Hand foot and mouth disease (HFMD) is a common childhood ailment. It is typically caused by coxsackie virus A16, and less commonly, coxsackie B and enterovirus 71. Physical manifestations are characterized by vesicles on the hands, feet and oral mucosa. HFMD in adults is less common and often more severe with atypical manifestations, such as widespread cutaneous involvement not limited to the hands and feet. Current literature is lacking in the characterization and outcomes of HFMD in adults. Because of the lesser frequency of HFMD in adults, it is often misdiagnosed and hence mismanaged. In this clinical vignette we describe two adult cases of HFMD to substantiate the literature on adult HFMD and guide health care providers’ management and treatment decisions.

The first case is a 37-year-old man with a history of anxiety and attention-deficit disorder who presented with acute onset of rash, sore throat, fever and malaise. Physical exam revealed generalized erythematous papules over the scalp, malar cheeks, torso, upper extremities, palms, hips and right ankle. Initial differential diagnosis included hand-foot-and-mouth disease, guttate psoriasis, pityriasis lichenoides or another reactive process. Swabs for HSV, VZV, bacteria and enterovirus were collected and a representative papule was biopsied. Biopsy results showed nonspecific inflammation, hemorrhage and epidermal changes. Swab results confirmed enterovirus infection and diagnosis of hand-foot-and-mouth disease was made.

The second case is a 32-year-old male with history of depression, anxiety and chronic pain who presented with acute onset of a rash that began on his face and scalp, slowly developing over his trunk, upper and lower extremities, including the palms and soles. Relevant history included recent self-limited HFMD in the patient’s daughter. Physical exam showed widespread morbilliform eruption with violaceous macules and vesicles on his scalp, face, neck, trunk and upper and lower extremities including hands and feet, as well as superficial erythematous erosions on his tongue and involving the hard palate. Differential included viral exanthem, erythema multiforme, disseminated herpes simplex and varicella infection, or Rocky Mountain spotted fever. Swab results were positive for enterovirus and diagnosis of hand-foot-and-mouth disease was made. The patient developed onychomadesis (nail shedding) shortly after diagnosis. In both cases, treatment was supportive care, including triamcinolone for the rash and hydroxyzine for itching. Both cases were self-limited.

Most cases of HFMD are seen in childhood. These cases illustrate the potential for hand-foot-and-mouth disease to present in adults and the features more common in adult HFMD, including widespread, generalized rash in addition to the classic locations of the hands and feet. HFMD must be considered in the appropriate clinical scenario to avoid unnecessary work-up and treatment.
| Victoria Blackhorse  
Dr. Brian Muthyala and  
Dr. Shemal Shah,  
Department of Medicine,  
University of Minnesota Medical School | Acetaminophen-induced hemolytic anemia in an undiagnosed case of Glucose-6-phosphate dehydrogenase deficiency  
A 22-year-old previously healthy male Burmese refugee was admitted to the medicine service for liver failure (AST 13,034; ALT 10,830) after a mixed acetaminophen and alcohol ingestion, thought to be a suicide attempt. He was started on N-acetyl cysteine with near complete resolution of his hepatic injury. 5 days into his hospitalization, with improving ALT 1931, AST 194, and INR 1.2, his hemoglobin dropped from 15 to 5.7 g/dL. A rapid drop in hemoglobin is either due to blood loss, which was not seen, or hemolysis. His workup revealed negative Coombs, low haptoglobin, elevated LDH, and “bite cells” on peripheral smear. As these findings were concerning for G6PD deficiency, a G6PD level was sent on blood collected on admission and it returned low (6.7 U/g Hb). A Repeat G6PD deficiency test was done as an outpatient two weeks after discharge, since during an acute hemolytic episode, G6PD can be falsely depressed. The laboratory value (1.8 U/g Hb) was shown to be consistent with G6PD deficiency. Hemolysis is self-limited and should resolve within a couple of weeks.  
Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an X-linked enzymatic red blood cell disorder that typically manifests in males, even though women can be asymptomatic heterozygous carriers. Affected patients are predisposed to denaturation of hemoglobin with oxidative stress leading to intravascular hemolysis. It is described primarily in individuals of Mediterranean and Asian descent. Homozygous G6PD deficient patients are asymptomatic unless they are exposed to certain triggers, such as certain foods (fava beans), infections, and drugs (sulfonamides and antimalarials). This case illustrates the exacerbation of a previously undiagnosed G6PD deficiency after acetaminophen ingestion. During periods of active hemolysis, G6PD levels may be spuriously low due to favored destruction of deficient erythrocytes; therefore, a sample should be used from before or after the acute hemolytic episode to avoid a false negative result. If testing is negative, and there is a high suspicion for G6PD deficiency, it is recommended to repeat within three months of the hemolytic episode, given a new set of circulating RBCs are produced. Previous case reports of known G6PD deficient patients going into hemolytic crisis with acute acetaminophen overdose have been readily described, however, the deficiency in our patient had not been previously identified, making this case unique. This case emphasizes the importance of back-to-basics problem solving to avoid missing a diagnosis and not overlooking adults, with a potential pediatric diagnosis, who have a hemolytic episode. |
| Johanna Blythe Reske  
Rena Singleton, MD | Drug Induced Lupus: A Rare Complication of a Common Medication  
An Uncommon Complication of a Commonly Used Medication  
Drug-induced lupus (DIL) is an autoimmune-mediated reaction to a medication. Associated with approximately 38 drugs, patients with DIL often present with less severe “lupus-like” symptoms. Renal involvement is less common and patients often recover after discontinuation of the offending medication and temporary treatment of drug-induced manifestations. An 80-year-old woman with a history of rheumatoid arthritis, heart failure, right splenic artery aneurysm repair, stroke and breast cancer treated with lumpectomy was transferred to the internal medicine service from the MICU after admission for acute hypoxic respiratory failure initially requiring intubation. She subsequently developed acute-onset anuric renal failure and ultimately required dialysis during admission. Initial exam findings were significant for diffuse inspiratory crackles, ulnar deviation in upper extremities, and no active synovitis or rash. It was noted that she was on hydralazine chronically for blood pressure management, and drug-induced lupus was considered in the broad differential for cause of her acute renal failure. Pertinent labs and studies during admission included a low C3 and C4 level, positive anti- |
PR3, positive anti-MPO, and positive anti-histone. A renal biopsy was completed and showed focal segmental necrotizing and crescentic glomerulonephritis and lupus-like glomerular immune complex deposition, consistent with an ANCA-associated vasculitis. Hydralazine was promptly discontinued and the patient was started on prednisone. Plasmapheresis was initiated followed by several doses of cyclophosphamide. Renal function improved, and before hospital discharge, the patient no longer required dialysis. Rituximab was initiated and the patient was discharged with close follow-up with Nephrology and Rheumatology.

This case represents an uncommon presentation of a known medication-induced complication. Hydralazine use has known association with an ANCA-positive vasculitis (typically a P-ANCA pattern), which can involve the kidney. On renal biopsy in DIL, often a necrotizing glomerulonephritis without immune complex deposition is seen, although an immune complex-mediated glomerulonephritis may be found, as it was with this patient. In retrospect, a pulmonary-renal syndrome due to drug-induced vasculitis is suspected in this patient, and ultimately she was diagnosed with a hydralazine-associated mixed drug-induced lupus/ANCA-associated vasculitis with drug-induced lupus nephritis. Early diagnosis and treatment by the multidisciplinary team caring for this patient was imperative; she was critically ill and at increased risk for significant morbidity and mortality--she had also clearly outlined her wishes to discontinue dialysis in the outpatient setting if her renal function did not recover. Identifying rare manifestations of drug-induced autoimmunity is challenging and requires a high degree of suspicion, but timely diagnosis and treatment is critical for improving patient outcomes. For this patient, early diagnosis and prompt treatment allowed for significant and meaningful recovery.

**Hafsa Chaudhry**
Jie Qu, M.D. and M. Rizwan Sohail, M.D.

**Fevers, Chills, and Eosinophils**

Introduction: Eosinophilia, defined as >500 eosinophils/microL, has a wide array of etiologies. Severe eosinophilia (>1500 cells/microL) has the potential for end-organ damage. Primary eosinophilia can be divided into either clonal or idiopathic processes. Secondary eosinophilia is commonly related to infectious, allergic and immunologic, or drug-induced causes. A thorough evaluation of eosinophilia is important to rule out treatable etiologies and to manage systemic complications.

A 78 year-old female with a history of iron deficiency anemia, asthma, and mild bronchiectasis presented with six weeks of intermittent fevers, chills, progressive fatigue, and nausea. Laboratory studies on admission were significant for anemia (Hgb 8.7 g/dL), leukocytosis (16,600 cells/microL), eosinophilia (3080 cells/microL), and elevated CRP (93 mg/dL) and ESR (58 mm/h). The patient denied any recent travel or changes in her home environment, new rashes or insect bites, and new medications or foods. She had no known sick contacts. Outside records from one month prior demonstrated eosinophilia of 7,000 cells/microL. Physical examination revealed a soft systolic murmur of the left upper sternal border and mild bibasilar rales.

Infectious Disease, Hematology, Pulmonology, and Rheumatology were consulted. A thorough workup was negative including: a PCR panel for several GI pathogens; ANCA serologies; tick-borne illnesses panel for Anaplasma, Lyme, and Ehrlichia; dimorphic fungal serologies; and testing for Strongyloides, Trichinella, and Toxocara. Blood cultures and stool tests for ova and parasites were also negative. A bone marrow biopsy demonstrated no morphologic features of mast cell disease, myeloproliferative neoplasm, granulomas, or lymphoma. Cytogenetic studies were also normal. CT scan of the chest showed atelectasis at the lung bases and baseline bronchiectasis. Transthoracic echocardiogram showed normal systolic function, mild diastolic dysfunction, and ejection fraction of 65%.

Over the course of her inpatient stay, the patient had persistent eosinophilia >3,000 cells/microL that ultimately declined to 1460 cells/microL upon discharge. Her fevers and eosinophilia were deemed to be idiopathic.
Discussion: The evaluation of a patient with eosinophilia involves consideration of a broad differential. This case demonstrates a thorough workup for eosinophilia. After ruling out secondary causes, including infectious, rheumatologic, hematologic, and immunologic etiologies, a diagnosis of idiopathic eosinophilia was made. Idiopathic eosinophilia is a diagnosis of exclusion; thus a broad differential diagnosis and a thorough history, examination, and initial assessment is imperative. If secondary causes are not identified, a bone marrow biopsy may be pursued to assess for primary etiologies. Additionally, echocardiography, electrocardiography, pulmonary function tests, and a CT scan of the chest may be necessary to assess for end-organ involvement, especially in cases of severe eosinophilia. Close observation has been recommended for asymptomatic patients with idiopathic eosinophilia, with serum troponin levels every 3-6 months and echocardiogram every 6-12 months. In symptomatic patients with idiopathic eosinophilia, prednisone is the initial drug of choice.

| Kathryn Del Valle  
Yelena Slinin, MD,  
Minneapolis VA Healthcare System, UMN |
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<td><strong>The Great Pretender Strikes Again: Sarcoidosis Presenting as Acute Renal Failure</strong></td>
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| Clinical renal disease is an uncommon but recognized manifestation of sarcoidosis. Most often it relates to abnormal calcium metabolism, and patients have hypercalcemia as well as extra-renal disease at presentation. However, rarely sarcoidosis can primarily present as granulomatous kidney disease causing acute renal failure.  
We present a case of a 66 y/o Caucasian male with a remote (35+ years prior) history of self-limited pulmonary sarcoidosis (diagnosed via lymph node biopsy) who presented with malaise, low grade fever, and muscle aches. Other past medical history included coronary artery disease, hypertension, stroke, Type 2 diabetes mellitus, hypogonadism, gout, chronic night sweats of unknown etiology, and obesity. No evidence had been found of prior sarcoid recurrence.  
Initial evaluation revealed acute renal failure in the setting of chronic kidney disease (CKD) Stage 3. His creatinine had nearly doubled from his previous baseline in less than 3 months: 2.4 in Sept. 2014 → 2.0 in March 2015 → 4.0 in June 2015. His serum calcium and serum ACE level were found to be high-normal at 9.7 (range 8.5-10.1) and 67 (range 9-67), respectively. Given the severity of AKI and lack of proteinuria suggesting worsening diabetic nephropathy, a kidney biopsy was performed. This showed focal granulomatous interstitial nephritis (GIN) and focal global glomerular sclerosis. Testing was performed for other known etiologies of GIN including paraproteinemias, tuberculosis, and HIV and found to be negative. A diagnosis of renal sarcoidosis was made.  
He was begun on prednisone 40mg per day and completed a gradual taper over a 12-month course. His renal function responded well, with his creatinine remaining generally stable on prednisone with continued fluctuations (1.7-2.3). Investigation for extra-renal sarcoid has included repeated chest imaging looking for pulmonary recurrence along with dermatologic and ophthalmologic evaluation, all negative. We noted that his testosterone levels increased into the normal range during his prednisone course, but the data was not definitive enough to determine whether this was sarcoid-related or merely coincidental. Shortly after completing his steroid course, his malaise and muscle aches returned but were accompanied by only a slight increase in his creatinine (to 2.5), and thus evaluation is ongoing to further characterize this return of symptoms.  
This case highlights the importance of including sarcoidosis in the differential for acute intrinsic renal failure, even in cases of known CKD. Furthermore, it illustrates that normocalcemia is not always a reliable metric through which to exclude renal sarcoidosis. Finally, this case demonstrates that renal disease can be the primary clinical presentation of sarcoidosis, even in those patients who have no confirmed evidence of this condition elsewhere. |
**Acquired pure red cell aplasia associated with multiple myeloma treated with cyclosporine.**

Pure red cell aplasia is a rare condition of profound anemia with low reticulocyte count and markedly decreased erythroid precursors in the bone marrow, usually do to immunological suppression. Multiple myeloma is the neoplastic proliferation of plasma cells with the production of monoclonal proteins in the serum, associated with pancytopenia, hypercalcemia, renal and bone disease. Here we describe a fascinating case of pure red cell aplasia associated with multiple myeloma with kappa free light chains. A 59-year-old man initially presented to the clinic with fatigue. The bone marrow biopsy performed revealed multiple myeloma with 30-40% kappa plasma cells but no erythroid precursors, consistent with pure red cell aplasia. No evidence of thymoma or parvovirus. Initially, it was hypothesized that red cell suppression was due to clonal plasma cell proliferation which in turn produced a monoclonal protein that suppressed erythropoiesis. In view of this hypothesis, he was started on treatment with cyclophosphamide, bortezomib and dexamethasone (CyBorD) chemotherapy to decrease his kappa free light chains. The kappa light chains decreased from 89.8 mg/dl to 23 mg/dl and plasma cells decreased from 20-25% to 5-10%, but he still had only 3% erythroid normoblasts. Since he continued to have anemia, reticulocytopenia and needed RBC transfusions it was concluded that his red cell aplasia was not responsive just to the treatment of myeloma. It was decided to add immune suppression with cyclosporine and prednisone to the regimen for his anemia. CyBorD was also continued for another 5 months. He had a gradual increase of his red blood cell and reticulocyte count on cyclosporine and became transfusion independent. At the end of the 5 months of cyclosporine, bone marrow showed around 40% erythroid normoblasts and he had minimal evidence of plasma cell neoplasm. Cyclosporine was continued for another 2 months following which it was gradually tapered. Since he was in a very good partial remission with normocellular bone marrow showing less than 5% plasma cells, autologous stem cell transplant was performed, to consolidate his remission, after priming with cyclophosphamide to collect stem cells and myeloablation with melphalan. Post-transplant his bone marrow biopsy at day 26 showed 22% erythroid cells and less than 5% plasma cells. His Hb on day 60 post-transplant fell to 6.7 g/dl and his retic count decreased to 7000/µL. Bone marrow showed rare kappa plasma cells and only 3% erythroid normoblasts consistent with RBC hypoplasia. Cyclosporine was then restarted along with prednisone. After 3 weeks of treatment, his reticulocyte count increased to 115,000/µL. He is presently transfusion independent and his myeloma is in very good partial remission. There have been only a handful of cases of pure red cell aplasia with multiple myeloma described in the literature.

**Support our trops** on dissecting medical emergencies

Aortic dissection is a cardiac and surgical emergency, which typically presents as a severe “tearing” or “ripping” chest pain with radiation to the back, arm, or neck, and may be associated with shortness of breath, stroke-like symptoms, or loss of consciousness. However, presentation can vary widely, especially in the elderly, leading to frequent initial misdiagnoses. An 84 year-old woman with a past medical history of atrial fibrillation, hypertension, left MCA stroke, and chronic kidney disease presented to the ED complaining of acute onset epigastric and neck pain associated with diarrhea and fecal incontinence. The patient denied chest tightness, arm pain, and shortness of breath. In the Emergency Department, the patient underwent standard evaluation including ECG and chest x-ray, as well as abdominal CT for evaluation of severe epigastric discomfort. Abdominal CT was negative for acute pathology and revealed incidental diverticulosis. Chest x-ray also was largely unremarkable, and revealed moderate cardiomegaly with normal pulmonary vascularity. ECG showed the pre-existing atrial fibrillation, global ST depression and T wave abnormalities. Troponin was slightly elevated at 0.04. At that time, this slight troponin increase was attributed to the patient’s
history of chronic kidney disease and previous record of elevated measurements without cardiovascular involvement. The patient was admitted for further monitoring, and underwent repeat ECG the following day. The ST changes had resolved, and the patient appeared comfortable, denying chest pain or any other discomfort. An initial diagnosis of NSTEMI was made. However, repeat troponin had increased to 0.16 and transthoracic echocardiogram was pursued. Surprisingly, echocardiogram revealed a type A aortic dissection extending from the aortic root to mid ascending aorta. Remarkably, the patient did not experience cardiac symptoms because the extensive margin of the dissection narrowly missed the origin of the coronary arteries and great vessels. CT angiography was confirmatory and cardiovascular surgery was urgently consulted. Unfortunately, the patient was deemed a poor surgical candidate due to advanced age, frailty, and cardiovascular complications. The patient was discharged in a medically stable condition on anti-hypertensive agents, anticoagulants, and comfort care. Unfortunately, the patient passed away two weeks later.

This case is a remarkable example of the heterogeneous presentation of ascending aortic dissection, and highlights the importance of monitoring the cardiac enzymes along with comprehensive cardiovascular workup for dynamic ECG changes. Although ECG readings may normalize and chest pain may not be present, trending cardiac enzymes can help detect cardiovascular pathology requiring urgent intervention.

Emily Karp

**Peritoneal carcinomatosis with prior diagnosis of Protein S deficiency**

Protein S deficiency is a rare, inherited disease characterized by increased risk of venous thromboembolism (VTE). Protein S is well known as a vitamin K-dependent glycoprotein that serves as a cofactor for coagulation inhibitor, protein C. Therefore, in the absence of protein S, protein C is inactive and procoagulant factors Va and VIIIa remain active placing the patient at higher risk for VTE. A handful of studies have reported functional effects of protein S independent of its anticoagulant function. They suggest protein S has a role in cell-cycle growth/survival/phagocytosis. Further supporting protein S deficiency playing a role in cancer pathogenesis, the glycoprotein was found to promote apoptosis and phagocytosis in rabbit models (Sassan and Bjorn, 2006). Case Description: A 55 year old male with past medical history of Protein S deficiency (DVT age 24, PE age 33, DVT 47), s/p IVC filter, hypothyroidism, and hyperlipidemia presented with drastic unintentional weight loss of 60 pounds in 5 months, sweats, fatigue, and general abdominal discomfort. Initial work up indicated thrombocytosis (730) and anemia (Hgb 12). On CT abdomen, peritoneal carcinomatosis of unknown origin identified. PSA normal and colonoscopy 3.5 years ago negative, per patient. At the time of this abstract submission, CA 125 and CA 19-9 pending. Further tissue biopsy by IR pending. Although the full work up has not been completed, this case of rapidly progressing cancer in a middle-aged male with history of protein S deficiency supports the hypothesis that protein S, in addition to its role in anticoagulation, may regulate cell-cycle and play a role in preventing tumorgenesis.
**Lucas Labine**  
David Lauterbach, MD, Samuel Ives, MD

**Undiscovered bullous emphysema and respiratory arrest; when ECMO becomes necessary**

Improvements in extracorporeal membrane oxygenation (ECMO) availability and use in patients with respiratory failure has allowed for more lifesaving treatment options. In patients who have little ability to self-oxygenate due lack of viable lung at baseline, ECMO becomes the only realistic option in times when the lungs are injured even further.

A 52-year-old man with known history of cigarette use presented to the Emergency Department with worsening dyspnea, fatigue, and intermittent hemoptysis. Four days prior, he was driving a city bus and was in a motor vehicle accident, causing the steering wheel to impact his left chest. At baseline, he could walk 1-2 miles without dyspnea, but now standing for 6 minutes took maximum effort. One day after his accident, he began having multiple episodes of bright red hemoptysis, each producing about a half cup of blood. Initially he was brought in by ambulance to the HCMC stabilization room for severe hypoxia with oxygen saturation of 76%, which rapidly improved with oxygen via nasal cannula. He had distant but clear breath sounds bilaterally, and no obvious deformity or ecchymosis near the impact site on exam. Imaging revealed massive bullous emphysema and a left lung infiltrate. This impressive bullous emphysema was unknown at the time of presentation. He was admitted overnight with oxygen and pain control, and reported increased dyspnea and pain in the morning. He then went into a respiratory arrest, which resulted in rapid sequence intubation and transfer to the MICU. Repeat imaging showing substantially increased bilateral pleural effusions and a worsening left lung infiltrate (thought secondary to pulmonary contusion). Given his lack of adequate ability to oxygenate with what little lung he had left, ECMO was initiated using venous-venous access on hospital day 2. After a prolonged ICU course, he was taken off of ECMO on day 15 and continues to be intubated with improvements of the infiltrate seen on chest imaging.

Advances in ECMO offer an additional method of oxygenation in patients with respiratory failure when other conventional treatments options are not appropriate. This case illustrates how a traumatic injury on top of chronic lung disease can dramatically change a patient’s respiratory status, and how ECMO allowed the patient to stabilize and begin the healing process with a hopeful recovery.

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**Karl Lafleur**  
Dr. Andrew Olson

**Are we related or not?**

A physician’s decisions are unavoidably influenced by cognitive biases. In the following case, the medical team was delayed in finding a correct diagnosis due to an anchoring bias and pursuit of an “interesting diagnosis”. A 32-year-old man with a history of polysubstance abuse was admitted with lethargy, rib pain, and bilateral shoulder pain from a bike accident. His blood cultures were positive for MRSA, and on the third hospital day, he developed ascending flaccid bilateral lower extremity paralysis and urinary retention. While the possibility of spread of infection to the spinal cord was considered, the presence of lower motor neuron signs was emphasized, and thus the differential diagnosis prioritized medication side effects, toxin-associated myopathy and Guillain-Barre syndrome. An MRI limited to the lumbar region was normal. When neurology was consulted on day 7 of admission, 4 days after onset of neurological symptoms, Guillain-Barre syndrome was considered most likely etiology despite the temporal relation to patient’s bacteremia. An LP revealed leukocytosis with marked elevation of protein but sterile cultures. A cervical/thoracic/lumbar MRI was performed that revealed a large epidural abscess with osteomyelitis in the cervical and thoracic spin. He was taken urgently for a laminectomy and evacuation of epidural abscess and has had a protracted recovery.

In this case, the team anchored on flaccid paralysis, its classic differential diagnosis, and it took significant time to move on to another diagnostic consideration. Over 150,000 patients in the US experience diagnosis-related harm on an annual basis, and research suggests 75% of diagnostic errors have at
least a partial cognitive origin. All clinicians experience cognitive errors, and residents, when specifically asked about cognitive errors, listed anchoring bias as the cognitive error they most commonly recognized themselves making retrospectively. One technique shown to increase diagnostic accuracy includes required reflection by residents. It is clear that educational and clinical innovations are needed to decrease diagnostic error and mitigate the effects of cognitive biases.

Katelyn Madigan
Rachel Busko

Anatomical Case Study: A Unique Perspective on Tetralogy of Fallot

As the most common cyanotic congenital heart defect, 5 out of every 10,000 infants is born with a complex cardiac condition classified as Tetralogy of Fallot. The shunting of oxygen-poor blood away from the lung vasculature into the systemic circulation often leads to cyanosis, due to the mixing of oxygen-poor blood with oxygen-rich blood. Defined as a congenital condition consisting of four cardiac defects: ventricular septal defect (VSD), overriding aorta, pulmonary stenosis, and right ventricular hypertrophy, the mortality of those living with Tetralogy of Fallot beyond age 6 was previously around 50% without surgical intervention.1 In this 14-year-old specimen procured from Lifesource, the patient underwent corrective Tetralogy of Fallot repair at 3 months of age. Specifically, the surgical intervention included pericardial outflow augmentation of pulmonary valve into main pulmonary artery and VSD closure. The purpose of this study is to create educational images of the novel cardiac anatomy of Tetralogy of Fallot from an internal and external perspective utilizing three-dimensional modeling and internal imaging of a perfusion-fixed heart.

Since neither heart nor lungs were viable for transplantation, this specimen was procured via Lifesource and donated for research. The cause of death was profound hypoxic ischemic encephalopathy following RV-to-PA conduit placement with a 24-mm pulmonary homograft with proximal CorMatrix patch augmentation.

First, images of the fresh heart-lung en bloc were obtained with care to maintain appropriate attitudinally correct anatomic positions: including the lungs while both inflated and deflated. Next, the great vessels were cannulated and the specimen perfusion fixed for 24 hours, in an end-diastolic state. Subsequently, the heart was rinsed in water for several days and then a fiberscope was utilized to record images of the internal anatomies of the various chambers and outflow. The great vessels were hooked up to a water low system so to mimic blood flow through the heart and to allow for additional structure dilation.

Additionally, external images of the heart-lung en bloc were obtained after the heart had been perfusion-fixed and cannulated. A CT scan of this specimen was also performed to obtain high resolution DICOM image stacks which then allowed us to produce 3D digital models using Mimics software. We generated three-dimensional models of heart tissue, coronary vasculature, blood volumes, as well as interactive models. Subsequently, the three-dimensional printing of these models provided for tangible tools to aid in visualizations.

Using the available methodologies within the Visible Heart® Laboratory, we hope to provide novel perspectives as to one patient’s Tetralogy of Fallot anatomical features. The resultant images and models should aid in a greater understanding of both internal and external anatomical alterations and the results of a post-surgical repair, as this condition commonly necessitates medical intervention early in the life of the patient.
Survived Cardiopulmonary Arrest in the Setting of Metastatic Carcinoid

A 61 year-old man with a long-standing history of metastatic carcinoid presented after cardiac arrest. The patient collapsed in his driveway and received immediate bystander CPR. Upon EMS arrival, he was found to be in ventricular fibrillation and was shocked twice before return of systemic circulation. Subsequent ECG revealed sinus tachycardia without ST elevations. The patient was stabilized in the Emergency Department where he was intubated for airway protection. His vital signs were normal and initial labs demonstrated mild hypokalemia (potassium of 3.3) and an undetectable troponin level. Computed tomography of the chest and abdomen showed a mesenteric soft tissue mass consistent with his known carcinoid tumor and innumerable liver lesions suggestive of metastatic disease. An arterial line and a femoral venous cooling catheter were placed and therapeutic hypothermia was initiated. Transthoracic echocardiography revealed normal left ventricular function but severe tricuspid regurgitation and moderate right atrial enlargement. Fixation of the septal tricuspid leaflet was present, consistent with carcinoid heart disease.

Following initial stabilization, additional history was obtained from the patient’s family. The patient had been diagnosed with carcinoid tumor 15 years prior and hadn’t seen his oncologist for many years. Instead, he’d traveled to Mexico several times for alternative treatments. His symptoms included episodic flushing and diarrhea. Recently, his bouts of diarrhea had increased in frequency, with several day-long episodes occurring each month. He also developed labile blood pressures with hypotensive episodes, prompting the recent discontinuation of his amlodipine and lisinopril.

After completion of the cooling protocol, the patient was rewarmed. He awoke and had no focal neurologic deficits, but exhibited moderate cognitive difficulty with short-term memory loss that gradually improved during his hospitalization. Continuous cardiac monitoring did not reveal an underlying arrhythmia. Coronary angiography demonstrated no significant atherosclerosis. At the recommendation of his cardiologist, the patient underwent placement of an automatic implantable cardiac defibrillator.

This case highlights a unique presentation of ventricular fibrillation and cardiac arrest in a patient with metastatic carcinoid tumor. Carcinoid tumors are rare neuroendocrine malignancies that release many vasoactive substances including serotonin, histamine, and bradykinin. This patient had evidence of carcinoid heart disease, reflecting chronically high levels of circulating vasoactive substances. We believe that this patient's ventricular fibrillation was most likely caused by sympathetic activation resulting in increased cardiac excitability. An alternative explanation for his ventricular fibrillation is notably absent. Although mildly hypokalemic on presentation, ECGs lacked characteristic changes of hypokalemia or QT prolongation. There are very few reported cases describing cardiac arrest in the context of carcinoid syndrome, however, at least one recent publication reported a case of carcinoid crisis-induced ventricular tachycardia.(Rupp 2016). Another case reported paroxysmal ventricular tachycardia in a dog with mesenteric carcinoid which resolved after resection of the tumor (Tappin, 2008).

Tertiary Syphilis: The Great Imitator

Since the introduction of penicillin in 1943, the number of cases of syphilis in the United States was trending downward until the late 1980s and early 1990s where there was a resurgence of primary and secondary syphilis. According to the CDC, the number of reported cases of tertiary syphilis has been rising since 2009, which may be a result of the outbreak in the late 1980s and early 1990s. Tertiary syphilis is considered a great imitator because of its ability to present with many symptoms including cardiovascular, neurologic, and dermatologic manifestations. Therefore, it should almost always be considered in a
differential for patients with multisystem symptoms without a unifying etiology. Case: A 66-year-old female with a past medical history of urinary and fecal incontinence, schizoaffective disorder, and peripheral neuropathy presented to the ED from a nursing home with increased confusion. She was admitted to the ICU and treated for sepsis thought to be secondary to either a UTI or an infection from her ulcerating leg wounds. The largest wound was located on her inner left thigh, measuring 6.5 x 7.3 x 2.5 cm, and was without pain during dressing changes. Her hospital course was complicated by HCAP and recurrent episodes of confusion. One day she suddenly lost consciousness for 3 minutes during rounds resulting in a stroke code. Emergent imaging and work-up was negative and she was back to baseline immediately. Amyloidosis was a concern given transient loss of conscience, ulcers, and presence of a protein gap. A previous skin biopsy of a skin lesion was negative with Congo red staining. As we worked up possible vasculitis causing the skin wounds, we decided to also test for syphilis with both an RPR and anti-treponema antibody screen. The RPR was negative, but the anti-Treponema was positive, suggesting either tertiary syphilis or previously treated syphilis. The RPR test has been found to be only 75-80% sensitive for tertiary/latent syphilis. A second antibody test confirmed this wasn’t a false positive. Given the patient’s skin manifestations, no reported history of syphilis and this result, it is very likely that this patient was presenting with tertiary syphilis. Furthermore, the patient was previously diagnosed with peripheral neuropathy without a history of diabetes, gait impairment for years, incontinence, confusion/dementia/mental health disorder, and possible transient seizures which could all be attributed to neurosyphilis. Unfortunately, many of these symptoms are irreversible given the late stage of the disease. She is being followed by Infectious Disease and will likely have treatment in hopes that some symptoms improve. It is unknown if the entirety of this patient’s symptoms can be explained by this diagnosis, but syphilis should be considered in patients with multisystem symptoms where other diagnoses have been ruled out.

Michael Rose

Tylenol Toxicity with a Twist: NAPQI Induced G6PD Hemolysis
Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common enzyme deficiency in humans, affecting 400 million people mostly of African, Asian, or Mediterranean descent. G6PD is inherited in a sex-linked recessive manner and offers protection against malaria. However, it increases susceptibility to hemolytic anemia from oxidative stress, often induced by infections or drugs. Acetaminophen is harmless at therapeutic levels, but at toxic doses the drug can overwhelm the liver’s conjugation system. This can lead to the production of the toxic metabolite NAPQI, the known cause of acetaminophen induced liver toxicity through oxidative damage.

A previously healthy Karen-speaking 22-year-old male presented with abdominal pain and nausea following intentional acetaminophen ingestion. History revealed suicidal ideation. Physical exam was notable for scleral icterus, lethargy and epigastric tenderness. Laboratory analysis revealed that the patient was in hyperacute liver failure with an AST of 13,034, ALT of 10,830, total bilirubin of 10.6 and direct bilirubin of 2. Acetaminophen level was 10.8 approximately three days post ingestion. The remainder of possible ingestion workup was negative. The patient was immediately started on N-Acetyl-Cysteine (NAC) protocol for his acetaminophen overdose.

His symptoms and liver function tests improved while on the NAC protocol. On hospital day four the patient was noted to have conjunctival pallor. A complete blood count was ordered revealing a hemoglobin of 5.7 down from 15.0 on admission. Hemoglobin had not been checked in the interim. Additional laboratory analysis revealed decreased haptoglobin and increased LDH concerning for hemolytic anemia. Coombs was negative. A peripheral smear showed bite cells with possible Heinz bodies. Given the patient’s ethnicity and smear findings, concerns for possible underlying G6PD deficiency were raised.
The patient received 2 units of packed red blood cells and his hemoglobin stabilized at 8.5. A G6PD level was sent from original blood tubes and confirmed the diagnosis of G6PD. The underlying inciting cause of his acute hemolysis was explored. As he had no signs of infection and no other medication exposures besides NAC, the most likely cause of hemolysis was deemed to be high levels of the toxic byproduct of acetyaminophen, NAPQI this triggered an acute severe hemolytic episode.

This case depicts acetaminophen overdose as a possible trigger for G6PD-associated hemolysis. It demonstrates the need for vigilance for signs and symptoms of G6PD hemolysis in susceptible populations when managing acetaminophen overdose.

<table>
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<th>Lacie Schulte</th>
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<td><strong>Syncope of unknown etiology</strong></td>
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<td>Introduction: Evaluation and diagnosis of syncope is complicated by the multitude of possible etiologies ranging from cardiac to neurogenic to orthostatic. Undiagnosed syncopal episodes can be devastating for patients, forcing them to drastically alter their lifestyle in some cases. This case presents a rare cause of syncope that is important to consider in diagnosing syncope of unknown etiology.</td>
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<td>Case Description: Fifty three year old Caucasian male with one and a half year history of syncopal episodes of unknown etiology admitted on 6/14/16 after three consecutive episodes of syncope while at the bank. Past medical history significant for chronic back pain controlled with tramadol, pregabalin, gabapentin, tizanidine, oxycodone, and flexeril, anxiety controlled with amitriptyline, and diabetes mellitus controlled with glipizide XL and metformin. The patient had been experiencing syncopal episodes over the past one and a half years. Patient noted that his symptoms began after an altercation involving strangulation. Previous work-up included an event monitor in early 2016 that showed syncopal events occurring during normal sinus rhythm. Thought to be unrelated to positional changes, including most recent episode. There was no prior TTE or neurological work-up.</td>
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<td>Emergency department evaluation revealed hemoglobin 11.0, elevated creatinine (3.56), negative troponin, and normal chest XR. Upon admission, the patient was placed on continuous cardiac monitoring. Amitriptyline and tizanidine were held due to possibility of contribution to syncope. Cardiology and neurology were consulted for further workup.</td>
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<td>The cardiology team performed carotid massage and this produced syncopal symptoms similar to the patient’s prior episodes There was a 3.5 second sinus pause noted on cardiac monitoring during this time. The patient was diagnosed with carotid sinus hypersensitivity and definitive management with pacemaker placement was pursued.</td>
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<td>Discussion: Carotid sinus hypersensitivity is a rare cause of syncope accounting for approximately one percent of syncope. It can be diagnosed using carotid sinus massage (CSM), performing CSM on both the left and right sides for ten seconds each in the supine and erect positions. A positive response including asystole for greater than three seconds, a drop in blood pressure, or a combination of both is diagnostic for the cause of syncope. Diagnosing carotid sinus hypersensitivity can be easily done with a CSM and thus should be part of the workup for syncope of unknown etiology.</td>
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<th>Frédérique St-Pierre</th>
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<td><strong>Psychic Moans: An Unusual Presentation of Hypercalcemia from Multiple Myeloma</strong></td>
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| Hallucinations are defined as the perception of an object or event in the absence of an external stimulus. Although visual hallucinations are commonly
associated with psychiatric disease, the differential diagnosis is in fact quite broad. It is important for physicians to maintain an adequate level of suspicion for serious and sometimes life-threatening underlying conditions. A previously healthy 65 year-old woman presented to the hospital with a five-day history of nausea and fatigue. She also had a recent history of visual hallucinations occurring sporadically throughout the day, each lasting for a few minutes. These hallucinations were distressing to her, and consisted of cursive writing on the walls. She had no apparent delusions, agitation, or disorganized speech. Past psychiatric history was negative. Her physical exam was unremarkable; she was fully alert, attentive and oriented. Laboratory investigations were significant for hypercalcemia with a total calcium of 14.1 mg/dL, acute kidney injury with a serum creatinine of 2.5 mg/dL, and normocytic anemia with a hemoglobin of 11.5 g/dL. She was treated with IV fluids and furosemide, and her visual hallucinations completely resolved within three days. Her calcium normalized quickly, but her creatinine remained elevated despite fluid administration. Further investigations revealed suppression of parathyroid hormone at 10 pg/mL, as well as elevated serum and urine protein with a serum IgG lambda M-spike of 1.4 g/dL. Renal biopsy showed evidence of cast nephropathy. Bone survey revealed no lytic lesions but did show scattered osteopenia. A bone marrow biopsy was performed and confirmed a diagnosis of an IgG lambda multiple myeloma. Psychosomatic manifestations of multiple myeloma, unrelated to hypercalcemia, have been described in the literature on a few occasions. Some case reports have documented mood disturbances such as depression or mania, and a study has reported four cases presenting with delirium. Isolated visual hallucinations, however, have rarely been described. A recent case report has documented a patient presenting with visual hallucinations three months prior to having overt symptoms of the malignancy. Potential causes for hallucinations in multiple myeloma include hypercalcemia, renal failure and infections. It has also been hypothesized that increased cytokine levels may be contributory. In this vignette, the clinical evolution suggests hypercalcemia as the most likely culprit. Visual hallucinations in patient with hypercalcemia have in fact been described, and are best underscored in the classic “painful bones, renal stones, abdominal groans, and psychic moans” of primary hyperparathyroidism. This case highlights the importance of keeping an elevated level of clinical suspicion for malignant causes of visual hallucinations, as these may be the first presenting symptom of cancer-associated hypercalcemia. Timely diagnosis and initiation of effective therapy directed at the underlying cause are essential in optimizing patient outcome and in reversing disturbing and anxiety-inducing symptoms of visual hallucinations.

Quality Improvement- Medical Students

Kellen Albrecht  
Kathryn Del Valle, Anita Krehnke, Albertine Beard

“Who Are You and What Do You Do?” Improving Team Member Role Clarity During Emergency Responses with Identification Stickers

Emergency responses in a healthcare setting are often chaotic and it is sometimes difficult to know who is performing which role – code leader, recorder, respiratory, nursing, anesthesia. Individual providers rarely know each other personally given large departmental sizes and rotating resident providers.

Various models of role clarity in code emergency responses have been designed and implemented to various degrees at hospitals throughout the United States. Examples of this include specific standing positions around a patient’s bedside and code leaders wearing brightly covered vests or hats. At the MVAHCS, there were “Code Leader” stickers on the code carts that were only occasionally being utilized. After extensive discussion with the code team members and leaders of the respective departments on the CPR committee, we decided that there was significant room for improvement in the area of role identification and clarity –
in other words, knowing which people were performing which roles in a particular situation. Often, 1-2 members of the team would personally know each other but then not know the other providers. Furthermore, we observed that it was quite rare for anyone to announce their role when they arrived at a code. Thus, we decided that role identification would be a valuable target for a quality improvement intervention. Starting in late November 2015, we distributed the above stickers, color-coded by professional role, to the core members of the code teams. These were intended to be placed on their upper chest as providers made their way to an emergency response. The stickers were utilized by staff in a variety of other ways as well – placed on equipment and badges. Code emergency responses are generally chaotic, but color-coded role stickers are one way to help alleviate confusion and frustration among code team members, as shown by survey results above. Overall compliance and employee buy-in to the program were large barriers to overcome. This may have masked more promising results, both in terms of employee satisfaction and outcome data.

Take-Home Points:

* Changing hospital culture is quite challenging—encountered resistance
* Interprofessional collaboration is crucial when implementing multidisciplinary change
* Compliance was actually lowest amongst MD providers overall
* Even when a problem is widely agreed upon (in this case, role clarity at codes), there is often significant resistance to any proposed solution/change

Future Plans:

After discussion with CPR committee, we are currently planning for the program to continue next year, with stickers being managed by VA Chief Resident of Quality and Safety.

| Oliver Jeremie  
| Archna Patel, John Bachman MD |
| Oral Rehydration Therapy Training and Clinical Simulation Experience in Preparation for International Medical Mission Trip to Nicaragua |
| In order to better prepare the medical, graduate and undergraduate students participating in our international medical mission trip to Nicaragua, we prepared and presented a discussion on Oral Rehydration Therapy (ORT) prior to the international experience. Additionally, a clinical simulation experience was incorporated into our pre-departure training to instruct the students on basic clinical skills, medical interviewing and teamwork. As a tool to measure the students’ prior knowledge on the topic of ORT, we designed a questionnaire which was distributed and collected prior to the training and simulation experience. Finally, one day after the ORT training and simulation experience, we distributed the same questionnaire and collected the results in order to measure the efficacy of the training and simulation, as well as the students’ retention of the information and skills taught. Our study population consisted of nine first-year medical students, one graduate student, and sixteen pre-medical students, all of whom participated in all aspects of the study. In the pre-training survey, only five of the students indicated that they could effectively explain or administer ORT to someone else. After collecting the results from the post-training survey, all of the students indicated that they could effectively explain or administer ORT to someone else. We concluded that the ORT training and clinical simulation experience, wherein students could actively apply the knowledge they gained on the administration of ORT to patients, are effective tools to aid in the preparation of medical, graduate and undergraduate students prior to embarking on international medical mission trips. |

| Kirsten Larson  
| Kayla Schenheit, Linda Olson Bergum, MD |
| Increasing Primary Care Physicians’ Understanding of Agent Orange Exposure and Type 2 Diabetes Mellitus in Vietnam Veterans |
| The Committee to Review the Health Effects in Vietnam Veterans due to Exposure to Herbicides has found that exposure to Agent Orange is linked to a number of chronic medical conditions including Type 2 Diabetes Mellitus. The |
American Diabetes Association estimates the average annual medical cost for an individual with Type 2 Diabetes to be over $13,000 a year. Fortunately, Vietnam veterans who were exposed to Agent Orange and who have been diagnosed with Type 2 Diabetes can apply for disability benefits to completely cover this cost. Unfortunately, we have noted that many Vietnam veterans and primary care physicians outside of the VA medical system are unaware of this. The results of both a literature review of Agent Orange exposure and its correlation to Type 2 Diabetes, as well as interviews of 15 Vietnam veterans suffering from Type 2 Diabetes will be presented. As more rural Minnesotan veterans are expected to access care from their local non-VA healthcare providers after the passing of the Veteran Access to Care Act, it is important to bring primary care physicians up-to-date on healthcare concerns specific to the veteran population, including the association between Type 2 Diabetes and previous Agent Orange exposure.

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<th>Research- Medical Students</th>
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<td><strong>Prakriti Gaba</strong></td>
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<td>Ammar M. Killu, MBBS;</td>
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<td>Niyada Naksuk, MD;</td>
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<td>Christopher V. DeSimone,</td>
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<td>MD,PhD; Samuel Asirvatham, MD, et al.</td>
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**Percutaneously Deployed Epicardial Defibrillation: A Novel Device-Based Therapy**

Current implantable defibrillation devices require surgical, primarily endovascular, access. This may result in endovascular complications and valve trauma, among other complications. While epicardial defibrillation has been utilized in the past, these devices were also complicated by surgical complications as well as device malfunction and notable extra-cardiac stimulation. In this study, our aim was to develop a percutaneously deployed epicardial defibrillation system with partially-insulated epicardial coils to decrease occurrence of defibrillation associated complications.

**Methods:** We created and tested 2 percutaneously deployed epicardial defibrillation systems, the first of which is a partially-insulated defibrillation coil and the second, a defibrillation mesh with a urethane balloon acting as an insulator to the face of the mesh not in contact with the epicardium. In both cases, the anode and cathode were located within the pericardial space to decrease the level of extra-cardiac stimulation. To measure workability and ability to terminate ventricular arrhythmia, we computed the average energy associated with a chance of successful defibrillation 75% of the time (ED75) and recorded the lowest energy resulting in successful defibrillation.

**Results:** Of 16 animal experiments, 13 (6 canines (29.8±4.0kg); 7 pigs (41.1±4.4kg)) were analyzed. Average ED75 was 12.8±6.7J (10.9±9.1J for canines; 14.4±3.9J in pigs \[P=0.37\]). The lowest ED75 was 2.5J in canines and 9.5J in pigs, while the lowest energy resulting in successful defibrillation was even lower (2J in canines and 5J in pigs). In all experiments, there was no evidence of coronary vessel injury, phrenic nerve damage (detected by pacing), or trauma to extra-pericardial structures including lung pleura.

**Conclusion:** Percutaneously-deployed epicardial defibrillation consisting of a partially insulated coil is feasible, safe, and associated with low defibrillation thresholds.

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<th>Chalene Gaw</th>
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<td>Aaron Leppin, MD, MSc</td>
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**Exploring primary care physicians’ readiness for clinical integration of evidence-based health promotion programs in communities**

Introduction: In 2018, Medicare will begin reimbursing community organizations for delivery of evidence-based health promotion programs, starting with the National Diabetes Prevention Program. It remains unclear whether effective community programs can be integrated with clinical practice and whether primary care physicians will be able and willing to engage. We sought to evaluate primary care physicians’ perceptions of their own readiness for integration of community-based programs.

**Methods:** As part of a parent project focused on implementing a community-based program called the Chronic Disease Self-Management Program (CDSMP), we contacted stakeholders from all (n=5) health systems across an 11 county region of Southeast Minnesota and asked for permission to survey
their actively practicing primary care physicians. We administered the 13-item survey over a 4-month period in the Spring of 2016 in either electronic or paper format and via complete or convenience sampling based on health system preference. Survey items assessed physician beliefs, knowledge about, and perceived barriers to integration of and referral to community resources generally, and the CDSMP specifically. We calculated response rates as feasible, used standard descriptive statistics to characterize respondents, and used chi square tests of association to test for key differences across groups. Results: We administered surveys to physicians from the 3 largest health systems in the region. 122 responded overall [65, 53% Family Medicine (FM); 38, 31% Internal Medicine (IM); 19, 16% other]. About half (54%) of the respondents cared for patients of low socioeconomic status and two-thirds (66%) cared for the elderly. 64 (53%) practiced in an urban or suburban setting, while the rest (47%) practiced in rural areas. Overall, 95% of the respondents reported that they believed community resources were important components of effective primary care and 69% felt they were underutilized in their practice. “Lack of awareness or education” about the CDSMP and its benefit was the most commonly reported barrier to referral, being cited by 69% of all physicians. These findings were consistent across clinical specialty (FM and IM) and urban or rural practice setting. IM physicians were more likely to cite lack of program feedback (P<0.01), lack of a system for referrals (P<0.01), and potential burden to patients (P<0.01) as referral barriers than their FM counterparts. FM physicians were more concerned about a lack of patient acceptance of the program (P<0.01).

Conclusion: Primary care physicians believe that evidence-based health promotion programs in community settings can benefit their patients and that they are underutilized. Physicians may require more specialty-tailored education about these programs and their benefit before they will feel comfortable referring their patients to them.

**Methods and Characterization of the Effects of Dietary Sulfur on Gut Microbiota H2S Production**

The emerging interest in gut microbiota have brought upon many investigations to explore its implications in human health. A characteristic increase in hydrogen sulfide (H2S) production in gut microbiota has been observed in patients with Inflammatory Bowel Disease (IBD). H2S is hazardous if accumulated in the colon and can directly inhibit cytochrome c oxidase, thereby preventing oxidation of short chain fatty acids that serve as 70% of the energy source used by colonocytes. In combination with the ability of H2S to directly damage DNA, this oxidative stress event can ultimately lead to break down of the gut mucosal barrier, cause translocation of pathogens from the lumen, and lead to chronic inflammation as associated with IBD. It is believed that altering the diet, specifically by reducing intake of sulfur containing foods such as protein, can directly modify the H2S production from sulfate reducing bacteria (SRB) and decrease inflammation.

In a pre-pilot study, a healthy volunteer participant was randomized to start on either a low suffer diet or a high sulfur diet for 4 days prior to a 3 day wash out period of normal diet before beginning any intervention. Fecal samples were collected throughout each period and were prepared for gas analysis through gas chromatography. Using the Nutrient Data Research System (NDRS), we were able to confirm relative total consumption of sulfur in both dietary interventions based on detailed food records. We found a statistically significant decrease in H2S production on a low sulfur diet compared to a high sulfur diet and observed an increase in H2S production on a high sulfur diet. The results of this study provide a stepping stone to an evidence-based dietary intervention that may serve as a promising alternative or adjunct to current invasive treatments used to manage IBD.
Predicting Bacterial Infection in Immunocompromised Patients: Procalcitonin compared with SIRS

Systemic inflammation due to bacteria continues to be a difficult to diagnose yet common cause of acute illness and mortality in healthcare. The diagnosis and treatment of bacterial sepsis is often complicated partly due to health care providers inability to differentiate systemic inflammation due to infection vs noninfectious causes. Both bacterial sepsis and noninfectious sources can lead to symptoms of pyrexia, tachycardia and tachypnea, often referred to as systemic inflammatory response syndrome SIRS. SIRS alone is often inadequate in diagnosing bacterial sepsis with some studies reporting that a significant proportion of patients with bacterial sepsis do not have SIRS at presentation. Given the consequences of missing a diagnosis of bacterial sepsis and the prognostic value of starting treatment, early researchers have recently turned to the biomarker Procalcitonin as a way to better the detection of bacterial sepsis and improve treatment decisions.

We conducted a retrospective cohort study of immunosuppressed adults at the University of Minnesota Medical center from 2011-2014 by comparing corresponding SIRS scores and PCT measurements collected within 24 hours of each other. Positive blood cultures within 3 days of the collected PCT indicated active bacteremia. SIRS was defined as having met two of the following criteria. WBC >12 <4 , temp >100.4, heart rate >90 and respiratory rate >20. In immunosuppressed patients with bacteremia, PCT was found to be significantly associated with bacteremia (OR 2.1660, 2.5295, p<0.005). By comparison, SIRS scores were not significantly associated. Using a multivariate logistic regression model log PCT we found that for each unit rise in log PCT the probability for bacteremia increased regardless of immuno status. Additionally, as log PCT increased the probability for exhibiting SIRS increased in immunocompetent patients. However, in immunosuppressed patients there was a lower probability of exhibiting a SIRS response at any given PCT level.

Procalcitonin is a more predictive test of bacterial infection than SIRS in immunocompromised patients.

Characterization of a novel Sos1 transcript in B-Cell Acute Lymphoblastic Leukemia

Introduction: B-cell acute lymphoblastic leukemia (B-ALL) is a rapidly progressing cancer of bone marrow lymphocytes caused by genetic alterations that increase progenitor B-cell survival and proliferation. Using a transposon-based mutagenesis screen we found that Sos1 was one of the most frequently targeted genes in B-ALL, resulting in truncation of its amino terminus and 3'UTR. Neither the exact location of the 5’ and 3’ truncations, nor the functional importance of the 3' UTR change are well understood.

Methods: The novel Sos1 transcript was characterized using 5’ and 3’ Rapid Amplification of cDNA Ends (RACE) and RNA sequencing analysis. The transcript was interrogated in various murine models of B-ALL, including Pax5 +/- x Ebf1 +/- mice, which spontaneously develop B-ALL. Independent RT-PCR-based validation was conducted to affirm the transcript defined using RACE. Luciferase assay analysis of the 3’UTR was conducted to understand its impact on transcript stability. The human TARGET database was examined to see if similar truncations occur in human B-ALL.

Results: The Sos1 gene is coded across 22 exons on chromosome 17. We observed a consistent 5’ truncation between exons 8 and 9 of Sos1. Using 5'RACE we discovered the presence of a Riken (F420015M16Rik) gene fused to the 5’ end of exon 9 within all truncated transcripts. Interestingly, Sos1 and the Riken gene are normally transcribed in opposite directions. Their fusion in B-ALL suggests that a genomic microinversion occurs at this locus during oncogenesis. RT-PCR-based validation confirmed the 5’ transcript fusion for multiple Pax5 +/- x Ebf1 +/- models. RNA sequencing of both Riken and Sos1 transcripts showed dramatic upregulation within the region of the truncated transcript. All other portions of both genes maintained normal expression,
suggesting one allele may be intact. In leukemias with 5’ Sos1 truncation, the 3’UTR was also consistently terminated approximately 1000 bps into the 3’UTR. To characterize the functional impact of this truncation, the truncated and full-length 3’UTR sequences were each cloned 3’ of a luciferase gene to assay for regulatory function. We observed reduction of luciferase expression (vs positive control) with the addition of each 3’UTR. This decreased stability aligns with the observed presence of various regulatory elements within the 3’UTR, such as microRNAs. Finally, multiple human B-ALL samples in the TARGET database exhibited increased expression of 5’ truncated SOS1 transcripts suggesting that this may be an important event in human B-ALL. Conclusion: We characterized an aberrant Sos1 transcript observed in multiple leukemia models and began to disentangle the network of interacting genomic changes contributing to B-ALL. By understanding the contribution of the truncated Sos1 transcript to B cell transformation, we may focus further studies on a key signaling pathway in disease pathogenesis, increasing our potential for therapeutic targeting in patients.

Jessica Sjoholm
Kevin O'Donnell, Lauren Reagan, Dr. Andrew Olson

Does This Patient Have a Necrotizing Soft Tissue Infection?
Background: Necrotizing soft tissue infection (NSTI) is a life-threatening condition with a high mortality rate that affects people of all ages. Making this diagnosis is often challenging because many clinical signs do not appear until late in the disease course and there are few validated, easily used clinical decision support tools to aid in diagnosis. A high index of suspicion is fundamental, since the diagnosis can only be definitively made at time of surgical exploration. However, it is not reasonable to have all patients with severe skin and soft tissue infection surgically explored and tools are needed to help improve this clinical decision.

Methods: We searched Medline for all studies pertaining to the diagnosis of NSTI, including history, physical examination, laboratory, and imaging tools. All studies with less than twenty patients were excluded. We maintained a strict reference standard requiring all diagnoses of NSTI to be confirmed by surgical exploration or histopathology; the absence of NSTI was defined as clinical resolution with medical treatment alone or negative histopathology and/or surgical findings. Two investigators screened all titles and abstracts for full text inclusion.

Results: Of 2424 studies screened, 146 studies have thus far met our inclusion criteria, of which 8 were prospective studies. A preliminary meta-analysis of these 8 collected prospective studies revealed a number of findings. Overall mortality rate among the studies was 24.6% (95% CI, 15.3-33.9%). A history of diabetes, a likely risk factor for NSTI, has a sensitivity of 0.203 (95% CI 0.101-0.365). The mean lactate for patients with surgically-confirmed NSTI is 4.132 mmol/l (±0.289). Most of these studies were case series, so we were unable to report any specificities for these findings. We will incorporate updated information and analysis for the final presentation.

Discussion: The mortality rate calculated in our meta-analysis is comparable to that found elsewhere in the literature. Further research is needed, especially in the form of prospective studies that contain patients both with and without NSTI. There is much data from Southeast Asia due to the presence of Vibrio vulificans and a seemingly higher incidence of necrotizing fasciitis, but large studies from other areas of the globe are lacking. There are also many studies that focus on risk factors for mortality, although we believe that the more helpful (still unanswered) clinical question is whether or not to perform surgical exploration in a patient with severe skin and soft tissue infection.

Lauren Ward
Michael F. Goldberg, Ph.D, Marc K. Jenkins, Ph.D.

Analysis of the intracellular niche of a phagosomal pathogen in the context of Salmonella enterica infection in mice
Salmonella enterica (Se) is an intracellular pathogen that persists within phagosomes of host antigen presenting cells. Se infection stimulates a strong CD4+ T cell response that activates microbicidal mechanisms within the infected phagocyte. Despite robust immune pressure Se persists in the
mesenteric lymph nodes (MLNs) throughout the lifetime of the host. We hypothesize that during Se infection, bacteria reside within mononuclear phagocytes in the MLN that localize to areas rich in circulatory and lymphatic vessels. In order to identify infected cells, a reporter strain of Se serovar Typhimurium SL1344 was developed that expresses the red fluorescent protein dTomato in the Salmonella chromosome behind the endogenous PhoN gene (Se-dTomato). 129x1/svJ mice were inoculated intragastrically with a solution containing 108 CFU of either Se-WT or Se-dTomato and were analyzed at D14 and D30 after infection. Single cell suspensions from MLNs of Se-WT and Se-dTomato infected mice were stained with fluorescent antibodies against myeloid cell markers, including CD11b, Siglec F, Ly6G, CD64, CD11c, and MHCII, and were analyzed by flow cytometry. Sections of fixed/frozen MLN from Se-WT and Se-dTomato infected mice were stained with antibodies against a variety of cellular and anatomical markers, including B220, CD11c, CD11c, CD169, CXCL9, CXCL10, LYVE-1, F4/80, Siglec F, Ly6G, and iNOS. Images were acquired on an epifluorescent microscope.

Results: Flow cytometry analysis revealed that 77% of Se-dTomato infected cells stained positive for the canonical monocyte/macrophage marker CD64 with the remainder found predominantly in Ly6G+ neutrophils. Further in situ experiments confirmed our flow cytometry-based findings about the identity of infected cell types. Myeloid markers frequently overlapped with Se-dTomato, further demonstrating the active infection of these cells, particularly macrophages, in vivo. We reproducibly found Se-bacteria within or near CD169+ macrophages in the subcapsular sinus and in close proximity to B-cell follicles. Se bacteria also overlapped with cells expressing inducible nitric oxide synthase (iNOS), a marker for an active Th1 response.

Conclusion: Our Se-dTomato strain was successfully used to identify and track infected cells in mice, and were predominantly found in monocytes and macrophages, localized near the subcapsular sinus of the MLN and towards the periphery of B-cell follicles, following intragastric infection of resistant mice. Se-dTomato was also seen within positive staining for an active Th1 response, consistent with infection control.

Residents

Quality Improvement- Residents

Ashley Dohlen, MD
Nick Boysen, MD

Predicting and preventing inpatient cardiac readmissions: an investigation of peri-hospitalization interventions in a Minnesota

Cardiac readmissions are an ever expanding burden spanning from patients, to hospitals, all the way up to the national healthcare system of the United States. Currently, there is a lack of consensus regarding appropriate inpatient screening tests for identifying patients at high risk for readmission, as well as peri-hospitalization disease management regimens aiming to prevent readmissions. Our clinical review examined cardiac patients and their risk of 7 day, all 30 day, and non-elective 30 day readmission rates, through the mini-cog mental examination as well as a set of ten peri-hospitalization interventions.

All cardiac admissions for a one year period from December 2014 to December 2015 at Regions Hospital, an urban tertiary center in Minnesota, were analyzed via EMR in a retrospective observational study. Each cardiac patient admitted during this time underwent mini-cognition evaluation with results recorded as either pass or fail. Additionally, each congestive heart failure patient’s chart was reviewed to assess which peri-hospitalization interventions he or she received. The ten interventions were: free weighing scales, MTM Pharmacist, complex disease management consultation, outpatient cardiology appointment within two weeks, community paramedic program, simplified heart failure booklet, heart failure refrigerator magnet, outpatient cardiac rehabilitation, inpatient cardiac rehabilitation, and a home health aide nurse. Chi square analysis was used to determine any association between mini – cog test and readmission. Similarly,
A 2x2 contingency table was constructed for each of the 10 interventions vs. each of the 3 binary outcome measures (7 day, all 30 day, and non-elective 30 day readmissions); chi-square statistics and the associated p-value (at significant level of 0.05) was computed for each table to evaluate the correlation between each intervention and outcome measure.

The frequencies for the all 7 day readmission rates, all 30 day readmission rates and non-elective 30 day readmission rates for all cardiac patients are 4.9%, 12.9% and 11.2% respectively. The chi-square analyses indicated that there is no strong association between the result of the mini cog test and readmission rates in all categories. However, the average length of stay was shown to be statistically significant in affecting the all readmission rates.

In review of interventions received by congestive heart failure patients, no intervention was found to have lower rates of readmission for 7 day readmission, all 30 day, and non-elective 30 day readmission.

A failed mini-cognition testing in all cardiac patients was not associated with higher readmission rates. However, in this analysis, it was found that a higher length of stay was statistically significant for higher readmission rates in all categories. In analyzing the congestive heart failure subset of cardiac patients, no one intervention received was found to have a statistically lower rate of readmission.

David Flood, MD
Kate Douglas, Vera Goldberg, Boris Martinez, Pablo Garcia, MaryCatherine Arbour, Peter Rohloff

Use of control charts to assess for longitudinal diabetes panel improvement: A quality report from a resource-limited setting

Quality improvement (QI) is a key element of strengthening health systems in low- and middle-income countries. There have been limited published applications of statistical process control methodologies like control charts in resource-limited settings or with longitudinal diabetes panels in high-income countries.

This study reports on a QI project in rural Guatemala. The primary aim was to show improvement in glycemic control of a small panel of adult ambulatory diabetes patients as measured by an absolute reduction in mean hemoglobin A1C and an increase in the proportion of patients meeting hemoglobin A1C goal.

This project utilized the Model for Improvement as its QI framework. A bundle of improvement activities was developed based on formative research. The analytic sample was comprised of 56 patents with five years of clinical data available. Traditional statistical testing and control charts were used to assess for improvement.

Mean hemoglobin A1C decreased from 9.1 ± 2.1% to 8.2 ± 1.9% after one year of the QI intervention (p=0.001) and 8.6 ± 2.1% after two years (p=0.01). The proportion of patients meeting goal hemoglobin A1C < 8% declined significantly after one year (p=0.049) but not after two years (p=0.39). Control charts of mean hemoglobin A1C and proportion of patients meeting target hemoglobin A1C showed statistically significant improvement as special cause were identified during the intervention period.

Diabetes quality improvement work is feasible in resource-limited settings in LMICs and can improve glycemic control among diabetes patients. Statistical process control charts are a promising methodology for use with panels or registries of ambulatory diabetes patients.

Teresa Fox, MD
Ryan Miller, MD, Benji Mathews, MD, Alex Ramirez, MD, Miguel Ruiz, MD

Diagnosing Our Documentation: An Electronic Peer-Feedback Program to Improve the Quality of Provider Notes

The advent of the Electronic Health Record (EHR) has changed the face of medical documentation. Illegibility and absence of data have all but disappeared, and EHRs can foster thoughtful assessments by providing a platform to craft differential diagnoses and note unanswered questions. However, EHRs have also introduced features like “copy and paste” and “blow in” templates that can compromise documentation quality. Additionally, providers must spend an increasing amount of time fulfilling legal and billing requirements that are linked to electronic documentation. Considering the
central role of EHRs in modern health care, there is a growing movement to define the characteristics of quality electronic documentation and encourage EHR users to adopt these features. Only a handful of prior documentation quality improvement projects have been published. One group validated a documentation evaluation tool, named the Physician Documentation Quality Instrument 9 (PDQI-9), which assists note reviewers in assessing nine note attributes. The few published studies utilizing this tool have been limited to residents and outpatient providers. The aim of our project was to improve the quality of inpatient progress notes written by hospitalists at a large tertiary care medical center through a structured peer evaluation system using the PDQI-9.

In the first phase of our project, thirty-nine hospitalists were anonymously assigned to evaluate one note from three different colleagues. Participants used the PDQI-9 tool to produce a numerical score in each of the nine categories and were also encouraged to provide free text commentary. In return, participants received feedback on three of their own progress notes. In the second phase, which is currently underway, we are repeating the evaluation process. After the completion of the project we plan to have participants complete a short post-project survey to assess their perceptions of the project.

While our study is not yet completed, we have preliminary results from phase one. The mean note score for all participants across the nine note attributes assessed in the PDQI-9 ranged from 4.27 – 4.68 (possible 0-5). The mean overall score for participants for the first phase was 40.38 (possible 0-45), with scores ranging from 24-45. After we have received the evaluations from the second phase we will compare the scores from phase one with those from phase two. We expect that after receiving feedback on notes participants will score higher in the second phase. We hope to foster a culture of high quality documentation among a group of hospitalist providers through this structured feedback project.

Although there are limited systematic mechanisms for providers to give and receive feedback about their documentation, establishing opportunities such as this is critical to improving note quality, in turn leading improved quality of care and diagnostic performance.

Tyler Gress, MD
Robert Miner, MD

Quality, Not Quantity: Improvement in Utilization of Routine Labs in a Hospital Setting

The United States spent 3 trillion dollars and 17.5% of its GDP on healthcare expenditures in 2014. Rising costs of medical care are a constant deterrent to adequate patient treatment and follow up, particularly in those with socioeconomic disadvantage. A paradigm shift toward improving resource utilization and efficiency is paramount to continued success and quality care. One area of significant expenditure is in the utilization of routine daily lab investigations in the hospital setting.

At Abbott Northwestern Hospital, we conducted a study within the residency program to improve upon this practice. For one month, data was collected from all patients admitted to the residency service regarding patient length of stay as well as quantity of CBC, CBC with differential, and Basic Metabolic Panels (BMPs) ordered, and presence of labs on day of discharge. The intervention was a 45 minute presentation which provided education regarding recommendations/indications for monitoring, lab study specifics (test variability, cost, etc.), and facility impact. Subsequently, data was again collected with the same parameters for another month to evaluate change.

The results of the CBC, CBC with differential, and BMP baseline data, reported in number of studies per patient day, were respectively 0.51, 0.21, 0.97, for a total of 1.69 labs/day. Post-intervention results were respectively 0.21, 0.21, 0.58 for a total of 0.99 labs/day (41.4% reduction).
This study is an example of a simple intervention which resulted in significant reduction in lab utilization in a residency program. Cost analysis suggests this intervention, if applied hospital-wide, would yield saving hundreds of thousands of dollars. It should be noted the focus of these efforts is based not only on cost reduction, but also to enhance patient experience and reduce unnecessary downstream workup.

Patrick Hoversten, MD  
Miguel Teixeira Silva, Ally Higgins, Greg Pajot, Jessica Slostad, Chung Sang Tse, Carina Preskill, John Ratelle

Enhancing provider-patient communication regarding inpatient medications: A QI project

The Affordable Care Act of 2010 attempts to improve the quality and safety of care for patients receiving acute-care inpatient stays through hospital value-based purchasing. Patient experience of care as measured in the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey accounts for 30% of the standardized total performance score of hospitals. Therefore, in order to enhance value of patient centered care delivered at our institution, we aimed to improve provider to patient communication surrounding indications and side effect profiles for new medications given in the inpatient setting.

Methods: We formed a multi-disciplinary group to review our most recent HCAHPS survey data. Through an iterative approach we identified the lowest rated items. We then evaluated patients on a general medicine floor at the Mayo Clinic, with the aim to improve patient-provider communication regarding new medications and side effects, as measured by improvement of 50% through a written survey by the end of July 2016. After developing a root cause analysis we surveyed randomly selected patients to obtain baseline data. Key stakeholders were identified and interviews were conducted with residents, pharmacists, nurses, and patients. The intervention was refined through plan-do-study-act (PDSA) cycles.

For the initial PDSA cycle, a resident generated flag in the electronic medical record (EMR) at the time of order entry for all new medications was created which in turn prompted nursing to discuss the medication and possible side effects with the patient prior to administration. Continued enforcement of the intervention was encouraged by personal communication, email, and visual-aids. Our outcome was measured via patient survey on how often 1) indication for medication was given and 2) whether possible side effects were discussed. Our process measure was the percentage of new medication orders for which residents flagged the EMR.

Results: Reminders to implement the intervention led to overall resident compliance increase from 2.2 to 14.8% during the first month of our study. Our outcome measure results indicated that patient-perceived frequency of communication about medication indication was no different after intervention with a mean score of 4.5/5 compared to 4.6/5. Whereas perceived frequency of discussion of side effects improved by 56.8% from a mean of 2.3/5 to 3.6/5.

Approximately 10 hours of resident work and reminders were needed throughout the month to improve adherence to intervention.

Conclusion: Limited and short term evidence suggest electronic order reminders provide a viable and effective way to improve patient-provider communication regarding medication side effects. The level of adherence to our intervention requiring intensive dissemination strategies raises questions about its sustainability. We are currently developing a clinical decision support tool to automatically identify new medications for patients and alert nursing to provide necessary education. More research is needed to determine its effectiveness.

Pierre Tawfik, MD  
Ryan Miller, Edra Nordstrom, Christine Lambert

Improving Lung Cancer Screening with low-dose helical CT in High Risk Patients using a Nursing-driven Protocol

Lung cancer is the third most common cancer and the highest cause of cancer death in the U.S.. Early detection of the most common lung cancer, i.e. non-small cell, improves prognosis. The U.S. Preventative Services Task Force (USPSTF) recommends low-dose chest CT’s in adults aged 55-80 with a 30 pack-year smoking history who are currently smoking or have quit within the
past 15 years. Despite this, the percentage of individuals who are screened is thought to be low due to lack of awareness, time, and a system that facilitates screening for the provider. There has been prior success within HealthPartners clinics using nurse-driven screening for issues such as colonoscopies and HIV testing. Nurses populate the electronic medical record (EMR) with a notification or unsigned order as they place patients in their rooms, which remind the provider to obtain the necessary test. There is no such process for lung cancer screening. Our goal was to improve the implementation of low-resolution CT lung cancer screening for qualifying patients using this mechanism. A pre-visit plan was created for and approved by nursing staff at the HealthPartners University Ave. clinic. The plan was implemented for all clinic visits. Included in the plan was a set of questions for obtaining accurate smoking history. Nurses entered an unsigned order for CT’s for patients meeting USPSTF criteria, which was then discussed with the patient and ordered by the provider. Baseline data on lung cancer screening rates was obtained from July to December 2015. A three month testing phase was conducted to adjust the above process. Then, screening data was collected from the subsequent four months from May to August 2016. The prior-to-implementation rate of chest CT’s ordered for qualifying patients was 15% (15/98), with 13% of the qualifying patients actually completing their chest CT (13/98). Following implementation of the pre-visit plan, the rate of chest CT’s ordered for qualifying patients rose to 86% (124/144) with 26% of qualifying patients actually completing their CT (38/144). The number of patients identified as meeting criteria rose from 0.5 to 1.2 patients per day. Overall, this nursing-driven procedure for obtaining smoking history and pending Chest CT orders markedly improved the number of CT’s ordered by physicians for qualifying patients. The number of CT’s that were completed only rose to 26% of qualifying patients. Our results suggest that a more automated process within the EMR such as utilizing the existing “Health Maintenance” tab would be beneficial for lung cancer screening. Further steps include process improvement to increase the number of CT’s that are completed, improving smoking history data collection, and making lung cancer screening part of the EMR.

Research - Residents

Jithma Abeykoon, MD
Jonas Paludo and Prashant Kapoor

Outcome of Young Patients with Immunoglobulin Light Chain (AL) Amyloidosis

AL amyloidosis (AL) is the most prevalent form of systemic amyloidosis with an estimated incidence of 1:100,000 person-years in western countries. The median age at diagnosis is approximately 64 years. Clinically relevant data of very young patients (≤ 40 years at AL diagnosis) are scant. Medical records of all consecutive patients with AL evaluated at Mayo Clinic, Rochester, MN between 01/01/1995 and 12/31/2015 were reviewed. The clinical characteristics, therapeutic approach and survival outcomes of patients ≤40 years at diagnosis were analyzed. The AL diagnosis date was used for all time-to-event analysis with the Kaplan-Meier method. Of 3,433 patients, 50 (1.4%) were ≤40 years at the time of diagnosis. The median time between the onset of symptoms and definitive diagnosis was 0.4 years (interquartile range [IQR], 0.26-0.89 years). Unusual initial features included spontaneous splenic rupture (2%) and erectile dysfunction (4%), observed 6-15 months prior to the diagnosis of AL. Forty-eight percent of patients had Eastern Cooperative Oncology Group (ECOG) performance status >2 and 24 (48%) patients had involvement of ≥3 organs at diagnosis. The median bone marrow plasma cell involvement was 10% (range: 1%-90%); 6 patients (12%) had concomitant multiple myeloma defined by CRAB criteria. The median follow-up was 11 years (95% CI: 7.6-12). The median overall survival (OS) was 12.7 years (95% CI: 4.0-NR), and 1 and 10-year OS from diagnosis was 73% and 51%, respectively. The estimated average years-of-life lost was 8.6 years over 20 years of follow-up. Cardiac involvement was associated with a worse OS with median OS of 3.2 years with cardiac
Of the 50 patients, 24 (48%) patients underwent upfront autologous stem cell transplantation (ASCT) (within 6 months of diagnosis). Median OS was NR (95% CI: NR-NR) in patients who underwent upfront ASCT vs 4.2 years (95% CI: 0.2-8) in patients who did not, p≤0.0001. Six (12%) patients underwent solid organ transplantation (kidney transplant in 5 patients, heart transplant in 1 patient) due to AL-related end-organ damage.

AL amyloidosis is infrequently encountered at the age of ≤40 years, but the loss of productive years of life and disease burden are substantial. A significant delay in diagnosis from the onset of symptoms was noted in our study. Cardiac involvement remains a primary determinant of prognosis in this very young cohort. Nearly half of the patients underwent upfront ASCT, an approach associated with a better outcome. Although over one-half of patients are alive at 10 years after the diagnosis, early 1 year mortality was substantial.

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<tr>
<th>Elizabeth Gilman, MD</th>
<th>Screening for breast cancer in women with dense and very dense breasts: A survey of primary care practice</th>
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<td>Jennifer Frank, Summer Allen, Denise Dupras</td>
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Introduction: Breast cancer risk is increased by as much as 3.25 percent in women with dense or very dense breasts. More than 50 percent of women screened by mammography have increased breast density. Many states require radiologists to notify women by letter that the mammogram shows increased breast density and encouraging them to discuss this with their doctor. The purpose of this survey was to determine breast cancer screening practices of primary care providers in women with dense and very dense breasts.  
Methods: A 16-question survey was designed to determine the use of supplemental screening and assess provider knowledge, approach, comfort level and educational preference in discussions with patients with dense and very dense breasts. The survey was administered via email using REDCap Survey was sent to primary care providers (physician and non-physician) at Mayo Clinic in Rochester, MN. The survey also collected optional demographic information. All responses were collected anonymously. This study was approved by the Institutional Review Board.  
Results: Eighty-one of 178 primary care providers responded (46%). Of the respondents, 53 were physician (MD/DO) and 28 were advanced practice providers (NP/PA); 50 were female (61%). The majority (89%) counsel patients some of the time that breast density is a risk factor for breast cancer and 65% of providers reported received questions monthly from patients about breast density. Ninety percent of providers offer supplemental breast cancer screening to some patients; however less than half of providers (48%) are moderately or completely comfortable discussing supplemental screening options with patients. Most providers would like additional guidance to help them decide which patients should be offered supplemental screening as only 3 respondents consider themselves extremely knowledgeable in that area and 13 (16%) were not comfortable at all in discussing supplemental screening options. The most influential resources regarding choice of supplemental screening were lectures heard at meetings (42%) and Ask Mayo Expert (58%). Although multiple options were selected, most providers (71%) would use a risk calculation tool that includes breast density as a risk factor.  
Conclusion: Primary care providers are aware of the risks of breast density and, in general, are comfortable having discussions with patients regarding risks and ordering supplemental screening tests. The majority, however, would appreciate additional aids for counseling patients with increased breast density on cancer risks and screening options. |

| Ben Henkle, MD | The rise of blood pressure: hypertension in rural southeastern Ghana |
| Bernard Trappey, MD; Edem Agamah, MD |  
Morbidity and mortality in the developing world is increasingly driven by non-communicable diseases such as hypertension. In the sub-Saharan country of Ghana, reported rates of hypertension have drastically increased over the past 40 years. Despite this increase, there is a paucity of research on hypertension in |
the rural areas of developing countries like Ghana. A pair of cross-sectional studies were conducted in 2011 and 2016. Data was collected at community-based blood pressure screening events in the Ketu North, Ketu South, Keta Municipal, and Akatsi districts of the Volta Region in southeastern Ghana. Blood pressure measurements were obtained and the prevalence, awareness, treatment, and control of hypertension was assessed. Hypertension was defined as a systolic blood pressure of 140 mmHg or higher and/or a diastolic blood pressure of 90 mmHg or higher or self-reported treatment of high blood pressure. Student’s t-tests, Chi-squared analyses, and logistic regression were used to evaluate significant differences between the occurrence of hypertension and its associated risk factors.

Results: 1028 participants were surveyed in 2011 and 1019 participants were surveyed in 2016 for a total of 2047 encounters. Overall, the average age of participants was 45 +/- 15 years and 74% were female. Between 2011 and 2016 there was no significant difference in populations age distribution, body mass index, smoking status, or diabetes. The prevalence of hypertension decreased from 36% in 2011 to 33.5% in 2016. Reported awareness nearly doubled from 46% to 80% during the time period and treatment increased from 43% to 60%. Control significantly improved from 17% to 32%.

Conclusion: From 2011 to 2016 baseline population characteristics were largely unchanged and hypertension remained greater than 30%. While the prevalence of hypertension remains significant, over a five-year period there have been significant improvements in awareness, treatment, and control of hypertension in rural southeastern Ghana.

Angie Lobo, MD
David Tierney, MD, FACP

Walking Tamponade: A Case Series Using Outpatient Internal Medicine Point-of-Care Ultrasound.

Introduction: Cardiac tamponade is a life threatening condition requiring a high index of clinical suspicion in order to make a timely and accurate diagnosis1. The emergency medicine literature has demonstrated that point-of-care ultrasound (POCUS) reveals meaningful pericardial effusions in a significant number of patients presenting to the emergency department with an otherwise negative workup for shortness of breath2,3. Our goal was to describe the use of POCUS in the outpatient internal medicine (IM) setting to facilitate early diagnosis of cardiac tamponade amongst more subtle, “walking” patient presentations.

Methods: Five patients presenting to our 2 IM outpatient clinics in whom POCUS was used to diagnose cardiac tamponade were retrospectively reviewed. Patient characteristics, archived POCUS images/clips, formal echocardiography results, hospital management, and patient outcomes were examined.

Results: Among 5 outpatients with cardiac tamponade detected using POCUS, all had dyspnea as their chief complaint. Only 3 of these patients had an abnormal traditional physical examination, with tachycardia being the most common abnormality in 3 out of 5 patients. On initial presentation to clinic, the median heart rate was 103 beats per minute (range: 74-120) and the median mean arterial blood pressure was 93 mmHg (range: 75-103). None of the patients demonstrated Beck’s triad (hypotension, jugular venous distension and distant heart sounds). POCUS demonstrated right ventricular collapse in all 5 patients and visible right atrial (RA) collapse in 2 (the other 3 patients either had poor visualization of the RA such that an assessment could not be made (n=2), or loculated effusions resulting in tethering of the RA (n=1)). Mitral Doppler inflow was performed in one patient and demonstrated >25% inflow variation consistent with tamponade. All patients, except for one that refused, underwent successful pericardiocentesis upon emergent/urgent direct admission from clinic to the hospital.

Conclusions: The use of POCUS in the outpatient IM setting facilitates accurate and early diagnosis of cardiac tamponade prior to more obvious symptoms or hemodynamic collapse. Lung POCUS is frequently used in our outpatient
Clinics to evaluate patients with shortness of breath, but the evaluation should routinely include cardiac POCUS as well. When identified early, treatment for tamponade becomes urgent rather than emergent. While outcomes of most procedures are worse in emergency situations, further research is needed to determine the impact of early diagnosis of tamponade with POCUS in the outpatient setting on patient outcomes.

**Impact of LVAD Implantation Site on Ventricular Blood Stagnation**

Treatment of end-stage heart failure includes cardiac transplantation or ventricular assist device (VAD) therapy. While increasingly prevalent, VAD therapy has many complications, including thrombosis. Studies have demonstrated that VAD implantation disrupts intra-cardiac blood flow, creating areas of stagnation that predispose thrombus formation, referred to as “hot spots.” Two surgical configurations exist for VAD implantation: through the apical or diaphragmatic surfaces of the heart. We hypothesized that diaphragmatic implantation causes more stagnation than apical implantation. We also hypothesized that intermittent opening of the aortic valve reduces stagnation of blood inside the ventricle when compared to a closed aortic valve. To test these hypotheses, a human left-ventricle geometry was re-created in silico and a VAD inflow cannula was virtually implanted in each configuration. A computational indicator-dilution study was conducted where “virtually-dyed blood” was washed out of the ventricle by injecting blood with no dye. Simulations demonstrated a substantial reduction in stagnation when the aortic valve opened intermittently vs permanently closed. In addition, virtual dye was cleared slightly faster in the apical configuration vs the diaphragmatic configuration. Our simulations demonstrate the clinical importance of configuring the VAD to allow intermittent opening of the aortic valve to prevent subvalvular stagnation, and also suggests that apical implantation might be more hemodynamically favorable than diaphragmatic implantation. Rather than drawing direct clinical conclusions, the results from this study should be used as an impetus to help design further computational, in-vivo, and clinical studies that will ultimately help further improve VAD therapy.

**Clinical Vignette- Residents**

**Umama Adil, MD**

**Scott Davies**

**A unique presentation of subacute cardiac tamponade**

Introduction: The use of point of care echocardiography by non-cardiologist in acute care settings such as the emergency department or the intensive care unit is very common. Unlike diagnostic echocardiography, the scope of such point of care exams is often restricted to address the clinical questions raised by the patient’s differential diagnosis or chief complaint in order to inform immediate management decisions. Pericardial effusion is frequently considered in the differential diagnosis for patients who present with or develop hypotension or shortness of breath in the ED or ICU. Despite the elegant physiology that underlies physical exam findings such as the pulsus paradoxus or Beck's triad, their lack of sensitivity has contributed to the evolution and adoption of point of care echo by clinicians seeking a more reliable diagnostic approach.

Case description: We present the case of a 66 year old Ecuadorian gentleman who presented with nausea / vomiting and RUQ pain. Vitals on presentation were significant for a HR of 117 and BP 100/76, afebrile. On exam, the patient had diffuse abdominal tenderness, more prominent in the RUQ. Labs were significant for a white count of 13 and LFT’s deranged with alkaline phosphatase 167, ALT 679, AST 550 and total bilirubin 1.4, with direct bilirubin being 0.8.

With concern for cholelithiasis / cholecystitis, the resident in the ED performed a bedside ultrasound, which showed a normal CBD and normal gallbladder. However, during her exam, while trying to find the IVC to assess volume status, she found the heart swinging in a very large pericardial effusion. This was followed by and EKG which showed textbook electrical alternans. The patient subsequently got a diagnostic and therapeutic pericardiocentesis per
Cardiology. The patient’s abdominal pain / nausea and vomiting improved and his LFT’s normalized. His presentation was attributed to congestive hepatopathy 2/2 subacute cardiac tamponade. The pericardial fluid tested positive for adenocarcinoma with a lung primary, with metastases to the bone, pericardium and brain. He is currently getting chemotherapy.

Discussion: The case highlights the utility of bedside ultrasound in the acute care setting. The accuracy and safety of emergency physician performed echo for has been well demonstrated in large prospective study of 515 patients where 103 pericardial effusions were detected and, using subsequent review by a cardiologist as the gold standard, produced a sensitivity of 96% and specificity of 98%. Furthermore, this case highlights how subacute cardiac tamponade can have varied presentations with abdominal symptoms being more pronounced than any cardiac manifestations.

Hamna Ahmad, MD

Chest pain with the tick bite
Lyme disease is a tick-borne multisystem disease which can lead to carditis in 1-4% reported cases. However, initial presentation only with cardiac symptoms is extremely rare.

This is a case of a previously healthy 32 years old male who presented to the ED with one day history of sharp positional chest pain that started after rock climbing. Patient was hemodynamically stable on admission and had no remarkable findings on clinical examination. On initial evaluation, he was found to have mild troponin elevation with EKG changes suggestive of early repolarization. Further work-up was done to rule out main differentials including ACS, pneumothorax and aortic dissection. Patient was admitted to the medicine service and a clinical diagnosis of pericarditis was made after ruling out other relevant causes. Treatment with Ibuprofen was initiated for pericarditis and patient was continuously monitored with serial troponin and EKGs.

With further careful history and detailed examination, patient was found to have a fading rash but did not recall any tick bites recently. This new finding on examination raised the suspicion for Lyme disease. Patient was discharged on Ibuprofen and Lyme serology was obtained prior to discharge. Lyme serology was equivocal initially but was found to have IgM positive subsequently. Patient was contacted to discuss the results and treatment with Doxycycline was initiated.

Cardiac involvement with Lyme disease is extremely rare and the principal manifestation of Lyme carditis is a self-limiting AV block and usually occurs during the stage II of illness. However, it can also present as pericarditis as seen in this patient. Lyme disease, when presenting with only chest pain and without stage I symptoms, can be diagnostically challenging. This case also illustrates the importance of a comprehensive history and a detailed physical examination. Early recognition and treatment of Lyme disease is important as it can lead to serious complications if left untreated.

S. Obaidullah Aseem, MD

Epididymo-orchitis in an Immunized, Immunocompromised Patient
Case: A 35-year-old male with past medical history significant for psoriasis with psoriatic arthritis on etanercept presented to the clinic for a two week history of fever. His fever was intermittent, highest being 104F, associated with chills, fatigue, malaise and myalgia. He denied any localizing symptoms such as cough, chest pain, shortness of breath, abdominal pain, or dysuria. He denied sick contacts. His immunizations were up-to-date. He lives with his wife and two young children who have received appropriate immunization. His vital signs were within normal limits except for a temperature of 38.1C. On examination, he appeared tired but non-toxic. He had mild oropharyngeal erythema and enlarged, non-tender tonsils. The rest of the exam was unremarkable. Chest x-ray was normal. Laboratory evaluation revealed neutrophil-predominant leukocytosis to 12.3 x10(9)/L (normal 3.5-10.5 x10(9)/L) and a C-reactive protein of 25.2 mg/L (normal <=8 mg/L). Cytomegalovirus (CMV), herpes simplex virus 1/2, Epstein–Barr virus and
tickborne panel testing were all unremarkable. Urinalysis, including culture, and blood cultures were also negative. Etanercept was stopped and symptomatic management recommended with a follow up appointment in a week. The patient returned to the clinic the next day with new right-sided scrotal pain and swelling, and persistent fever. Examination revealed an erythematous right scrotum, and edematous, tender testicle and epididymis with pain radiating to the groin. There was no parotid swelling or tenderness. Screening for sexually transmitted infections and adenovirus testing were negative. Parvovirus B19 testing was consistent with remote infection, while Rubella testing was consistent with his known immunization status. However, mumps IgG and IgM were both positive suggestive of an acute infection. He was, therefore, diagnosed with mumps epididymo-orchitis. Symptomatic management with NSAIDs and acetaminophen was recommended. He was advised to wear a surgical mask around his family for as long as his fever persisted. He gradually improved over 3 weeks.

Discussion: This case illustrates an uncommon presentation of mumps in a previously immunized but immunocompromised adult presenting with fevers and epididymo-orchitis without parotitis. Mumps infection is uncommon in the United States. However, mumps outbreaks have become increasingly more frequent over the last 5 years. We are not aware of any outbreaks in the Southeast Minnesota region around the time of mumps diagnosis in this patient. He was predisposed to infections due to his immunosuppression by etanercept. The previous year, before starting etanercept, he had CMV mononucleosis resulting in 2 months of recurrent fever. Evidence suggests that patients with psoriasis have impaired T-cell function predisposing them to infections regardless of exposure to immunosuppressive treatment. This, in part, explains patient’s unusually prolonged symptoms with viral infections. Mumps infection should be considered in a febrile patient with epididymo-orchitis regardless of immunization status, particularly if immunocompromised.

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<th>Tori Bahr, MD</th>
<th><strong>Soft tissue mass of childhood, finally diagnosed as an adult</strong></th>
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<td>An otherwise healthy 32 year-old woman presents to clinic for a preventive health visit where she casually reports some left lower leg discomfort which has been ongoing since eleven years of age. The pain is localized to the left calf and extends up to behind her knee. Movement exacerbates her pain. Occasionally this area is pruritic and at times she finds that it gets firmer. On exam the left lower extremity is larger in size than the right, without a clearly defined mass. The area is firm, but there are no palpable thrills. There are no overlying skin changes. She has reduced dorsiflexion of the ankle on the left. The patient was referred to orthopedics where she underwent an MRI of the lower extremity showing a large heterogeneous mass measuring 4.6cm by 5.6cm by at least 14.6cm consistent with a benign soft tissue hemangioma. Given the restricted range of motion of ankle flexion and her pain, surgical intervention was offered which the patient is planning for in the next couple of months. Given the extent of her hemangioma she now holds her foot in a persistently plantarflexed position and will likely requiring a lengthening of the Achilles tendon as well as a potential ankle capsular release in addition to the resection. This case highlights the importance of identifying soft tissue masses early to minimize long-term sequelae. The appropriate workup of soft tissues will be discussed including the concerning signs and symptoms for primary care physicians to watch out for when evaluating these masses within the primary care setting. The differential for soft tissue mass varies significantly from benign lipomas to aggressive sarcomas, but the consequences of missing a diagnosis can be severe.</td>
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<th>Abdo Barakat, MD Ryan Anderson</th>
<th><strong>It May Seem Neoplastic, but It Is Oddly Infectious.</strong></th>
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<td>Introduction: Progressive disseminated histoplasmosis complicates about 0.05% of acute Histoplasma capsulatum infections. Diagnosis is often delayed given its non-specific initial presentation, especially when the differential is initially biased towards a neoplastic process. To note, histoplasmosis is the most</td>
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prevalent endemic mycosis in the United States. 
Case Presentation: This is the case of a 56 year-old woman with a past medical history significant for eosinophilic fasciitis, hypertension, and hypothyroidism. She was diagnosed with eosinophilic fasciitis 4 months prior to admission (PTA), and started on high dose prednisone for 2 weeks, followed by a prolonged taper. Methotrexate was then added, and discontinued after 5 weeks due to liver toxicity. She presented to an outside hospital for worsening generalized malaise, non-productive cough, chills, and exertional dyspnea. She had been experiencing marked unintentional weight loss and paroxysmal flares of subjective fever and night sweats. She was transferred to our institution for further evaluation.

On admission, laboratory workup revealed pancytopenia and findings consistent with DIC; low haptoglobin, high PT/PTT, low fibrinogen, and high LDH. CT angiogram was remarkable for acute bilateral segmental pulmonary emboli and RLL consolidation suggestive of an infarct. A lower extremity ultrasound was positive for DVT. CT abdomen/pelvis showed a near-occlusive thrombus of the infra-hepatic IVC extending into the left lower extremity and splenomegaly with innumerable hypo-enhancing foci.

Her clinical presentation prompted further hematologic workup. Of note, the patient had a bone marrow biopsy 4 months PTA as a part of her workup for eosinophilic fasciitis, which is often associated with hematologic disorders. It was negative for malignancy, with no apparent clonal abnormalities on cytogenetics. Bone marrow biopsy this admission revealed small budding yeast associated with histiocyte clusters that were morphologically consistent with Histoplasma capsulatum. Histoplasma capsulatum later grew from the bone marrow culture. Her previous bone marrow biopsy had not been sent for culture or silver staining.

She was started on a 2-week course of IV amphotericin B and transitioned to oral itraconazole for an anticipated duration of 12 months. On follow-up 5 weeks after initiation of antifungals, she was improving, but still quite ill. Discussion: A presentation that includes fever, fatigue, weight loss, pancytopenia, DIC, and splenomegaly points more commonly to an active neoplastic process. A recent diagnosis of the rare eosinophilic fasciitis only steered our differential closer to neoplasia, as this could be a presenting feature. However, when findings do not point to a specific hematologic cause, prompt consideration of other etiologies could be lifesaving; e.g. invasive fungal infections. Untreated acute disseminated histoplasmosis is progressive and fatal over a 2-12 week course. Despite amphotericin B treatment, mortality risk may be as high as 50%.

David Bartlett, MD
Danae A. Delivanis M.D.,
Ben Nordhues M.D.,
Diana S. Dean M.D.

A New Form of Auto-Immune Pituitary Disease

Introduction: Immune checkpoint inhibitors are becoming an important part of cancer therapy. Cytotoxic T-lymphocyte antigen-4 (CTLA4) and programmed death-1 (PD-1) are two co-inhibitory receptors that are expressed by T cells on activation [1]. Antibodies blocking the activity of these receptors enhance the immune system to attack tumor cells and have been shown to have significant survival benefit in some types of cancer. Unfortunately, the use of these immune checkpoint inhibitors can also induce autoimmune/inflammatory side effects causing endocrinopathies.

Case Presentation: The patient is a 42 year old female with a history of metastatic melanoma who has been on nivolumab (PD-1) and ipilimumab (CTLA-4) therapy for 4 weeks. She presented to her oncology appointment with nausea, vomiting, abdominal pain, right-sided frontal headache, fatigue, and flu-like symptoms for four days. She denied any vision changes. She was found to have orthostatic hypotension in the office, and was admitted to the hospital. Her family also noted an increase in skin pigmentation of her face to a more darkish gray color since initiation of immunotherapy. An ACTH level was obtained on admission and was found to be < 5.0 pg/mL consistent with secondary adrenal insufficiency. She received a brain MRI for concerns of hypophysitis caused by her immune checkpoint inhibitor therapy
which showed no signs of inflammation, enlargement of the pituitary gland, or metastases. The patient was started on high dose prednisone and all of her symptoms resolved the next day. Her pm cortisol was 14 mcg/dL and am cortisol was 2.6 mcg/dL, however this was drawn after receiving one dose of prednisone. Her TSH was 0.3 mIU/L and Free T4 was 1.8 ng/dL, sodium 135 mmol/L, potassium 4.8 mmol/L. Fortunately, the patient continued to improve on high dose prednisone and she was discharged home on this treatment for presumed hypophysitis from her immunotherapy. 

Discussion: Endocrinopathies induced by immune checkpoint inhibitors are infrequent, but include hyperthyroidism, hypothyroidism, adrenal insufficiency, and hypophysitis. While rare, hypophysitis has emerged as a distinctive endocrine side effect of anti-CTLA4-mAbs and represents a new form of autoimmune pituitary disease [1]. Hypophysitis can also occur with PD-1-mAbs, but this is rare. Headache is the most commonly reported presenting symptom. Other symptoms are rather nonspecific, but are similar to lymphocytic hypophysitis [2]. MRI is an important tool in evaluation however, not all cases have reported findings on imaging. As immune checkpoint inhibitors increase in use, the frequency of drug induced hypophysitis will likely increase. As a result, knowledge of this complication will become important when evaluating this patient population.

Mohammad Bashir, MD
John Matulis, III DO

Not all that pulsates is pertinent: Hepatic Schistosomiasis presenting with a pulsatile neck mass

A 67 yo female, Sudanese immigrant with no known medical history presented to establish care and for evaluation of a non-tender, pulsatile, right-sided neck mass. The mass has been present and stable for many years. Recent complaints include low-grade fevers (~100 degrees F) associated with bilateral neck pain radiating into her head approximately 2-3 times per month. This is associated with blurry vision which worsens during her headache episodes.

Physical exam was notable for pulsatile, non-tender, non-erythematous, anterior cervical neck mass and a II-III/VI holosystolic murmur heard best at the apex. CBC was significant for microcytic anemia with a hemoglobin of 11 g/dL with a mild eosinophilia. Peripheral blood smear was negative for parasites. C-reactive protein, HIV, and blood cultures were negative. Transthoracic echo showed mild mitral regurgitation.

CTA showed a tortuous, but otherwise normal appearing right common carotid artery. However, the subcarinal and retrocarinal region was ill-defined with soft tissue abnormality concerning for infiltrative disease adenopathy. A subsequent, dedicated chest CT showed that the subcarinal/mediastinal soft tissue abnormality likely represented a distended azygos vein and esophageal varices. Further, there appeared to be a fibrotic, deformed liver with periportal fat hypertrophy. Portal hypertension, splenomegaly, and esophageal varices were present. Subsequent evaluation showed normal liver enzymes and synthetic function. Hepatitis B serologies were consistent with prior infection. Hepatitis C antibody was negative. Stool and urine examinations were negative for parasites. Schistosoma IgG was positive.

She was initiated on antihelminthic therapy and underwent subsequent management of her esophageal varices.

-Schistosomiasis can be classified as immediate, acute, and chronic disease.
-Immediate manifestations include a maculopapular dermatitis at the site of parasite penetration; it is often seen in travelers to endemic regions. Swimmer’s itch, by contrast, is a hypersensitivity-mediated dermatitis that presents after re-exposure to schistosomes.
-Acute schistosomiasis, also known as Katayama fever, is type III hypersensitivity reaction mediated by immune complexes resulting in a variety of symptoms including: fevers, chills, myalgias, diarrhea, RUQ pain, urticaria, and angioedema.
-Chronic infection leads to a granulomatous inflammatory response to schistosome ova antigens which leads to fibrosis and obstruction of host organs.
<table>
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<tr>
<th>Caitlin Baxter, MD</th>
<th><strong>Acute Myocardial Infarction with Thrombotic Thrombocytopenic Purpura</strong></th>
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<tr>
<td></td>
<td>Thrombotic thrombocytopenic purpura (TTP) is a rare condition with a</td>
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<td>mortality rate of 90-95% in untreated patents but with a prognosis of 80-90%</td>
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<td>survival in patients who are treated early with plasma exchange. Early</td>
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<td>treatment is dependent upon early identification.</td>
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<td>A 69 year-old woman was sent to the emergency department with history of</td>
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<td>fever, altered mental status, nausea, and vomiting. An electrocardiogram was</td>
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<td>consistent with an acute ST elevation myocardial infarction and the cardiac</td>
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<td>catheterization lab was activated. A complete blood count (CBC) revealed</td>
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<td>anemia and profound thrombocytopenia. While the patient was undergoing</td>
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<td>coronary angiography, a pathologist reviewed a peripheral smear and identified</td>
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<td>schistocytes. Thrombocytopenia, schistocytes, fever, altered mental status,</td>
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<td>and acute kidney injury formed the clinical diagnosis of TTP. Concurrently,</td>
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<td>the patient was found to have a thrombus in the distal LAD. The diagnosis of</td>
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<td>TTP was communicated to the interventionist and the patient was treated</td>
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<td>medically for the acute myocardial infarction. The patient was transferred</td>
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<td>to the intensive care unit and plasma exchange therapy was initiated. Within</td>
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<td>48 hours the platelet count and lactate dehydrogenase normalized and plasma</td>
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<td>exchange therapy was discontinued after five days. The patient was</td>
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<td>subsequently found to have a mitral valve mass presumed to be thrombotic in</td>
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<td>nature as an infectious evaluation was negative. Dual-antiplatelet therapy</td>
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<td>was initiated due to the acute myocardial infarction and mitral valve mass.</td>
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<td>No further events occurred during hospitalization and she was discharged</td>
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<td>home in stable condition. This case demonstrates both the importance of</td>
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<td>early detection and communication of TTP and a rapid response to plasma</td>
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<td>exchange. Had the patient’s CBC not been promptly reviewed with a peripheral</td>
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<td>smear by a pathologist, it is possible the patient could have undergone</td>
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<td>coronary intervention and additional anticoagulation. That possibility, in</td>
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<td>addition to progression of TTP and delay of plasma exchange, would have</td>
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<td>very likely proven fatal. This outcome was avoided by accurate identification</td>
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<td>and efficient communication and treatment of a rare but deadly disease.</td>
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| Anne Becker, MD  | **Three Cases of Respiratory Failure due to Severe Viral Pneumonia in a      |
|                  | Residential Facility**                                                     |
|                  | Introduction: Adenovirus is known to cause upper respiratory infection       |
|                  | including sore throat and coryza and is usually self-limited. There are case |
|                  | reports describing outbreaks in under chlorinated swimming pools, and in the |
|                  | military after discontinuation of a vaccine, among others. Described here is |
|                  | a series of patients admitted during July and August 2016 from the same     |
|                  | residential facility with severe pneumonia leading to respiratory failure, all |
|                  | with adenovirus.                                                            |
|                  | Case Description: Case 1: A thirty-eight year old man living at Residence X |
|                  | with history of latent tuberculosis, obesity, obstructive sleep apnea,      |
|                  | tobacco use, and schizophrenia, presented with several days of worsening     |
|                  | dyspnea and wheezing. Developed hypoxic respiratory failure and was         |
|                  | intubated. On HD3 tested positive for Adenovirus. Progressed to ARDS and     |
|                  | required VV-ECMO for 12 days. He received two doses of cidofovir. Eventually |
|                  | required tracheostomy and discharged to long term acute care hospital (LTACH)|
Case 2: A forty-two year old man living at Residence X with history of traumatic brain injury, obesity, hypertension, asthma, tobacco use, and schizoaffective disorder, presented 7 days after Case 1 with cough and dyspnea. Found to be febrile and developed hypoxic and hypercapnic respiratory failure requiring intubation. On HD2 tested positive for Adenovirus. Developed ARDS and required proning. Underwent tracheostomy and discharged to LTACH after 28 days in hospital.

Case 3: A sixty-two year old man living at Residence X with history of tuberculosis, tobacco use, anemia, and schizophrenia presented 10 days after Case 2, via ambulance. He was found to be in septic shock and was started on antibiotics for pneumonia after chest x-ray showed opacity. On HD1 he tested positive for Adenovirus. He developed hypoxic respiratory failure requiring intubation and then ARDS. He was successfully extubated after two days and discharged to a subacute rehabilitation facility after 10 days in hospital.

Discussion: These cases demonstrate the potential for severe viral pneumonia in close contacts living at the same mental health residential facility. Other commonalities between them include a history of mental illness, smoking, and lung disease. The patients presented during summer months and two had chest x-rays without a well-defined infiltrate; a reminder to consider viral pneumonia in all seasons. The spread of adenovirus can be prevented by use of droplet (surgical mask) and contact (gown and glove) precautions. The Minnesota Department of Health, HCMC Infection Prevention and Infectious Disease consultants were involved in management of these cases. The main treatment for adenovirus is supportive. In severe cases, ECMO and antivirals can be tried. In this outbreak, adenovirus pneumonia resulted in severe morbidity and extended hospitalization among three close contacts.

Manuel Bonfim Braga Neto, MD
Elie F. Berbari, M.D.

Bacterascites: to treat or not to treat?

INTRODUCTION: Bacterascites is a relatively common phenomenon in patients with chronic liver disease undergoing frequent paracentesis. It is defined as a positive ascitic fluid culture and negative fluid analysis for SBP (<250 neutrophils/mcL). It is thought to be a self-limited process in most cases not requiring antibiotic therapy. However, in selected patients, antibiotics may be warranted. The microbiology epidemiology of such infections is similar to those with spontaneous bacterial peritonitis (SBP), where gram-negative bacteria predominate. CASE: We present a case of a 58-year-old male with cryptogenic cirrhosis, chronic kidney disease (baseline creatinine of 1.4) and esophageal varices that presented to the Emergency Department (ED) with altered mental status and subjective fever. Of note, patient had undergone therapeutic paracentesis earlier that day, with 2.5L removed. His peritoneal fluid analysis showed 309 nucleated cells/mcL (18% neutrophils) and protein of 0.6g/dl. In the ED, patient was afebrile and normotensive. Pertinent labs include hemoglobin of 8.1g/dL, platelets 152,000, creatinine 2.0mg/dl, bilirubin 2.3mg/dL, and ammonia 74mcl/L. No recent history of melena or hematemesis. He endorsed a lack of full compliance with lactulose/rifaximin oral therapy. Peritoneal fluid culture showed gram-positive bacillus on the direct gram stain. Patient was given lactulose and cefotaxime and admitted to the hospital. Due to cefotaxime shortage, he was transitioned to parenteral ceftriaxone. Infectious Disease consulted on day 4 of hospitalization regarding appropriate antibiotic therapy and need for long-term prophylaxis in the setting of peritoneal fluid culture positive for Clostridium sp. Given low peritoneal fluid protein and impaired renal function, recommendation was to complete a 5-day course of parenteral ceftriaxone and use subsequent prophylaxis with oral ciprofloxacin. His mental status improved throughout hospitalization. A repeat paracentesis on day 7 showed total nucleated cells of 395/mcL (4% neutrophils), bacterial culture negative. Patient was discharged on day 11. DISCUSSION: A review of the literature demonstrated only few cases of SBP or bacterascites due to
Clostridium sp. Bacterascites should be differentiated from SBP, defined as peritoneal fluid analysis with ≥ 250 neutrophils with or without positive culture. While SBP requires antibiotic therapy, most cases of bacterascites are self-limited and do not require targeted treatment, unless patient is high risk for infection. Furthermore, positive peritoneal fluid cultures can also be a consequence of contamination during paracentesis, especially when organisms also found in the skin flora are involved, typically gram positive bacteria. Clostridium species, however, are not part of the skin flora and are known to colonize the GI tract. Bacterial translocation is a known phenomenon and could explain the patient’s positive culture. Given he was at high risk for infection in the setting of low peritoneal fluid protein, we favored completing a 5-day course of parenteral antibiotic therapy followed by oral prophylaxis with ciprofloxacin.

Hoofbeats from a Zebra: Colorectal Cancer in a patient with Systemic Sclerosis

Systemic scleroderma (SSc) can be a devastating progressive disease and over 90% of patients can develop gastrointestinal (GI) manifestations including gastroesophageal reflux, bowel dysmotility, and malabsorption. Interestingly, while there appears to be increased cancer risk in SSc patients, studies have found higher incidence of lung malignancies, whereas incidence of colorectal cancer is rare. We report the rare case of colon cancer in a systemic sclerosis patient without traditional risk factors.

CASE REPORT: A 57-year-old woman with systemic scleroderma on chronic immunosuppression presented with hematochezia while on warfarin for a previous line associated clot. Her past medical history was remarkable for 20-year smoking history at a pack per week, non-Hodgkin’s lymphoma treated by chemo without radiation in 1980, no family history of colorectal cancer or polyps, and no previous screening colonoscopy.

Upon admission, she was hemodynamically stable with supra-therapeutic INR at 5.3. Unfortunately, colonoscopy revealed a sigmoid annular mass which pathology revealed infiltrated moderately differentiated adenocarcinoma. Staging CT was negative for metastasis. While the goal of her hospitalization became optimizing nutrition for possible surgery in the future, given her primary gut failure and contraindications for parenteral nutrition due to renal failure and immunosuppression, she bravely transitioned to comfort care.

DISCUSSION: Despite her minimal traditional risk factors, systemic scleroderma is known to have a higher risk of cancer compared to patients without scleroderma with standardized incidence ratios (SIRs) ranging from 0.99-1.99. Most studies have found a stronger correlation with lung cancer with SIRs ranging from 2.1 to 5.2. Nevertheless, colorectal cancer risk in SSc is rare, with at most 5 patients in a registry of 769 SSc patients. The pathophysiology behind this increased cancer risk is unclear. One study found that positive anti-RNA polymerase antibody was associated with at least twofold increased hazard ratio for cancers, especially within 36 months of SSc onset. This correlates with our patient’s presentation with weakly positive RNP antibodies three years prior to diagnosis of cancer.

This rare case of colorectal cancer in a patient with systemic sclerosis demonstrates several important clinical lessons. First and foremost, colon cancer preventive screening is crucial, as a colonoscopy in this patient seven years earlier may have prevented progression to invasive malignancy. Second, though non-bleeding duodenal ulcers were seen on EGD initially in the setting of melena, given her persistent transfusion requirements and eventual hematochezia in a patient without previous colorectal cancer screening, anchoring bias should be avoided and the possibility of a lower GI source should be entertained. Finally, while systemic scleroderma is not an established risk factor for colorectal cancer, there is association with increased overall risk of cancer, further supporting the importance of preventive screening in our scleroderma patients.
| David Brennan, MD  
Timothy G. Call, Juliana Perez Botero, Dong Chen, William Nichols | **Hermansky-Pudlak Syndrome: A rare cause of oculocutaneous albinism that can present with early-onset pulmonary fibrosis**  
Hermansky-Pudlak Syndrome (HPS) is a rare form of oculocutaneous albinism with mild bleeding diathesis from platelet dense granule deficiency caused by defects in intracellular vesicle trafficking. There are different subtypes that present with varying degrees of albinism, platelet dysfunction, immunodeficiency, granulomatous colitis and early-onset pulmonary fibrosis. Early recognition and diagnosis of this disorder enables appropriate monitoring for detection of pulmonary and gastrointestinal complications that can be fatal.  
Case Presentation: A 40 year old man from Iowa presented to a tertiary medical center for lung transplant evaluation. He has a lifelong history of oculocutaneous albinism and horizontal nystagmus without genetic testing. He was otherwise healthy and active until two years prior when he developed a dry cough, which persisted despite proton pump inhibitor therapy. One year later he developed progressive dyspnea on exertion. CT scan showed peripheral honeycombing in both lungs consistent with pulmonary fibrosis. Pulmonary function testing (PFT) revealed significant restriction with reduced diffusing capacity. PFT did not improve after three months of corticosteroids. Bronchoscopy was unrevealing, and auto-immune testing was negative. Pulmonary function deteriorated requiring continuous oxygen therapy and the patient was started on pirfenidone.  
Physical exam showed an albino male on high-flow oxygen. Horizontal nystagmus was present. No conjunctival or oral hemorrhages identified. No significant bruising. Whole mount electron microscopy of platelets was remarkable for absence of delta granules consistent with a diagnosis of HPS. Genetic testing is currently pending. The patient has no known Puerto Rican ancestry.  
Discussion: HPS is a rare form of oculocutaneous albinism caused by mutations in genes related to intracellular vesicle formation and trafficking. This impairs the function of melanocytes, platelets, and other cell types to varying degrees. It is usually identified in childhood by the classic findings of oculocutaneous albinism and absent platelet dense granules. There are 10 variants and the milder forms may not be identified until adulthood. Some subtypes (HPS-1 and HPS-4) are associated with development of pulmonary fibrosis, usually in the fourth decade. There are no FDA-approved medical therapies, but increasingly patients are pursuing lung transplantation. Prior to surgery, bleeding risk must be assessed by history and platelet function testing. DDAVP and/or platelet transfusion can be used prophylactically when appropriate.  
HPS is most common in Puerto Ricans with an incidence as high as 1:1800. There are over 4.5 million Puerto Rican-Americans in the U.S., with over 10,000 living in Minnesota. Outside of the Puerto Rican population the incidence is between 1:500,000 and 1:1,000,000. Regardless of ethnicity, HPS should be considered in all patients with oculocutaneous albinism as the bleeding diathesis can be mild. Whole mount electron microscopy of platelets is the gold standard to identify a delta granule deficiency. Genetic testing is recommended to identify the pathogenic variant. |
| Andrew Briggler, MD | **Big-hearted and Broken-hearted: An Overview of Cardiac Masses**  
Cardiac masses are uncommon, often asymptomatic, and can be due to several very different etiologies, including thrombus, vegetation, and tumor. Fortunately, cardiac tumors are rare and the majority are benign, of which myxoma is the most common. A malignant cardiac mass is most likely metastatic. Primary cardiac malignancies are extremely rare, but can be sarcomas, mesotheliomas, lymphomas, or paragangliomas.  
CASE DESCRIPTION: A 47-year-old gentleman with a history of seizure disorder and recently treated pericarditis complicated by acute kidney injury and pericardial effusion was urgently transferred from an outside hospital following PEA cardiac arrest. ROSC was achieved after 6 minutes of CPR, and the therapeutic hypothermia protocol was initiated. He arrived to the medical ICU intubated, paralyzed, and sedated. |
Workup prior to transfer included a CT scan of the chest which showed concern for a mass in the lateral wall of the right atrium. Initial laboratory evaluations were significant for hemoglobin 8.3, potassium 3.2, magnesium 2.0, and creatinine 3.7 (baseline 1.0). Physical exam was notable only for sinus bradycardia, without adventitious heart or lung sounds. Neurological status was unable to be assessed due to the sedation and paralysis.

The patient underwent urgent bronchoscopy, which showed progressively bloody return without visible endobronchial lesions. A broad workup was performed to further evaluate the alveolar hemorrhage, which included complements, ANCA panel, ANA, hepatitis B and C, HIV, Histoplasma, Blastomyces, tuberculosis, and Pneumocystis jirovecii, all of which returned negative. PET/CT showed a 2x4cm hypermetabolic mass abutting the right atrium with pleural thickening, bilateral pulmonary nodules, and diffuse metabolically active lymph nodes.

The patient was rewarmed after 24 hours and successfully extubated. He was subsequently transferred to a general floor, but developed worsening tachycardia and dyspnea, with ongoing intrapulmonary hemorrhage. Ultimately, it was deemed too risky to attempt a biopsy, and the patient ultimately elected to be made comfort cares and soon passed. Cause of death was ruled due to widely metastatic cancer, most likely from primary cardiac sarcoma.

**DISCUSSION:** Over 75% of cardiac masses are benign, and include myxomas, papillary fibroelastomas, rhabdomyomas, fibromas, teratomas, and lipomas. In general, these are usually asymptomatic and no intervention is undertaken unless they grow large enough to require surgery. Myxomas, however, often have cardiovascular manifestations secondary to transient mitral valve obstruction, and should be surgically removed as they can lead to sudden death. 15% of cardiac tumors are malignant, of which most are metastatic, especially from melanoma, lung, breast, and esophageal primaries. Primary cardiac tumors are extremely rare, and are most commonly sarcomas, but can also be mesothelioma, paraganglioma, or lymphoma. Sarcomas are usually widely metastatic at diagnosis, and thus have a dismal prognosis of months, despite aggressive surgeries and systemic chemoradiation.

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**Fiorela Calderon Sandoval, MD**

**Recurrent aspiration pneumonia in the setting of a rare esophageal dysmotility disorder.**

Hypertensive peristalsis or Nutcracker Esophagus is a relatively rare esophageal motility disorder first diagnosed in the 1970s, that accounts for just 4.1% of patients referred for manometric evaluation in consecutive series in tertiary referral centers. With an incidence of about 1 case in 100,000 population per year in the USA, esophageal spasm, in general, seems to be more common in white women. Also known as "Spastic Nutcracker" and "Jackhammer Esophagus", it is caused by the overactivity of excitatory innervation. In contrast to other esophageal spasms disorders, only a small proportion of patients are symptomatic: mainly with non-cardiac chest pain. This pathology is distinguished from other dysmotility disorders by normal sequential contractions in the smooth muscle esophagus of excessive amplitude or duration: mean value > 220 mmHg or >6 sec respectively.  

**CASE DESCRIPTION:** A 45-year-old Caucasian female with a past medical history of HTN, IDDM, CKD-Stage 3, COPD, GERD, chronic pancreatitis, HIV/AIDS on HAART therapy and morbid obesity who presented with a 3-day history of a productive cough, congestion, SOB and worsening hypoxia particularly with exertion. ROS positive for dysphagia with both solids and liquids and daily reflux with every meal. Physical exam remarkable for mild inspiratory crackles on bases, expiratory and inspiratory wheezing; as well as mild tenderness on the epigastrium and periumbilical area, without peritoneal signs. Chest x-ray notable for worsening bilateral interstitial opacities and esophagogram with evidence of small hiatal hernia and diffuse esophageal dysmotility with multiple tertiary contractions consistent with Nutcracker
esophagus, (later confirmed by Manometry testing). Esophageal impedance was performed as part of the workup with evidence of 100 reflux events/day as the likely cause of recurrent aspiration with resulting pneumonitis. Initially, the patient was started on calcium channel blocker for symptomatic control and later, despite the risk of worsening dysphagia, Nissen fundoplication was performed associated to Heller myotomy after utilizing shared decision-making.

DISCUSSION: This case illustrates a patient with a history of multiple admissions for hypoxic respiratory failure in the setting of recurrent aspiration pneumonia partially to refractory GERD. A new finding of nutcracker esophagus during an extensive workup complicated the course of action in a patient with increased risk of morbidity and mortality. According to Patti and colleagues comparative studies, surgical myotomy in patients with DES and Nutcracker esophagus might be more effective than medical treatment, becoming an alternative modality for difficult-to-treat patients. This is a case that clearly reflects the importance of decision-making when benefits outweigh the risks in specific clinical situations.

Nian En Chiang, MD
John Ratelle, M.D.,

Refeeding a young and healthy mother
Introduction: Although refeeding syndrome is a well recognized phenomenon in anorexic and critically ill patients, it can occur in well-nourished individuals with increased energy expenditure and decreased caloric intake. This case demonstrates refeeding syndrome in an otherwise healthy individual.
Case: An obese 25-year-old female with no previous past medical history presented to the emergency department for a 2 day history of nausea and vomiting. She had been trying to lose weight by restricting carbohydrates and caloric intake to less than 1000 calories per day for the past 3 weeks, and her weight decreased from 210 pounds to 200 pounds (BMI 33). On presentation, she had mild sinus tachycardia which was attributed to dehydration. Her laboratory evaluation was significant for metabolic acidosis with pH of 7.11, an anion gap of 30 and bicarbonate of 8, and an elevated beta hydroxybutyrate of 8.1. Her extended electrolytes including potassium, magnesium, calcium, and phosphate were all within normal limits. A diagnosis of starvation ketoacidosis was made given the normal osmolar gap, glucose, lactate, and renal function in addition to a negative drug screen for alcohol, aspirin and acetaminophen levels. Overnight, her nausea, tachycardia and acidosis all resolved after gentle intravenous hydration and a meal consisting of pizza. She complained of mild fatigue and weakness and was subsequently found to have significant electrolyte abnormalities including an extremely low phosphorous level of 1. Her potassium was 3 and magnesium was 1 with a normal calcium level. Additional history revealed that she had been breastfeeding her 6-month-old child. She required replacement of phosphorus, potassium, and magnesium for 2 days before her electrolytes normalized and was discharge from the hospital.
Discussion: The risk of refeeding syndrome is well recognized in anorexic and critically ill patients. This case illustrates the potential for refeeding syndrome in well-nourished people and those with increased energy expenditure, such as a breastfeeding mother who is trying to lose weight. Awareness of these risk factors is important to the institution of appropriate monitoring and prevention of severe complications from electrolyte disturbances. These complications can be especially detrimental to this otherwise healthy population.

Daniel Childs, MD
Stephenson, Chris, MD

Unusual presentation of recurrent diffuse large B-cell lymphoma: non-infiltrative hepatic dysfunction
Introduction: In case series, liver involvement of non-Hodgkin’s lymphoma has been reported both in the form of a localized mass of B-cell origin and diffuse lymphomatous infiltration. Here, we report a unique case of recurrent diffuse large B-cell lymphoma presenting with liver dysfunction in the absence of imaging or histologic evidence of hepatic involvement.
Case Description: A 60 year old man was transferred to our facility with 3 months of progressive fevers, chills, night sweats, fatigue, weight loss, and
jaundice. His history was notable for stage 3 diffuse large B cell lymphoma in complete radiographic remission, which had been achieved 7 years prior after 6 cycles of R-CHOP. He also had a history of pulmonary tuberculosis that had been successfully treated with a multidrug regimen. This was considered in his evaluation. The patient’s initial laboratory assessment revealed significant hepatic dysfunction: total bilirubin 14.5 mg/dL with a direct fraction of 11.4 mg/dL, alkaline phosphatase 252 U/L, AST 118 U/L, ALT 66 U/L, INR 1.9, and albumin 2.1 g/dL. As diagnostic testing was being pursued over the next few days, his hyperbilirubinemia continued to worsen, finally peaking at 19 mg/dL. Serologic testing for hepatotropic viruses was negative, as was evaluation for autoimmune inflammatory causes of liver dysfunction. No extrahepatic biliary ductal dilation was seen on ultrasonography. A liver biopsy had been performed prior to transfer to our facility and showed only mild, focal portal inflammation with mild hepatocellular cholestasis. Ultimately, a positron emission tomography scan revealed cervical, mediastinal, and upper abdominal lymphadenopathy. Excisional lymph node biopsy confirmed the diagnosis of recurrent diffuse large B cell lymphoma, and the patient was treated with high dose steroids and Rituximab.

Interestingly, there were no lymphoid cells identified on the liver biopsy, and the positron emission tomography scan showed no FDG avidity within the liver. Taken together, these findings suggest that a paraneoplastic process, such as a variant of Stauffer’s Syndrome, was mediating his marked liver function test abnormalities rather than biliary ductal obstruction, hepatic mass or direct infiltration of the liver. Following initiation of lymphoma-directed therapy, liver function tests rapidly normalized.

**Discussion:** Stauffer’s Syndrome is a paraneoplastic phenomenon, thought to be mediated by a potent pro-inflammatory cytokine, IL-6, that causes liver dysfunction in the absence of hepatic metastasis and biliary ductal obstruction. It was first described in relation to renal cell carcinoma but has since been associated with other malignancies. To our knowledge, this is the first report of Stauffer’s syndrome in association with a hematological malignancy.

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**Janice Cho, MD**

**George Saffouri, MD;**

**Thomas Smyrk, MD;**

**Thomas Viggiano, MD**

**Asymptomatic anemia in a patient with melanoma**

**Introduction:** Metastatic melanoma is often found in the gastrointestinal tract. The most common sites are the liver and small bowel but less commonly metastases can be found in the stomach. We present a patient with metastatic melanoma to the gastric body who presented with moderate normocytic anemia.

**Case Description:** A 60-year-old male had a background 7 year history of malignant melanoma metastatic to the right chest wall, right and left axillary lymph nodes, right breast, and left lower lung. All metastatic disease was treated with surgical resection. In routine follow-up, he presented with minimal bright red blood per rectum and a new normocytic anemia. He had no intestinal symptoms other than the rectal bleeding. Colonoscopy showed sigmoid diverticulosis and non-bleeding internal hemorrhoids. An upper endoscopy demonstrated 4 ulcerated, non-circumferential polyoid masses in the gastric body. Biopsies were taken which revealed tumor cells positive for S-100, melan A, and HMB45 confirming the diagnosis of metastatic melanoma. Positron emission tomography scan showed a large mass with increased uptake in the mid-portion of the stomach. Partial gastrectomy was discussed, but due to concern for surgical morbidity due to pulmonary hypertension from severe obstructive sleep apnea, systemic therapy with pembrolizumab and indoximod was ultimately pursued.

**Discussion:** This case illustrates an atypical metastatic focus of melanoma. No metastases were found in the lower gastrointestinal tract. Melanoma metastases to the GI tract are quite common with liver and small bowel making up the majority of gastrointestinal involvement. Anemia is commonly found in these patients who often do not present with clinically evident blood loss. Gastric resection is a treatment option for those with low cardiopulmonary morbidity but oftentimes metastatic melanoma will require systemic chemotherapy. In any
patient with a history of malignant melanoma and unexplained anemia, it is important to consider gastrointestinal involvement despite lack of clinical symptoms. New or worsened anemia should prompt further evaluation including endoscopy.

**Kevin Chodnicki, MD**  
**Hafsa Chaudhry, Korosh Sharain, MD**

**Back pain, lung nodules, and a cardiac device**

Introduction: Implantable cardioverter-defibrillators (ICDs) are one type of cardiovascular implantable electronic device (CIED). They are effective at reducing sudden cardiac death in a variety of clinical scenarios. Implantation of ICDs has increased worldwide. Understanding the prevalence and management of ICD complications is important in counseling patients before implantation and caring for them afterwards.

Case Description: A 66-year-old man presented to the emergency department with progressively worsening back pain and recurrent falls. His medical history included diabetes mellitus, chronic kidney disease, and ischemic cardiomyopathy with placement of an ICD. Several months prior to presentation, he was upgraded to a biventricular pacemaker with placement of a left ventricular lead. He had an intentional 30 to 40 pound weight loss over this time and endorsed fatigue and intermittent night sweats. He denied fever, chills, recent travel, and bowel or bladder dysfunction. Examination was notable for tenderness to palpation over the lumbar and lower thoracic spine but was negative for focal neurologic deficits and saddle anesthesia. Laboratory studies were remarkable for a normal white blood cell count but elevated inflammatory markers (CRP of 87.2 mg/dL and ESR of 74 mm/h). Thoracic and lumbar spine CT showed irregular soft tissue thickening at the T10-11 interspace with endplate changes along with incidental basilar lung nodules. A formal chest CT demonstrated multiple cavitary, solid, and ground-glass lung nodules bilaterally. An evaluation was initiated for bacterial and fungal pulmonary infections, vasculitis, and malignancy. However, blood cultures from admission grew methicillin-resistant coagulase-negative Staphylococcus epidermidis after 34 hours and he was started on vancomycin. Imaging consistent with vertebral osteomyelitis in the setting of positive blood cultures raised concern for endocarditis. Therefore, a transesophageal echocardiogram (TEE) was performed but did not demonstrate vegetation. Given persistently positive blood cultures despite antibiotics he underwent ICD explantation and pocket washout. The ICD device leads, pacemaker pocket, and T10-T11 vertebral body biopsy all grew S. epidermidis. He was diagnosed with ICD related endocarditis with septic emboli to the lungs and vertebrae. He was discharged on vancomycin and rifampin for synergy. He underwent ICD replacement and antibiotics were planned for six weeks.

Discussion: The differential for multiple lung nodules includes malignancy, vasculitis, vascular malformations, occupational exposures, and anaerobic, mycobacterial, or fungal infections. One must also consider septic emboli from endocarditis or CIED infections when present. Risk factors for CIED infections include heart failure, diabetes mellitus, kidney disease, and pocket manipulation. Staphylococcus species are the most common cause of CIED infections. With positive blood cultures and a negative TEE, a new CIED can be implanted if blood cultures after CIED removal are negative for 72 hours. If valve vegetations are identified, the CIED replacement should be delayed 14 days from the first negative blood culture.

**Nathan Clarke, MD**  
**Dr. Derek Ebner, MD**

**Purpura Fulminans: An unusual skin manifestation of Rocky Mountain Spotted Fever**

Purpura fulminans is an acute thrombotic disorder which manifests itself as bruising and discoloration of the skin and eventually necrosis and disseminated intravascular coagulation (DIC). Mostly associated with defects in the coagulation pathway, it has been rarely associated in episodes of severe sepsis. A 51-year-old lady presented to the emergency department with a one week history of malaise following a trip to her family’s lake house in northern
Minnesota. She was otherwise healthy, without a significant medical history but
also endorsed two days of diarrhea, non-bloody emesis and a Tmax of 103°F.
She was alert and oriented and had no physical exam findings. Her initial labs
showed multiple abnormalities including thrombocytopenia to 22000,
schistocytes on peripheral smear and classic associations consistent with DIC.
Within 12 hours of admission her mental status acutely decompensated. She
subsequently developed hypotension requiring vasopressors with secondary
hepatic failure, a subdural hematoma from T12-L2 and renal failure requiring
renal replacement therapy. An extensive infectious work up was initially
negative including a tick-borne panel, and the patient’s antibiotic coverage was
broadened to include piperacillin-tazobactam and doxycycline. In the setting of
DIC and septic shock, she developed symmetrical dusking of her hands and feet
that subsequently developed into dry gangrene of multiple fingers as well as all
toes. Though initially believed to be related to vasospasm injury from continued
vasopressor medications, purpuric patches were also noted on the upper
extremities with occasional hemorrhagic bullae. These findings suggestive of
purpura fulminans lead to repeat rickettsia testing, one week following her
initially negative panel. This time, however, serologies showed a positive titer,
and she was diagnosed with Rocky Mountain Spotted Fever (RMSF). The
diagnosis of RMSF is often elusive due to its non-specific presentation and
limitations of laboratory confirmation. Purpura fulminans is a frequently fatal
syndrome that may follow a bacterial infection. Although its association with
RMSF is rare, its recognition may cue a provider towards the diagnosis. Signs
of DIC, evolving gangrene of the sacral areas and microangiopathic changes on
peripheral smear blood smear characterize purpura fulminans. Management
often requires intensive care, managing of DIC, peripheral gangrene and the
underlying cause.

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<tr>
<th>Don Chamil Codipilly, MD</th>
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<td>Allan S. Jaffe, M.D.</td>
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Infective endocarditis is usually considered a relatively overt diagnosis, but it
can be subtle and detection is important as it can cause substantial morbidity
and mortality. Antibiotic treatment is the cornerstone of treatment, but there
also are surgical indications that internists must be aware of.
A 63 year old male with a past medical history of metastatic colon cancer
(treated with sigmoid colectomy, chemotherapy, and ablation of liver
metastases) presented for a routine outpatient follow up. The patient had a
history of enterococcus liver abscesses secondary to a biliary stricture.
However, at this time, the patient offered no complaints. He was afebrile.
Routine computed tomography scan of the abdomen was done to evaluate for
recurrence of his colorectal adenocarcinoma. This imaging revealed findings
consistent with a new liver abscess. Blood cultures were obtained and
eventually grew enterococcus faecalis. The patient was hospitalized and started
on broad spectrum antibiotics.
Vital signs were stable, and the patient continued to feel well. At this point, the
patient’s physical examination was notable for hepatomegaly, but the
cardiopulmonary examination was reported to be unremarkable.
Blood cultures were persistently positive over the course of the next four days.
On day four, a presumably new holosystolic murmur was heard best at the right
upper sternal border. The patient denied shortness of breath or feeling ill.
A transesophageal echocardiogram was obtained which showed severe aortic
regurgitation and native valve endocarditis involving the aortic valve, with a
perforation through the right coronary cusp.
The patient underwent urgent aortic valve replacement with a bioprosthetic
valve after his systemic infection was blunted (i.e blood cultures turned
negative). His postoperative course was marked by hematemesis, and EGD
revealed esophageal varices, which were successfully banded.
The patient completed a 6 week course of antibiotics from the time of surgery.
There have been no signs of cardiac compromise or recurrence of liver
abscesses since then.
We present the case of a patient who developed endocarditis with perforation
through an aortic valve leaflet secondary to a liver abscess and systemic infection. Interestingly, the patient claimed he was asymptomatic. Our case highlights several key points:
Persistent positive blood cultures in patients on appropriate antibiotics should commence a search for insidious foci of infection, such as endocarditis.
Repetitive cardiac auscultation is mandatory.
It is important for internists to understand when to treat medically and when to proceed to valve surgery in patients with endocarditis (chart will show indications).
Providers must have a high degree of suspicion for endocarditis, as patients may not be overtly symptomatic and may not appear severely ill. However, often subtle findings suggesting this diagnosis can be found if one is vigilant.

Caitrin Coffey, MD
Danqing Hu, MD; Majd El-Harasis, MD; Will Schouten, MD

A Forgettable Family Meal
Transient global amnesia (TGA) is the sudden onset of anterograde amnesia without other neurologic deficits or explainable cause that resolves in less than 24 hours. Prognosis is good, and early recognition can help avoid unnecessary and costly workup.
A 71-year old man with history of Parkinson’s disease was brought to the Emergency Department with acute alteration in mental status for approximately 1-2 hours. He was observed by family wandering around a restaurant parking lot after getting up from a meal to use the restroom. He was confused, disoriented to place and time, but not person, and could not remember any details about recent events since the meal. Physical examination was normal upon presentation, aside from inability to complete finger to nose testing. Laboratory evaluations including toxicology screen, glucose, electrolytes, lactate, ABG, urinalysis, blood and urine cultures were all negative. Creatinine was slightly elevated to 1.7, but normalized with IV fluids. EKG, chest X-ray, and head CT/CTA were unremarkable.
A few hours after hospital admission, he was oriented and at his baseline, though he could not recall any details about the episode. He remained asymptomatic until his discharge the following day.
TGA typically occurs in adults 50-70 years of age. The clinical presentation typically consists of sudden loss of ability to understand the current situation, often accompanied by repetitive questioning. The differential diagnosis includes stroke or TIA, metabolic encephalopathy, encephalitis, intracranial tumor, seizure, or psychogenic dissociation. TGA is often a diagnosis of exclusion. Notably, patients with TGA do not have focal neurologic impairment and do not lose orientation to self. The etiology of TGA is not completely understood. Studies have associated TGA with history of migraine, though migraine symptoms do not typically accompany TGA episodes. Transient ischemia due to venous congestion or TIA, seizure activity, and cortical spreading depression, as seen with migraine, have also been implicated as potential etiologies however none of these can consistently explain TGA. Brain MRI may show punctate hippocampal lesions on diffusion-weighted imaging, though this is not always present and imaging is not necessary for diagnosis. There is evidence to suggest that patients with TGA have a more favorable cardiovascular risk profile than those with TIA/CVA. Patients with TGA can be managed conservatively, as this is a self-resolving condition with low risk of recurrence or progression. The described patient had full resolution of his anterograde amnesia within hours of hospital admission, and was discharged with reassurance only. TGA can be diagnosed clinically in patients with acute onset of anterograde amnesia, lack of other neurologic findings, epileptic signs, or identity loss, and supporting history provided by an unaffected observer, after clinically ruling out other causes for amnesia.

Daniel Cole, MD
Richard McGowan

Diffuse Lymphadenopathy Secondary to Syphilis in a Patient with Newly Diagnosed HIV
Lymphadenopathy in the setting of HIV/AIDS has a wide differential diagnosis,
including acute HIV, malignancy, and a multitude of infections. The diagnostic challenge of such a broad differential can be mitigated with a thorough history and physical.

A 51-year-old man with a history of alcohol dependence and recently diagnosed HIV was admitted for work up of several months of malaise, 35-pound weight loss, and diffuse lymphadenopathy. History revealed recent onset unilateral hearing loss and physical exam was notable for cachexia, hyper-pigmented maculopapular rash over both palms and soles, profound cervical, axillary, and inguinal lymphadenopathy, hard palate mucosal lesions, and a healed chancre over the dorsum of the penis. Lab work significant for CD4 count of 350, viral load >100,000 cop/ml and a positive RPR titer of 1:256 with a reactive Treponema pallidum antibody. Patient was diagnosed clinically with secondary syphilis with presumed neurologic involvement of hearing loss and blurry vision. Lymph node biopsy was performed on hospital day 3 which revealed spirochetes visualized with anti-treponemal antibody stain consistent with syphilis as the primary cause of his lymphadenopathy. He was started on IV penicillin with noted improvement in his rash, oral lesions, visual changes, and constitutional symptoms.

This case illustrates several points including the importance of maintaining a wide differential diagnosis and the value of a good history and physical exam when presented with lymphadenopathy in a patient with HIV. Secondary syphilis typically presents with a constellation of signs and symptoms including maculopapular rash over the palms and soles, constitutional symptoms, mucosal lesions, and skin eruptions. However, also known as “the great masquerader”, syphilis may present in a variety of ways including diffuse lymphadenopathy. Neurosyphilis can present in any stage of syphilis and is a clinical diagnosis. Syphilis is an important risk factor for HIV, and neurosyphilis may present earlier during the course of illness in immune suppressed patients secondary to impaired cellular/humoral immunity.

Maros Cunderlik, MD

An Acute ST-Segment Elevation In An Unresponsive Patient – A Clear Case Of STEMI?

A finding of an acute ST-segment elevation on electrocardiogram (ECG) in an unstable patient raises an immediate concern for an evolving ST elevation myocardial infarction (STEMI). While STEMI is rightfully considered a “cannot miss diagnosis” in this context, normal variants and other etiologies should always be considered.

Case: A 35 year old woman with past medical history of anxiety, depression, and drug use presented to a hospital emergency department (ED) by emergency medical service (EMS) after being found unresponsive earlier at her home. Prehospital ECG was concerning for STEMI thus cardiac catheterization lab was activated. Upon arrival to the ED, the repeat ECG showed convex down sloping 4+mm ST-segment elevation in precordial V1 and V2 leads, wide QRS complex, and large T waves. On physical exam, the patient was found to be unresponsive with cool extremities, with needle marks in antecubital fossa of both upper extremities and tense right lower leg edema with blistering. Initial investigations showed poor global cardiac function, no wall motion abnormality, and concern for dilated right ventricle on bedside echocardiogram. With the diagnostic uncertainty of encephalopathy and poor cardiac function, early reperfusion therapy was temporarily delayed until further evaluation was completed. Given the findings on echocardiogram emergent computed tomographic pulmonary angiography (CTPE) was considered however prior to the initiation of the study the patient was found to have elevated creatinine and hyperkalemia above the upper limit of measurement range (> 9.4mEq/L). Severe hyperkalemia was treated with calcium gluconate, bicarbonate, insulin, dextrose, and albuterol and repeat ECG in two hours showed no ST-segment elevation and no QRS complex duration prolongation. Patient was admitted to the intensive care unit where she was found to have severe rhabdomyolysis with creatinine kinase nadir of 306,000 IU/L due to lower extremity compartment
syndrome. After a prolonged hospitalization complicated by stress cardiomyopathy, acute kidney injury requiring hemodialysis, cardiac arrest, and repeat fasciotomies and myomectomies the patient was discharged to acute care rehabilitation facility for her right leg injury. Prior to discharge the repeat transthoracic echocardiogram showed normal cardiac function.

In conclusion, the evaluation of patients with acute ST-segment elevation meeting STEMI ECG criteria should promptly include additional investigations aimed at ruling out other etiologies such as acute pericarditis, pulmonary embolism, left bundle branch block, and hyperkalemia. As demonstrated in this case, rhabdomyolysis can cause a severe hyperkalemia resulting in striking ST-segment elevations in V1 and V2 leads. Therefore understanding the morphology of ST-segment changes in hyperkalemia as compared to STEMI is important in differentiating these two entities during the time sensitive period when early reperfusion therapy is being considered.

JAIME De La Fuente, MD
Jennifer E. Clark M.D., Daniel K. Partain M.D., David A. Froehling M.D., Anjali Bhagra M.B.B.S

To Lyse or Not to Lyse: Managing Extensive Venous Thrombosis in the Oncology Patient

It is well known that patients with active malignancy have a higher risk of venous thrombosis. Unfortunately, these patients often also have an increased bleeding risk with anticoagulation therapy, making medical decision-making and risk-benefit discussions complex – especially in the setting of other systemic illnesses such as liver disease.

Case Description: A 61-year-old man with a history of cirrhosis and Hepatitis C infection presented to his local emergency department with bilateral asymmetric lower-extremity (LE) edema of acute onset. He was initially treated with oral furosemide, without any reported improvement in his symptoms; after returning a week later, furosemide dosing was increased and a LE ultrasound was ordered. This study was performed two days later and revealed no acute LE deep venous thrombosis (DVT). Subsequently, computed tomography (CT) imaging of the abdomen/pelvis was completed, reporting a hepatic mass with extensive thrombus involving the right hepatic vein and intrahepatic inferior vena cava (IVC), extending superiorly to the cavoatrial confluence. The patient subsequently presented to our institution due to persistence of symptoms. Physical examination was notable for asymmetric LE and scrotal edema. Laboratory data revealed thrombocytopenia 45, INR 1.3, d-dimer 2545, and creatinine 1.2. Abdominal CT confirmed a hepatic mass showing arterial phase enhancement with venous washout, indicative of hepatocellular carcinoma, and an occlusive thrombus in the upper abdominal IVC. Transthoracic echocardiogram was performed, revealing a large echo-dense structure in the IVC protruding into the right atrium without tricuspid obstruction.

The patient was monitored closely considering the high clot burden. Medical vs interventional management options were discussed. Given his degree of thrombocytopenia, catheter-directed thrombolysis was deemed too high-risk. Heparin nomogram was initiated, with continued close monitoring of platelets and signs of active bleeding. LE ultrasound was repeated, revealing occlusive thrombus in the IVC extending through the common iliac veins, but none distally. LE compression therapy was initiated. After his goals of care and preferences were explored through discussion, he was dismissed to outpatient follow-up with LMWH, 1 mg/kg, injected SQ twice daily to minimize bleeding risk while ideally preventing further extension of the thrombus.

Discussion: This case illustrates the complex decision-making involved in the management of venous thrombosis in cancer patients. These cases require a patient-centered, multidisciplinary, and individualized assessment before the initiation of anticoagulation with contingency planning in place. The size of this patient’s thrombus warranted urgent intervention, but his thrombocytopenia, likely extensive tumor thrombus, and increased risk of bleeding due to end-stage liver disease made him a poor candidate for thrombolytic therapy. CHEST 2016 guidelines recommend the use of LMWH over warfarin or direct oral
anticoagulants for cancer-associated DVT/VTE, with no scheduled stop date for therapy. Such management warrants continued goals of care discussions with patients and reassessment at periodic intervals.

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<th>Brinda Desai, MD</th>
<th>Is all that Bleeding because of Me(ckel’s)?</th>
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<td>62Y M with a history of thalassemia minor (baseline Hemoglobin of 11.5) was admitted lightheadedness and fatigue found to have acute anemia (hemoglobin of 7.5) of unknown etiology. EGD was done on hospital day 2 without evidence of upper GI bleed source. Pt was transfused with a unit of PRBC with an appropriate response. However, on the second day of admission, patient had several episodes of large hematochezia, had a syncopal episode, and hemoglobin of 6. CT abdomen/pelvis was negative for acute bleed. Patient was transferred to the ICU on the third day of admission for ongoing hematochezia and hypotension despite 6 units PRBC s. Patient was urgently taken for tagged RBC scan to evaluate for source of bleed; however, study was negative. Patient continued to have hematochezia and required multiple more transfusions. Urgent colonoscopy performed given persistent evidence of lower GI source without a source. Colonoscopy positive for erythematous mucosa in the terminal ileum with blood in the entire colon. Site of bleeding was suspected to be in the right colon, specifically around the ileocecal valve/proximal ascending colon but exact location of lesion was not identified. Mesenteric arteriogram was also unable to pinpoint the culprit lesion. Given the unclear source of lower GI bleed despite multiple procedures, surgery was consulted and decision was made to proceed with ex-lap. During the procedure, a large Meckel’s diverticulum with multiple inflamed distal small bowel loops and retroperitoneal inflammation consistent with what appeared to be Crohn’s disease (later confirmed by final pathology). The right colon, distal small bowel and portion of the retroperitoneal mass along with the Meckel’s diverticulum were incised with a primary anastomosis. Patient recovered well, had slow return of bowel function, and did not have repeated episodes of hematochezia with stabilization of hemoglobin. Meckel's diverticulum is a congenital condition due to incomplete involution of the omphalomesenteric tract, appearing as an out-pouching of the intestine located approximately 60 cm from the ileocecal valve. Several case reports discuss cases of Meckel’s in patients with Chron’s disease in both pediatric and adult patients. This case illustrates the importance of broadening the differential in patients admitted with acute anemia with suspicion for lower GI bleed without clear etiology. Although classically thought of as a pediatric condition, Meckel’s Diverticulum can be seen in the adult population. This case along with several reports does raise the question of whether patients with Chron’s disease should be checked for Meckel’s Diverticulum or vice versa. The existing literature on the matter is controversial and addresses the need for more studies looking at the association between the two conditions.</td>
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<th>Jaspreet Dhilliwal, MD</th>
<th>Moyamoya syndrome associated with Sickle Cell disease resulting in hemorrhagic stroke.</th>
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<td>Moyamoya Syndrome is a rare chronic cerebral occlusive vasculopathy resulting in progressive narrowing of the major intracranial vessels. Subsequently, occlusion of the supraclinoid internal carotid arteries and the circle of Willis occur, accompanied by proliferation of arterial collaterals in proximity to the site of occlusion at the base of the brain. Moyamoya syndrome has been associated with diverse pathological conditions such as Down’s syndrome, neurofibromatosis, sickle cell disease, trauma, and radiation exposure. Moyamoya, which translated means “puff of smoke,” was the term coined by Suzuki and Takaku in 1969 to describe the appearance of the network of collaterals. Case Description: 32 year old male with history of homozygous S Sickle cell disease, past acute chest syndrome, two cerebrovascular accidents, recurrent priapism, and pulmonary hypertension. He presented to the hospital after being found down at the light rail station and altered.</td>
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On examination, he was aphasic and plegic on the right side. Labs showed Hb-8.7, WBC-12.2 and Hct -25.5 and INR-1.3. The differential included ischemic stroke, hemorrhagic stroke, seizure, toxic encephalopathy, traumatic epidural hematoma.

His Head CT scan demonstrated a large left basal ganglia hemorrhage with intraventricular extension. There was obstructive hydrocephalus along with early uncal herniation. The patient had an external ventricular drain placed and was taken to the operating room for evacuation of the hematoma and a decompressive craniectomy.

He then underwent a formal diagnostic cerebral angiogram. The angiogram provided the diagnosis of Moyamoya syndrome demonstrating the left supraclinoid internal carotid artery stenosis and basal collaterals supplying the left middle cerebral and anterior cerebral territory.

Discussion: Patients with Sickle Cell disease and associated Moyamoya Syndrome cerebral vasculature are at increased risk for stroke and hemorrhage. The fragile Moyamoya vessels that form at the base of the brain are thin-walled and dilated or thick walled and stenotic and are prone to hemorrhage. It is important to consider the diagnosis of Moyamoya syndrome in patients with a past history of cerebrovascular accidents. Timely diagnosis and treatment could prevent life threatening hemorrhagic strokes in this population.

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<th>Daniel Dudenkov, MD</th>
<th>Coughing up rocks? A case of broncholithiasis.</th>
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<td>Sumedh Hoskote, MBBS</td>
<td>A 69 year old woman presents with a 10-year history of cough, previously treated for GERD and asthma. Over the last several months, she reports intermittently “coughing up small rocks”. Chest X-ray reveals calcified lymph nodes in the mediastinum with the possibility of some calcified material in the right mainstem bronchus. CT scan of the chest demonstrates subcarinal calcified lymphadenopathy with evidence of erosion into the right mainstem bronchus. Bronchoscopy reveals several broncholiths in the right mainstem bronchus with obstruction of the bronchus intermedius. Four broncholiths are removed, with the largest one measuring about one centimeter. The patient’s symptoms improve afterwards. The patient has broncholithiasis, a condition characterized by the presence of broncholiths, or calcified material, in the bronchial tree. Broncholiths are usually the result of calcified lymph nodes that have slowly eroded through the bronchial wall. These calcified lymph nodes are often late sequelae of remote fungal infections, most commonly histoplasmosis in the United States and tuberculosis worldwide. Patients can present with complications such as hemoptysis, post-obstructive pneumonia or mediastinal fistulas. However, in many cases such as this one, patients can simply have a chronic nonproductive cough. If a patient with chronic cough also reports “coughing up small rocks”, it is a good idea to take them seriously because they may have broncholithiasis.</td>
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<th>Nirjhar Dutta, MD</th>
<th>Acute Renal Failure in a Patient Enrolled in Clinical Trial of Finerenone for Diabetic Nephropathy</th>
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<td>Introduction: Finerenone is a mineralocorticoid receptor antagonist (MRA) which is thought to be more specific for the kidneys than spironolactone and cause less hyperkalemia than eplerenone. MRAs are thought to reduce proteinuria when used with an ACE-I or ARB. Finerenone was evaluated in a 90 day phase 2 dose-finding trial of 823 patients with T2DM with albuminuria, already on an ACE-I or ARB, and doses of 7.5mg to 20mg per day resulted in a dose dependent reduction in albuminuria compared to placebo. 1 Case Description: 65 y/o M w/PMH of HTN, bladder cancer s/p cystectomy and ileal conduit in 2010, CKD stage III with microalbuminuria, and T2DM (diet controlled) was sent to the ED from the endocrine clinic due to AKI on 8/18/16. Patient was started on Finerenone for diabetic nephropathy on 7/20/16 (confirmed by endocrinologist that patient was on Finerenone arm) and his lisinopril dose was also increased from 10mg to 20mg. A few days later patient developed diarrhea, nausea, poor appetite, progressively got weaker,</td>
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lightheaded, and had decreased UOP. Patient was also using ibuprofen TID two weeks for neck/back pain. At presentation patient had normal vitals, was mentating well, but was found to have K 4.4, HCO3 of 9, BUN of 117, Cr 6.38 (baseline 1.3), and pH of 7.08. Patient was fluid resuscitated and dialyzed once. Patient’s UOP increased, and Cr was down trending without HD and was discharged home with oral bicarbonate; Finerenone, Lisinopril, and NSAIDs were discontinued. Labs on 9/8/16 showed Cr 1.53, BUN 19, and HCO3 of 26. Discussion: AKI was thought to be due to a combination of diarrhea, increased Lisinopril use, NSAID use, and finerenone. In the Finerenone trial, 3% of participants developed diarrhea and 2.2% had decrease in GFR. Providers should be vigilant about renal failure in patients on MRA.

Michael Eastman, MD  

**An Unwelcome Surprise: Hyperemesis Gravidarum**

Hyperemesis Gravidarum is a relatively common complication of pregnancy affecting 0.3 – 1.0% of all pregnant women. In severe cases, however, the treatment of this condition can be just as dangerous as the condition itself, as shifting of electrolytes can result in dangerous imbalances which can lead to respiratory failure, arrhythmias, seizures, and death.

A 27 year old G2P0010 woman who was approximately 16-weeks pregnant and with no past medical history was seen in the emergency room after several months of nausea and vomiting since nearly the beginning of her pregnancy. This had worsened over the last several weeks to the point where she was unable to keep down any food and barely any liquids and she was brought to the emergency department when “My mom came and started freaking out.” In the emergency department she was noted to be tachycardic, jaundiced, and with a soft but tender abdomen in the right upper quadrant and epigastric area. She was treated symptomatically with anti-emetics and intravenous fluids. Her serum potassium level was noted to be 2.3mEq/L and her anion gap, lipase, liver enzymes, and bilirubin levels were all slightly elevated. Her platelet and hemoglobin counts were normal. A urinalysis was significant for ketonuria, proteinuria, and bilirubinuria. A vaginal wet prep was positive for bacterial vaginosis and she was started on Metronidazole. Abdominal ultrasounds showed a viable fetus with size consistent with the stated period of pregnancy, as well as sludge in the gallbladder without cholecystitis. Obstetrics was consulted in the emergency department but the patient was admitted to the general medicine floor for evaluation of her elevated liver enzymes and lipase.

On the floor, she was treated with further intravenous fluids, IV thiamine and folate, anti-emetics, and potassium replacement. Upon rechecking her electrolytes, however, it was noted that her potassium levels failed to improve and her relatively mild hypophosphatemia (2.0mg/dL) dropped to as low as 0.4mg/dL, despite early replacement. A manual read of her EKG also revised her QTc from 440ms to 585ms. QT-prolonging medications were stopped and anti-emetic control was achieved with Phenergan suppositories. Her QTc interval subsequently normalized and her electrolytes were aggressively replaced and subsequently normalized over the course of the next four days at which time she was discharged home.

This case illustrates the profound, refractory, and dangerous electrolyte balances that can result when treating a relatively common condition: hyperemesis gravidarum. A careful history will alert the provider of the potential severity of this condition and the need for close monitoring and aggressive electrolyte replacement.

Melissa Eelkema, MD

**A Respiratory Complication of Laparascopic Gastric Banding**

Laparoscopic gastric banding surgery is growing in popularity and importance as a treatment for obesity and for prevention of obesity-related metabolic diseases. However, this procedure is not without long-term consequences, even beyond its well-known gastrointestinal side effects. It is important to recognize the significant impact that bariatric surgery can have on other organ systems. Physicians must also remember to consider previous bariatric surgeries when
developing a differential diagnosis for complaints that seem unrelated to these procedures, as in this case of progressive dyspnea. A 72-year-old female presented to a follow up cardiology clinic appointment for heart failure. She had a complicated past medical history, including moderate persistent asthma, atrial fibrillation (status post conversion), coronary artery disease, heart failure with preserved ejection fraction, dilated cardiomyopathy (status post pacemaker/ICD placement), type 2 diabetes, and obesity (status post lap band surgery) who gave a history of progressive dyspnea and fatigue over the previous several weeks. She was observed in clinic to have dyspnea at rest that was far worse than her baseline. She was directly admitted to the hospital due to concern for heart failure exacerbation. She also reported intermittent chest discomfort and low-grade fevers at home to 101. Her work up included an EKG that was unchanged from previous, negative troponins, a normal BNP, and a trans-thoracic echocardiogram that was unchanged from previous. Her chest x-ray had no acute pathology and no evidence of pulmonary edema. Chest CT showed evidence of multifocal aspiration and inflammation in the setting of a hiatal hernia and inflated lap band. For management, the gastric lap band was evacuated. The patient improved almost immediately. Her dyspnea improved immediately and her fatigue and low-grade fevers resolved over the next few days. She also received a one week course of empiric antibiotics for aspiration pneumonia. At follow up, the patient had continued to feel well without a recurrence of this dyspnea. The plan is to leave her lap band deflated indefinitely.

This case presents a rare but important complication of bariatric surgery. The patient’s clinical picture was initially convincing for a heart failure exacerbation, but further investigation revealed aspiration pneumonia. While the benefits of bariatric surgery often outweigh its risks, internal medicine physicians must remain cognizant of the wide-reaching effects these procedures can have on our patients.

**Majd El-Harasis, MD**

Margaret Cupit-Link;

Caitrin Coffey; Will Schouten

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**Found down and confused: A diagnosis you CAAn’t miss**

Cerebral amyloid angiopathy (CAA) is a common small vessel disease of the brain characterised by β-amyloid deposition in cerebral vessels. Associated vascular wall weakening can result in lobar hemorrhage, microhemorrhage, and microinfarcts.

A 68-year-old man with no known past medical history and limited prior contact with the healthcare system was admitted to the hospital after being found pinned under a bookshelf in his apartment. He was unable to provide any history due to encephalopathy. Physical examination revealed a dishevelled male oriented only to person, with multiple abrasions on his body. Laboratory evaluation revealed severe hypernatremia, acute kidney injury (AKI), and rhabdomyolysis. Initial CT head showed chronic right lacunar and right cerebellar infarcts, with no evidence of acute hemorrhage or infarct. His hypernatremia, AKI, and rhabdomyolysis resolved with intravenous hydration. The patient’s encephalopathy persisted, despite resolution of his metabolic derangements. He developed two staring spells with eye deviation, thought to represent dyscognitive seizures. The patient’s family revealed that he had been experiencing progressive cognitive decline in recent months. MRI brain showed multifocal subacute microinfarcts throughout the cerebral and cerebellar hemispheres and brainstem, along with diffuse leukoaraiosis suggestive of chronic small-vessel ischemia. Gradient-recalled echo sequence demonstrated innumerable focal hypointesities suggestive of diffuse microhemorrhage. In sum, the history and imaging findings were thought to represent probable CAA. CAA is common and under-recognized, with prevalence and severity increasing with age. Microhemorrhages and microinfarcts are often asymptomatic, but can result in progressive cognitive decline, seizures, or headaches. The differential diagnosis includes amyloid β-related angiitis (ABRA) and primary angiitis of the central nervous system (PACNS). Brain MRI usually shows leukoaraiosis in all three conditions, but multiple lobar microbleeds are hallmarks of CAA,
whereas acute infarcts are more characteristic of ABRA and PACNS. Furthermore, myelopathy is suggestive of PACNS as spinal vessels are spared from β-amyloid deposition. Although brain biopsy (not pursued in this case) is required for definitive diagnosis of CAA, a probable diagnosis can be made based on history and imaging, according to diagnostic criteria. CAA is managed by avoiding anticoagulants and anti-platelets, to prevent further hemorrhage. Statins may also be held, as some evidence suggests that lower LDL levels increase the risk of hemorrhage. Steroids may be helpful in ABRA and PACNS, but not in CAA.

The patient’s care was complicated by findings of calf deep vein thrombosis and pulmonary embolism, thought related to prolonged immobilization. Anticoagulation was initiated with close monitoring, as the risk of recurrent thromboembolism was thought to outweigh that of further cerebral hemorrhage in the setting of CAA.

This case highlights an interesting cause of persistent confusion following a fall with prolonged immobilization as well as a clinical dilemma regarding anticoagulation.

Jessica Gaulter, MD

**Running Into Darkness: A Transient Case of Amaurosis Fugax**

Amaurosis fugax is a transient loss of vision in one or both eyes that is caused by a number of conditions ranging from benign to serious. Frequent causes include atherosclerotic disease of the internal carotid or ophthalmic artery, giant cell arteritis, optic neuropathies, ocular migraine, vasospasm, and acute angle closure glaucoma.

A healthy and active 33-year-old man with a history of pterygium presented to clinic with multiple episodes of painless complete vision loss in his left eye. The vision loss occurred 1 or 2 times per month and began 5 months prior to his clinic visit. The episodes occurred while exercising. They lasted about 5 minutes after he stopped exerting himself. The patient did not experience any pain during the episodes and denied accompanying headache. He had no history of migraine headaches. The patient was evaluated by ophthalmology. Slit lamp exam revealed nasal pterygium in left eye and nasal and temporal pinguecula in right eye. External, slit lamp and fundus exam were otherwise normal. The patient was started on 81 mg of aspirin daily and noticed a mild decrease in symptoms. Due to the concern for atherosclerotic disease, further work-up was obtained. An MRI of brain, transthoracic echocardiogram, and EKG were unremarkable. Based on his negative work-up and lack of risk factors, the patient was given a diagnosis of exercise-induced vasospastic amaurosis fugax. He decided against starting treatment given the infrequency of his symptoms.

While rare, exercise-induced vasospastic amaurosis fugax is well described in the literature. It is a diagnosis based on history and exclusion of other causes. Nifedipine, a calcium channel blocker, is an effective treatment. The need for treatment is based on the severity and frequency of symptoms. It is important to keep a broad differential and take a detailed history when considering amaurosis fugax.

Aaron Goldish, MD

Pezhman Roohani, MD.

Peter Lund, MD

**I Get kNO2cked Down**

Introduction: Vitamin B12 deficiency through inadequate nutrition or malabsorption can cause subacute combined degeneration with symptoms of sensory ataxia and loss of proprioception. Habitual nitrous oxide canister inhalation (AKA “whip-its”) can inactivate Vitamin B12 causing subacute combined degeneration. This diagnosis is an important consideration as nitrous oxide is legal and easy to obtain, without laboratory testing to detect its use.

Case Presentation: A 22 year old male presented with 2 weeks of steadily worsening lower extremity weakness, ascending numbness and frequent falls. He was transferred to hospital from neurology for evaluation of ataxia. On admission he stated he followed a normal diet without restrictions and denied any substance abuse. His girlfriend had similar lower extremity numbness and weakness 6 weeks prior and was suspected to have B12 deficiency and possible
Radiculopathy at L5-S1. His exam was notable for stable vital signs with poor foot proprioception, incomplete numbness up to T4 dermatome, positive Rhomberg test, Lhermitte’s sign, sensory ataxia, and hyperreflexia over biceps and patellar tendons. Cranial nerve examination was normal for all extremities. Initial serum and CSF analyses were normal. Vitamin B12 level was normal at 373 with elevated methylmalonic acid (MMA) at 5.47. MRI of the spine revealed active demyelination and enhancement over the distal cervical and dorsal thoracic cord.

EMG testing was done the following day and returned normal. During the EMG, the patient admitted to nitrous oxide abuse of up to 50 canisters daily for the past 15 months. Nitrous oxide abuse was stopped and he was supplemented with Vitamin B12. He was discharged to a rehab center where over the course of the next 3 weeks he was able to recover independent ambulation.

Discussion: Nitrous Oxide is an inhalant commonly used for its anesthetic effects, but in higher concentrations causes euphoria with auditory and visual hallucinations lasting 1-5 minutes. Nitrous oxide, if abused chronically, oxidizes and inactivates cobalt within cyanocobalamin. Cyanocobalamin levels can range from low to normal, with occasional elevation in MMA levels. This inhibits the formation of methionine, which is required for myelin sheath maintenance and DNA & RNA synthesis. Neurotoxicity develops, presenting as polyneuropathy or ataxia.

In Minnesota, nitrous oxide is legal for household use in food products, but is illegal to sell to minors or as an intoxicant. The 2014 National Survey on Drug Use and Health showed that over half a million people over the age of 12 reported current use of inhalants. This case demonstrates the important consideration of inhalant abuse in patients that may not readily admit to its use. The inability to test for these compounds further emphasizes the need for healthcare providers to consider its use in patients who present with myeloneuropathy.

**Stephen Groves, MD**

**Neuroleptic Malignant Syndrome and Serotonin Syndrome Following Low Doses of Psychotropic Medications**

Introduction: Neuroleptic Malignant Syndrome (NMS) and Serotonin Syndrome (SS) are rare, but life-threatening conditions both induced by administration of psychotropic medications. Sharing similar presentations, clinical differentiation is often difficult, and diagnosis may be overlooked if insufficient doses of the offending drugs are suspected.

Case Description: A 60 year old male was admitted to the intensive care unit with agitation, diaphoresis, muscle rigidity, hypertension, unresponsiveness, and fever after treatment for a steroid-induced psychosis with haloperidol. Prior to his initial hospitalization, he had been suffering from degenerative disc disease and anxiety. A back pain exacerbation resulted in a tapered regimen of methylprednisolone that lead to increasing paranoia and delusional thinking. He had also been initiated on escitalopram for his anxiety and had taken one pill prior to presentation. Continued pain and altered mental status lead to hospitalization, where a diagnosis of steroid-induced psychosis was made. The patient was treated with several doses of lorazepam and three separate doses of haloperidol totaling 12.5mg. After treatment with haloperidol, the patient became increasingly agitated and febrile. His extremities developed rigidity and he became diaphoretic. He demonstrated 3+ patellar reflexes bilaterally and exhibited 4 beats of clonus in his left ankle. His agitation required continuous sedation with propofol and the patient was intubated for airway protection.

Although clonus is the most sensitive differentiator for SS, the timeline was more consistent for NMS, and cotreatment with bromocriptine and cyproheptadine was initiated. Over the proceeding 12 days, the patient’s exam waxed and waned. Fevers intermittently recurred, the patient occasionally followed commands, and clonus persisted. On day 13, the patient began to answer yes and no questions and his agitation improved with lower sedation requirements. Within a week, the patient recovered to baseline and walked out of the hospital.
Discussion: This case demonstrates the difficulty in differentiating between NMS and SS and emphasizes that small doses of either offending drug class can trigger these conditions. Furthermore, time to recovery and effectiveness of traditional pharmacotherapies is variable among studies, highlighting the significance of supportive care in recovery.

Justin Grunewald, MD

Wheezeing Lost in Translation

Justin Grunewald (Associate), Lisa Callies (Fellow): Abbott Northwestern Hospital, Minneapolis, MN

Shortness of breath and wheezing are frequently encountered problems in both the clinic and hospital setting. Although this finding is commonly associated with asthma and chronic obstructive pulmonary disease (COPD), when patients are not adequately responding to treatment, different etiologies for their presentation should be pursued.

An 81 year old Somali female presented to the hospital for shortness of breath and wheezing. She carried a diagnosis of severe persistent asthma, despite no pulmonary function testing on record. She had been hospitalized four times in the previous four months for a similar presentation. She also had many outpatient office encounters for persistent wheezing with two different primary care physicians. Over this period, she had been treated with multiple inhalers and systemic steroids. She was discharged home from her last hospitalization on duoneb inhalers, Advair, extended prednisone taper, along with home nurse visits to ensure compliance.

Compliance was thought to be the likely reason for lack of improvement, despite adequate treatment for asthma. On admission, oxygen saturation level was in the lower 90’s on 4L nasal cannula. Exam was notable for diffuse wheezing. She endorsed significant shortness of breath but stated she was compliant with both inhalers and Prednisone 40mg daily. Pulmonary function testing was performed on hospital day one that showed restrictive lung disease, with no response to bronchodilators. An ENT consult was placed; direct laryngoscopy revealed paroxysmal vocal cord dysfunction. The patient’s steroids were eventually tapered and bronchodilators were discontinued. The patient began speech therapy and is still having continued improvement in symptoms. This patient had been treated for multiple years with systemic steroids, resulting in cushingoid features and uncontrolled type 2 diabetes mellitus.

It is very atypical for a patient to be diagnosed with new obstructive lung disease in their eighth decade of life. Multiple medical conditions can cause wheezing, including, but not limited to, postnasal drip, paroxysmal vocal cord motion, laryngeal edema, airway tumors, obesity, tracheal stenosis, asthma, COPD, pulmonary edema, aspiration, pulmonary embolus, carcinoid syndrome, and parasitic infections.

If a patient is not responding to standard treatment for COPD/asthma and is having multiple hospitalizations, laryngoscopy is a fairly simple procedure to rule out many of the extra thoracic upper airway causes of wheezing and is also a low risk procedure.

Jordan Gunn, MD
Korosh Sharain M.D.

Takotsubo, An Annual Recurrence

A 59-year-old female with coronary artery disease and LAD stent, stress cardiomyopathy (SCM) in 2013 and 2014, chronic pain on opioids, major depressive disorder and undiagnosed psychotic disorder was brought to the ED by her husband for altered mental status. She was hypotensive with systolic pressures in the eighties. She was unresponsive on exam and there was suspicion for opioid overdose, therefore, Narcan and IV fluids were given with improvement in mental status and vitals. A CT of the head was unremarkable. Her ECG was normal and troponins were elevated but had no significant delta. Her creatinine was elevated to 2.8 from a baseline of 0.9 thought to be secondary to dehydration and hypotension. She was admitted for further evaluation.
Her mental status and vitals resolved the following day. However, she developed sudden onset shortness of breath with desaturation to 85% on room air, tachypnea and tachycardia. A STAT chest x-ray demonstrated flash pulmonary edema, and she was transferred to the ICU. Repeat troponins were up trending, and a bedside echocardiogram revealed an EF of 33% with regional wall motion abnormalities, hypokinesis/akinesis in the base and mid-ventricle with preservation of the apex (echocardiogram on admission demonstrated an EF of 63%). The following day she underwent left heart catheterization which showed no significant occlusions but revealed hemodynamics consistent with cardiogenic shock. Cardiac MRI revealed findings consistent with the echocardiogram and a diagnosis of inverted stress cardiomyopathy was made. The patient’s heart failure was managed with Lasix, Carvedilol and Imdur.

SCM, also known as Takotsubo Cardiomyopathy, is an acute decline in systolic function of the left ventricle that cannot be explained by an area supplied by one epicardial vessel. Presentation involves chest pain, dyspnea, ST segment changes, troponin elevation and decreased ejection fraction. Therefore, SCM should be included in the differential of acute coronary syndromes. More than 80% of individuals with SCM have troponinemia and ischemic changes on ECG; so initial diagnosis is challenging. SCM occurs more often in women (9:1 ratio). Most occurrences are preceded by a physical or emotional trigger. Over half of cases occur in patients with neurologic or psychiatric disorders. Although SCM recurrence is rare, with a rate of 2%, it should remain in the differential diagnosis of acute heart failure. Apical hypokinesis or akinesis of the left ventricle is seen in 80% of cases, hence the name of apical ballooning syndrome. Rarer presentations include midventricular, basal and focal types. Beta-Blockers and ACEIs are used for treatment; however, only ACEIs have benefit in survival. Beta-blockers do not prevent recurrence. Complications include ventricular tachycardia, thrombus and rupture. An echocardiogram should be repeated after a few days to weeks to evaluate for resolution of the EF and regional wall abnormalities.

**Stephen B. Hicks, MD**

Geoffrey Huntley, Michael Ruff, MD, Micah Yost, DO, and Jimmy Fulgham, MD

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The “Snake Eye Sign” in Spinal Cord Cavernoma: A case report of a unique finding in a rare disease

Introduction: In case series, cavernous malformations have been reported to occur in both sporadic and familial forms. The familial form accounts for one fifth of cases and is more frequent in Hispanic-Americans. Here, we report a unique case of cavernous malformations presenting with ascending flaccid paraplegia.

Case Description: A 58-year-old right-handed Hispanic gentleman without significant past medical history developed ascending flaccid paraplegia. He was transferred to our institution two months after symptom onset. The patient’s symptoms began with back pain and left lower extremity radicular symptoms during a workout at the gym. His symptoms were first attributed to a “bulging disk,” and treated conservatively. He ambulated under his own power for two weeks until his symptoms progressed over a period of 48 hours when he developed constipation, urinary retention, and asymmetric onset of bilateral lower extremity weakness and falls. MRI of the spine was significant for a lesion at spinal level T11 and increased T2 signal with a “snake eyes” appearance indicative of spinal cord ischemia. MRI of the brain demonstrated innumerable cavernous malformations. He underwent an extensive evaluation which included CSF microorganism evaluations and spinal angiography, which were unrevealing of causative pathology. Upon our initial assessment, motor examination revealed intact strength, reflexes, and sensation in the bilateral upper extremities with flaccid paralysis and anesthesia from the xiphoid process inferiorly with areflexia and mute plantar responses. Notably during our initial interview, the patient endorsed a family history of intracerebral hemorrhage in paternal family members and a deceased paternal aunt “to spinal cord swelling”.

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His stepwise deterioration was attributed to recurrent bleeds at the T11 lesion, resulting in vascular congestion and cord ischemia. Neurosurgical extirpation of the T11 cavernoma was performed at our institution without incident. Given the significant family history of brain bleeds and spinal cord edema, Medical Genetics was engaged, and he was found to have a heterozygous mutation on exon 13 of the KRIT1 (CCM1) gene, which is consistent with autosomal dominant familial cerebral cavernous malformations. Discussion: Cerebral cavernous malformations (CCM) is a rare, hemorrhagic stroke disease affecting up to 0.5% of North Americans. Loss of function mutations in three genes are responsible for the development of cavernomas: CCM1 (KRIT1), CCM2, and CCM3 (PDCD10). The specific protein lost causes the formation of cavities which lack subendothelial support. The endothelium is fragile, and repetitive micro hemorrhages ensue and lead to focal hemosiderosis and reactive gliosis. This case illustrates that early recognition of genetic syndromes is critical to the application of appropriate screening modalities and therapy. Furthermore, it is possible that more expedited surgical intervention could have led to a better clinical outcome in this patient.

Alexandra Higgins, MD
Henry J. Schultz, M.D., MACP

My Achy-Brachy Colon: Colonic spirochetosis presenting as hematochezia

Intestinal spirochetosis is a condition defined histologically by the presence of spirochetes of the family Brachyspiraceae attached to the apical cell membrane of colonic epithelium. There is increased prevalence in poorly developed regions as well as HIV-infected patients. The clinical significance of intestinal spirochetosis has not been well characterized, but has been associated with diarrhea, abdominal pain, and bloody stools.

Case Description: A 44 year old Hispanic female presented to primary care internal medicine with a six day history of hematochezia. Her past medical history was significant for type 2 diabetes, severe COPD, pulmonary hypertension, and latent tuberculosis. The patient’s hemoglobin was 14 and physical exam was unremarkable. She had not used NSAIDs. A colonoscopy was ordered, but the procedure was delayed for a month secondary to the patient’s lack of citizenship and insurance. At the time of colonoscopy, she complained of progressive watery stools with continued presence of hematochezia. She also complained of diffuse nonspecific abdominal pain and bloating. Further history revealed over one year of abdominal discomfort and diarrhea, which had become significantly worse over the last month when she began noticing the bloody stools. The patient denied recent travel outside the United States. Colonoscopy revealed several small 1- to 2-mm ulcers in the terminal ileum. There were no masses. Random colonic biopsies were taken to evaluate for microscopic colitis. Pathology of the colonic biopsies revealed spirochetosis by Warthin and immunostaining. There was no histologic evidence of invasion beyond the epithelium. The ulcers showed mild active chronic ileitis without granulomas and negative Warthin’s stain. CBC, liver function tests, and CT of the abdomen and pelvis were all unremarkable. HIV, syphilis, and celiac testing were negative. Given the otherwise unrevealing diagnostic work-up, the patient was treated with metronidazole 500 mg TID for 14 days for intestinal spirochetosis. She had subsequent resolution of her hematochezia, diarrhea, and abdominal pain.

Discussion: Patients who are either HIV-infected or from poorly developed countries may be at increased risk for symptomatic intestinal spirochetosis by Brachyspira, presenting as abdominal pain, diarrhea, and even bloody stools. Random colonic biopsies are necessary for diagnosis as the colonic mucosa generally grossly appears normal. If spirochetosis is found, the patient should be screened for HIV if not already done. The most effective treatment based on literature review is metronidazole.

Katherine Hoversten, MD
Roberto Leon-Ferre, M.D.

Breast cancer in pregnancy: Challenges in diagnosis, staging, and management

The approach to cancer during pregnancy poses challenging decisions.
Extensive imaging, although important for staging and treatment decision-making, can pose risks to the fetus. In addition, many effective anticancer agents are contraindicated during pregnancy. All of these factors need to be carefully weighted when evaluating pregnant patients with cancer.

CASE DESCRIPTION: A 24-year-old woman at 14-weeks gestation presented to clinic with a new tender right breast lump. Her history was notable for a Wilms tumor at age 5 involving both kidneys and lungs, which was treated successfully with nephrectomy, chemotherapy and whole lung radiation. Biopsy of the new breast mass was consistent with high-grade, invasive ductal carcinoma, ER+, PR+, HER-2/Neu +. The patient strongly desired to carry her pregnancy to term, and her treatment team was supportive of this. She underwent bilateral mastectomies which revealed a 1cm tumor of similar characteristics as initial biopsy. Axillary lymph node dissection revealed 3 positive lymph nodes. Given her pregnancy, usual staging with PET/CT or CT chest and abdomen and bone scan could not be carried out. Instead, she underwent a chest x-ray and liver ultrasound. The liver ultrasound showed two concerning lesions, and the chest x-ray showed nodularity that raised concern for metastasis versus changes resultant from her previously radiated Wilms tumor metastasis. To further characterize the lung lesions, a CT of the chest with abdominal shielding was pursued and showed multiple cavitary pulmonary lesions, along with several bony lesions in the vertebral bodies. A biopsy of a spinal lesion was performed and surprisingly returned negative for malignancy, although a repeat scan 2 months later did show progression of the skeletal lesions. Four cycles of chemotherapy with doxorubicin and cyclophosphamide were carried out with deferment of endocrine and HER-2 directed therapies until after pregnancy due to their inherent fetal risks. A PET/CT has been planned for after delivery at which point further therapy will be guided by burden of disease. The patient’s pregnancy is meanwhile being managed by High Risk Maternal and Fetal Medicine with a plan for delivery at 34-weeks gestation. At 33 gestational weeks, there is no sign of harm to the baby.

DISCUSSION: This unfortunate case illustrates the importance of monitoring for secondary cancers in patients with previously treated malignancies, particularly with a history of prior radiation. In addition, this case showcases the challenges faced by a diagnosis of cancer during pregnancy. It is important to note that in some malignancies, including breast cancer, termination of pregnancy does not improve outcomes. If pregnancy is continued, staging and timing of therapy should be adjusted to best protect the developing fetus. Finally, management of such a complex case is best approached by a collaborative multidisciplinary team.

Marie Hu, MD
Vania H. Phuoc, Thomas J. Beckman

Babesiosis: A Rare Cause of Hemophagocytic Lymphohistiocytosis

Hemophagocytic lymphohistiocytosis (HLH) is a syndrome of excessive immune activation and tissue destruction that can be life-threatening. It is almost always associated with an underlying trigger that disrupts immune homeostasis. The most common triggers include malignancy (predominantly lymphomas), infection (especially viruses like EBV and CMV), and rheumatologic disorders.

A 66-year-old male with no past medical history presented to the emergency department with a three-week history of profound fatigue, lightheadedness, abdominal pain, fevers, night sweats, and weight loss. On presentation, he was febrile to 39.4°C and initial labs were significant for pancytopenia (Hgb 9.4, WBC 2.4, platelets 89), so he was started on empiric cefepime and vancomycin. A full work-up of viral (Parvo, EBV, CMV, HSV, VZV, HIV, HCV), fungal, and autoimmune etiologies of pancytopenia were all negative. Further testing revealed elevated inflammatory markers (ESR 50 mm/hr, CRP 91 mg/L), undetectable haptoglobin, LDH 414, and ferritin 1838. PET/CT showed FDG avidity diffusely in the spleen with mild splenomegaly but no abnormal uptake in the bone marrow and or lymph nodes. Bone marrow biopsy showed normocellular bone marrow with morphologically normal trilineage.
hematopoiesis and few hemophagocytic histiocytes consistent with HLH. Therefore, he met five of the eight criteria for HLH. Upon further questioning, it was discovered that the patient enjoyed hiking weekly along various trails in Southern Minnesota and had observed a tick on his arm about one month prior to development of symptoms. A tick-borne panel subsequently returned positive for Babesia microti, and negative for Lyme, Ehrlichia and Anaplasma. The peripheral smear confirmed organisms compatible with Babesia species. The patient was then initiated on a 10-day course of azithromycin and atovaquone. By Day 2 of treatment he felt much improved, and by Day 5 all of his cytopenias had nearly resolved. He was discharged home with close follow-up to ensure full recovery of his pancytopenia.

To our knowledge, there have been only two published cases of HLH resulting from babesiosis. A diagnosis of HLH should be considered in patients presenting with fever, cytopenias, hepatosplenomegaly, and an extremely elevated ferritin level. For formal diagnosis, at least five of the following 8 criteria should be met: fever, splenomegaly, cytopenias in multiple cell lines, hypertriglyceridemia, hemophagocytosis on pathology, hyperferritinemia, impaired NK-cell activity, and elevated soluble CD25. Timely diagnosis is crucial to prevent fatal complications of this disease. This case also highlights the importance of identifying an underlying cause of HLH. With proper identification and treatment of the trigger, many patients with mild HLH can experience full recovery and avoid aggressive therapies such as chemotherapy or hematopoietic stem cell transplant.

Rocky Mountain Spotless Fever

Rocky Mountain Spotted Fever (RMSF) is a rare life-threatening condition. It is the most common fatal tickborne disease in the United States. Although unusual in Minnesota, it remains an important possibility in rapidly deteriorating patients. Empiric treatment should be considered in patients with fever, hyponatremia, and hepatitis, even if no rash is present. Digit necrosis secondary to infectious purpura fulminans is a potential complication.

A 51 year old previously healthy female presented to an urgent care center with fever, malaise, cough, emesis, and diarrhea. One week prior to admission, she was outdoors at an all-day fishing excursion and afterwards felt as if she had “heat stroke.” Over the next several days, she developed a non-productive cough, fevers to 103 F, chills, night sweats, diarrhea, and non-bloody emesis. Travel history was negative. No rash was observed at any point. At the urgent care center, she was found to have multiple laboratory abnormalities including severe hyponatremia to 120, lactic acidosis, and acute hepatitis (AST 246, ALT 154, TBili 1.6, DBili 1.5). She was directly admitted to the medical ICU for evolving sepsis. Urinalysis and chest x-ray were unremarkable. Abdominal ultrasound was consistent with acute hepatitis. Infectious workup with negative, including HIV, hepatitis viruses, CMV, EBV, HSV, Tuberculosis, Ehrlichia, Anaplasma, Babesia, Lyme, West Nile, Leptospirosa, Histoplasma, Legionella, and other bacterial, viral, protozoan, and fungal diarrheal pathogens. Autoimmune workup was negative, including cryoglobulin, ANCA, ANA, dsDNA, and phospholipid panel. Lake water from her fishing excursion was negative for cyanobacteria. Spotted fever group antibodies were initially negative on admission. In the ICU, she continued to decompensate despite broad antibiotic coverage with cefepime, metronidazole, vancomycin, doxycycline, and acyclovir. The patient’s long ICU stay was complicated by septic shock requiring 3 vasopressors, intubation for hypoxic respiratory failure, and hemodialysis for sepsis-related ATN. While on vasopressors she developed dark discoloration of her fingers and toes resembling frostbite thought to represent infectious purpura fulminans. Despite the lack of travel history and the rarity of RMSF in Minnesota, there was clinical concern for the disease based on her clinical presentation. Spotted fever group antibodies were repeated one week after admission. Both IgM and IgG titers were positive at 1:64 and 1:256 respectively, confirming the diagnosis. She gradually recovered over the next
This case highlights the complexity of diagnosing and treating RMSF. Although native cases are unusual in Minnesota, it is an important life-threatening possibility to consider for a rapidly deteriorating patient as serologies may not become positive until weeks after symptom onset. The symptom constellation of fever, hyponatremia, and hepatitis should raise suspicion for tickborne illness even in the absence of a rash. Complications may include digit necrosis from infectious purpura fulminans.

**Brandon Huffman, MD**  
Jeff Wiisanen, MD; Min Shi, MD, PhD; Ronald Go, MD

**Feeling run down: Extreme exercise-induced pancytopenia**

**Introduction:** Overexercise-induced malnutrition can lead to deleterious effects including a mixture of nonspecific findings, including pancytopenia, hypogonadism, bradycardia, and hypothermia. Gelatinous transformation, also referred to as serous fat atrophy or starvation marrow, can be seen in malnourished patients on bone marrow biopsy and is a potentially reversible cause of pancytopenia.

**Case description:** An 18-year-old young male consulted his primary care provider for fatigue and poor athletic performance. He was a competitive cross country runner who ran up to 80 miles weekly, and he began noticing that short distances would cause him significant pain and extreme exhaustion. He had no significant past medical history. No family history of bone marrow disorders. He was up to date on his immunizations and denied any recurrent infections. On examination, he was bradycardic at 54 bpm, normotensive, and hypothermic at 35.6 degrees Celsius. He appeared fit with a body mass index of 20. There was mild conjunctival pallor. Otherwise, exam was normal. Basic laboratory testing showed mild transaminase elevation, decreased testosterone, decreased luteinizing hormone, mild leukopenia (WBC 3.1), macrocytic anemia (Hgb 11.1 with MCV of 103), and thrombocytopenia (131). Liver biopsy showed nonspecific findings. Acute hepatitis panel, HIV, hemochromatosis, autoimmune hepatitis, and celiac disease panel were negative. The peripheral smear showed no morphologic abnormalities. Hematology was consulted. Bone marrow biopsy showed profoundly decreased cellularity of 5%. An amorphous eosinophilic substance near completely replaced the marrow sample. Congo red stain, reticulin, and trichrome stains were negative. Findings were consistent with gelatinous transformation of the bone marrow or serous fat atrophy. Flow cytometry did not reveal a monoclonal B-cell population or paroxysmal nocturnal hemoglobinuria. Chromosome analysis was normal. Parvovirus B19 PCR was positive in the bone marrow, but negative from the peripheral blood. Fanconi sensitivity studies and telomerase mutations were negative. Antinuclear antibody, copper, zinc, EBV IgG, EBV DNA, and CMV IgG were all normal/negative. Given his extreme exercise schedule and physical manifestations of malnutrition, inpatient treatment for a suspected eating disorder was recommended.

**Discussion:** The differential for pancytopenia is wide and includes congenital or acquired bone marrow failure syndromes, marrow space-occupying lesions, peripheral destruction of hematopoietic cells, autoimmune disorders, infection, and ineffective marrow production. Initial evaluation should include detailed clinical history, medication, recreational drug, and environmental exposure history. Bone marrow biopsy and hematology consultation is usually indicated. When serous fat atrophy is identified as the likely cause of pancytopenia, malnutrition secondary to cancer, heart failure, anorexia nervosa, or alcoholism should be considered, as it is a rare pathologic finding of unclear etiology. These changes have been reported to be reversible depending on the inciting nature of the disease. This patient’s constellation of symptoms and exam findings make malnutrition the most likely diagnosis.

**Joseph Huguelet, MD**  
Amy Holbrook, MD

**Oh, by the way, I may have ebola**

January of 2015, an ophthalmologist from Monrovia, Liberia presented to the emergency department with hematuria. He reported a history of benign prostatic
hyperplasia and hematuria following a prostate resection. At the triage desk, the patient denied recent travel. After being placed in a room he acknowledged that he had just flown from Monrovia to Ghana, then to Amsterdam, Atlanta and finally Minneapolis the day prior. Hematuria had begun on his flights but had worsened overnight. Despite being a physician from Liberia, he reported that he taught in the medical school, had no ill contacts or known Ebola exposure, and hadn’t attended any funerals. He denied fevers, diaphoresis, nausea, emesis, myalgias or arthralgias but endorsed mild chills after urinating. He also denied dysuria, diarrhea, hematochezia or melena.

The patient was placed in an isolated room and the Minnesota Department of Health was contacted. They confirmed that he had undergone the proper exit and entrance screenings and that his symptoms weren’t consistent with Ebola. They agreed that he could be admitted into the hospital and no specific contact precautions were recommended. A urinalysis showed frank blood and concern for infection. Urology began continuous bladder irrigation and he was started on ceftriaxone for a presumed urinary tract or prostatic infection.

On hospital day 2, the patient had a new fever of 100.6°F and was diaphoretic. A urine culture showed ESBL Klebsiella pneumoniae only susceptible to carbapenems. He was switched to imipenem. The patient’s hemoglobin had fallen to 6.6 mg/dl so a unit of packed red blood cells (PRBC) were ordered. 30 minutes after beginning PRBC transfusion, the patient became more diaphoretic, uncomfortable and febrile to 102°F and staff were temporarily reluctant to enter his room. Their perception was that the patient was now a higher Ebola risk and screening may have been insufficient. They also argued that nursing staff had been told that they wouldn’t take care of patients with risk any concern for Ebola. The patient had no further fevers after hospital day 2. On hospital day 6 the patient underwent cystoscopy and transurethral resection of his prostate. The patient did well over the following days without further hematuria or fevers and was discharged with orders for daily outpatient infusions of ertapenem for 7 days.

This case highlights issues faced by many healthcare facilities in response to the West African Ebola epidemic. A clear understanding of Ebola, its symptoms and how to stratify individual risk weren’t universally known. Nationally and in our hospital, protocols for potential exposure were also not universally understood or implemented. Learning from these mistakes will allow for better preparedness during future disease outbreaks and more consistent delivery of quality healthcare.

Isabel Hujoel, MD
Gwen E. Thompson, James S. Newman

**Hereditary condition presenting as severe rhabdomyolysis**

The possible etiologies of rhabdomyolysis can be divided into three main categories: traumatic, nontraumatic exertional, and nontraumatic nonexertional. When a patient presents with rhabdomyolysis a detailed history will help to differentiate between these categories and therefore limit the differential. Herein, we describe a rare cause of rhabdomyolysis where a careful history was crucial in diagnosis.

A 35 year-old previously healthy male was admitted with acute renal failure secondary to rhabdomyolysis. Two days before admission, he was moving a heavy desk when he experienced significant muscle contraction of his legs. The following day, his urine output decreased and he developed nausea and vomiting. On presentation his creatinine kinase (CK) was over 200,000 and his creatinine was 5. He was admitted and started on dialysis. His course was complicated by the development of seizures secondary to posterior reversible encephalopathy syndrome (PRES).

Further history revealed that in the month prior to hospitalization, he was undergoing evaluation for increasing fatigue and elevated liver enzymes. Family history revealed that his sister had similar symptoms of fatigue accompanied by weakness. He was on no medications and denied illicit drug use. The physical exam was notable for tenderness over his bilateral quadriceps and normal strength.
Work-up found elevated inflammatory markers and an elevated AST of 91 and an ALT of 147 (upper limits of normal being 48 and 55 respectively). Further investigation revealed a normal pyruvate kinase and TSH. An analysis of carnitine and acylcarnitine panel showed mildly elevated acylcarnitines in no specific pattern. Ultimately, a muscle biopsy from his left quadriceps was obtained that showed McArdle disease (myophosphorylase deficiency). The patient continued to improve during hospitalization and after discharge. His kidney function recovered and he no longer required dialysis.

In approaching rhabdomyolysis, a thorough history is imperative both for diagnosis and to identify treatable causes. In this case, several clues pointed to the ultimate diagnosis of McArdle’s disease, which is a metabolic myopathy that is a rare cause of nontraumatic exertional rhabdomyolysis. These included the absence of multisystem involvement, late onset of symptoms, history of elevated liver enzymes, and family history of similar symptoms. This patient’s diagnosis carried implications not only for therapy with dietary changes and exercise, but also for his young daughter given the autosomal recessive nature of the condition.

Ashley Husebye, MD

When broad-spectrum antimicrobials are not enough

A 53-year-old female with past medical history significant for rheumatoid arthritis on chronic immunosuppression (rituxan, cellcept, and chronic prednisone) and leukoclastic vasculitis was transferred to HCMC after having several months of complications following a cystoscopy. She initially presented three months prior with severe abdominal discomfort. CT imaging demonstrated thickened bladder and she was treated with a course of antibiotics for presumed UTI. When her symptoms did not improve, cystoscopy was performed with evidence of inflammation. She had a procedure called bladder instillation which involved placing heparin, sodium bicarbonate, lidocaine, and solu-medrol in the bladder. Spinal anesthesia was used during this procedure. A few days later, she developed severe abdominal and back pain. MRI of the back showed an epidural abscess from T9-T11 with evidence of spinal cord impingement. Neurosurgery performed a T9 and T10 decompression with T10 open laminectomy with evacuation of abscess. Multiple urine cultures were negative. Epidural abscess cultures were negative. She was maintained on broad-spectrum antibiotics of meropenem and vancomycin. Follow up imaging a month later was concerning for developing T10 osteomyelitis. Over the next month, she continued to have issues with fevers, back pain, and drainage tracts from her back. She developed a T10 compression fracture and was placed in a TLSO brace. Neurosurgery brought the patient back to the OR twice for debridement. One of culture grew MSSA of unclear significance. Remaining cultures including RNA sequencing were negative.

The patient was transferred to HCMC for hyperbaric treatment. At the time of transfer, she had been treated with ceftazidime/avibactam, daptomycin, caspofungin, and ciprofloxacin for over three weeks. She was continued on broad-spectrum antibiotics on admission. MRI showed worsening epidural abscess, T8-T10 osteomyelitis, and a new abscess under the right scapula. Culture of the right scapula abscess did not grow anything on routine bacterial or fungal cultures. A 16S rDNA sequencing was sent and positive for ureaplasma parvum. Doxycycline was started with stabilization of her disease. Ureaplasma parvum is a type of mycoplasma species. Mycoplasma species are the smallest free living organisms and lack a cell wall, which means they can be difficult to identify, do not have a gram stain reaction, and therefore are not susceptible to many antibiotics. Mycoplasma species are typically found in the respiratory and urogenital tracts. Ureaplasma have been associated with invasive joint infections as well as respiratory infections, typically related with bacteremia in the setting of humeral immunity. Since this patient was on rituxan, she likely was at increased risk for an ureaplasma infection, which is difficult to identify on culture and not treated by typical broad spectrum antibiotic coverage.
### Decent into Madness: An Increasingly Common Cause of Post-Partum Psychosis in Young Women

Case: A 28-year-old Caucasian female with a past medical history of epilepsy presented for direct admission to the inpatient neurology unit from an outside hospital after developing generalized tonic-clonic seizures. She had been suffering from what was thought to be post-partum blues, but now presented with new-onset psychosis. Her depressive symptoms lasted for one week and were followed by a two-week-long state of hyperactivity, delusions of grandiosity, rapid mood changes, auditory hallucinations, and insomnia. She had remained seizure free for four years prior to this episode, and had continued her antiepileptic regimen through pregnancy.

**Case Presentation:**

- **History:** A 28-year-old female with a past medical history of epilepsy presented for direct admission to the inpatient neurology unit from an outside hospital after developing generalized tonic-clonic seizures. She had her first spontaneous vaginal delivery three weeks prior to presentation, and had been suffering from what was thought to be post-partum blues.

  - **Symptoms:** Depressive symptoms lasting for one week, followed by a two-week-long state of hyperactivity, delusions of grandiosity, rapid mood changes, auditory hallucinations, and insomnia.

  - **Medical Workup:** Extensive medical work up for both seizure and post-partum psychosis, including: CBC, BMP, calcium, LFTs, TSH, B12, hepatitis panel, HIV, FTA-ABS, UA, blood cultures, and serum autoimmune workup was negative. Serum level of Lamotrigine was low and Levatiracetam was normal.

  - **Imaging:** MRI of the brain showed only nonspecific findings, and EEG did not capture any epileptogenic activity.

  - **Lumbar Puncture:** Under fluoroscopy due to active psychosis, revealed lymphocytic pleocytosis.

  - **Treatment:** IVIG was initiated promptly, due to high clinical suspicion of anti-NMDA receptor encephalitis.

  - **Discussion:** Anti-NMDA receptor encephalitis is frequently associated with an underlying neoplasm, most often an ovarian teratoma. Therefore, a transvaginal ultrasound and PET scan was obtained, but did not reveal an ovarian or extra-ovarian teratoma. A paraneoplastic epilepsy panel was also obtained, and revealed NMDA receptor antibodies. Patient continued to receive treatment with weekly infusions of rituximab following a 5-day course of IVIG.

  - **Outcome:** Presently, the patient's positive psychotic symptoms have resolved, though she remains altered with facial dyskinesia, catatonia, and occasional dystonic posturing. Her current antiepileptic regimen was optimized, to daily lacosamide and levetiracetam.

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### Not All Bladder Masses are Transitional Cell Carcinoma: An Unusual Presentation of a Lymphoproliferative Disorder

Case: An 83-year-old female presented with a two-week history of worsening low back pain, radiating to the pelvis and groin, with an increase in baseline urinary frequency and nocturia. Past medical history was significant for: atrial fibrillation on anticoagulation (Xarelto), monoclonal gammopathy, mitral insufficiency, pulmonary hypertension, hypothyroidism, diabetes, and prior hysterectomy. Physical exam was remarkable for obesity, irregularly irregular rhythm, systolic bruit, and right lower quadrant tenderness. Admission labs included: hemoglobin 11.7 g/dL, white blood cell count 7.1 k/cumm, platelet count 233 k/cumm, mean corpuscular volume 111.2 fl, creatinine 0.6 mg/dL, BUN 18 mg/dL, alkaline phosphatase 293 U/L, and a normal calcium level.

**Discussion:** The patient's presentation was concerning for a lymphoproliferative disorder, as evidenced by her history of monoclonal gammopathy and mitral insufficiency. The differential diagnosis included multiple myeloma, Waldenström macroglobulinemia, and primary systemic amyloidosis. Further evaluation with bone marrow biopsy and serum free light chain analysis were ordered to confirm the diagnosis.
mg/dL, total protein 8.0 mg/dL, albumin 3.2 mg/dL, total bilirubin 0.6 mg/dL, alkaline phosphatase 492 IU/L, AST 62 IU/L, and ALT 59 IU/L. Abdominal-pelvic computed tomography (CT) scan with contrast showed two foci of hyperdense bladder wall thickening (1.1 x 1.7, 2.9 x 1.7 cm), bilateral inguinal lymphadenopathy (left, 3.4 x 2.9 cm; right, 2.5 x 1.7 cm); left internal/external iliac and left para-aortic lymphadenopathy; hepatic steatosis. Cystoscopy revealed firm, circumferential lower vaginal nodules (4-10 mm) and two masses appearing external to the bladder causing significant distortion: one large mass encompassing the bladder trigone, and a second left posterior bladder wall mass. There was mild mucosal edema over the masses, but no papillary changes typical with urothelial malignancy. Vaginal/bladder biopsies revealed an extensive nodular lymphoid infiltrate with intervening fibrosis characterized by increased vascularity, and subepithelial collections of small mature lymphocytes, admixed with histiocytes, eosinophils, plasma cells, and scattered Reed-Sternberg cells/variants and mummified cells. Most background lymphocytes were CD3/CD45-positive; Reed-Sternberg cells/variants were positive for EBER ISH/CD15/CD30/PAX5, and CD3/CD20/CD45-negative. Morphologic and immunophenotypic characteristics were consistent with Hodgkin lymphoma, suggestive of classic mixed cellularity subtype. Subsequent PET/CT showed uptake in a left supraclavicular lymph node and an ill-defined uterine area mass invading the posterior bladder wall. Bone marrow was normocellular for age with no evidence of Hodgkin lymphoma (HL). For her Ann Arbor stage 3 disease, ChlVPP (chlorambucil, vinblastine, procarbazine, prednisone) therapy was initiated.

HL accounts for 10% of all lymphomas, with disease generally beginning in a solitary lymph node, then spreading through contiguous lymphatic chains; extranodal presentations as in our patient are uncommon, comprising 5-10% of all cases. Reported extranodal sites include the lung, stomach, intestine, liver, bone, breast, kidney, epidural space, and head/neck. In small series, there is a male predominance, with half of patients having Ann Arbor stage 1-2 disease. Biopsy is essential in making the diagnosis. Treatment is as in nodal HL, with a favorable prognosis. Our case should prompt physicians to consider HL in the differential diagnosis of any tumor, as prognostic and therapeutic implications are significantly different.

Michael Jaeger, MD
Dr. Rishi Kumar

When Things Aren't Entirely as They Seem
Case Description: 67 year old male, presents to the ED with weakness. Patient too weak to get out of bed at shelter, brought in by ambulance for evaluation. Initially no complaints, not sure why he was brought into the ED. Physical Exam: 144/78, 101, 12, 98%; General: No acute distress, unkempt, disheveled, somewhat confused. HEENT: Atraumatic; CV: RRR, No murmurs Respiratory: Non-labored breathing on room air, rhonchi with consolidation posteriorly throughout nearly all lung fields. No wheezes Abdomen: Normal body habitus, normoactive bowel sounds, non-tender, non-distended MSK: radial and pedal pulses 2+ bilaterally, 1+ pitting edema bilaterally. Neuro: AAOx2 (place and person, no date, does know season), CN2-12 intact, Strength 5/5 bilaterally arm flexion and extension, hip flexion and extension, leg flexion and extension, planar and dorsiflexion, EHL and FHL. Biceps and patellar reflexes normal. SILT at all dermatomes bilaterally Skin: Overall skin is in an unkempt condition Investigative studies: CXR: Multifocal airspace opacities, concern for underlying malignancy vs multifocal pneumonia Chest CT: Nodular confluent opacities in both upper and lower lobes, cystic lunacies and cavitation of nodules. Heat CT: 1.1 cm hyper-dense round mass in the cerebellar vermis just to left of midline without any obvious surrounding edema Positive AFB smear. Patient's progress and outcome. Patient was admitted and started on treatment for Tuberculosis. Due to his
unstable housing he was kept in the hospital until his AFB smear was negative x3, or had negative AFB cultures. The mass seen in his brain was presumed to be a tuberculoma. His smears and cultures continued to be positive and he was completing 2 months of treatment. His initial culture showed pan-sensitive TB. Despite adequate treatment, he continued to show clinical deterioration. Serial imaging of his brain mass showed continued growth. After discussions with the patient the decision was made to undergo biopsy of his brain. After surgical resection of the mass, pathology came back showing adenocarcinoma. It was presumed that this was a lung primary that was obscured by the large cavitary lesion in his chest.

Discussion: There is a known association between a history of pulmonary TB and the development of adenocarcinoma. However, the learning point for myself was seeing a patient that was receiving adequate treatment for his diagnosed disease, but continued to deteriorate. I saw how taking another closer look at the differential pushed us to do more diagnostic testing and confirm a different diagnosis as well.

Mithulan Jegapragasan, MD
Dr. Sumedh Hoskote

Crazy Paving Misbehaving
Cough and dyspnea has a long differential and workups should be guided when possible by the past medical history.
CASE PRESENTATION: 45 year old female with a past medical history of exercise induced asthma and gestational diabetes presents with acute onset of cough, dyspnea, and left-sided chest pain. She had childhood episodes of bronchitis in the winter and was diagnosed with exercise-induced asthma several years ago. She was given a rescue inhaler, which she has not used. She has travelled to Eastern Europe on missionary work and has no pets or exposures.

After developing the above symptoms, she was initially evaluated at an outside emergency department where she was found to have a large left sided pneumothorax. She had initial management with a large bore chest tube and was admitted for one week. CT scan was concerning for possible interstitial lung disease and given this, she was discharged on a prednisone taper. She had follow-up with a pulmonologist and underwent a BAL. BAL was negative for infectious causes but the retrieved fluid was milky in quality. GM CSF was positive at 12,800 and VAT’s biopsy was consistent with pulmonary alveolar proteinosis (PAP). She was treated with bilateral lung lavage and discharged on nebulized GM CSF 450 mcg twice a day.

DISCUSSION: Pulmonary alveolar proteinosis was first described in 1958 and since that time less than 500 cases have been cited in the literature. Three different types of PAP exist: idiopathic, secondary, and congenital. Like in our patient, most cases are idiopathic and present at an average age of 40 years old. Secondary causes include industrial exposures including fiberglass, cement duct, and silica particles.

Clinical presentation is most often dyspnea and cough, but can at times be non-specific and often very mild. Pneumothorax is a rare presentation for PAP and has been described in the literature once prior. CT scan can aid with diagnosis with imaging showing a geographical appearance with geometric shapes referred to as “crazy paving”. Diagnosis is confirmed with biopsy. PAP should remain in the differential for patients presenting with cough and dyspnea of unknown cause.

Ryan Jelinek, MD

The Diagnosis of a Rare Fibrosis
Retroperitoneal fibrosis (RPF), is a rare disease with some studies estimating it’s incidence to be as small as 1 case per one million people. RPF is commonly idiopathic and causes profound inflammation and scarring of the retroperitoneum. Patients can present with symptoms related to urethral obstruction or entrapment of other local structures; however, many have non-specific complaints. The diagnosis of RPF requires a high degree of suspicion, as the frequency and empiric treatment of other causes of renal colic can delay
DS is a previously healthy 28 year-old man who presented with one month of vomiting and weight loss and two weeks of progressive left-sided flank pain. He had already been seen twice at another local hospital and diagnosed with constipation and suspected ureterolithiasis, even though a CT scan had not demonstrated any stones. On presentation he had an elevated heart rate, left lower quadrant tenderness and left-sided flank pain. Labs revealed leukocytosis, elevated serum creatinine and proteinuria. Repeat CT of the abdomen/pelvis with IV contrast was obtained and showed an enlarged left kidney with rim-enhancing fluid at the left inferior pole concerning for abscess. Reactive left periaortic and iliac chain lymphadenopathy was also noted. Findings were concerning for perinephric abscess; consequently, IV antibiotics were initiated. Urology was consulted and performed a retrograde pyelogram which showed narrowing in the distal left ureter. A stent was placed and resulted in rapid relief of the patient’s pain, nausea and vomiting and normalization of his creatinine. Upon review of the images, Urology felt the location of the ureteral stenosis along the retroperitoneal wall was concerning for possible RPF or lymphoma. A CT-guided biopsy of the retroperitoneum was obtained and confirmed retroperitoneal fibrosis. Serum IgG levels were done and showed diffuse elevation with a predominance of IgG4. Final diagnosis was IgG4-related retroperitoneal fibrosis. Patient was started on prednisone and referred to a rheumatologist.

This case illustrates an extremely rare cause of ureteral obstruction which is amenable to treatment if the proper diagnosis is made. The patient’s constellation of symptoms – flank pain, nausea, vomiting, weight loss – together with ureteral obstruction on imaging in the absence of a confirmed stone should raise suspicion for RPF. CT and MRI remain the imaging tests of choice; however, in this case the diagnosis was made only after CT failed to reveal a cause of obstruction, after which the differential diagnosis was broadened. This case underscores the need to maintain a broad differential in patients presenting with renal colic and ureteral obstruction, particularly in cases where stones are not confirmed. This poster will highlight this case as a review to the diagnosis and management of RPF.

Kimi Johnson, MD
Miguel Teixeira,

**A Case of Methamphetamine Induced Reverse-Takotsubo Cardiomyopathy**

Methamphetamine is the second most commonly abused substance in the world. It has many known possible adverse effects on the cardiovascular system including a drug-induced cardiomyopathy leading to heart failure with a spectrum of presentations from a reverse Takotsubo (RT) pattern to global hypokinesis with permanent fibrosis of the myocardium. Younger women with relatively less chronic abuse may more often present with the RT findings. The RT compared to classical takotsubo dysfunction may be due to the relative concentrations of adrenergic signals induced by drug-use compared to a natural stress response, and also the concentration distribution of the adrenergic receptors in different segments of the ventricle. Characteristics of the dysfunction pattern and particular MRI findings may help elucidate the likelihood of improvement following cessation of the drug for those with cardiomyopathy.

A 31 year old woman with a past medical history of methamphetamine use presented to the ED with a two-day history of substernal chest pain associated with dizziness and diaphoresis. Her last use of methamphetamine was three days earlier. She was found to have orthostatic blood pressures, T-wave inversions of the inferior leads on ECG, an elevated Troponin I of 0.12, and positive urine toxin screen for methamphetamines. She was given fluids, aspirin and nitroglycerin, followed by coronary catheterization, which found normal coronary arteries. The following day, she continued to have chest pain that was made worse with standing and improved with recumbency. Her troponins remained elevated at 0.12 throughout the day. CRP was 3.2 and Pro-BNP was 1516. Cardiac MRI revealed severe hypokinesis in the mid ventricular lateral
and anterolateral walls as well as in the inferolateral walls, with preserved basal and apical function (LVEF 40%). Mild myocardial edema was noted in the hypokinetic segments, but no resting perfusion defect or abnormal delayed enhancement was identified. The following day her troponin had risen to 0.14, her blood pressures remained orthostatic, and her chest pain symptoms were still present intermittently, but improving in frequency and severity. Follow up echocardiogram showed improvement of LV dysfunction. She was discharged with plan to follow up as outpatient for resolution of symptoms.

Our patient’s case of methamphetamine-induced cardiomyopathy displayed an unusual Takotsubo pattern with sparing of the both the apical and basal regions of ventricle. Her lack of fibrosis and lack of other chronic remodeling findings increase her likelihood of recovering ventricular systolic function in <6 weeks. Amphetamine induced cardiomyopathy is still an emerging area of research and identification of prognostic features at presentation will be important for managing further care of these patients.

Brianna Johnson-Rabbett, MD

Rifampin induced thrombocytopenia
Introduction: Thrombocytopenia is commonly encountered in clinical practice. Having a broad differential is important to identify less common and potentially easily reversible etiologies.
Case description: The pt is a 47F with a significant PMH including recent subependymoma/ependymoma resection from the posterior fossa and latent tuberculosis. She presented to urgent care with complaints including bruising/rash as well as nose and gum bleeding and was subsequently sent to the ED for further evaluation. On interview, it was noted that she was compliant with rifampin therapy, for which she had been recently initiated on for treatment of latent TB. On physical exam, pt was noted to have ecchymoses and scattered petechiae. Plt count returned at 2, and on additional questioning pt endorsed new and different headaches. Head CT was negative for acute pathology. Other cell lines were WNL, repeated coags, bilirubin, fibrinogen were normal, bench smear demonstrated no evidence of schistiocytes. Glucocorticoids were initiated as primary ITP can initially be indistinguishable from DITP. Pt received plt transfusion and repeat plt count was 59, remaining stable on subsequent repeat testing. IVIG administration was deferred given response. Of note, pt had been partially treated for tuberculosis with regimen including rifampin in the past, with most recent drug exposure within 3-4 months of presentation. Laboratory studies for rifampin related platelet antibody as well as other studies to rule out infectious or nutritional etiologies were also sent. Later, rifampin related plt ab returned positive, supporting the diagnosis of rifampin induced thrombocytopenia. Plt count returned to normal at follow up post discontinuation of rifampin.
Discussion: Severe thrombocytopenia is life threatening and needs to be addressed immediately, and in this case was complicated by recent neurosurgery. Emergent etiologies to rule out immediately include TTP, DIC, HIT, acute leukemia. History and physical, chart review, and bench review of blood smear can rule out most of these etiologies. Especially in the context of very low plt counts, ITP needs to be strongly considered. Thorough history and chart review to identify possible causes of drug induced ITP is necessary, as the treatment of ITP and DITP diverge. DITP should resolve post discontinuation of causative agent.

Daniel Johnsrud, MD

A Hypertension Essential to Diagnose
A 62 year old woman with a two day history of abdominal pain, vomiting presented to the emergency department. Past history was significant only for hypertension and essential tremor. Initial vital signs were significant for hypertension to 180/120, tachycardia to 105 with exam significant for mild abdominal tenderness. Labs showed a leukocytosis as well as elevation in lipase and creatinine. CT of the abdomen showed a large right sided abdominal mass concerning for renal cell carcinoma. Due to the symptomatic nature of the mass
as well as her abnormal vital signs she was admitted for inpatient evaluation. Further history revealed about one year of worsening, difficult to control hypertension despite escalation of therapy including moderate to high doses of propranolol, nifedipine and lisinopril. She additionally described several years of chronic, progressive, vague symptoms including upper and lower extremity weakness, paresthesias of the scalp and extremities. Symptoms were noted to be worse with her morning showers and additionally while bending over to tie her shoes. Additionally she reported several years of constipation and no bowel movements at the time of admission for the past several days. Lab recheck showed a normal lipase, stable creatinine, stable leukocytosis. Blood pressure was managed with her home antihypertensive regimen plus hydralazine as needed. Urology was consulted for possible resection, and noting the superior nature of the mass, requested MRI be performed to assess for adrenal involvement which suggested compression of the superior renal pole with an intact layer of fat between the mass and kidney. The mass measured 10.7 x 9.3 x 10.4 cm with no involvement of renal vessels or IVC. Plasma metanephrine was obtained and found to be elevated to 52 nmol/L (normal <0.5). Twenty four hour urine metanephrines were subsequently obtained at 54,894 mcg (normal 30-180). Endocrinology and General Surgery were consulted for assistance with surgical and medical management of suspected pheochromocytoma. The patient received 9 days of phenoxybenzaprime with salt tablets to prevent orthostasis and proceeded to the operating room for resection. Pathologic examination confirmed the diagnosis. Post operative course was complicated by pulmonary embolism; however, the patient otherwise recovered well with complete resolution of hypertension. Although the diagnosis was eventually obtained with laboratory and imaging findings, several important clues were present in the history – namely, worsening, resistant hypertension concurrent with spells of a hyperadrenergic character. Additionally, although most pheochromocytomas are around 5 cm in size at diagnosis, this example was significantly larger. Nevertheless, careful diagnosis prior to surgical intervention prevented a possibly disastrous outcome if the diagnosis had not been made prior to operation.

Amrit Kamboj, MD
Thomas G. Cotter, Cyril Varghese

A Case of Relapsing Polychondritis with Myelodysplastic Syndrome

Background: Relapsing polychondritis (RP) is an exceedingly rare immune-mediated condition, occurring in approximately 3.5 per million individuals annually. Approximately, one-fourth of all RP cases are associated with myelodysplastic syndrome (MDS).

Objective: To describe a case of RP with dramatic auricular, cranial nerve (CN), and polyarthritis involvement in the setting of underlying MDS.

Case Report: A 65-year-old man presented with a 3-month history of neck and shoulder pain before developing left-sided CN VII palsy, bilateral ear pain and swelling, and right-sided hearing loss. His medical history was significant for high-grade transfusion-dependent MDS. On initial testing, laboratory studies revealed hemoglobin 9.1 g/dL, platelet count 112 x 109 cells/L, sodium 125 mmol/L, and BNP 13300 pg/mL. CRP and ESR were elevated to 161.1 mg/L and 47 mm/1hr respectively. A comprehensive infectious workup for viruses, bacteria, fungi, and parasites was negative. ANA, ANCA, MPO, PR3 were also negative. CT chest with inspiratory and expiratory views was unremarkable. A spine MRI illustrated diffuse epidural thickening and enhancement of cervical and upper thoracic spine consistent with extramedullary hematopoiesis in the setting of known MDS. An audiogram revealed profound bilateral mixed hearing loss. A bone marrow biopsy confirmed MDS with 7% bone marrow blasts and no circulating blasts. The patient was diagnosed with RP based on the combination of auricular chondritis, non-erosive seronegative inflammatory polyarthritis, and audiovestibular damage. The patient was treated with a 3-day course of IV Solu-Medrol 1 g followed by oral prednisone 60 mg with significant improvements in neck pain, bilateral ear inflammation, and left-sided hearing.
Discussion: RP is an autoimmune condition that involves inflammation of cartilaginous structures in the body. The diagnosis of RP is classically based on the McAdams criteria where at least 3 of the following 6 clinical features must exist: bilateral auricular chondritis, non-erosive seronegative inflammatory polyarthritis, nasal chondritis, ocular inflammation, respiratory tract chondritis, and audiovestibular damage. Our patient had multi-system manifestations of RP involving auricular, audiovestibular, polyarthritis, and cranial nerve findings. The most common feature of this disease at presentation is unilateral or bilateral ear inflammation seen in approximately 43% of patients. Auricular inflammation can persist from days to weeks and can progress to sudden hearing loss and tinnitus. While auricular chondritis is the hallmark feature of the disease, other anatomic areas including the eyes, nose, airways, heart, joints, vascular system, skin, and nervous system can also be affected to varying degrees. RP can present as a primary disorder or in association with other disorders such as systemic vasculitis and MDS. Patients with co-involvement of RP and MDS are more likely to be male and have lower survival rates due to the underlying malignancy.

Anna Karoline Lange, MD
Anya Jamrozy, MD

A Case of Rhombencephalitis
A 73-year-old man presented to the emergency department with fever after an unwitnessed fall at home. His medical history was significant for hemoglobin S/beta thalassemia and recent diagnosis of prostate adenocarcinoma. On the evening prior to presentation, the patient described eye pain and headache to his wife, who found him early the next morning unresponsive and shaking on the floor. On admission, the patient had a fever to 102.8°F and was alert, but confused. He was unable to follow simple commands and grimaced with passive neck flexion. A few small pustules were noted on his neck and forearms. Laboratory evaluation showed baseline anemia. A CT scan of his head was negative for acute pathology. CSF analysis showed slightly cloudy CSF, WBC 284, RBC 5, cell count 100, neutrophils 83%, lymphocytes 4%, monocytes 13%, glucose 52, protein 146. Gram stain was notable for 2+ WBC and no organisms were seen. CSF tests for HSV, VZV, EBV, Enterovirus and S. pneumococcus were negative. Treatment was started promptly in the ED after LP with Vancomycin, Meropenem (Penicillin allergy) and Acyclovir. Over the next few days in the hospital, the patient continued to have fevers, became increasingly somnolent and developed disseminated pustules. Concern was raised for aspiration and post-pyloric feeding tube was placed. Brain MRI showed swelling of the pons with extension into the cerebellar white matter suggestive of rhombencephalitis. Blood and CSF cultures showed no growth. Skin lesion cultures returned negative and biopsy pathology was unrevealing. Repeat LP showed positive EBV PCR and serum EBV DNA copies were also confirmed. Acyclovir was continued for possible benefit in EBV infection and TMP-SMX was added for increased activity against Listeria. Paraneoplastic panel was notable for mildly positive calcium channel binding antibody, which was felt to be positive due to known prostate malignancy and unlikely the cause for rhombencephalitis. Patient completed anti-infective therapy with slow gradual improvement and was discharged to a rehab facility after 31-day hospitalization.

Rhombencephalitis is an inflammatory condition affecting the hindbrain (brain stem and cerebellum) and has infectious, autoimmune and paraneoplastic causes. Without prompt treatment, this condition can potentially be life threatening. CSF analysis and CT scan are often negative and MRI is needed to confirm the diagnosis. Clinical findings include cranial nerves palsies, ataxia, tremor, and decreased level of consciousness. Respiratory failure is common. Listeria is the most common infectious organism, but can be detected in only about half of cases. EBV is a less common cause for RE and it remains unclear whether detectable viremia in this patient represented reactivation of dormant EBV and/or was the causative organism.
| Kathryn Larson, MD  
Nick Oblizajek, Eric Matteson | **Recalcitrant Sinusitis**  
Introduction and Background: Granulomatosis with polyangiitis (GPA) is an uncommon disease with an estimated prevalence of 3 per 100,000. It classically involves the upper and lower respiratory tract and kidneys with necrotizing granulomatous inflammation. Involvement of the upper airways is present in 95% of affected patients with symptoms such as paranasal sinus pain and drainage of purulent and bloody nasal discharge. It may progress to nasal septal perforation and saddle nose deformity. A positive c-ANCA and positive PR3 are present in greater than 90% of cases of severe generalized disease; 20-30% of patients with limited GPA may be ANCA negative. Cervicofacial actinomycosis is the “great masquerader” of head and neck disease. Infections may progress to formation of multiple abscesses, fistulae, and draining sinus tracts which are often dental in origin. Histology reveals acute and/or chronic inflammatory granulation tissue and may include granulomas. These infections may be highly destructive and require repeated debridement, resulting in significant scarring and fibrosis despite appropriate surgical and antibiotic therapy.  
Case Description: A 73 year old male presented to his primary care doctor with a chief complaint of sinus congestion for three weeks. The patient had undergone an uneventful molar extraction three weeks prior for extensive dental caries. Over concern for a developing abscess, the patient was given amoxicillin. During the next few weeks, the patient developed worsening eye and face pain. CT scan of the sinuses revealed maxillary, frontal, and ethmoid sinusitis. The patient was taken to the OR for washout and debridement. Intraoperative cultures grew Actinomyces odontolyticus. Postoperatively, the patient developed sinus pressure, headaches, and purulent nasal discharge. Repeat imaging showed extension of the infection into the orbit, sphenoid, ethmoid, frontal sinus, parotid glands, and possibly into the pachymeninges. Physical exam at the time revealed painful bilateral parotid nodules and peri-auricular abscesses. The patient returned to the operating room six times for repeated debridements with parotidectomy and extensive resection of necrotic sinus tissues. Infectious Disease consultation was obtained for recalcitrant Actinomyces infection. Antibiotics were escalated, and hyperbaric oxygen therapy was initiated. Pathology was repeatedly consistent with sinusitis, however, a single specimen revealed the presence of necrotizing granulomas. He began to develop a prominent deformity of the nasal cartilage. Recognizing that some infectious diseases may be associated with necrotizing granuloma, the clinical course raised the possibility of underlying GPA. Serologies for vasculitis were obtained, revealing c-ANCA positivity with positive proteinase 3; p-ANCA and myeloperoxidase antibody were negative. Fungal and mycobacterial serologies were negative. The patient was started on methotrexate and prednisone with excellent clinical response. Conclusion: This case illustrates the importance of widening the diagnostic considerations in patients with recalcitrant infections of the upper respiratory tract including the possibility of concurrent vasculitic disease. |
| Thuy Tien Le, MD | **Adults are just like big children**  
The patient was a 32 year old woman with a history of ulcerative colitis who presented with sudden onset of polyarthralgia and distal extremity swelling associated with severe throbbing pressure and pain. Due to the pain, she presented to the Emergency Department for evaluation and was found to have arthritis in her right elbow, left wrist, right knee, and both ankles. She had a fever to 101 and sore throat one day prior to presentation. She consulted a telemedicine service and was diagnosed with bacterial sinusitis and given doxycycline. Hours after her first dose, the joint and extremity pain and swelling began. She had also developed multiple non-painful papules on her elbows, knees, and shins. |
She reported similar symptoms once before, when she had Streptococcal pharyngitis and was given azithromycin. After two doses of the azithromycin, she experienced swelling and pain in her extremities, so she discontinued the medication and her symptoms resolved after 1 week.

On exam, she appeared well and was afebrile and hemodynamically stable. She had joint swelling and reduced range of motion and pain in her elbows, wrists, and ankles, though her joints were not hot or red. Both forearms and feet appeared swollen without pitting or erythema. Her posterior oropharynx was erythematous with white exudate. She had scattered flesh colored, non-tender, non-pustular papules.

Her left wrist fluid contained >100,000 WBCs with 82% neutrophil predominance and no crystals. The fluid culture as well as blood cultures were negative. Aspiration of both ankle joints yielded no fluid. Rapid Strep antigen testing was positive. WBC count was 13.3 k/uL and CRP was 5.9 mg/dL. Skin biopsy of the papules revealed a neutrophilic dermatosis.

Orthopedic Surgery and Infectious Disease were initially consulted for evaluation for septic arthritis, though her clinical picture appeared more consistent with an auto-inflammatory process. Rheumatology was thus consulted and she was diagnosed with a post-Group A Strep reactive arthritis. Her Strep pharyngitis with three doses of ceftriaxone and her pain and swelling improved rapidly after initiation of antibiotics and she ultimately did not require any corticosteroids.

Discussion: Group A Streptococcal pharyngitis is associated with a broad range of complications, but because the infection more frequently occurs in children, it is easily missed in adults. Post-Streptococcal reactive arthritis is increasingly described in adults and should be considered in the differential diagnosis of acute polyarthritis. Adult providers should also be aware that while patients with reactive arthritis can subsequently develop valvular heart disease, and though guidelines recommend prolonged antibiotics for secondary prophylaxis of acute rheumatic fever in children, there is no evidence to support the same practice in low-risk adult patients.

**Persistent MRSA Bacteremia from Mycotic Abdominal Aortic Aneurysm**

Existing aortic aneurysms are at risk for becoming infected in the setting of bacteremia. Infected aneurysm is associated with significant morbidity and mortality.

An 80 year old man with history of atrial fibrillation, abdominal aortic aneurysm (AAA), severe peripheral arterial disease status post femoral-peroneal arterial bypass 8 weeks prior, and status post right 1st metatarsal head resection for MRSA osteomyelitis 6 weeks prior with non-healing right foot wound, presented with low back pain 2 weeks after an apparent mechanical fall at home that worsened after chiropractic adjustment. He was found to have new T11 and L5 compression fractures, possible right scaphoid fracture, dehydration, and atrial fibrillation with RVR. CT aortic angiogram on admission showed stable size of known AAA at 5.6cm diameter and 5.9cm length. Neurosurgery was consulted and he was placed in a Jewitt brace to stabilize his vertebral fractures, and Podiatry was consulted for foot wound cares. He was also found to have MRSA bacteremia with persistent positive blood cultures over 10 days despite treatment with vancomycin and then daptomycin. The source for bacteremia was initially felt to be his right foot given recent MRSA osteomyelitis, however there was no radiographic evidence of ongoing infection and the wound bed was clean. TTE did not demonstrate any obvious vegetations, and TEE could not be performed, initially due to delirium, and then due to development of RVR when it was attempted. MRI spine demonstrated compression fractures without osteomyelitis. He had previously had a synthetic vascular graft which had been removed during recent femoral-peroneal bypass, and other than bilateral iliac stents, he had no other hardware or implants to serve as nidus of infection. On HD#11 a CT abdomen was repeated to search for occult infectious source. This revealed a significant interval enlargement in the patient's AAA, now measuring...
up to 7.8cm in both diameter and length, with associated para-aortic stranding concerning for early leak or infection. Vascular Surgery was consulted emergently, but given the high risk of morbidity/mortality from the proposed open repair and reconstruction, the patient declined intervention. He was discharged home with hospice and died three weeks later. This case illustrates the need for thorough workup to identify the source of persistent bacteremia, as well as the high risk for morbidity and mortality that comes with infected abdominal aortic aneurysm. Diagnosis in this patient was challenging due to initial focus on potential osteomyelitis, development of hospital delirium, and an alternative explanation for his worsening low back pain. In the absence of a clear source for persistent bacteremia, further diagnostic workup should be undertaken until a source is identified.

### Localized ST Elevation: Always a STEMI?

CW was a healthy 35 year old woman who presented to the emergency department with 5 days of low grade fevers, chills and tachycardia. This was followed by progressive exertional dyspnea, chest pain, and epigastric pain that improved with sitting up. In the emergency department her temperature was 36.8, pulse 130, BP 121/81, and respirations 18. On exam, her heart rate was regular with no murmurs or gallops, lungs were clear, and there was no peripheral edema. Chest x-ray showed clear lung fields with slight cardiac enlargement. ECG showed ST elevation in leads V1, V2, and V3. Her initial troponin T was elevated to 1.7 ng/ml. Coronary angiography revealed normal coronary arteries. She developed a fever of 38.7, was persistently tachycardic to the 130s, and continued to have chest discomfort which improved with sitting forward. An echocardiogram revealed global LV hypokinesis, an ejection fraction of 43%, and a small pericardial effusion. Further laboratory evaluation included ESR of 31 mm/hr, CRP of 89 mg/L, AST 149 U/L, ALT 174 U/L, normal bilirubin, and an NT-pro-BNP of 5593 pg/mL. Viral studies for hepatitis, CMV, adenovirus, and enterovirus were all unremarkable. She was started on captopril for management of heart failure. The following day, cardiac MRI revealed diffuse myocardial edema without delayed myocardial hyperenhancement but with mild pericardial hyperenhancement suggestive of acute myopericarditis. Over the next two days her heart rate and symptoms improved. Captopril was titrated up and transitioned to lisinopril. Carvedilol was started prior to dismissal. Follow-up echo three weeks later revealed normalization of LV structure and function and a normal appearing pericardium.

**Discussion:** Acute pericarditis and myocarditis often occur together and on occasion can mimic acute myocardial infarction as in this case with ST segment elevation. The term myopericarditis is used for cases with conjoint pericardial and myocardial inflammation, as demonstrated by elevated biomarkers and/or evidence of myocardial inflammation on imaging (ie, cardiac MR). The clinical presentation varies depending on whether there is predominantly pericardial or myocardial involvement. In patients with more myocardial involvement, the presentation usually is associated with heart failure symptoms. With pericarditis, chest pain is more predominant. Elevations of troponin imply a myocardial component and ECG changes in these patients are common with diffuse ST elevation and PR depression. Subsequently, there is normalization of ST and PR segments and diffuse T wave inversion. Localized ST elevation as in our patient is uncommon. In one study of 274 patients with acute pericarditis, 40 were found to have myopericarditis and of those localized ST elevation and T wave inversion was seen in only 17 (43% of those with myopericarditis and 6% overall). Most of these patients (15), as in our case underwent coronary angiography.

### Atypical presentation of squamous cell carcinoma of pancreas

Squamous cell carcinoma of the pancreas is extremely rare with most of its literature presented in the form of case reports. We report a case of squamous
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<td>Benyam Addissie, MD, Amindra Arora, MB, BChir</td>
<td>Cell Carcinoma of the Pancreas with an Atypical Presentation</td>
<td>A 61-year-old male presented to the Emergency Department with melena, concerning for a gastrointestinal bleed in the setting of recently diagnosed 6.5 x 5.9 cm mass in the pancreatic head, most compatible with pancreatic malignancy with hepatic metastasis. Emergent esophagogastroduodenoscopy revealed a fungating mass invading the duodenum from the pancreas with diffuse bloody oozing. Histopathology of the biopsy revealed infiltrating squamous cell carcinoma. Interestingly, our patient had significant leukocytosis as high as 74 without infectious or hematologic etiologies during subsequent hospitalizations for repeat bleeding. Squamous cell carcinoma of the pancreas is a poorly understood phenomenon. The pathophysiology is still unknown, as the pancreas is typically devoid of squamous cells. Presentation with leukemoid reaction has not been previously described or reported in association with squamous cell carcinoma of the pancreas. This case illustrates the need for further investigation into squamous cell carcinoma of the pancreas.</td>
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<td>Caroline Lochungvu, MD Ryan Kelly</td>
<td>The Nose Knows: When Rhinitis is More Than Meets the... Eye</td>
<td>The Nose Knows: When Rhinitis is More Than Meets the... Eye Introduction: Sinus congestion is a very common presenting symptom in primary care clinic. Non-classic presentations should alert clinicians to consider causes beyond sinusitis. A primary frontoethmoidal encephalocele is a type of congenital malformation defined as herniation of the meninges with or without brain matter through a defect in the frontal and ethmoid bone resulting from defective neural tube closure. It typically presents between 15.5 and 21 months of age as a skin-covered mass over the nasal bridge which enlarges with crying and is associated with CSF rhinorrhea. Rarely, they can present as a CSF leak older in life. A missed diagnosis can result in meningitis. Case Presentation: A 48 year-old Somali woman with no significant past medical history presented to the clinic with 11 days of clear, left-sided rhinorrhea, facial pain, and new onset headache. She had been seen in the ED 4 days prior to presentation where she was diagnosed with allergic rhinitis and discharged home with a nasal steroid spray. Symptoms persisted, thus she presented for further evaluation. She had no prior history of headaches, sinusitis, or head trauma. She did not have any fever, neck pain, or photophobia. Her physical exam was remarkable for clear, thin rhinorrhea from the left nostril when leaning forward, improved when leaning backward. There was tenderness on palpation of the left maxillary sinus. Due to concern for CSF leak, the patient was sent for urgent maxillofacial CT which demonstrated a mass-like protrusion into the left ethmoid cells suspicious for a frontoethmoidal encephalocele, with complete opacification of the left maxillary and frontal sinuses. The patient was sent to the ED, where ENT performed a bedside fiberoptic endoscopy revealing a mass lateral to the middle turbinate. A beta-2 transferrin on the fluid was positive, confirming CSF fluid. A brain MRI was done and showed herniation of the frontal lobe into the frontoethmoidal recess and CSF fluid in the left anterior ethmoid air cells extending into the left maxillary sinus. She was admitted and underwent an endoscopic endonasal resection of the encephalocele by Neurosurgery and leak repair with vascularized nasal septal flap by ENT. She was discharged home with left nasal packing and completed a 2 week course of cephalexin. Discussion: This case describes an unusually late presentation of a frontoethmoidal encephalocele in an adult with no known inciting head trauma. It also highlights the importance of broadening the differential in patients with non-classic symptoms of sinusitis, as a delayed diagnosis of a CSF leak could result in meningitis.</td>
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<td>Susan Lou, MD Brian Hanson, MD</td>
<td>Urachal Adenocarcinoma Eroding the Posterior Curvature of the Stomach Presenting as Syncope and Life Threatening GI bleed</td>
<td>Urachal adenocarcinoma is a subtype of bladder cancer that arises from the urachal remnant, also known as the median umbilical ligament. The urachal remnant is formed early in embryonic life from the allantois, which drains the fetal urinary bladder. In the majority of cases, the urachus coalesces...</td>
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with the umbilical arteries to form the umbilical ligament and is obliterated by birth. Urachal adenocarcinoma is rare and does not present with “classic” bladder cancer symptoms such as hematuria, given that the bladder wall is involved instead of the luminal surface.

Clinical Case: A 62 year old man with history of urachal adenocarcinoma status post partial cystectomy and removal of urachus with negative surveillance, presented with syncope, hemoglobin of 5.3, and melena. Initial esophagogastroduodenoscopy (EGD) showed a 5x8cm gastric ulcer with a large adherent clot and otherwise normal appearing gastric mucosa concerning for primary gastric cancer versus metastatic cancer. Endoscopic techniques were unsuccessful in removing the clot. The ulcer continued to bleed. Interventional radiology and surgery were consulted, however the unclear etiology of the patient’s bleeding and clinical instability precluded radiological or surgical interventions. Supportive measures were continued and the patient initially responded to blood transfusion. Unfortunately, hematemesis recurred followed by hemodynamic instability leading to cardiac arrest and death. Autopsy was granted and revealed mucinous adenocarcinoma with gastric ulcer measuring 8.0x5.0cm. Interestingly, the pathology was identical to that of the patient’s remote urachal cell adenocarcinoma making the ultimate diagnosis late recurrence of metastatic urachal cell cancer.

Discussion: In summary, a wide differential should be considered during evaluation of gastric ulcers, including metastatic disease. Recurrence of malignancy despite negative surveillance should be considered. This case highlights the importance of a detailed medical history and showcases an uncommon cause for a very common disease.

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<th>Lan Luu, MD</th>
<th>A Rare Case of Dyspnea</th>
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| Vertebbral osteomyelitis accounts for about 1 to 7% of all bone infections with the cervical region being the most uncommon (3-10% of cases). Although cervical spine infections are rare, it has been reported as a complication of head and neck cancers treated with radiation therapy that can present many years after treatment. This vignette describes a 65-year-old man with a past medical history of hypertension, gout, and nasopharyngeal squamous cell carcinoma status post surgery and radiation therapy 8 years ago who presented with dyspnea and bilateral foot pain. Patient had been having shortness of breath for about 3 weeks, particularly with lying down. He did not have a cough, fevers, chills, or any recent URI illness. Examination showed patient to be in mild respiratory distress with pursed lip breathing and difficulty finishing a sentence. Patient was also tachycardic with bilateral lower extremity edema and warmth to dorsums. Chest Xray was negative for infiltrates, consolidation, or any abnormalities. Initial work up included EKG, NT-proBNP, CBC, and BMP, which were all unremarkable. CTA chest was also obtained for concerns of pulmonary embolism that was negative. More history was later obtained from patient and he revealed that he had some neck pain about 6 weeks ago that was treated with a course of prednisone and physical therapy with improvement. This history prompted further imaging of patient's neck. MRI of the cervical spine was obtained and showed osteomyelitis at C3/C4 with phlegmon at the ventral epidural region that extends towards midline causing severe bilateral foraminal stenosis and moderate central canal stenosis. Neurosurgery was consulted to drain this abscess which later grew Group B streptococcus and he was treated with IV ceftriaxone with a plan to complete a 6 weeks course. Patient’s difficulty breathing is thought to be secondary to phrenic nerve injury caused by the C3/C4 spinal abscess; therefore, a Sniff Test was performed and confirmed left diaphragm paralysis. Given the lack of literature in phrenic nerve injury due to an epidural abscess, it is difficult to determine if and when patient’s dyspnea would improve. Patient will be monitored closely as outpatient with a follow up cervical MRI in the near future.
This case illustrates very common chief complaints of shortness of breath and neck pain with an unusual etiology. Osteomyelitis of the cervical spine is fairly uncommon let alone one that would result in a phrenic nerve injury. Risk factors for vertebral osteomyelitis includes surgical interventions/instrumentation, diabetes, immunocompromised state, IV drug use, and one that is often not considered is history of head and neck cancer with radiotherapy. It is important for clinicians to consider the possibility of cervical pathology in patients with pertinent history of head and neck cancer.

Dyspneic and Expecting: A case of mediastinal adenopathy in pregnancy
Ryan Lyerla, MD
Lisa Callies, MD (fellow);
Lisa Tsai, MD

Hormonal and anatomical changes in pregnancy can result in a constellation of non-specific symptoms including dyspnea, cough, and even night sweats, leading to a delayed diagnosis of lymphoma, the most common malignancy in pregnancy. Once diagnosed, it can be especially difficult to manage and treat as it involves two persons, the mother and the fetus.

A G2P1 31-year-old 26 weeks pregnant NICU nurse consulted her doctor because of increasing dyspnea on exertion, night sweats, and dry cough. A clinical diagnosis of bronchitis was made and the patient was treated empirically with a 7-day course of Augmentin. She also tried a course of ranitidine, but neither treatment provided relief of her cough. She presented to the ED one month later with tachycardia and hypoxia. Additional history revealed that she had lost five pounds during the pregnancy despite normal fetal development. On admission, she was found to have mild leukopenia and anemia. A CXR revealed potential cardiomegaly, however her subsequent echocardiogram was normal. Due to worsening hypoxia, a CT chest was ordered which showed a large mass in the mediastinum, with adjacent lymphadenopathy collapsing the entire lingula of the left upper lobe. Core needle biopsy was performed and a diagnosis of nodular sclerosing Hodgkin’s Lymphoma was made. Neonatology, maternal fetal medicine, oncology, internal medicine, and the patient and husband met to discuss next steps. Several issues were addressed, including the risk of chemotherapy to the fetus, risk of delayed treatment of the mother given her current symptoms, and risk of prematurity to the fetus, if delivered early. Ultimately, the mother concluded the risk of chemotherapy to the fetus and the delayed treatment of her aggressive, yet curable, lymphoma outweighed the risk of preterm delivery. The decision was made to proceed with induction and delivery at 32 weeks 5 days, followed by staging and chemotherapy.

This case illustrates two important concepts. (1) Symptoms of malignancy can overlap with common symptoms of pregnancy such as dyspnea and night sweats; weight loss, however, in an otherwise healthy pregnancy should raise red flags and requires further work-up. (2) When deciding how to proceed with management of Hodgkin’s lymphoma in pregnancy, it is important to involve a multidisciplinary team of neonatologists, maternal fetal medicine physicians, and oncologists to help patients determine the best course of action for both the mother and her unborn child.

Polycythemia Vera and Budd-Chiari Syndrome
Thomas Michael Malikowski, MD

Acute hepatic vein thrombosis, also known as Budd-Chiari syndrome, is characterized by an acute liver injury that can be life threatening. The most common etiology of this disorder is Polycythemia Vera, a myeloproliferative disorder associated with increased production of erythrocytes.

Case Description: A 57-year-old woman with no significant prior medical history presented to the emergency department with worsening right upper quadrant abdominal pain and nausea of 1-day duration. Her vital signs included the following: temperature, 36.6°C; heart rate, 93 beats per minute; respiratory rate, 14 breaths per minute; and blood pressure, 164/86 mmHg. Physical examination was notable for absent breath sounds at bilateral lung bases,
abdominal distention with shifting dullness, moderate tenderness on palpation of the right upper abdominal quadrant with a tender, smooth liver edge, and 2+ pitting edema up to the knees bilaterally. There were no stigmata of chronic liver disease. Laboratory evaluation revealed: hemoglobin, 18.9 g/dL [13.5-17.5 g/dL]; mean corpuscular volume, 86.5 fl [81.2-95.1 fl]; leukocyte count, 19.9 X 10^9/L [3.5-10.5 X 10^9/L]; sodium, 134 mmol/L [135-145 mmol/L]; potassium, 4.4 mmol/L [3.6-5.2 mmol/L]; chloride, 100 mmol/L [98-107 mmol/L]; creatinine, 1.5 mg/dL [0.8-1.3 mg/dL]; aspartate aminotransferase, 2538 U/L [8-48 U/L]; alanine aminotransferase, 2563 U/L [7-55 U/L]; alkaline phosphatase, 702 U/L [46-118 U/L]; total bilirubin, 2.0 mg/dL [0.1-1.0 mg/dL]; direct bilirubin, 0.9 mg/dL [0.0-0.3 mg/dL]; and INR, 1.7. A CT abdomen/pelvis was obtained and showed an abnormality within the hepatic vein along with a normal sized heterogenous liver, abdominal ascites, and bilateral pleural effusions. Viral hepatitis B and C serologies were negative. An acetaminophen level was undetectable. Doppler ultrasonography of the liver was performed and showed multiple thrombi with little to no flow in the hepatic veins. An intravenous heparin nomogram was initiated. Paracentesis was performed. Analysis of the ascitic fluid was suggestive of Budd Chiari syndrome with an ascites protein level ≥2.5 and a SAAG ≥1.1. Cytology revealed no evidence of malignancy. A TIPS procedure was successfully performed. Hemoglobin level was noted to be persistently elevated at >18 g/dL. Erythropoietin (EPO) level was measured and was suppressed. JAK2 testing was performed and was positive for genetic mutation. Bone marrow biopsy was performed and confirmed a diagnosis of polycythemia Vera.

Discussion: Budd-Chiari syndrome, or acute hepatic vein thrombosis, leads to hepatic congestion and subsequent ischemic necrosis. It presents clinically with abdominal pain, ascites, and abnormalities in liver function testing. In most cases, the etiology of hepatic vein thrombosis can be identified. Etiologies include hypercoaguable states, obstructive lesions (infectious, benign, neoplastic), and a variety of systemic disorders. Polycythemia Vera is the most common etiology. Without treatment, the syndrome can lead to significant morbidity and mortality. Early recognition is critical to ensure good clinical outcomes.

Matthew McElwee, MD

Unexpected Infectious Disease Challenges in Stem Cell Transplant

Immunosuppression in bone marrow stem cell transplant is fraught with risks. These risks may be even higher in patients who originate from areas endemic for higher burdens of infectious disease.

A 34 year old male who emigrated from Ghana 9 years previously who initially presented with fatigue and abdominal pain and found to be thrombocytopenic, hypercalcemic with a lymphocytosis. After a peripheral smear found atypical lymphocytosis irregular nuclear contours and occasional prominent nucleoli/chromatin center and flow cytometry showed a malignant T-cell population expressing CD2, CD3, CD5, CD25, CD38 and CD45. Initial screening was negative for hepatitis A, B and C was negative, EBV IgG and EBNA antibody were positive and rapid HIV-1 and 2 screens were negative but HTLV-1 antibody was found to be positive. The patient was diagnosed with HTLV-1-associated adult T-cell leukemia/lymphoma. A CT was concerning for pulmonary and abdominal metastases, and the patient was started on zidovudine and interferon-alpha. After a month, the patient had worsening neutropenia, thrombocytopenia and splenomegaly requiring hospitalization and was started on hyperCVAD therapy, which was complicated by neutropenic fever, myocarditis and a detectable hepatitis B viral load. The patient was started on tenofovir. Three months after hyperCVAD therapy was started, the patient was admitted for myeloablative umbilical cord blood transplant.

At the time of transplant, the patient was on levofoxacin, micafungin, and acyclovir. Tenofovir, zidovudine and interferon had been stopped pending recovery of blood counts and improvement in LFTs. His post-transplant course was almost immediately complicated by abdominal pain with watery stool and
he was found to have C. difficile. Unfortunately, the O&P was also positive for Strongyloides larvae, for which he was started on ivermectin. His post-transplant course was additionally complicated by persistent neutropenic fever, renal failure, BK-associated hemorrhagic cystitis, Staphylococcus mitis bacteremia, and disseminated adenovirus. He ultimately developed ARDS, pleural effusions, hypotension requiring four pressors and a PEA arrest. His family elected to withdraw life-sustaining treatment.

In addition to the typical risks of infectious disease associated with immune suppression in allogeneic stem cell transplant, this patient had concomitant HTLV-1, Strongyloides and chronic hepatitis B infections. This case highlights the potential challenges of immune suppression in patients who originate from areas with higher burdens of infectious disease.

**Human Granulocytic Anaplasmosis as an Underlying Cause of Acquired Hemophagocytic Lymphohistiocytosis**

A 73-year-old man with no significant past medical history presented to the emergency department with altered mental status when he was found confused at home. He was found to be somnolent and arousable only to sternal rub. His vitals were significant for a fever to 39 C, HR 120, RR 36, BP 190/148, and saturating 94% on 2L NC. Initial labs were significant for Hgb 13 g/dL, WBC 2.7x10^9/L, platelets of 23x10^9/L, creatinine 1.0 mg/dL, AST 404 U/L, ALT 216 U/L, total bilirubin 1.0 mg/dL. He was started on vancomycin, cefepime, ampicillin, and acyclovir for suspected meningoencephalitis in the setting of leukopenia. He was immediately intubated for worsening mental status.

A CT of the chest, abdomen, and pelvis was significant for splenomegaly to 14.4 cm. MRI of the head was negative. Further labs were obtained including a ferritin which was 65,270 mcg/L. Further history taking per his wife revealed that the patient had been chopping wood the day before. Therefore, tick borne testing was performed. A peripheral smear demonstrated intracytoplasmic inclusion bodies, or morulae, in neutrophils consistent with Human Granulocytic Anaplasmosis (HGA) infection. Therefore, IV doxycycline was added. PCR returned positive for Anaplasma phagocytophilum and negative for other tick-borne infections including Ehrlichiosis, Lyme, Rocky Mountain spotted fever, and Babesiosis.

Given the significantly elevated ferritin in the setting of a febrile illness, there was concern for Hemophagocytic Lymphohistiocytosis (HLH). A bone marrow biopsy was obtained which demonstrated histiocytosis with hemophagocytosis. Therefore, he met 5/8 criteria for HLH including fever >38.5, fasting triglycerides >265 mg/dL (388), splenomegaly, ferritin > 500 ng/mL, and hemophagocytosis seen on bone marrow biopsy. He was diagnosed with HLH secondary to anaplasmosis. He completed two weeks of IV doxycycline and was discharged from the hospital with complete return to his baseline.

**DISCUSSION:**

This case highlights the importance of considering acquired HLH in a patient with fever, cytopenia, and hyperferritinemia. There are less systematic studies on acquired HLH in adults compared to primary or familial HLH generally found in children. If HLH is considered in the differential diagnosis, diagnostic criteria for HLH can guide testing. At least 5/8 of the following criteria must be met to diagnose HLH, which include: (1) fever; (2) splenomegaly; (3) cytopenias in 2 or more cell lines; (4) hypertriglyceridemia (triglyceride level > 265 mg/dL) or hypofibrinogenemia (fibrinogen level <150 mg/dL); (5) hemophagocytosis in the bone marrow, spleen, or lymph nodes; (6) hyperferritinemia (ferritin level >500 ng/mL); (7) impaired NK cell function; and (8) elevated soluble CD25. The common causes of acquired HLH include infections, autoimmune disorders, and malignancy. Management is treatment of the underlying cause, in this case, doxycycline for the treatment of HGA. Anti-inflammatory medication with corticosteroids can also be considered.

**Don't Blame the Lungs: an Unusual Case of Malignancy Presenting as**
David Raslau

**Dyspnea**

Introduction: Diffuse intravascular coagulation (DIC) is a syndrome resulting from inappropriate activation of coagulation mechanisms, causing widespread thrombosis formation within the vasculature. Consumption of platelets and clotting factors can lead to increased risk of bleeding. Multiple clinical conditions can trigger DIC, most commonly infection, trauma, and malignancy. Here we describe a case of fulminant DIC secondary to metastatic breast cancer. 

Case Presentation: An active 60 year old female with a past medical history significant for type II diabetes mellitus and end-stage renal disease, status post living donor renal transplant, presented to the emergency department with a three week history of progressive dyspnea on exertion, new hypoxia, and a 24 hour history of melena. Chest x-ray demonstrated minimal bilateral pleural effusions, and she was admitted for further workup of her dyspnea. She had previously been seen in the emergency department 1.5 weeks prior to admission for the same concern. At that time she had a new mild thrombocytopenia, and D-dimer was noted to be >2000. CT with contrast was negative for evidence of pulmonary embolism but noted unexplained left breast dermal thickening and mild left axillary lymphadenopathy. Diagnostic mammogram demonstrated a mass with associated calcifications concerning for malignancy. Ultrasound guided biopsy was conducted two days prior to her admission, at which time biopsy results were not yet available. Physical exam on admission was notable for ecchymosis and oozing at her biopsy site, but was otherwise negative for petechiae or purpura. The remainder of her exam was unremarkable. Laboratory studies revealed a mild normocytic anemia, leukocytosis, lactic acidosis, acute kidney injury, mild transaminitis, and hyperbilirubinemia. Platelets were 71, and fibrinogen was <60. Urinalysis revealed granular casts and renal epithelial cells; renal ultrasound was unremarkable. Right upper quadrant ultrasound noted multiple hypoechoic hepatic lesions up to 2 cm in diameter.

Empiric treatment for DIC was initiated with cryoprecipitate and heparin. Extensive infectious workup was negative, and therefore a diagnosis of acute on chronic DIC secondary to malignancy was made. Despite therapy, DIC was progressive, and the patient developed signs of diffuse microvascular occlusions. Breast and axillary lymph node biopsy results both returned positive for triple-negative adenocarcinoma of the breast. In light of this information, the patient and her family opted for a comfort-oriented approach, and she passed away within days of her diagnosis.

Discussion: DIC secondary to malignancy is a common entity, but is usually a chronic and slowly progressive process. This case is unique due to its acuity and severity, ultimately leading to death. It is important for clinicians to maintain awareness for this process in patients with malignancy. More broadly, this case is a reminder that unexplained thrombocytopenia should always be investigated, especially in the setting of other unexplained symptoms.

Warda Niaz, MD

**Drug Induced Lupus**

Certain drugs are known to induce an autoimmune state with lupus like features known as drug induced lupus (DILE). The most common being isoniazid, hydralazine and procainamide. There are only a few case reports of trimethoprim/sulfamethoxazole resulting in drug induced lupus.

Case Description: A 28 year old female presents to the Rheumatology clinic with 1 month history of diffuse joint pain and stiffness which developed after taking trimethoprim/sulfamethoxazole. Symptoms initially improved after stopping antibiotics but subsequently developed similar symptoms on restarting trimethoprim/sulfamethoxazole for treatment of acne. Work up revealed positive ANA, positive RNP antibody, elevated inflammatory markers, positive double stranded DNA, positive anti-histone antibodies and positive SM antibodies. Started on therapy with low dose steroids which she initially responded to. 6 months later presented to ED with malar rash, oral ulcers, high
grade fevers (101F) and polyarticular joint pain. Inflammatory markers elevated with elevated ANA and positive double stranded DNA suggesting active lupus symptoms. Started on high dose steroids and azathioprine with improvement in symptoms. Follow up in clinic after 6 months showed improvement in symptoms and normal inflammatory markers but persistent anti-histone antibodies confirming drug induced lupus as most likely cause of patient’s disease course.

Discussion: This case demonstrates development of autoimmune process with symptoms similar to SLE caused by exposure to trimethoprim/sulfamethoxazole. This is a rather rare side effect of this class of antibiotics but it is important to be aware of such a complication since it is used very commonly in both inpatient and outpatient settings. DILE should always be on the differential for a patient presenting with lupus like symptoms on sulfa class of drugs and they should be used cautiously in these patients.

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<th><strong>Fever in a Returning Traveler</strong></th>
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<td>Rodney Thompson, M.D.</td>
<td>Global travel and immigration are increasingly common and it is important to be aware of common infections, their presentations, and appropriate treatment for these diseases in order to best care for our patient population. We present a case of a 25 year old male who presented to the emergency department with intermittent fevers up to 39.4 C associated with headaches and nausea. He moved to the United States from India in 2014 and is attending graduate school. He recently traveled back to India to visit family for a total of three weeks. He reported several days of non-bloody diarrhea at the beginning of his trip which had since resolved. He ate both raw and cooked meals, primarily vegetarian. He denied any obvious insect or animal bites. The day after returning to the United States, he developed high fevers, headaches, arthralgias and generalized weakness prompting presentation to the emergency department. In the emergency department was tachycardic (HR 146 bpm), hypotensive (99/62 mmHg), and febrile (39.4 C). Lab work revealed anemia, thrombocytopenia, elevated creatinine, but no leukocytosis. He was admitted for supportive management. Malaria smears and Hepatitis A IgM were negative. Dengue and Chikungunya serology were consistent with prior infections. Blood cultures were drawn and grew gram negative rods at 12 hours. He was initiated on empiric Piperacillin/Tazobactam. Blood cultures initially resulted as Salmonella, not typhi. He began to clinically improve, but remained intermittently febrile for another 48 hours after treatment was initiated. Blood cultures cleared after 36 hours on IV antibiotics. The primary team placed orders to deescalate antibiotics to ciprofloxacin, however due to concerns regarding resistance patterns he was treated with Ceftriaxone. After further speciation at the Minnesota Department of Health the cultures were finalized as Salmonella Typhi, quinolone resistant. Typhoid fever is the predominant cause of enteric fever worldwide. It is transmitted by fecal-oral transmission through contaminated food or water. On an individual basis, definitive diagnosis is made by culturing bacteria from the blood, although blood cultures are only 66% sensitive. Travelers vising friends and relatives have been reported to have a disproportionately high risk for developing travel associated infectious disease. Vaccinations are effective for prevention and should be considered in all people traveling to endemic areas, although they have not been widely adopted as a public health method for protecting whole populations. Salmonella, and other enteric pathogens from much of Asia are increasingly resistant to fluoroquinolones, and these agents should not be used for empiric treatment. Definitive treatment of fluoroquinolone sensitive isolates is appropriate. Patients incontinent of stool should be placed on contact precautions and food-workers should have stool test showing they no longer carry bacteria before returning to work.</td>
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### Dave Bartlett, M.D., Kianoush Kashani, M.D.

**Introduction:** Torsades de Pointes (TdP) is a malignant arrhythmia associated with prolonged QT intervals. Patients undergoing hemodialysis may experience rapid fluctuations in electrolytes that can lead to ventricular ectopy, abnormalities in myocardial repolarization, and precipitation of malignant dysrhythmias. Sudden cardiac death secondary to malignant dysrhythmias remains the most common cause of death in hemodialysis patients.  

**Case Presentation:** The patient was a 71 year old man with end-stage renal disease secondary to membranoproliferative glomerulonephritis who has been maintained on home hemodialysis 6 days per week. He awoke with pleuritic chest pain and acute dyspnea on exertion. Upon initial evaluation, he was hypoxic into the 80s on room air. A chest CT was suggestive of pulmonary vascular congestion and was negative for pulmonary embolism.  

Laboratory evaluation was notable for stable chronic anemia with Hgb 8.6 g/dL, potassium of 4.5 mg/dL, and a bicarbonate of 28 mg/dL. A troponin assay was performed and trended from 0.06 to 0.12 to 0.10 ng/mL. A 12-lead ECG revealed normal sinus rhythm with a new left anterior fascicular block and no new ischemic changes. Notably, his QTc was 518 msec, increased from his baseline of 493 msec. He had no known family history of sudden cardiac death. A routine magnesium level was 2.3 mg/dL five days prior to admission. All QT prolonging medications were held, and none had been recently started. 

He underwent hemodialysis with removal of 500 mL of fluid over 3 hours. His post-dialysis potassium value was 3.2 mg/dL. He subsequently experienced an episode of TdP requiring cardiopulmonary resuscitation, magnesium administration, and cardioversions x 2 resulting in the return of spontaneous circulation. 

A 12-lead ECG was repeated and was notable for a QTc of 626 msec, lateral T-wave inversions, and many premature ventricular contractions. With transition from a 3K to a 4K dialysate, the ventricular ectopy significantly improved. He was also bradycardic in the 50s and was placed on an isoproterenol drip for a target heart rate of 100 bpm to minimize the risk of a repeat R on T phenomenon. He was evaluated with coronary angiography which was negative for significant occlusive disease. Fortunately, he made a complete recovery and was discharged to home. Prior to hospital discharge, his QTc normalized to 421 msec. He elected for a DNR/DNI status, and no ICD was placed. 

**Discussion:** Patients undergoing hemodialysis experience rapid fluctuations in electrolytes that may precipitate ventricular ectopy. Patients at high risk for sudden cardiac death, including patients with long-QT syndrome may experience cardiac arrest around the time of hemodialysis. Patients with prolonged QT intervals should have extra caution applied to medications that may further prolong the QT interval and caution should be exercised during hemodialysis to minimize rapid shifts in electrolyte concentrations.

### Daniel O'Leary, MD  
Evan Mariash MD

**MALAT lymphoma masquerading as metastatic carcinoma**  
An 83 year old man with remote history of prostate cancer status post resection and history of colon polyps presented with recurrent lower left-sided abdominal pain. He was seen in the ED on multiple occasions and and found to have a solitary pulmonary nodule; his flank pain was attributed to herpetic neuralgia. Chest x-ray showed a 2.1 x 2 cm pulmonary nodule in the left lung, suspicious for malignancy. A malignancy work-up was planned. However, after presenting to the ED 4 times in 10 days for abdominal pain, the patient was admitted and a PET/CT performed. This study demonstrated a 1.5 cm solid renal mass in the lower pole of the right kidney, multiple pulmonary nodules (1.7 x 1.2 cm and 2.1 x 1.4 cm), and a hyper-metabolic focus in the stomach, concerning for a metastatic cancer of unknown primary. Given the accessibility of the stomach mass, the patient underwent upper endoscopy with biopsy. Biopsy results surprisingly revealed H. pylori and lymphoma of mucosa-associated lymphoid tissue (MALAT lymphoma, also known as extranodal marginal zone lymphoma), an uncommon indolent B-cell lymphoma often associated with H. pylori infection. The patient subsequently underwent biopsy of a lung lesion which
also revealed MALT lymphoma. Gastroenterology started the patient on clarithromycin to treat the patient’s H. pylori infection, with resultant improvement of his abdominal pain. He was referred to medical oncology with a diagnosis of stage IV MALT lymphoma. Repeat scanning 5 months after treatment showed the persistence of spiculated nodules in the lungs and the solid mass in the kidney. He has otherwise done well without chemotherapy or immunotherapy.

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<th>Takeshi Onizuka, MD</th>
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<td><strong>A case of Aortoenteric fistula: rare complication of endovascular abdominal aortic reconstruction (EVAR)</strong></td>
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<td>Aortoenteric fistula (AEF) is a rare complication of endovascular abdominal aortic reconstruction (EVAR). Classical herald bleeding or even massive bleeding can occur. Bleeding can, however, be intermittent and in small amounts. It is challenging to diagnose AEF when patients have comorbidities which can cause anemia in the setting of no GI bleeding symptom.</td>
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<td>Case Description: A 82-year-old male with history of chronic kidney disease stage IV secondary to polycystic kidney disease, status post EVAR for AAA with type 2 leak s/p embolization who presented with 3 month-history of ongoing anemia. The patient had been admitted to another hospital with anemia and polymicrobial bacteremia with E. Coli and Pseudomonas with presumed infected AAA graft stent 2 months before presentation. At the previous hospital, esophagogastroduodenoscopy (EGD), colonoscopy, and bone marrow biopsy had been performed and the results had been unremarkable. He was transfused and discharged with IV antibiotics. He continued to receive occasional RBC transfusion. At scheduled clinic visit, he was found to be anemic that brought him to the hospital. His anemia was already noted since one year ago, and he had received EPO but it was more acute on chronic change. He denied any bleeding symptoms. On arrival, the patient appeared pale and fatigued but normotensive, afebrile, and without abdominal tenderness. Hb was 5.2 g/dl and Cr 2.6 mg/dl, Absolute Reticulocyte 0.05 M/ul. No findings of iron deficiency anemia or B 12 deficiency were seen. He continued to receive cefepime for recent bacteremia/graft infection. He was transfused 3 units of RBCs. On 2nd day of admission, he had melena. Push enteroscopy revealed blood pooling in the fourth part of the duodenum adjacent to another extrinsic compression area, which was suspected as aortoenteric fistula. CT angiogram showed findings highly suspicious for Aortoduodenal fistula between the thrombosed aneurysm sac and the loop of bowel/duodenum. There is a new type I endoleak with aneurysm diameter 10.9 cm, which was increased in size. Gass bubbles seen in the aortic sac. Definitive treatment was surgical intervention. However, it was thought to be too high risk so the patient and family opted for comfort care.</td>
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<td>Discussion: AEF is a rare complication of EVAR, which was reported in 0.7% of patients in one review. But AEF should be included in the differential diagnosis of anemia in patients with a history of EVAR or aortic interventions, especially if they present with graft endoleak or infection. Not all the patients have GI bleeding symptoms and negative EGD doesn’t exclude AEF. In this particular case, AEF was overlooked in the setting of multiple comorbidities that could cause anemia. A high index of clinical suspicion leads to early diagnosis which could save patients even the mortality rate is high in AEF patients.</td>
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<th>Salma Patel, MD</th>
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<td><strong>Resolution of obstructive sleep apnea after surgery for acromegaly</strong></td>
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<td>Acromegaly occurs as a result of hypersecretion of growth hormone. In over 95% of cases the cause is a somatotroph adenoma of the pituitary. The prevalence is about 6 per million and average age of diagnosis is 40-45 years old. Obstructive sleep apnea (OSA) is common in acromegaly with overall prevalence of 40-50%. This is thought to be due to craniofacial deformities, macroglossia, and enlargement of the soft tissues of the pharynx and larynx. Treatment of acromegaly often impacts severity of OSA. Here we review a case of acromegaly with a large growth hormone-producing pituitary macroadenoma</td>
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that underwent a transsphenoidal resection and the impact of surgery on OSA. Case: A 45-year-old man with a past medical history of acromegaly, large growth hormone-producing pituitary macroadenoma, and transsphenoidal resection two months prior was referred for an abnormal overnight oximetry. He had increasing hand size, foot size, and changes in his facial structure that started about four to five years ago. These had already started to improve after his surgery. He slept alone and was unaware of any snoring or apnea. He had not noted any snort arousals. He woke up in the morning feeling refreshed without headache, dry mouth, or sore throat. He was mildly sleepy in the daytime, dozing watching boring TV or sitting with friends. After driving two hours, the car could drift off the road. His Epworth Sleepiness Scale score was 12 (normal <11).

Physical examination revealed frontal bossing and large hands and feet. Jaw position was normal with posterior oropharyngeal crowding (Friedman grade III). The base of the tongue was prominent, but there was no generalized macroglossia

Pre-operative MRI was notable for a pituitary macroadenoma (21 x 23 mm). Post-operative MRI had no evidence of residual neoplasm. There was a significant decrease in IGF-1 and growth hormone levels post transsphenoidal resection. Pulse oximetry, performed 2 days prior to surgery, showed multiple oscillatory desaturations, with an oxyhemoglobin desaturation index of 38/hour, minimum SpO2 of 55% and SpO2 below 90% for 38% of the night, consistent with severe sleep-disordered breathing.

A repeat oximetry test 2 months postoperatively was within normal limits and thus a polysomnogram was not performed.

Discussion: OSA in some patients with acromegaly secondary to a pituitary macroadenoma may resolve after surgery. As illustrated by this case, acromegalic patients with OSA preoperatively should be retested a few months after successful surgery to determine whether OSA is still present.

Guilherme Piovezani Ramos, MD
Kianoush Kashani

Binge Correction

BACKGROUND: Severe hyponatremia (HNa) is associated with high morbidity and mortality, which can be worsened by rapid corrections. Ethanol abuse can lead to HNa through different mechanisms. Identifying the primary process is crucial to correct sodium (Na) appropriately and prevent complications.

CASE-REPORT: A 40-year-old male presented with a week history of confusion and frequent falls. He had history of significant alcohol abuse. There were no deficits on neurologic exam. Laboratory evaluation showed: Na 103mmol/L, creatinine 6.5mg/dL and BUN 89mg/dL – unknown baseline. Urine revealed osmolality 230mOsmol/L and Na 50mmol/L. Following admission to the ICU 0.9% NaCl replacement was started with the goal of correcting <10mmol/L/24hours. After 12-hours, Na was 115 mmol/L and 0.45% NaCl started. Na continued to increase, peaking at 121mmol/L, after 18-hours when all infusions were stopped, and urine output (UOP) was 12L. On day 3, he developed agitation refractory to alcohol withdrawal protocol. MRI-Brain was normal. Examination on day 8 showed truncal ataxia, dysarthria and worsening cognition with a repeat MRI-Brain confirming osmotic demyelination syndrome (ODS)

DISCUSSION: Beer Potomania (BP) is an unusual cause of HNa, at a high risk of osmotic ODS from rapid correction. Beer has minimal electrolytes and carbohydrate load suppresses urea production. As a result, daily solute excretion falls below 250 mosmol/L, leading to a decrease the capacity of free water excretion and this, in turn, results in HNa. Re-introduction of solute will lead to brisk diuresis and rapidly correct Na, despite free water replacement. Management of BP should include 1)ICU admission with q2h sodium checks; 2)NPO for the first 24 hours with D5W for the caloric intake to promote solute diuresis; 3)intravenous fluids should be limited to symptomatic patients and
| Sasha Prisco, MD  
Sarah Kiel, MD | **A Cautionary Tale: Stress Induced Cardiomyopathy After Administration of Epinephrine for Anaphylaxis**  
Introduction: Catecholamine induced cardiomyopathy is a rare but characterized entity. There are published case reports of stress cardiomyopathy after a clinically appropriate dose of epinephrine for an allergic reaction. Since epinephrine is the cornerstone for treatment of anaphylaxis, awareness of the risk of epinephrine induced cardiomyopathy is important.  
Case Description: A 19 year old female with a history of beta thalassemia minor and anemia presented with an urticarial rash, subjective shortness of breath, and facial swelling consistent with an allergic/anaphylactic reaction possibly secondary to the use of amoxicillin for an upper respiratory tract infection. Her only other outpatient medication was a topical cream for hyperhidrosis. Past medical and family history were negative for any autoimmune or congenital cardiac disorders or premature cardiac death. Social history was negative for tobacco, alcohol, or illicit drug use or sexual activity. She presented without any hypoxia, evidence of respiratory distress, tachycardia, or fever and was hemodynamically stable with an unremarkable physical exam except for a rash. After inadvertently receiving epinephrine 0.3 mg administered intravenously (~0.007 mg/kg) instead of intramuscularly, she developed acute hypoxic respiratory failure secondary to flash pulmonary edema requiring intubation and tachycardia and hypotension consistent with cardiogenic shock. Chest x-ray showed new diffuse bilateral opacities. Initial EKG showed ST segment elevation in the lateral leads. Initial troponin I was 0.44 µg/L and peaked at 9.158 µg/L. Echocardiogram on the day of admission showed severe diffuse hypokinesis and ejection fraction (EF) at 23%. Right heart catheterization demonstrated normal filling pressure. Cardiac MRI showed reduced LV and RV systolic function and no abnormal hyperenhancement to suggest a myocardial scar/inflammation/infiltration. Myocardial biopsy showed no evidence of myocarditis and HIV, EBV, CMV, Coxsackie virus, Parvovirus, Legionella, Streptococcus, sputum culture, ANCA, rheumatoid factor, complement levels, and anti-citrullinated cyclic peptide were negative, suggesting that the etiology of the cardiomyopathy was epinephrine administration. Echocardiogram on day of discharge showed improvement with EF of 45-50%. The patient was discharged with metoprolol succinate and lisinopril. She has followed up regularly with Cardiology and a subsequent echocardiogram three months post-hospitalization showed a normal EF.  
Discussion: We report a case where administration of intravenous epinephrine for anaphylaxis led to reversible stress induced cardiomyopathy. This case is a cautionary tale that highlights the importance of the route of epinephrine administration. While the dose of epinephrine administered in this case was supratherapeutic, there are case reports where appropriately dosed intramuscular and intravenous epinephrine for anaphylaxis also led to stress induced cardiomyopathy. Epinephrine is commonly used for anaphylactic reactions, thus, awareness of the potential risk of epinephrine induced cardiomyopathy is essential. |  |
| Robert Cole Pueringer, MD  
Dr. Samuel Ives, Dr. Vanessa Dayton, Dr. Siddhant Yadav | **Difficult Case of Pancytopenia with Acquired Hemolytic Anemia**  
Case Presentation: A 62-year-old man with metastatic lung adenocarcinoma cancer and chronic hepatitis C presented with progressive weakness, anorexia, loose stools, and a recent diagnosis of Clostridium difficile colitis (1 week prior). He had recently started metronidazole and is currently not on chemotherapy.  
Initial labs showed a severe acute kidney injury and marked pancytopenia while |  |
imaging, pan-cultures, and sepsis evaluation were unrevealing. Further testing showed evidence of hemolytic anemia and peripheral blood smear (reviewed by a hematopathologist) revealed a marked normocytic anemia with pyropoikilocytosis (erythrocyte morphology), leukoerythroblastic blood, and severe thrombocytopenia. Given the recent diagnosis of Clostridium difficile colitis and the specific finding of pyropoikilocytosis on blood smear there was concern for infection leading to toxin-mediated hemolysis. Recent chemotherapy, malignancy, and severe Clostridium difficile infection led to bone marrow stress and suppression with peripheral red cell destruction. The patient and his blood counts improved in parallel over the next week with aggressive treatment of colitis and bacteremia.

Discussion: This case demonstrates a number of learning points including the etiology and approach to pancytopenia, characterization and differential of hemolytic anemia, the specific finding of acquired pyropoikilocytosis on peripheral blood smear only known to be associated with hyperthermia (seen in burn patients) and gram negative toxins in the blood, but in this case due to disseminated Clostridial infection.

Take away points:
1. Causes of pancytopenia can broadly be categorized as either disorders of increased peripheral destruction or disorders of decreased bone marrow function subcategorized as normal bone marrow that is replaced, absent, or ineffective.
2. Hemolytic anemia is typically characterized as either hereditary or acquired. Hereditary hemolytic anemias are disorders of erythrocyte hemoglobin, cytoplasmic enzymes, or membranes including hemoglobinopathies, GlPD deficiency, and membranopathies like hereditary spherocytosis. Acquired hemolysis is more common, and is due to microangiopathy (mechanical disruption from erythrocyte circulation), autoimmunity (antibodies to erythrocyte surface antigens), or infections (malaria, babesiosis, Clostridium infections).
3. Acquired pyropoikilocytosis is a specific finding on peripheral blood smear only known to be associated with hyperthermia (seen in burn patients) and bacterial toxins in the blood (particularly Clostridium difficile toxin).

Sravanti Rangaraju, MD

Severe Depression: Is it the problem or a sign?
Evaluation for depressed mood, memory impairment, and progressive personality changes are common presenting complaints at any primary care clinic. Often the syndromes of severe depression and dementia are overlapping, however with the use of some common office tools these can be differentiated better. Standard of care focuses on a good history and physical as well as using screening tools such as the PHQ-9, MoCA, Mini Mental state, etc. The diagnostic workup of dementia usually includes laboratory and neurodiagnostic imaging, while the role of these in the work up of depression is not clearly defined.

Case: A 70-year-old female with an extensive history of depression including previous admissions for severe depression, presented to our clinic for the first time to be evaluated for progressively worsening easy distractibility, forgetfulness, decreased ability to interact with family members, emotional detachment and weight loss over 2-3 months. The patient had minimal insight into her symptoms and her primary concern was knee pain. Physical examination was notable for a flat affect, but no other focal neurological signs. A brief office MoCA score was 30 (normal) and PHQ 9 was 32 (severe depression). Given the concern for severe depression the patient was sent to the psychiatry emergency department (ED) for evaluation for inpatient admission. During the course of her ED evaluation the patient reported a headache since arrival to the hospital, which prompted evaluation with a non-contrast CT head. While laboratory workup was unremarkable, the CT head revealed a right frontal lobe tumor with extension into the corpus callosum. Further evaluation
as an inpatient revealed a primary CNS lymphoma of the right frontal lobe with extension to the left and significant mass effect. The patient has since gone on to achieve remission with appropriate chemotherapy and her symptoms have improved significantly.

Discussion: Keschner et al reported that 78% of 530 study patients with brain tumors had psychiatric manifestations but 18% presented with purely psychiatric manifestations at initial diagnosis. Although it is difficult to extrapolate whether this patient’s initial diagnosis of depression prior to evaluation at our clinic was due to the CNS lymphoma, the improvement in her symptoms with treatment strongly suggest that her initial diagnosis and recent flare up of severe depression were related to the tumor. This case brings to light the importance of a high index of suspicion on the part of primary care providers, especially in patients presenting with new onset or recurrence of previously controlled psychiatric symptoms, and in patients not responding to optimal anti-depressant therapy. Further studies may be warranted to identify subsets of patients that may benefit from early imaging in the evaluation of severe depression.

Praful Ravi, MD
Roberto Leon Ferre

Anemia, thrombocytopenia and coagulopathy - the answer is in the blood (film).

Anemia and thrombocytopenia are commonly found in adult inpatients, but the coexistence of both should alert the clinician to consider the possibility of thrombotic microangiopathy (TMA).

Case Description: A 47-year old woman with a history of recurrent rectal cancer was admitted with a 1-day history of fatigue, feeling generally unwell and subjective fever, on a background of chronic, low-volume rectal bleeding. On presentation, she was tachycardic (HR 125), hypotensive (84/55) and had a low-grade fever (37.8°C). Examination was notable for tenderness in both lower quadrants of the abdomen. Initial laboratory evaluation revealed a normocytic anemia (Hb 7.7, MCV 84), neutrophilic leukocytosis (WBC 19, neutrophils 17), thrombocytopenia (PLT 16) and evidence of a coagulopathy (PT 34, APTT 52) with an elevated fibrinogen (415) and D-dimer (1830). A peripheral blood smear identified schistocytes, with no evidence of platelet clumping; additional testing was significant for an elevated LDH (332) and total bilirubin (1.8), low haptoglobin (<14) and a negative direct antiglobulin test, consistent with hemolysis. Testing of individual coagulation factors revealed deficiency of vitamin K-dependent factors, with improvement in the PT and APTT after vitamin K administration. ADAMTS13 activity was noted to be extremely low, with the detection of an inhibitor, consistent with the diagnosis of acquired thrombotic thrombocytopenic purpura (TTP). The patient was commenced on high-dose prednisone and plasma exchange (PLEX), with resultant improvement in her platelet count and normalization of ADAMTS13 activity after 9 days, at which point she was discharged on a slow taper of prednisone.

Discussion: While TTP is a rare TMA with an incidence of 3 per 1,000,000 adults per year, the presence of its cardinal features, microangiopathic hemolytic anemia (MAHA) and thrombocytopenia, should prompt the clinician to seek its diagnosis. It is almost always an acquired condition where an autoantibody inhibits the ADAMTS13 enzyme, deficiency of which leads to accumulation of ultra-large vWF multimers and development of platelet thrombi in small vessels. TTP is fatal if left untreated, and PLEX and high-dose glucocorticoids should be commenced even while awaiting results of confirmatory testing of ADAMTS13 activity.

This case highlights the importance of considering TTP when assessing a patient with anemia and thrombocytopenia, and the need to proceed with diagnostic evaluation in a systematic manner to identify its key features but also to avoid a delay in treatment while awaiting results of confirmatory tests. In our case, the coexistence of a coagulopathy could have led to premature diagnostic closure, with a presumptive diagnosis of disseminated intravascular coagulation.

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(DIC), for which PLEX and steroids play no role. Patients with TTP, especially in the setting of malignancy, can have additional coagulopathies, and TTP should therefore not be excluded solely on the basis of abnormal clotting parameters.

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<th>Michael Richter, MD</th>
<th>Looking Past Psychiatric Labels: A Not-So-Hidden Cause of Catatonic Depression</th>
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<td>Adrian Vella, MD</td>
<td>While psychiatric conditions can often masquerade as systemic illness, it is important to be alert to the possibility that psychiatric disturbances are a manifestation of an underlying medical condition. This poses a diagnostic challenge in patients who may only have subtle signs of a systemic disease. A 33-year-old man presented acutely for a second opinion regarding his severe depression. He had an eight-month history of progressive fatigue, weakness, depressed mood, and periods of confusion with memory impairment. A recent hospitalization for encephalopathy, which included evaluation by neurology, neurosurgery, and psychiatry, resulted in a diagnosis of catatonic depression with possible conversion disorder. His medical history was also significant for hypertension, diabetes mellitus, and obesity. These comorbidities were all diagnosed within the past two years. Upon admission, physical exam revealed facial flushing, prominent preauricular and supraclavicular fat pads, central obesity, and proximal muscle weakness. Laboratory workup revealed an elevated 24-hour urine free cortisol at 1933µg/24h, and a morning cortisol of 13µg/dL after dexamethasone suppression test. MRI of the pituitary gland noted a 9mm heterogenously hypoenhancing mass in the anterolateral right sella. CT scan of the chest, abdomen, and pelvis was unremarkable. He was diagnosed with ACTH-dependent pituitary Cushing's disease and underwent transsphenoidal resection of the mass. Pathology confirmed the diagnosis with staining positive for ACTH and chromogranin. His was treated with a post-operative course of prednisone for symptoms and signs of adrenal insufficiency, and one month later he resumed working and reported significant improvement in all of his presenting symptoms. This case illustrates the neuropsychological symptoms that can be associated with Cushing’s syndrome and emphasizes the high degree of clinical suspicion necessary for diagnosis. This can be a unique challenge as many of the typical disease features, namely obesity, hypertension, insulin resistance, and depression, are remarkably common in the general population.</td>
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<th>Camille Robichaux, MD</th>
<th>Joining Forces</th>
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<td>Evidence based medicine often relies on specialty association guidelines and statistically proven algorithms to diagnose and treat medical diseases. While this improves patient outcomes, it cannot be applied to each specific case. Not only that, but being a physician can sometimes feel like simply following a recipe. In this case, a series of common pathologies were brought to uncommon extremes. Subspecialists from pulmonology and gastroenterology worked together to develop a creative strategy for diagnosing an acquired tracheoesophageal fistula. Our patient was transferred from an outside hospital with aspiration pneumonia. She is a 55 year old female with a history of end-stage COPD. She underwent a bilateral single lung transplant one year prior to her presentation. The recovery period was complicated by atrial fibrillation requiring a trans-esophageal echocardiogram followed by cardioversion. Her respiratory status only worsened after the cardioversion, and chest CT later revealed an esophagopleural fistula with leakage of tube feedings into the pleural space. This was attributed to a perforation from the TEE, a rare but known complication. Her condition improved gradually after an extensive cardiothoracic surgery which included a thoracotomy with wash-out, muscle flap repair of the esophageal defect, and placement of an esophageal stent, tracheostomy, and PEG tube. For the next six months prior to her current presentation she suffered chronic nausea and abdominal pain due to...</td>
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gastroparesis related to her steroid induced diabetes and chronic opioid use.

Even prior to her arrival to our hospital, aspiration of tube feeds was suspected based on bronchoscopic imaging. Review of her medical history revealed a patient with a predisposition to gastric reflux, increased esophageal pressures, esophageal diverticula, and inflammation within the pulmonary system. Chest CT obtained per cardiothoracic surgery recommendations was unrevealing, but a tracheoesophageal fistula continued to be high on the differential.

Pulmonology and gastroenterology planned a creative procedure to identify the cause of her pneumonia. Esophagogastroduodenoscopy revealed an edematous area of the middle esophagus. The inferior side of the swelling was poorly visualized, but flushing with saline caused bubbles to develop around this area. When methylene blue was injected, the team was initially unable to determine whether or not a fistula was present. Immediately after the EGD however, the pulmonary team obtained bronchoscopic imagining of methylene blue within the co-responding area of the trachea, confirming the presence of a tracheoesophageal fistula. Through team work and innovative problem solving, two services were able to identify a small hole that led to a huge problem.

### Angeline Sabol, MD

**Stephanie Hansel**

**Pancreatic Adenocarcinoma? But oh how it grows!**

**Learning Objectives:**
1. Identify undifferentiated pancreatic carcinoma with osteoclast-like giant-cells (UC-OGCs)
2. Assess treatment options for UC-OGCs

**Case:**
A 65 year old male presented to an outside hospital with abdominal cramping and decreased appetite for 2 months. CT scan was obtained and showed a pancreatic mass with liver metastases. Two months later he presented to our institution with presyncopal symptoms and decreased oral intake. He was admitted to the hospital for an EGD-guided nasojejunal tube placement to improve nutrition. Labs were concerning for an acute anemia which led to a repeat CT scan. Results showed multiple new abnormalities including substantial tumor progression with necrosis, a concomitant hematoma, and near-complete compression of the portal confluence and proximal superior mesenteric and splenic veins. Notably the CA 19-9 was within normal limits.

After a failed ultrasound-guided liver biopsy, an endoscopic ultrasound-guided biopsy demonstrated UC-OGC. A single-agent regimen with gemcitabine was initiated due to the patient’s debilitated status. Follow up is pending.

**Discussion:** UC-OGC is a rare and aggressive tumor, accounting for <1% of all pancreatic cancers (1). The average age of diagnosis is 60 years, affecting males and females equally (2). It is similar to those found in long bones but can rarely occur in extraskeletal tissues (3). Radiographically the tumor is vascular differentiating it from adenocarcinoma (2). It is composed of two types of cells: osteoclast-like giant cells and mononuclear cells. The origin of the giant cell is likely mesenchymal, staining positive for CD68 (2). In our patient, CK AE1/AE3 immunostain of the non-giant cells was positive, which is most consistent with epithelial origin (2). The prognosis is poor with median survival time of less than 1 year. Surgery is an option if the tumor is localized (3). Gemcitabine has been shown to be effective in a patient without liver metastases, with complete remission attained in 5 months and no evidence of recurrence at one year (1). In a report of a patient with liver metastases, cisplatin, etoposide, and ifosamide were used with 50% reduction in size (2). These agents, along with gemcitabine, are options for those patients for whom surgery is not feasible. Larger numbers are needed for more definitive treatment recommendations.

### Wil Santivasi, MD

Rachel M. Wiste, Jacob J. Strand

**Acute-onset ataxia as an adverse effect of amiodarone**

Amiodarone is highly effective in the management of ventricular and supraventricular tachyarrhythmias, but adverse effects occur frequently. Most
commonly, amiodarone is associated with corneal depositions, nausea/vomiting, skin discoloration/rash, bradyarrhythmia, and thyroid dysfunction, with neurologic dysfunction including ataxia occurring in an estimated 4-9% of patients.

Case Presentation: A 74-year-old man with a history of pancreatic adenocarcinoma, atrial fibrillation on amiodarone for rhythm control, and chronic kidney disease presented for admission with a two-week history of confusion and gait instability with falls. Neurologic examination was significant for isolated truncal ataxia localizing to the cerebellar vermis. Mental status examination revealed mixed hypoactive and hyperactive delirium. MRI of the brain demonstrated no acute changes. Extensive serologic and CSF workup for autoimmune, infectious, and paraneoplastic etiologies was unrevealing. Haloperidol was initiated, resulting in improvement in his mental status, but not his ataxia. Amiodarone was held due to concerns that it might be contributing to these symptoms. Within 48 hours, the patient’s truncal ataxia and delirium began to resolve, requiring decreasing quantities of as-needed haloperidol. Within one week, he returned to his neurologic baseline and no longer required pharmacologic intervention. Amiodarone was permanently discontinued in favor of quinidine, but recurrent atrial arrhythmias over the next several months required repeated cardioversion and ultimately atrioventricular nodal ablation with implantation of a cardiac resynchronization therapy pacemaker.

Discussion: This case illustrates the importance of maintaining a broad differential diagnosis in the evaluation of patients with ataxia. Ataxia can be due to focal insults to the cerebellum, autoimmune disease, paraneoplastic phenomena, alcohol toxicity, and other etiologies, but medication effect must also be considered. Classic drug associations include amiodarone, antiepileptic medications, benzodiazepines, and chemotherapeutic agents. Amiodarone-induced ataxia can be managed with discontinuation of the offending agent, but alternative rhythm control must be implemented for recurrent dysrhythmia.

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**John Schempf, MD**

**Vacation Cut Short by Eosinophilic Myocarditis Due to Chlorthalidone**

Eosinophilic myocarditis (EM) is a life-threatening disease characterized by eosinophilic inflammation within the myocardium. A 72y male presented with acute dyspnea, chest pain, recurrent fevers and night sweats. Three weeks prior to admission, he was treated for sepsis from a recent urologic procedure resulting in bacteremia, transthoracic echocardiogram (TTE) at the time showed no evidence of bacterial endocarditis. Initial treatment with vancomycin was transitioned to minocycline to facilitate travel to Australia, Tonga, and Sri Lanka. Four days prior to presentation, while overseas, he developed fevers, headaches, non-exertional chest pain, and dyspnea. He presented to an international hospital, work-up revealing elevated CRP and negative blood cultures. He was started on Augmentin and immediately returned to Minneapolis. En route, he experienced episodic chest pain, prompting presentation from the airport to the Veterans Affairs ED, where he developed 10/10 chest pain. Vitals were stable and he was afebrile. EKG showed an old LBBB and new onset atrial fibrillation. Pertinent labs included a normal WBC count but an absolute eosinophil count of 0.71 K/cmm, ESR 82mm/hr, CRP 101 mg/mL, troponin I 0.327 ng/mL. CT chest with contrast showed ground glass opacities, new mediastinal lymphadenopathy, and no pulmonary embolism. He was given aspirin, metoprolol, heparin, amiodarone, and broad-spectrum antibiotics. His symptoms subsided and he was admitted with concerns for ACS and infection. Past medical history included hypertension and nephrolithiasis, and pertinent outpatient medications included chlorthalidone, which was started 2 months prior to admission. TTE on day 1 showed preserved ejection fraction (EF) with mild/moderate mitral regurgitation (MR). No clear infection was found, so antibiotics were discontinued. On day 4, his exertional dyspnea progressed, eosinophil count increased to 1.78, and repeat TTE showed EF of 30-35% and severe MR. He underwent coronary angiogram with biopsy the same day, and started solumedrol for presumed sarcoidosis, eosinophilic or
giant cell myocarditis. Biopsy results confirmed the diagnosis of eosinophilic myocarditis. Parasite serology, aspergillus, histoplasma, blastomyces, CMV, tuberculosis, mycoplasma, and viral serology were negative/normal. ANA, ANCA, complement, hepatitis serology, cryoglobulin, and IgG subclasses were negative/normal. His chlorthalidone, held on admission, was believed to be the culprit of his eosinophilia. On day 5, TTE showed normalization of EF and improvement in MR, and his eosinophilia resolved. With near complete symptom resolution, he discharged on day 8 with lisinopril, carvedilol, and oral prednisone with plans for tapering. Without treatment, EM can be deadly. The causes of EM vary, including medications, infection, malignancy, hypereosinophilic syndrome, and autoimmune disease. In our patient, chlorthalidone was the cause and has been known to cause peripheral eosinophilia. Many patients do well with corticosteroids and removal of the offending agent or treatment of the underlying cause.

**Michelle Schmugge, MD**

Matthew Bartlett

### Aortic thickening as a key finding in fever of unknown origin

In patients with prolonged fever of unknown origin, the differential diagnosis initially remains broad. In this patient, an unexpected finding on imaging ultimately led to a diagnosis.

A 57-year-old woman with a history of hypothyroidism and hyperlipidemia presented to the hospital with daily fevers for the past three months. The fevers occurred regularly three times a day and were associated with headaches, myalgias, and a dry cough. She also unintentionally lost 10 pounds and had night sweats during this period. Age appropriate screening was all normal. Prior to admission, she had already undergone an extensive work-up. Broad infectious testing including a tick-borne panel (Anaplasma, Ehrlichiosis, and Lyme), herpes simplex virus, HIV, hepatitis panel, blood cultures, and parasite smear were all negative. The patient also had a CT chest, abdomen, and pelvis which was unrevealing. Shortly after admission, the patient had an episode of fever and tachycardia. Physical exam was normal with no rashes. Laboratory studies indicated a worsening normocytic anemia, leukocytosis, and thrombocytosis. Inflammatory markers including ESR and CRP were elevated and she had a mild transaminitis. Thyroid stimulating hormone was normal. The differential for her fever of unknown origin initially remained broad. While she endorsed B-cell type symptoms, imaging did not reveal lymphadenopathy or hepatosplenomegaly. There were no renal masses seen on imaging which would suggest renal cell carcinoma. She had no history of familial inheritable febrile syndromes. She did not take any drugs known to induce fever. Broad infectious work-up was unrevealing. A repeated CT chest, abdomen, and pelvis revealed concentric wall thickening of the thoracic aorta without evidence of luminal dilation or narrowing. The finding of aortic wall thickening narrowed the possible diagnosis significantly. She was tested for syphilis to rule out this infectious cause of aortitis. She was also tested for immunoglobulin and G4-related systemic disease (IgG4-RD), which can present with aortitis and periaortitis. These tests were negative. Given her headaches, anemia, and elevated inflammatory markers, large vessel vasculitis was suspected. Her age favored giant cell arteritis over Takayasu. She denied vision changes, jaw claudication, or scalp tenderness. The patient underwent a whole body PET scan, which revealed diffuse metabolic uptake along her thoracic aorta, confirming large vessel vasculitis. She was initiated on prednisone. In less than a week of treatment, her fevers resolved.

This case highlights the broad work-up often performed before a vasculitis is diagnosed. The finding of aortic wall thickening points to a short list of inflammatory and infectious diseases. In this patient, proper diagnosis with initiation of treatment led to swift resolution of symptoms.

**Sarah Schneider, MD**

Zelalem Temesgen, MD

### A Pain in the Neck

A 76 year old male presented with one week of gradual onset left-sided neck pain. It was constant, sharp, and non-positional in nature. He reported subjective fevers, but denied any other symptoms. Past medical history was significant for
a right vertebral artery dissection one month prior and polymyalgia rheumatica, without recent steroid use. This patient presented afebrile with normal and stable vitals. Exam revealed a non-toxic patient with substantial tenderness and edema of the left neck. Laboratory findings were significant for a white count of 18, erythrocyte sedimentation rate of 23, and C-reactive protein of 231. Due to his recent right vertebral artery dissection, CT angiogram was performed and negative for acute dissection of the neck vessels. CT of the head and neck with contrast exposed a loculated fluid collection in the left paraspinal musculature. This area underwent ultrasound-guided aspiration. Final cultures from the aspiration grew only Streptococcus anginosus. He was initiated on intravenous Piperacillin/Tazobactam at 3.375 grams every six hours. The patient proceeded to the operating room (OR) for debridement of the loculated collection. Within a day following debridement, he developed an excruciating pain in the neck (worse than before) which appeared out of proportion with exam findings. He was urgently taken back to the OR with concern for necrotizing fasciitis. Pathology from the procedure confirmed this suspicion. The patient ended up returning to the OR for continued debridements on a daily basis over the following two weeks to ensure viable tissue on pathology. MRI of the neck over this course of time additionally revealed C3-C7 facet involvement. He additionally underwent seventeen hyperbaric oxygen treatments. Aside from infectious disease, ENT, neurosurgery, and thoracic surgery were involved in his care. Despite his poor prognosis, he experienced an excellent recovery after over one month of hospitalization requiring a total of twelve surgical irrigations, debridements and a cervical laminectomy. Although Streptococcus anginosus showed susceptibility to penicillin, the antibiotic coverage was kept broad due to the clinical severity of his illness. Piperacillin/Tazobactam was continued at the same dose for a six week course. The lesson to be learned from this case is that Streptococcus anginosus has the ability to cause necrotizing fasciitis and to be on the lookout for the clinical presentation. The infection in general is life-threatening, but adding the proximity to the neurologic structures, as in this case, makes the prognosis quite poor. The fact that this patient lived through the infection was owed not only to antibiotic coverage, but to the heroic efforts of the surgeons involved.

Jessica Schultz, MD

**The Critically Ill Pregnant Patient: A Case That Causes Most Internists to Run in Fear**

Case of a pregnant patient who developed Acute Respiratory Distress Syndrome (ARDS) secondary to H1N1 Influenza that went on to develop acute renal failure, ventilator-associated pneumonia (VAP), and persistent multi-drug resistant Pseudomonas bacteremia. Risk of mortality for both patient and fetus was near 95%, but because of excellent communication between multi-disciplinary teams and taking some risks with dialysis and antibiotics, the patient made a full recovery and delivered a healthy full term baby. A 32-year-old previously healthy female who was 21 weeks pregnant was admitted with 5 days of progressive dyspnea. She quickly developed ARDS and was diagnosed with H1N1 on a respiratory viral panel. She was intubated, started on nitric oxide and epoprostenol, and required high levels of sedation with midazolam, ketamine, propofol, and hydromorphone drips. She developed septic shock necessitating norepinephrine, and within one week of admission developed acute renal failure and was started on continuous renal replacement therapy (CRRT). Within several more days she developed VAP secondary to Pseudomonas, which two weeks into her course led to multi-drug resistant Pseudomonas bacteremia. Multiple antibiotic courses were tried including colistin, meropenem, and newest cephalosporin/beta-lactamase inhibitor ceflozane/tazobactam (intermediate susceptibility), but the bacteremia persisted for 7 days. The strain of Pseudomonas was found sensitive only to aminoglycosides (class D pregnancy category). At 3 weeks post-admission one of many care conferences was held between the patient’s parents, ICU team, Maternal Fetal Medicine, Infectious Disease, Nephrology, and Palliative Care to discuss prognosis (very poor) and goals of care. It was estimated with her multiple co-morbidities and gestational age of the fetus, mortality for both was
close to 95%. With the combined expertise from the various teams and family consent, the plan was to start a hybrid dialysis regimen mixed of daily intermediate hemodialysis along with CRRT, start IV tobramycin despite fetal ototoxicity risk, and keep the patient alive until a planned 28 week cesarean section for earliest fetal viability. Her bacteremia cleared immediately with tobramycin, and 6 weeks later was discharged breathing on her own and off all dialysis. She went on to have an uneventful delivery at 37 weeks to a healthy baby boy with a normal hearing test after birth.

This case illustrates how pregnancy brings most Internist-trained physicians out of their comfort zones, and requires them to think differently. We aren’t just taking care of one patient with typical hemodynamics, but instead all medications (like aminoglycosides) and treatments need to be assessed for teratogenicity and fetal risk. Also, in this case because of increased fluid removal needs in the setting of hypotension, an unorthodox dialysis schedule was implemented. Above all without strong communication and coordination of care between the multiple specialties, the outcome would not have been as successful.

Conor Senecal, MD
David Brennan, MD
Thomas C. Gerber, MD  Ph.D

**Refractory Vasospastic Angina with Complete Heart Block: A Knife Through the Chest**

Coronary Artery Vasospasm or Prinzmetal’s Angina is a relatively rare and difficult-to-diagnose variant of coronary artery disease. It typically presents during the 5th decade of life and classically manifests with ST segment elevations on EKG that resolve with the administration of nitrates.

**Case Presentation:** A 48 year old woman with a past medical history of well-controlled diabetes mellitus type 2 and hypertension presented to outpatient cardiology clinic for evaluation of recurrent chest pain. Six months prior she had been lying in bed when a sensation of numbness began in the ulnar aspect of her left hand. This quickly progressed to chest pain described as “a knife through my chest” radiating to the back, accompanied by shortness of breath. She was evaluated in an emergency room; however the pain had resolved by the time she was seen and EKG and troponins were normal. She experienced approximately 50 additional similar chest pain episodes over the next 6 months. She underwent a full cardiology evaluation including treadmill exercise testing (normal), echocardiogram (structurally normal heart) and coronary angiogram (normal coronary arteries). During an 8-days hospitalization for continuous cardiac monitoring and further evaluation, the patient was observed to have intermittent ST segment elevation and 3rd degree atrioventricular block with bradycardia during episodes of chest pain. Nitroglycerin, amlodipine, nifedipine, metoprolol and hydrochlorothiazide all failed to prevent recurrent chest pain episodes.

Due to concern for coronary vasospasm, provocative testing was performed. During selective catheterization, intracoronary injection of methylergonovine at doses of 75 mcg, 150 mcg, and 225 mcg did not provoke spasm. However, the final dose of 450 mcg of intracoronary methylergonovine produced marked focal spasm of the distal right coronary artery and immediate onset of her typical symptoms. Intracoronary administration of nitroglycerin quickly resolved the spasm. The location of observed spasm was consistent with her history of 3rd degree atrioventricular block, presumably due to atrioventricular node ischemia. The patient was discharged on diltiazem extended release 240 mg daily, with plans to titrate to a daily dose of 600 – 900 mg daily as tolerated.

The patient returned to the care of her primary care physician and has had a dramatic reduction in the frequency of her episodes.

**Discussion:** In a patient whom obstructive coronary artery disease has been ruled out and coronary vasospasm is suspected, nitroglycerin acutely and calcium channel blockers chronically are the standard of care to reduce the frequency and severity of chest pain episodes. In refractory cases, provocative testing with intracoronary administration of acetylcholine or methylergonovine can be performed to confirm the diagnosis. Prognosis depends on concurrent obstructive coronary disease: in patients without obstructive coronary disease 5-year survival is approximately 94%, whereas in patients with diffuse coronary
Sphingomonas paucimobilis Endocarditis

Sphingomonas paucimobilis is an aerobic, non-fermenting Gram-negative bacillus. It is typically regarded as having minor clinical significance. In healthcare settings, it is most often identified in association with contaminated solutions (ex. distilled water, drug carrier solutions, dialysis fluid). Despite not being a typical pathogen, S. paucimobilis has been identified as a source of invasive infection in a variety of cases. Due to the infrequency with which S. paucimobilis acts as a pathogen, there is a paucity of information on optimal treatment regimens for the various infections it may cause.

A 54-year-old male with a history of a bicuspid aortic valve s/p valve replacement and aortic grafting presented to his PCP with complaints of intermittent, but worsening night sweats and fever. Blood cultures resulted positive for Sphingomonas paucimobilis. Repeat cultures were positive for the same organism. Unfortunately, due to the fragile nature of the species, antibiotic susceptibility testing was unsuccessful. The case was discussed with infectious disease, and the patient was started on levofloxacin and scheduled for a TEE given bacteremia in the setting of a mechanical valve. TEE revealed new perivalvular insufficiency around the aortic valve. The patient was subsequently hospitalized, started on meropenem, and then discharged home to complete a 2-month course of meropenem via PICC.

The patient felt well on this regimen for several weeks until he woke one morning with fever and diaphoresis – febrile to 101.8°F. He presented to his cardiology clinic for further evaluation. Admission was recommended. On admission, a grade II/VI systolic ejection murmur was noted, but no peripheral stigmata of endocarditis were identified. Cardiac CT demonstrated a normal functioning mechanical aortic valve with prominent low-attenuation material surrounding the ascending aortic graft – concerning for infection. Further evaluation via cardiac PET scan was also consistent with infection. CV surgery recommended attempting medical treatment rather than proceeding directly to surgery. Tobramycin was added to the antibiotic regimen for synergy with meropenem. After discharge, patient completed 2 weeks of tobramycin and 3 weeks of meropenem (total 6 weeks of meropenem). At the time of his last follow-up, the patient remained symptom free though is still felt to be high risk for medical failure and may yet require surgical intervention.

This case illustrates a rare occurrence of S. paucimobilis endocarditis. Literature review suggests only one previous case of S. paucimobilis endocarditis has been described. Limited in vivo studies have been completed to examine antibiotic resistance patterns for S. paucimobilis, but the largest study as well as the structural similarities between S. paucimobilis and Pseudomonas spp. suggest fluoroquinolones, third-generation cephalosporins, and carbapenems are the best initial therapies. Though not well studied, the synergistic efficacy of tobramycin makes it a reasonable second agent if a two-drug regimen is required.

Cutaneous Manifestations of Henoch-Schönlein Purpura Mimic Numerous Dermatological Conditions

Henoch-Schönlein Purpura (HSP) is an IgA-mediated small vessel vasculitis that is usually seen in children. When HSP affects adults it may be confused with other dermatological conditions.

CASE PRESENTATION: A 67-year old male with a history of vitiligo presented to the ED with left lower extremity cellulitis. He was treated with cefadroxil and was released to home. The next day, he returned to the ED with palpable purpura on his legs and buttocks. Physical examination revealed a markedly swollen and erythematous left lower extremity, scattered palpable purpura and petechiae over the legs and buttocks, and patches of vitiligo on the upper extremities. Notable labs included an elevated ESR of 56 and CRP of 42.1. The patient was admitted for further management of worsening cellulitis,
which was treated with vancomycin and ciprofloxacin. The patient’s purpura was attributed to a cefadroxil reaction. The patient became hypertensive, so he was treated with amlodipine before being discharged to home. The next day he developed facial angioedema, leading to the discontinuation of amlodipine. The presence of vitiligo, palpable purpura, and angioedema raised concern for an underlying malignancy, so he underwent a PET CT and bone marrow biopsy which were unremarkable. A negative autoimmune workup included compliment levels, ANA, ANCA panel, and antibodies to SSA/SSB, Sm, RNP, Scl, and Jo1. Subsequently, the patient’s systolic blood pressure elevated into the 220s and his creatinine increased from 1.2 to 2.1. A skin biopsy revealed IgA vasculitis and a renal biopsy showed IgA nephropathy, yielding the diagnosis of HSP. By this time the patient’s renal function was improving so he was managed expectantly with observation alone. Over the following weeks his renal function and blood pressure normalized.

**DISCUSSION:** This case highlights the variable presentations and misdiagnosis of HSP purpura, which resulted in delayed treatment. Confusing HSP with other dermatological conditions is particularly common in adults. The proximity between cefadroxil treatment and the appearance of purpura caused a false perception that the patient had developed a drug reaction. The constellation of cutaneous findings also raised suspicion for malignancy. Consequently, the diagnosis of HSP was delayed until long after hospital discharge, resulting in acute kidney injury and severe hypertension that might have been prevented if the diagnosis had been made sooner.

**Neil Siekman, MD**  
**Ryan Uselman**

**TTP in a healthy community-dwelling adult**

TTP is a rare but life threatening condition, which fortunately does have a number of effective treatments if implemented early. As such, this disease process must remain high on any clinician's differential diagnosis for a large number of common symptomatic complaints and laboratory abnormalities, most notably including thrombocytopenia, anemia, acute kidney injury, fever, altered mental status. The following case provides a clear and sobering example of early diagnosis and effective treatment of acquired TTP in an otherwise healthy, community-dwelling adult.

**Case Description:** The patient is a 58 year old male with PMH significant for OSA and HTN who was transferred to our facility with 3 days of abdominal pain, nausea, and intermittent vomiting. Preliminary laboratory evaluation revealed platelets of 4, creatinine of 1.76, hemoglobin of 9. Further evaluation for hemolysis revealed an LDH of 2119, total bilirubin of 3.8, negative DAT, and a peripheral smear which revealed microangiopathic hemolytic anemia characterized by marked normochromic, normocytic anemia; numerous red blood cell fragments, occasional bite cells. Hematology rapidly consulted who agreed with diagnosis of TTP, suggested initiation of treatment with daily plasma exchange and high dose steroids (solumedrol 125mg IV BID). ADAMTS13 activity and ADAMTS13 inhibitor studies were sent, which came back several days later confirming a diagnosis of acquired TTP: ADAMTS13 activity of < 5% with inhibitor units of 1.5 (reference range < 0.4). This patient improved rapidly over ensuing 5 days with the aforementioned treatment: platelets returned to 130; hemoglobin remained stable; creatinine normalized to 1.0; and patient's abdominal pain, nausea, and vomiting all resolved. As such, plasma exchange was stopped after 6 treatments, steroids were tapered down to prednisone 100mg daily and patient was discharged home. At 1 month follow up, patient remained stable without any decline in blood counts; he will continue to be followed closely as outpt for continued tapering of steroids.

**Parvati Singh, MD**

**Hypertensive Emergency and Finding that Zebra**

When young individuals present with hypertensive emergency in the setting of drug abuse, it is easy to forget to evaluate for other secondary causes. In this case, a 30 year old male with a past medical history of Chronic DVT, NSTEMI, IV drug use, PRES, Obesity, and Essential HTN presented to the hospital with hypertensive emergency. On admission, he had a BP of 230/140, chest pain,
diaphoresis, headache, elevated troponin, and an AKI. This clinical picture was in the setting of a urine drug screen positive for cocaine and amphetamine. Due to elevated blood pressure and nature of the chest pain, a CT aortic angiogram was completed to evaluate for aortic dissection. Instead of aortic dissection, imaging incidentally showed a 3.5 cm nodule on the left adrenal gland. Work-up of the mass found a normal RAAS axis, elevated 24 hour urine catecholamine and metanephrines, and elevated plasma metanephrines. This diagnosis of pheochromocytoma in a young individual was likely delayed due to drug use and further workup for his HTN was only pursued due to an adrenal incidentaloma. Though his obesity and drug use can explain some of his medical issues, the pheochromocytoma helps to tie together some of the patient’s other conditions inducing Takotsubo cardiomyopathy, pre-diabetes, PRES, and chronic DVT. Thus, this case illustrates the importance of considering secondary causes of HTN in young patients.

Grace Skemp-Dymond, MD
Peter Lund

The Right Side Won’t Flow and the Left Side Won’t Blow
A 63 year old female with a past medical history of smoking and asthma presented with a chief complaint of dyspnea, increased sputum production and wheezing for one week. In the ED her vitals were notable for HR 140, RR of 35 and spO2 82% requiring intubation. CT PE study showed extensive right sided pulmonary emboli and an obstructive mass in the left main bronchus. She was given Lovenox, tenectaplase and transferred to a quaternary care center. Bronchoscopy was performed revealing an obstructing, white, multi-lobed mass within the proximal left main bronchus. She underwent bronchoscopic debulking and cryotherapy. Pathology revealed typical bronchial carcinoid tumor with hallmark low mitotic figure count and positive staining for synaptophysin. Lung sparing surgery was considered but deemed high risk. She was anticoagulated. 24-hour urine 5HIAA and serum chromogranin A were normal. Octreotide scan was negative for metastatic disease. She is currently doing well and CT scans have been stable without any evidence of reoccurrence of disease. Discussion: Bronchial carcinoid tumors are neuroendocrine neoplasms stemming from enterochromaffin cells. Bronchial carcinoid tumors are a rare types of pulmonary malignancy, accounting for only 1-2%. They typically present in the 3rd through the 7th decade of life with initial symptoms of hemoptysis, cough or obstructive pneumonia. The bronchial carcinoid tumor is characteristically located in one of the central airways. Tissue sampling of the mass is imperative for diagnosis. Histopathology allows differentiation of typical versus atypical carcinoid based on mitotic figures, size, necrosis, and cell morphology. Typical bronchial carcinoid tumors are slow growing and present at earlier stages and atypical bronchial carcinomas present more aggressively and at a later stage. Surgical resection is the treatment of choice. Typical bronchial carcinoid tumors have a good prognosis after surgery with ten year survival rate > 80%.

Thrombophilia is a frequently associated with underlying malignancy but there is little reported on the incidence of thromboembolism and bronchial carcinoid. There has been a case reported of a tumor embolism from a bronchial carcinoid tumor mimicking an arterial thromboembolism, but this was not a true thromboembolism. To our knowledge, this is the first reported case of simultaneously diagnosed pulmonary thromboembolism and obstructive typical bronchial carcinoid tumor. Upon analysis of the case, the simplest explanation would be that her underlying bronchial carcinoid tumor led to the development of a thromboembolism. However, given the dearth of related cases, this may be a unique presentation of two unrelated events.

Aaron Smith, MD

Borrelia burgdorferi Infection with Splenic Infarction
A 22-year-old female with developmental delay, epilepsy, and hypothyroidism presents to the emergency department for intermittent recurrent fevers over the past 10 days and acute-onset left shoulder pain. She was evaluated at an outside hospital days earlier and received a thorough workup, including an abdominal CT scan, with no identified source of infection. She is admitted to the hospital
for further evaluation. On exam she is febrile to 103.8 degrees Fahrenheit, is profusely diaphoretic and writhing in discomfort without localized symptoms of infection. An abdominal CT shows splenic wedge-shaped hypodensities concerning for infarction. The patient receives an exhaustive work-up for infectious, hematologic, and malignant etiologies without confirmation of a diagnosis. She completes a course of broad spectrum antibiotics with resolution of the fevers and left-sided shoulder pain. She discharges home with a plan for close follow up. Lab results show a positive ELISA for Lyme disease, confirmed with Western Blot. The patient’s mother reveals the patient recently attended a summer camp in Minnesota. The patient completes a course of doxycycline and remains without a recurrence of her symptoms.

Although case reports have described splenic infarction in patients with babesiosis, another tick-borne illness, Lyme disease has been described in association with splenic infarction on only one occurrence in the medical literature. In our case, the patient has no other medical problems or co-morbidities that would explain her new-onset splenic lesions. Given the proximity of symptoms and concomitance with her acute Lyme disease presentation, the association of splenic infarction with Borrelia burgdorferi infection can be appropriately inferred in this patient.

Dharma Sunjaya, MD
Luke Hafdahl

Acute Abdominal Pain in an Adult with Paraesophageal Hernia

Abdominal pain with nausea and vomiting is one of the most common clinical presentations in both the inpatient and outpatient setting. The etiology of abdominal pain includes both gastrointestinal and non-gastrointestinal causes. In this case, we will discuss a rare and uncommon cause of acute abdominal pain.

Case description: An 80 year-old woman with history of gallstone pancreatitis complicated by pseudocyst, chronic esophageal hiatal hernia, aortic stenosis, and pulmonary hypertension presents for evaluation of epigastric pain, nausea, and vomiting. Her history was notable for five days of progressively worsening epigastric pain that radiated from the left to the right further complicated by nausea and a single episode of coffee-brown emesis. Her symptoms were not affected by position or eating. Physical exam revealed a new irregularly irregular heart rate and palpable mass in the epigastric region with diathesis concerning for ventral hernia. Initial laboratory findings showed mild anemia (Hb 13.4 gm/dL), mild elevation in serum lactate level (2.8 mmol/L) normal lipase level (<10 U/L), and elevated BUN and Creatinine level consistent with acute kidney injury (BUN and Cr: 39mg/dL and 1.5 mg/dL), which responded to an administration of IV normal saline. Abdominal and pelvis CT with contrast showed enlargement of a right inguinal hernia, multiple small ventral abdominal wall hernias, walled off pancreatic necrosis, and stable large hiatal hernia with inversion of the greater and lesser curvatures of the stomach, representing organoaxial volvulus. No gastric outlet obstruction or intestinal ischemia was noted on imaging. EGD was performed the following day to evaluate for hematemesis, which showed a grade D esophagitis and 10 cm hiatal hernia. Due to the severity of esophagitis on endoscopy and persistent abdominal pain, open transabdominal repair with nissen fundoplication was subsequently performed, along with gastrostomy tube placement. The patient tolerated the surgery well and was discharged home in good condition.

Lesson: Organoaxial volvulus or gastric volvulus is an uncommon cause of acute or recurrent abdominal pain in adults, especially in the setting of a known paraesophageal hernia. The clinical symptoms associated with volvulus are often nonspecific and often includes abdominal pain, nausea, and vomiting. This diagnosis can be confirmed using radiograph, fluoroscopy, or computed tomography. Prompt diagnosis is necessary to prevent complications such as bowel ischemia or infarction.

Nicholas Tan, MD
Shounak Majumder, M.B.B.S; Meera

A Malignancy Gone Viral: Metastatic Epstein-Barr Virus Positive Lymphoepithelioma-Like Cholangiocarcinoma

Lymphoepithelioma-like cholangiocarcinoma (LEL-CCA) is a rare subtype of
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intrahepatic CCA that is strongly associated with Epstein-Barr virus (EBV) infection. Although patients with LEL-CCA have more favorable outcomes compared to other variants of intrahepatic CCA, it can sometimes present with extensive tumor burden and aggressive disease.

Case Description: A 22 year-old man presented with several weeks of generalized weakness and right upper quadrant abdominal pain. His medical history was significant for ulcerative colitis that was previously treated with corticosteroids, azathioprine, and adalimumab. Abdominal magnetic resonance imaging (MRI) showed massive intra-abdominal lymphadenopathy, innumerable hepatic masses demonstrating central T2 hyperintensity with peripheral rim enhancement, and biliary dilatation with multifocal strictures consistent with previously undiagnosed primary sclerosing cholangitis (PSC). He underwent a liver biopsy which demonstrated a poorly differentiated tumor characterized by syncytial growth and prominent intratumoral lymphocytes. In-situ hybridization testing for EBV was positive in the neoplastic cells (Figure 2B); additionally, immunohistochemistry (IHC) staining was positive for CDX2, CAM5.2, and MOC31. Overall, the liver biopsy findings suggested a gastrointestinal or biliary origin.

Esophagogastroduodenoscopy and colonoscopy were negative for masses, although interestingly, colonic mucosal biopsies revealed malignant cells within an ulcer base that had EBV positivity and an IHC profile similar to that from the liver; this was felt to represent a metastasis rather than a primary colorectal tumor. He then underwent an endoscopic retrograde cholangiopancreatography with brushing of a dominant stricture just above the cystic duct insertion. Cytology was positive for adenocarcinoma; fluorescent in-situ hybridization studies demonstrated loci amplification of MCL1, EGFR, MYC, and CDKN2A. A final diagnosis of EBV-associated LEL-CCA with nodal and colonic metastases was made.

The patient underwent 2 cycles of 5-fluorouracil, folinic acid, and oxaliplatin (FOLFOX) chemotherapy along with 2 cycles of pembrolizumab. Imaging demonstrated interval shrinking of some hepatic masses and lymphadenopathy. Unfortunately, he was admitted with septic shock shortly afterwards and passed away despite aggressive supportive therapy in the intensive care unit.

Discussion: LEL-CCA is an uncommon cause of biliary cancer, with only 25 other cases reported thus far. It is more frequently found in Asia, affects middle-age individuals, has a strong female predominance, and is highly associated with EBV positivity. No known link between LEL-CCA and inflammatory bowel disease – or medications used in its treatment (e.g. azathioprine and anti-tumor necrosis factor therapy) – currently exists. LEL-CCA typically portends a better prognosis than other subtypes of intrahepatic CCA; however, this case clearly illustrates the possibility of an aggressive disease course if left unrecognized.

In conclusion, LEL-CCA should be considered in the differential diagnosis for patients presenting with hepatic masses that are EBV-positive on histology. Thorough investigation including imaging, histopathology, and endoscopic studies should be undertaken to establish the diagnosis for therapeutic and prognostic purposes.

Miguel Teixeira, MD
Andrew Greenlund, MD PhD
Laura Greenlund, MD PhD

Point-of-Care Ultrasonography: A Valuable Tool in the Diagnosis of Early Polymyalgia Rheumatica

Polymyalgia Rheumatica (PMR) is a common chronic inflammatory rheumatic disease without universal diagnostic criteria, usually managed by internists. The diagnosis is usually made on the basis of characteristic symptoms including morning muscle pain and stiffness in the neck, shoulder, or pelvic girdle in the older patient (>50 years) that lasts for more than two weeks duration in the background of elevated inflammatory markers. Although usually elevated, ESR levels may be ≤ 30 mm/hour in 6%-20% of patients with PMR. Today, ultrasonography has a role in the diagnosis and management of PMR and has recently been integrated into ELAR/ACR.
diagnostic scoring algorithm. Not only do ultrasonographic findings of such as bilateral shoulder bursitis provide higher sensitivity and specificity in diagnosis of PMR, they may be a timelier indicator of disease than traditional blood inflammatory markers.

CASE DESCRIPTION: Our patient is a 76 year old man with four months of bilateral shoulder pain in the setting of known mild degenerative joint disease. He was initially treated for presumed rotator cuff tendinopathy and arthritis and with physical therapy and NSAIDS with no improvement. He subsequently developed bilateral hip pain. Inflammatory markers were not elevated (ESR 8; CRP 8.2) arguing against polymyalgia rheumatica. A corticosteroid injection of the shoulder was done and a point of care ultrasound exam at the time of injection demonstrated bilateral bicipital tendinitis. Following bilateral biceps tendon sheath corticosteroid injection, the patient had marked improvement of his shoulder symptoms as well as his hip pain, which relapsed several weeks later. Follow up inflammatory markers were drawn two months from the initial testing were noted were then elevated (ESR 51; CRP 56). The patient was diagnosed with PMR and started on a low dose steroid taper with resolution of his symptoms.

DISCUSSION: Using ultrasonography may be particularly beneficial when inflammatory markers are normal despite clinical suspicion of PMR. We show that bilateral bicipital tendinitis appears to predate the elevation of inflammatory markers. Our case illustrates the role for point-of-care ultrasound as helpful tool in the diagnosis of PMR, especially when inflammatory markers might still normal.

Chung Sang Tse, MD
Joshua C. Ellis, Garen S. Wolff, and Eddie L. Greene

An Over-the-Counter Poison: Bleeding Gums, Sky High INR, and No Warfarin

An 89-year old woman presented with a one-day history of acute gingival bleeding. Her medical history included osteoarthritis and coronary artery disease status post stent placement. Her only medication was aspirin 81 mg. On presentation, she was hemodynamically stable. Physical exam was notable for small amounts of dried blood on the lips, trace red blood on the buccal surfaces, and left lower extremity edema.

Laboratory studies revealed Hgb 9.6 g/dL, WBC 15.0 x 10^9/L, platelets 349 x 10^9/L, creatinine 1.1 mg/dL, AST 26 U/L, ALT 10 U/L, and ALP 103 U/L. Coagulation studies were markedly abnormal: INR > 9.0 (normal 0.8-1.2), APTT 115.3 seconds (23.0-36.0 seconds), and PT > 120 seconds (8.5-11.5 seconds). Products of the coagulation pathway were mildly abnormal: plasma fibrinogen 490 mg/dL (200-430 mg/dL), fibrinogen equivalent units 0.52 mcg FEU/mL (<0.50 mcg FEU/mL), and d-dimer 260 ng/mL (<250 mg/dL).

Serum salicylate was in the toxic range of 45.5 mg/dL (therapeutic 3.0-10.0 mg/dL; toxic >30 mg/dL). Serum acetaminophen was <5 mcg/mL. Serum warfarin level was < 1.0 mcg/mL (therapeutic 2.0-5.0 mcg/dL). Venous blood gas revealed pH 7.44, pCO2 23.6, pO2 < 40, and HCO3 16.

On further history, she admitted to taking three aspirin 81 mg per day for >10 years for arthritic pain. Chronic salicylate toxicity was diagnosed and she was treated with sodium bicarbonate infusion with close monitoring of urine pH and serum pH, potassium, glucose, and serum aspirin concentration. Vitamin K 10 mg PO was administered. Within 12 hours, the serum aspirin level was < 30 mg/dL and the sodium bicarbonate infusion was discontinued. The serum aspirin level and INR normalized over the next four days and she was discharged home in stable condition.

DISCUSSION: Salicylate is a common compound contained in many over-the-counter pharmaceutical products and is used for its analgesic, antipyretic, and anti-inflammatory properties. In rare cases, salicylate toxicity can cause hepatotoxicity and interfere with vitamin K metabolism leading to coagulopathy with elevated INR. Treatment includes alkalization of urine to promote salicylate elimination. Another important diagnosis to consider is disseminated intravascular
coagulopathy (DIC), a systemic process that initiates the clotting cascade and can lead to a deficiency in clotting factors and subsequent hemorrhage. It presents with varying degrees of severity; ranging from clinically insignificant to life threatening. The International Society of Thrombosis and Haemostasis published diagnostic guidelines for DIC and developed a scoring system assessing platelet count, PT, fibrinogen, and D-dimer values. Our patient had a total score of 4, just below the cutoff of ≥5 for DIC.

In summary, in cases of bleeding with significantly elevated INR, salicylate toxicity should be considered in the absence of warfarin overdose, chronic liver disease, disseminated intravascular coagulopathy, or hereditary coagulation factor deficiency.

**Ryan Uselman, MD**
**Dr. Neil Siekman**

**A clear case of acquired TTP**

TTP is a rare but life threatening condition that has effective treatments when implemented early. It must remain high on any clinician's differential diagnosis, as it is characterized by common symptomatic complaints and laboratory abnormalities, most notably thrombocytopenia, anemia, acute kidney injury, fever, and altered mental status. The following case provides a clear and sobering example of early diagnosis and treatment of acquired TTP in an otherwise healthy, community-dwelling adult.

Case Description: The patient is a 58 year old male with PMH significant for OSA and HTN who was transferred to our facility with 3 days of abdominal pain, nausea, and intermittent vomiting. Preliminary laboratory evaluation revealed platelets of 4, creatinine of 1.76, hemoglobin of 9. Further evaluation for hemolysis revealed an LDH of 2119, total bilirubin of 3.8, and a negative DAT. Peripheral smear revealed microangiopathic hemolytic anemia characterized by marked normochromic, normocytic anemia, numerous red blood cell fragments, and occasional bite cells. Hematology was rapidly consulted, agreed with the diagnosis of TTP, and suggested initiation of daily plasma exchange and high dose steroids (solumedrol 125mg IV BID).

ADAMTS13 activity and ADAMTS13 inhibitor studies were sent, which confirmed a diagnosis of acquired TTP: ADAMTS13 activity of < 5% with inhibitor units of 1.5 (reference range < 0.4). He improved rapidly over the next 5 days with the aforementioned treatment: platelets returned to 130; hemoglobin remained stable; creatinine normalized to 1.0; and his abdominal pain, nausea, and vomiting all resolved. Plasma exchange was stopped after 6 treatments, steroids were tapered down to prednisone 100 mg daily, and he was discharged to home. At 1 month follow up, he remained stable without any decline in blood counts; he is followed closely as an outpatient for continued monitoring and tapering of steroids.

Discussion: Acquired TTP is a thrombotic microangiopathy caused by an inhibitory autoantibody directed against ADAMTS13 leading to severe functional ADAMTS13 deficiency. It occurs in about 3 per 1 million adults annually in the United States. Given the 90% improvement in mortality rate with early plasma exchange and high dose corticosteroid treatment, TTP must remain high on any clinician's differential for thrombocytopenia and/or microangiopathic anemia. Although this case highlights rapid improvement with plasma exchange and corticosteroids, recurrence is relatively common: 48 percent in the first year, 30 percent in the subsequent 2 years, and 22 percent in the following 10 years. Therefore, close outpatient monitoring is essential. In closing, we feel this case is particularly illuminating, given the unambiguous ADAMTS13 studies and rapid recovery. It is a helpful reminder that acquired TTP is a serious illness that requires rapid diagnosis and treatment, albeit an incredibly rare one that few clinicians have the opportunity to witness firsthand.

**Sravya Vinnakota, MD**
**Josh S. Shapiro, Bradley R. Salonen**

**Linear IgA Bullous Dermatosis: A Rare Manifestation of Vancomycin Hypersensitivity**

Vancomycin is one of the most widely used antibiotics. Due to its prevalent use, a number of side effects have been observed like ‘red man’ syndrome,
Clostridium difficile diarrhea, agranulocytosis, ototoxicity, and nephrotoxicity. In addition, it has also been associated with anaphylaxis and drug hypersensitivity reactions like Linear IgA Bullous Dermatosis (LABD). Although multiple case reports have documented Vancomycin as the most frequent inciting factor for LABD, formal studies validating the causal relationship are lacking as it remains a relatively uncommon phenomenon.

Case: An 88 year old male with a past medical history of hypertension, diabetes, coronary and peripheral arterial disease underwent an amputation of second left toe and was subsequently treated with Vancomycin, Zosyn, Meropenem and Levofoxacin for post-operative fever. Two weeks later, he presented with fever, hypotension, altered sensorium, and a diffuse rash. The rash consisted of multiple urticarial, well-delineated plaques with superimposed clear, fluid-filled, flaccid bullae with a characteristic "crown of jewels" distribution. No mucosal involvement was noted which ruled out erythema multiforme major and Stevens-Johnson syndrome. Upon admission, he was resuscitated with fluids and blood and urine cultures were obtained. As his fever subsided and cultures remained negative, an infectious cause was deemed unlikely. Clinical appearance of rash was characteristic of LABD, which is known to be associated with Vancomycin use. The last dose of Vancomycin was administered five days prior to admission. He was empirically treated with topical Triamcinolone and oral Prednisone 40 mg, which was tapered over two weeks. The diagnosis was confirmed by skin biopsies demonstrating strong linear deposition of IgA along the basement membrane on direct immunofluorescence. Clinically, the patient responded well with no new lesions and resolution of existing lesions.

Discussion: Linear IgA Bullous Dermatosis is a rare blistering skin disorder that is characterized by deposition of IgA antibodies along the basement membrane. It may be idiopathic or drug-induced. Vancomycin has been recognized as a common inciting factor. Other associated medications include NSAIDs, furosemide, captopril and lithium. The clinical presentation is often similar to dermatitis herpetiformis that is associated with gluten-sensitive enteropathy. With LABD, symptoms begin within one month of exposure to the inciting agent and may persist for several weeks after drug cessation. New lesions may continue to erupt for up to 2 weeks after cessation. The diagnosis is confirmed by a perilesional skin biopsy demonstrating linear IgA deposition along the basement membrane on direct immunofluorescence. Drug-induced LABD usually resolves spontaneously with cessation of the drug, but severe cases may require prednisone and/or dapsone with a quick taper over 4-6 weeks. Prolonged systemic therapy is rarely needed. Cutaneous lesions heal over several weeks without scarring, but mucosal lesions may be complicated by stricture formation and scarring.

Elizabeth Wight, MD

Calcinosis Cutis: An Unusual Mimic of Cellulitis

Cellulitis is a common superficial skin infection that is usually easily identified and treated. When cellulitis frequently recurs or fails to respond to appropriate antimicrobial therapy, other diagnoses should be considered as many conditions can masquerade as cellulitis, including calcinosis cutis, as observed in this case. A 57 year-old female with a history of steroid-dependent asthma, on chronic prednisone, diabetes mellitus, seronegative rheumatoid arthritis and recurrent cellulitis presented to the Emergency Department for evaluation of increasing left lower extremity pain and erythema despite being on IV antibiotic therapy for previously diagnosed cellulitis.

Over the preceding year, the patient was hospitalized on ten separate occasions for several reasons including respiratory failure related to reactive airway disease, generalized weakness, olecranon bursitis, and multiple hospitalizations for cellulitis in her upper and lower extremities. Due to concern for health-care associated pathogens, she was treated aggressively with antibiotics including vancomycin, piperacillin-tazobactam, cefepime, metronidazole and daptomycin. In the month prior to this admission the patient had undergone a bone marrow
biopsy at the left hip as part of a work-up for macrocytic anemia. Unfortunately, she had difficulty with wound healing and the presence of the left hip wound heightened awareness and concern for recurrent infection in that extremity. She was diagnosed with cellulitis due to erythema, warmth and pain at the left lower extremity and discharged on daptomycin. The patient returned to the ED with increasing pain, having just completed her course of daptomycin without any significant improvement. There had been no interval history of trauma, fevers or constitutional symptoms. Ultrasound for DVT was negative. Exam demonstrated subtle erythema overlying scattered small subcutaneous nodules, slight warmth and mild tenderness over the left knee and medial thigh. She was initially started on broad-spectrum antibiotics. Upon further evaluation, there was no clinical evidence of active infection and the lack of response to appropriate antibiotic therapy raised questions about the accuracy of the cellulitis diagnosis. Antibiotics were stopped and Dermatology performed a skin punch biopsy of a nodular lesion with overlying mild erythema on the left thigh. Surprisingly, pathology revealed calcinosis cutis. Topical sodium thiosulfate therapy was started and the patient was discharged. This case illustrates the need to critically evaluate the diagnosis of cellulitis with frequent recurrence or failure to respond to appropriate therapy, especially in the presence of other confounding factors. In this case, the patient’s history of previous episodes of cellulitis with documented microbiology, chronic immunosuppression on prednisone, and nonhealing left hip biopsy site all raised suspicion may have been red herrings. Unfortunately, delay in diagnosis in this patient led to months of unnecessary IV antibiotic therapy and exposed her to risks associated with treatment while postponing initiation of appropriate therapy.

**Hives Again? When Steroid And Antihistamines Are Not The End**

Urticaria is one of the most common rashes that physicians encounter, however relapsing chronic urticaria represents a challenging and critical diagnostic entity. 44-year-old man presented with recurrent hives for 2 weeks. Initially, treated with a 10-day course of prednisolone with an improvement of the rash but suffered a relapse shortly after stopping the steroid. Basic workup including CBC w/diff, ESR, ANA-EIA, RF and Lyme serology were unremarkable. Prednisolone was restarted with a prolonged course and dermatology referral however the rash did not return and the patient did not show for his dermatology visit. 3 months later and 4 days off prednisolone, the patient developed progressive lower extremity edema, lip swelling, erythematous papules on his back and intermittent arthralgia involving the PIP, MCP, and wrist. Laboratory work up was repeated including CBC, ESR, ANA-EIA, RF, CRP, and UA. Results were remarkable for significant hematuria, proteinuria>300mg/dl, Cr1.49mg/dl, Albumin1.9g/dl and 3g reduction of Hb from the previous visit and the patient was subsequently hospitalized. Further work up revealed a Urine Protein to Creatinine ratio (UPCR) of 11.6g/gCr and total urine protein of 6.9g/24 hr. There were granular casts and oval fat bodies on urine microscopy. He had a worsening AKI with Cr up to 2.5 mg/dL, hypocomplementemia with C3(60mg/dl) and C4(14mg/dl), negative ANA-EIAx2 and positive anti-dsDNA at 32IU/ml. With the concern of urticarial rash, anti-C1Q IgG and complement C1Q level were sent with pending result initially. Other serologies including viral hepatitides, ANCA, cryoglobulin, and antiGBM were negative. Renal biopsy showed immune complex mediated necrotizing and crescentic glomerulonephritis and mild acute tubular injury. Diagnosis of hypocomplementemic urticarial vasculitis syndrome (HUVS) was entertained given the history of recurrent urticaria and finding in kidney biopsy, which can closely mimic the lupus nephritis ‘full house’ immunofluorescence pattern. Anti C1QAb was later reported to be positive, complement C1q level was normal at 160 µg/ml and repeat ANA-IFA turned out positive at 1:160 speckled pattern. The patient was treated with 1g of methylprednisolone IV for 3 days and MMF 1000 mg bid which was later
switched to cyclophosphamide 1500 mg IV with the concern for crescentic findings on renal biopsy. His Cr gradually came down to 2.0mg/dl with a significant reduction of UPCR. Later in the course of treatment, the patient again developed multiple discrete erythematous papules at posterior neck area while on the immunosuppressant. Skin biopsy revealed subepidermal vesicular dermatitis with neutrophils, which could represent an early process of autoimmune dermatitis. This case illustrates the utilities of diagnostic workups for chronic urticaria. Careful selection of repeat laboratory workups in conjunction with clinical findings may be worthwhile when a definite diagnosis is challenging.

Katarina Wrzos, MD

A Curious Case of Mucomycosis

Introduction: Despite its causative agents being ubiquitous in nature, mucormycosis is a rare disease that carries a high mortality rate. It is an opportunistic infection primarily affecting those in an immunocompromised state, e.g. solid organ transplant, diabetic ketoacidosis, or malignancy, most commonly presenting as pulmonary or rhino-orbital-cerebral disease. The challenge in diagnosis arises when patients do not present in a “typical” fashion. This case features one such event.

Case Description: The case begins with a 60 year-old previously healthy man with history of well-controlled type 2 diabetes mellitus and hypertension. He initially presented to an outside hospital (OSH) with acute onset abdominal pain and was diagnosed with gallstone necrotizing pancreatitis. His course was complicated by sepsis, acute kidney injury requiring dialysis, and atrial fibrillation (Afib) with rapid ventricular response, prompting transfer on hospital day 4 for a higher level of care. On hospital day 15 he had his first of several maroon stools and eventually required 5 units of packed RBCs. Heparin, which had been started at the OSH for Afib, was stopped. In the days prior to this event, he also coped with persistently high blood glucose, malnutrition, and rising WBC. Colonoscopy on hospital day 18 showed inflamed, ulcerated, and edematous appearing lesions in the terminal ileum that were concerning for ischemia vs. malignancy. The lesions were biopsied; however, infection was not yet on the differential and no tissue was sent for culture. Pathology was significant for acute and granulomatous inflammation, necrosis, and many branching hyphal elements suggestive of Zygomycetes or Aspergillus. At this point, Infectious Diseases was consulted and biopsied tissue was sent out for fungal PCR. Empiric posaconazole therapy was initiated due to concern for invasive fungal infection. On hospital day 33 fungal PCR results returned positive for Rhizopus species and a diagnosis of gastrointestinal mucormycosis was confirmed. The patient elected to pursue medical management only with surveillance colonoscopy in several weeks. He has returned home and is doing well.

Discussion: Gastrointestinal mucormycosis carries the risk of infarction, perforation, and shock, demonstrating a rare and potentially fatal infectious process. Ultimately, a successful and efficient diagnosis, accomplished by employing a complement of diagnostic tools and disciplines, allowed for the initiation of early treatment and a favorable outcome for this patient. This case highlights the diligence required to workup and diagnose a rare presentation of a rare disease, furthering the importance of keeping a broad differential in the face of nonspecific symptoms and exam findings.

Jennifer Wu, MD

A Confounding Case of Cough

The pulmonary-renal syndromes are a source of significant clinical concern, both from a nephrologic and a respiratory standpoint. The differential includes many entities; classically Goodpasture’s but includes many other etiologies. We present a case of mistaken respiratory infection subsequently determined to be due to renal disease.

Case Description: A 37 year old Somali man presented with worsening cough and respiratory distress. He had been seen at an outside hospital one week prior
for the same complaint and was discharged with antibiotic therapy for hazy bilateral infiltrates, presumed to be atypical pneumonia. At the time of admission, his infiltrates had appreciably worsened and his creatinine, which had been elevated at that time, was even higher at 1.9. His respiratory status deteriorated and he was ultimately intubated. Due to this, his case was concerning for a pulmonary-renal syndrome, though he had no history of hemoptysis. A bronchoscopy obtained revealed a low degree of hemosiderin-laden macrophages, making the diagnosis of true hemoptysis concerning but not entirely clear. A renal biopsy was performed, as well as a serologic workup, which was negative on initial light microscopy and staining for any immune complex deposition, negative immunofixation (including IgA), and negative for crescent formation. His serologic panel was overall negative, including anti-GBM, ANA, ANCA, IgA, and ASO titers. Based on his clinical course and serologic studies, a diagnosis of pauci-immune (ANCA-negative) vasculitis causing pulmonary-renal syndrome was made. Hemodialysis for acute renal failure and ultrafiltration was started, and fluid removal did not impact his respiratory status. Near the time of biopsy, empiric high-dose steroid pulse and cyclophosphamide therapy were initiated without significant clinical improvement. He was then initiated on plasmapheresis after biopsy results were finalized with rapid improvement in his respiratory function, and was able to be extubated within 48 hours of pheresis initiation. Ultimately, he remained dialysis-dependent during the completion of his pheresis course but was able to return home to complete ongoing Cytoxan therapy.

Discussion: Pulmonary-renal syndromes are defined as diffuse alveolar hemorrhage along with glomerulonephritis and encompass a number of pathologies, including the prototypic Goodpasture’s syndrome as well as other autoimmune causes, vasculitides, connective tissue disorders, as well as drug-induced etiologies. Early diagnosis relies on appropriate data, including serologic studies, biopsy results, as well as confirmation of alveolar hemorrhage via history or diagnostics. Keeping a wide differential for these presentations can lead to appropriate diagnostics and treatment.

Omar Yasin, MD  
Alberto Rubio-Tapia MD,  
Maurice Enriquez-Sarano MD

**Wellens’ Syndrome With Syncope But Not Chest Pain – A New Variant?**

Acute coronary syndromes can have atypical presentations without chest pain and are a rare cause of syncope to keep in mind. This is a case of a woman in her 70s presenting to the emergency department with syncope. She had sudden loss of consciousness while standing in her kitchen. She could not clearly recall the details of the episode or any specific prodromal symptoms other than possible lightheadedness. She has no history of chest pain, palpitations or any other symptoms before, during or after the episode and has never had syncope before. By the time she was admitted to the hospital she was completely asymptomatic. Her initial troponin level was 0.05 and then was stable at 0.04 at three and six hours. Electrocardiogram showed deep inverted T-waves in leads V1 to V3, and QTc of 521ms. Labs otherwise were within normal limits. Computed tomography (CT) and CT-angiography of the head and neck did not show any evidence of hemorrhage or carotid dissections. CT-pulmonary angiography ruled out a pulmonary embolus. Given elevated troponins, lack of ST segment changes, and characteristic T-wave findings, her presentation resembled that of Wellens’ Syndrome—all except for the lack of chest pain. Her diagnosis was confirmed with angiography, which showed a critical left anterior descending artery (LAD) occlusion. Our patient received two drug eluting stents to the LAD and was started on dual antiplatelet therapy, beta-blockers and an angiotensin-converting enzyme inhibitor. She remained asymptomatic after the intervention and did not have any evidence of heart failure, arrhythmia or reinfarction. With the lack of chest pain this could represent a new variant of Wellens’ Syndrome.

Many diseases can present with T-wave inversions and syncope including electrolyte abnormalities, medications, intracranial hemorrhage, pulmonary embolism, and other cardiac diseases. In the setting of myocardial infarction...
Syncope is precipitated by arrhythmias or by exaggerated neurally-mediated responses that lead to a transient decrease in cardiac output. The composite of clinical presentation, biomarkers and electrocardiogram should guide to prompt coronary angiogram when acute coronary syndrome is suspected.

### Antibiotics and Complement-directed Therapies in Hemolytic Uremic Syndrome

Shiga-toxin producing bacterial infections are generally treated by supportive measures and avoiding the use of antibiotics due to the risk of exacerbating toxin production and precipitation of Hemolytic Uremic Syndrome (HUS). This clinical vignette explores controversies regarding the use of complement-directed therapies and antibiotics in HUS.

We investigate a case of HUS in a 67-year-old female who transferred to us from an outside hospital with Shiga-toxin producing E. coli O157 (STEC). The patient initially presented with bloody diarrhea and was treated with piperacillin-tazobactam before stool testing revealed STEC, prompting stoppage of antibiotics. She subsequently developed colitis and peritonitis with CT demonstrating free abdominal fluid. She was transferred to St. Mary’s Hospital where she received another dose of piperacillin-tazobactam due to concern for colonic bacterial translocation into her abdominal fluid, before emergently undergoing hemicolecotomy. Post-operatively, antibiotics were changed to azithromycin and metronidazole; however the patient ultimately developed HUS as characterized by microangiopathic hemolytic anemia, thrombocytopenia, acute renal failure and severe neurological dysfunction. Historically, certain antibiotics have been known to precipitate HUS by inducing further Shiga-toxin production, and this has prompted recommendations that all antibiotics are contraindicated in STEC. However, small case series suggest that azithromycin does not increase the rate of HUS, and may in fact be used to treat complications related to HUS. While no clinical studies have demonstrated that macrolides prevent HUS, laboratory studies have shown that macrolides such as azithromycin inhibit Shiga-toxin production in vitro and that fluoroquinolones and sulfonamides induce toxin production. In addition to the use of antibiotics, this patient received plasma exchange (PLEX) and eculizumab, which are typically reserved for treatment of atypical-HUS. PLEX and eculizumab were instituted based on limited empirical evidence that complement-directed therapies may also be beneficial in treating HUS itself, supported by the notion that both HUS and atypical-HUS share the commonality of deranged complement activation. Unfortunately, there are no randomized control trials studying macrolides, PLEX or eculizumab in HUS. Based on the available literature, it would be reasonable to treat HUS with strong indications for antibiotics with macrolides. Similarly, patients with severe neurological dysfunction in HUS should be treated with complement-directed therapies such as eculizumab. Our patient survived HUS with full recovery from hemicolecotomy and persistence of moderate neurological symptoms secondary to multiple small intracerebral infarcts.

### How much clot warrants a workup?

The value of routinely performing a thrombophilia evaluation in a patient with an acute thrombus has been questioned, as laboratory findings can be of dubious importance and may have little impact on the patient’s treatment course. However, these evaluations are still often performed in patients.

Case: A 35 year old woman presented with facial swelling. She had an extensive past medical history, including coronary artery disease requiring 3 stents, ischemic systolic heart failure, diabetes, chronic kidney disease, catheter-associated DVT, LV thrombus on warfarin therapy, and an episode of ischemic kidney injury. On admission she was noted to have marked edema of her face, arms, and legs. She was found to have bilateral internal jugular, subclavian, and deep femoral DVTs, several PEs, and several SVTs throughout her limbs. She
had been off warfarin for 2 weeks and her INR was 1.5 on admission. She was admitted, placed on a heparin drip, and received an IR thrombectomy and lytic therapy. Her edema resolved but her hospital course was complicated by acute kidney failure requiring two sessions of hemodialysis, acute hepatic injury, heparin induced thrombocytopenia, and pleural effusions requiring thoracentesis. She was discharged off of dialysis to rehab unit with plan for lifelong anticoagulation with warfarin.

We performed an extensive thrombophilia workup given her dramatic presentation of venous clotting and history of arterial clotting. The patient has no family history of clot. We found Factor II and V and non-nephrotic change proteinuria. Rheumatology was consulted for consideration of vasculitis which they thought was unlikely and serologies for ANCA and ANA were negative.

Discussion: This case raises important questions about the utility of thrombophilia workups, especially in the inpatient setting with active clot. We did not change management based on the results, as she would have warranted lifetime anticoagulation regardless of these mutations. Additionally, these mutations do not explain the extreme presentation nor why she presented with her first clots two years ago rather than earlier in life or during her two pregnancies. Given that even our positive results do not explain her clinical picture, this case raises the question if there truly is no utility in thrombophilia workups, no matter the extent of the clot burden.

Breanna Zarmbinski, MD
Peter Lund, MD (Fellow)

*When Slow Flow Needs Fast Action: A Case of Hyperviscosity Syndrome and Waldenstrom Macroglobulinemia*

A 70 year old man with a past medical history of TBI, hyperlipidemia, and hypertension presented to the emergency room with one month of epistaxis, bloody stools and fatigue. On exam, he was found to be hypertensive and had cervical, axillary, inguinal and supraclavicular adenopathy. Laboratory studies revealed a anemia, lymphocytosis, thrombocytopenia, acute kidney injury and elevated INR. CT of the chest, abdomen and pelvis was notable for diffuse lymphadenopathy and splenomegaly. A peripheral smear was ordered, and he was discharged with plans to follow-up with outpatient oncology.

After discharge, the patient noted worsening shortness of breath, vertigo, headache, ataxia and fatigue, so he returned to the hospital. Review of the patient’s peripheral smear showed a B cell lymphoproliferative disorder with plasmacytic features. Serum electrophoresis was positive for a monoclonal (IgM) protein spike. The patient’s serum viscosity was also elevated. Given this finding and his neurologic complaints, he was diagnosed with hyperviscosity syndrome and underwent plasmapheresis with symptomatic improvement. Subsequent bone marrow biopsy revealed a lymphoplasmacytic lymphoma. He was diagnosed with Waldenstrom macroglobulinemia. He began rituximab and discharged to home. His disease progressed, and his chemotherapy regimen was adjusted several times and he continued to necessitate periodic plasmapheresis.

**Teaching Points:**

Waldenstrom macroglobulinemia (WM) is an abnormal clonal proliferation of B cells that leads to:

1. Infiltration of bone marrow and lymphoid organs
2. High amounts of monoclonal IgM

WM often presents with anemia, hyperviscosity syndrome, bleeding diathesis, and lymphadenopathy. Virtually any organ system may be involved via paraprotein tissue infiltration. Diagnosis is made with both a bone marrow biopsy and SPEP.

Hyperviscosity syndrome is most often associated with diseases of increased gamma globulins, such as WM or multiple myeloma, but can also occur in disorders of erythrocytosis or significant leukocytosis. In WM, IgM pentamers accumulate to increase serum viscosity. As a result, blood flow in microcirculatory beds is decreased. The most common symptoms of hyperviscosity syndrome include headache, encephalopathy, dizziness and visual disturbances. Hyperviscosity syndrome is considered a life-threatening emergency, as if left...
untreated, it can lead to CNS and limb ischemia. It is treated with plasmapheresis, which removes IgM molecules from the intravascular space and leads to almost instant relief of symptoms. Definitive treatment includes chemotherapy to eradicate the monoclonal proliferation. Bleeding or hypercoagulable disorders occur in paraproteinemias such as WM. As mentioned previously, hyperviscosity leads to impaired blood flow and can consequently result in thrombus formation. Patients with WM are also more prone to bleeding, as IgM proteins can inhibit fibrin polymerization and clot formation as well as interact with platelet surface membrane glycoproteins to impair platelet function and aggregation.

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<th>Michael Zhang, MD</th>
<th>Polymicrobial sepsis and hemolysis in a patient with a prior Whipple procedure</th>
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<td>Phillip Plager, Jutarat Sangtian, David Griffin, Dimitri Drekonja</td>
<td>A 67 year-old man with a history of pancreatoduodenectomy 25 years ago to treat choledocholithiasis with impaction presented with fevers, chills, jaundice, nausea and red urine. One day prior, he underwent a percutaneous ultrasound-guided liver biopsy as part of the evaluation of a one year history of asthenia, mild elevation in alkaline phosphatase, and 1:80 positive titer for anti-smooth muscle antibodies. Exam was significant for mild scleral icterus, jaundice, a large well-healed abdominal chevron scar, and a mildly ecchymotic post-biopsy site. Blood cultures revealed Gram positive cocci in chains, Gram positive bacilli and Gram negative bacilli. The same day, the patient’s hemoglobin decreased from 13.5 g/dL to 11.6 g/dL, serum haptoglobin decreased to 8.6 mg/dL (normal range 30-200 mg/dL), lactate dehydrogenase was not measurable due to continued hemolysis, but fibrinogen remained within normal range. A peripheral smear and a Coomb’s test were obtained. An abdominal CT scan revealed a 6.0 x 4.2 cm fluid and air collection in the right lobe of the liver. Blood cultures were finalized as Streptococcus infantarius, Clostridium perfringens, Escherichia coli and Klebsiella oxytoca. The fluid and air collection was drained via CT-guided needle aspiration, with cultures from the aspirate mirroring the blood culture results. Given the recent history of liver biopsy, remote history of pancreatoduodenectomy, and a history of long-standing pneumobilia, the patient’s sepsis and fluid and air collection was attributed to systemic inoculation of intestinal bacteria that likely chronically colonized his biliary tree in the setting of his pneumobilia. The hemolysis was self-limited and was attributed to release of C. perfringens alpha toxin. The patient was treated with piperacillin-tazobactam and his hemoglobin stabilized by hospital day 2. Once subsequent blood cultures remained negative for 48 hours, the patient was discharged home on intravenous ertapenem for 4 weeks with infectious diseases clinic follow up. A literature review revealed only two cases of liver abscess after liver biopsy in a post-pancreatoduodenectomy patient, but both cases involved preexisting lesions; our patient received a nonspecific liver biopsy after an ultrasound ruled out any apparent liver lesions. Overall, the experience with our patient raises the question of whether peri-procedural antibiotics should be considered when conducting a liver biopsy in the setting of known pneumobilia, which may be indicative of bacterial colonization of the biliary tree.</td>
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<th>Xin Zhang, MD</th>
<th>A Confusing Case of Persistent Confusion</th>
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<td>Wil Santivasi, MD, Donna Miller, MD</td>
<td>Case Presentation: A 69-year-old Hmong man, originally from Thailand, was transferred from an outside hospital for a two-week history of progressive encephalopathy. His medical history was notable for severe COPD, severe systolic heart failure due to ischemic cardiomyopathy (EF 25%), and chronic kidney disease. He had initially presented with acute left hemiparesis and was found to have a right MCA ischemic stroke. He developed intermittent fevers and was treated for pneumonia, but was later readmitted for worsening mental status, functional decline, hypotension, and continued low grade fevers. Repeat MRI demonstrated new multifocal acute strokes in watershed areas. Blood cultures and TEE were negative. He was transferred to our institution for further</td>
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management. On transfer, he was afebrile and vitally stable with a 2-liter oxygen requirement. Labs were notable for hyponatremia, transaminits, elevated inflammatory markers, and normal WBC with lymphopenia. Lumbar puncture revealed neutrophil-predominant pleocytosis, decreased glucose, elevated protein, and negative gram stain and bacterial cultures. HIV screening was negative. He was started on empiric broad spectrum antibiotics and tuberculosis (TB) induction therapy. Mycobacterium tuberculosis PCR returned positive on the second of three serial CSF specimens, confirming TB meningitis. His treatment was complicated by his comorbidities, poor functional status, and identification of multi-drug-resistant TB. Because of his COPD, induced sputum was difficult to obtain. Upon discussion with infection control, gastric aspirate samples were deemed to be adequate to rule out pulmonary tuberculosis. These returned negative on triplicate PCR and mycobacterial culture. His mental and functional status gradually improved, and he was successfully discharged to complete a protracted course of amikacin, ethambutol, moxifloxacin, pyrazinamide, linezolid, and ethionamide.

Discussion: Although rare, tuberculous meningitis must be considered as a cause of encephalopathy in high-risk populations. Tuberculosis is a rare diagnosis in natural-born American citizens. In fact, foreign immigrants account for 66.5% of cases in the United States. Rarer still, tuberculous meningitis comprises only 5% of cases with extrapulmonary involvement. This case demonstrates that TB meningitis can present with insidious onset of non-specific symptoms such as headache and low grade fever. It further shows that definitive diagnosis requires testing serial CSF samples to increase diagnostic yield. In patients who are unable to produce sputum, gastric aspirates may be a low-cost and low-risk alternative to rule out pulmonary involvement. To this end, the sensitivity and specificity for combined gastric aspirate PCR and acid-fast smear are similar to those for combined bronchoalveolar lavage PCR and acid-fast smear. In all patients with confirmed tuberculosis, it is also important to rule out HIV coinfection.

A Case of Adrenal Insufficiency after Nivolumab Therapy

This is a case of a patient who presents with adrenal insufficiency after initiating palliative treatment with Nivolumab for his NSCLC. It illustrates the importance of understanding the potential adverse side effects of new immunotherapy drugs.

A 58 year-old male with a past medical history significant for type 1 diabetes and stage IV adenocarcinoma of lung with metastasis to the brain, status post radiation and chemotherapy, presents with one month of worsening fatigue, dizziness, weakness and decreased appetite. On admission to the hospital he was found to be hypotensive, but otherwise vitally stable. Physical exam was significant for left sided weakness and a wide based, unsteady gait. His labs revealed an elevated creatinine, hypoglycemia, hyperkalemia, and hyponatremia, suspicious for adrenal insufficiency. Random plasma cortisol was in normal range. However, a cosyntropin stimulation test was performed and he was found to have an inadequate response to ACTH. A CT scan of the abdomen was obtained and ruled out adrenal hemorrhage. MRI of the brain did not show progression of metastasis. The patient’s adrenal insufficiency was ultimately thought to be due to his second-line chemotherapy treatment with Nivolumab, which he had started four months ago. He was started on stress dose corticosteroids and an insulin drip, and his symptoms and electrolyte abnormalities improved markedly over the course of a few days. On discharge from the hospital he was started on a steroid taper, and continued treatment with Nivolumab.

Recent advances in understanding of antitumor immune responses have led to the development of monoclonal antibodies in the treatment of cancer. Nivolumab is a human IgG4 antibody blocking the programmed cell death-1 receptor, an immune-checkpoint receptor, which is overexpressed on the surface...
of tumor cells. Originally used in patients with melanoma, it is now being used in the treatment of metastatic squamous NSCLC that has progressed despite first line platinum-based chemotherapies. Despite important clinical benefits, checkpoint inhibition is associated with potentially significant immune related adverse events including but not limited to endocrinopathies. This case highlights a known but rare and potentially critical side effect of Nivolumab – adrenal insufficiency. It goes without saying that it is always important to consider side effects of medications when coming up with a differential diagnosis or treatment plan. This is particularly important in an era when many new immune-modulators are entering the market.