From the Residency Program Director

The goal of a Residency Program in Internal Medicine is to strive to train the next generation of practitioners and academicians in Medicine who will become physicians-scholars, scientists, teachers, and humanists.

We are excited that many of our residents are pursuing research opportunities in the laboratory or clinic. Such participation is a requirement for training at Jefferson. In addition, this journal serves as an outlet for scholarly work of a variety of types. We are pleased to support another issue of the Jefferson Forum to continue to highlight this work. This represents the sixth installment of the Jefferson Forum, which debuted in 1999. The journal is supported entirely through private contributions and unrestricted educational grants.

Subscriptions to the members of the Department of Medicine are provided at no cost. The editors have maintained complete editorial independence to assemble and peer review the submissions for this installment.

The editors deserve our praise for a job well done. Please recognize that the creation of this journal is accomplished by a small team who still have to contend with the daily rigors of residency including night call, teaching their inpatient teams, long days, and preparing for boards. I thank them for extending Jefferson's tradition of excellence in education and enhancing the experience of our residents.

Gregory C. Kane M.D.
Associate Professor of Medicine
Residency Program Director
Department of Medicine

Welcome to the 6th Edition of the Jefferson Medicine Forum

We are very excited to bring you this new and improved volume of the Forum because it exhibits the talents of the Internal Medicine Residents. This edition showcases many of the residents' strengths in writing scholarly projects, creating research studies, and interpreting modern diagnostic imaging. Whether it is a discussion of an interesting case report or a perplexing electrocardiogram, all the work is truly original and academic. We applaud the contributing authors for all their creativity and dedication to excellence. All of these articles are the result of a lot of hard work in and out of the hospital.

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An 83 year-old African-American female with a history of hypertension, frequent urinary tract infections, atrial fibrillation, and a cerebrovascular accident (CVA) on Coumadin presented two days after a fall. A family member stated she was walking normally and tripped on uneven concrete, hitting her chin on a fence. Two days after the incident, the patient was found at home slumped over in a chair with blood oozing from her chin wound. The patient was brought to the emergency department where she was lethargic but responsive. The patient denied any chest pain, shortness of breath, lightheadedness, dizziness, blurry vision, weakness or incontinence. Her speech was slightly slurred. The patient also denied nausea, vomiting, headache or fevers. She did report some pain over her jaw. There was no other significant past medical, surgical, or family history. Her home medications included 3mg of Coumadin and 12.5mg of Toprol daily. She had no known drug allergies.

On physical exam, the patient was found to have a fever of 102.7 F, a heart rate of 68 beats per minute, a blood pressure of 115/67 mm Hg, a respiratory rate of 16 breaths per minute and an oxygen saturation of 99% on 2 liters of oxygen. Her blood sugar was 26 mg/dL on admission and she was given intravenous (IV) dextrose. She was lethargic but arousable and responded to both verbal and tactile stimuli. Orientation was difficult to assess, but the patient was not at her baseline as per her family. Her extraocular movements were intact and her pupils were equal round and reactive to light. She had an area of ecchymosis and an abrasion over her chin. Her heart rate was irregularly irregular. There were no murmurs, rubs or gallops. Her lung exam was clear bilaterally. Her abdomen was soft, nontender and nondistended. She had normal active bowel sounds and was heme negative rectally. She had no edema in her extremities. Her neurological exam was difficult to assess secondary to lack of cooperation. She did have spontaneous movements in all four extremities.

Laboratory data on admission showed a white blood cell count of 4k/L (4 -11), a hemoglobin of 12.4 g/dL (12.5-15), and a platelet count of 146k/L (140-400). She had a sodium of 135 mmol/L (135-146), potassium of 4.9 mmol/L (3.5-5.0), chloride of 100 mmol/L (98-109), bicarbonate of 28 mmol/L (24-32), BUN of 8 mg/dL (12-27), creatinine of 0.9 mg/dL (0.7-1.4), and a glucose of 56 mg/dL (60-110). Her calcium was normal. Her PTT was 30 sec (22-36), her PT was 24.2 sec (13.4-15.8) and her INR was therapeutic at 2.03. In the emergency room, she had a head CT which showed no focal abnormalities and no signs of hemorrhage. Her urine drug screen was negative and a urinalysis showed no evidence of infection. Her troponins were negative times three. Blood and urine cultures were sent. She had a CXR which showed no active disease. An EKG on admission showed atrial fibrillation at a rate of 93 beats per minute. A TSH was 0.91 uIU/ml (0.4-4.8). B12 and folate levels were normal as well.

The patient started to become more confused and so a lumbar puncture was performed. The CSF findings were unremarkable. The patient defervesced and all cultures were normal. Neurology recommended an EEG which was consistent with multi-infarct dementia and metabolic encephalopathy. An MRI of the brain showed no acute infarcts or hemorrhage. There was evidence of old ischemia and a slightly enlarged pituitary gland.

Her sodium had dropped significantly during her hospital stay to a low of 119 mmol/L and her blood pressure dropped to a systolic range of 80-90mmHg. At that time, a cortisol level was checked and was found to be 1.3 mcg/dL. A repeat TSH was 0.68 uIU/mL. She had a free T4 of 0.5 ng/dL and a total T3 of 69 ng/dL, both of which were low. An endocrine consult was obtained and a dedicated pituitary MRI was recommended as well as IV steroids (hydrocortisone 100gms IV every 8 hours was used). The patient was also started on 25mcg of Synthroid daily. Her hyponatremia improved dramatically as did her mental status. An ACTH level was low at 8 pg/mL (9-52) and a somatomedin-C level was low at 19 ng/mL (71-290). A prolactin level was normal at 19 ng/mL (0-19) and an IGF-1 was ordered but not completed. The dedicated pituitary MRI showed diffuse hemorrhage involving the pituitary gland with a probable underlying macroadenoma. It was presumed that the patient had pituitary apoplexy.
Discussion

Pituitary apoplexy is a rare but serious condition caused by sudden hemorrhage or infarction of the pituitary gland. Typically, there is an underlying pituitary adenoma. A classic presentation is characterized by sudden headache, vomiting, visual impairment and meningismus. Headache is usually the most common presenting symptom. Some precipitating factors of pituitary apoplexy include anticoagulation and head trauma, both of which were present in this case. Other precipitating factors include hypertension, radiation therapy, recent surgery, bromocriptine therapy and dynamic pituitary function testing. The clinical presentation can vary greatly ranging from a mild headache to hemodynamic compromise. If blood enters the subarachnoid space, meningitis-like symptoms including fever, meningismus, vomiting and altered mental status can occur. These patients deteriorate very rapidly. The urgency of surgical decompression depends on the presentation, and many of these cases are managed conservatively.

The key to diagnosis is to first recognize the condition. Initial laboratory data should include a complete blood count, coagulation studies, electrolytes, a baseline cortisol level and thyroid function tests. Pituitary hormone deficiency is very common. Hypogonadism, growth hormone deficiency, and prolactin abnormalities occur in many cases. Acute adrenal insufficiency (AI) can be very serious and is found in 2/3 of cases. Hypothyroidism is found in about 42% of cases. Diabetes insipidus can occur from damage to the posterior pituitary gland and is seen in only about 4% of cases. Electrolyte disturbances, especially hyponatremia, are also common. Hyponatremia can occur from inappropriate ADH secretion, secondary AI, or secondary hypothyroidism. Laboratory data to check for hypopituitarism include TSH, prolactin, LH, FSH, cortisol, GH, estradiol in females and testosterone in males. A lumbar puncture can be performed to rule out meningitis and subarachnoid bleed. Radiologic studies are used to confirm the presence of pituitary apoplexy. Imaging by CT is often used acutely, however MRI is preferred because it is more sensitive and is often used in the subacute setting. Management involves supportive care, “stress-dose” steroids, and a neurosurgical evaluation. Hydrocortisone 100mg IV every 6-8 hours is often used or dexamethasone 4mg IV every 8 hours or equivalent. Pituitary hormone replacement is used when necessary. Transsphenoidal surgery may be indicated if there are visual changes. Radiotherapy is not indicated immediately since the risk of recurrence is negligible. Careful follow-up is recommended.

References

The patient is a 34 year-old G1P1 Caucasian female with no medical history who was transferred from an outside hospital after an emergent Cesarean section for increasing jaundice with elevated liver enzymes, abnormal coagulation times and acute renal failure. The patient was healthy until 33 weeks gestation when she noted dizziness, headache and visual changes. Blood pressure at that time was elevated at 140/90 and she had trace lower extremity edema. No proteinuria was detected. The clinical picture was consistent with mild pre-eclampsia. The patient was followed until 35 weeks gestation when she developed vaginal bleeding and abdominal pain. At that time, an emergency C-section was performed due to a non-reassuring fetal heart rate. On the first night after the surgery, she became anuric and laboratory tests demonstrated acute renal failure, coagulopathy, and elevated liver enzymes. She became progressively jaundiced and she was transferred for further management. On admission, she complained of nausea and malaise. She denied abdominal pain, chest pain, dyspnea, lightheadedness or headache.

Her past medical history was only significant for endometriosis. Her past surgical history included laparoscopic treatment of endometriosis several years ago and ovarian cyst removal several years ago. Her medications included Phenergan, Percocet, Lasix and Dulcolax. She had allergies to Augmentin and Ceclor which caused a rash. Her family history was non-contributory. The patient noted occasional tobacco use, denied alcohol or other substances. Her review of systems was only significant for mild dyspnea, nausea, mild gingival bleeding, and mild pruritis.

Vital signs showed a temperature of 99.0F, pulse of 84 beats per minute, respirations of 22 breaths per minute, blood pressure of 130/70 with blood oxygenation at 99% on room air. Her physical examination was significant for scleral icterus; her heart rate was regular without murmurs, rubs or gallops; her lungs had bibasilar crackles; her abdomen was soft with some tenderness at her incision site with minimal oozing; she had moderate lochia and was hem negative rectally; she had 2+ pitting edema on her bilateral lower extremities; neurologic examination was intact with some asterixis noted.

Her laboratory findings on admission were significant for a sodium of 122mg/dL, potassium of 5.2mmol/L, bicarbonate of 17mmol/L, BUN of 33mg/dL, creatinine of 3.3 mg/dL, PT of 55.6 sec, PT of 23 sec, INR of 2.5, fibrinogen of 94mg/dL, protein of 3.9g/dL, albumin of 2.0g/dL, total bilirubin of 9.7mg/dL, direct bilirubin of 5.4mg/dL, AST of 124mg/dL, ALT of 104mg/dL, alkaline phosphatase of 390U/L, ammonia of 57mol/L, white blood cell count of 15.6k/L, hemoglobin of 9.6g/dL, platelets of 174k/L, and a urinalysis with 3+ protein.

Her chest X-ray showed mild pulmonary vascular congestion. A right upper quadrant ultrasound showed decreased flow in hepatic vein and mild ascites. Her MRI/MRA/MRV of the abdomen showed narrowing of hepatic vein and inferior vena cava (IVC). The renal ultrasound showed no hydronephrosis.

Discussion
This case allows the discussion of liver disease during pregnancy, however the focus of this discussion will be on the Budd-Chiari Syndrome (BCS).

Pathogenesis
The patient in this case had signs and symptoms consistent with BCS or hepatic venous outflow obstruction. BCS describes a group of disorders that cause outflow obstruction at the level of the hepatic venule, large hepatic veins, inferior vena cava or right atrium. Hepatic veno-occlusive disease refers to obstruction at the level of the center of sub-lobular hepatic veins. Hepatic venous outflow tract obstruction results in increased sinusoidal pressure and portal hypertension. Early in the disease, portal venous perfusion is diminished which may result in portal vein thrombosis. Venous stasis leads to centrolobular necrosis, fibrosis and eventually cirrhosis. If a portosystemic shunt is created or portal venous collaterals develop, liver function improves by reducing sinusoidal pressure. About 75% of patients have an identifiable cause of BCS. Hereditary and acquired hypercoagulable states are a common cause. Myeloproliferative disorders are the most common cause of BCS, most notably polycythemia vera. Other causes include paroxysmal nocturnal hemoglobinuria, antiphospholipid syndrome, inherited deficiencies of proteins C and S and antithrombin III. BCS has been described in pregnancy and the immediate post-partum period.

Clinical Manifestations
BCS can be grouped into fulminant, acute, subacute and chronic depending on the speed which the hepatic veins become occluded and whether collateral circulation...
Abdominal pain, hepatomegaly and ascites are the most common findings. Nausea, vomiting and jaundice are more common in the fulminant and acute forms. Splenomegaly and esophageal varices are more common in the chronic forms. IVC occlusion usually causes dilated venous collaterals on the back and flanks. Patients with acute BCS have ascites, hepatic necrosis, symptoms of short duration and lack of venous collaterals. Hepatic necrosis and ascites are usually minimal in the subacute form because venous collaterals have decompressed the hepatic sinusoids. The subacute form is the most common form of BCS. A careful cardiovascular examination can separate BCS from cardiac causes of diminished hepatic venous outflow. Right atrial myxoma, tricuspid regurgitation and constrictive pericarditis can cause similar symptoms to BCS. Lack of hepatojugular reflux is indicative of BCS on physical examination.

**Diagnosis**

Laboratory evaluation shows AST and ALT to be five times the upper limit of normal in fulminant and acute forms of BCS. The subacute form has lower values. Alkaline phosphatase and bilirubin levels are also elevated. Serum-ascitic fluid albumin gradient is high. Doppler ultrasound is the diagnostic imaging of choice with a sensitivity and specificity of 85%. MRI can show hepatic vein thrombosis and may be better for delineating acute from subacute and chronic forms. Hepatic venography is used as a confirmatory test when ultrasound is negative but there is a strong clinical suspicion. The classic “spiderweb” pattern is often seen. The patient in this case had an MRI which showed narrowing of the hepatic vein and IVC which is consistent with BCS.

**Management**

Medical management focuses on treating the underlying cause, anticoagulation to prevent extension of thrombosis and efforts to reduce ascites. Diuretics such as furosemide and spironolactone as well as paracentesis and sodium restriction are used to reduce ascites. Heparin is used initially with conversion to warfarin with a goal INR of 2.0 to 2.5. Medical management is generally recommended for patients with few symptoms, no hepatic necrosis and minimal ascites. Patients with coagulopathy, encephalopathy and hepatorenal syndrome have a poor prognosis and require immediate relief of hepatic venous obstruction.

Thrombolytics can be used in the acute form of BCS particularly when an acute thrombus is seen on angiography. TPA or urokinase is directly infused by catheter for 24 hours. The overall success rate is low with thrombolytics, but positive results have occurred as far as two to three weeks after onset of symptoms. Percutaneous or transhepatic angioplasty of segments of the narrowed hepatic vein can also be performed. Symptom relief occurs in up to 70% of patients, but restenosis rates are high.

Transjugular intrahepatic portosystemic shunts (TIPS) are typically used in patients who have an occluded IVC when the portal vein-infrahepatic vena caval pressure gradient is less than 10 mm Hg and when there is poor hepatic reserve. TIPS can also be used in acute BCS after failure of thrombolytic therapy. TIPS can be used as a bridge to liver transplantation. Even if the shunt occludes, it may allow enough time for collaterals to develop and decrease sinusoidal pressure.

Surgical options include excision of IVC webs followed by angioplasty of the vena cava, although portosystemic shunting and liver transplantation are the most common surgical treatments for BCS. Surgical portosystemic shunts are recommended in subacute forms of BCS when the underlying etiology has a favorable outcome, the patient is a good surgical candidate and when liver biopsy shows ongoing hepatic necrosis. A portal vein and IVC pressure gradient of more than 10 mm Hg is associated with a successful long-term outcome. Examples of surgical shunts include side-to-side portacaval shunt, central splenorenal shunt, and a mesocaval shunt. The five-year survival rate after surgical shunting is between 75% and 94%.

The five-year survival rate for liver transplantation in patients with BCS is 95%. Indications are an underlying disease associated with a favorable prognosis, fulminant hepatic failure, cirrhosis, and failure of portosystemic shunt. Not all patients require long-term anticoagulant therapy after liver transplantation, but it may be reasonable to anticoagulate since patients with BCS have multiple underlying etiologic factors.

**References**

Case Reports

Woman with a Bleeding Diathesis
Bo Kim MD, PGY-3

61 year-old Indian female with history of hypercholesterolemia presents to an outside hospital (OSH) with worsening vaginal bleeding, hematochezia, nausea, and vomiting starting three days prior to admission. Patient also had a global persistent headache for approximately 24 hours at the time of admission. Otherwise, the patient denied any fever, chills, abdominal pain, or trauma. The patient noted no previous episodes of bleeding or easy bruising in her past. She notes that her menstrual periods were always regular and not subjectively heavy. Last menstrual period was 10 years ago. Patient has had two pregnancies in her obstetric history for which she delivered vaginally without bleeding complications. The patient denied recent antibiotic use. She had no change in diet and no prior transfusions. At the OSH, the patient was noted to be orthostatic at presentation with mild tachycardia but was stabilized with intravenous fluids and transfusions of packed red cells. Patient's nausea and vomiting resolved with antiemetics at the OSH. Nasogastric lavage was negative for blood. Laboratory results revealed patient to have markedly elevated prothrombin time (PT) and activated partial thromboplastin time (aPTT) with an INR greater than 20. The patient was initially treated with fresh frozen plasma (FFP) and high doses of vitamin K. The patient denied any warfarin use and she did not know anyone currently on the medication. CT scan of the head showed left subdural hematoma without midline shift or hydrocephalus. The patient was immediately transferred to the Jefferson Neurosurgical service. The patient was subsequently deemed a poor surgical candidate and was continued on supportive treatment with blood products and vitamin K. At time of transfer to the medicine service, the patient developed respiratory distress with severe hypoxia requiring intubation. The patient was admitted to the intensive care unit (ICU) for ventilator-dependent respiratory failure secondary to Transfusion Related Acute Lung Injury (TRALI). After five days, the patient was extubated and transferred to the medicine floor team in stable condition for further management of her bleeding diathesis.

The patient's past medical history was significant only for hypercholesterolemia but the patient was on no medications. The patient had a cholecystectomy 12 years ago and a laminectomy 7 years ago. Psychiatric history was notable for depression with prior suicide attempt five years prior to admission. Family history was negative for any bleeding disorder or malignancy. Social history revealed no alcohol use, substance use, or smoking. The patient was a homemaker.

On physical exam after transfer from the ICU, the patient was afebrile with a pulse of 85 beats per minute, a respiratory rate of 16 breaths per minute, and a blood pressure of 132/72mmHg. In general, the patient was in no acute distress. She was well nourished, well developed, and appeared her stated age. The patient's head was normocephalic and atraumatic. Her eyes showed equally round and reactive to light pupils and anicteric sclera. Her extra-ocular muscles were intact. Her mucous membranes were moist, her oropharynx was clear, and there were no petechiae or stomatitis in the oral cavity. Her neck was supple with no lymphadenopathy, no thyromegaly, no JVD or carotid bruits. Her heart was regular with no murmurs, gallops, or rubs. Her lungs had minimal scattered bilateral rales and mild bibasilar crackles. Her abdomen was soft, non-distended, non-tender. There were no appreciable masses or organomegaly. Her rectal exam revealed moderate hemorrhoids. There was normal rectal tone, stool was dark brown and heme positive. There was no frank blood. There was no clubbing, cyanosis, or edema in the extremities. Her neurologic exam revealed no focal deficits with cranial nerves II-XII grossly intact. There was also no nystagmus, no dysmetria on finger to nose, and deep tendon reflexes were equal and symmetric. Her skin revealed small ecchymoses on upper extremities. See Table 1 for the baseline laboratories at time of transfer to the medicine floor service.

The remainder of the hospital course was notable for the continued elevations in her PT. Multiple transfusions of FFP and multiple injections of high-dose vitamin K initially normalized the PT and aPTT at the time of transfer from the neurosurgical service. Subsequent coagulation labs revealed a continually rising PT requiring the titration of the vitamin K dose from 10mg daily to 50mg twice daily. For two weeks, the patient had high doses of vitamin K and any dose...
taper led to a rapid rise in PT (See Table 2). The platelet count remained stable and hemolysis labs were negative. Her DIC panel revealed a mildly elevated D-dimer and a markedly elevated fibrinogen. Mixing studies performed on the second day of admission revealed normalization of elevated coagulation factors with mixing indicating a deficiency of factors rather than a presence of an inhibitor. Despite the elevated PT, there was no further evidence of active bleeding during the remainder of the hospitalization. Repeat head CT revealed a slowly resolving subdural hematoma and the hemoglobin remained stable. The patient was seen by gynecology and gastroenterology but no active interventions were planned as an inpatient.

Of concern was the patient’s psychiatric history with a prior suicide attempt. The patient was initially placed on one to one nursing especially given the continuing elevations in her hemostatic labs. The patient repeatedly denied depression or suicidal ideations. She was evaluated by the psychiatry department at Jefferson and was deemed safe for discharge home. Approximately one month after discharge, the patient’s PT was stable on oral vitamin K.

### Table 2.

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**Daily Vit K dose**
- 10mg
- 20mg
- 40mg
- 50mg
- 100mg
- 100mg
- 20mg
- 20mg

* Or transfer to the medicine floor

### Discussion

The history and presentation of the patient suggest a diagnosis of an acquired hemostatic disorder rather than an inherited or congenital disease. The patient did not have any memorable episodes of bleeding in her past and no one in her family had a problem with bleeding that she could report. Acquired bleeding diathesis can be categorized into two major categories, platelet defect versus coagulation disorder.

A quantitative platelet disorder can induce bleeding usually with platelet counts below 50,000. Diseases such as idiopathic thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP), or heparin induced thrombocytopenia (HIT) can precipitously drop the platelet count. The patient did not have a significant decline in her platelet count, nor did she show any clinical signs of TTP (mental status changes, fever, renal failure, hemolytic anemia). The patient had also never been on heparin. A qualitative platelet dysfunction can be medication-induced (ASA, NSAIDs, clopidogrel, ticlopidine), or associated with a medical condition such as uremia, myelodysplastic syndrome (MDS), or von Willebrand disease (VWD). The patient was not on any medications and had good renal function. The diagnosis of MDS can be one of exclusion especially when an elderly patient presents with anemia (typically macrocytic) or pancytopenia with no clear etiology. Diagnosis was not pursued because of low clinical suspicion and a bone marrow biopsy was clearly not indicated in this case. VWD is the most common inherited bleeding disorder with a prevalence of approximately 1%. A negative family history does not rule out VWD since the clinical presentation can be variable and subclinical. Most women with milder VWD
will usually report heavy menstrual periods and postpartum bleeding. The patient presented with heavy bleeding for three days of sudden onset. Inherited VWD would be very unlikely in this case since more severe forms of VWD would manifest at a much earlier age. Acquired VWD is a possibility but the disorder is associated with comorbidities such as malignancies and autoimmune disorders that were not evident in the patient. Furthermore, VWD can cause an elevation of the aPTT because it is the carrier of factor VIII, but it will not cause critical elevations of PT and aPTT. Ristocetin cofactor assay to test qualitative function of von Willebrand factor was not performed.

Acquired coagulation disorders with elevated PT and aPTT can be caused by liver disease, deficiency or inhibitors to factor V or X, deficiency of fibrinogen or prothrombin, disseminated intravascular coagulation (DIC), or high doses of warfarin with or without heparin. Vitamin K deficiency alone would not cause elevations in aPTT. The patient had normal liver function and had mixing studies that normalized during the hospitalization. A mixing study mixes the plasma of the patient with elevations in PT or aPTT with plasma that has normal coagulation function. A normalization of the coagulation labs would indicate a deficiency of factors that were replaced by the normal plasma whereas a continued elevation in PT or aPTT would indicate the presence of an inhibitor (antibody or medication). Acute DIC is most commonly associated with trauma, sepsis, or malignancy and treatment is aimed at the underlying cause. Supportively, the patient can be treated with FFP or cryoprecipitate if the fibrinogen is low. The patient only had a mild elevation in the D-dimer (fibrin degradation product) and elevation in fibrinogen (acute phase reactant). There was no evidence of hemolysis and the platelet count was stable.

The marked elevations in the PT and aPTT that responded to vitamin K are most consistent with warfarin toxicity. The patient denied any use of the medication and she could not have ingested the drug accidentally. Also concerning was the difficulty of normalizing her coagulation defect even weeks after the inciting event. Rodenticides are warfarin derivatives with extremely high potencies. They are designed to be antagonists of vitamin K but they are much more fat soluble and their half lives are many weeks compared to the 2-3 days of coumadin. The patient had a urine test performed during the hospitalization to detect levels of the commonly used “super-warfarins” of rodenticides like bromodiolone and difenacoum but the test result was negative. Three weeks into the hospitalization, a serum assay for a specific warfarin derivative called brodifacoum was sent to an outside laboratory. The result was positive for 0.1µg/mL. This chemical is a second-generation anticoagulant with a half-life of 157 days. It is retained in tissues at high rates and can remain in organ systems for years. The chemical is rapidly absorbed by the gut and quickly causes gastrointestinal hemorrhage. The mystery of how the patient ingested rodenticide was confounded by her psychiatric history of depression and prior suicide attempt. She repeatedly denied suicidal ideations and the psychiatry department did not feel she was a threat to herself at this time. Criminal investigation was discussed but quickly dismissed when the patient clearly expressed her desire not to pursue inquiries. The patient was discharged on day 32 with instructions for close follow-up.

References
A 26 year-old Cambodian monk presents with complaints of a three week history of fatigue and malaise. The patient reports that four days prior to presentation he developed fevers to 103F, chills and a severe headache. The patient reports that he had returned from Cambodia one week prior to initiation of symptoms. He denies any sick contacts and denies any neck stiffness, photophobia, visual changes or abdominal pain. The patient does report diarrhea for one week with approximately 8-10 bowel movements per day. The patient denies any risk factors for IV. The patient had been seen in the Emergency Department one day prior to admission. His temperature was 102F, pulse was 110 beats per minute, respirations were 20 breaths per minute and blood pressure was 110/80mm Hg. A lumbar puncture was performed, blood cultures and stool cultures were sent. The patient was discharged with a prescription for Percocet.

On the following day, the blood cultures yielded gram negative rods. The cerebrospinal fluid (CSF) was sterile and the patient was contacted and admitted to the hospital.

On examination, the temperature was 103.6F, pulse was 110 beats per minute, respirations were 18 breaths per minute and blood pressure was 102/66mm Hg. The patient had erythematous linear lesions on trunk and back, sclera was anicteric and there was no lymphadenopathy. Heart was regular without murmurs, lungs were clear to auscultation and abdomen was benign without evidence of organomegaly. Rectal exam was negative for occult blood. Laboratory examination revealed a normal white cell count. The patient's chemistries were also within normal limits. Liver tests revealed an AST and ALT of 219 and 192 respectively. Stool studies were negative and blood parasite smear was negative.

During his hospitalization, the patient was started on broad spectrum antibiotics and blood cultures grew out Salmonella typhi.

Discussion
Typhoid fever is a systemic infection with the bacterium S. typhi. Typhoid fever occurs mainly in the developing world such as India and Vietnam where sanitary conditions remain poor. Typhoid is usually contracted by ingestion of food or water contaminated by fecal or urinary carriers excreting S. typhi.

Salmonella organisms multiply within mononuclear cells in the lymphoid follicles, liver and spleen. The most common sites of secondary infection are the gallbladder, Peyer's patches and the bone marrow. The incubation period is 7-14 days.

The clinical manifestations of typhoid start initially as an asymptomatic period of 7-14 days. Patients then develop fever and malaise, a dull frontal headache, anorexia and nausea. A tender abdomen, hepato/splenomegaly and a relative bradycardia are common. The fever in typhoid is initially low grade but rises progressively and by the second week is sustained. Occasionally, patients may develop rose spots on the abdomen and chest. Lab work usually reveals a normal white cell count, normal hemoglobin and platelets. Liver enzymes are usually two times the upper limit of normal.

The most important complications of typhoid are intestinal perforation, encephalopathy, and gastrointestinal bleeding. Relapse usually occurs two to three weeks after resolution of fevers and is usually milder than the initial attack. Fatality rate is less than one percent.

Blood cultures are the standard diagnostic method of detecting typhoid. They are positive in 60-80% of patients with typhoid. Typhoid can also be detected in the bone marrow with approximately 80-95% sensitivity. Typhoid needs to be distinguished from other endemic subacute febrile illnesses such as malaria, dengue, brucellosis, leptospirosis and tuberculosis.

The introduction of chloramphenicol for the treatment of typhoid transformed a debilitating disease into a treatable one. The emergence of resistance to chloramphenicol and other antimicrobials has been a major setback. The fluoroquinolones are the most effective drugs for the treatment of typhoid fever. Patients should be treated for a minimum of 10-14 days. Third generation cephalosporins are also effective. Chloramphenicol is appropriate in areas where the bacterium is susceptible.

Control of typhoid required the provision of safe drinking water, effective sewage disposal and hygienic food preparation. The typhoid vaccine is recommended for travelers to areas where typhoid is endemic.

References
A 39 year-old African-American male with past medical history significant for uncontrolled hypertension presents with a sudden onset of weakness and numbness on the left side of his face, left arm, left leg, and right leg while watching television twenty hours prior to presentation. At that time, the patient did have a mild headache. The patient initially thought that it was positional, but soon realized that he could not move the affected extremities at all. He also began to have some difficulty swallowing and minor difficulties with speech as well.

Two hours after the initial onset of symptoms, the patient was able to ambulate without difficulty. Shortly afterwards, he regained function and sensation in his left upper extremity. His dysarthria and dysphagia also resolved but he had a persistent drooping of his left lip with numbness on the left side of his face.

On review of systems, he admitted that he had run out of medications 3 days prior to presentation. He had also noted a rash on the lateral portion of his left upper extremity but he did not recall when it started. The rash was pruritic for 2 days and then resolved without further treatment. The patient denied fevers, chills, neck pain, visual changes, diplopia, tinnitus, dizziness, and lightheadness. The patient denied urinary or bowel incontinence.

His past medical history is significant for uncontrolled hypertension with multiple visits to the emergency department; atypical chest pain, with a normal stress test 2 years prior to admission; gastroesophageal reflux and hiatal hernia; hepatitis A; a positive PPD, treated with a full course of prophylactic isoniazid; superficial perivascular lymphocytic dermatitis diagnosed in 2000, currently stable; and condyloma acuminatum, excised by urology five months prior.

His medications included atenolol 100 mg twice daily, clonidine 0.1 mg twice daily, nifedipine (SA) 90 mg daily, enalapril 20 mg daily, rabeprazole 20 mg daily, sertraline 50 mg daily, and hydrocortisone cream twice daily as needed. He had a syncopal reaction to loratadine. He had a positive smoking history but he quit in 1999. He has never used illicit drugs. He was a former prison guard, served in the Navy in the 1991 Persian Gulf War and is currently active in the US Army. His father died in his 50s of prostate cancer.

Physical examination revealed a 39 year-old male in no acute distress with an initial blood pressure of 204/106. Vital signs were otherwise stable. The patient had decreased sensation to pinprick and dull pressure on his left face. The patient also had weakened muscles of mastication on his left side and flattened left nasolabial folds. His strength, sensation, and reflexes in his extremities were all within normal limits. He had normal Babinski reflexes bilaterally with normal gait. He also had a hyperpigmented rash noted on his left upper extremity and scars on the lateral aspect of the left neck and on his right thigh from old stab injuries. He had cardiovascular, pulmonary, abdominal, and extremity examinations were benign. Fundoscopic examination revealed changes attributable to hypertension but no papilledema. His main facial findings are shown in Figure 1. (Permission was granted by the patient prior to the picture being taken; this is documented with the paper chart from this admission).

Laboratory data was significant for a slight hypokalemia (3.3mmol/L), elevated glucose (120mg/dL), an elevated ALT (205U/L), and a normal complete blood count. A CT of the head without contrast was obtained showing no acute bleed or pathology. Initial ECG (Figure 2) shows sinus rhythm with left ventricular hypertrophy and left-sided/lateral strain.

He was initially admitted to the intensive care unit with a presumptive diagnosis of transient ischemic attack secondary to the presence of significant hypertension. Appropriate measures were taken to reduce systolic pressure. A neurology consult was obtained the next morning that discovered that much of his recent Army training had been in wooded areas. Although the possibility of hypertensive stroke/TIA could not be ignored, Lyme neuropathy and neurosarcoidosis were now on the differential due to this new information. Serum Lyme titers, as well as a lumbar puncture with CSF Lyme titers and angiotensin-converting enzyme, were recommended.
Serum Lyme titers were negative. A lumbar puncture showed colorless, clear fluid with 6 RBCs, 2 WBCs (both neutrophils), glucose 63mmol/L, and protein 5mg/L. Gram stain and culture were negative for cells or organisms. Titers for VDRL and HSV were both negative. An ACE-I level from the cerebrospinal fluid was within normal limits. However, Lyme titers from the cerebrospinal fluid returned positive at 1:52 (nmL 1:10). An MRI was performed which demonstrated mild enhancement near the location of the left seventh nerve.

The patient had been started on ceftriaxone because it took several days for the Lyme titers from the cerebrospinal fluid to return. His facial signs slowly improved and eventually resolved over the next few weeks.

Neuroborreliosis is only seen in approximately 10 percent of untreated Lyme disease. Clinical presentations are variable but there are distinct time periods during which they arise. Aseptic meningitis, cranial nerve palsy (usually involving the facial nerve), and radiculoneuritis (severe localized radicular pain or motor weakness, with variable sensory deficits) usually occur during early disseminated disease (1-3 months). Aseptic meningitis and peripheral neuropathies may also occur with reactivated disease. Headache and neck stiffness are usually mild. Asymmetric dermatomal and myotomal abnormalities, also known as lymphocytic meningoradiculitis or Bannwarth's syndrome, can be seen. These cases are usually seen in Europe, although rare cases can be seen in North America. Encephalopathy and chronic encephalomyelitis are usually manifestations of late persistent infection (> 3 months). Neuroborreliosis is treated effectively with one month of intravenous ceftriaxone. Oral doxycycline is an option in isolated facial nerve palsy, but due to the severity of cerebrospinal fluid inflammation, intravenous antibiotics are usually preferred.

References
What's Your Diagnosis?

A 35 year-old Caucasian woman with history of Systemic Lupus Erythematosus (SLE) complicated by Lupus glomerulonephritis presented to the Emergency Department complaining of worsening bilateral lower extremity rash and leg pain. The rash had been present for over a month and a recent biopsy of the lesion revealed leukocytoclastic vasculitis. Her usual dose of prednisone 120mg every other day had been increased to 60mg daily over the past few weeks with the worsening rash. In addition to the rash and leg pain, she also reported some right-sided pleuritic chest pain. Otherwise, the patient noted no shortness of breath, cough, fevers, or chills. Of note, she was recently treated for both pneumonia and a pulmonary embolism at an outside hospital.

Past medical history for this patient was significant for the diagnosis of SLE made six months prior along with diffuse proliferative glomerulonephritis for which she had undergone therapy with Cytoxan twice and Cellcept. She was unable to tolerate either of these treatments and was switched to oral prednisone. Two months ago, she was started on intermittent dialysis via a permacath that had been placed.

Physical exam on admission revealed an afebrile young woman with stable vital signs who was visibly uncomfortable due to the pains in her legs. She had normal heart sounds with no murmurs or rubs. Her lung exam was significant for decreased breath sounds over the right lung base, but otherwise her lungs were clear to auscultation. Abdominal exam was unremarkable. Examination of her lower extremities revealed macular patches of an erythematous rash with scattered patches of palpable purpura that were all tender to touch. Her blood work was remarkable for a white blood cell count of 28,000 with 97% neutrophils, platelets of 73,000, hemoglobin of 10.2g/L, hematocrit of 34%, creatinine of 2.2 mg/dL and a C-reactive protein of 4.8mg/dL.

The patient was admitted to the hospital and treated with pain medications and high dose intravenous steroids for her progressive vasculitis. The leg pain and rash showed signs of improvement over the course of several days, however she continued to complain of worsening pleuritic chest pain. A chest X-ray (Figure 1) revealed a right lower lobe opacity while a ventilation/perfusion scan showed a low probability for pulmonary embolism. CT scan of the chest without contrast (due to her impaired renal function) was performed on day 6 of hospitalization (Figure 2).

On day 7 of hospitalization, the patient developed respiratory distress requiring emergent intubation. Bronchoscopy was performed revealing copious amounts of purulent secretions in the right main-stem bronchus along with its associated branches. An ultrasound-guided thoracentesis of the right side was performed and the fluid was sent for analysis. Figures 3 and 4 show two stains that were obtained from pleural fluid specimen. Please also see inside front cover for another pleural fluid specimen.

Lung Cavitary Lesion
Bassem Elgohary MD, PGY-3 and Betty Lim MD, PGY-2

A 35 year-old Caucasian woman with history of Systemic Lupus Erythematos (SLE) complicated by Lupus glomerulonephritis presented to the Emergency Department complaining of worsening bilateral lower extremity rash and leg pain. The rash had been present for over a month and a recent biopsy of the lesion revealed leukocytoclastic vasculitis. Her usual dose of prednisone 120mg every other day had been increased to 60mg daily over the past few weeks with the worsening rash. In addition to the rash and leg pain, she also reported some right-sided pleuritic chest pain. Otherwise, the patient noted no shortness of breath, cough, fevers, or chills. Of note, she was recently treated for both pneumonia and a pulmonary embolism at an outside hospital.

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What's Your Diagnosis?

Figure 1 – Chest X-ray – Right lobe opacity

Figure 2 – Non-contrast CT of the chest – multiple nodular air space consolidations in the right middle and right lower lobe with cavitation at the right base.

Figure 3 – Gram stain from pleural fluid specimen. Delicate filamentous gram positive rods are seen.

Figure 4 – Modified Acid-Fast Stain (Kinyoun) from pleural fluid specimen. Gram positive branching filamentous rods that are partially acid fast.

What's Your Diagnosis?
Turn the page for the diagnosis and discussion.
**Diagnosis: Nocardia**

Nocardia is part of the actinomyces species which includes Mycobacterium and Actinomyces. They are considered aerobic bacteria which appear as filamentous, branching gram-positive rods on gram stain. In contrast to Actinomyces, Nocardia species are positive by modified acid-fast stains (Kinyoun stains) secondary to the mycolic acid content in their cell walls.

Nocardia is found worldwide in the soil, decaying vegetable matter, and aquatic environments. It can become airborne and ultimately inhaled or directly inoculated as a result of trauma, surgery, catheters, or animal bites and scratches. Initially, the host response involves neutrophils and macrophages engulfing the bacteria. Then a T cell-mediated response occurs which enhances this phagocytic process and helps eliminate the bacteria. Since cell-mediated immunity is so important, Nocardia causes disease mainly in immunocompromised individuals such as those with HIV/AIDS, prolonged steroid use, hematological malignancies, transplant recipients, and even diabetics and alcoholics (~60% of cases). However, nocardiosis can also occur in those with intact immune systems (~40% of cases).

Nocardia is known for its ability to affect any organ system. The most common organ involved is the lung, followed by skin and then central nervous system (CNS). Lung involvement can be acute, sub-acute, or chronic and manifested by a variety of symptoms such as cough, SOB, fevers/chills, night sweats, hemoptysis, or pleuritic chest pain. Imaging studies may reveal lobar consolidation, interstitial infiltrates, single or multiple nodules, lung masses (with or without cavitations), or pleural effusions. Skin involvement is also diverse and can be manifested by cellulitis, ulcerations, pyoderma, or subcutaneous abscesses. CNS involvement occurs as a result of special affinity of Nocardia to neuronal cells and results in brain abscesses with signs and symptoms such as headaches, fevers and chills, meningismus, seizures, and focal neurological deficits.

There have been no prospective randomized trials ever performed to determine what the best treatment options are for nocardial infections. Most of the data in the literature stem from experienced clinicians, microbiology/antibiotic studies, and animal models. The antibiotic of choice is trimethoprim-sulfamethoxazole (TMP-SMX) which has good tissue penetration including the CNS. Other agents include amikacin, imipenem, 3rd generation cephalosporins, and minocycline. In addition to antibiotics, surgical intervention is necessary for any abscesses.

Former cases of nocardiosis suggest it has a tendency to relapse, but those treated for a prolonged period of time can achieve complete remission. It is recommended that immunocompetent patients with pulmonary or non-pulmonary involvement, other than CNS, be treated for 6 months. Patients who are immunocompromised or have CNS involvement should be treated for 12 months. Cure rates depend on the virulence of the Nocardia species and the host immune response, but in general: skin ~100%, pulm ~90%, non-pulm/CNS ~60%, and CNS ~50%.

**Discussion**

Our young patient fits the profile of those who become susceptible to disseminated nocardiosis. She was indeed immunocompromised not only from her chronic high dose steroid use but also from her past exposure to Cytoxan and Cellcept therapies. The fact that the organisms were so readily visualized by gram stain from pleural fluid samples emphasizes the large organismal burden as well as its dissemination. Upon modified acid-fast stain confirmation, the patient was started on high dose TMP-SMX. Since speciation and sensitivities were still pending at that time, she was also started on combination therapy with ceftriaxone and linezolid. The organism was eventually confirmed as Nocardia asteroides sensitive to TMP-SMX. Ceftriaxone was stopped but linezolid was continued for possible synergy in combination therapy as had been recently reported. A chest tube was placed on the right lung for drainage of the purulent effusion. Three days after being intubated, the patient was extubated without complications. A head CT showed no signs of any intracranial cavitary lesions. Her steroid regimen was quickly tapered over the next two weeks and all plans for restarting Cytoxan treatment were put on hold. On day 24 of hospitalization, the patient was discharged home on oral prednisone 5mg twice a day, oral linezolid 600mg twice a day, and TMP-SMX DS two tablets twice a day.

**Reference**

What's Your Diagnosis?

A 23 year-old Caucasian female with no past medical history presents with one week of easy bruising and increasing “red spots” on her arms and chest. She does not recall any history of trauma that may have lead to the bruises. She denies any fever or chills. She has no history of bleeding problems and underwent dental procedures last year without any complications. On review of systems, she had vague left abdominal pain over the past week and 3 days of right ear pain that was recently treated with cefuroxamine as directed by her primary care doctor. Family history is noncontributory. She drinks occasional alcohol on weekends and denies any tobacco or drug use. She takes no medications.

Hematology Slide Review
Jane Choi MD, PGY-2

On physical exam, the patient is afebrile and vital signs are stable. She is a well-developed, healthy female in no acute distress. Multiple petechiae are noted on her upper extremities and anterior chest wall. Several ecchymoses are present over sites of blood draws. The spleen tip is felt approximately 2cm below the costal margin. She is hemoccult negative rectally. The rest of the physical exam is within normal limits.

Labs reveal white blood count 8,200, hemoglobin level of 7,900 and platelet count of 16,600.

Below are her blood smears. What's Your Diagnosis?
The patient is a 78 year-old male with a past medical history of hypertension and duodenal ulcer presenting with 2 months of increasing abdominal girth. The patient reports 1 month of loose bowel movements and a 2 week history of early satiety. He notes that in the last week he has been nauseous at the smell and thought of food. He denies fevers, chills, excessive alcohol intake, history of blood transfusions, intravenous drug use, melena or bright red blood per rectum. The patient states he has never undergone a colonoscopy and to his knowledge there is no family history of malignancy.

The patient was admitted to the hospital and a diagnostic study was performed. The images from a CT scan demonstrate multiple loculated fluid collections with enhancing walls within the peritoneal cavity. The largest mass was located anteriorly within the peritoneal cavity and measured 30cm x 14 cm (transverse x AP) and extended from the liver to the bladder. These finding were consistent with a pseudomyxoma peritonei and the patient was taken to surgery for an exploratory laparotomy. The patient underwent an evacuation of the gelatinous tumor and an ileocecal resection with primary ileoascending colostomy. The pathology report revealed the origin of the mucinous secretions was in fact an appendiceal cystadenocarcinoma.

Pseudomyxoma peritonei is a rare condition resulting from rupture of a mucocoele of the appendix, a mucinous ovarian cyst, or mucin-secreting intestinal or ovarian adenocarcinoma. It is two to three times more common in females than in males. It is often an unexpected finding during a laparotomy and is said to be found in 2 of every 10,000 laparotomies.

The primary treatment remains surgical debulking although the rate of recurrence in the twelve-year Mayo Clinic series was 76% with 50% of recurrences in the first 2.5 years. It is not clear if adjuvant radiotherapy and/or chemotherapy is beneficial. The five-year survival rate ranges from 53 to 75%, but outcomes vary widely between relatively benign and malignant subgroups. Patients with appendiceal cystadenocarcinomas with pseudomyxoma peritonei have a 25% five-year survival rate, with most deaths attributed to intestinal obstruction or renal failure. The study of pseudomyxoma peritonei is limited by the rarity of the condition and the small number of cases collected in published series.

References
The following case demonstrates small bowel varices without esophago-gastric varices as an unusual cause of gastrointestinal bleeding in a patient with chronic liver disease.

The patient is a 47 year-old man who presented to the hospital with several days of back pain and weakness. The work-up of his symptoms revealed a L3-L4 phlegmon on MRI of the lumbar spine. A biopsy of this lesion yielded focal nonviable bone.

The day after his biopsy, the patient was noted to have two episodes of melena followed by bright blood mixed with stool. The patient complained of some light-headedness.

His medical history included cirrhosis from alcohol, hepatitis C and hypertension. He drank six to ten cans of beer a day and smoked half a pack of cigarettes a day. He quit intravenous heroin ten years prior to admission. The patient noted no allergies and was maintained on lactulose, furosemide, and spironolactone at home. Vancomycin was started in the hospital.

On examination, the patient’s temperature was 97.2°F orally, pulse was 106 beats per minute, respirations were 16 breaths per minute, and blood pressure was 140/78 mmHg. The patient appeared comfortable. He had pale conjunctivae and scleral icterus, heart was tachycardic, lungs were clear, abdomen was mildly distended and non-tender with normal bowel sounds. There was no abdominal ascites and there was trace pitting edema. The rectal exam revealed bright red blood. The patient was promptly transferred to the intensive care unit.

Laboratory values revealed that the hemoglobin decreased from 8.8 g/dL to 4.4 g/dL. The patient’s platelets were 93,000/mm³. The chemistry panel was normal and the liver function tests showed protein 2.9 g/dL, albumin 2.0 g/dL, total bilirubin 2.7 mg/dL, direct bilirubin 1.4 mg/dL, aspartate aminotransferase 89 U/liter, alanine aminotransferase 38 U/liter, and alkaline phosphatase 34 U/liter. The prothrombin time was 20.1 seconds, partial thromboplastin time was 38 seconds, and the international normalization ratio was 1.56.

A prompt bedside nasogastric tube lavage revealed bilious aspirate. The patient was transfused with four units of packed red blood cells (PRBCs) and eight units of fresh frozen plasma without a change in his hemoglobin. Bedside upper endoscopy revealed no esophageal varices or other sources of bleeding. He was transfused with an additional four units of PRBCs with an increase in hemoglobin to 7.6 g/dL. Although hemodynamically stable, he continued have bright red blood per rectum and a decision was made to proceed with an angiogram.

The angiogram revealed no site of arterial extravasation during superior mesenteric and celiac arteriography. Several clusters of varices within the small bowel were deemed to be the bleeding sites. (Figure 1)

Emergent transjugular intrahepatic portosystemic shunt (TIPS) was placed to decompress the small bowel varices. This produced a reduction in the mean portosystemic gradient from 33 to 9 mmHg. The patient received an additional seven units of PRBCs during the procedure.

Over the next two days, the patient continued to have melena and required an additional six units of PRBCs. Patient’s bleeding subsequently ceased and he remained stable for seven days after the TIPS procedure.

Unfortunately, on the eighth day after the TIPS procedure, he developed Staphylococcus aureus sepsis leading to hemodynamic compromise and death.

This case demonstrates that in patients with cirrhosis and gastrointestinal hemorrhage, non-traditional bleeding sources, such as small bowel varices, should be considered in the absence of esophago-gastric varices.

**Figure 1**

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Small Bowel Varices Without Esophago-gastric Varices: A Cause of Massive Gastrointestinal Hemorrhage

Sivakumar Srinivasan MD, PGY-3 and Kuntal Thaker MD, PGY-6, Gastroenterology Fellow
A 43 year-old Chinese woman who immigrated to the United States in 1994 was seen because of several years of chronic, intermittent coughing that was productive of voluminous, thick, green sputum with occasional blood streaking. The cough was accompanied by right anterior pleuritic chest pain. She had no fevers, chills, or night sweats. Her medical history included childhood pneumonia at the age of 18 months, a prior right pneumothorax that required chest tube placement, and a positive PPD. She was a nonsmoker. Despite her symptoms, she was fully functional with activities of daily living but unable to tolerate exercise. She worked as a part-time seamstress and had no environmental exposures. Review of systems was significant only for a 20lb weight loss in the past 2 years.

On exam, she was a thin Asian female weighing 94 lbs in no acute distress and with no labored breathing. On lung auscultation, crackles were heard diffusely and, at the right upper lobe, adventitial sounds and a pleural friction rub were also appreciated. She had no lymphadenopathy and physical exam was unremarkable otherwise.

Bronchoscopy and sputum analysis were performed. Bronchial brushings showed mucopurulent secretions in the right upper lobe, but both bronchial samples and sputum samples were negative for acid fast bacilli (AFB). Heavy growth of Pseudomonas aeruginosa was seen in both sputum and bronchoscopy specimens. CT scans of the thorax were obtained and are shown above.

The patient’s CT scans showed extensive dilatation of the bronchi throughout the entire right lung with thickening of the bronchial walls. Air fluid levels can also be seen, suggesting mucous secretion entrapment in the dilated airways. The lung parenchyma is fibrosed and collapsed with large bullae occupying the lung base.

Bronchiectasis is a disease defined by its morphology; the irreversible dilatation of bronchi damaged from a primary insult such as infection (MAI, pneumonia, pertussis), hypersensitivity reaction (ABPA), cystic fibrosis, primary ciliary dyskinesia, or congenital airway obstruction. The primary disease promotes infiltration of the area with neutrophils and T-lymphocytes, with increased release of elastase, IL-8, TNF-a, and prostanoids. The resulting inflammation leads to further obstruction and damage of the bronchial airways, thereby initiating a new cycle of inflammation and bronchial wall injury. Symptoms include chronic cough, hemoptysis, foul-smelling sputum, and dyspnea.

Management consists of antibiotics to control acute infections; P. aeruginosa, H. influenza, S. pneumonia, and MAI are common pathogens. Inhaled corticosteroids and bronchodilators can help relieve symptoms by reducing airway inflammation. Chest PT and postural drainage help address the issues of mucous overproduction. There are reports of successful surgical outcomes if bronchiectasis is unilateral, where removal of the diseased lung can be curative in some patients. The use of inhaled tobramycin in bronchiectasis is also currently being studied. Initial studies have shown a decrease in sputum P. aeruginosa in approximately 2/3 of patients with minimal side effects, however, more studies are needed to better assess its efficacy and long term outcome.

References
A 48 year-old male with a past medical history of gout, degenerative disc disease, and T cell lymphoma treated with chemotherapy and autologous peripheral blood stem cell transplant, currently in remission, presented seven days status-post a non-myeloablative allogeneic transplant with an acute onset of excruciating left hip and groin pain and a low-grade fever. The physical exam did not reveal any obvious cause of his extreme pain.

The CT imaging revealed extensive inflammation of the left retroperitoneum and psoas muscle with a large focus of gas. The patient was taken emergently for exploratory surgery that revealed extensive myonecrosis of the left psoas muscle with air and foul-smelling serous fluid. The pathology of the surgical soft tissue specimen revealed Clostridium perfringens.

Clostridial myonecrosis, also known as gas gangrene, is a severe, rapidly progressive infection with devastating results. It is usually the result of trauma or surgical complication, but a small percentage of cases are spontaneous. The spontaneous cases are often associated with either a gastrointestinal malignancy, or in the case of our patient, a hematological malignancy. Clinical findings include severe pain out-of-proportion to physical exam findings, low-grade fevers (less than 101°F), and tachycardia. The overlying skin may vary in color – it may be completely unchanged, very pale, bronze in color, or even a purplish-red color. These color changes may also be associated with bullae. Gas may be palpated in the tissues.

Complications of this infection include a brisk hemolysis, jaundice, liver necrosis, shock, renal failure, ARDS and death. The mortality is 20-30% if the infection occurs in an extremity and is treated rapidly and aggressively. However, truncal or spontaneous cases are often associated with a mortality of 67-100%, even with proper treatment. Treatment is multifactorial and includes appropriate antibiotics, usually penicillin and/or clindamycin. Aggressive surgical debridement is essential. Hyperbaric oxygen therapy may also be effective as an adjunct to antibiotics and surgery; however, studies have failed to show a consistent benefit.

Mortality usually occurs within 24-36 hours of infection, and even when the patient survives, severe disability usually results from the numerous and radical surgeries required to debride infected tissue.

References
Mr. B is an 84 year-old African-American male veteran with a history of type 2 diabetes and hypertension who was admitted to the VA hospital for hypertensive urgency. In the ICU, he became unresponsive and pulseless. T-gram showed “ventricular fibrillation” which spontaneously converted to sinus rhythm. An echocardiogram showed an ejection fraction of 60%. An ECG performed prior to the ventricular arrhythmia is shown below.

The major findings of this ECG are bradycardia, QT prolongation, U waves, and T wave alternans (TWA) best seen in leads V3, V4, and V5. With these findings, it is important to ask if the patient was really in ventricular fibrillation.

Ventricular fibrillation rarely spontaneously remits. The findings of QT prolongation and TWA prior to the event are suggestive of a ventricular tachyarrhythmia. This patient had normal electrolytes and was on no drugs that typically cause QT prolongation. He was sent to a hospital with an electrophysiology department and given the diagnosis of long QT syndrome and TWA. Mr. B’s risk of developing another tachyarrhythmia was considered very high therefore an Automatic Implantable Cardioverter Defibrillator (AICD) was placed.

TWA is a variation in the shape of the T waveform seen every other beat representing a change in the intrinsic repolarization of the heart. It is a highly sensitive and specific marker of susceptibility to ventricular arrhythmias and sudden cardiac death. TWA often precedes conditions like Prinzmetal’s angina, acute myocardial infarction, electrolyte imbalances and long QT syndrome. TWA is detected by measurement of microvolt level. TWA on surface Laplacian ECG is commonly associated with long QT syndrome. TWA seen by the naked eye on ECG is a rare finding. Testing for TWA may identify patients at increased risk who fulfill MADIT II criteria for AICD placement.

Thank you to Dr. Reddy for this interesting ECG.

References
Mr. K, a 57 year-old Caucasian male with a history of coronary artery disease, dilated ischemic cardiomyopathy, ventricular fibrillation arrest status post implantable cardioverter defibrillator (ICD) placement was admitted to telemetry for two syncopal episodes. The patient described multiple episodes of dizziness with fatigue over the week prior to admission, the last two episodes resulting in loss of consciousness with bladder incontinence. He was home alone when these episodes occurred and was unsure of how long he had been unconscious. Mr. K was not aware of any recent firing of his ICD. He denied any shortness of breath, chest pain, diaphoresis, recent fevers or chills.

His medical history was significant for hypertension, coronary artery disease status post two vessel coronary artery bypass grafting, dilated cardiomyopathy, and ventricular fibrillation arrest with subsequent ICD placement four years ago. His most recent echocardiogram was four years ago, showing an ejection fraction of 15%. The patient’s medications included enalapril, carvedilol, amiodarone, warfarin, ezetimibe, digoxin, atorvastatin, furosemide, aspirin and niacin. He had no known drug allergies. Mr. K was a retired train conductor. He smoked half of a pack of cigarettes a day and had an 80 pack-year smoking history. He had a history of alcohol, cocaine, and amphetamine abuse, but he quit these drugs 15 years prior. He denied any history of intravenous drug use.

Physical examination on admission was significant for elevated jugular venous pressure, a grade II/VI systolic ejection murmur over the left sternal border, diffuse wheezes on lung exam, and 2+ lower extremity edema. Laboratory results showed a B-type natriuretic peptide level of 662 pg/ml, a creatinine of 1.0 mg/dL, and a digoxin level of 1.6 ng/mL. Chest X-ray showed moderate pulmonary edema. His electrocardiogram (ECG) is shown in Figure 1.

The patient was admitted to telemetry and ruled out for myocardial infarction by serial enzymes. His ICD was interrogated on hospital day 1, revealing three episodes of ventricular tachycardia, which correlated with his

![Figure 1](image-url)

(Continued on next page)
symptoms. The settings of his ICD were adjusted, and the electrophysiology service recommended reloading the patient with oral amiodarone. The patient was started on amiodarone 400 mg three times a day for the next five days. For treatment of his congestive heart failure exacerbation, the patient was diuresed with intravenous furosemide with a goal negative balance of one to two liters per day. The patient was also started on nebulizers for suspected chronic obstructive pulmonary disease and spironolactone to optimize his heart failure regimen. The patient reported feeling improvement over the next four days.

On the morning of hospital day #5, Mr. K complained of feeling very uncomfortable with a sensation of fullness and bloating in his abdomen, which the patient attributed to being constipated. He reported no bowel movements in the past few days. He also complained of increased weakness, shortness of breath and an episode of chills, nausea and emesis overnight. On physical exam, he was afebrile, heart rate was 60 beats per minute and blood pressure was 124/77 mmHg. His abdomen was distended but nontender with active bowel sounds. No rebound or guarding was present. An arterial blood gas was attempted but was felt to be venous. The pH of the venous blood gas was 7.37. Stool softeners and laxatives were ordered and an extra dose of furosemide was given.

A few hours later, the patient called the nurse complaining of feeling poorly. The nurse noted the patient to be diaphoretic and cyanotic. She attempted to take his blood pressure and could not detect a pressure by manual cuff. The primary team was called to evaluate the patient and detected a systolic blood pressure of 54 mmHg by doppler. A fluid bolus of one liter of normal saline was given with improvement of the systolic blood pressure to 82 mmHg by doppler. The patient complained of an uncontrollable gasping for air but denied any chest pain. Central venous access was obtained, and the critical care unit team was called to evaluate the patient for hypotension and cyanosis.

Physical examination revealed the patient to be alert in moderate distress with cyanotic lips. After a one liter fluid bolus, the patient had a heart rate of 70 beats per minute and respirations were 30 breaths per minute. A pulse oximetry reading was unobtainable due to cyanotic extremities. Jugular venous pressure was estimated at 10mmHg. The systolic murmur was unchanged from prior exams. Lung exam demonstrated wheezes diffusely with 1+ lower extremity edema. A stat echocardiogram was ordered to evaluate the possibility of cardiac tamponade given the patient’s hypotension. Echocardiogram showed an ejection fraction of 10%, severe left ventricular enlargement with global dysfunction, mild to moderate mitral regurgitation, but no pericardial effusion.

An electrocardiogram was obtained and is shown in Figure 2. Compared to his previous ECG on admission which showed mostly ventricular paced beats, the patient now had a sinus rhythm with widened QRS complexes (duration 640ms) and peaked T waves. Hyperkalemia was suspected, and the patient was given two ampules of calcium gluconate and 10 units of insulin intravenously with one ampule of dextrose 50%. The patient’s blood pressure fell to the 70s/40s mmHg and continuous dopamine infusion was started. The patient was placed on a 100% non-rebreather mask and urgently transferred to the cardiac intensive care unit.

Stat laboratory results returned showing the serum potassium to be 6.8 meq/L (compared to 4.0 meq/L the day before), serum bicarbonate of 19 meq/L (previously 31 meq/L), calcium 2.0 mg/dL (from 4.2 mg/dL) and creatinine of 1.7 mg/dL (from 1.0 mg/dL). The patient was given three more ampules of calcium gluconate and two ampules of sodium bicarbonate for his hyperkalemia.

Approximately 10 minutes after arrival to the CCU, the patient began to complain of extreme shortness of breath. His heart rate rapidly decreased to the 50s, and the patient became unresponsive and pulseless. Cardiopulmonary resuscitation was initiated for pulseless electrical activity and three doses of epinephrine were given. The patient’s rhythm converted to pulseless ventricular fibrillation, and defibrillation was attempted three times without change in rhythm or recovery of pulse. An intravenous bolus of amiodarone was also given without any response. Resuscitative efforts were continued for 20 minutes before the patient was pronounced dead.

Discussion
Post-mortem, a serum digoxin level sent earlier that morning showed a level of 5.8 ng/ml. This level was well above the upper limit of therapeutic (0.5 to 2 ng/ml).
Digoxin toxicity was likely a contributing factor in this unfortunate case. The patient had multiple known risk factors for digoxin toxicity, including cardiac disease, potential electrolyte abnormalities from diuresis, acute renal insufficiency, and the addition of medications that interfere with digoxin metabolism.

Digoxin acts by inhibiting the sodium-potassium adenosine triphosphatase (ATP-ase) pump in myocytes. With each action potential, sodium enters but a decreased amount of sodium exits leading to an increase in intracellular sodium and a decrease in intracellular potassium. Through the sodium-calcium exchange, the increase in sodium results in increased intracellular calcium. This increases myocardial contractility and enhances automaticity while slowing conduction through the atrioventricular node. The decrease in intracellular potassium may cause a relative increase in extracellular potassium leading to elevated serum potassium levels.

The most important method of diagnosing digoxin toxicity is to maintain a high level of suspicion. Signs and symptoms of digoxin toxicity are often subtle and nonspecific. Patients may experience nausea, vomiting, abdominal pain, fatigue, blurred vision, headache, dizziness, confusion, delirium, and altered color vision (classically described as seeing yellow halos around lights). No single ECG abnormality is pathognomonic of digoxin excess. However, the combination of enhanced automaticity and impaired conduction (e.g., atrioventricular (AV) block accompanied by an accelerated junctional pacemaker) is highly suggestive of toxicity even when serum levels are within the “accepted” therapeutic range. The first presenting sign of digoxin toxicity may be a cardiac arrhythmia. Almost any arrhythmia may be associated with digoxin toxicity, though the most frequent is ventricular ectopy. Sinus bradycardia, sinus arrest, paroxysmal atrial tachycardia, heart block, junctional rhythms, ventricular tachycardia and fibrillation are also commonly seen.

Digoxin is excreted through the kidneys proportional to the glomerular filtration rate and is therefore dependent on creatinine clearance. Renal insufficiency is then a predisposing factor for digoxin toxicity. In our patient, the acute renal insufficiency was likely secondary to aggressive diuresis.
Amiodarone, among many other drugs, is known to increase serum digoxin levels through decreased renal excretion at the tubular level and may also displace bound digoxin from tissue. (See Table 1 for a list of other commonly used medications that affect digoxin levels.) It is recommended that patients being started on amiodarone should have their maintenance doses of digoxin decreased by 50 percent with close monitoring of serum digoxin levels. In our patient, his maintenance digoxin dose while on amiodarone 200 mg daily was 0.25 mg with a digoxin level within therapeutic range (1.6 ng/mL). He was also started on spironolactone during his hospitalization, which like amiodarone, increases digoxin levels by decreasing renal clearance. The patient's rapid increase in serum digoxin level was likely due to decreased renal excretion from the combination of the oral amiodarone load, the addition of spironolactone, and acute renal failure.

As previously mentioned, digoxin toxicity may also be associated with hyperkalemia by inhibiting sodium-potassium exchange into the myocyte. In this case, Mr. K had three potential causes of hyperkalemia: acute renal failure, spironolactone use, and digoxin toxicity. The treatment he received for his hyperkalemia included multiple ampules of calcium gluconate which may have further potentiated the effects of digoxin.

Elevated serum calcium levels increase ventricular automaticity and this effect is at least additive to, and may be synergistic with, the effects of digoxin. Administration of intravenous calcium to patients taking digoxin may provoke lethal ventricular arrhythmias, in particular, refractory ventricular tachycardia and fibrillation. Thus, calcium gluconate administration is problematic in hyperkalemia if digoxin toxicity is suspected and generally not recommended. In Mr. K’s case, the cause of his cardiac arrest may have been primarily hyperkalemia which would correlate with his rhythm of pulseless electrical activity. However, his rhythm then converted to ventricular fibrillation that was unchanged after multiple attempts at defibrillation. This may have been the effect of the five ampules of calcium gluconate that were unknowingly administered in the context of digoxin toxicity.

In severe cases of digoxin toxicity, digoxin-specific antibody fragments (Digibind) may be used to treat patients. Digibind rapidly binds circulating digoxin (as digoxin has an increased affinity for the antibody fragment over the sodium-potassium pumps) thus inactivating the drug. Indications for use of Digibind include an acute ingestion of greater than 10 mg of digoxin, plasma digoxin levels greater than 10 ng/ml, and potassium levels greater than 5 meq/L in the presence of a life-threatening arrhythmia, as in this case. The antibody fragments are given intravenously over 30 minutes, unless cardiac arrest has occurred, in which case the solution is given as a bolus. Side effects are few with Digibind but include worsening congestive heart failure and hypokalemia.

Would the outcome of Mr. K’s case have been different if digoxin toxicity had been suspected and Digibind administered? We hope that by highlighting this case of digoxin toxicity with associated hyperkalemia, we will heighten awareness for the diagnosis and never have to ask ourselves this question in the future.

References


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<th>Drug</th>
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<td>Rifampin</td>
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Effect Of Endogenous Noradrenaline Release On Peak Exercise Heart Rate In Subjects With Chronic Heart Failure Receiving Carvedilol Versus Metoprolol

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Background
Dose equivalency of metoprolol and carvedilol for beta-1 blockade remains subject of ongoing debate. The degree of beta-1 blockade is best assessed in vivo by blunting of the exercise induced heart rate. Accordingly, we examined baseline and peak exercise heart rate in subjects with chronic heart failure (CHF) treated with carvedilol or metoprolol. To correct for possible differences in norepinephrine (NE) release due to beta-2 blockade, we also measured NE levels at baseline and peak exercise.

Methods
Thirty-three subjects treated chronically with carvedilol (34.5 ±3.4 mg; n=23) or metoprolol XL (77.5+17.3 mg; n=10) referred for cardiopulmonary exercise testing were studied prospectively. All subjects were in normal sinus rhythm, achieved RER > 0.95, and received the long acting form of metoprolol, metoprolol XL, which has 75% bioavailability of the short acting metoprolol IR. Carvedilol versus metoprolol XL subjects did not differ (p < 0.05) with respect to age (52 vs 56 yrs), LVEF (25 vs 29 %), LV ED D (6.2 vs 6.3 mm), MAP (83.5 vs. 88.3 mmHg), baseline HR (73.6+2.4 vs 71.5+4.7 bpm), peak VO2 (16.7 vs 15.7 ml/kg/min), exercise time (9.3 vs 9.1 min), or baseline (3.49 vs 4.01 nmol/l) plasma norepinephrine (NE) levels. However, despite similar peak NE levels (17.1±4.8 vs 18.6+4.9 nmol/l), heart rate at peak exercise was higher in subjects receiving carvedilol (131.7 + 4.6 bpm) compared to those receiving metoprolol (112.6 +6.0 bpm), p=0.029.

Conclusion
Similar NE release and more complete beta-1 blockade as assessed by peak heart rate is observed in otherwise well matched subjects with CHF treated with a mean daily dose of 77.5 mg metoprolol XL as compared to 35.5 mg carvedilol. Assuming a 75% bioavailability of metoprolol XL, 58 mg metoprolol IR should provide a higher degree of beta-1 blockade than 35 mg carvedilol.

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Abstracts

Resident and Faculty Feedback: The Student’s Perspective
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Background
Feedback from faculty members and residents is a critical component of undergraduate medical education. Little is known about how students assess the adequacy of feedback from faculty and residents.

Purpose
To report medical students’ evaluations of clinical teacher feedback and to determine if students assess feedback given by residents differently than they assess feedback given by faculty.

Methods
Data were retrospectively collected from medical students’ responses to end-of-clerkship questionnaire items that evaluated feedback from residents and attending physicians. The mean ratings of faculty feedback in four clerkships were compared with the mean ratings of resident feedback within each academic year from 1998 to 2002.

Results
Overall, the 1198 student evaluations of clinical teacher feedback were positive. Resident feedback was rated equal to or higher than faculty feedback in every clerkship; 5 of the 16 comparisons (31%) reached statistical significance.

Conclusions
Students believe feedback from residents is at least as valuable as feedback from faculty. Higher resident feedback ratings may have been due to a greater frequency of resident-student interactions as well as a more peer-level relationship between students and residents.

Background
Feedback refers to information describing students’ performance in a given activity that is intended to guide future performance in that activity. Medical students who receive feedback have been shown to perform better on objective outcome measures than students who do not receive feedback. Accordingly, feedback is recognized as an important part of medical education.

Effective feedback is timely, expected, frequent, non-judgmental, non-threatening, and specific (based on direct observation of behaviors). Feedback that lacks these characteristics may fail to communicate useful information to the student. Because of the potential for variability in feedback, it is important for medical schools to monitor feedback given to students.

Typically, clinical faculty and residents are both responsible for teaching medical students and giving them feedback. Because attending physicians tend to have more teaching experience than residents, they might be expected to provide better feedback. However, on most clinical rotations residents spend more time with students and therefore have the opportunity to provide more frequent, specific feedback. Little is known about whether students value feedback from residents differently than they value feedback from attending physicians.

The purpose of this study is to report medical students’ evaluations of clinical teacher feedback and to determine if students assess feedback given by residents differently than that given by faculty. To our knowledge, this is the first study that specifically compares student ratings of feedback from residents with feedback from faculty.

Methods
The University of Florida College of Medicine administers a questionnaire to third-year medical students at the end of each clinical clerkship. All questionnaires contained the same 2 items to assess feedback: (1) “Attending physicians provided regular feedback on student performance,” and (2) “Residents provided regular feedback on student performance.” Possible responses ranged from “poor” (1) to “excellent” (5) on a 5-point Likert scale. This study involved a retrospective analysis of student responses to these two items.

Questionnaires from Internal Medicine, Neurology, Pediatrics, and Surgery were included. Questionnaires from clerkships that did not provide feedback data from all 4 years relating to both the faculty and residents were excluded. For each clerkship within each academic year, mean student ratings of resident feedback were compared with mean ratings of faculty feedback using a t-test.

Results
Overall, the 1198 student evaluations of clinical teacher feedback were positive. Resident feedback was rated equal to or higher than faculty feedback in every clerkship; 5 of the 16 comparisons (31%) reached statistical significance.

Conclusions
Students believe feedback from residents is at least as valuable as feedback from faculty. Higher resident feedback ratings may have been due to a greater frequency of resident-student interactions as well as a more peer-level relationship between students and residents.
Discussion
In this study, student responses to end-of-clerkship questionnaires were retrospectively analyzed to assess and compare student perception of feedback given by attending physicians and residents. On average, students rated feedback from all clinical teachers (residents and attending physicians) as good or better. Resident feedback was rated equal to or better than faculty feedback. The difference was statistically significant for 31% of the faculty-resident comparisons.

Several factors may have contributed to higher ratings of resident feedback. One is amount of time spent with trainees. A study of internal medicine clerkship students found that the amount of time clinical teachers spent with students was related to student ratings of overall teaching effectiveness. Residents generally spend more time with medical students because faculty-student interactions tend to be limited. Therefore, time spent with students may have contributed to higher resident ratings.

Another factor that may have contributed to higher ratings of resident feedback is that students considered feedback from residents more personally acceptable. As previously stated, effective feedback is non-threatening. Generally, students and residents are closer in age and experience than students and attending physicians. Students and residents, therefore, have more of a peer relationship. Most likely, students feel less threatened by residents than by attending physicians.

We recognize several limitations of the present study. The first limitation is that the questionnaire wording, e.g., “Attending physicians provided regular feedback on your performance,” prevents drawing a precise conclusion about student perception of the effectiveness of feedback given. The next limitation relates to the difficulty of interpreting these subjective data. Even though feedback from residents was rated significantly higher in 5 of the 16 comparisons, it is difficult to know the educational or clinical significance of this difference. The important conclusion to draw is that students rated feedback from residents and faculty as poorly equivalent, with a slight favoring of feedback from residents. In addition to the limitations imposed by questionnaire wording and subjective data, there is also the potential for recall bias as a result of student inability to always recognize feedback.

Future studies could address these limitations to better assess and compare resident and faculty feedback. A more useful instrument to measure the effectiveness of feedback would be a questionnaire that specifically addresses the component parts of effective feedback. Another valuable approach might be to train students in recognizing and receiving feedback. Such training has been shown to improve students' ratings of feedback given. To address the issue of feedback recall, students could be surveyed multiple times during a clerkship.

In conclusion, this study shows that while medical students were satisfied generally with the level of feedback from all clinical teachers, they considered feedback from residents as good as or better than feedback from faculty. Because residents play a critical role in undergraduate medical education, it is valuable to assess feedback from residents as well as faculty. Further research is needed to more objectively determine the effectiveness of feedback given by residents and faculty.

References
The Use of Non-Primed Peripheral and Central IV Tubing for Nesiritide Infusion is Reliable and Cost-Effective

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Background
Prescribing information of nesiritide mandates priming of intravenous tubing with 25 mL of nesiritide prior to connecting the intravenous (IV) line to the patient, since the drug may partially absorb to the line. Thus, 10% of a reconstituted vial is wasted, with a cost of $40-50 per line used. No study has quantified the binding effect of nesiritide to intravenous tubing, tested binding properties of different materials, or analyzed binding effect of central lines, where priming cannot occur. Furthermore, prescribing information states that nesiritide must not be administered through a central heparin-coated catheter, since it may bind to heparin. However, no study quantified this binding effect.

Methods
1.5 mg vials of nesiritide were reconstituted into 250 mL 0.9% NS bags. A 23.3mL bolus, followed by 7mL/h 2-hour infusion (2ug/kg bolus, 0.01ug/kg/min infusion for a 70kg pt) were run, in duplicate, through 5 separate experimental tubing systems: 1) Standard PVC peripheral IV tubing primed with a 25 mL of nesiritide; 2) Standard non-primed PVC peripheral IV tubing; 3) Non-primed polyethylene peripheral IV tubing, commonly used for NTG infusion; 4) Non-primed PVC peripheral IV tubing, connected distally to a central IV polyurethane catheter; 5) Non-primed PVC peripheral IV tubing, connected distally to a heparin-coated pulmonary artery PVC catheter. Nesiritide concentration was measured, in triplicate, in the initial bags and samples collected from the five IV settings, using Biosite BNP test (Beckman Coulter).

Results
More than 95% of nesiritide was recovered from all five IV settings. Priming of PVC tubing with nesiritide improved drug recovery by 2% during IV bolus and 2-hour infusion compared to non-primed PVC tubing. Polyethylene tubing improved drug recovery also by 2% at 1- and 2-hour time points, suggesting that polyethylene saturates faster than PVC. Connecting a triple lumen or heparin-coated pulmonary artery catheter distally to non-primed PVC tubing did not further impact percentage of drug recovery.

Conclusions
Priming of peripheral IV tubing with 25mL of nesiritide minimally improves drug release to patients since more than 95% of drug is delivered even without priming. Polyethylene IV tubing further minimize drug binding and offers an even more reliable, yet inexpensive, alternative to priming. Elimination of priming may result in $40-50 saving per line used. Use of central lines or heparin-coated pulmonary artery catheter does not result in significant binding. Thus, changes in nesiritide prescribing information are warranted.

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Cover Art “Untitled,” Watercolor by Manav Segal, 2004
Manav Segal MD is currently a Third-Year Internal Medicine Resident. This is his second year displaying artwork for the cover of the Jefferson Forum. Dr. Segal uses watercolor and chalk to create his works of art. His passion lies in creating abstract portraits. This piece was created during this past spring and the Jefferson Forum is its feature display.