII levels. Local hemostatic measures, such as fibrin sealants and suturing, are very important.

Dental professionals ought to confer with hematologists to mitigate bleeding dangers and guarantee secure treatment planning.

Factor IX (Christmas Factor):

Not having enough of it produces hemophilia B, which has the same bleeding hazards as hemophilia A.

Dental Relevance: Patients with hemophilia A need factor IX replacement before invasive operations, just like people with hemophilia B. Dentists need to be careful when doing surgery and use hemostatic medications to stop bleeding.

Considerations: Before treatment, it is important to work with a hematologist to change the amounts of factors.

Von Willebrand Factor (vWF):

Significance: vWF aids in platelet adherence to injured arteries and stabilizes factor VIII. Von Willebrand disease (VWD) is the most prevalent inherited bleeding illness. It happens when there isn't enough of a certain protein or it doesn't work right.

Dental Relevance: Patients with VWD may experience significant bleeding during dental operations, particularly extract ions or periodontal surgery. You could need desmopressin or vWF concentrates, as well as local hemostatic measures like mouthwash with tranexamic acid.

Things to think about: It is very important to diagnose VWD since mild cases may go unnoticed until a dental operation causes too much bleeding.

Fibrinogen (Factor I):

Significance: Fibrinogen is transformed into fibrin, constituting the structural framework of the clot. Deficiencies, such as afibrinogenemia or dysfibrinogenemia, can result in hemorrhage or paradoxical thrombosis.

Dental Relevance: Patients with fibrinogen abnormalities may experience extended bleeding following dental operations. You might need to replenish fibrinogen or use antifibrinolytic drugs.

Before invasive surgeries, fibrinogen levels should be checked, and local hemostatic methods (such gelatin sponges) are sometimes utilized.

Factor XIII (Fibrin-Stabilizing Factor):

Why it's important: It stabilizes fibrin clots by connecting fibrin strands together. A lack of this can cause bleeding to happen later, which may not be obvious right after an operation.

Dental Relevance: People with factor XIII insufficiency are worried about bleeding that happens after dental extractions. Patients may need cryoprecipitate or factor XIII concentrates.

Things to think about: Dentists should keep an eye out for prolonged bleeding and make sure that follow-up care is done after the surgery.

Platelets and Their Interaction with Clotting Factors:

Importance: Platelets collaborate with clotting factors, mainly vWF, to make the first platelet plug at the site of a blood vessel lesion.

Dental Relevance: Thrombocytopenia or platelet dysfunction (e.g., from drugs like aspirin or systemic disorders) can make bleeding worse during dental work. Clotting factors such as vWF are essential for platelet adhesion.

Before doing any invasive procedures, you should check the platelet counts and function, especially in patients who are on antiplatelet treatment.

Why These Are Important for Dentists

Bleeding Risk: Patients with clotting factor deficits may bleed a lot during dental treatments, especially extractions, implant placements, or periodontal surgery.

Patient Management: Patients with bleeding disorders (e.g., hemophilia, VWD) necessitate customized treatment protocols, encompassing pre-procedural factor replacement, antifibrinolytics (e.g., tranexamic acid), and localized hemostatic interventions (e.g., absorbable hemostats, sutures).

Anticoagulant Therapy: A lot of individuals take anticoagulants (such warfarin and direct oral anticoagulants) that change how coagulation factors work (like factors II, VII, IX, and X). Dentists need to talk to doctors to decide if they need to change the treatment.

Post-Procedure Care: Delayed bleeding, which is prevalent in factor XIII deficiency or VWD, needs close monitoring after the procedure and patient education.

Things to think about in dental practice

Assessment Before Treatment: Get a full medical history to find out if the person has a bleeding issue or is taking anticoagulants. You might need to get certain lab tests, such PT/INR, aPTT, or a platelet count.

Hemostatic Measures: Use local hemostatic treatments such oxidized cellulose, fibrin glue, or tranexamic acid mouthwash to stop the bleeding.

Collaboration: Work with hematologists or medical teams to care for individuals who have bleeding disorders or who are taking anticoagulants. Techniques that are minimally invasive: Choose atraumatic methods to lower the danger of bleeding. **[8-12]**

Key Bleeding Disorders for Dental Practitioners [7-12]

1. Hemophilia A (Factor VIII Deficiency):

Description: An X-linked recessive condition caused by a lack of or malfunctioning factor VIII, which is an important clotting factor in the intrinsic coagulation pathway. It causes bleeding that lasts longer than normal, often after surgery or an injury.

Dental Relevance: Patients may have excessive bleeding during or after dental operations, including spontaneous gingival bleeding or persistent bleeding post-extraction. In severe circumstances, bleeding can be life-threatening.

Management: For mild cases, it is necessary to contact with a hematologist about pre-procedure factor VIII replacement treatment or desmopressin (DDAVP). It is also important to use local hemostatic treatments such fibrin sealants, tranexamic acid mouthwash, and suturing. Don't have intrusive operations done without enough planning.

Things to think about: Check the levels of factor VIII and the person's bleeding history. When possible, dentists prefer to use non-invasive methods**.**

2.Hemophilia B (Factor IX Deficiency):

Definition: An X-linked recessive condition caused by a lack of or malfunctioning factor IX, which is also part of the intrinsic coagulation pathway. It looks a lot like hemophilia A, but it's not as common.

Dental Relevance: Bleeding risks are about the same as those of hemophilia A, and bleeding can last longer after dental work. Delayed bleeding may happen if the clot isn't stable enough.

Management: Needs factor IX replacement therapy before invasive surgeries, which should be planned with a hematologist. Bleeding is controlled with local hemostatic medicines and antifibrinolytics, such as tranexamic acid.

Things to think about: Make sure the diagnostic and factor levels are correct before treatment. It is very important to keep an eye on things after the procedure to find any delayed bleeding.

3.Von Willebrand Disease (VWD):

Description: The most prevalent inherited bleeding condition is caused by a lack of or malfunctioning von Willebrand factor (vWF), which helps platelets stick together and keeps factor VIII stable. There are three varieties of it: Type 1 is a partial deficiency, Type 2 is a malfunctioning vWF, and Type 3 is a severe deficiency.

Dental Relevance: Patients may develop mucosal bleeding, extended seeping following extractions, or gingival bleeding. Type 3 VWD might look a lot like severe hemophilia. Mild cases that haven't been diagnosed may show up unexpectedly following dental work.

Management: Desmopressin (DDAVP) for Type 1 and some Type 2 instances; vWF concentrates for severe cases (Type 3 or unresponsive Type 2). Tranexamic acid mouthwash, absorbable hemostats (such gelatin sponges), and stitches are all local treatments. Don't take aspirin or other NSAIDs.

Things to think about: Check for a history of bleeding (for example, nosebleeds or heavy periods). You could need lab testing including vWF antigen, activity, and factor VIII levels.

4.Fibrinogen Disorders (Afibrinogenemia, Hypofibrinogenemia, Dysfibrinogenemia):

Description: Uncommon conditions characterized by nonexistent, diminished, or malfunctioning fibrinogen (factor I), which constitutes the fibrin clot. Afibrinogenemia produces heavy bleeding, and dysfibrinogenemia can cause either hemorrhage or thrombosis.

Dental Relevance: Bleeding that lasts a long time following dental work, notably extractions or operations. Dysfibrinogenemia may manifest as erratic bleeding or clotting tendencies.

Management: Fibrinogen replacement, such as cryoprecipitate or fibrinogen concentrate, may be necessary. Local hemostatic drugs and antifibrinolytics are very important. Watch for bleeding that happens later or thrombosis.

Things to think about: Check the levels and function of fibrinogen. For complicated cases, work with a hematologist.

5.Factor XIII Deficiency:

Description: A rare autosomal recessive condition that leads to low levels of factor XIII, which helps keep fibrin clots stable. It causes bleeding that doesn't happen right away (hours to days after the procedure) and wounds that don't heal well.

Dental Relevance: A common sign of delayed bleeding following dental extractions or procedures is that it may not be seen right away. Patients may have a history of bleeding from the umbilical cord or have miscarriages over and over again.

Management: You may need factor XIII concentrates or cryoprecipitate before and after the surgery. It is important to use local hemostatic measures and follow up for a long time.

Things to think about: Keep an eye out for bleeding that happens later. It is very important to teach patients about the indicators of bleeding.

6.Platelet Function Disorders (e.g., Glanzmann Thrombasthenia, Bernard-Soulier Syndrome):

Definition: Uncommon conditions that impact platelet function, hindering primary hemostasis. Glanzmann thrombasthenia is a condition in which platelets don't stick together properly. Bernard-Soulier syndrome is a condition in which platelets don't stick to each other because they don't have enough glycoprotein Ib-IX-V.

Dental Relevance: After the operation, patients may have mucosal bleeding, gingival leaking, or bleeding that lasts a long time. These conditions exhibit symptoms similar to VWD.

Management: Platelet transfusions for severe cases, desmopressin for some illnesses, and antifibrinolytics (e.g., tranexamic acid). Local hemostatic drugs are very important. Don't take aspirin or NSAIDs.

Things to think about: You could need platelet function testing, like aggregometry. Work with hematology to manage.

7.Acquired Bleeding Disorders:

Conditions such as vitamin K deficiency (which affects factors II, VII, IX, and X), liver disease (which lowers the production of clotting factors), or drug-induced coagulopathy (such as warfarin, direct oral anticoagulants [DOACs], or antiplatelet drugs) can make it harder for the body to stop bleeding.

Dental Relevance: This is common in people who use anticoagulants or have other health problems, like liver illness. Procedures can lead to significant bleeding, particularly in people on warfarin (which affects vitamin K-dependent variables) or DOACs.

Management: Check the INR for people on warfarin; they may need to switch to heparin or stop taking it for a short time (with a doctor's advice). You might need to change the dose of DOACs or use reversal agents, like idarucizumab for dabigatran. We apply local hemostatic techniques and antifibrinolytics.

Things to think about: Look into the patient's prescription history and talk to their doctor. Do not change your anticoagulant therapy without talking to a doctor beforehand.

Practical Considerations for Dental Practitioners

Pre-Treatment Assessment: Collect a comprehensive medical history, encompassing bleeding tendencies (e.g., epistaxis, bruising, extended postoperative bleeding), familial history, and pharmacological usage. Laboratory testing include PT/INR, aPTT, platelet count, and vWF assays may be necessary.

Hemostatic Measures: To stop bleeding, use local hemostatic agents including oxidized cellulose, gelatin sponges, and fibrin glue, as well as tranexamic acid mouthwash and sutures. Use atraumatic methods to reduce trauma.

Collaboration: Work with hematologists or primary care doctors to take care of patients who have bleeding disorders or are taking anticoagulants. You might need to change your medications or replace some factors before the treatment.

Patient Education: Tell patients about the dangers of bleeding and how to care for themselves after the procedure, including how to tell if bleeding is delayed.

Planning the procedure: Choose techniques that are as little intrusive as feasible. Plan high-risk treatments in places where hematology assistance is available, including hospital-based clinics. [**7-12]**

Prosthodontic Treatment Procedures in Patients with Bleeding Disorders and Deficient Clotting Factors: Protocols and Precautions. [11-28]

Prosthodontic treatments, including fixed partial dentures (FPDs) and dental implants, restore function and aesthetics; however, they present distinct challenges for patients with bleeding disorders (e.g., hemophilia A/B, von Willebrand disease [VWD], factor XIII deficiency) or clotting factor deficiencies due to the heightened risk of excessive bleeding, hematoma formation, and delayed healing. These procedures require cooperation between multiple specialists, including hematologists, because they include manipulating soft tissue, preparing bone, and possibly performing surgery (for example, preparing teeth for FPD abutments or placing implants with or without grafting). General concepts encompass preoperative factor replacement to attain hemostatic levels (e.g., 50–100 IU/dL for factor VIII/IX), antifibrinolytic therapy (e.g., tranexamic acid [TXA]), atraumatic procedures, and postoperative surveillance.

General Protocols and Precautions for Prosthodontic Procedures

- Preoperative Assessment: Collect a detailed medical history, encompassing bleeding phenotype (e.g., HEMSTOP questionnaire score ≥2 necessitates hematology referral), familial history, and inhibitor status. Tests done in the lab include activated partial thromboplastin time (aPTT), prothrombin time (PT/INR), factor levels, von Willebrand factor (vWF) assays, and platelet function. Talk to a hematologist or hemophilia treatment center (HTC) 1–2 weeks before. If you haven't already, be vaccinated against hepatitis A and B.
- Preparation for Hemostasis: For simple procedures (like FPD impressions), raise deficient factors to 50–80 IU/dL, and for major procedures (like implant surgery), raise them to 80–100 IU/dL. For mild VWD or hemophilia A that responds to treatment, provide desmopressin (DDAVP) via IV or intranasal (0.3 mcg/kg). Start taking TXA (25 mg/kg orally or IV every 8 hours) or epsilon-aminocaproic acid (EACA; 50–100 mg/kg every 6 hours) one day before the procedure and keep taking it for 5–7 days after. Don't use NSAIDs or aspirin; instead, take acetaminophen for pain.

Methods of surgery: Use approaches that are as less invasive and traumatic as possible, like guided implant surgery and flapless techniques. Use local anesthetic using a vasoconstrictor, such as lidocaine 2% with epinephrine 1:100,000, by infiltration. Avoid nerve blocks till the factors have returned to normal. During the surgery, use local hemostats such gelatin sponges, oxidized cellulose (Surgicel), or fibrin glue.

- Care after surgery: Keep an eye on them for 1–2 hours after the procedure; for high-risk situations, keep an eye on them overnight. Infuse factors/TXA for 3 to 7 days. A soft diet, ice packs, and raising the head; chlorhexidine rinses from day one. Check in 24 to 48 hours later, then once a week for two weeks to see how the bleeding and healing are going.
- Type of Procedure: No factor cover is needed for low-risk (FPD try-ins and modifications). Moderate-risk (FPD tooth preparation): Factor to 50 IU/dL plus TXA. For high-risk procedures such implant implantation and grafting, the dose should be 80–100 IU/dL plus TXA and local measures.

1. Hemophilia A (Factor VIII Deficiency) and Hemophilia B (Factor IX Deficiency)

- Patients with Hemophilia A/B (severe: <1 IU/dL; moderate: 1–5 IU/dL; mild: 5–40 IU/dL) are at risk of prolonged bleeding following tooth preparation or implant osteotomy. Protocols follow the standards of the World Federation of Hemophilia (WFH), which stress replacing factors.
- FPD Procedures: o Protocol: For crown/bridge preparation, provide recombinant factor VIII (Hem A) or IX (Hem B) 30–60 minutes before the operation at a dose of 50–80 IU/dL (weight [kg] times target rise [IU/dL] × 0.5 for VIII; ×1 for IX). TXA mouthwash (4.8%, 10 mL rinse four times a day) after prep. Impressions: Use atraumatic retraction cords that have been soaked in TXA.
- Precautions: Wait to do deep subgingival preps; use a laser to handle soft tissue to cut down on hemorrhage. When using inhibitors, employ bypassing agents like rFVIIa 90 mcg/kg.

- Results: Low risk of bleeding with prophylaxis; one research found no problems in 71 mild to moderate cases with buccal infiltration exclusively.
- Implant Procedures: o Protocol: Before surgery, raise factors to 80–100 IU/dL; then keep them at 40–60 IU/kg every 12–24 hours for 3–5 days. Add platelet-rich fibrin (PRF) for sinus lifts and grafting. Placement with guidance or no flap is recommended. TXA and stitches after surgery.
- Precautions: Use single-stage implants to cut down on procedures; don't load them right away in very bad situations. Check INR/aPTT every day at first. Case reports reveal that preoperative factor coverage works 100% of the time.
- Results: With multidisciplinary treatment, about 95% of people survive, and bleeding is controlled in 90% of instances.

2. Von Willebrand Disease (VWD)

VWD (type 1: partial vWF deficiency; type 2: dysfunctional; type 3: severe) impairs platelet adhesion; most frequent hereditary condition (prevalence ~1%). Dental implants and FPDs can cause mucosal leakage.

FPD Procedures: o Protocol: DDAVP for type 1 (0.3 mcg/kg IV 30 min pre-op; elevates vWF 2–6x). For types 2 and 3, give vWF/FVIII concentrate (like Humate-P; 40–60 IU/kg) to get vWF:RCo/FVIII levels over 50 IU/dL. TXA before and after surgery. To avoid hurting tissue, use silicone impression materials.

Precautions: Check how DDAVP works before surgery; don't give it to older people or anyone with other health problems (risk of hyponatremia). Gingival retraction using drugs that don't have epinephrine in them.

Results: 63 examples of effective hemostasis with only local TXA; no transfusions required.

Implant Procedures: Protocol: vWF concentrate to >80 IU/dL before surgery; keep it up for 5–7 days. Mix with TXA and local hemostats, like fibrin sealant. Surgery with guidance lowers flap elevation.

Precautions: Wait for uncontrolled bleeding phenotype; keep an eye out for delayed hemorrhage (up to 72 hours). Case study: Successful implantation of four implants with DDAVP and TXA, with no problems.

Results: Implant survival rate is over 90%, and guided methods lower the risk of complications.

3. Factor XIII Deficiency and Other Rare Clotting Factor Deficiencies (e.g., Fibrinogen Disorders)

Rare (prevalence <1:1,000,000); danger of delayed bleeding and poor clot durability.

FPD Procedures: o Protocol: Infuse factor XIII concentrate (e.g., 10–20 IU/kg) or cryoprecipitate to >30 IU/dL pre-op. TXA for 7 days. Very little tooth loss.

Take care: Don't do too much preliminary work; utilize PRF to make things more stable.

Implant Procedures: o Protocol: Factor to >50 IU/dL; infusions every 3–5 days after surgery. It is important to place the flapless.

Precautions: Watch for delayed bleeds for a long time (up to 2 weeks); fibrinogen levels must be above 100 mg/dL.

Outcomes: There isn't much data, but it worked with a customized replacement.

4. Acquired Bleeding Disorders (e.g., Anticoagulant-Induced Factor Deficiencies)

- Common in older people (for example, warfarin affects II/VII/IX/X); balance the risks of thrombosis and hemorrhage.
- FPD Procedures: o Protocol: INR <3.0; no break for minor preps. TXA if INR is between 2.5 and 3.5.
- Precautions: Talk to a doctor first; utilize DOAC reversal if necessary (for example, idarucizumab for dabigatran).
- Implant Procedures: o Protocol: Stop taking warfarin 2–3 days before the surgery (INR <2.0); if there is a high risk of thrombosis, use heparin as a bridge. For DOACs, stop for 24 to 48 hours.
- Precautions: Local precautions are required; a meta-analysis reveals that continuing for single implants does not increase bleeding.
- Outcomes: The risk of bleeding is low (OR 1.11) with local hemostasis, and the survival rates are similar to those of the controls.

Challenges and Future Directions

Some of the problems are making inhibitors, getting to concentrations, and differences in global guidelines. New trends: Non-factor therapy (such emicizumab for hemophilia A) and guided surgery cut down on the requirement for comprehensive prophylaxis. Adherence leads to success rates of over 90%, however 59% of mild cases are over-treated. **[12,16, 21-28]**

Advancements in the Management of Bleeding Disorders and Deficient Clotting Factors from a Dental Treatment Perspective. [12,16, 21-28]

The management of bleeding disorders, including hemophilia A and B (deficiencies in factors VIII and IX), von Willebrand disease (VWD; von Willebrand factor [vWF] dysfunction), Glanzmann's thrombasthenia (platelet function defects), factor XIII deficiency, and bleeding disorders of unknown cause (BDUC), has advanced significantly between 2023 and 2025. These changes are all about making prophylaxis better, cutting down on the number of treatments needed, and improving hemostasis. This is especially important for dental operations where there is a significant risk of bleeding, like extractions, root canal therapy, and periodontal surgery. From a dental point of view, new technologies make treatments safer, less invasive, and more likely to be done as outpatient operations. They also eliminate the need for high-dose factor replacement, which can lead to issues including prolonged bleeding or hematoma formation. Some of the most important trends are non-factor therapy, medications with longer half-lives, rebalancing agents, new devices, local hemostatics, and standardized instruments for assessing risk.

1. Non-Factor Therapies: Bispecific Antibodies and Mimetics

- Non-factor therapies imitate the activity of clotting factors or improve coagulation without directly replacing them. They can be given subcutaneously and are resistant to inhibitors (antibodies that neutralize factors). These are life-changing for patients with inhibitors, who used to have a higher risk of bleeding during dental work.
- Emicizumab (Hemlibra): A bispecific antibody that acts like factor VIII. It is approved for hemophilia A and is now in phase 3 trials for severe VWD (2024–2025). It is given under the skin once a week or once a month, and it cuts down on bleeding by 50% to 80%. In juvenile patients with inhibitors, it has changed protocols from on-demand to prophylactic usage, along with recombinant activated factor VIIa (rFVIIa) during procedures. Mim8 (84% zero-bleed rate in trials), NXT007 (longer half-life), and Inno8 (possible oral version) are new mimetics that improve on this and are more powerful.
- Dental Implications: For dental extractions or root canals in children with hemophilia A and inhibitors, emicizumab prophylaxis facilitates safer procedures when combined with rFVIIa (90 μg/kg pre- and post-procedure) and local agents (e.g., gelatin sponges, fibrin glue), achieving hemostasis without complications in the majority of cases. In VWD, it stabilizes low factor VIII levels, which may help stop bleeding from the mucous membranes after gum surgery. Dentists can do outpatient treatments with fewer factor dose, but they need to talk to other specialists to avoid thrombotic hazards from combinations like emicizumab and activated prothrombin complex concentrate (aPCC).

2. Rebalancing Agents

- These subcutaneous medicines block natural anticoagulants such tissue factor pathway inhibitor (TFPI) or antithrombin to make thrombin production go up. The FDA approved them for hemophilia A/B with or without inhibitors in 2024–2025.
- • Concizumab (Alhemo), Marstacimab (Hympavzi), and Fitusiran (Qfitlia): Concizumab blocks TFPI every day, and marstacimab blocks it every week. Fitusiran reduces antithrombin every other month. They lessen bleeding without needing to replace factors, and you don't have to stop taking them for small procedures. Concizumab is becoming a treatment for BDUC that makes hemostasis better in cases where the cause is not known.
- • Dental Implications: For BDUC patients who need extractions, concizumab could work with tranexamic acid (TXA) or desmopressin (DDAVP) to lower the risk of bleeding after surgery (36–84% of untreated cases). For hemophilia, these drugs keep prophylaxis going during oral surgery, which cuts down on breakthrough bleeds. Dentists should keep an eye out for clots during big procedures and employ local treatments like sutures and haemostatic dressings at the same time. This makes it possible to use atraumatic procedures and tele-video follow-up, which makes it easier for people who are afraid of going to the dentist to get care.

3. Extended Half-Life Clotting Factor Products

Bioengineered recombinant factors lengthen duration, lowering infusion frequency.

•Altuviiio (Efanesoctocog Alfa): A factor VIII with a longer half-life that keeps protective levels for about 7 days and stops bleeding in many patients through tailored pharmacokinetics. Similar products for factor IX are getting better.

• Effects on teeth: For individuals with hemophilia, lower doses (250–1500 IU before the procedure) are enough for extractions, and there have been no reports of severe bleeding. This helps dental care for those who don't stay overnight, especially for kids, where personalized prophylaxis stops serious disease and encourages preventive checkups. For outpatient settings, higher doses may be needed than for inpatient settings. This shows how important it is to standardize.

4. Novel Devices and Targeted Therapies for Platelet Disorders

OhmBody Vagus Nerve Stimulator: In trials, it increased platelet function and cut excessive bleeding by 50%. Large studies are scheduled for 2025–2026.

- Designer Antibody for Glanzmann's Thrombasthenia: Phase 2 data (2025) demonstrate over 50% reduction in bleeding, marking the initial effective treatment for this condition.
- Dental Implications: These could help stop mucosal bleeding in people with platelet problems during treatments like scaling or implants. For Glanzmann's, better platelet aggregation helps stop bleeding without needing blood transfusions, which makes oral surgery safer.

5. Local Hemostatic Agents and Risk Assessment Tools

Fibrin Sealants and Adjuncts: Matched cohort studies (2024) validate enhanced hemostasis during dental surgery in comparison to conventional techniques. Along with TXA (20–25 mg/kg) or DDAVP for BDUC or VWD.

The HEMSTOP Questionnaire is a reliable way to find out how likely someone is to bleed before surgery for BDUC. If the score is 2 or above, the person should see a hematologist.

Dental Implications: Fibrin sealants make extractions less likely to cause problems, especially in kids with inhibitors. HEMSTOP standardizes screening, which makes it easier for different types of doctors to work together and makes sure that oral health isn't ignored. For BDUC, TXA is enough for minor extractions, but combinations are needed to stop bleeding in more serious cases.

6. Standardized Guidelines and Multidisciplinary Approaches

Recent evaluations stress the need for uniform clotting factor procedures to deal with differences around the world. They also stress the need for preventive care starting in childhood. The World Federation of Hemophilia's guidelines (2020, with modifications for 2024–2025) include emicizumab and rebalancing agents.

Dental Implications: Customized plans lower the number of hospitalizations and make it possible to do operations in primary care settings. Dentists should work with hematologists on high-risk clients, employing technologies like HEMSTOP and local medications to keep BDUC or inhibitors under control.

These improvements will lead to fewer bleeding problems, better patient compliance, and better oral health results in dental practice. But there are problems, such as the risk of thrombosis, the difficulty of getting to low-resource areas, and the need for more trials. **[29-35]**

Future trends in the management of Bleeding disorders & Deficient clotting from a Dental Treatment Perspective. [29,30,36-40]

The care of bleeding disorders, including hemophilia A (factor VIII deficiency), hemophilia B (factor IX deficiency), von Willebrand disease (VWD; von Willebrand factor dysfunction), factor XIII deficiency, and bleeding disorders of undetermined origin (BDUC), is advancing swiftly. These improvements are meant to make dental operations safer, easier to conduct, and less likely to cause bleeding, which is a common danger because they are intrusive (e.g., extractions, implants, periodontal surgery). From a dental perspective, these trends underscore the importance of maintaining stable clotting factor levels to reduce pre-procedure prophylaxis, fostering interdisciplinary collaboration, enhancing preventative treatment, and implementing standardized methods to tackle global disparities in factor utilization.

1. Gene Therapy for Sustained Factor Production

Gene therapy is a revolutionary method that uses adeno-associated virus (AAV) vectors to transfer functional genes (for example, F8 for factor VIII in hemophilia A). This could lead to long-lasting or even permanent factor expression and cut down on the number of infusions needed. Valoctocogene roxaparvovec (Roctavian®) and other approved treatments have kept factor VIII levels steady (for example, the mean level was 41.9 IU/dL at 1 year in phase 3 trials) and cut the number of bleeding episodes by more than 80%. Giroctocogene fitelparvovec and dirloctocogene samoparvovec are two investigational possibilities that show dose-dependent factor increases. Some patients even reach normal levels. New CRISPR-Cas9 editing fixes mutations like F8 intron inversions and gives permanent fixes.

Dental Implications: Sustained factor levels could render invasive operations "risk-free" by lowering the need for supplementary prophylaxis and bleeding problems including delayed hemorrhage after extraction. For example, individuals receiving gene therapy may necessitate reduced factor replacement for extremely invasive operations (e.g., numerous extractions or implants), facilitating safer outpatient dental care. However, long-term monitoring for liver toxicity and blood clotting hazards is necessary. This may require collaboration between hematologists and dentists to choose when to perform procedures. Preventive dental measures in youngsters may avert severe caries, which are more common in individuals with bleeding disorders due to inadequate care.

2. Non-Factor Therapies and Rebalancing Agents

Non-factor therapies work around missing clotting factors by imitating their activity or blocking anticoagulants. They can be given under the skin and are resistant to inhibitors. Bispecific antibodies such as emicizumab (for hemophilia A) and Mim8 (with greater potency) augment thrombin production, leading to a 50–80% reduction in bleeding episodes. RNA interference drugs, such fitusiran (given once a month under the skin), diminish antithrombin, while TFPI inhibitors, like concizumab and marstacimab, raise coagulation. Recombinant von Willebrand factor therapy are growing for VWD, especially for women and girls who have excessive menstrual bleeding. Concizumab is becoming available for BDUC, and it helps with hemostasis in cases when the cause is not clear.

Dental Implications: These treatments could make managing patients around procedures easier by establishing stable hemostasis, which would mean less intravenous factors are needed for things like extractions or scaling. Antifibrinolytics (e.g., tranexamic acid, aminocaproic acid) combination with these medications improve clot stability during dental surgery, with tranexamic acid alone adequate for uncomplicated extractions in BDUC. In hemophilia, they facilitate flapless implants or orthognathic surgery with minimal supplementary prophylaxis. Future trends involve the integration of these approaches for juvenile patients to enhance oral health-related quality of life, tackling elevated caries rates and infrequent dental visits.

3. Bioengineered Extended Half-Life Clotting Factors

Bioengineered recombinant factors, including factor VIII/IX with PEG conjugation or fusion proteins, make the half-life longer, which means that infusions happen less often, from 2–3 times a week to once a week or less. This takes care of immunogenicity and short bioavailability in standard treatments.

Implications for teeth: Longer factor activity could minimize the dose needed before a procedure (for example, 200–3000 IU for extractions), making therapies easier to get in primary care settings. For severe hemophilia, this backs up atraumatic methods like laser pulpotomy or rapid implants that don't require long hospital stays. Standardizing the doses for dental operations is a major necessity for the future. This is because there are differences around the world, such as larger outpatient doses, that show that the doses are not always the same.

4. Standardization of Guidelines and Multidisciplinary Education

There is an increasing demand for standardized guidelines for the use of clotting factors in dental treatment, considering the significant disparities in prophylactic doses globally. To help dentists feel more confident in treating patients, it is suggested that they get more training, have guidelines in their local language, and work with hemophilia treatment centers. New tools and research, such the HEMSTOP questionnaire for assessing bleeding risk, are coming out.

Dental Consequences: Standardized criteria could improve hemostasis for invasive procedures, which would cut down on unneeded treatments like referrals. Multidisciplinary approaches encourage preventive care from a young age, which helps keep oral health from getting worse. In Hungary and places like it, training initiatives are meant to get more care to primary dentists.

5. Advanced Local and Minimally Invasive Techniques

Trends include flapless implants, local hemostats (such fibrin glue and gelatin sponges), and antifibrinolytics that don't affect the whole body for mild instances. More and more high-risk patients are getting tele-video follow-up and operations in hospitals.

Dental Implications: These lower the risk of bleeding in those with BDUC or mild hemophilia, making extractions or implants safer. Avoiding NSAIDs and taking preventive antibiotics makes things even safer.

Overall, these developments offer safer, easier-to-get dental care by lowering the risks of bleeding and the burdens of treatment, with a focus on preventive and customisation. **[29,30,36-40]**

Conclusion

Bleeding disorders, such as hemophilia A (factor VIII deficiency), hemophilia B (factor IX deficiency), von Willebrand disease (VWD), factor XIII deficiency, and uncommon platelet disorders like Glanzmann thrombasthenia, pose considerable challenges in prosthodontic treatments, including fixed partial dentures (FPDs) and dental implants, due to the risk of excessive bleeding, hematoma formation, and compromised wound healing. These treatments, which include preparing teeth, moving soft tissue, or cutting bone, need careful planning and a team of doctors, including hematologists, to make sure they are safe. Protocols stress the importance of assessing risk before surgery with tools like the HEMSTOP questionnaire, personalized factor replacement to reach hemostatic levels (50–100 IU/dL), desmopressin for instances that respond to it, and antifibrinolytics like tranexamic acid to keep clots stable. To lower the danger of bleeding, it is important to use local hemostatic treatments (like fibrin glue and gelatin sponges) and atraumatic procedures (such flapless implant implantation). Recent breakthroughs, such as longer half-life clotting factors, non-factor therapy like emicizumab, and rebalancing agents like concizumab, have changed the way we treat people by making it possible to do procedures in the office and reducing the number of treatments needed. Standardized global guidelines and preventive dental treatment make things even safer and more effective, which leads to better prosthodontic outcomes and a better quality of life for people with bleeding disorders.

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