

## Easy Bruising and Bleeding in the Adult Patient: A Sign of Underlying Disease

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**A** chief complaint of easy bruising and bleeding should alert the clinician to the possibility of a serious underlying disease process. The evaluation includes a careful history and a complete physical examination. As many bleeding disorders are inherited, a detailed family history should also be obtained. Laboratory investigations should be guided by the clinical impression.

In general, easy bruising is associated with platelet disorders, whereas easy bleeding is associated with coagulation disorders. There is significant overlap, however, and platelet and coagulation disorders may coexist. Platelet disorders as well as coagulation abnormalities must be considered in any patient with bruising or bleeding that is disproportionate to the offending trauma (Table 1).<sup>1</sup> Common complaints associated with platelet and coagulation disorders include epistaxis, gingival bleeding, menorrhagia, gastrointestinal bleeding, ecchymosis, purpura, and petechia. Physical abuse is always a consideration but must not be assumed.<sup>2</sup> This article reviews the approach to evaluating patients who present with easy bruising or bleeding. Two illustrative cases are presented.

The definitions of petechia, purpura, and ecchymosis differ among sources, but the definitions used here are as follows: *Ecchymoses* are large areas of bruising that occur out of proportion to the offending trauma. *Petechiae* are pinpoint (1–3 mm), nonraised, reddish purple lesions that result from intradermal or submucous hemorrhage. *Purpura* are larger (> 3 mm) red to purple nonblanching lesions that also result from bleeding into the skin and mucous membranes. Unlike bruising, petechiae and purpura do not result from trauma.

### APPROACH TO THE PATIENT WITH EASY BRUISING

Bruises are large areas of subcutaneous bleeding. Bruising is considered abnormal if it is out of proportion to the offending trauma. Not all patients with easy bruising have a serious underlying disorder, however.

### SIGNS—EASY BRUISING AND BLEEDING

#### Easy bruising

Ecchymoses  
Purpura  
Petechiae

#### Easy bleeding

Epistaxis  
Gastrointestinal/rectal bleeding  
Gingival bleeding  
Hemarthrosis  
Hematuria  
Menorrhagia  
Prolonged bleeding during surgery/tooth extraction

Senile purpura, seen in elderly patients, is a benign process caused by capillary fragility associated with weakened connective tissue and is not a sign of a serious underlying disease. In addition, certain medications, such as aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and anticoagulants may be associated with purpura. Bruising restricted to the lower limbs is usually normal. (This is not always true, however, as illustrated in the case presented.) Easy bruising over the trunk, neck, and face warrant further hematologic evaluation.<sup>3</sup> Although easy bruising is more commonly associated with thrombocytopenia, coexistence with coagulation disorders is common.

### Clinical Evaluation

The history should focus on the onset of easy bruising as well as a family history of hematologic disorders. A detailed history of medication use is critical. The

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**Table 1.** Clues to the Diagnosis of Easy Bruising and Easy Bleeding

	Finding	Possible Cause
<b>Easy bruising</b>	<b>History</b>	
	Bruising out of proportion to the offending trauma	Platelet disorder
	Advanced age	Senile purpura
	Family history of easy bruising	Qualitative platelet disorder
	Medication use (eg, heparin, warfarin, aspirin, steroids, NSAIDs)	Platelet inhibition, coagulopathy
	<b>Physical examination</b>	
<b>Easy bleeding</b>	Multiple bruises, petechiae	Severe thrombocytopenia
	Lymphadenopathy, splenomegaly	Hematologic malignancy
	<b>History</b>	
	Prolonged bleeding from minimal trauma (eg, minor surgery, tooth extractions)	Coagulation disorder and/or platelet disorder
	Menorrhagia, spontaneous bleeding (eg, epistaxis, hemarthrosis, hematuria, rectal bleeding)	Coagulation disorder and/or platelet disorder
	Family history of easy bleeding	Hemophilia, qualitative platelet disorder
<b>Physical examination</b>	Medications (eg, heparin, warfarin, aspirin, steroids, NSAIDs)	Platelet inhibition, coagulopathy
	<b>History</b>	
	Hemarthrosis	Hemophilia
	Spider angiomas, scleral icterus, ascites, gynecomastia	Chronic liver disease

NSAID = nonsteroidal anti-inflammatory drug.

physical examination is essential in elucidating an underlying cause. Take note of which areas are bruised. Bruises on the lower extremities are not considered quite as abnormal as bruising elsewhere, but petechiae, which are typically seen on the lower extremities, are a sign of severe thrombocytopenia. Evidence of hematologic malignancy should be sought, including lymphadenopathy and splenomegaly. Laboratory investigations should include a complete blood count, platelet count, prothrombin time (PT), and partial thromboplastin time (PTT). Hematologic malignancy may be uncovered with a complete blood count with peripheral smear.

### Platelet Disorders Associated with Easy Bruising

Platelet disorders can be divided into quantitative and qualitative abnormalities.<sup>4,5</sup> Quantitative disorders are characterized by thrombocytopenia resulting from sequestration, peripheral destruction, or decreased production of platelets (Table 2).<sup>4,5</sup> Bone marrow disorders causing thrombocytopenia include aplastic anemia, myelodysplasia, and hematologic malignancies. Chronic alcoholism can also cause marrow suppression. Nonmarrow disorders causing thrombocytopenia include disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, liver failure, hypersplenisms, and autoim-

mune disorders (including immune thrombocytopenic purpura).

Qualitative platelet disorders can be either congenital or acquired.<sup>4,5</sup> Patients with qualitative platelet disorders have prolonged bleeding times despite a normal platelet count. A family history is important in evaluating a patient with a qualitative platelet disorder. Congenital disorders include Glanzmann's thrombasthenia and Bernard-Soulier syndrome, both of which are rare autosomal recessive disorders. Acquired platelet disorders can result from uremia and certain drugs (eg, aspirin, NSAIDs). Uremia causes abnormal platelet function by unknown mechanisms.

### Illustrative Case

**Case presentation.** A 50-year-old woman presents with a 3-week history of easy bruising and fatigue. Physical examination is significant for an obese woman with scattered areas of ecchymosis predominantly on the lower extremities (Figure 1). Laboratory examination reveals a leukocyte count of  $200 \times 10^3/\text{mm}^3$  (normal,  $4.8\text{--}10.8 \times 10^3/\text{mm}^3$ ), hemoglobin concentration of 9 g/dL (normal, 12.0–15.5 g/dL), and a platelet count of  $20 \times 10^3/\text{mm}^3$  (normal,  $150\text{--}450 \times 10^3/\text{mm}^3$ ). A differential cell count shows 83% blasts. Results of coagulation studies, including PT and activated PTT (aPTT), are normal.

**Table 2.** Causes of Thrombocytopenia

**Decreased platelet production**

- Leukemia
- Lymphoma
- Aplastic anemia
- Myelodysplasia
- Chronic alcoholism
- Vitamin B<sub>12</sub> deficiency
- Folic acid deficiency

**Splenic sequestration**

- Cirrhosis with congestive splenomegaly
- Myelofibrosis with splenomegaly

**Nonmarrow disorders**

- Idiopathic thrombocytopenic purpura
- HIV infection
- Drugs (heparin, quinidine, quinine, sulfa-containing)
- Disseminated intravascular coagulation (cancer, sepsis)
- Thrombotic thrombocytopenic purpura
- Hemolytic-uremic syndrome
- Paroxysmal nocturnal hemoglobinuria

**Discussion.** In this case, a middle-aged woman presents with nonspecific complaints of easy bruising and fatigue. She reports that the largest bruise, which is on her left thigh, is the result of insignificant contact with a waste can. The resulting bruise is out of proportion to the force of contact. Although the patient has severe thrombocytopenia, petechiae are not present. Results of coagulation studies are normal, but the complete blood count reveals a markedly elevated leukocyte count, anemia, and severe thrombocytopenia. The peripheral smear shows a predominance of blasts. Acute leukemia, specifically acute myelogenous leukemia, was subsequently diagnosed.

Acute myelogenous leukemia accounts for 80% of acute leukemias in adults and acute lymphocytic leukemia accounts for the remaining 20%.<sup>6</sup> Acute lymphocytic leukemia is primarily a childhood leukemia. The median age of patients with acute myelogenous leukemia is about 50 years.<sup>6</sup> Approximately one third of patients present with easy bruising or easy bleeding. The leukocyte count is elevated and blasts are seen on the peripheral blood smear. Moderate anemia is present and the platelet count is often less than  $20 \times 10^3/\text{mm}^3$ .

**APPROACH TO THE PATIENT WITH EASY BLEEDING**

A bleeding disorder should be considered in a patient with easy bleeding, recurrent epistaxis, menorrhagia, hemarthrosis, prolonged bleeding during oper-



**Figure 1.** Area of ecchymosis (a large bruise).

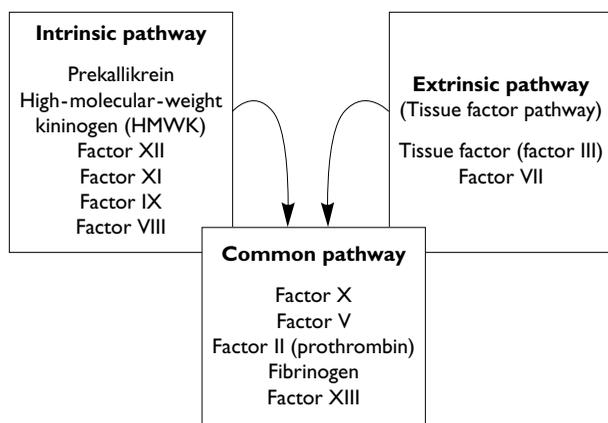
ations and tooth extractions, hematuria, or rectal bleeding. Although any of these conditions can occur alone, spontaneous bleeding from multiple sites (eg, epistaxis, hematuria, rectal bleeding) further raises the suspicion of a bleeding disorder. A bleeding disorder should be especially considered in a patient with any of the aforementioned conditions together with a family history of a bleeding disorder. In general, easy bleeding is associated with coagulation disorders, although coexistence with platelet disorders can occur. Qualitative platelet disorders are more likely to cause easy bleeding than quantitative disorders unless severe.

The history should focus on the onset of easy bleeding as well as a family history of hematologic disorders. A long history of easy bleeding is an indication of an inherited disorder, whereas acute onset of easy bleeding is indicative of an acquired disorder. A detailed history of medication use is essential. Anticoagulants such as warfarin and heparin can prolong the PT and PTT. Aspirin and NSAIDs can prolong the bleeding time by inhibiting platelet aggregation. Take note of the sites of bleeding. Spontaneous bleeding from multiple sites is a red flag for underlying coagulopathy.

The physical examination is useful in finding clues to an underlying cause. Lymphadenopathy and splenomegaly are signs of possible hematologic malignancy. Chronic liver disease can lead to easy bleeding due to depletion of vitamin K-dependent clotting factors. Signs of chronic liver disease include scleral icterus, spider angiomas, gynecomastia, palmar erythema, and digital clubbing. Laboratory investigation of patients with easy bleeding should include a complete blood count, platelet count, PT, aPTT, bleeding time, and liver function tests.

**Coagulation Disorders Associated with Easy Bleeding**

Coagulation disorders can be either inherited or



**Figure 2.** A simplified version of the coagulation pathway showing the involved clotting factors.

acquired.<sup>7</sup> Inherited disorders are likely to manifest in childhood whereas acquired disorders present later. In evaluating a patient for coagulation disorders, a careful history should include inquiries about excessive bleeding during previous procedures such as tooth extractions. Hereditary disorders of coagulation can be elicited through a detailed family history.

Laboratory evaluation of the coagulation pathways incorporates 4 tests: PT, aPTT, thrombin time, and fibrinogen assays. The aPTT and PT are the most commonly performed tests of hemostasis. An understanding of the coagulation cascade is important (**Figure 2**). The extrinsic, or tissue factor, pathway is the mechanism by which coagulation is initiated in response to tissue trauma. In this pathway, released tissue factor activates factor VII.<sup>5,8</sup> The intrinsic pathway is activated when blood comes in contact with an injured vessel wall, activating factor XII.<sup>5,8</sup> Both pathways proceed to a common pathway that leads to the formation of a clot by cross-linking of fibrin.

### Causes of Prolonged PT

The PT evaluates the extrinsic pathway of coagulation (factors II, V, VII, X, and fibrinogen). Causes of prolonged PT include liver disease, vitamin K deficiency, warfarin, and factor VII deficiency (**Table 3**). The PT has a normal range of 11 to 15 seconds. The clotting factors are synthesized in the liver; patients with liver failure, therefore, whether acute or chronic, are likely to develop coagulopathy evidenced by a prolonged PT disproportionate to the aPTT. Patients on prolonged antibiotic therapy are also prone to developing coagulopathy secondary to deficiency of the vitamin K–dependent factors (factors II, VII, IX,

**Table 3.** Causes of Coagulation Disorders

#### Causes of prolonged prothrombin time

Liver disease  
Vitamin K deficiency  
Warfarin  
Factor VII deficiency

#### Causes of prolonged partial thromboplastin time

Factor deficiencies:  
Factor XII  
Factor XI  
Factor VIII (hemophilia A)  
Factor IX (hemophilia B)  
von Willebrand's disease  
Heparin administration  
Lupus anticoagulant  
Acquired factor inhibitors

and X). The PT is used to monitor patients on warfarin therapy.

### Causes of Prolonged aPTT

The aPTT evaluates the intrinsic coagulation pathway. The test is most sensitive for factors VIII, IX, XI, and XII. The most common cause of prolonged aPTT is incorrect collection of blood through an indwelling catheter that has been flushed with heparin. The aPTT has a normal range of 22 to 38 seconds. The aPTT test is preferred to the original PTT test.

Hemophilia A (factor VIII deficiency) is the most common hereditary disorder of blood coagulation. The next most common disorders are hemophilia B (factor IX deficiency) and von Willebrand's disease. Both hemophilia A and hemophilia B are X-linked recessive disorders—only males are clinically affected and females may be carriers. von Willebrand's disease is an autosomal dominant disorder. Acquired factor inhibitors (autoantibodies) can also develop.<sup>9</sup> The most common acquired inhibitor is that against factor VIII.

### Illustrative Case

**Case presentation.** A 70-year-old man presents with a 2-week history of hematuria, melena, and easy bruising and bleeding from minor trauma. His past medical history is otherwise unremarkable. Physical examination is remarkable for a thin elderly man with scattered areas of ecchymosis. Rectal examination reveals guaiac-positive stool. Laboratory examination reveals a leukocyte count of  $8.0 \times 10^3/\text{mm}^3$ , hemoglobin of

8 g/dL, platelet count of  $170 \times 10^3/\text{mm}^3$ , PT of 11 seconds (normal, 11–15 seconds), and an aPTT of 84 seconds (normal, 22–38 seconds). Laboratory results from 1 year ago (including coagulation studies) are normal.

**Discussion.** In this case, an elderly man presents with episodes of spontaneous bleeding and easy bruising. His laboratory results from 1 year ago are normal, thereby providing evidence that his coagulopathy is newly acquired. A family history for bleeding disorders is negative. The patient has an isolated elevation of the aPTT. An acquired inhibitor was suspected.

Spontaneous inhibitors are autoantibodies to coagulation factors.<sup>8</sup> The most common factor involved is factor VIII. Factor VIII inhibition prolongs the aPTT but not the PT. A simple test that checks for the presence of an inhibitor (an inhibitor screen) can be performed by incubating mixtures of patient plasma and normal plasma. Failure of the normal plasma to correct the prolonged aPTT indicates the presence of an inhibitor.

#### **CONCLUSION**

Although easy bruising and easy bleeding are often normal, they can be ominous signs of a serious underlying disease process. Platelet disorders and coagulation disorders must be considered. A detailed family history is important because many bleeding disorders

are inherited. Laboratory examination must include a complete blood count and coagulation studies, including PT and aPTT.

**HP**

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