

# Bleeding and Bruising: Primary Care Evaluation

Pamela R. Hughes, MD; Meghan N. Lewis, MD; and Shalease S. Adams, DO

Easy bruising and bleeding are commonly seen in primary care. Use of a bleeding assessment tool and a comprehensive history, physical examination, and patient-provided photographs can help identify causes of abnormal bleeding and bruising. Family history can aid diagnosis of a heritable cause. Nonaccidental trauma should be considered, especially in vulnerable populations. Initial laboratory testing includes a complete blood cell count, peripheral blood smear, prothrombin time (PT), international normalized ratio, activated partial thromboplastin time (aPTT), and fibrinogen. Normal PT and aPTT results may indicate a platelet disorder. A normal PT result with a prolonged aPTT result indicates a disorder of the intrinsic coagulation pathway, and a prolonged PT result with a normal aPTT result may indicate a disorder of the extrinsic coagulation pathway. Consultation with a hematologist is recommended when initial evaluation indicates a bleeding disorder or when suspicion remains high despite a normal laboratory workup result.

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asy bruising and bleeding are commonly seen in primary care. Heavy menstrual bleeding (47%), epistaxis (25%), and easy bruising (18%) are commonly reported in healthy patients without an underlying disorder. Causes include trauma, medications, vitamin deficiencies, platelet disorders, clotting factor deficiencies and inhibitors, pregnancy, malignancy, liver disease, and connective tissue disease. Abnormal bleeding and bruising may be caused by defects in both primary and secondary hemostasis due to an acquired or inherited disorder.

A comprehensive history, physical examination, and validated bleeding assessment tool may help identify an underlying bleeding disorder. <sup>4,5</sup> Physicians can initiate this workup and consult with a hematologist for diagnosis of unidentified disorders or advanced testing.

### **PATHOPHYSIOLOGY**

The extent of bleeding can provide insight into underlying pathology.<sup>6</sup> Nonblanchable spots that appear due to damage in small blood vessels include petechiae (less than 2 mm in diameter) and purpura (2 to 10 mm in diameter). Bruising is the outward appearance of a subcutaneous hematoma that has formed in the extravascular soft tissue.

In healthy patients, endothelial vessel damage prompts a cascade of events to repair the injury and contain bleeding. First, vasoconstriction reduces blood flow to the injured area, and primary hemostasis occurs as platelets and von Willebrand factor form a platelet plug. The platelet plug further adheres to the site of endothelial injury via additional circulating von Willebrand factor, collagen, and factor VIII. Then, secondary hemostasis stabilizes the platelet plug with fibrin to form a clot through the coagulation cascade (Figure 18). Finally, maintenance and the eventual breakdown of the fibrin clot occur during tertiary hemostasis.

### **HISTORY**

The patient's history (eg, age, sex, diet, trauma, personal and family history, medications, detailed descriptions of bleeding events) is integral to the investigation of the source of abnormal bleeding or bruising. Age at symptom onset is significant, because severe inherited disorders typically present in infancy or early childhood. Age-related thinning of the skin, subcutaneous tissue atrophy, and weakened capillaries in older patients increase the likelihood of bruising. A careful review of medical history should focus on conditions known to increase bleeding and bruising, such as connective tissue disease or hemophilia. Dietary history can indicate possible vitamin C and K deficiencies, which are required components for collagen formation and clotting factors, respectively.

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The International Society on Thrombosis and Haemostasis Bleeding Assessment Tool standardizes assessment of history with a focus on the type of symptoms, their frequency and severity, and treatment required. Although it was developed for specialist assessment of bleeding disorders, it can guide history-taking in primary care. Scores should be interpreted in consultation with hematology. Abnormal scores are more than 3 in adult males, more than 5 in adult females, and more than 2 in children. An excerpt is summarized in Table 1, and the full tool is available online at https://www.isth.org/resource/resmgr/ssc/isth-ssc\_bleeding\_assessment.pdf.

# **Bleeding History**

The clinician should elicit a thorough description of the type, location, size, duration, and frequency of any bleeding or bruising episodes. <sup>14</sup> Events surrounding a bleeding episode (eg, trauma, vaginal delivery, dental procedure) may offer insight into a potential etiology<sup>4,9</sup> (Table 2<sup>4,15</sup>). Investigation into the treatments required for each episode of bleeding can gauge the severity of symptoms. <sup>4</sup>

Menstrual history includes an estimate of the duration of bleeding, perceived volume, and quantity of menstrual protection items needed during each cycle since menarche. 16,17 Menstrual bleeding is considered heavy when it impairs quality of life, lasts at least 8 days, is described as "flooding" or "gushing," saturates one or more menstrual protection items within 2 hours on multiple days, requires simultaneous use of multiple menstrual protection items or changing items overnight, features the repeated passing of blood clots the size of a quarter or larger, or has a pictorial blood loss assessment chart score of more than 100.16,17 Heavy menstrual bleeding that begins after the age of 20 may indicate an acquired bleeding diathesis. 6 Up to 40% of people who menstruate report heavy bleeding, and approximately 20% of adolescents with heavy menstrual bleeding are diagnosed with a bleeding disorder. 16,17

Platelet disorders (eg, von Willebrand disease [vWD], idiopathic thrombocytopenic purpura) should be suspected in patients with mucocutaneous bleeding, whereas coagulation disorders (eg, hemophilia) should be suspected in patients with spontaneous hemarthroses and muscle hematomas. Bleeding from two or more mucocutaneous sites, more than five episodes of epistaxis per year or one episode that lasts more than 10 minutes, bleeding that lasts more than 10 minutes after a cut, heavy menstrual bleeding, severe or unexplained postpartum hemorrhage, three bleeding episodes from a single site, and a bleeding episode requiring blood transfusion are clinically significant and warrant further evaluation. 6,16

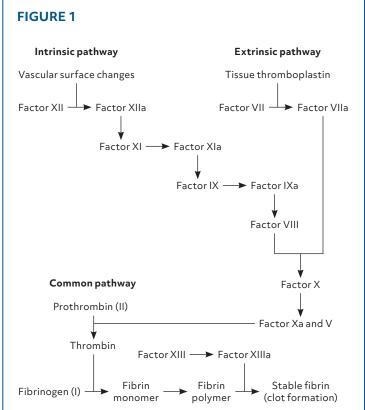
### **Medication History**

Common medications and supplements that can increase the likelihood of bruising and bleeding or

unmask a bleeding diathesis are listed in Table 3.4,15 Discontinuation should be considered for patients with abnormal bleeding or bruising.4,18 Injectable medications commonly cause local bruising and are not in themselves a cause for concern.19 Druginduced thrombocytopenia should be strongly considered when a sudden rise in platelet count occurs after discontinuation of the potentially offending medication.4 If bleeding symptoms or low platelet count persists 10 days after discontinuation, further evaluation for a bleeding disorder should be initiated.

# **Family History**

A comprehensive family history should focus on relatives with abnormal or frequent bleeding. The timing and severity of symptoms and sex of the family member may identify hereditary patterns. Reviewing several generations and evaluating the history of extended family members can indicate X-linked recessive hemophilia, connective tissue disease, and vWD due to incomplete penetrance and variable expression. A suggestive family history is particularly important in children who



Note: A simplified version of the coagulation cascade. An abnormality in the extrinsic pathway results in prolonged prothrombin time. An abnormality in the intrinsic pathway results in prolonged activated partial thromboplastin time. An abnormality in the common pathway results in a prolongation of both.

## Coagulation cascade.

Adapted with permission from Cohen AR. Rash—purpura. In: Fleisher GA, Ludwig S, et al., eds. *Textbook of Pediatric Emergency Medicine*. 3d ed. Williams & Wilkins; 1993:430-438.

**TABLE 1** 

# International Society on Thrombosis and Haemostasis Bleeding Assessment Tool

Symptoms	Severity, frequency, or required treatment (score)					
(to the time of diagnosis)	0*	1*	2	3	4	
Epistaxis	None/ trivial	> 5 per year or one episode lasting lon- ger than 10 minutes	Consultation only†	Packing, cauteriza- tion, or antifibrinolytic therapy	Blood transfusion, replace ment therapy (use of hemostatic blood com- ponents and recombinant activated factor VII), or desmopressin therapy	
Cutaneous symptoms	None/ trivial	≥ 5 bruises (> 1 cm in diameter) in exposed areas	Consultation only†	Extensive treatment	Blood transfusion, sponta- neous hematoma	
Bleeding from minor wounds	None/ trivial	> 5 per year or one episode lasting lon- ger than 10 minutes	Consultation only†	Surgical hemostasis	Blood transfusion, replacement therapy, or desmopressin therapy	
Oral cavity symptoms	None/ trivial	Present	Consultation only†	Surgical hemostasis or antifibrinolytic therapy	Blood transfusion, replacement therapy, or desmopressin therapy	
Gastrointestinal bleeding	None/ trivial	Present (not associated with ulcer, portal hypertension, hemorrhoids, or angiodysplasia)	Consultation only†	Surgical hemostasis or antifibrinolytic therapy	Blood transfusion, replacement therapy, or desmopressin therapy	
Hematuria	None/ trivial	Present (macroscopic)	Consultation only†	Surgical hemostasis or iron therapy	Blood transfusion, replacement therapy, or desmopressin therapy	
Bleeding during or after dental procedure	None/ trivial	In ≤ 25% of all procedures; no intervention‡	In > 25% of all procedures; no intervention‡	Resuturing or packing	Blood transfusion, replacement therapy, or desmopressin therapy	
Surgical bleeding	None/ trivial	In ≤ 25% of all procedures; no intervention‡	In > 25% of all procedures; no intervention‡	Surgical hemostasis or antifibrinolytic therapy	Blood transfusion, replacement therapy, or desmopressin therapy continues	

Note: Scores > 3 in adult males, > 5 in adult females, and > 2 in children warrant further evaluation. Full tool available at https://www.isth.org/resource/resmgr/ssc/isth-ssc\_bleeding\_assessment.pdf.

<sup>\*—</sup>The distinction between 0 and 1 is of critical importance; 1 means that the symptom is judged as present in the patient's history but does not qualify for a score of 2 or higher.

 $<sup>\ \ \, \</sup>dagger \text{--The patient sought medical evaluation and was referred to a specialist or offered detailed laboratory investigation.}$ 

<sup>‡—</sup>For example, a score of 1 is assigned for four extractions or surgeries in which only one resulted in bleeding (25%); a score of 2 is assigned for one extraction or surgery resulting in bleeding (100%), for two extractions or surgeries in which only one resulted in bleeding (50%), or for three extractions or surgeries in which only one resulted in bleeding (33%).

<sup>§—</sup>If already available at the time of collection.

<sup>¶—</sup>Includes umbilical stump bleeding, cephalohematoma, cheek hematoma caused by sucking during breastfeeding or bottle feeding, conjunctival hemorrhage, and excessive bleeding after circumcision or venipuncture. When these conditions occur in infants, detailed investigation is required independent from the overall score.

### TABLE 1 (continued)

#### International Society on Thrombosis and Haemostasis Bleeding Assessment Tool Severity, frequency, or required treatment (score) Symptoms (to the time 0\* 4 of diagnosis) 1\* 2 3 Menorrhagia None/ Consultation only†; Missed work Combined antifibri-Acute menorrhagia requiring trivial changing pads more or school more nolytic and hormone hospital admission and frequently than than twice per therapy; or present emergency treatment; blood every 2 hours, clotyear; antifisince menarche and transfusion, replacement ting and flooding, brinolytic, longer than 12 months therapy, or desmopressin or scoring > 100 on hormone, or therapy; or dilation and pictorial blood loss iron therapy curettage, endometrial ablaassessment chart§ tion, or hysterectomy Postpartum None/ Consultation only†; Iron or anti-Blood transfusion, Any procedure requiring trivial fibrinolytic critical care or surgical interhemorrhage oxytocin; lochia replacement therlasting > 6 weeks therapy apy, desmopressin vention (eg, hysterectomy, internal iliac artery ligation, therapy, examination under anesthesia, uterine artery embolization, uterine brace sutures) or the use of uterine balloon/package to tamponade the uterus Muscle Never Post-trauma, no Spontaneous, Spontaneous or Spontaneous or traumatic, hematomas no therapy traumatic, dessurgical intervention or therapy blood transfusion mopressin or replacement therapy Hemarthrosis Never Post-trauma, no Spontaneous, Spontaneous or Spontaneous or traumatic, therapy no therapy traumatic, dessurgical intervention or blood transfusion mopressin or replacement therapy Central nervous Never Never Never Subdural, any Intracerebral, any system bleeding intervention intervention Other None/ Present Consultation Surgical hemosta-Blood transfusion, bleeding¶ trivial only† sis, antifibrinolytic replacement therapy, or

Note: Scores > 3 in adult males, > 5 in adult females, and > 2 in children warrant further evaluation.  $^{12,13}$  Full tool available at https://www.isth.org/resource/resmgr/ssc/isth-ssc\_bleeding\_assessment.pdf.

therapy

Adapted with permission from Rodeghiero F, Tosetto A, Abshire T, et al.; ISTH/SSC joint VWF and Perinatal/Pediatric Hemostasis Subcommittees Working Group. ISTH/SSC bleeding assessment tool: a standardized questionnaire and a proposal for a new bleeding score for inherited bleeding disorders. *J Thromb Haemost*. 2010;8(9):2063-2065.

desmopressin therapy

<sup>\*—</sup>The distinction between 0 and 1 is of critical importance; 1 means that the symptom is judged as present in the patient's history but does not qualify for a score of 2 or higher.

<sup>†—</sup>The patient sought medical evaluation and was referred to a specialist or offered detailed laboratory investigation.

<sup>‡—</sup>For example, a score of 1 is assigned for four extractions or surgeries in which only one resulted in bleeding (25%); a score of 2 is assigned for one extraction or surgery resulting in bleeding (100%), for two extractions or surgeries in which only one resulted in bleeding (50%), or for three extractions or surgeries in which only one resulted in bleeding (33%).

<sup>§—</sup>If already available at the time of collection.

<sup>¶—</sup>Includes umbilical stump bleeding, cephalohematoma, cheek hematoma caused by sucking during breastfeeding or bottle feeding, conjunctival hemorrhage, and excessive bleeding after circumcision or venipuncture. When these conditions occur in infants, detailed investigation is required independent from the overall score.

may not have encountered a hemostatic challenge such as surgery or menses. 4,14,15 However, the absence of personal or family history of easy bleeding or bruising does not rule out the possibility of a bleeding disorder. 4,20

### PHYSICAL EXAMINATION

The physical examination should note any evidence of bleeding (eg, bruises, scabs) and stigmata of underlying causes, such as body habitus, hepatomegaly, hypermobility, jaundice, or splenomegaly. 4,6,12,15 The clinician should perform a comprehensive skin and oral examination and document the number, size, and location of purpura, petechiae, telangiectasias, bruises, and hemarthroses. Findings that suggest a bleeding disorder include truncal bruising, five or more bruises greater than 1 cm in diameter, and atraumatic petechiae or hematomas.9 Furthermore, signs consistent with anemia, such as conjunctival pallor and tachycardia, may provide insight into the severity or chronicity of bleeding. Patient-provided photographs can be compared with physical examination findings, and in-office photographs may aid in monitoring progression or resolution.9

### SPECIAL CONSIDERATIONS

Abuse and nonaccidental trauma should be considered as causes of bruising in children and patients who are older or disabled. 20-24 When abuse is suspected, the patient should not be released until further investigation has been completed. Bruises that may indicate elder abuse tend to be large (more than 5 cm) and located on the face, lateral aspect of the right arm, and posterior torso. 23 Bruising patterns that may indicate child abuse are distinct from those occurring from developmentally consistent accidental trauma (eg, from learning to walk or ride a bicycle) and include object or hand patterns and bruises located on the ears, neck, and genitals. 20

The TEN-4-FACESp clinical decision rule is highly sensitive (95.6%) and specific (87.1%) in differentiating bruising from abuse and accidental injury in children younger than 4 years.<sup>25</sup> Potential signs of child abuse include any bruising that is patterned; noted in an infant younger than 5 months; or located on the torso, ear, neck, frenulum, angle of the jaw, fleshy part of the cheek, eyelids, or subconjunctival area. The clinical decision rule and the approach to and

### **TABLE 2**

Differential Diagnosis of Bleeding and Bruising Disorders			
Diagnosis	Key clinical features		
Bleeding Disseminated intravascular coagulation	Bleeding from multiple sites		
Factor inhibitors	Sudden onset of joint or soft tissue bleeding without family history		
Hemophilia (A or B), or other factor deficiencies	Joint or soft tissue bleeding with family history		
Hereditary hemor- rhagic telangiectasia	Telangiectasias over oral mucosa, nasal cavity, skin; epistaxis		
Leukemia	Abnormal complete blood cell count or peripheral blood smear result, weight loss, fatigue, night sweats; hepatosplenomegaly may occur		
Platelet disorders (qualitative or	Lifelong history of bleeding despite negative diagnostic workup		
functional)	May be a glycoprotein disorder (Bernard-Soulier syndrome, Glanzmann thrombasthenia), storage pool disease, von Willebrand disease, May-Hegglin anomaly, or Wiskott-Aldrich syndrome		
Platelet disorders (quantitative)	Bleeding, bruising, petechiae, or purpura; spleno- megaly may occur		
	May be idiopathic thrombocytopenic purpura, thrombocytopenic purpura, heparin-induced thrombocytopenia, malignancy, or viral infection		
Trauma	Deep lacerations, intracranial trauma		
Vasculitis or cryoglobulinemia	Purpura; neuropathy; pulmonary-renal involvement		
Vitamin K deficiency	Likely due to malabsorption (bacterial overgrowth, celiac disease, chronic pancreatitis, irritable bowel syndrome, short gut syndrome), poor diet (malnutrition, alcoholism, total parenteral nutrition), or vitamin K-binding medications (cholestyramine)		
Bruising			
Alcohol use disorder	Social history, screening tools (CAGE, AUDIT), hepatomegaly, cirrhosis, jaundice		
Cushing disease	Facial plethora; hirsutism; hyperglycemia; hypertension; striae		

management of child abuse were reviewed by *AFP* in 2022 (https://www.aafp.org/pubs/afp/issues/2022/0600/p661.html and https://www.aafp.org/pubs/afp/issues/2022/0500/p521.html). Nonmobile patients with bruises should undergo an evaluation for abuse and bleeding disorders unless there is an independent witness of accidental trauma.<sup>20</sup>

Bruises in infants younger than 6 months are rarely seen in the primary care and emergency departments, with a prevalence of 0.6% in both settings.<sup>26,27</sup> When infants younger than 6 months are presented with bruising, administration of neonatal vitamin K should be confirmed.20 Vitamin K deficiency should be suspected in infants who did not receive a dose of vitamin K.<sup>28</sup> Bleeding of the umbilical stump, excessive bleeding after circumcision, numerous and large bruises, and bruising at the sites of object pressure points (eg, car seat buckles or clothing clasps) are strongly suggestive of an underlying bleeding disorder in infants.<sup>20,21</sup> Any child with an intracranial hemorrhage should be evaluated for a bleeding disorder.<sup>20</sup>

# LABORATORY EVALUATION Initial Testing

Laboratory tests should be ordered for patients with symptoms or a suspicious history.<sup>4,12</sup> The workup for a suspected bleeding disorder includes a complete blood cell count, peripheral blood smear, and coagulation

studies. Coagulation studies include assessment of prothrombin time (PT), international normalized ratio, activated partial thromboplastin time (aPTT), and fibrinogen. 4,5,12,29-31

### TABLE 2 (continued)

# Differential Diagnosis of Bleeding and Bruising Disorders

Diagnosis	Key clinical features		
Bruising (continued)			
Ehlers-Danlos syndrome or connective tissue disease	Atrophic scarring; joint dislocations; hypermobile joints (per Beighton hypermobility scale); skin hyperextensibility		
Marfan syndrome	Enlarged aortic root; ocular involvement; mitral valve prolapse; scoliosis; pectus excavatum; striae; tall and slim body habitus with long limbs and digits		
Physical abuse (including child or elder abuse)	Atypical pattern of bruising or bleeding that may be object-related; bruising in nonmobile persons; history inconsistent with patient's injuries		
Purpura simplex (easy bruising)	Bruising typically found on the upper thighs and arms		
Senile purpura	Dark ecchymoses in aged, thin skin; typically found on extensor surfaces of forearms		
Trauma	Ecchymoses from underlying soft tissue injury, fracture		
Vitamin C deficiency	Dietary and social history, malaise, coiled hair, failure to thrive, gingival bleeding, tooth loss		

Adapted with permission from Ballas M, Kraut EH. Bleeding and bruising: a diagnostic

work-up. Am Fam Physician. 2008;77(8):1118, with additional information from reference 4.

If prothrom - Normal PT and aPTT results may indicate a platelet disorder.

Normal PT and aPTT results may indicate a platelet disorder. A normal PT result with a prolonged aPTT result indicates a disorder of the intrinsic coagulation pathway, and a prolonged

### TABLE 3

# Medications Known to Cause Bleeding and Bruising

Antibiotics	Anticoagulants	Anticonvulsants and	Anti-inflammatories	Miscellaneous
Cephalosporins	Aspirin	antidepressants	Corticosteroids	Metaxalone
Linezolid	Direct thrombin	Carbamazepine	Nonsteroidal anti-	Propylthiouracil
Nitrofurantoin	inhibitors	Selective serotonin	inflammatory drugs	Thiazide diuretics
Penicillins	Factor Xa inhibitors	reuptake inhibitors	Antineoplastic agents	Supplements
Quinine	Heparin	Tricyclic antidepressants	Imatinib (Gleevec)	Fish oil
Rifampin	Warfarin	Valproic acid	Interferons	Ginkgo biloba
Sulfonamides				Gold
Vancomycin				Testosterone

Adapted with permission from Neutze D, Roque J. Clinical evaluation of bleeding and bruising in primary care. *Am Fam Physician*. 2016;93(4):283, and Ballas M, Kraut EH. Bleeding and bruising: a diagnostic work-up. *Am Fam Physician*. 2008;77(8):1122.

PT result with normal aPTT result may indicate a disorder of the extrinsic coagulation pathway. Because vWD is the most common inherited bleeding disorder in female patients, testing for it should be considered initially.<sup>5,30,31</sup> The differential diagnosis based on initial results and recommended next steps

are summarized in Table 4<sup>3,5,29,31-36</sup> and Figure 2.<sup>4,5</sup> A low platelet count should be confirmed by recollecting the blood in a citrated or heparinized tube, because ethylenediaminetetraacetic acid sensitivity can lead to a false-positive result for thrombocytopenia due to platelet clumping.<sup>29</sup> A peripheral blood smear

TABLE 4			
Laboratory Evaluation of Bleeding and Bruising			
Test results	Inherited etiology	Acquired etiology	Further testing*
Normal PT and normal aPTT	Mild vWD Factor XIII deficiency Alpha₂ antiplasmin deficiency	Impaired fibrinolysis	von Willebrand fact antigen and activity Factor VIII level Platelet function Genomic analysis
Prolonged PT and normal aPTT	Extrinsic coagulation pathway disorder: factor VII deficiency	Mild vitamin K deficiency Liver disease Early DIC Medications (eg, warfarin)	Specific factor measurement
Prolonged PT and prolonged aPTT	Common coagulation pathway disorder: factor X, V, II (prothrombin), I (fibrinogen) deficiency Combined factor deficiencies Primary hyperfibrinolysis* (see low fibrinogen)	DIC Liver disease Severe vitamin K deficiency Factor X, V, II,* I inhibitors Factor X deficiency due to amyloidosis Medications (eg, warfarin, direct thrombin inhibitors)	Mixing study Thrombin time Genomic analysis Specific factor measurement
Normal PT and prolonged aPTT	Intrinsic coagulation pathway disorder: Factor VIII (hemophilia A), IX (hemophilia B), XI deficiency Factor XII deficiency† vWD	Factor VIII, IX, XI, XII inhibitors Acquired von Willebrand syndrome Hemophilia A Factor V deficiency Lupus anticoagulant Medications (eg, heparin, direct Xa inhibitors)	Mixing study Specific factor measurement Genomic analysis
Abnormal blood smear	Macrothrombocytopenia (gray platelet syndrome)  Neutrophil inclusion bodies (May-Hegglin anomaly)  Thrombocytopenia (DIC, thrombotic or idiopathic thrombocytopenic purpura)	Platelet clumps in an ethylene- diaminetetraacetic acid tube (pseudothrombocytopenia) Medications (eg, carbamazepine)	Repeat complete blood cell count in a citrated or heparin- ized tube Genomic analysis

 $a \label{eq:potential} PTT = activated \ partial \ thrombop last in time; \ DIC = disseminated \ intravascular \ coagulation; \ PT = prothrombin \ time; \ vWD = von \ Willebrand \ disease.$ 

<sup>\*—</sup>May require consultation with hematology.

<sup>†—</sup>Factor XII deficiency causes abnormal test results but is not associated with an increase in the tendency to bleed or bruise. Further investigation into the etiology may be necessary.

# TABLE 4 (continued)

# Laboratory Evaluation of Bleeding and Bruising

Test results	Inherited etiology	Acquired etiology	Further testing*
Abnormal	Type 2 or 3 vWD	vWD	Light transmission
platelet func-	Albinism	Uremia	aggregometry
tion test	Glanzmann thrombasthenia	Medications (eg, tricyclic antidepressants, selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, nonsteroidal anti-inflammatory drugs)	Lumiaggregometry
	Bernard-Soulier syndrome		PFA-100
			Flow cytometry
			von Willebrand factor antigen and activity
			Genomic analysis
			Whole blood impedance aggregometry
Low fibrino- gen, elevated D-dimer	Alpha <sub>2</sub> antiplasmin deficiency	DIC	Thromboelastography
	Plasminogen activator inhibitor-1	Cirrhosis	Genomic analysis
	deficiency	Acute promyelocytic leukemia	
	Quebec platelet disorder	Trauma	
	Primary hyperfibrinolysis	Postpartum hemorrhage	

 $a PTT = activated\ partial\ thrombop last in\ time;\ DIC = disseminated\ in\ travascular\ coagulation;\ PT = prothrombin\ time;\ vWD = von\ Willebrand\ disease.$ 

Information from references 3, 5, 29, and 31-36.

# **SORT: KEY RECOMMENDATIONS FOR PRACTICE**

Clinical recommendation	Evidence rating	Comments
A comprehensive history, including family history, is integral to the investigation of abnormal bleeding and bruising. <sup>4</sup>	С	Consensus, expert opinion
Use of the International Society on Thrombosis and Haemostasis Bleeding Assessment Tool as a standardized approach to a patient's history can be initiated in primary care alongside history of present illness, but scores should be interpreted in consultation with hematology. 4,10,12,13	С	Consensus, expert opinion, and disease-oriented outcomes
The TEN-4-FACESp clinical rule can aid in differentiating bruising from abuse and bruising from accidental trauma in children younger than 4 years. <sup>25</sup>	В	Prediction rule from large prospective cross-sectional study
Initial laboratory evaluation of suspected bleeding disorders should assess complete blood cell count, prothrombin time, activated partial thromboplastin time, peripheral blood smear, and fibrinogen level, with additional consideration for von Willebrand disease analysis. 4,5,12,29-31	С	Consensus, expert opinion
Although light transmission aggregometry remains the clinical standard for platelet function testing, PFA-100 is a more available initial option for testing. <sup>29,32</sup>	С	Consensus, disease-oriented outcomes

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afpsort.

 $<sup>\</sup>hbox{$^*$--May require consultation with hematology.}\\$ 

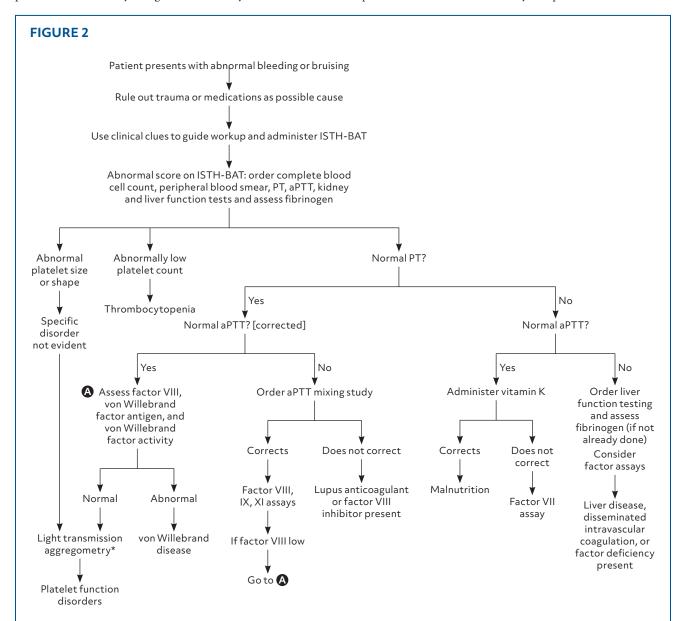
<sup>†—</sup>Factor XII deficiency causes abnormal test results but is not associated with an increase in the tendency to bleed or bruise. Further investigation into the etiology may be necessary.

evaluates platelet morphology and can suggest a qualitative or quantitative platelet disorder. When both the PT and aPTT are prolonged, liver function should be evaluated.  $^4$ 

### **Further Testing**

Disorders of primary hemostasis can be evaluated with platelet function tests such as light transmission aggregometry and platelet function analysis (eg, the PFA-100 system). <sup>29,32</sup> Platelet

dysfunctions include low quantity of platelets or qualitative abnormalities and should be suspected after normal coagulation study results.<sup>29,37,38</sup> Bleeding time was historically used to assess platelet aggregation but is no longer favored due to standardization difficulties and low sensitivity.<sup>39</sup> Light transmission aggregometry is considered the clinical standard for platelet function analysis, but standardization is less reliable than expected, and the test is technically complex.<sup>29</sup> Platelet function



aPTT = activated partial thromboplastin time; ISTH-BAT = International Society on Thrombosis and Haemostasis Bleeding Assessment Tool; PT = prothrombin time.

\*—This test should be ordered only by a hematologist. Platelet function analysis (eg, using the PFA-100 system) is another option for initial screening.

Evaluation of abnormal bleeding and bruising.

Adapted with permission from Neutze D, Roque J. Clinical evaluation of bleeding and bruising in primary care. *Am Fam Physician*. 2016;93(4):284, with additional information from reference 5.

analysis has sensitivity up to 80% for severe platelet dysfunctions and type 2 and 3 vWD; however, sensitivity is 24% for mild platelet dysfunctions and type 1 vWD, and the nuances of these results are best interpreted by a hematologist. <sup>29,31,32</sup>

Genomic analysis is an area of rising interest and is becoming more widely available and cost-efficient. <sup>5,14,29,40</sup> Real-time functional testing of blood clotting and fibrinolysis, such as thromboelastography, is not routinely used for initial bleeding evaluation, because the validity and applicability for disease diagnosis are questionable. Thromboelastography is more often used to manage acute bleeding in trauma, surgery, and obstetric hemorrhage. <sup>29,33</sup> Measurement of fibrinogen and D-dimer levels can assess fibrinolytic processes that lead to bleeding by disruption of a hemostatic platelet clump, deactivation of fibrinolytic inhibitors, or by a quantitative deficiency. <sup>34</sup>

# **CONSULTATION**

Hematology consultation should be pursued when the initial laboratory evaluation reveals a specific disorder or is nondiagnostic with a concerning history, a patient with a suspected or confirmed bleeding disorder is undergoing a procedure, or there is a request for prenatal counseling. It is also appropriate any time the primary care physician may need expert consultation. If an obstetric patient has vWD or another inherited bleeding disorder, consultation with hematology, maternal-fetal medicine, and anesthesiology is warranted. Up to 60% of referred symptomatic patients may have a bleeding disorder of unknown cause.

This article updates previous articles on this topic by Neutze and Roque<sup>4</sup> and Ballas and Kraut.<sup>15</sup>

Data Sources: A PubMed search was completed in Clinical Queries using the key terms bleeding and bruising. The search included meta-analyses, randomized controlled trials, clinical trials, and reviews. The Agency for Healthcare Research and Quality Effective Healthcare Reports, the Cochrane database, DynaMed, and Essential Evidence Plus were also searched. We critically reviewed studies that used patient categories such as gender. The included references used biologic sex when related to heritable conditions. Search dates: October and December 2023 and May and October 2024.

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