Thrombocytopenia and Avoiding Bleeding Complications

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Note: Certain lab values were incorrectly stated in the magazine version of this article. All lab values in this online version of this article are correct. A correction will be published in the January 2010 issue of Dentistry Today.
Thrombocytopenia and Avoiding Bleeding Complications

LEARNING OBJECTIVES:

After reading this article, the individual will learn:

- The roles of platelets in hemostasis.
- Causes of thrombocytopenia, how to identify a patient with thrombocytopenia, and how to minimize bleeding in a surgical patient with thrombocytopenia.

ABOUT THE AUTHORS

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INTRODUCTION

Hematologic disorders are relatively common in the elderly but are often undetected. Dentists can frequently predict a bleeding disorder by taking a good medical history and by evaluating the general physical attributes of a patient's face, neck, hands, feet, and oral cavity. In order to prevent serious post-treatment hemorrhage in such patients, special care should be practiced when performing invasive dental procedures.

This article discusses the etiology and pretreatment recognition and considerations of thrombocytopenic purpura, a common bleeding disorder. This will be followed by a case report focused on preprosthetic surgery on an elderly patient treated by a general dentist in a community care setting. The information presented in this article may be applied to other invasive dental procedures, such as exodontia and periodontal surgery. However, a general dentist should always consider his/her skill level and assess the patient’s bleeding risk before performing such procedures. Referral to an oral-maxillofacial surgeon should be made if the dentist does not feel prepared to manage potential complications.

BACKGROUND, SIGNS, AND SYMPTOMS

Thrombocytopenia is a blood disorder characterized by an inadequate number of platelets, resulting in a decreased ability to clot after injury to blood vessels. Platelets, also known as thrombocytes, are non-nucleated cells that circulate in the peripheral blood. They form in the bone marrow by fragmenting from giant precursor cells called megakaryocytes. Platelets survive for only 7 to 10 days. However, bone marrow continuously replenishes the platelet pool under the direction of thrombopoietin, a growth protein derived primarily from the liver.1

Repair of a severed blood vessel requires vascular constriction, platelet activity, and the coagulation cascade process. Platelets promote hemostasis through 4 mechanisms of action: adhesion, aggregation, secretion of several clotting factors, and procoagulant activity. Platelet adhesion begins when platelets arrive at the site of endothelial injury and adhere to local collagen.

Aggregation, or clumping, occurs through the binding of platelets with von Willebrand's factor and plasma fibrinogen. Activated platelets secrete a variety of granules that encourage formation of a thrombus. These substances include adenosine diphosphate (ADP), thromboxane, serotonin, platelet derived growth factor, fibronectin, and additional fibrinogen.2

ADP and epinephrine cause further activation of platelets, while thromboxane and serotonin cause vasoconstriction and promote platelet aggregation.2 Platelet derived growth factor, along with serotonin, exerts a
mitogenic and reparative effect on injured vascular smooth muscle. During procoagulant activity, platelets release phospholipids that help activate the coagulation cascade.

The final steps of this cascade process involve the conversion of prothrombin to thrombin, which then converts fibrinogen and the platelet plug into a cross-linked fibrin clot.3

Platelet disorders can be either quantitative (too few platelets as seen in thrombocytopenia) or qualitative (impaired function affecting adhesion or aggregation).4

Thrombocytopenia can lead to events such as prolonged and extensive bleeding following trauma or surgery, hematoma, and intracranial or gastrointestinal bleeding.5 Signs and symptoms are described below; however, definitive confirmation is made through the results of laboratory tests.

Persons with thrombocytopenia often present with red or purple nonblanching skin and mucosal manifestations referred to as purpura. Categorization of thrombocytopenic lesions varies, but for the purpose of this article they are classified as petechiae (tiny, flat bleeding spots that tend to occur in clusters), hemorrhagic vesicles, and larger hematomas or ecchymoses (bruising).6 An initial sign of a platelet deficiency is the development of petechiae on the hands or feet. Other typical signs include epistaxis, shaving-induced petechiae, hematuria, hematomas from blunt trauma, brushing induced or spontaneous periodontal pocket hemorrhage, and blood-filled lesions on the tongue, lips, or buccal mucosa. The presence of oral mucosal hemorrhagic bullae, also known as wet purpura or blood blisters, is prognostic for life-threatening hemorrhage, and increased collaboration with the patient’s physician is necessary prior to dental treatment.7

Symptoms vary depending on the cause, but may include localized or generalized pain, prolonged menstruation, fatigue, headache, seizures, cardiac arrhythmias, visual disturbance, dizziness, confusion, and altered mental state.8

**TYPES OF THROMBOCYTOPENIA**

A shortage of platelets in the peripheral blood can occur for various reasons. Some cases have an unknown etiology and are termed idiopathic thrombocytopenia. However, most cases are secondary to other conditions, either singularly or synergistically. Both primary and secondary thrombocytopenia can be immune mediated. The following list is not all-inclusive but presents common situations.

1. Decreased platelet production9,10
   a. drugs (Table 14,11,13-16).
   b. bone marrow failure or aplasia, cancer metastases, or acute leukemia.
   c. genetic factors.
   d. Epstein-Barr or viral infections that damage megakaryocytes (Human immunodeficiency virus [HIV], hepatitis B or C).
   e. alcohol toxicity, vitamin B12 or folic acid deficiency, and pregnancy.
2. Increased platelet destruction or consumption11:
   a. drugs (Table 1).
b. disseminated intravascular coagulation (widespread clots often due to cancer or sepsis), thrombotic thrombocytopenia, acute venous thromboembolic disease, antiphospholipid syndrome (a coagulation disorder).

c. meningitis.

d. pregnancy or labor, particularly with pre-eclampsia.

e. hemolytic uremic syndrome (as seen in *Escherichia coli* food poisoning).

f. systemic lupus erythematosus, severe rheumatoid arthritis, or other immune problems such as idiopathic thrombocytopenia.

g. Epstein Barr virus, malaria, or HIV.

3. Dilutional thrombocytopenia: due to a large volume transfusion, which is unlikely to be encountered in an ambulatory dental patient.

4. Sequestration of platelets: the spleen normally stores 30% of a person’s platelets but gross accumulation of up to 90% can occur. The most common cause of splenomegaly is portal hypertension due to cirrhosis of the liver.

**HISTORY, EXAMINATION, AND TESTS TO DETERMINE PRESENCE OF A PLATELET DISORDER**

**Taking a History**

Ask the patient about current and past problems, including family history. Ask about drug or alcohol use, viral infections, cancer, blood pressure problems, spontaneous bleeding or bleeding events from prior surgeries and pregnancies, recent blood transfusions, hematuria, abnormal menstrual bleeding, nosebleeds, diets that might predispose deficiencies in vitamin K, vitamin B12, or folate; and medications or supplements that affect clotting mechanisms.

**Examination**

Extraorally, look for signs of bruising or petechiae on face, neck, hands, legs, and feet. Shaving nicks are common (Figure 1). Palpate the lymph nodes to feel for lymphoma. The spleen is only palpable if there is an enormous sequestration and when the patient is supine. Intraorally, look for gingival bleeding and nonblanching purple or reddish lesions.

**Suggested Lab Tests**

Sometimes platelet disorders do not present any signs or symptoms and are only detected by routine lab tests (Table 217-24).

**PRETREATMENT PRECAUTIONS**

A dentist can minimize surgical risks for patients with thrombocytopenia by avoiding drugs that exacerbate the condition, managing blood pressure, and following guidelines to minimize trauma. Consult the patient’s physician so that he/she can adjust medications if necessary. Whenever possible, use only local measures to manage bleeding rather than reduce or discontinue anticoagulants. This will minimize systemic blood clot risks. During invasive surgery, use epinephrine-containing local anesthetic in the area of the surgery and consider radiosurgery, electrosurgery, or a laser instead of a scalpel to minimize bleeding. Consider the use of efficient hemostatic agents such as Surgicel (Ethicon) or BloodStop gauze (Lifesience PLUS), and obtain primary closure when possible. The use of large gauze sponges and close postoperative supervision of patients will ensure that biting pressure is maintained on bleeding sites. Tranexamic acid can be administered intravenously or topically as a postoperative oral rinse and on a gauze pack if excessive bleeding is encountered.

**CASE REPORT**

Note: Verbal and written patient consent was obtained for sharing the images and information about this case.
Examination and Treatment Planning

A 71-year-old fully edentulous gentleman presented with a chief complaint of postoperative pain associated with extractions of teeth Nos. 22 and 23 performed 2 weeks earlier. Both the mandibular and maxillary arches exhibited several areas of prominent bony exostoses that precluded the ability to wear dentures. A root or bony fragment was noted in the lower anterior alveolus and was removed under topical anesthesia. An impression was obtained of the lower arch and a study model was prepared. Impression of the maxillary arch was not possible due to bilateral bony projections (Figures 2 to 4).

At the first visit, the objectives of treatment were discussed with the patient. The treatment plan consisted of osteoplasty and lingual tori reduction followed by full removable maxillary and mandibular prostheses. Due to the short height of the maxillary ridge, an implant-retained maxillary denture would have been preferable, but for financial reasons this option was ruled out. The patient’s medical history was reviewed in detail, and vital signs were recorded. Past dental records described hematoma of the lower face associated with a mandibular molar extraction performed the previous year.

The patient had multiple health conditions, including a diagnosis of “idiopathic thrombocytopenia,” atrial fibrillation, depression, hypertension, hypothyroidism, chronic sinusitis, and a history of candida infections. He also had experienced acute hepatic coma, and tested positive for the hepatitis C virus. He was taking Prozac and Doxepin (for depression), Atenolol, Synthroid, Methadone, Vicodin, and a daily 325 mg aspirin.

Severe ecchymoses were present on the patient’s hands at every dental visit (Figure 5). The patient reported that he accidentally bumped himself but staff at his assisted living facility could not explain why the patient always had bruising. Normally, bruising would resolve over the course of a few weeks, even in a person with thrombocytopenia, as

Table 2. Suggested Laboratory Tests for Platelet Disorders17-24

<table>
<thead>
<tr>
<th>Test Description</th>
<th>Reference Ranges (human)</th>
<th>Notes/Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Complete blood count: platelet count, red blood count, white blood count, hemoglobin, and hematocrit.</td>
<td>Platelet count: normal range is 150 to 400 million/ml. Extensive bleeding after invasive dental treatment may occur with platelet counts less than 50 million/ml.17</td>
<td></td>
</tr>
<tr>
<td>2. Platelet with collagen/epinephrine and platelet with collagen/adenosine diphosphate (ADP):</td>
<td>our lab provided reference ranges of 77 to 170 seconds and 62 to 117 seconds respectively.</td>
<td>ADP, collagen, and epinephrine are platelet activators and these tests measure platelet function.18</td>
</tr>
<tr>
<td>3. Prothrombin time/international normalized ratio (PT/INR):</td>
<td>Our lab’s reference range was 12.1 to 14.4 sec/0.9 to 1.1 for the PT/INR but these values can vary depending on the assay and reagents used.</td>
<td>INR is a calibrated method for measuring PT, and lab reports often express both PT and INR values. A normal INR reference range is 0.9 to 1.2. A higher number predicts more postsurgical bleeding. For patients with a risk of clotting, stroke, or heart attack, a recommended INR target is between 2.0 and 3.5. A safe INR target for invasive dental surgery is usually 1.5 or less, but this should always be confirmed with the patient’s physician. The PT test evaluates the tissue factor or extrinsic pathway and is recommended for patients who use warfarin.19</td>
</tr>
<tr>
<td>4. Activated partial thromboplastin time (aPTT) bleeding time.</td>
<td>The aPTT test evaluates the intrinsic pathway and is recommended for patients taking heparin. Both PT and aPTT tests evaluate the common pathway and should be given for any patient suspected of having a coagulation deficiency.20</td>
<td></td>
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<tr>
<td>5. More sophisticated tests should be ordered by the physician if there are still concerns about coagulation and platelet function:</td>
<td>platelet function analyzer-100, von Willebrand’s factor tests, bone marrow function, and aggregation tests are examples.22</td>
<td></td>
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<tr>
<td>6. Human immunodeficiency virus.23</td>
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<tr>
<td>7. Hepatitis C Viral Load (HCV RNA):</td>
<td>Our lab classifies HCV RNA detected below the limit of quantification for 1.9 to 2.3 log IU/ml, and reports as quantifiable for readings more than 2.3 log IU/ml. Having a negative result does not assure that HCV is not present. Additionally, this value varies among different labs. However, knowing that the viral load is high may determine the degree of platelet deficiency or impairment as HCV has been implicated as a cause of thrombocytopenia.24</td>
<td>The dentist can also use the viral load to assess the patient’s disease transmission potential.</td>
</tr>
</tbody>
</table>

Figure 2. Mandibular arch preoperative condition.

Figure 3. Mandibular arch preoperative study models.
long as trauma does not recur. It is likely that the patient's thrombocytopenia was actually a result of one or more of his medications and/or the hepatitis C virus (HCV) infection. Thyroid dysfunction tends to occur concurrently with thrombocytopenia, but treatment of hypothyroidism only occasionally improves the thrombocytopenia.25

**TESTS AND PRESURGICAL PROCEDURES**

A panoramic radiograph revealed no significant findings (Figure 6). The patient's physician was informed of the planned procedures and an oral-maxillofacial surgeon was consulted for advice. The oral surgeon advised testing for hepatitis C virus load (HCV RNA) and obtaining a complete blood count including prothrombin time/ international normalized ratio (PT/INR) and a platelet count. The surgeon also recommended a blood platelet transfusion if indicated. Each unit of platelets raises the platelet count approximately 7 to 10 million/ml depending on the size of the patient.26 However, platelet transfusion carries risks, is effective only in certain situations, and must be administered immediately before the surgery. After repeating the platelet count, it was decided to forgo the platelet transfusion, as the patient's current count was at 70 million/ml of blood, above the critical 50 million/ml mark suggesting a need for transfusion.26 Due to the very invasive nature of the planned surgeries and the larger 325 mg dose of daily aspirin usage, the patient was directed to stop using aspirin 7 days prior to each of the operative dates, and to restart aspirin 5 days postoperatively. Antibiotic coverage (Pen VK 500 mg, qid) was prescribed for 7 days, beginning with the day before each surgery. Ideally, the patient should consult a hematologist, although in this case specialty care was not financially feasible. It should also be noted that tests were not necessarily performed at an ideal time as the patient lived in a nursing care facility and coordination of the procedures was rather difficult. For example, the PT/INR should be performed on the same day as the surgery. Any adjustments to anticoagulants should always be made under the supervision of the patient's physician.

**THREE PHASES OF SURGERY**

**Armamentarium:** Macan electrosurgery unit with angled loop or single incising electrode; Minnesota retractor; Dr. Thompson color transfer applicator (Great Plains Dental) for marking the alveolar ridge with an easy to remove ink, disposable scalpel; Molt periosteal elevator; surgical handpiece; diamond or carbide football and round taper burs; sterile saline solution; 4-0 and 6-0 black silk sutures; BloodStop hemostatic gauze; hemostat and surgical scissors; gauze;
chlorhexidine; and local anesthetic (Septocaine 4% with epinephrine 1:100,000, [Septodont USA]).

**Phase 1. Mandibular Left Quadrant Surgery**

Surgery was performed for anterior labial undercuts and left lingual torus. However, the left buccal shelf exostosis was deemed too large for surgical revision.

**Results of preoperative tests:**
- Blood pressure, heart rate and respiration: normal.
- HCV RNA: 5.9 log IU/ml.
- Platelet count: 76 million/ml.
- PT/INR: 15.1 sec/1.18. The relatively normal readings may be attributed to the fact that some conditions causing platelet shortage or dysfunction do not necessarily affect the PT/INR reading. Conditions that have the greatest effect on INR readings include warfarin usage and coagulation factor deficiencies. The patient had neither of these conditions but was diagnosed as having “idiopathic thrombocytopenia.”
- Platelet with collagen/epinephrine and platelet with collagen/ADP: The patient's physician ordered these tests, which measure platelet function. The results were over “300” for the collagen/epi and 171 for the collagen/ADP, signifying significant platelet dysfunction.

**Procedure:** Anesthesia was obtained and incision lines were drawn on the alveolar ridge using a Dr. Thompson’s color transfer applicator. In order to obtain hemostasis and also to reduce the risk of disease transmission to the clinician and assistant, electrosurgery was used to make most of the incisions. Care was taken to prevent heat from being transmitted to the bone by using a light brush stroke, irrigating with water/saline, then waiting 30 to 45 seconds before making each additional cut. A horizontal incision was made along crest of the ridge starting from the incisor region and extending to the retromolar pad. Vertical releasing incisions were made in the anterior labial and lingual torus area. Using the periosteal elevator, a full thickness flap was reflected to expose the bony exostoses. The bone was reduced using diamond burs, bone files, and chisel and mallet. The lingual torus was not reduced completely but just enough to allow for comfortable wear of the proposed denture.

The tissue flaps were re-approximated and sutured together (Figure 7). There was a fair amount of steady hemorrhage from the lingual torus area that was eventually controlled within 20 minutes after the placement of a BloodStop square, several water-moistened 4 x 4 gauze sponges, and firm pressure applied. The BloodStop gauze is a resorbable cellulose sponge that becomes gelatinous and forms a seal when it contacts blood. Estimated blood loss was approximately 40 cc (8 tsp) during this procedure and an
additional 20 cc postoperatively. In a study performed in England, average blood loss during third molar extraction was considered to be excessive if the estimated blood loss was over 100 cc.27 The patient was dismissed in good condition with a chlorhexidine prescription and postoperative instructions.

The patient was seen 2 days and 7 days postoperatively. The patient stated that he had no pain but the nursing home staff reported that the patient habitually rubbed the surgical areas with his bare fingers, introducing bacteria and debris into the wounds. At the 2-day postoperative visit a large area of ecchymosis developed over the skin of the anterior lower left jaw, along with some hematoma and swelling over the ridge (Figure 8). By the seventh day postoperative visit, he also had a 2 cm hematoma in the floor of the mouth and a bony dehiscence over the lingual torus (Figure 9). However, the hemostatic gauze had created a firm, clear gelatin-like film over the bare bone that helped to hold the edges of the soft tissue flaps together.

Phase 2. Bilateral Maxillary Arch Surgery

One month after the mandibular arch surgery, maxillary posterior buccal exostoses were removed. No biopsy was performed due to the identical appearance of the projections on each side.

Preoperative test results:
• Normal blood pressure, heart rate, and respiration.
• Platelet count: 70 million/ml.
• PT/INR: 16.6 sec/1.33.

Procedure: Electrosurgery incisions were completed over the crest of the ridge from the tuberosity to the first bicuspid and vertically over the bony projections as a T diagram bisecting the projections. Full thickness flaps were raised and the projections were removed with burs, bone rongeur, and bone files. The soft tissue margins were re-approximated and sutured together with a combination of 4-0 and 6-0 black silk. The 6-0 silk worked nicely with the thin tissue of the exostoses. Good hemostasis was achieved in both operative sites as the buccal corridors held the chlorhexidine-moistened gauze firmly in place. Estimated blood loss during these procedures was about 25 cc for each side, with a total of 50 cc (Figures 10 to 14).
The patient was seen the next day for follow-up. Since he had only mild pain and no bruising, it was decided to perform surgery for the mandibular right quadrant at this visit.

**Phase 3. Mandibular Right Quadrant Surgery and Maxillary Surgery Follow-up**

**Procedure:** Incisions were made horizontally over the crest of the ridge superior to the right buccal exostosis and vertically over the exostosis several millimeters distal to the frenum paralleling the frenum pull. Full thickness flaps were raised just above the base of the bony ledge and excess bone was removed using diamond burs. Flaps were sutured together (Figure 15). Estimated blood loss for this visit was about 25 cc.

The patient returned one week later for follow-up and removal of sutures for both mandibular and maxillary surgical sites (Figure 16).

**RESULTS AND FINAL OUTCOMES/PROSTHESES**

Two weeks after the final surgery visit, preliminary alginate impressions were taken for the fabrication of custom trays. The 2-week postoperative condition of the mandibular right quadrant is shown in Figure 17. Study models made at approximately one month postoperative for the maxillary arch and 2 months postoperative for the mandibular arch are shown in Figure 18. In retrospect, more of the mandibular lingual torus should have been reduced. However, a semipermanent soft liner can be placed if there is friction on the torus area. The patient is very happy with the outcome and is being followed up as necessary for comfort and function (Figures 19 and 20).

**CONCLUSION**

General dentists who wish to perform oral surgery for patients with a suspected bleeding disorder should be familiar with various hematologic conditions and consult with the patient’s physician to obtain necessary tests that would help give a clearer understanding of the patient’s status. Basic tests to order include the complete blood

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**Figure 15.** Mandibular right quadrant surgery completed.

**Figure 16.** Maxillary right quadrant one-week postoperative, mild incision line opening.

**Figure 17.** Mandibular arch postoperative (approximately 2 weeks on right, 6 weeks on left).

**Figure 18.** Models postoperative (approximately one month maxilla, 2 months mandible).

**Figure 19.** Prostheses delivered.
count, PT, activated partial thromboplastin time, and HCV RNA. Evidence of a bleeding disorder does not necessarily correlate with a platelet deficiency. If concern remains, then more tests may be needed, such as platelet aggregation studies or a von Willebrand's workup. Elderly patients in particular may require extensive testing to prevent bleeding diathesis.

As described in this article, the patient only required local hemostatic measures and the discontinuance of aspirin for a short period of time. However, when platelet counts are below 50 million/ml, or if there are high INR readings, or other abnormal findings, additional strategies may be required. This article presents a highly simplified protocol for dental management of thrombocytopenia. There are excellent hematology textbooks available for the practitioner who desires more information. With proper planning and strict follow-up, most surgical patients with mild to moderate thrombocytopenia can be treated predictably and successfully in a general dental practice setting.

ACKNOWLEDGEMENT

The author expresses sincere appreciation for the surgical assistance received from Dr. John Uniat and the hematology advice provided by Dr. Anne Deucher. Both individuals made a significant contribution to the completion of this case. Special appreciation is also extended to Dr. Brian Chun, Dr. John Pavel, Dr. Joy Wang and Dr. Chitra Shikaram for their support. John's Dental Lab, San Jose, Calif, fabricated the complete dentures in the clinical case presented.

REFERENCES

Thrombocytopenia and Avoiding Bleeding Complications


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**POST EXAMINATION QUESTIONS**

1. How should a patient be screened for thrombocytopenia?
   a. Medical history.
   b. General physical evaluation of head, neck, and extremities.
   c. Blood tests.
   d. All of the above.

2. What are common causes of thrombocytopenia?
   a. Some cancers.
   b. Medications.
   c. Viral infections.
   d. All of the above.

3. Purpura are soft tissue lesions which are commonly found on the buccal mucosa and the lips. These lesions blanch with firm pressure.
   a. Both statements are true.
   b. First statement is true, second statement is false.
   c. First statement is false, second statement is true.
   d. Both statements are false.

4. When performing a single extraction, what is the best method to prevent excessive and prolonged bleeding in an individual with platelet deficiency or dysfunction?
   a. Local measures such as pressure packs and hemostatic agents.
   b. Discontinuation of anticoagulation medication.
   c. Both a and b.
   d. None of the above.

5. The prothrombin test is the only reliable method to test for surgical bleeding risk. International normalized ratio reading should be brought to 1.0 prior to performing invasive dental surgery on a patient.
   a. Both statements are true.
   b. First statement is true, second statement is false.
   c. First statement is false, second statement is true.
   d. Both statements are false.

6. What is the mechanism of action that some viral infections exhibit in affecting platelets?
   a. Direct damage to megakaryocytes.
   b. Immune mediated process.
   c. Impaired function of platelets.
   d. All of the above.

7. According to a study about tranexamic acid and dental extractions, what amount of blood loss is considered to be excessive?
   a. 25 cc.
   b. 65 cc.
   c. 85 cc.
   d. 100 cc.
8. When is a platelet transfusion advisable prior to invasive oral surgical procedures?
   a. Platelet count is below 100 million/ml of blood.
   b. Platelet count is below 75 million/ml of blood.
   c. Platelet count is below 50 million/ml of blood.
   d. None of the above.

9. What is the lifespan of a platelet?
   a. 7 to 10 days.
   b. 14 days.
   c. 30 days.
   d. None of the above.

10. The spleen normally stores approximately what percentage of a person's platelets?
    a. 10% to 20%.
    b. 30%.
    c. 90%.
    d. None of the above.

11. In what way(s) do drugs cause bleeding disorders?
    a. Decrease production of platelets.
    b. Impair platelet function, adhesion, or aggregation.
    c. Both of the above.
    d. None of the above.

12. What are the mechanisms of action of platelets?
    a. Adhesion, aggregation, secretion, procoagulant activity.
    b. Adhesion, vasoconstriction, aggregation, secretion.
    c. Both a and b.
    d. Neither a nor b.

13. How are thrombocytes produced?
    a. From red blood cells.
    b. From megakaryocytes in the bone marrow.
    c. Directed by proteins derived mainly in the bone marrow.
    d. Both b and c.

14. In what ways can platelets be affected in thrombocytopenia?
    a. Decreased production.
    b. Increased consumption.
    c. Sequestration.
    d. All of the above.

15. Abnormal bleeding stems from:
    a. Platelet disorders.
    b. Vascular integrity.
    c. Coagulation factor deficiencies.
    d. All of the above.

16. Patients with a known bleeding tendency and behavioral risk factors should be tested for:
    a. Hepatitis C.
    b. HIV.
    c. Both of the above.
    d. Neither of the above.
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