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# Special Care Dentistry: Part 3. Dental Management of Patients with Medical Conditions causing Acquired Bleeding Disorders

**Abstract:** The second paper in this three part series discussed the dental management of patients with drug-related acquired bleeding disorders. This paper will discuss and outline the dental management of patients with acquired bleeding disorders that can result from medical conditions. Again, these may be associated with vascular defects, platelet defects or coagulation defects. In an age when people are living longer, and medical interventions are continually becoming more advanced, clinicians will need to be aware of systemic disorders and treatments that may cause complications in the dental setting.

**Clinical Relevance:** Being able to recognize which medical conditions, including their management, may cause bleeding problems at an early stage will lead to good patient management, particularly in planning and delivering treatment involving any invasive dental procedures that can cause bleeding. Whilst most patients can be successfully treated in general dental practice, the clinician may need to make a decision on whether or not to refer a patient to specialist services for all dental treatment, or to share care between primary care and specialist services.

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There are many acquired medical conditions in which the patient may be on some of the drugs described in paper 2, therefore leading to increased bleeding tendencies. For example, some patients with heart valve

replacement will be taking anticoagulants, or patients that have had organ transplants may be on corticosteroids.

However, there are several acquired medical conditions that can directly affect normal haemostasis. In this paper, acquired conditions in the following groups will be discussed:

- Liver disease;
- Renal disease;
- Bone marrow disorders;
- Immune disorders;
- Other relevant acquired conditions.

## Liver disease

The liver plays a major role in haemostasis as:

- It produces coagulation factors such as Factors I (fibrinogen), II, VII, IX, X and XI.

- It produces thrombopoietin, a glycoprotein hormone which regulates platelet production by the bone marrow.

- Failure of normal function of the liver can lead to malabsorption of fat soluble vitamins, such as vitamin K, which is required for the synthesis of blood-clotting factors.

- Both Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) are prolonged in chronic liver disease and severe bleeding can occur after dental extractions in these patients.<sup>1</sup>

Alcohol misuse is one of the causes of liver disease leading to cirrhosis, which has been attributed to 3000 deaths per year in England and Wales. It is estimated that up to 10% of the United Kingdom population have problems with their liver, most likely linked to lifestyle

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■ Ascites
■ Skin rashes
■ Flushed facial appearance
■ Spider naevi which are vascular lesions consisting of a central arteriole surrounded by smaller blood vessels due to hormonal changes. These occur in a third of cases. <sup>25</sup>
■ Bruising/bleeding due to decreased production of clotting factors.
■ Palmar erythema. Mottling of the palm due to altered sex hormone metabolism.
■ Dupuytren's contracture. Thickening and shortening of palmar fascia that leads to flexion deformities of fingers. This is attributed to fibroblast proliferation and collagen deposition. It occurs in 33% of patients.
■ Acne rosacea
■ Skin blemishes
■ Swollen eyes
■ Foetor halitosis
■ Coated tongue
■ Itchy skin due to bile products deposited in the skin.
■ Excessive sweating causing offensive body odour.
■ Jaundice. Yellow discolouring can be seen in the skin, eye and mucous membranes due to increased bilirubin (2–3 mg/Dl) which is usually excreted through bile.

**Table 1.** Signs of chronic liver disease.

factors such as heavy drinking, obesity and diabetes. Average alcohol consumption in this country has risen steadily and it is estimated that 26% of the adult population in this country drink in excess of the recommended limits for sensible drinking. Alcohol misuse is implicated in up to 22,000 deaths per year in England and Wales.<sup>2</sup> Post-operative bleeding is a common complication in alcohol-dependent patients as a result of:

- Liver cirrhosis leading to decreased production of clotting factors;
- Bone marrow suppression and folate deficiency causing thrombocytopenia;
- Malnutrition due to heavy drinking which can decrease synthesis of vitamin K-dependent clotting factors, leading to further coagulation problems;<sup>3</sup>

- Alcohol prolonging bleeding time produced by aspirin and NSAIDs.<sup>4</sup>

**Hepatitis**

The Health Protection Agency (HPA) Centre for infections has reported that there have been about 1,200 cases per year of Hepatitis A since 2000 in England and Wales. The figures underestimate the true number as people with mild symptoms are under reported.

As many cases of hepatitis remain undiagnosed and other risk factors for liver disease are on the increase, such as obesity and drinking, it is important for clinicians to look for external signs (Table 1) and recognize symptoms of liver disease.

Hepatitis may co-exist with HIV in patients that have contracted the virus

through blood transfusions and this may further complicate the bleeding tendency with thrombocytopenia. According to the UK NHS Blood and Organ Donor statistics,<sup>5</sup> there are currently around 600 liver transplants carried out each year, with an 85% success rate after one year.

**Dental management of bleeding tendencies caused by acquired liver disease**

- Any patient with a history of liver disorder or high alcohol intake should have blood taken for liver function tests and clotting screens prior to invasive dental treatment, such as dental extractions.<sup>6</sup>
- In patients at risk of vitamin K malabsorption, such as those with obstructive jaundice, intravenous vitamin K may be required beforehand. Therefore, consultation with the patient's physician is essential.
- Any patient with jaundice has an increased risk of bleeding and may require a pre-operative infusion of fresh frozen plasma.<sup>6</sup> Again, consultation with the patient's physician will be necessary for this.
- Local haemostatic measures should always be used (Table 2).

**Renal disorders**

The kidneys play a vital role in excretion of waste products and maintaining fluid and electrolyte balance. They produce the hormone erythropoietin which stimulates red cell production in the bone marrow, as well as vitamin D, which plays a vital role in bone metabolism. Haemostasis is impaired in patients with chronic renal failure owing to:

- Impaired platelet production as thrombopoietin hormone, which stimulates megakaryocytes to proliferate and mature into platelets, is produced in the kidney's proximal convoluted tubular cells;<sup>7</sup>
- Impaired platelet adhesion due to defective von Willebrand's factor as glomerular endothelial cells express von Willebrand's factor;
- A decrease in platelet factor 3 (thromboxane) which impairs conversion of prothrombin to thrombin in the clotting cascade;
- Vasodilation from raised prostacyclin levels (PGI)<sup>8</sup>;
- Haemodialysis patients taking heparin to facilitate their treatment.

<p><b>1. Local Anaesthetic</b></p> <ul style="list-style-type: none"> <li>■ Use local anaesthetic with a vasoconstrictor;</li> <li>■ Avoid regional nerve blocks where possible. If necessary, then ensure an aspirating syringe is always used.<sup>26</sup></li> </ul>
<p><b>2. Minimize Trauma</b></p> <ul style="list-style-type: none"> <li>■ As with all extractions, the aim is to minimize trauma as much as possible.</li> </ul>
<p><b>3. Haemostatic Agents</b></p> <ul style="list-style-type: none"> <li>■ Consider the use of a haemostatic resorbable dressing following an extraction, such as oxidized regenerated cellulose (Surgicel®), synthetic collagen or gelatine sponge to promote and stabilize clot formation by providing a mechanical matrix.<sup>27</sup></li> </ul>
<p><b>4. Suture</b></p> <ul style="list-style-type: none"> <li>■ Suture the socket with resorbable sutures to achieve primary closure where possible and then apply pressure to the socket with a gauze pack until haemostasis is achieved.</li> </ul>
<p><b>5. Post-operative instructions</b></p> <ul style="list-style-type: none"> <li>■ Give clear post-operative instructions to the patient, both verbal and written.</li> </ul>
<p><b>6. Tranexamic Acid Mouthwash</b></p> <ul style="list-style-type: none"> <li>■ The use of tranexamic acid post-operatively is not routinely advocated in patients on warfarin as it can be expensive, difficult to obtain and, when used in combination with other haemostatic measures, provides little additional reduction in post-operative bleeding.<sup>28</sup></li> <li>■ However, tranexamic acid mouthwash may be useful as an antifibrinolytic agent for patients with congenital and other acquired bleeding disorders.</li> </ul>

**Table 2.** Local haemostatic measures.

General Signs	Oral Signs
Anaemia as kidneys produce erythropoietin	Loss of lamina dura
Bruising due to decreased thromboxane production which impairs conversion of prothrombin to thrombin	Osteolytic lesions
Bleeding from mucous membranes due to platelet abnormality and defective von Willebrand's factor	Secondary hyperparathyroidism leading to giant cell lesions
Skin pigmentation and pruritus due to excess urea.	Halitosis
Anorexia, nausea, vomiting, diarrhoea	Metallic taste
CNS effects such as confusion, coma and fits due to metabolic disturbances.	Dry mouth
	Oral ulceration/pale mucosa due to anaemia

**Table 3.** Signs of chronic renal failure.

### Chronic renal failure (CRF)

Chronic renal failure is an irreversible condition which requires treatment with dialysis. It occurs after progressive kidney damage, resulting in depression of the glomerular filtration rate persisting over 3 months or more.

Prediction modelling by the UK renal registry<sup>9</sup> suggests an increase in the numbers receiving dialysis treatment. The incidence of renal disease is influenced by several factors, including a previous history of renal disease, hypertension and diabetes. Both hypertension and diabetes are common among people of Afro-Caribbean or South Asian descent, making them more prone to developing renal disease.

Clinicians may need to be aware of signs and symptoms of renal failure, especially in patients who have a history of poorly controlled hypertension or diabetes (Table 3).

Patients with chronic renal failure may require dialysis. There are two main types of dialysis:

- Haemodialysis; and
- Peritoneal dialysis.

Patients on haemodialysis typically attend a hospital renal unit three times a week for a 3–5 hour period. The dialysis machine filters out waste products from the patient's circulation returning cleansed blood. Heparin is added to the dialysis circuit to facilitate the process. Patients on other forms of dialysis, such as peritoneal dialysis, are not treated with heparin.

### Dental management of bleeding tendencies caused by acquired renal disorders

- The renal physician or haematologist should be consulted.
- Although dialysis should improve platelet function in general, patients on haemodialysis are heparinized. Therefore, invasive dental treatment should not be carried out on the same day as dialysis.
- Bleeding tendencies should be excluded prior to giving a nerve block local anaesthetic or carrying out invasive dental treatment.
- Local haemostatic measures as described in Table 2 are essential.
- To avoid haemostatic problems, once local measures have been used,

Desmopressin (DDAVP), which can be taken intranasally chairside, may help with haemostasis for up to 4 hours and can be prescribed by the patient's specialist unit.<sup>8</sup>

## Bone marrow disorders

The bone marrow produces haemopoetic stem cells, which can be divided into three lineages:

1. Erythroid cells which form erythrocytes;
2. Lymphoid cells which form T and B cells and contribute towards humoral immunity;
3. Myeloid cells, which include granulocytes, megakaryocytes (which form platelets) and macrophages. These cells play a significant role in both innate and humoral immunity, as well as haemostasis.

Normally, only mature cells are released from the bone marrow into the circulation. Any disorder causing an abnormality in the production of immature precursor cells, or mature cells, can cause a bone marrow disorder. Normal function can be disrupted by infections such as tuberculosis or malignancies such as leukaemias (Table 4).

### Dental management of bleeding tendencies caused by bone marrow disorders

The main points to consider are:

- Any invasive dental procedures that can cause bleeding, including inferior dental block local anaesthetics, must be carried out with extreme caution.
- Prior consultation with the patient's haematologist or physician is essential to discuss the bleeding risk.
- Local haemostatic measures must always be used (Table 2).
- For patients with haematological malignancies, the timing of the procedure is important. Invasive dental procedures should be carried out when the patient is in remission and between chemotherapeutic regimes, when the cell count and platelet count is optimal.<sup>10</sup>
- Prior to chemotherapy, radiotherapy and bone marrow transplants, it is essential that a thorough dental assessment is carried out so that any teeth with poor prognosis can be removed before treatment commences.

Preventive advice, including oral hygiene instruction and diet advice, are essential to minimize dental problems. The aim is to prevent carrying out invasive dental treatment when there are decreased platelet and white cell counts, which will increase the risk of bleeding and infection.

■ Patients with thrombocytopenia may require platelet transfusions prior to invasive dental treatment, depending on their platelet levels. Full blood and platelet counts should be checked before surgery:

-At least 30 x 10(9)/l is required to administer regional dental block injections.

-At least 50 x 10(9)/l is required for minor oral surgery.

-At least 75 x 10(9)/l is required for major surgery.<sup>11</sup>

Local haemostatic measures and the use of DDAVP and tranexamic acid can reduce the need for platelet and factor transfusions.

■ Patients that have had bone marrow transplantation may be leucopenic and thrombocytopenic for up to 6 months after. Therefore, it is advised that dental treatment be deferred until then. Any procedures thereafter must be done following medical consultation.<sup>12</sup>

## Immune disorders

Disorders of the immune system can affect haemostasis due to immune destruction of platelets, effects on vessel walls, effects of drugs taken to control the disorders or effects on the spleen.

### Idiopathic thrombocytopenic purpura (ITP)

Also known as auto-immune thrombocytopenic purpura, this is a condition where there is immune destruction of platelets leading to thrombocytopenia, which is defined as a platelet count of less than 150 x 10(9)/L.

The acute form of ITP can be seen in children following a viral infection. The chronic form is seen mostly in adult women. Normal platelet count is usually slightly decreased during pregnancy owing to the dilution effect. However, it is possible to develop ITP during pregnancy which usually resolves postpartum.<sup>13</sup> ITP is usually idiopathic but

may occur in conjunction with other auto-immune disorders, such as systemic lupus erythematosus, thyroid disease and some viral infections such as HIV.<sup>14</sup>

Clinical features are similar to those seen in platelet disorders, such as bleeding from mucous membranes, epistaxis, and menorrhagia.

As platelets are consumed quickly in active ITP, management includes corticosteroid therapy or alternative immunosuppressant drugs, such as mycophenolate mofetil, azathioprine, to manage the auto-immune condition. In severe cases, a splenectomy might be indicated followed by thrombopoietin medication. Thrombopoietin stimulates megakaryocytes to differentiate into platelets. This has been useful in avoiding the problems associated with platelet transfusions, such as graft versus host disease, bacteraemia, repeated transfusions becoming inadequate and high cost.<sup>15</sup> At present, there are two thrombopoiesis stimulating drugs that are NICE approved and licenced to use in the UK. These are the orally administered Revolade (Eltrombopag) and the subcutaneously administered Nplate (Romiplostim).

### Human immunodeficiency virus (HIV)

Clinically significant haematological problems can be commonly seen in people with HIV. This is due to impaired haemopoiesis, immune-mediated thrombocytopenia and altered coagulation. These are attributable to HIV infection itself, or as sequelae of HIV-related opportunistic infections, malignancies such as lymphoma, or as a result of treatment for HIV itself or associated conditions. In addition, HIV may co-exist with hepatitis or haemophilia, conditions which further exacerbate haematological problems. Several studies, including a London-based study, have shown that thrombocytopenia is frequently associated with HIV infection. HIV-ITP is often an early manifestation of HIV infection, occurring before the CDC AIDS defining condition develops. However, ITP improves as HIV progresses. Treatment is usually reserved for those people with clinically significant symptoms, such as epistaxis or gastro-intestinal haemorrhage. Standard treatment for ITP, such as corticosteroid therapy, chemotherapy, IV immunoglobulin infusions, have proved unsatisfactory.<sup>16,17,18</sup>

Bone Marrow Disorder	Disorder results from:	Treatment	Bleeding tendency caused by:
Myeloproliferative Disorders (rare)	Increased production of one or more precursor cell lines resulting in inhibition of other cells	Spontaneous recovery/ Bone marrow transplant/ Immunosuppressive treatment	Decreased production of platelets/Transformation to leukaemia/ Immunosuppressive treatment
Myelodysplastic Syndrome (rare)	Abnormal cell production leading to underproduction of normal cells	Spontaneous recovery/ Bone marrow transplant/ Immunosuppressive treatment	Decreased production of platelets/Transformation to leukaemia/ Immunosuppressive treatment
Myelofibrosis	Fibrosis due to abnormal precursor cells stimulating fibroblasts	Hydroxyurea and Bisulphan/ Splenectomy	Decreased production of platelets/Transformation to leukaemia
Leukaemia (2% of all cancers in the UK) <sup>29</sup>	Malignant neoplasm of haemopoietic stem cells that can infiltrate bone marrow and enter circulation – 4 main types	Chemotherapy/ Radiotherapy/ Bone marrow transplant	Decreased production of platelets from disease and from treatment
Lymphoma (Non-Hodgkin's more common than Hodgkin's; 4% of all cancers in the UK) <sup>29</sup>	Neoplastic transformation of normal B or T cells in lymphoid tissue – 2 main types	Chemotherapy	Bone marrow infiltration causes thrombocytopenia
Graft versus Host Disease	Severe complication that can follow bone marrow transplant	High dose corticosteroids	Liver involvement/ Thrombocytopenia/ Corticosteroid treatment
Multiple Myeloma (1% of all cancers in the UK) <sup>29</sup>	Malignant disease of bone marrow plasma cells	Chemotherapy/ Bone marrow transplant	Bone marrow infiltration leading to thrombocytopenia/ Hyperviscosity leading to further bleeding tendency/ Association with renal failure

**Table 4.** Bone marrow disorders.

However, several authors have suggested splenectomy in HIV ITP to be a more successful alternative, whilst others remain cautious owing to the immunosuppressive effect advocating splenic irradiation as a possible alternative to surgery.<sup>19 20</sup>

**Systemic lupus erythematosus (SLE)**

Systemic lupus erythematosus is a multisystem auto-immune disease characterized by a variety of auto-antibodies, including antinuclear antibodies (ANA),

antibodies to double stranded DNA, as well as anti-Rho, anti-La, anti-SM, anti-RNP and anti-phospholipid antibodies. It is ten times more common in females than in males. Causative factors include virus, sunlight, drugs, hormones or exposure to occupational agents, such as pesticides.<sup>21</sup> It has a genetic basis with a defect in immune regulation which is thought to be virally induced. Thrombocytopenia can be a complication of SLE.

As this is a multi-system disorder there is a variety of clinical features: facial

(butterfly) rash, alopecia, arthralgia, arthritis, pleuritis, glomerulonephritis, renal failure, anaemia, neutropenia, thrombocytopenia, stroke, seizures, neurological symptoms, fever, lymphadenopathy and photophobia.

Management is with NSAIDs, corticosteroids, hydroxychloroquine, although newer therapies such as anti-TNF alpha agents, and anti-CD20 rituximab have also proven to be effective.<sup>22</sup>

Patients with SLE have a bleeding tendency from thrombocytopenia, circulating lupus coagulants and steroid medication.<sup>21</sup>

Some patients may be on anticoagulation medication such as warfarin. Therefore, it is necessary to know the INR as well as the platelet count and to use local measures to achieve haemostasis (Table 2).

#### Antiphospholipid syndrome (APS)

Antiphospholipid syndrome (also known as Hughes syndrome) is a coagulation disorder which predisposes people to thrombosis in arteries and veins, as well as pregnancy-related complications related to miscarriage, pre-term delivery or severe pre-eclampsia. The most common complication is usually deep vein thrombosis involving deep veins of the legs. The most common arterial event is stroke. Thrombocytopenia is also associated with APS. It is more common than SLE and usually affects young women.

There is auto-immune production of antibodies directed against phospholipid which constitutes cell membrane or plasma proteins which are bound to anionic phospholipids.

Diagnosis depends on the presence of these antibodies, as well as thrombosis or recurrent abortion. It is managed by aspirin to inhibit platelet activation in mild cases, or warfarin in more severe cases, where the INR should be maintained between 3–4.<sup>23</sup> During pregnancy, low molecular weight heparin and low dose aspirin is advocated in women with recurrent history of miscarriage as warfarin is teratogenic.

#### Disorders of the spleen

The spleen has several functions, such as phagocytosis of old red cells, synthesis of antibodies, removal of antibodies coated with bacteria, and acts as a storage site for red cells and platelets, enabling rapid mobilization when necessary. Pluripotential

stem cells, such as megakaryocytes, reside in the spleen and proliferate in conditions of severe haematological stress (extramedullary haemopoiesis, where haemopoiesis usually occurs in the bone marrow).

Splenomegaly usually occurs secondary to other disorders. Common causes of splenomegaly (Table 5) also cause bleeding problems.

Hypersplenism can result from splenomegaly and results in sequestration of platelets causing thrombocytopenia and pancytopenia. Management involves treating the underlying condition, splenectomy and vaccination against infections post surgery.

#### Dental management of bleeding disorders caused by immune system disorders

The main points to consider are similar to the sections above:

- Prior to any dental procedures that may cause a bleeding episode (extractions, scaling, inferior dental block anaesthesia) it is important to consult the patient's physician and to check the patient's full blood and platelet count.
- If the patient is on anticoagulants, then manage as described in paper 2.
- Always use local haemostatic measures, as described in Table 2.

### Other causes of acquired bleeding disorders

#### Acquired thrombocytopenia

There can be many other causes of thrombocytopenia which inevitably results in a patient being more prone to bleeding (Table 6).

Other rarer causes of acquired bleeding disorders include:

- Acquired haemophilia – a disorder resulting from auto-antibodies to Factor VIII.

Haemophilia has been discussed in detail in paper 1.

- Blood transfusion reactions, such as post transfusion purpura. This can occur 7–10 days after a blood transfusion due to antibodies developing against the human platelet antigen 1a leading to auto-immune destruction of platelets.
- Disseminated intravascular coagulation – a disorder where there is overactivation of the clotting cascade leading to consumption of platelets and coagulation factors, and widespread generation of fibrin within blood vessels. This can occur after major trauma, infection, surgery or cancer. Therefore, this condition is more likely to be seen in hospitalized patients.
- Scurvy – this rare condition results from a depletion of vitamin C in the body. This can result in malnourished elderly patients or anorexic patients. Severe deficiency results in haemarthrosis, gingival haemorrhage and sub-periosteal haemorrhage. Studies have shown that anorexia nervosa is on the rise. The General Practitioner database in the UK found a mean incidence of 4/100,000 in people aged between 10–39 years. Therefore, it is important to identify patients who might be at risk of haemostatic problems as a result of anorexia nervosa.<sup>24</sup>

### Conclusion

As we live in a society where medical interventions are continually advancing, people are living longer and medical conditions are extremely diverse, it is important for the dental clinician to be able to recognize medical conditions and treatments that may cause bleeding complications following dental treatment. This paper outlines many of these conditions and suggests ways to identify and manage these patients to prevent

Haematological	Hepatic	Auto-immune	Infective
Myeloproliferative	Cirrhosis	SLE	Chronic malaria
Myelofibrosis	Portal hypertension	Rheumatoid arthritis	Endocarditis
Leukaemias		Sarcoidosis	Typhoid
Lymphomas			Tuberculosis

**Table 5.** Causes of splenomegaly.

Decreased Platelet Production	Splenic Sequestration	Other
Leukaemia Lymphoma Aplastic anaemia Myelodysplasia Chronic alcoholism Vitamin B <sub>12</sub> deficiency Folic acid deficiency	Cirrhosis with congestive splenomegaly Myelofibrosis with splenomegaly	Idiopathic thrombocytopenia purpura (ITP) HIV Drugs (heparin) Disseminated intravascular coagulation (DIC) Thrombotic thrombocytopenia purpura (TTP)

**Table 6.** Causes of acquired thrombocytopenia.<sup>25</sup>

such an episode occurring in the dental surgery. Through detailed risk assessment and treatment planning, the clinician can provide safe dental treatment and use a shared care approach when necessary.

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## CPD ANSWERS November 2013

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|------------|----------|
| 1. C       | 6. A, B  |
| 2. C       | 7. A     |
| 3. D       | 8. D     |
| 4. D       | 9. B, D  |
| 5. A, B, D | 10. C, D |