Overview of the ACE live session and instructions to Facilitators

Introductions (Start at 8:30 am: 5-10 minutes)
- Start the live session by introducing yourself
- Meet the students and let them introduce themselves
- If you are familiar with the students, take a few minutes to check in on them and how they are doing
- Let the pre-designated student/students connect the computer/laptop to the AV system to log on and bring up the google doc forms to be used in the session

Clinical Approach Questions (Start no later than 8:40 am: 15 minutes)
- Start with the Clinical Approach Questions document on the screen:
  - Ask each clinical approach question and elicit a response from the students (as a large group)
  - If students are not volunteering or speaking up, go around the room and call on them or use the student roster provided in your folder
  - If students are not giving the expected/correct answers, guide them further
  - Ensure that you fill in gaps, if students are missing important points, or necessary information relating to the learning objectives

ACE Table (Start no later than 9:00 am: 40 minutes)
- Next direct the students to bring up the ACE Table document on the screen:
  - Students will need to work together to fill in the table (via google docs)
  - They can access the electronic “Resources folder” at any time
  - Divide your large group into smaller subgroups of 2-3 students
  - Assign each smaller subgroup of 2-3 students, a diagnosis and let them fill in the missing information—allow about 10-15 minutes
  - Circulate or check on them periodically and guide them as needed
After the table is filled, let each subgroup present what they worked on—allow about 25-30 minutes.

Let each student present if possible.

Discuss or challenge them if you see gaps in the information provided or if there are erroneous information.

Once completed, the students are allowed to keep this table for their educational purposes.

**Practice Clinical Cases (Start no later than 9:40 am: 20-25 minutes)**

- Next, direct the students to the Practice Clinical Cases document on the screen:
  - As a large group, work to discuss the practice clinical cases.
  - Rotate through the students to elicit responses to the questions in each practice clinical case and direct the discussion as needed.
  - Reveal the “working diagnosis” for each clinical case after all the questions have been answered.
  - Alternatively, if you have ample time, divide your large group into smaller subgroups and give each subgroup a clinical case to work on (10 minutes) and let each subgroup present (15-20 minutes).

**Quiz and feedback (Start no later than 10:00 am: 15-20 minutes)**

- Ensure that all students log into eCampus and access the Quiz under the course/CSIE ACE folder/Quiz.
- Access the brown envelope in your maroon folder and read out loud the quiz password.
- If a student experiences technical issues, access the brown folder for a backup copy.
- The quiz will take 10 minutes to complete.
  - During the quiz, please access the one page student evaluation form (in the brown envelope) and evaluate each student using the given grading rubric.
  - When all students are done with the quiz, briefly go over the quiz questions/answers (5-10 minutes).
- Conclude the session and release the students by 10:20 am.
- Leave the completed student evaluation form in the brown envelope within the maroon folder.

**PLEASE ENSURE THAT ALL FILLED-IN STUDENT EVALUATIONS ARE IN THE BROWN ENVELOPE BEFORE YOU LEAVE THE ROOM.**

**Quick Overview of Student Expectations and Assessment:**

**Student Expectations**

- Students are expected to arrive on time, in professional dress, white coat and badge.
- Students are expected to actively participate, show professional behavior such as appropriate listening skills and refraining from disrupting the session (please see the student evaluation rubric for more details).
- Students are expected to have prepared for the live session by reading the preparation guide and assigned reading material to prepare them for the live session.

**ACE Assessment**

- This CSIE ACE comprises of 3% of the overall block grade in the following way:
  - 1.5% for the individual quiz given at the end of the session.
  - 1.5% for the student evaluation form (provided by you as the facilitator).

Texas A&M University, College of Medicine
ACE Easy Bleeding/Bruising Learning Objectives:

1. Develop a clinical approach to the chief complaint of easy bleeding/bruising.
2. Name the organ systems commonly associated with easy bleeding/bruising.
3. Develop a differential diagnosis for easy bleeding/bruising based on history, physical exam findings, and diagnostic tests.
4. List likely causes of easy bleeding/bruising in a younger versus an older patient.
5. List child abuse as a potential cause of bruising.
7. List major life threatening causes of easy bleeding/bruising.
8. Identify the physical exam findings indicative of severe bleeding.
9. Differentiate between different causes of easy bleeding/bruising (e.g. Von Willebrand disease, vs. hemophilia, vs ITP, TTP, DIC, leukemia, child abuse etc.) given key clinical features.
10. Identify appropriate diagnostic testing to further evaluate easy bleeding/bruising.
11. Identify the common hematologic laboratory abnormalities associated with bleeding disorders.

CC: Easy bleeding/bruising

Clinical Approach & Questions:

Approach to the Patient with Easy Bleeding/Bruising

1. What organ systems are commonly associated with easy bleeding/bruising?
   - Hematologic, Vascular, Oncologic, Psychosocial, Other (hepatic, drugs, normal)

2. Within these systems, what is your differential diagnosis for each?
   - Hematologic
     - Platelet deficiency (quantitative):
       - Decreased survival- TTP, ITP, HUS
       - Splenic sequestration- hypersplenism
       - Bone marrow failure/replacement: fibrosis, infections, malignancies
     - Platelet defective function (qualitative):
       - Inherited disorders- Bernard Soulier, Glanzmann’s thrombasthenia, Von Willebrand Disease
       - Acquired- Aspirin use, uremia
     - Coagulation factor deficiency or dysfunction:
       - Inherited- Hemophilia A, hemophilia B, Von Willebrand Disease
       - Acquired- DIC, vitamin K deficiency, factor inhibitor, meds or drugs
3. What are some conditions that can cause easy bleeding/bruising in children versus adults?

- **Children**: Trauma, leukemia, child abuse, poisoning (rodenticide ingestion), post-viral ITP, Von Willebrand disease (most common inherited coagulation disorder)
- **Adults**: Medications/drugs (Aspirin, warfarin, steroids, alcohol), liver disease, vitamin K deficiency (warfarin use for example), aging (senile purpura), physical abuse, malignancy (leukemia/DIC), uremia (kidney disease), Von Willebrand disease (most common inherited coagulation disorder), idiopathic

4. What are life-threatening causes of easy bleeding/bruising?

- Leukemia, DIC (due to sepsis or malignancy- e.g. APL- acute promyelocytic leukemia or leukemia with very low platelet counts), abuse, severe trauma, poisoning, thrombotic thrombocytopenic purpura (TTP), heparin induced thrombocytopenia (HIT), certain severe coagulation factor dysfunctions (e.g. hemophilia)

For additional info on HPI questions/exam findings/labs and procedures etc., see “Further information for the ACE Table and its discussion“ below. This document will only be discussed with students in context of the ACE Table discussion.

Further information for the ACE table and discussion

What pertinent ROS questions and exam findings would you look for?

- Onset, duration, timing
  - Abrupt versus chronic
    - Chronic bleeding and bruising maybe leukemia, vasculitis, or chronic use of aspirin
  - Isolated versus repetitive
Spontaneous versus induced

- Quality
  - Clotting of menstrual periods may indicate a problem with coagulation

- Location
  - Petechiae of lower extremities is more indicative of platelet dysfunction or vasculitis where petechiae of the upper extremities in the elderly maybe considered benign
  - Deep hematomas and knee hemarthrosis is suggestive of a problem with coagulation
  - Bleeding gums and nosebleeds are nonspecific but may be a sign of platelet dysfunction

- Associations
  - Severe infections and fatigue can be associated with leukemia
  - Neuropathy, pulmonary-renal involvement, GI tract involvement, and arthritis are seen in vasculitis
  - Neural manifestations, fever, renal involvement maybe seen with TTP

- Context
  - Was a deep hematoma associated with minor trauma?
  - Did excessive bleeding occur with minor surgery/procedure?
  - Epistaxis- maybe related to rhinitis, trauma (even nose picking in children), dry air

**Physical Exam:**

**Vitals:**
- Is the patient hypotensive from blood loss? Orthostatic vitals can reveal clinical hypovolemia
- Tachycardia can be a sign of anemia
- High fever with neutropenia can point towards leukemia
- High blood pressure might indicate a glomerulonephritis from vasculitis
- Pulmonary hemorrhages from vasculitis will show tachypnea with respiratory distress with possible low oxygen saturation

General appearance: Look for pallor (maybe difficult to assess, see HEENT)

HEENT: Look for mucocutaneous bleeding in your oral exam. Look for conjunctival and sublingual pallor.

Cardiovascular exam: You might hear a flow murmur with anemia. You might see peripheral or generalized edema from glomerulonephritis due to small vessel vasculitis.

Lungs: Typically is normal. Small vessel vasculitis may involve lungs and demonstrate lung exam findings consistent with pulmonary hemorrhage or pleural effusions.

GI: Look for HSM (leukemia/lymphoma) and stigmata of advanced liver disease (e.g. ascites)

Skin: Palpable vs non-palpable purpura? Is petechiae located in the upper or lower extremities?
Musculoskeletal exam: Examine the knees for knee effusions that might be due to hemarthrosis

What other pertinent elements of the patient’s history would you focus on?

- **Past history**
  - History of other episodes of bleeding
    - Bleeding following surgical procedures (i.e., tooth extractions, circumcision)
    - Heavy periods
    - History of epistaxis, cutaneous bruises, bleeding from minor wounds, oral cavity bleeding (i.e., gums), GI bleed, hemarthrosis, CNS bleed, muscle hematomas, hemarthrosis
  - Onset of bleeding at birth or childhood points to inherited cause
  - History of iron-responsive anemia
  - History of blood transfusions
  - Positive family history increases the risk of a bleeding disorder

- **Medications**
  - Aspirin, NSAIDS, Beta lactam antibiotics, Clopidogrel, Warfarin

- **Social history**
  - Alcohol use, physical abuse

What laboratory values and/or studies would you order to narrow your differential diagnosis? (Depending on the clinical data, not all will be ordered on each patient)

- When the diagnosis is not immediately apparent, order a CBC (to check platelet count), PT, and aPTT

Normal PT, aPTT, and platelets:

- If there is a high suspicion of platelet disorder (i.e., mucocutaneous bleeding), consider platelet function disorder, factor XIII deficiency, or vascular integrity diseases
- **Platelet disorders**
  - Von Willebrand disease and Inherited platelet dysfunction are considerations
  - Order peripheral blood smear and PFA-100
    - If **PFA-100 is prolonged** with *both collagen/epinephrine membrane and collagen/adenosine membrane*, consider Von Willebrand Disease and test for vWF
    - If **prolonged aggregation with only collagen/epinephrine**, consider drug effect (e.g., Aspirin)
  - If all the above mentioned tests are negative, then consider factor XIII deficiency, fibrinolytic defects, and disorders of vascular integrity
  - Von Willebrand disease
    - Present with moderate to severe mucocutaneous bleeding depending on the subtype
    - Can present with a prolonged aPTT due to a concomitant deficiency of factor VIII (e.g. subtype 3)
• Levels will normalize with certain medical conditions, hiding the disorder (i.e., pregnancy, oral contraceptives, and liver disease)
• Initial screening includes immunoassay for VWF antigen, ristocetin cofactor activity and factor VIII activity level. *(Warning: results may vary and retesting might be indicated.)*
  o Platelet dysfunction (inherited and rare)
    • Bernard-Soulier syndrome
      ● Defect of GP Ib/IX/V complex
      ● Has giant platelets and greater than expected bleeding for the degree of thrombocytopenia
    • Glanzmann thrombasthenia
      ● Defect of GP IIb/IIIa complex
      ● Normal platelet count, and morphology with abnormal platelet aggregation
    • Storage pool disease
      ● Common: due to aspirin, NSAIDS, beta-lactam antibiotics, uremia, myeloproliferative and myelodysplastic syndrome.
      ● Rare: Wiskott-Aldrich syndrome, thrombocytopenia with absent radii syndrome, Chediak-Higashi syndrome, and Hermansky-Pudlak syndrome.

• Coagulation disorders
  o Factor XIII deficiency
    • Factor XIII stabilizes and cross links fibrin strands
    • May present with delayed bleeding (i.e. 24-36 hours after surgery or trauma or spontaneous bleeding
    • Normal PT, aPTT, and TT (thrombin time)
    • Diagnosis made by measurement of reduced plasma factor XIII activity, an immunoassay for factor XIII, or demonstration of clot dissolution in 5 molar urea or monochloroacetic acid
  
  Normal PT and **prolonged aPTT**

• Factor deficiencies
  o Due to derangement of intrinsic pathway (plus common pathway) factors
  o Inherited disorders include factor VIII deficiency (Hemophilia A), von Willebrand disease (severe type 3), factor IX deficiency (hemophilia B), and factor XI deficiency
  o Hemophilia A and B present with lifelong recurrent soft tissue and joint bleeding
  o Factor XI deficiency has a variable and unpredictable bleeding history and occurs after surgical procedures
  o *Factor XII deficiency, and deficiencies of prekallikrein will prolong aPTT but do not cause excessive bleeding*
Acquired inhibitors
- Antiphospholipids antibodies prolong aPTT but cause thrombosis (lupus anticoagulant)
- Antibodies to factor VIII, IX, and XI can cause catastrophic bleeding
- Inhibitors to factor V have variable effects on PT and aPTT

Measure aPTT after mixing study:
- If normalizes then it is likely a factor deficiency (i.e., VIII, IX and XI, which all have assays). **If Factor VIII is low, check also for vWF!**
- If mixing study does not normalize, then the problem is an inhibitor such as an antibody (i.e., lupus anticoagulant, acquired factor VIII inhibitor etc.)

**Prolonged PT and normal aPTT**
- Abnormality of the extrinsic pathway (plus common pathway) factors
  - Suggests factor VII deficiency which has a wide range of bleeding symptoms
- Seen commonly with warfarin, early liver disease, and Vitamin K deficiency
- Seen in early DIC
- Vitamin K can be given as a “challenge” to see if PT will correct
  - If PT corrects, then likely Vitamin K deficiency from inability of gut to absorb (i.e., Cystic fibrosis, chronic pancreatitis)
  - If PT does not correct, then check assays for factor VII

**Prolonged PT and aPTT**
- Indicates a disorder of the common, extrinsic and intrinsic pathways
- Disorders of factor X, V, prothrombin (II), or fibrinogen (I) are extremely rare
- Afibrinogenemia and dysfibrinogenemias are also rare
- Vitamin K deficiency, liver disorder, DIC, and fibrinolysis
  - Difficulty to distinguish between them
  - Liver disease and Vitamin K def. will cause low factor II, VII, IX, and X
  - Factor V is independent of vitamin K, and if low may point towards liver disease or increased consumption from DIC
  - Factor VIII is not made from the liver so if lower would point towards DIC
  - First step is to exclude abnormality of fibrinogen and can be measured in plasma fibrinogen concentration and the thrombin time. Test also for D-dimer or fibrin split products
  - If there is a history of inherited coagulation disorder and normal fibrinogen, check for deficiencies of factor V, X, and prothrombin
  - Rarely, acquired factor X deficiency is seen with primary amyloidosis
ACE Table
Chief Complaint – Easy Bleeding and Bruising (Students will fill in 8 diagnoses below; see yellow highlights)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>System</th>
<th>History</th>
<th>Physical Exam Finding</th>
<th>Labs</th>
<th>Radiology/Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Idiopathic/immune thrombocytopenic purpura (ITP)</strong></td>
<td>Hematology</td>
<td>Acute form (children): self-limited, post-viral, usually presents as petechial rash, may have epistaxis, or bruising</td>
<td>Petechiae and purpura common, mucosal bleeding if more severe</td>
<td><strong>CBC</strong> – thrombocytopenia with other cell lines usually normal</td>
<td>Consider bone marrow aspirate/biopsy if concern for leukemia (multiple cell lines abnormal, lymphadenopathy, hepatosplenomegaly)</td>
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<tr>
<td></td>
<td></td>
<td>Chronic form (adults): ITP may be primary or secondary to another disorder (e.g., HIV, SLE)</td>
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<td><strong>Smear</strong> - shows enlarged, immature platelets</td>
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<td></td>
<td><strong>PT/INR and PTT</strong> - Normal</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>ANA panel</strong> - for chronic ITP</td>
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<tr>
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<td></td>
<td></td>
<td><strong>Consider bone marrow aspirate/biopsy if concern for leukemia (multiple cell lines abnormal, lymphadenopathy, hepatosplenomegaly)</strong></td>
<td></td>
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<td></td>
<td><strong>Imaging of area of concern may be needed, BUT SHOULD NOT DELAY FACTOR ADMINISTRATION IN A KNOWN HEMOPHILIAC.</strong></td>
<td></td>
</tr>
<tr>
<td><strong>2. Hemophilia (A, B, C)</strong></td>
<td>Hematology</td>
<td>Severe cases bleed in infancy at circumcision or have multiple hemorrhage</td>
<td>Macro-hemorrhage - large palpable ecchymosis, hematomas, hemarthrosis</td>
<td><strong>CBC</strong> – normal unless anemia due to bleeding</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderate cases have occasional hemorrhage</td>
<td></td>
<td><strong>PT/INR</strong> – normal</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Mild cases may be missed until dental or surgical procedures</td>
<td></td>
<td><strong>PTT</strong> - prolonged</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Family history – A &amp; B x-linked recessive, C autosomal recessive</td>
<td></td>
<td>Hemophilia A – low factor VIII levels</td>
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<td>Hemophilia B – low factor IX levels</td>
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<td></td>
<td></td>
<td></td>
<td>Hemophilia C – low factor XI levels</td>
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<td><strong>NOTE: DO NOT NEED TO CONFIRM FACTOR LEVEL IN A KNOWN HEMOPHILIAC PRIOR TO GIVING FACTOR REPLACEMENT IF</strong></td>
<td></td>
</tr>
</tbody>
</table>

**NOTE:** PAIN = BLEEDING IN KNOWN HEMOPHILIAC UNTIL PROVEN OTHERWISE

Texas A&M University, College of Medicine
| 3. Von Willebrand Disease (vWD) | Hematology | Presents with concerns for mucosal bleeding. Menorrhagia common presentation in females. Family history may be positive (autosomal dominant forms) | Micro-hemorrhage – mucous membrane bleeding, epistaxis, petechiae, purpura | CBC – normal unless anemia due to bleeding | DDAVP trail – to determine if DDAVP responsive 
Note: O blood types have lower levels of vWF (50-75% of other blood types) |
|---|---|---|---|---|---|
| Acute Lymphoblastic Leukemia (e.g. B-ALL) | Oncology | Peak age 4; rare over age of 50 Fatigue, fever (from infections), bleeding or bruising, bone pain, neural manifestations | Mucosal bleeding, petechiae, lymphadenopathy, hepatosplenomegaly, check testes in males, neuro exam | CBC – more than one cell line abnormal, often all 3 (Lymphocytosis or – lymphopenia, anemia, thrombocytopenia, Elevated LDH and uric acid (rapid cell turnover) | Bone marrow biopsy and aspirate (send for molecular/cytogenetic/flow cytometry studies) 
Lumbar puncture – to look for CNS involvement (B-ALL is the most likely leukemia to involve the CNS) |
| Non-accidental trauma (Child Abuse) | Psychosocial | Always consider with unexplained bruising or bruising in unusual locations, age and developmental level important | Pattern of bruising (ex - belt, handprint, bite mark) 
Bruising to unusual locations - Bruising to cheeks, neck, genitals, buttocks and back | Diagnosis of exclusion 
CBC – normal, but may have anemia with severe bleeding 
PTT, PT/INR - normal 
PFA-100, VWF testing – normal | Osseous survey – looking for occult fractures 
CT of Head – looking for head trauma 
Dilated Eye exam – looking for retinal hemorrhages |
<table>
<thead>
<tr>
<th>Condition</th>
<th>Category</th>
<th>Description</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Senile purpura</td>
<td>Dermatologic/Vascular</td>
<td>Elderly with thin skin, chronic sun exposure and drugs may exacerbate</td>
<td>None generally needed but CBC and Coagulation studies normal if performed</td>
</tr>
<tr>
<td>Vitamin K deficiency</td>
<td>Nutrition</td>
<td>Deficiency may not be noted until hypothyroidism is present. Easy bruising and mucosal bleeding. Identify susceptible groups – malnutrition, fat malabsorption, medications. Hemorrhagic disease of newborn if not given vit K at birth (home birth).</td>
<td>Ecchymosis, petechiae, hematomas, oozing of blood from injury</td>
</tr>
<tr>
<td>None needed</td>
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</tr>
<tr>
<td>Medication Effect [Aspirin, clopidogrel, heparin, warfarin]</td>
<td>Pharmacology/Toxicology</td>
<td>Common: Aspirin, Clopidogrel, Heparin, NSAIDs, Warfarin- ask if patient is taking any of these</td>
<td>Dermal or mucosal bleeding</td>
</tr>
<tr>
<td>None needed</td>
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</tbody>
</table>

Note: recognition of heparin induced thrombocytopenia (HIT) very important given risk for life threatening bleeding.
| Liver disease | Hepatic | Alcohol abuse, jaundice, cirrhosis, acute liver failure | Jaundice, pale, ascites, caput medusa, spider angiomata, shock with severe variceal bleeding, enlarged spleen | Heparin – prolonged PTT  
Warfarin - PT/INR prolonged  
Clopidogrel – PFA-100 may be normal  
Liver disease  
Hepatic  
Alcohol abuse, jaundice, cirrhosis, acute liver failure  
Jaundice, pale, ascites, caput medusa, spider angiomata, shock with severe variceal bleeding, enlarged spleen  
CBC – mild to mod thrombocytopenia, anemia  
PT/INR – may be prolonged  
PTT – may be prolonged  
D-dimer – elevated with severe disease  
Abnormal LFTs (liver function tests) | Note: Labs poor predictor of bleeding because they only reflect changes in procoagulant factors. |
| --- | --- | --- | --- | --- | --- |
| **6. Acute Disseminated Intravascular Coagulation** | Hematology | Recent history of trauma, sepsis, malignancy (especially acute promyelocytic leukemia), or ABO-incompatible blood transfusion | Bleeding, especially oozing from sites of trauma, catheters, or drains | CBC – thrombocytopenia, anemia  
PT/INR and PTT – prolonged  
D-dimer – elevated  
Plasma fibrinogen – low  
PBS – microangiopathic changes- schistocytes | If measured - Increased thrombin time, reduced levels of procoagulant factors such as factors VII, X, V, and II (prothrombin), reduced levels of coagulation inhibitors such as antithrombin (AT), protein C, and protein S |
| **7. Thrombotic thrombocytopenic purpura (TTP)** | Hematology | Clinical features: classic pentad (thrombocytopenic purpura, fever, renal failure, neurologic changes, microangiopathic | Confusion, AMS, diffuse petechial hemorrhages or purpura, neurologic symptoms, fever | CBC – anemia (hemolytic) and thrombocytopenia | Note: perform emergent plasmapheresis- otherwise, TTP can be fatal |
| 8. Iron deficiency anemia (Non-nutritional) | Hematology | Fatigue, pale, near-syncopy, unrecognized excessive bleeding (teenage female with menorrhagia), occult bleeding may be asymptomatic until anemia detected, Pica | Pale skin and mucous membranes, orthostatic hypotension and tachycardia as worsens, may hear systolic flow murmur, glossitis, koilonychia | CBC – microcytic hypochromic anemia | Iron studies – low iron and ferritin, high TIBC | PFA, Coagulation studies - normal | May need endoscopy/colonoscopy depending on age to identify source of occult GI bleeding, Stool hemoccult, U/A |
| Henoch-Schonlein Purpura (HSP) | Vascular | Child/adolescent, recent URI, rash, fever, malaise, polyarthralgia, and colicky abdominal pain | Dependent palpable purpura and petechiae (predominantly on buttocks and lower extremities), diffusely tender abdomen, edema and HTN with renal disease | CBC, PT/INR normal With renal involvement – transient renal failure (Elevated BUN creatinine), hematuria, proteinuria on U/A | Ultrasound if concern for intussusception (due to bowel wall edema). Renal biopsy with persistent renal ds – resembles IgA nephropathy |

**ACE- Easy Bleeding/Bruising PRACTICE CLINICAL CASES (3 cases)**

**Case 1**

CC: “My child has a spotty rash”
A 15-month old female infant is brought to clinic with a concern for a spotty rash noticed last evening on one arm, now has spread over arms, legs, trunk and face. Exam shows a diffuse pin-point non-blanching erythematous rash.

1. What is your differential diagnosis?
   ITP, HSP, HUS, child abuse, leukemia
2. What is common in this age group?
   Same as above
3. What other pertinent HPI questions would you ask the parents?
   Ask about recent viral URI
4. What pertinent ROS questions would you ask the parents?
   - Fever (none reported)
   - Weight loss (none)
   - Bone pain (none)
   - Prior bleeding or bruising (none)
   - Arthralgias or abdominal pain- HSP (none)
   - Diarrhea (none)
   - Family history of bleeding (none)
5. What pertinent exam findings would you look for or expect for this patient?
   - Petechiae (yes, that is the rash she is presenting with)
   - Mucosal bleeding- nares or gums (none on exam)
   - Lymphadenopathy (none)
   - Hepatosplenomegaly (none)
   - Tender abdomen (none)
6. What studies would you order?
   - CBC (PLT count is 7,000/mm^3, remainder within normal range)
   - PT/INR, PTT (normal)
7. Would the patient need close observation in the hospital?
   Given generally self-limited condition, most don’t need admission or treatment (American College of Hematology), but given severity of thrombocytopenia and young age in this particular case (risk for falls) most would admit with hematology consult. Treatment considerations include IVIG, steroids, and IV Rho immunoglobulin in Rh-positive patients.

**Diagnosis for case 1:** Idiopathic/immune thrombocytopenic purpura

**Case 2**

CC: “My baby is bleeding from the circumcision site”

A 3-day-old baby boy presents to newborn follow up clinic after discharge from the hospital yesterday. The first-time parents have noted that the circumcision site has been oozing blood ever since the procedure, but they were given reassurance that this was expected at the time of discharge. Exam reveals a blood soaked diaper with active bleeding at circumcision site.
1. What is your differential diagnosis?
   - Hemophilia, Von Willebrand Disease, type 3, Hemorrhagic disease of newborn, TORCH Infections, DIC due to sepsis or shock, Factor XIII deficiency
2. What is common in this age group?
   - Same as above
3. What other pertinent HPI questions would you ask the parents?
   - Family history of bleeding (none reported)
4. What pertinent ROS questions would you ask the parents?
   - Other signs of illness (they report none)
5. What pertinent exam findings would you look for or expect for this patient?
   - General (he is alert and interactive)
   - Vital signs (his heart rate is 190s at rest- tachycardia due to anemia)
   - Mucous membranes (pale mucous membranes- anemia)
   - Jaundice (none)
   - Limb abnormalities or dysmorphic features (none)
   - Bruising, ecchymoses, petechiae, hematomas (none found)
6. What studies would you order?
   - CBC (WBC 17,000, Hgb/HCT 7/21, PLT 250,000)
   - PT INR (normal)
   - PTT (65 sec – prolonged)
   - Factor VIII (very low, 2%)
7. Would the patient need close observation in the hospital?
   - Yes bleeding newborn with anemia and coagulopathy. Will need local control of bleeding, factor replacement, and possible transfusion.

**Diagnosis Case 2: Hemophilia A**

**Case 3**

CC: “Abdominal pain and bruising”

This is a 37-year-old man who is presenting with severe abdominal pain and bruising to both flanks. Exam reveals an anxious white male with a diffusely tender and somewhat rigid abdomen with infrequent bowel sounds. He has a positive Turner sign. Serum amylase and lipase are both elevated (indicating pancreatitis).

1. What is your differential diagnosis?
   - Traumatic (intramuscular or intraabdominal)
   - Non-traumatic – hemorrhagic pancreatitis
   - Acquired factor inhibitor
   - Leukemia
2. What is common in this age group?
3. What other pertinent HPI questions would you ask the patient?
   Medication use (none reported)
   Social Hx (on social history he reports heavy alcohol use- chronic alcoholism without cirrhosis)
   PMHx (two episodes of pancreatitis in the past. No prior bleeding.)
   Family history: (Family history of alcoholism)

4. What pertinent ROS questions would you ask the patient?
   Fever (101)
   Acute or gradual (he reports acute onset of diffuse abdominal pain)
   Vomiting/diarrhea (reports vomiting. No diarrhea)

5. What pertinent exam findings would you look for or expect for this patient?
   Vitals: BP 110/60, P 110 bpm, RR – 16 bmp, Temp 38 C
   Turner sign- bluish discoloration of flanks – retro or intra peritoneal bleeding

6. What studies would you order?
   - CBC (Hgb/HCT: 11/33, WBC 16,000, PLT 110,000)
   - LDH (1,000 IU/L)
   - PT (15.1 seconds [nl<14 sec])
   - PTT (42 sec [22-35 sec])
   - Mixing study (PTT corrects, no evidence of circulating anticoagulant)
   - Fibrinogen (120 mg/dl [nl 150-400 m/dl])
   - D- dimer (980 ng/ml [nl 500 ng/ml])
   - Peripheral blood smear (normocytic, normochromic, with small numbers of fragmented RBCs-schistocytes, polychromasia, and increased numbers of granulocytes)

7. Would the patient need close observation in the hospital?
   Patient is critically ill and will need admission to ICU with close monitoring and blood component therapy (PLTs to keep > 100,000, FFP and Cryoprecipitate to keep fibrinogen above 100 mg/dl and the PTT within normal range).

Diagnosis Case 3: DIC as a complication of necrotizing pancreatitis

ACE Easy Bleeding/Bruising Quiz Questions:

1) Beyond the hematologic and oncologic causes of easy bleeding/bruising, what other organ system/category is commonly associated with causing easy bleeding/bruising?
   a. Endocrine
   b. Respiratory
   c. Neural
   d. Vascular
   e. Cardiac
2) Which of the following laboratory test/s is/are useful in the workup of a bleeding problem?
   a. Platelet Function Assay
   b. Complete Blood Count
   c. Activated Partial Thromboplastin Time
   d. Prothrombin Time
   e. All of the above

3) During an annual health exam, a 70-year-old woman is found to have dark purple ecchymosis generally confined to the extensor surfaces of hands and forearms. She has no history of bleeding difficulties. She has no other complaints. Which of the following is the most likely cause of her physical exam findings?
   a. Acute lymphoblastic leukemia
   b. Hemophilia B
   c. Senile purpura
   d. Thrombotic thrombocytopenic Purpura
   e. Ehlers-Danlos disease

4) A 16-year-old male with known Hemophilia A presents with a painful swollen left elbow after a fall off his skateboard. He has a subcutaneous Port-a-cath to his right upper chest, and he brings his supply of recombinant Factor VIII. In addition to immediate infusion of his supply of Factor VIII via his Port-a-cath to ensure stopping any possible bleeding, what laboratory findings would you expect?
   a. Thrombocytopenia
   b. Decreased factor IX levels
   c. Prolonged PT
   d. Prolonged PTT
   e. Vitamin K deficiency

5) A 30-year-old woman presents with complaints of fever for the past 3 days. She comes to the emergency department today due to inability to speak clearly and tingling/numbness over both lower extremities for the past 3 hours. She has no significant past medical history. She is concerned that she is suffering from a stroke. Physical exam confirms the fever and neurological deficits, without any other localizing findings. A CBC is significant for low hemoglobin/hematocrit and thrombocytopenia. The peripheral blood smear reveals many schistocytes. Which of the following is her most likely diagnosis?
   a. Heparin Induced Thrombocytopenia
   b. Thrombotic thrombocytopenic purpura
   c. Abuse
   d. Idiopathic/immune thrombocytopenic purpura
   e. Von Willebrand disease

6) A 73-year-old man is hospitalized for a pulmonary embolus. He is receiving heparin infusion for management of his PE. Which of the following laboratory abnormalities is most expected?
a. Thrombocytosis  
b. Prolonged Activated Partial Thromboplastin Time  
c. Leukopenia  
d. Prolonged Prothrombin Time  
e. Low Factor IX level

7) A 63-year-old man is on Coumadin (warfarin) therapy for a history of atrial fibrillation. He comes in for increased bleeding after a recent dose change. Which of the following laboratory abnormalities is most expected?  
a. Thrombocytosis  
b. Prolonged Activated Partial Thromboplastin Time  
c. Leukopenia  
d. Prolonged Prothrombin Time  
e. Low Factor IX level

8) After a recent viral URI, an otherwise healthy 6-year-old boy is brought in by his parents for a rash on both of his lower extremities. Physical exam is only significant for a pin point petechial rash on the boy’s bilateral lower extremities. Which of the following laboratory abnormalities is most likely in this patient?  
a. Low factor VIII levels  
b. Prolonged Activated Partial Thromboplastin Time  
c. Thrombocytopenia  
d. Low VWF antigen levels  
e. Prolonged Prothrombin Time

9) A 2-year-old boy is brought in by his mother for an asthma exacerbation. On physical exam, the physician notices bruising on the child’s cheeks, neck, buttocks and back. The mother denies any prior history of bruising or easy bleeding. She denies prolonged bleeding at the time of his circumcision procedure. Aside, from the wheezing and above bruising, there are no other significant findings on physical exam. This pattern of bruising in a child would be concerning for which of the following?  
a. Immune thrombocytopenic purpura  
b. Hemophilia A  
c. Von Willebrand disease, type 3  
d. Glanzmann thrombasthenia  
e. Child abuse  
f. Bernard Soulier disease

10) What laboratory finding would be most likely in a patient with known Von Willebrand disease?  
a. Abnormal mixing studies  
b. Decreased Ristocetin induced platelet aggregation  
c. Prolonged Prothrombin Time  
d. Thrombocytopenia  
e. Low Vitamin K levels
Answers:
1. D (Objective 1,2)
2. E (Objective 1,10)
3. C (Objective 1,6)
4. D (Objective 11)
5. B (Objective 3,4,7,9)
6. B (Objective 10,11)
7. D (Objective 10,11)
8. C (Objective 9,11)
9. E (Objective 3,4,5,7)
10. B (Objective 10,11)

ACE Easy Bleeding and Bruising Learning Objectives:

1. Develop a clinical approach to the chief complaint of easy bleeding/bruising.
2. Name the organ systems commonly associated with easy bleeding/bruising.
3. Develop a differential diagnosis for easy bleeding/bruising based on history, physical exam findings, and diagnostic tests.
4. List likely causes of easy bleeding/bruising in a younger versus an older patient.
5. List child abuse as a potential cause of bruising.
7. List major life threatening causes of easy bleeding/bruising.
8. Identify the physical exam findings indicative of severe bleeding.
9. Differentiate between different causes of easy bleeding/bruising (e.g. Von Willebrand disease, vs. hemophilia, vs ITP, TTP, DIC, leukemia, child abuse etc.) given key clinical features.
10. Identify appropriate diagnostic testing to further evaluate easy bleeding/bruising.
11. Identify the common hematologic laboratory abnormalities associated with bleeding disorders.